

**The Perception of Fatigue and Associated Neurophysiological and
Psychophysiological Effects during Sustained Physical Activity in Healthy
Humans**

Aaron Greenhouse-Tucknott

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ABSTRACT

The perception of fatigue is a universal, debilitating psychological phenomenon. Yet, despite acknowledgement that fatigue undermines physical performance, its specific role in the regulation of physical activity has yet to be clearly defined. The presented thesis attempted to address this by examining the effect of a physically induced, perceived state of fatigue on behavioural, neurophysiological, and psychophysiological responses to sustained physical activity. Four experimental studies were conducted based on a common paradigm, designed to separate effects associated with the subjective experience of fatigue from concomitant influences of motor fatigability, examining the effects of demanding physical activity performed in the upper body on performance in non-active muscle group of the lower body. To establish the veracity of this paradigm, the first study assessed the impact of demanding physical activity in the upper body on indices of neuromuscular function in the lower body. Minimal effects were observed for the intervention, indicating that neuromuscular function in the lower limbs remained largely preserved following activity in the upper body. Subsequently, the second study examined how upper body activity influenced psychophysiological responses during a sustained contraction performed in the lower limbs. A perceived state of fatigue evoked by prior activity in the upper body was shown to indirectly limit endurance performance in the lower limbs by altering how effortful and pleasurable the task was perceived to be. Striving to replicate this effect and establish causal associations between perceptions of fatigue and the regulation of performance, the third study investigated whether the responses to sustained activity were modulated by the subjective intensity of the pre-induced state of fatigue. In addition, the association between individuals' interoceptive ability and their perceptual and affective experience of physical activity was explored. A perceived state of fatigue was again shown to impair performance, altering perceptual (i.e. effort) and affective responses. Yet, interestingly, no differences were observed between the two experimental manipulations of fatigue. The perception of fatigue, across all conditions, was associated with a meta-awareness of interoceptive judgements. Finally, the fourth study examined how the decision to exert effort in a forced-choice task was impacted under a perceived state of fatigue. Though participants indicated no difference in choice preferences when fatigued, confidence in ones' ability to complete chosen actions was reduced, indicating an association between fatigue and a (meta)awareness of perceived performance capacity. In conclusion, the findings of the thesis implicate the perception of fatigue as a top-down cognitive factor, associated with higher-order self-representations of physiological function and performance capacity, which influences perceptual and affective responses during sustained physical activity. Though these effects do not necessarily translate directly to changes in value-based decision-making, the perception of fatigue is identified as an important constraint limiting action.

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the influence of sensory evidence on updates to model predictions (i.e. posterior) (**A**). Conversely, when prediction errors are relatively imprecise, they have little impact on the posterior belief (**B**). Precision itself must be estimated (second-order predictions; system not shown explicitly here) and is established by descending predictions (blue dashed line). The relative precision of prediction errors at every level of the system is believed to be controlled by neuromodulatory actions that gate or control the gain of error carrying neuronal units (grey arrows). Schematic adapted from combined works of: Ainley et al. (2016); Seth and Friston (2016). Taken from Greenhouse-Tucknott *et al.* (2022).

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Figure 8.2. A graphical representation of the predictive processing framework underlying the emergence of exertional fatigue. The engagement of protracted physical exertion requires internal models to accurately anticipate the sensory states that will be encountered during transitions towards future goal states, to have the body reside within a (predictable) limited range of states that will sustain its biological integrity (i.e. maintain homeostasis). The subjective perception of fatigue may serve an adaptive function representing the ability of internal models to accurately predict transition states during the pursuit of temporally distal goal states. (1) Under resting conditions or even low-intensity (physical) exertion, evidence of sensory states (green arrow) may be largely predictable (i.e. black posterior distribution dominated by blue prior beliefs). This may see the minimization of prediction error predominated by (autonomic) reflexes at the lowest level of the hierarchy. (2) However, as demands increase and internal conditions become more unstable, physiological perturbations may be associated with greater prediction errors. Increasing strength of the prediction error (i.e. red distribution curve) may force error to ascend further up the levels of the hierarchy, necessitating deeper explanation, increasing its influence on posterior probabilities. This may generate attentional changes or perceptual updates across these lower levels. As pursuit of temporally-distal goal states is driven by increasingly higher-levels, action will continue if the precision of these distal goal beliefs enables it to dominate prior updates and therefore contextualise the levels beneath (i.e. posterior distribution still dominated by prior beliefs). (3) Across time, the performance of the model's overall ability to predict transition states within goal pursuit is monitored by a metacognitive layer. Persistent detection of error within the hierarchy signals an inability to exert effective (allostatic) control of internal states during this pursuit of (longer term) goal states. This signals that the model may provide bad predictions about the present and, importantly, future condition of the body. This perceived lack of control over bodily states undermines allostatic control self-efficacy, which is experienced as the subjective experience of exertional fatigue. Computationally, the emergence of fatigue may be associated with declining precision estimates afforded to predictions driving goal-directed behaviour, signalling increasing uncertainty within the model and weakening prediction's influence on posterior beliefs (dashed black line). The development of exertional fatigue is progressive, thus lower precision beliefs concerning goal-directed predictions result in greater prediction error throughout the levels of the hierarchy, which further undermines control capabilities during goal pursuit. Eventually, changing precision will see prediction error afforded more weight and cause high-level, goal-directed beliefs to be updated (i.e. shift in posterior distribution towards prediction error) which may shift control priorities towards the resolution of more immediate prediction error. This may be achieved through action (i.e. rest). Over time, rest may restore self-efficacy in control over bodily states as through the experience of agency (i.e. accurate predictions) in the restoration of homeostasis. Fatigue is consequently alleviated. However importantly, due to the significant challenge to model evidence encountered, restoration of perceived mastery of the body and homeostasis may be protracted. This is because precision estimates of predictions may be so low that prediction error is exacerbated during the recovery period. Therefore, the detection of accurate allostatic predictions may be bestrewn with prediction error which prolongs the subjective experience of fatigue. *Red arrows represent ascending prediction error, blue arrows represent descending predictions and green arrows represent ascending sensory evidence from the body. Dashed blue line represents effects on precision estimates.* Taken from Greenhouse-Tucknott *et al.* (2022).

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RESEARCH OUTPUTS FROM THESIS

Manuscripts

GREENHOUSE-TUCKNOTT, A., BUTTERWORTH, J., WRIGHTSON, J.G., SMEETON, N., CRITCHLEY, H., DEKERLE, J., HARRISON, N. A. (2022). Towards the unity of pathological and exertional fatigue: A predictive processing model. *Cognitive, Affective and Behavioral Neuroscience*. 22(2), 215–228. <https://doi.org/10.3758/s13415-021-00958-x>

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*This thesis is dedicated to the loving memory of my mum,
Christine Mary Tucknott.
Forever with me.*

DECLARATION

I declare that the research contained in this thesis, unless otherwise formally indicated within the text, is the original work of the author. The thesis has not been previously submitted to this or any other university for a degree and does not incorporate any material already submitted for a degree.

Signed: 

(Aaron Greenhouse-Tucknott)

Dated: 28/06/2022

NOMENCLATURE

[K ⁺]: concentration of interstitial potassium ions	FS: feeling scale
[La ⁻]: muscle lactate concentration	GABA: gamma-aminobutyric acid
[P _i]: concentration of inorganic phosphate	GDPR: general data protection regulation
ACC: anterior cingulate cortex	GLMM: generalized linear mixed model
ADP: adenosine diphosphate	Gr: granular
Agr: agranular	group Ia: primary muscle spindle
AIC: anterior insula cortex	group Ib: Golgi tendon organ
ANCOVA: analysis of covariance	group II: secondary muscle spindle
ANOVA: analysis of variance	group III/IV (A-δ/C-): ergoreceptors/metabo-nociceptors
ATP: adenosine triphosphate	H ⁺ : Hydrogen ion
b[La ⁻]: blood lactate concentration	HBD: heartbeat discrimination task
BB: <i>biceps brachii</i>	HG: handgrip
BF: <i>biceps femoris</i>	HR: heartrate
CI: confidence interval	HRA: health research authority
CMEP: cervicomedullary evoked potential	ICC: intraclass correlation
CNS: central nervous system	ICF: intracortical facilitation
CO: cardiac output	IFA: index flexor abductors
CON: control condition	IMP: inosine monophosphate
CP: critical power	<i>IQR</i> : interquartile range
CR10: category ratio 0-10 scale	ITT: interpolated twitch technique
CR100: centiMAX RPE scale	KE: knee extensors
CSP: cortical silent period	KSS: Karolinska sleepiness scale
DASS: depression, anxiety and stress scale	LMM: linear mixed model
dIPFC: dorsolateral prefrontal cortex	M1: primary motor cortex
Dys: dysgranular	MAP: mean arterial blood pressure
ECG: electrocardiogram	<i>Mdn</i> : median
EEG: electroencephalography	ME/CFS: myalgic encephalomyelitis/chronic fatigue syndrome
EF: elbow flexors	MEP: motor evoked potential
EMG: electromyography	MFI: multidimensional fatigue inventory
ERT: estimated resting twitch	MOD: moderate RoF condition
ESS: Epworth sleepiness scale	MPF: mean power frequency
FDI: <i>first dorsal interosseous</i>	MRFD: maximal rate of force development
FDR: false detection rate	MRI: magnetic resonance imaging
FNS: femoral nerve stimulation	MRR: maximal rate of relaxation

MSLT: multiple sleep latency test

MSO: maximal stimulator output

MVC: maximal voluntary contraction

M_{wave} : muscle compound action potential

NLMF: non-local muscle fatigue

NMFA: neuromuscular function assessment

NTS: nucleus of the solitary tract

OFC: orbitofrontal cortex

PAG: periaqueductal gray

PB: parabrachial nucleus

PCr: phosphocreatine

PMC: pre-motor cortex

POMS: profile of mood states

Q_{tw} : twitch force

RF: *rectus femoris*

RMS: root mean square

ROC: receiver operating characteristic curve

RoF: ratings of fatigue

RPE: ratings of perceived exertion

rTMS: repetitive transcranial magnetic stimulation

S1: somatosensory cortex

SD : standard deviation

SE : standard error

SEID: systemic exertion intolerance disease

SESOI: smallest effect of interest

SEV: severe RoF condition

SICI: short interval cortical inhibition

SIT: superimposed twitch force

SMA: supplementary motor area

S_tO_2 : local tissue saturation of oxygen

TEA: task effort and awareness scale

TMS: transcranial magnetic stimulation

TOST: two one-sided t -test

TTF: time to task failure

VA: voluntary activation

VAS: visual analogue scale

VA_{TMS} : cortical voluntary activation

$\dot{V}_E/\dot{V}CO_2$: ventilatory equivalent of carbon dioxide

\dot{V}_E : volume of minute ventilation

VL: *vastus lateralis*

vIPFC: ventrolateral prefrontal cortex

VM: *vastus medialis*

VM_b : basal ventral medial nucleus of the thalamus

vmPFC: ventromedial prefrontal cortex

VM_{po} : posterior ventral medial nucleus of the thalamus

$\dot{V}O_2$: volume of oxygen consumption

VP: ventroposterior nucleus of the thalamus

W' : power-duration curve constant

WMA: world medical association

W_{peak} : peak power

CHAPTER 1 - INTRODUCTION

The experience of fatigue is, for many, an all too familiar encounter. It is an important and ubiquitous experience present in both health and disease. As an illustration of its pervasiveness, within a sample ($n = 15,283$) of the general adult population of the south of England, 38% self-reported experiencing substantial fatigue, with 18% recounting undiminishing symptoms for 6 months or longer (Pawlikowska *et al.*, 1994). Other estimates place the prevalence within the community between 7-46% (Bültmann *et al.*, 2002; Chen, 1986; Lewis & Wessely, 1992; Loge *et al.*, 1998; Lerdal *et al.*, 2005; Ricci *et al.*, 2007). The widespread prevalence of fatigue has notable implications within the population at large, reflecting an important demand on medical care (e.g. Andrea *et al.*, 2003), a determinant of the incidence of occupational injury (e.g. Swaen, 2003), a predictor of premature mortality (e.g. Basu *et al.*, 2016) and a source of significant financial cost due to a loss of productivity (e.g. Ricci *et al.*, 2007). The consequences of fatigue are broad, and depending upon the context, the resulting outcomes may be stark. At one extreme, for patients suffering from neurological illness, fatigue is a common and unrelenting feature of day-to-day living (see Kluger *et al.*, 2013), regularly cited as a key contributor to reduced function and self-reported quality of life (Havlikova, Rosenberger, *et al.*, 2008; Ramírez-Moreno *et al.*, 2019; Ruban *et al.*, 2021). At another, for the competitive athlete, fatigue (or more specifically, offsetting its development) is an important determinant of performance and may be the difference between success and failure.

Fatigue is a disabling symptom. Recent taxonomical frameworks have proposed that fatigue may be principally defined across two independent, but interactive, attributes: 1) its conscious perception, and 2) its objective or physical manifestation, defined by a decline in magnitude or rate of some performance criterion (i.e. fatigability) (Kluger *et al.*, 2013; Enoka & Duchateau, 2016; Skau *et al.*, 2021). Fundamentally, it is our subjective perception of fatigue (here after, simply referred to as fatigue) that is of principal significance to the phenomenon (Dittner *et al.*, 2004; Penner & Paul, 2017; Noakes, 2012), which within both healthy individuals and as a signature of many illnesses, serves to limit the output of physical and cognitive activity (Enoka & Duchateau, 2016; Chaudhuri & Behan, 2004). Yet despite both its prevalence and universal relevance, over a century of dedicated scientific research has witnessed comparatively modest progress in our understanding of this debilitating perception. Progress has been hampered by various issues within the study of fatigue, most notably by those relating to methodology, including adopted definitions and utilised measurement instruments (Dittner *et al.*, 2004). For example, for the definition and conceptualisation of fatigue, important issues include: 1) the possible confounding influence of related, but separate constructs, due to similar or shared descriptors within what is conventionally ascribed to the subjective experience of fatigue, and 2) the conflation and surrogation of fatigue for other related, but ultimately distinct psychological constructs (e.g. the perception of effort).

In health, fatigue is principally a product of exertion; be that physical or cognitive. Within the study of the limits of our physical endurance capacity, prominent models contend that our subjective experience of fatigue is a vital component of a centrally orchestrated control of behavioural outputs enacted by the brain in order to maintain biological integrity (Noakes, 2012) or, more simply, in response to the momentary desirability of the task

(Marcora, 2019). However, among several limitations levelled at current models of central regulation, a persistent issue continues to be the depiction of this complex, psychophysical control process based on evidence drawn from the assessment of just a single psychological construct, such as ratings of perceived exertion (RPE; e.g. Crewe *et al.*, 2008; Eston *et al.*, 2007). Consequently, our appreciation of the dynamics between different conscious percepts and the implication of these interactions for behaviour remains severely lacking (Venhorst *et al.*, 2017). Importantly, the attribution of changes in RPE as fatigue (e.g. Noakes *et al.*, 2005; Tucker, 2009) may hinder the identification of the specific role of the perception of fatigue, *per se*, and thus compound our lack of understanding regarding of this debilitating feeling state.

During physical activity, various sensations arise in response to the work performed. Perception of these sensations may encompass distinctly experienced discriminatory (i.e. what), affective (i.e. how) and cognitive (i.e. why) components (Hutchinson & Tenenbaum, 2006). Importantly, individuals possess the ability to disassociate fatigue from other exertion-related perceptions (e.g. effort) both during and following physical activity (McAuley *et al.*, 1999; Micklewright, St Clair Gibson, *et al.*, 2017). Similarly, fatigue can also be disassociated from more basic affective states, such as valence (McAuley *et al.*, 1999). This suggests an independency of psychological constructs which may be relevant to the central regulation of performance, but to what the perception of fatigue relates to remains unclear. Though the perception of fatigue is associated with the processing of homeostatic inputs (Harrison *et al.*, 2009; Herbert, Ulbrich, *et al.*, 2007; Pollak *et al.*, 2014), it may actually be evoked by a higher-order, evaluative (meta)awareness of one's ability to exert effective control over the body in response to perturbation (Stephan *et al.*, 2016). As both the perception of effort and affective valence are sensitive to cognitive inputs, including an individuals' self-judgement of performance capacity (Focht *et al.*, 2007; Halper & Vancouver, 2016; Hutchinson *et al.*, 2008; McAuley & Courneya, 1992; McAuley *et al.*, 1999) and contextual expectancies (Azevedo *et al.*, 2021), a perceived state of fatigue may be an important modulating factor influencing these key regulatory variables and, consequently, decision-making processes determining whether or not to continue to engage in physical activity. However, our subjective appraisal of task demands are not infallible and may not necessarily translate accurately onto behaviour (Meyniel *et al.*, 2014). Thus, there is not only a need to understand how a state of fatigue interacts with other subjective experiences arising from physical activity, but also how fatigue alters the conversion of our perceptions of task demands and outcome rewards into motivated behavioural outcomes (Iodice *et al.*, 2017).

The principal aim of the present thesis was therefore to examine the effect of a perceived state of fatigue on the perceptual and affective responses to prolonged physical activity and the control of physical performance. Three experimental chapters ([chapters 5-7](#)) are presented which investigate the relationships between perceptual and affective responses during physical activity, as well as effort-based decision making, when performed under a perceived state of fatigue. A significant obstacle to causally establishing the specific function of the perception of fatigue within the central regulation of physical performance is the concomitant physical manifestation of fatigue on functional capacity (e.g. Whittaker *et al.*, 2019). Thus, to understand the role of the subjective component within the central regulation of performance specifically, there is a need to separate the perception of fatigue from a change in motor fatigability. Several experimental paradigms are available that may address this problem. Of particular interest is the observation that prior physical activity in a region of the body separate from that used to assess task performance, appears to modulate the perception of task activity and performance independently of

functional changes in the force-generating capacity of the investigated muscle groups (Amann *et al.*, 2013; Johnson *et al.*, 2015; Aboodarda *et al.*, 2020). Accordingly, [chapter 4](#) examined the challenges imposed on neuromuscular function of a non-activated muscle group following physical activity in another part of the body, in order to justify the adopted experimental paradigm and contribute to a growing interest in the topic (Behm *et al.*, 2021; Halperin *et al.*, 2015). A brief outline of the structure of the thesis is provided below:

- [Chapter 2](#) provides a review of the literature relevant to the construction of the research questions of the thesis. This includes the phenomenology of fatigue, the central regulation of physical performance, the neurophysiology of our perceptions and affective responses to physical activity and possible processes mediating their interactions, concluding with an evaluation of emerging paradigms that may enable an evaluation of the perception of fatigue on the regulation of physical performance.
- [Chapter 3](#) provides an account of the methods common to all the experimental chapters of this thesis.
- [Chapter 4](#) details an empirical examination of the acute effect of prior physical activity on the neuromuscular function of a non-activated muscle group.
- [Chapter 5](#) examines how interactions between different perceptual and affective responses may interact in the regulation of physical activity.
- [Chapter 6](#) evaluates how the subjective intensity of a perceived state of fatigue and individual sensitivity to interoceptive sensory inputs alters the central regulation of physical activity.
- [Chapter 7](#) investigates how a perceived state of fatigue modulates effort-based choice behaviour during a forced-choice task.
- [Chapter 8](#) discusses the findings of the experimental chapters and details a broader framework through which the results may account for the causes and consequences of fatigue during acute physical activity. Contributions to the progression of the research area, limitations of the studies and future directions are also discussed.
- [Chapter 9](#) presents the conclusion of the thesis.

CHAPTER 2 - REVIEW OF THE LITERATURE

2.1. Introduction to the Review of the Literature

This chapter will present a review of the literature, focussing on the perception of fatigue and the regulation of physical activity. [Section 2.2.](#) initially considers conceptualisations of fatigue and the multiple dimensions, terminologies and definitions used within its study. The relation between the subjective experience of fatigue and other psychological phenomena is also briefly explored to delimit the definition of fatigue adopted within the present thesis. [Sections 2.3. – 2.5.](#) present a review of prevalent models of exercise regulation and their principal perceptual (i.e. effort) and affective components. Within these sections, understanding of the neurophysiological basis of these constructs is discussed, enabling putative interactions with the perception of fatigue to be explored. In [section 2.7.](#), evidence from emerging experimental paradigms, utilising both prior cognitive and physical activity to separate the perceptual and physical/performance components of fatigue, is presented in justification of the experimental approach taken within the present thesis. Finally, [section 2.9.](#) presents the research aims and hypotheses arising from the review of the literature.

2.2. Defining Fatigue

2.2.1. The Term Fatigue

Etymologically, *fatigue* (n.) was introduced into the English language from the French around the mid-17th century, which was originally derived from the Latin word *fatigare* – ‘to weary, to tire out’¹. It replaced the now obsolete *fatigate*, a direct borrowing from Latin used in the 16th century. Although a concept of fatigue is firmly embedded within modern life and on the surface its meaning clear to all, colloquial understanding of what is conveyed when describing oneself as fatigued can be highly diverse. Present dictionary definitions of fatigue include i) “*extreme tiredness resulting from mental or physical exertion or illness*”, ii) “*a reduction in the efficiency of a muscle or organ after prolonged activity*”, iii) “*a lessening in one’s response to or enthusiasm for something, caused by overexposure*” (Oxford Dictionaries, 2013). Thus, fatigue may often be used to describe a broad combination of physical, sensory and cognitive epiphenomena. Consequently, colloquial and scientific use of the word fatigue may not always prove harmonious, generating ambiguity which may serve to complicate its formal study (Ream & Richardson, 1996). Indeed, fatigue has been described as an ‘enigma’ (Rasker, 2009), highlighting the inherent complexity of its study due, predominantly, to the multidimensionality of the construct (Karshikoff *et al.*, 2017; Pattyn *et al.*, 2018). The study of fatigue has therefore seen wide use of specialised definitions based on largely reductionistic approaches relating to the properties of fatigue of most interest within specific research fields including, for example, biomedicine, immunology, cognitive psychology, affective neuroscience and the exercise sciences. The emerging landscape is therefore one of dichotomies and semantic ambiguities which has, in part, caused a fragmentation within fatigue research and served to hinder the transfer of knowledge (Pattyn *et al.*, 2018; Skau *et al.*, 2021). For example, within these fields, fatigue has been partitioned

¹ Transcending its anthropological basis, the concept of fatigue started to be attributed to the properties of materials (e.g. metals) in the 19th century as a by-product of the industrial revolution (Schijve, 2003).

and conceptualised separately as a physiological process (Allen *et al.*, 2008; Gandevia, 2001), an affective symptom (Hartman *et al.*, 2019; Noakes, 2012) and as a cognitive/motivational factor (Boksem & Tops, 2008). Examples of definitions used in the description of fatigue across different fields may be found in [Table 2.1](#).

2.2.2. The Multidimensions of Fatigue

The emergence of some of the classic dichotomies evident throughout much of present day fatigue research may be traced back to the early work of Italian physiologist Angelo Mosso (1891), in which sensory and motor effects, central versus peripheral components and mental and physical influences were first described. In addition, the distinction between non-pathological and pathological symptoms of fatigue must also be considered. Accordingly, any discussion of fatigue must appreciate the full breadth of its multidimensionality. Presented below is a brief description of conventional dichotomies associated with fatigue that may be found in the literature.

2.2.2.1. Exertional vs. Pathological Fatigue

The ‘normal’ or exertion-related fatigue we all at some point experience is an acute, transient, non-pathological symptom with an identifiable cause (e.g. some form of physical or cognitive exertion), which wanes with the removal of the stressor; that is, through rest (Jason *et al.*, 2010). On the other hand, pathological fatigue is the prolonged (1-5 months) or chronic (> 6 months) experience of symptoms (Jason *et al.*, 2010), which is unalleviated by rest (Wrightson & Twomey, 2021). Prolonged or chronic fatigue may be defined as either an idiopathic symptom of a disease or specifically diagnosed as Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS; also termed Systemic Exertion Intolerance Disease; SEID) based on certain diagnostic criteria (Fukuda *et al.*, 1994). In relation to pathological fatigue, it is also important to differentiate primary fatigue from secondary fatigue (i.e. that which develops from the presence of other circumstances or disease) and comorbid fatigue (i.e. that which develops in the presence of other circumstances or diseases, but is not causally related to the primary disease or the circumstances or context) (Penner & Paul, 2017). Indeed, fatigue is a prevalent, debilitating symptom of many neurological and non-neurological conditions, including Parkinson’s disease (Herlofson & Kluger, 2017), multiple sclerosis (Krupp *et al.*, 2010), stroke (De Doncker *et al.*, 2018), post-poliomyelitis syndrome (Trojan & Cashman, 2005), cardiovascular disease (Nasiri *et al.*, 2016), traumatic brain injury (Mollayeva *et al.*, 2014), rheumatic arthritis (Nikolaus *et al.*, 2013) and cancer (Bower, 2014).

Exertional and pathological fatigue are typically conceptualised as distinct, with different underlying aetiology. Evidence indicates that a momentary state of fatigue may be disassociated from the chronic, or trait² experiences of fatigue as seen, for example, in stroke (Tseng *et al.*, 2010) and traumatic brain injury (Malloy *et al.*, 2021). Qualitative reports from patients indicate differences in both the severity and quality of fatigue experienced in disease (e.g. Flinn & Stube, 2010; Repping-Wuts *et al.*, 2008; Scott *et al.*, 2011) adding further support to this

² ‘Trait fatigue’ refers to a person’s perceived predisposition for fatigue over a period of time. The term can be a source of some confusion as it has also been used to refer to the chronicity of fatigue (i.e. the experience of symptoms over a protracted period of time), which does not necessarily reflect an individual’s beliefs about their propensity to experience fatigue.

Table 2.1. Select definitions of fatigue available within the current literature, separated into general/combined, objective, and subjective conceptualisations.

Author	Fatigue Definition
<i>General/Combined</i>	
Boksem & Tops (2008)	“[Cognitive fatigue] ... <i>a complex psychophysiological state involving changes in mood, information processing and behaviour.</i> ”
Chaudhuri & Behan (2000)	“... <i>the failure to initiate and/or sustain attentional tasks (mental fatigue) and physical activities (physical fatigue) requiring self-motivation.</i> ”
Enoka & Duchateau (2016)	“... <i>a disabling symptom in which physical and cognitive function is limited by interactions between performance fatigability and perceived fatigability.</i> ” <ul style="list-style-type: none"> ○ “[Performance fatigability] ...<i>the decline in an objective measure of performance over a discrete period.</i>” ○ “[Perceived fatigability] ... <i>changes in the sensations that regulate the integrity of the performer.</i>”
Enoka & Stuart (1992)	“... <i>a general concept intended to denote an acute impairment of performance that includes both an increase in the perceived effort necessary to exert a desired force and an eventual inability to produce this force (includes cognitive/perceptual and physiological components, in addition to describing the point of exhaustion).</i> ”
Hockey (2011)	“... <i>an adaptive state, serving to maintain effective overall (system-wide) management of goals.</i> ”
Phillips (2015)	“... <i>a suboptimal psychophysiological condition caused by exertion.</i> ”
Tanaka <i>et al.</i> (2014)	“... <i>a condition or phenomenon of declined ability and efficiency of mental and/or physical activities caused by excessive mental or physical activities, or illness; fatigue is often accompanied by peculiar sense of discomfort, desire to rest, and reduced motivation, referred to as fatigue sensation.</i> ”
<i>Objective</i>	
Bigland-Ritchie <i>et al.</i> (1983)	“[Muscle fatigue] ... <i>the reduction in the force-generating capacity of the neuromuscular system that occurs during sustained activity.</i> ”
Enoka <i>et al.</i> (2021)	“[Objective fatigability] ... <i>magnitude of the change in a performance metric after completing a prescribed task.</i> ”
Gandevia (2001)	“[Muscle fatigue] ... <i>any exercise-induced reduction in the ability of a muscle to generate force or power.</i> ” <ul style="list-style-type: none"> ○ “[Central fatigue] ... <i>a progressive reduction in voluntary activation of muscle during exercise.</i>” ○ “[Peripheral fatigue] ... <i>fatigue produced by changes at or distal to the neuromuscular junction.</i>”
Kluger <i>et al.</i> (2013)	“[Performance fatigability] ... <i>the magnitude or rate of change in a performance criterion relative to a reference value over a given time of task performance or measure of mechanical output.</i> ”

Author	Fatigue Definition
Skau <i>et al.</i> (2021)	"[Performance fatigability] ... <i>the decrement in magnitude or rate of change in a performance criterion relative to a reference value over a given time of task performance.</i> "
<i>Subjective</i>	
Aaronson <i>et al.</i> (1999)	"... <i>the awareness of a decreased capacity for physical and/or mental activity due to an imbalance in the availability, utilization, and/or restoration of resources needed to perform activity.</i> "
Dantzer <i>et al.</i> (2014)	"... <i>a feeling that relates to the lack of motivation to deploy resources and engage in high-effort performance to cope with their situation.</i> "
Davis & Walsh (2010)	"... <i>an overwhelming sense of tiredness at rest, exhaustion with activity, lack of energy that precludes daily tasks, inertia or lack of endurance, and loss of vigour.</i> "
Dittner <i>et al.</i> (2004)	"... <i>extreme and persistent tiredness, weakness or exhaustion - mental, physical or both.</i> "
Enoka <i>et al.</i> (2021)	"... <i>feelings of tiredness, lack of energy, low motivation, and difficulty in concentrating.</i> "
Kluger <i>et al.</i> (2013)	"... <i>subjective sensations of weariness, increasing sense of effort, mismatch between effort expended and actual performance, or exhaustion.</i> "
Krupp & Pollina (1996)	"... <i>an overwhelming sense of tiredness, lack of energy and feelings of exhaustion</i> "
Kuppuswamy (2017)	"... <i>a percept arising from alterations within the activational systems that inform voluntary action.</i> "
Micklewright <i>et al.</i> (2017)	"... <i>a feeling of diminishing capacity to cope with physical or mental stressors, either imagined or real.</i> "
Ream & Richardson (1996)	"... <i>a subjective, unpleasant symptom which incorporates total body feelings ranging from tiredness to exhaustion creating an unrelenting overall condition which interferes with individuals' ability to function to their normal capacity.</i> "
Riley <i>et al.</i> (2010)	"... <i>from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that is likely to decrease one's ability to carry out daily activities, including the ability to work effectively and to function at one's usual level in family or social roles.</i> "
Skau <i>et al.</i> (2021)	"... <i>the sensation of (i) feeling the need for rest or (ii) mismatch between effort expended and actual performance.</i> "
Tajima <i>et al.</i> (2010)	"... <i>an indispensable bio-alarm to avoid the exhaustive state caused by overwork and stress.</i> "
Wrightson & Twomey (2021)	"[Pathological fatigue] ... <i>a persistent feeling or perception of weariness, tiredness or exhaustion that is not alleviated by rest, is not proportional to activity levels and is a disabling negative symptom that interferes with daily activities and impairs quality of life.</i> "

(continued)

distinction. However, it is also possible that this separation may be, at least in part, exacerbated by the different instruments used to assess chronic versus acute symptoms (c.f. Tseng et al., 2010). Instruments used to assess protracted or trait-like experiences of fatigue may involve an integration of related and/or unrelated factors other than fatigue, which may only further this disassociation (Malloy *et al.*, 2021; [section 2.2.4.1.](#)). Accordingly, it is not entirely clear currently whether pathological and exertional fatigue can be considered truly distinct phenomena³. Interestingly, a common feature of pathological fatigue is an exacerbation of symptoms following some form of acute exertion (e.g. Nijs et al., 2010), thus it is conceivable that exertional fatigue is a fundamental component encompassed within the broad pathological experience of fatigue, supporting a proposed commonality between symptoms in disease and health in which both ultimately serve to regulate energy expenditure and work output (Chaudhuri & Behan, 2004).

2.2.2.2. *Objective vs. Subjective Fatigue*

Distinction may be made between the objective, or behavioural, emergence of fatigue - often referred to as fatigability, performance fatigability or objective fatigue/fatigability (see [section 2.2.3.](#)) - and its subjective experience. The former is assessed through declines in some performance criterion, while the latter is assessed through changes in self-reported measures (Zwarts *et al.*, 2008). Though the perception of fatigue and fatigability have been shown to be intrinsically associated both in health (e.g. Whittaker *et al.*, 2019) and disease (e.g. Coates *et al.*, 2020), it has also been shown that objective and subjective responses may not always correspond, demonstrative of the independence of these dimensions of fatigue (e.g. Prak *et al.*, 2019).

2.2.2.3. *Physical vs. Cognitive Fatigue*

The symptom of fatigue is also commonly distinguished based on its domain of origin. That is, physical fatigue is often used to describe some difficulty in performing physical tasks while cognitive fatigue⁴ develops in response to protracted cognitive work. In relation to physical performance, although performance is ultimately determined holistically by an integration of physical, technical, decision-making and psychological components, all of which are 'fatigable' (Knicker *et al.*, 2011), physiologists have commonly defined physical fatigue (sometimes referred to as muscle fatigue or neuromuscular fatigue) in reference to its lowest level (i.e. the contractile output) as "*any exercise-induced reduction in the ability of a muscle to generate force or power*" (Gandevia, 2001). While this reduction in capacity may be accompanied by changes in how activity is perceived in broader perspectives of fatigue (Enoka & Stuart, 1992), studies adopting this definition predominantly focus on the underlying processes residing within the motor system and the assumption that its function directly relates to an individuals' ability to carry out physical tasks. In contrast, cognitive fatigue may be conceptualised as a "*psychophysiological state*

³ For example, some perspectives hold that pathological fatigue reflects an amplified sense of normal (physiological) fatigue (Chaudhuri & Behan, 2004).

⁴ The term 'cognitive fatigue' and 'mental fatigue' are used varyingly throughout the literature (with their usage typically linked to particular research domains) to denote the emergence of fatigue arising from protracted engagement with a cognitive task. Ackerman and Knafer (2009) propose that due to the type of task typically adopted in this line of research, cognitive fatigue may represent the more precise term. Others argue that 'mental fatigue' is more appropriate as it encompasses the emotional and motivational effects of the task (Van Cutsem *et al.*, 2017). In the present thesis, the terms are not distinguished, and 'cognitive fatigue' will be consistently used throughout.

involving changes in mood, information processing and behaviour” (Boksem & Tops, 2008), which may thus see cognitive fatigue refer to a feeling state, changes in neuronal activity and/or declines in cognitive performance. Though the involvement and physiologic changes within networks supporting task performance clearly differ between physical and cognitive tasks (Kluger *et al.*, 2013)⁵, the phenomenological experience of fatigue is seemingly comparable between domains (and may be defined as such; Skau *et al.*, 2021), which may see fatigue - that is, the perception - identified with a common process during physical and cognitive exertion (Müller & Apps, 2019). In keeping, it has previously been proposed that “*the gap between [cognitive] and physical fatigue is not very broad*” (Inzlicht & Marcora, 2016; p.5). This distinction will be discussed further in [section 2.7.1](#).

2.2.2.4. Central vs. Peripheral Fatigue

Identification of the locus of the deleterious effect of fatigue is often associated with peripheral (i.e. factors outside the central nervous system; CNS) and central factors (i.e. factors within the CNS). However, definitions and the use of terms vary across different domains of fatigue research. In the context of physical fatigue, peripheral fatigue conventionally refers to declines in force or power attributable to “*changes at or distal to the neuromuscular junction*”, while central fatigue represents a decline in force arising from “*a progressive reduction in voluntary activation of muscle*” (Gandevia, 2001). The separate peripheral and central sites of motor impairment may be evaluated through electrical and/or magnetic stimulation techniques applied at different points along the motor pathway (Millet *et al.*, 2012; Todd *et al.*, 2016).

Alternative perspectives, however, use the distinction between peripheral and central fatigue in a way that is more analogous to that of physical and cognitive fatigue, or objective and subjective fatigue, outlined above. Indeed, peripheral fatigue is relevant to physical fatigue but not typically to cognitive fatigue (Chaudhuri & Behan, 2000), while central fatigue has been, rather ambiguously, used to refer to the subjective perception of fatigue, an effect on the function of the CNS, or in relation to motivational/cognitive deficits (Chaudhuri & Behan, 2000; Chaudhuri & Behan, 2004; Friedman *et al.*, 2007; Leavitt & DeLuca, 2010).

2.2.3. Proposed Taxonomies for the Study of Fatigue

In response to the evident ambiguity in the use of terms and definitions prevalent throughout the study of fatigue, a number of taxonomical frameworks have recently been proposed in order to clearly demarcate the various causes and consequences of fatigue and facilitate shared conceptual frameworks, clear communication, scientific progress within and across interested fields (Kluger *et al.*, 2013; Enoka & Duchateau, 2016; Enoka *et al.*, 2021; Skau *et al.*, 2021). These proposed taxonomies have been applied to both pathological fatigue (Kluger *et al.*, 2013) and transient, exertional fatigue (Enoka & Duchateau, 2016)⁶. Broadly, fatigue is described, first and foremost, as a disabling symptom in which physical and cognitive function is impaired through the interaction between two dimensions (Enoka & Duchateau, 2016): a subjective dimension (‘perceived fatigue’) and/or an objective

⁵ Though it is often not acknowledged that most tasks involve both physical and cognitive components to greater or lesser degrees.

⁶ This was principally created in reference to the fatigue-performance relationship attributable to physical or motor tasks.

dimension ('performance fatigability'⁷), the latter denoting a reduction in some marker of (physical and/or cognitive) performance (Kluger *et al.*, 2013). Causal factors that influence the perception of fatigue are associated with homeostatic factors and the psychological state of the individual, while the factors affecting performance fatigability are attributed to the effects acting both peripherally (i.e. within the muscles) and centrally, reflecting changes in cortical/subcortical networks and output from the CNS (Kluger *et al.*, 2013; Enoka & Duchateau, 2016; Enoka *et al.*, 2021). Though specific causal factors are attributed to specific dimensions, it is proposed that there exists significant interactions between the two. For example, the homeostatic changes acknowledged to give rise to the perception of fatigue will also concomitantly limit the ability of the contractile machinery in producing force and therefore lead to performance fatigability (Enoka & Duchateau, 2016).

The taxonomies proposed within the study of pathological (Kluger *et al.*, 2013) and more broadly, with reference to exertional fatigue in health (Enoka & Duchateau, 2016), differ on the conceptualisation of the subjective component of fatigue, however. Enoka and Duchateau (2016) propose that the symptom of fatigue arises through interactions between performance and *perceived* fatigability. Perceived fatigability defines any change in perception that aids in regulating the performer (Enoka & Duchateau, 2016). Examples may include the perceived level of effort required to perform the task (e.g. Staiano *et al.*, 2018) and/or some change in affective valence felt (e.g. Hartman *et al.*, 2019) - the role of these psychological constructs in the regulation of physical performance will be discussed in detail in later sections. Though combining multiple axes under one broad rubric has appeal for describing the complex, multifaceted and constantly changing perceptual experience involved in the control of performance, one fear may be that the concept of 'perceived fatigability' risks further confusing an already complicated and multifactorial phenomenological experience such as fatigue. Moreover, within this proposed taxonomy it is unclear whether the perception of fatigue (i.e. the self-reported symptom) is separable from perceived fatigability or can be (and is) represented by both. If the latter, the definition could risk becoming circular (Skau *et al.*, 2021). Recently, in reference to clinical conditions (i.e. multiple sclerosis) 'perceived fatigability' was disassociated from the state (i.e. momentary) perception of fatigue (Enoka *et al.*, 2021). 'Perceived fatigability' was aligned to the experience of trait fatigue, reflecting a subjective estimate of ones' past or future work capacity based on a perceived disposition to experience fatigue (Enoka *et al.*, 2021). This is very different to the original definition of perceived fatigability, highlighting the potential for confusion in the application of the concept. Furthermore, the subjective component of fatigue is often conflated and/or used interchangeably with concepts such as the perception of effort (Enoka & Stuart, 1992; Marcora, 2019). Though related, the perception of effort and fatigue do represent distinct constructs (Halperin & Emanuel, 2020). As the perception of fatigue and the perception of effort are often used synonymously, empirical evidence of this difference is sparse. However, alongside what small evidence there is, some practical examples can be useful in articulating the difference. For example, the perception of fatigue may be experienced for a period post-exertion, during rest, but the same is not true for the perception of effort, which cannot be experienced in the absence of goal-directed action (Micklewright, St Clair Gibson, *et al.*, 2017; Massin, 2017). Similarly, the performance of a brief maximal contraction may require maximal perceived effort, however it is unlikely to cause a severe perception of fatigue (Smirmaul, 2012). More recently, divergent effects across effort and fatigue were shown to

⁷ Fatigability is used to denote a measure of physical or cognitive work capacity (Enoka *et al.*, 2021); a change in performance that is relative both to the individual and the task.

be mediated by interest. That is, interest was shown to increase participation in higher effort tasks, yet despite the engagement of greater effort, perceived fatigue was demonstrated to be attenuated (Milyavskaya *et al.*, 2021). The distinction between the perception of fatigue and effort is discussed further in [sections 2.3.2.](#) and [2.4.4.](#) Accordingly, it is believed that ‘perceived fatigability’ may dilute appreciation of the specific contributions and distinct roles of specific feeling states, particularly that of fatigue, in relation to the control of behaviour. For this reason, the present thesis will conform to the original dimensions proposed by Kluger *et al.* (2013), attributing fatigue to interactions between performance fatigability and the perception of fatigue (ignoring perceived fatigability), in order to facilitate a clear categorisation of the attributes of fatigue discussed. Performance fatigability may be defined as “*the decrement in magnitude or rate of change in a performance criterion relative to a reference value over a given time of task performance*” (Skau *et al.*, 2021). Below, the subjective experience of fatigue is explored in more detail in order to offer the most appropriate definition for the present thesis.

2.2.4. The Perception of Fatigue

A longstanding question remains, what does it mean to feel fatigued? Despite calls for more information on the phenomenology of fatigue (Lewis & Wessely, 1992), it has been noted that little attention has been dedicated to understanding this ubiquitous experience across both health and disease (Morris, 2019). In disease, this may be a particularly complicated task considering the vast variability in patients’ descriptions of their personal experiences (e.g. Institute of Medicine, 2015). Presently, there remains no universally accepted definition of the phenomenological experience of fatigue. This presents one of, if not, the most important issue faced by fatigue research. Without a clear definition of the phenomenological experience of fatigue, precise measurement is hindered, which in turn serves to obscure understanding of the phenomenology of fatigue (Dittner *et al.*, 2004). At present, numerous psychometric scales exist for the assessment of fatigue. However, the information gained from each is, in part, dependent upon the developers’ own conceptualisation of fatigue, which may lead to the measurement of different aspects of fatigue, or indeed, different constructs altogether (Dittner *et al.*, 2004). Discussion of the various merits of each instrument is beyond the scope of this literature review, but the interested reader is directed to the following articles for discussion on the topic: Dittner *et al.* (2004); Hjollund *et al.* (2007); Shen *et al.* (2006); Whitehead (2009).

Broadly, two thematic conceptualisations of the subjective experience of fatigue would seem to be evident within the current literature. One refers to a conventional, or perhaps colloquial, feeling associated with an “*overwhelming sense of tiredness, lack of energy and feelings of exhaustion*” (e.g. Karlsen *et al.*, 1999; Krupp & Pollina, 1996). The other offers an more indeterminate but reflective phenomenological experience associated with a feeling of reduced capacity (or motivation) to cope with experienced demands (e.g. Aaronson *et al.*, 1999; Dantzer *et al.*, 2014; Micklewright *et al.*, 2017; Steele, 2021; André *et al.*, 2019). To identify the experience of fatigue, and subsequently an appropriate means of assessment, it may be pertinent to evaluate how such conceptualisation specifically relate to fatigue such that it can be disassociated from other related phenomena and therefore delineate the phenomenological space within which fatigue occupies⁸. What follows offers a very brief

⁸ Based on the discussion above, it is important to highlight that any distinction must be viewed with some scepticism due to the absence of a clear definition of fatigue and the use of different instruments.

description of evidential and hypothesised boundaries distinguishing fatigue from other related perceptual and affective constructs.

2.2.4.1. Separating the Perception of Fatigue from Related Constructs

As stated, one conceptualisation of fatigue references extreme feelings of tiredness. Common definitions of tiredness define “*the state of wishing for sleep or rest*” (Oxford Dictionaries, 2013). Shared descriptions of complaints (i.e. being tired) between sleepiness and fatigue has seen interchangeable use of terms within many research contexts (Shen *et al.*, 2006). This may be exacerbated by a difficulty in differentiating qualitative assessments (Neu *et al.*, 2010). However, though related, sleepiness and fatigue have been shown to reflect distinct subjective experiences (Hossain *et al.*, 2005; Mairesse & Neu, 2016; Neu *et al.*, 2010; Shen *et al.*, 2006). For example, subjective sleepiness recorded using the Epworth Sleepiness Scale⁹ (ESS; Johns, 1991) was not shown to contribute to the variance explained across fatigue domains assessed using the Multidimensional Fatigue Inventory¹⁰ (MFI; Smets *et al.*, 1995) in Parkinson’s patients (Havlikova, van Dijk, *et al.*, 2008). Moreover, objective markers of sleep propensity (i.e. the multiple sleep latency test, MSLT) may also be disassociated from the subjective fatigue reported by patients with sleep disorders (Lichstein *et al.*, 1997). However, the distinction may not always be clear. People with ME/CFS have been shown to display sleep latencies within a normal range, but report heightened perceptions of fatigue and, compared to sleep apnoea patients, also report similar levels of subjective sleepiness (Neu *et al.*, 2008).

The distinction between sleepiness and fatigue appears to relate to the fact sleepiness necessitates sleep specifically for its alleviation, while in non-pathological fatigue, symptoms may be abated through sufficient rest and/or change in the environmental stressor (Mairesse & Neu, 2016). It has been proposed that sleep serves a clear and specific biological function (i.e. restoration), while the function of fatigue may potentially be broader (Leavitt & DeLuca, 2010). Interestingly, the distinction between sleepiness and fatigue may be particularly evident when contextualised to acute, physical activity (Driver & Taylor, 2000). While exacerbation of the subjective perception of fatigue is a common consequence of physical (or cognitive) exertion in both health (e.g. Micklewright *et al.*, 2017) and disease (e.g. Loy *et al.*, 2016), acute activity can transiently relieve subjective sleepiness (Leproult *et al.*, 1997; Matsumoto *et al.*, 2002). A primary drive for sleep is underpinned by interactions between the body’s circadian rhythms and homeostatic functions, generating an innate biological function in response to extended periods of wakefulness (Borbély *et al.*, 2016). Fatigue on the other hand is particularly sensitive to preceding and/or prospective exertion. While sleepiness may promote sleep for restoration, fatigue is often conceptualised as a protective mechanism, safeguarding against excessive homeostatic perturbation through exertion (Boulloasa & Nakamura, 2013), offering different roles for the two phenomena. Indeed, fatigue has been associated with reduced, self-initiated activity, though similar associations between excessive sleepiness and reduced physical behaviour are not necessarily always evident (Matsangas & Shattuck, 2018). Importantly, when individuals are

⁹ A measure of subjective propensity to sleep.

¹⁰ A 20-item instrument used to quantify the severity of fatigue experienced over the last week across 5 dimensions (general fatigue, physical fatigue, mental fatigue, reduced motivation, reduced activity).

provided with a clear distinction between the two phenomena they are capable of accurately distinguishing between fatigue and sleepiness (e.g. Benoit *et al.*, 2019). Consequently, in order to avoid a conflation of constructs, it has been proposed that fatigue should be operationalized as “*weariness, weakness and depleted energy*” with no direct reference to feelings of tiredness (Pigeon *et al.*, 2003).

However, this operationalization presumes that fatigue and energy are equivalent, residing on the same continuum (i.e. high fatigue is synonymous with low energy). Loy *et al.* (2018) refute this suggestion, proposing that energy (and its descriptors of vigour and vitality) and fatigue may in fact represent distinct perceptual states. The basis of the authors’ hypothesis originates from the differentiation between energy and fatigue factors within several mood questionnaires (e.g. the Profile of Mood States [POMS]; Heuchert & McNair, 2012). Experimental evidence indicates that these factors may change independently of each other (see Loy *et al.*, 2018). Consequently, feelings of energy and fatigue may serve distinct functions, facilitating adaptive approach- and avoidance-orientated behaviours, respectively. The phenomenological differentiation of feelings of vigour and fatigue continues to be debated (Deng *et al.*, 2015).

Fatigue is also conventionally related to motivational functions (Boksem & Tops, 2008; Hockey, 2011; Müller & Apps, 2019; Pageaux, 2014). Accordingly, it may often be difficult to distinguish fatigue from other related disorders involving motivational deficits, including depression, boredom and apathy. In particular, the disassociation of fatigue from depression is problematic since co-occurrence is so common, which may indicate shared underlying mechanisms (Corfield *et al.*, 2016)¹¹. Yet, disassociations between fatigue and depression have been found (Skorvanek *et al.*, 2015; Douven *et al.*, 2017) suggesting the need for further inquiry with greater nuance to understand this difference (e.g. Stephan *et al.*, 2016).

Differentiation of boredom from fatigue may be easier to understand, at least theoretically, with the difference defined by the level of arousal evoked by the perceived demands of the task. That is, low work demands (‘underload’) may give rise to boredom, whereas high work demands may elicit fatigue (Pattyn *et al.*, 2008). This relationship, however, may not be as simple as first viewed. Based on the bi-dimensional model of subjective boredom proposed by Hill and Perkins (1985), boredom is characterised by both cognitive (i.e. the perceived or evaluated task demands) and affective components (i.e. the interpretation of those demands, for example, frustration). The interaction between these two components may hold important implications for the experience of fatigue. Indeed, Pattyn *et al.* (2008) proposed that if the affective component of boredom dominates, then the potential experience of frustration may induce a certain level of stress, which in turn may increase arousal eventually leading to a fatigue-associated state. Alternative perspectives propose that fatigue and boredom are underpinned by the opportunity costs of persisting with current actions over foregone rewards across internal and external worlds, respectively (Agrawal *et al.*, 2021)¹². Specifically, the experience of fatigue reflects the value of rest and the use of offline mental simulations to improve the association between action and rewarding outcomes,

¹¹ As stated previously, this may also be exacerbated by self-reported measures of fatigue which require retrospective recall of its impact and thus introduce other biases (i.e. depression) within the assessment of fatigue (Malloy *et al.*, 2021).

¹² The authors acknowledge that this distinction may be a little blurred, as mental simulations may enable the value of gathering information through exploration to be propagated through the brain’s underlying computational models, which may account for interactions between fatigue and boredom (Agrawal *et al.*, 2021).

while boredom represents the value of information that may be gained (and currently not accessed) through exploration (Agrawal *et al.*, 2021).

The relationship between apathy and fatigue has been understudied, with a limited number of investigations indicating an unsurprisingly close association between constructs (Cochrane, Rizvi, *et al.*, 2015; Skorvanek *et al.*, 2015; Sáez-Francàs *et al.*, 2013). The two phenomena may develop over a similar time course based on shared comorbidities (i.e. depression; Douven *et al.*, 2017). However, like depression, evidence of a disassociation between fatigue and apathy has also been reported (e.g. Martino *et al.*, 2016). Apathy is conceptualised as a multidimensional construct, defining a loss of motivation and interest, comprising behavioural/social, cognitive and emotional aspects (Ang *et al.*, 2017; Marin, 1991). While both constructs are related to deficiencies in self-initiated, goal-directed behaviour, Kuppuswamy (2017) proposed that the important distinction between apathy (and depression/anhedonia) and fatigue may concern the property of motivation affected. Classic motivational theory proposes motivated behaviour to be characterised by both activation (i.e. the vigour and persistence of an action) and directional (i.e. towards or away from an object) facets (Salamone & Correa, 2012). The proposed distinction between fatigue and apathy offers that apathy primarily arises from changes in directional aspects of motivated behaviour, impairing individuals 'want' to initiate actions, while fatigue is associated with deficits in activation-related systems, with individuals displaying a want to initiate action but feeling unable to do so (Kuppuswamy, 2017). This may hold important implications for understanding the aetiology of both apathy and fatigue (Müller & Apps, 2019). This hypothesis, however, remains untested. Interestingly, a recent evaluation of the dimensions of apathy suggests apathy and fatigue may also differ based on the degree of emotional engagement (Ang *et al.*, 2017). Negative correlations between emotional apathy (i.e. blunted affect) and fatigue (Ang *et al.*, 2017) suggests that the symptom of fatigue is a highly affective construct, while apathy may be associated with reserved emotional investment.

2.2.5. Conclusions drawn from the Conceptualisations and Definitions used within the Study of Fatigue

The study of fatigue has been plagued by semantic ambiguity for many years which has served only to limit progress across interested research areas. Indeed, a recent attempt to provide a unified set of definitions applicable across a wide variety of fields proposed thirteen separate definitions to cover the full range of its usage (Skau *et al.*, 2021). Though other taxonomical frameworks offer a more streamlined framework through which to translate findings across different fields interested in fatigue, similar issues related to the outlined definitions are still apparent when considering the proposed dimensions of fatigue (e.g. Enoka & Duchateau, 2016).

Ultimately, fatigue is a self-reported symptom. Focus on markers of (performance) fatigability, particularly in relation to exertional fatigue, may capture only a small part of the total 'fatigue process'. That is, performance may be maintained through goal-orientated control processes at the expense of a change in the perception of fatigue (Hockey, 2011; Hockey, 2013). Moreover, acute performance decrements¹³ may emerge following

¹³ There is need to also highlight a distinction between performance fatigability and task failure, which are sometimes used equivalently in fatigue research. Failure may be viewed as an event and may not necessarily correspond to any objective change in physical or cognitive function. For example, there could be a conceivable instance where an extremely unmotivated individual disengages with a task well before any functional changes occur.

protracted exertion in response to transient, affective states other than fatigue, such as boredom ([section 2.2.4.1.](#)), thus cannot necessarily be used to conform the presence of fatigue. What definitively defines fatigue is its subjective experience. However, its phenomenology remains difficult to define clearly and unequivocally, such is the need of continued investigation. As briefly outlined, it appears that the subjective experience of fatigue occupies its own phenomenological space, in that it can be disassociated from other related states. Fatigue is a highly affective subjective experience, typically associated with motivational changes. However, colloquial descriptors, including a feeling of extreme tiredness, may confuse understanding and lead to a misinterpretation of fatigue with other related constructs. Accordingly, definitions based on a broader, but more indiscriminate feelings, related to a perceived reduction in work capacity – or at least, a perceived challenge to one’s ability to exert effect control over actions - may present the most broadly acceptable conceptualisation currently available. Micklewright *et al.* (2017) have developed and validated a single-item scale¹⁴ for evaluating individuals’ rating of their present perceived state of fatigue, with the perception of fatigue defined as “*a feeling of diminishing capacity to cope with physical or mental stressors, either imagined or real*”. Accordingly, this definition was adopted for the assessment of the perception of fatigue within the present thesis.

2.3. The Limits of Physical Endurance Performance

Increased metabolic activity arising from sustained or repeated contractions of skeletal muscle(s) disrupts the resting homeostasis of multiple (if not all) tissues and organs of the body, and a series of complex, coordinated interactions between biological systems emerge to deal with this imposed challenge (Hawley *et al.*, 2014). A consequence of these internal perturbations is the development of ‘fatigue’(Ament & Verkerke, 2009). In line with the different conceptualisations and dichotomies within the study of fatigue outlined in the previous section, perspectives on the mechanisms limiting the performance of physical activity¹⁵ are also varied. Exercise physiologists have typically focussed on impairments in muscles’ capacity to produce force ([section 2.2.2.3.](#)). One of the earliest models on the limits of physical activity proposed that, ultimately, physical activity is limited by cardiac output, developing skeletal muscle anaerobiosis and the accumulation of lactic acid (Hill & Lupton, 1923; Hill *et al.*, 1924). Current understanding of lactate production in the development of metabolic acidosis and its implications for performance presents a very different perspective to that of Hill and colleagues’ original proposal¹⁶, with ‘lactic acid’¹⁷ disassociated from metabolic acidosis and lactate evidenced as an important energy substrate in skeletal muscles, the brain and other organs (Cairns, 2006; Hall *et al.*, 2016). However, limitations to the production of high-energy phosphates and the impairment of muscle force or power production as a result of

¹⁴ This is also important, as single-item instruments may be more appropriate for study of the transient emergence of fatigue during and/or after an acute bout of physical exertion than multi-item instruments due to the time required to complete the latter (Dittner *et al.*, 2004).

¹⁵ Physical activity is defined as “*a potential disruption to homeostasis by muscle activity that is either exclusively, or in combination, concentric, eccentric or isometric*” (Winter & Fowler, 2009). It is equivalent to exercise and the two terms may be used interchangeably (Winter & Fowler, 2009). However, it is believed that exercise continues to hold stronger connotations with structured and planned physical activity, relating to particular types of activity (e.g. walking, jogging, cycling, etc). Physical activity was used throughout this thesis to in an attempt to emphasise the broader consequences of fatigue in response to physical action.

¹⁶ The basic premise however, that ‘lactic acid’ is universally detrimental to physical performance largely endures in popular beliefs.

¹⁷ That is, the disassociation of lactic acid into its conjugate base, lactate⁻, and hydrogen ion (H⁺).

inadequate oxygen supply to the working muscles is still considered the cornerstone of exercise physiology and a primary determinant of physical endurance performance (Bassett Jr & Howley, 2000; Joyner & Coyle, 2008). Within this, further reductionist approaches, separating and investigating biological processes across finer constituent parts, has seen the development of multiple models of motor performance fatigability (Abbiss & Laursen, 2005). Largely, these models have been termed ‘catastrophic’ (see Abbiss and Laursen, 2005; Noakes, 2012), since they predict that termination of physical activity is a physical event underpinned by dyshomeostasis and a failure of the (motor) system to produce the output required to meet task demands (see Burnley & Jones, 2018)¹⁸.

Counter to ‘catastrophic’ perspectives on the limits of physical endurance performance, a body of evidence indicates that there exists a functional force/power reserve immediately following the termination of physical activity¹⁹. That is, during whole-body physical activity (i.e. bipedal cycling tasks)²⁰, maximal power production upon termination has been shown to exceed the power required during constant-load, submaximal tasks (Marcora & Staiano, 2010) and the end power required during maximal incremental exercise (Cannon *et al.*, 2016; Coelho *et al.*, 2015; Morales-Alamo *et al.*, 2015; see also Ferguson *et al.*, 2016²¹). Though these studies have received some methodological criticisms (e.g. Burnley, 2010), the presence of a reserve appears to persist when such concerns are accounted for (e.g. Staiano *et al.*, 2018). Moreover, further evidence of a functional reserve may be seen through centrally-acting, psychological interventions such as, for example, the ergogenic effect of placebos (e.g. Pollo *et al.*, 2008). The presence of a functional reserve at the limit of exercise tolerance would indicate a need to focus on factors other than cardiorespiratory capacity and neuromuscular function as the prime limiting factors of physical activity²² and places greater attention on the psychological factors involved in physical performance (Marino *et al.*, 2011). Indeed, the volitional decision to both engage and disengage with physical activity is, fundamentally, an output of the brain (Kayser, 2003). Accordingly, several models have emerged to describe the central regulation of physical activity, yet two have proceeded to dominate discussion ([Figure 2.1](#)); namely, the central governor model of exercise regulation (Noakes *et al.*, 2001) and the psychobiological model of endurance performance (Marcora, 2008; Pageaux, 2014)²³.

¹⁸ Paralleling this, resource accounts of self-control within cognitive psychology are also often referenced in relation to the development of ‘cognitive fatigue’ (Baumeister *et al.*, 2007). The depletion of a finite physical or biological resource (i.e. glucose; Gailliot *et al.*, 2007) is proposed to lead to an inability to exert effective control. However, like ‘catastrophic’ perspectives of physical performance, several lines of evidence have questioned this account of self-control (Beedie & Lane, 2012; Kurzban *et al.*, 2013; Inzlicht *et al.*, 2014).

¹⁹ It should be highlighted that it has been argued that the evidence of a functional force/power reserve examined *after* task failure means that it cannot indicate, precisely, what caused task failure and thus its presence *during* the task (Burnley & Jones, 2018).

²⁰ Similar effects have been reported at the end of submaximal isometric contractions in single limbs (Neyroud *et al.*, 2012).

²¹ The authors report a mean increase in power of 12% above task demands at the point of task failure, but this was not statistically significant ($p = 0.116$), despite the large effect size (Cohen’s $d = 0.81$). For discussion see Morales-Alamo *et al.*, (2016) and Ferguson, Cannon, *et al.* (2016).

²² Though it is obvious (and this fact should not be detracted from) that physiological capacities clearly set the foundation of athletic performance.

²³ Alternative models may be found within the literature but are not discussed in detail in this thesis since they were either based on the described models or share too many similarities to the central governor model and/or psychobiological model to warrant further detailed discussion (e.g. the flush model is based on the central governor model; Millet, 2011).

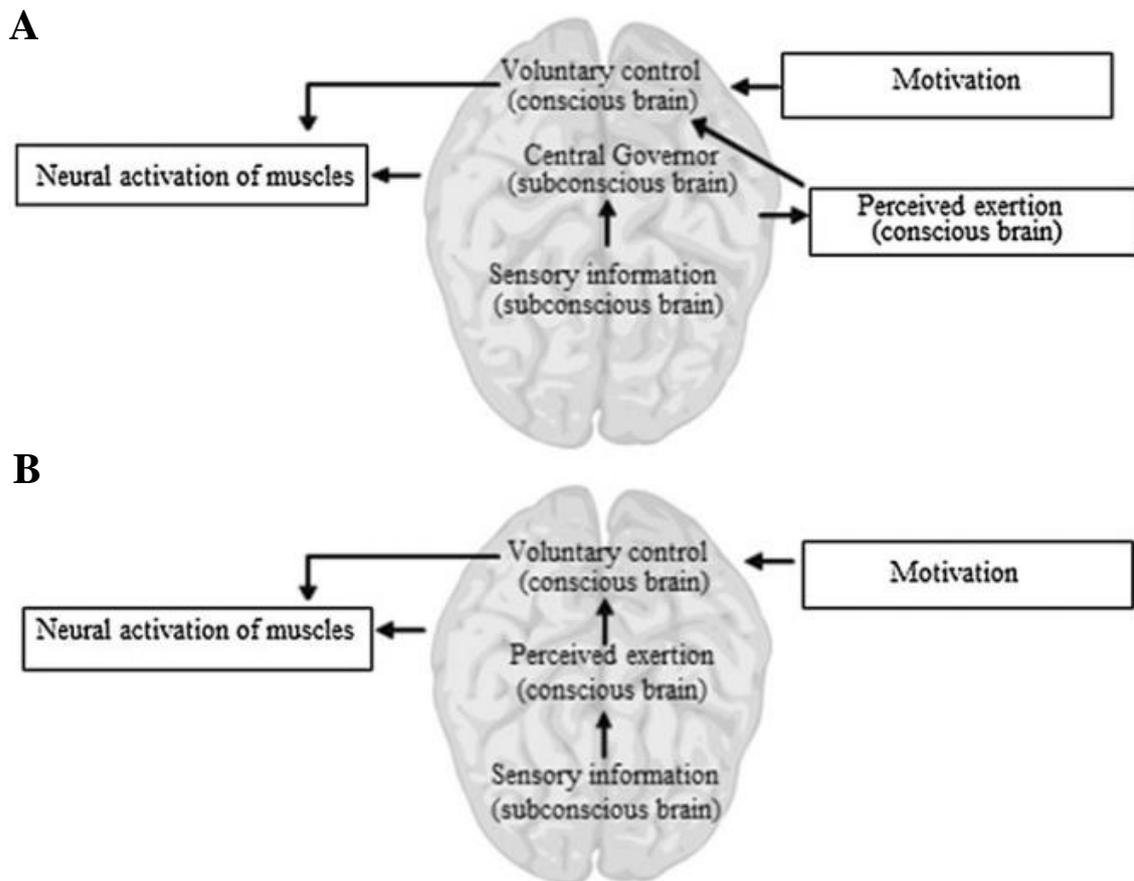


Figure 2.1. Visual comparison of models of the central regulation of physical activity: The central governor model of exercise regulation (**A**) and the psychobiological model of endurance performance (**B**). Adapted from Edwards and Polman (2013).

2.3.1. Models of the Central Regulation of Physical Activity

2.3.1.1. *The Central Governor Model of Exercise Regulation*

Presenting one of the first formal frameworks for understanding the limits of exercise tolerance, Ulmer (1996) described a closed-loop model of extracellular regulation. In this model, feedforward efferent motor commands do not simply determine the temporal and spatial biomechanical parameters of locomotion (e.g. stride length and stride rate), but additionally set the rate of muscular metabolism in line with anticipated endpoints in order to prevent the development of premature exhaustion. During sustained physical activity, somatosensory feedback, signalling the present metabolic rate and the conscious percept of exertion ([section 2.4.3.1.](#)), is entered alongside the forecasted efferent strategy into an algorithm performed by an undefined ‘regulator’ within the CNS, constructing an integrated control of physical performance based on current muscle metabolism, energy reserves and known task endpoints. This integrated feedforward-feedback loop is referred to as teleoanticipation (Ulmer, 1996).

The concept of teleoanticipation was later integrated within a controversial, yet pioneering model of central regulation based on the control of homeostasis. The central governor model of exercise regulation posits that exercise intensity is controlled by a central regulator in the CNS (i.e. brain) which functions to protect internal

homeostasis from excessive perturbations and thus harm (Lambert *et al.*, 2005; Noakes, 2012; Noakes *et al.*, 2001; Noakes *et al.*, 2004; Noakes *et al.*, 2005; St Clair Gibson & Noakes, 2004; St Clair Gibson *et al.*, 2006). According to the authors, the central governor acts at a sub-conscious level and initially anticipates the level of motor-unit recruitment (i.e. exercise intensity) that may be sustained over a given task based on internal and external environmental states (Noakes *et al.*, 2005). It is important to note that in the original conceptualisation of the central governor, conscious agency or volition is, for all intents and purposes, removed, with decisions and subsequent actions determined solely by the putative sub-conscious regulator (Venhorst *et al.*, 2017). Deviations from pre-planned homeostatic set points arising from dynamic, nonlinear interactions between biological systems and the environment (Lambert *et al.*, 2005) subsequently lead to constant adjustments in active motor unit recruitment based on feedforward-feedback loops that ensure no one biological system is overwhelmed (Noakes, 2011; Noakes *et al.*, 2004; St Clair Gibson *et al.*, 2006). To this end, rather than a conspicuous physiological event (i.e. an inability of locomotor muscles to produce the requisite force), the central governor model suggests that performance fatigability (i.e. reduction in speed or possibly the termination of exercise) is a relative process and emphasises the importance of fatigue as an emotional feeling (further discussed in [section 2.5.4](#)) - a conscious awareness of homeostatic feedback (Baron *et al.*, 2011; Noakes, 2012; St Clair Gibson *et al.*, 2003). Indeed, proponents of the central governor model view fatigue as a sensory perception²⁴ (Noakes *et al.*, 2005; St Clair Gibson & Noakes, 2004; see St Clair Gibson *et al.*, 2003). A conscious awareness of fatigue arises from the subconscious controller indicating the level of effort required to maintain homeostasis (St Clair Gibson & Noakes, 2004), which maps onto the implemented motor-unit recruitment strategy and serves as a deterrent to the volitional over-ride of this strategy, which could jeopardise biological integrity (Noakes *et al.*, 2005) ([Figure 2.1.A](#)). Tucker (2009) proposed an anticipatory feedback model in which the conscious perception of physical exertion was the variable of interest. The rate of change in the perception of exertion, predicted in anticipation based on prior experience and features of the task (e.g. duration, intensity, environmental conditions), is used to control the intensity of activity (and homeostasis) in order to ensure tasks are terminated before any harm may be incurred. In this model, subjective perceptions are generated based on both top-down (i.e. duration/distance of the task) and bottom-up factors (i.e. homeostatic afferent feedback), reflecting a form of perceptual hazard score (i.e. the potential danger of maintaining a given intensity given the estimated duration of the task; de Koning *et al.*, 2011).

A strength of the central governor model was that it provided an explanation of several features of physical performance that were not readily compatible with traditional ‘catastrophic’ perspectives (see Noakes, 2011). This includes, for example, the capacity to increase power/speed toward the end of a task (i.e. the end-spurt; e.g. Smits *et al.*, 2016; Wingfield *et al.*, 2018), typically the point of greatest metabolic disruption. This observation suggested that performance is tightly regulated to ensure tasks are completed within pre-defined homeostatic boundaries and that a reserve can be utilised only when the brain is confident that the ‘costs’ over a short duration will not pose biological systems any physiological harm. Moreover, the rise in the subjective perceptions of physical exertion has been shown to be set in anticipation of the exercise task across a range of environmental contexts, dependent upon antecedent information, and shown to predict time on task reflective of a form of central regulation (e.g. Crewe *et al.*, 2008; Eston *et al.*, 2007; Faulkner *et al.*, 2008). Despite this, the central governor

²⁴ Though it must be stated, a definition of this subjective experience is not clearly outlined by the authors.

model has provoked much debate, with some heralding it as a scientific revolution in the study of physical performance (Pires, 2012), while others suggesting the original premise and subsequent revisions to the central governor model have left it more akin to ‘pseudoscience’ through not adhering to the fundamental cornerstone of the scientific method - falsification (Robergs, 2017). Several concerns regarding the legitimacy of the central governor model as a complete account of performance fatigability have been levelled against it (Hudson & Hasan, 2022; Inzlicht & Marcora, 2016; Shephard, 2009; Weir *et al.*, 2006). For example, some detractors highlight the fact that significant homeostatic perturbations (e.g. myocardial ischaemia; Bogaty *et al.*, 2003) and the fact that rare, but possibly dramatic consequences²⁵ can arise from demanding voluntary exercise argues against a governor, or at the very least, an effective one (Shephard, 2009). However, the complexity of the proposed, non-linear interactions between multiple physiological systems means that the evidence from constituent systems is not necessarily sufficient to fundamentally disprove the model (Micklewright & Parry, 2010). The concept of a sub-conscious central governor has also been likened to a paradoxical, all-knowing homunculus, necessitating a conscious awareness within the subconscious brain (Edwards & Polman, 2013; Inzlicht & Marcora, 2016). Edwards and Polman (2013) posit that rather than a sub-conscious black-box (i.e. central governor), physical performance may be regulated throughout the conscious brain, operating across different levels of conscious awareness. Micklewright, Kegerreis, *et al.* (2017) suggest that the conscious-subconscious dichotomy involved in the description of performance regulation and fatigability is, in itself, a problem, arguing that this dichotomy should be replaced by a dual-process framework based on intuitive and deliberate decision-making processes, which could provide greater insight into the multidimensional processes underlying pacing behaviour during physical activity. Further criticisms of the central governor model focus on its philosophical underpinnings (Hudson & Hasan, 2022).

Since its original conception, the central governor model has witnessed several revisions, and multiple related models have been formed on some of the core principles of the model. For example, Rauch *et al.* (2013) proposed that the ‘governor’ may not in fact be represented by the function of a single, discrete brain region, but the overall neurochemical balance between cortico-basoganglionic-thalamo-cortical circuits which motivate physical behaviour based on economic (i.e. integration of costs and rewards) principles. Indeed, St Clair Gibson *et al.* (2018) updated the central governor model by incorporating facilitatory psychological drives that may explain how exercise behaviour is initiated and maintained in the face of homeostatic challenges. The resulting ‘integrative governor model’, proposes that performance is regulated through competing influences of mainly facilitative psychological, goal/success-orientated drives and mainly inhibitory physiological drives arising from homeostatic feedback. The sub-conscious governor is replaced by an undetermined ‘decision-making algorithm’ that takes into the account the weighting afforded to each respective drive at a given moment in time (St Clair Gibson *et al.*, 2018). In this regard, the continued reference to a central governor may be slightly misleading, or at least confusing, if referenced to the original conceptualisation. The new integrated governor would appear to align closer to other frameworks which propose performance fatigability to be the product of competing facilitatory and inhibitory neural networks (Tanaka & Watanabe, 2012) or an integrative network which aids and forms decisions regarding activity in light of internal and external environmental contexts (Robertson & Marino, 2016). Indeed,

²⁵ Though the author does recognise that predisposing factors may account for these unfortunate events.

the issue with an increasingly prominent role of motivational functions with reference to the original description of the central governor is that it undermines its principal function; that is, if the threat to homeostasis can be ignored or overcome with sufficient incentives, then the role of the governor (i.e. prevention of catastrophic failure of physiological systems) would be invalidated (Inzlicht & Marcora, 2016).

2.3.1.2. *The Psychobiological Model of Endurance Performance*

Alternatively, Marcora and colleagues argue against the need for a “*unnecessarily complex*” central governor, advocating performance regulation to be a conscious and volitional decision making process (Marcora, 2008; Marcora, 2019; Marcora & Staiano, 2010; Pageaux, 2014) ([Figure 2.1.B.](#)). Founded on the theory of motivational intensity (Brehm & Self, 1989), the psychobiological model of endurance performance initially attributed performance to five cognitive/motivational factors: 1) the perception of effort, 2) potential motivation (i.e. the maximal effort one is willing to exert to satisfy a motive), 3) knowledge of distance/time to cover, 4) knowledge of distance/time remaining and 5) previous experience or memory of the perception of effort during exercise of varying duration and intensity (Pageaux, 2014). The latter three factors appear to influence performance through effects on potential motivation which, alongside the perception of effort, represent the primary variables of the model (Marcora, 2019). According to the psychobiological model, an individual will disengage with a task when perceived effort (i.e. task difficulty) exceeds the maximum level they are willing to invest to satisfy some outcome (i.e. their potential motivation), or when task demands are perceived to be impossible (Marcora, 2019). Consequently, any effect altering either effort perception and/or potential motivation are believed to influence the conscious decision to invest or withdraw effort, thus regulating performance and determining the limits of exercise tolerance (Marcora, 2008). The psychobiological model also differs from the propositions outlined within the central governor model in that it argues that the perception of effort is independent of homeostatic afferent feedback, and is instead determined by the processing of corollary discharge of efferent motor commands (Marcora, 2009). This is further discussed in [sections 2.4.3.1.](#) and [2.4.3.2.](#)

As stated, the psychobiological model makes two very clear, testable hypotheses: 1) any physiological and/or psychological manipulation that increases perceived effort (for a constant potential motivation) will impair exercise tolerance (with the opposite true for reductions in perceived effort) and 2) any manipulation that increases potential motivation (assuming a constant perception of effort) will improve exercise tolerance (again, and vice versa) (Marcora, 2019). Support for these propositions have been taken from various sources including, for example, evidence that bouts of demanding prior cognitive activity has been shown to increase the perception of effort reported during subsequent physical activity, limiting performance during sustained (Brownsberger *et al.*, 2013; MacMahon *et al.*, 2014; Pageaux *et al.*, 2014) and intermittent (Smith *et al.*, 2014) whole-body exercise (though see [section 2.7.1.](#)). Moreover, stimulating effects of financial incentives (e.g. Cabanac, 1986) and the presence of competitors (e.g. Stone *et al.*, 2012; Ansdell *et al.*, 2017) are believed to improve physical performance through altering potential motivation. However, to date, the psychobiological model has yet to undergo a full evaluation and several limitations and concerns should be acknowledged when interpreting findings in reference

to the proposed framework²⁶. One particular issue is that to fully assess the model, the measurement of two constructs (i.e. perceived effort and potential motivation) would appear necessary. However, this is not the case in much of the cited evidence. This may therefore introduce implicit assumptions within the interpretations of key findings. Specifically, compared to the perception of effort, individuals' potential motivation is rarely captured within the supporting evidence. If it is recorded, it is often only assessed once, typically immediately before participants engage with a physical task, and is subsequently assumed to remain constant (e.g. Marcora *et al.*, 2009). Limited information is currently available regarding the temporal dynamics of potential motivation across physical tasks, yet it is unlikely that potential motivation remains constant across a bout of demanding physical activity. The break-away cyclist giving their all during the final steep climb must presumably experience a challenge to their potential motivation if overtaken by a competitor during the ascent. The psychobiological model suggests that the perception of effort is a relative experience, defined by the upper limit of what one is willing to invest (i.e. potential motivation) (Stewart *et al.*, 2009). That is, ratings of perceived effort are always referenced to this maximal investment. Accordingly, single item ratings of perceived effort, recorded in the absence of any assessment of potential motivation, cannot be interpreted as an exclusive change in perceived effort (thus generating ambiguity), since ratings intrinsically reflect the combination of two constructs. The continued absence of some assessment of (potential) motivation may possibly reflect the difficulty in interpreting its psychological underpinnings, particularly in response to manipulations which aren't specifically designed to effect it, and/or the inherent reporting bias that may be evident in such self-reported measures (particularly under laboratory conditions). Future work is required to address these issues in order to facilitate understanding of the interactions between the perception of effort and potential motivation during physical activity and the applicability of the psychobiological model as an account of exercise regulation.

2.3.2. Perceptions Involved in the Regulation of Physical Activity

Though issues surround the central governor and psychobiological model as complete accounts of exercise regulation, they represent important steps in our understanding of the influences determining human performance and continue to shape and influence views on the topic (McMorris, Barwood, & Corbett, 2018; Balagué *et al.*, 2020). Arguably one of their most important contributions to our understanding of the regulation of physical activity has been the increased attention afforded to psychological factors including motivation and perceptions, resulting in an increased interest in perception-action coupling since their conception. Both models place the subjective experience of the individual at the core of the 'fatigue process' and thus force one to consider to what this subjective experience relates.

Both the psychobiological and central governor model have almost exclusively relied on a single-item rating of RPE (Borg, 1970; Borg, 1998). As stated, the rate increase in RPE has been shown to predict the duration of physical activity (e.g. Crewe *et al.*, 2008), suggesting it provides a suitable means of estimating the perceived proximity to a conceptual sensory tolerance limit (Hureau *et al.*, 2016) – a hypothetical 'threshold', beyond which

²⁶ For example, the psychobiological model proposes that the decision to terminate a task is volitional. However, volitional task disengagement is refuted by some (Balagué *et al.*, 2020). For further discussion, please see [section 8.4](#).

physical activity become sufficiently unattractive causing a change in behaviour (Gandevia, 2001). However, the use of a single rating scale to depict the regulation of physical performance is clearly an oversimplification of what is a complicated, psychophysical process (Hardy & Rejeski, 1989; Hutchinson & Tenenbaum, 2006; Venhorst *et al.*, 2017), which necessitates greater eclecticism in the constructs studied in order to understand this control process fully (Venhorst *et al.*, 2018c). This has subsequently led to the development of multidimensional frameworks for the conceptualisation of the perceptual regulation of physical performance, which attempt to capture the perceptual, affective and cognitive interactions that define the control of behaviour. Drawing on gate-control theory of pain (Melzack & Wall, 1965), in which the transmission of nociceptive signals in the dorsal horn of the spinal cord and the subsequent perception of pain is modified by psychological (i.e. efferent or ‘top-down’) factors, Tenenbaum *et al.* (1999) developed a questionnaire to assess runners’ perceptions of discomfort. Here, the authors took the reported experiences of runners and integrated them with the dimensions outlined in the gate-control theory of pain, with physiological perceptions (i.e. proprioceptive, leg, respiratory stomach and head symptoms plus feelings of dryness and heat) associated with a sensory-discrimination dimension of discomfort (i.e. information of the quality, location and intensity of the discomfort). Mental toughness was associated with a motivation-affective dimension (i.e. the engendered affective and arousal facilitating approach or avoidance behaviour), while the cognitive-evaluative dimension (i.e. the volitional control over the other two dimensions) reflects runners’ experience of disorientation and thoughts concerning task completion (Tenenbaum *et al.*, 1999). Hutchinson and Tenenbaum (2006) applied this framework for the description of ‘perceived effort’ (see [section 2.4.2.](#)), with the sensory-discrimination dimension defined by feelings of muscle aches, pain and fatigue, the motivational-affective dimension associated with feelings of concentration, determination and mental toughness, and the cognitive-evaluation dimension ultimately representing the experienced perception of effort and/or exertion defining task aversion. The authors demonstrated that individuals could distinctly perceive the separate dimensions of ‘effort’ during both isolated, small muscle mass contractions ([Figure 2.2](#)) and whole-body aerobic exercise (Hutchinson & Tenenbaum, 2006).

Venhorst *et al.* (2017) indicated that the original subordinate structure of Tenenbaum *et al.*'s (1999) framework may have led to the potential misallocation of constructs within certain dimensions. For example, mental toughness was initially assigned part of the motivational-affective dimension, but arguably, may be better described as a cognitive strategy reflecting the exertion of volitional control over the desire to disengage from the task (Venhorst *et al.*, 2017). Subsequently, Venhorst *et al.* (2017) proposed a new three-dimensional framework for the perceptual and cognitive regulation (i.e. perceived fatigability) of physical performance based on current psychological theories and clearly differentiated constructs. The sensory-discrimination dimension was comprised of the separately perceived cognitive (i.e. the effort invested into and/or required to continue with the task) and physical strain (i.e. exercise related sensations caused by the task but separate from affective constructs such as pain or discomfort) experienced during a task. The affective-motivation dimension pertained to an individuals’ core affect, which holds both a primary and mediatory role in the regulation of exercise performance - the latter arising through effects on cognitive control strategies. Finally, the cognitive-evaluation dimension represented the experience of an action crisis between continued goal pursuit and goal disengagement. The authors studied these interactions using a structural equation modelling approach to examine the proposed causal relationships during physical activity, indicating support for their assertion that performance fatigability is predicted by increased

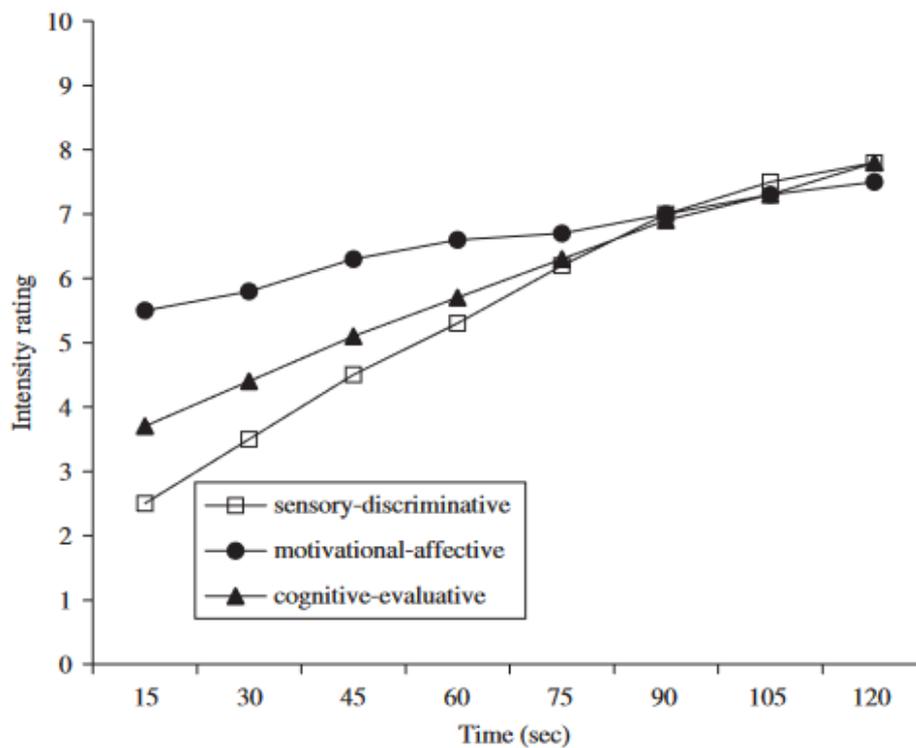


Figure 2.2. Interactions between sensory-discriminative, motivational-affective and cognitive-evaluative dimensions of ‘perceived effort’ during a sustained (25% MVC) handgrip contraction. The observed dimension x time interaction was taken as support for participants’ ability to distinctly perceive the separate dimensions of ‘perceived effort’ Figure taken from Hutchinson and Tenenbaum (2006).

perceptions of physical strain, fostering a reduction in affective valence, which subsequently evokes an experience of an action crisis (Venhorst *et al.*, 2018a; Venhorst *et al.*, 2018b).

The findings of Venhorst and colleagues highlight the diverse and complex interactions between psychological factors involved in the regulation of physical behaviour. However, a conspicuous omission from Venhorst *et al.*'s (2017) framework is any specific reference to the perception of fatigue, *per se* (see [section 2.2.4.](#)). Hutchinson and Tenenbaum (2006) incorporated feelings of fatigue within the physical sensations responsible for the perception of effort arising from physical activity. In line with this proposition, processing of interoceptive²⁷ inputs are believed to be central to the subjective experience of fatigue (Pollak *et al.*, 2014). Indeed, perceptions of fatigue evoked through experimental homeostatic perturbations (e.g. acute inflammation) are associated with increased activation of core interoceptive centres of the brain (Harrison *et al.*, 2009; Harrison *et al.*, 2015). Identified good interoceptive perceivers on a heartbeat detection task were observed to freely exercise at more conservative intensities, and thus incur less physiological perturbations, than those classified as poor perceivers (Herbert, Ulbrich, *et al.*, 2007). Yet despite the difference in physiological strain experienced between the two groups, the perception of fatigue was similar, indicating that the development of fatigue and behavioural

²⁷ Interoception refers collectively to the processing of internal bodily stimuli by the nervous system (Khalsa *et al.*, 2018; see also Critchley & Harrison, 2013; Craig, 2002). The interoceptive system represents the physiological status of all tissues of the body and is functional distinct from proprioceptive and exteroceptive systems (Craig, 2002).

regulation is dependent upon the sensitivity of the individual to interoceptive inputs (Herbert, Ulbrich, *et al.*, 2007). This indicates that homeostatic/allostatic control is a defining feature of fatigue perception. However, Hutchinson and Tenenbaum (2006) also noted that during sustained contractions, participants' reported feelings of fatigue showed a slightly different response across time compared to the other classified physical perceptions (e.g. muscle aches and pain). This may suggest that the perception of fatigue may be, in part, influenced by, or involve, additional psychological factors. This may also raise questions regarding what part of the perceptual-affective-cognitive regulation of physical performance does the perception of fatigue concern²⁸. As previously stated, the perception of fatigue has been conceptualised as both an emotion (Noakes, 2012; Hockey, 2013) and motivational deficit (Kuppuswamy, 2017; Müller & Apps, 2019). Furthermore, dispositional and situational cognitive factors including, for example self-efficacy, have been shown to influence perceptual-affective-cognitive symptoms of physical exertion, particularly at low or moderate intensities (e.g. Hutchinson *et al.*, 2008). Self-efficacy defines an individual's task-specific judgment of their capability to execute an action and attain a desired outcome (Bandura, 1997). Importantly, the perception of fatigue and self-efficacy have recently been described as “*extensionally equivalent*” - both representing an individuals' perceived capacity to meet task demands or exert effective control (Steele, 2021). Indeed, self-efficacy and perceptions of physical exhaustion have been shown to be inversely related during exercise (Treasure & Newbery, 1998; Focht *et al.*, 2007). In the study of pathological fatigue, a similar association has been proposed, in which reduced efficacy in one's perceived ability to effectively control internal states of the body, detected through higher-order (meta)cognitive processing, is the basis of fatigue development (Stephan *et al.*, 2016). In several clinical populations, nascent evidence indicates that altered metacognitive beliefs may maintain or exacerbate the subjective experience of fatigue (Siciliano *et al.*, 2021; Maher-Edwards *et al.*, 2011). Metacognition is positioned as an important (but understudied) facet of self-regulation during endurance performance (Brick *et al.*, 2016) and, alongside interoceptive processing, cortical regions supporting meta-cognition have been implicated in the development of exertional fatigue (Müller & Apps, 2019). Mechanistic accounts of metacognition highlight the role of the lateral prefrontal cortex, including dorsolateral prefrontal cortex (dlPFC), and its intricate connections to interoceptive control centres, in generating a general felt (meta-)awareness of performance (Fleming & Dolan, 2012). In relation to physical activity, the dlPFC has been postulated to feed forward predictions of the interoceptive consequences of activity in order to generate a current awareness state based on a comparison performed in anterior insula cortex (AIC) (McMorris, Barwood & Corbett, 2018) ([Figure 2.3.](#)). It has been associated with the development of a subjective state of perceived fatigue (Tanaka *et al.*, 2013; van der Schaaf *et al.*, 2018) and the regulation of motor output under conditions of fatigue (Matsuo *et al.*, 2022).

The resulting suggestion is thus: that the ‘perception of fatigue’ is not simply a conscious awareness of the homeostatic state of the body, to which it is often referred. Instead, it may involve other cognitive processes (see St Clair Gibson *et al.*, 2003), which may see it exert influence over perceptual-affective components of physical performance regulation. However, the exact role and/or influence of a perceived state of fatigue within the

²⁸ It must be stated, that Hutchinson and Tenenbaum (2006) indicated that the dynamics of the perception of fatigue displayed no obvious similarities to constructs within the other dimensions the authors defined.

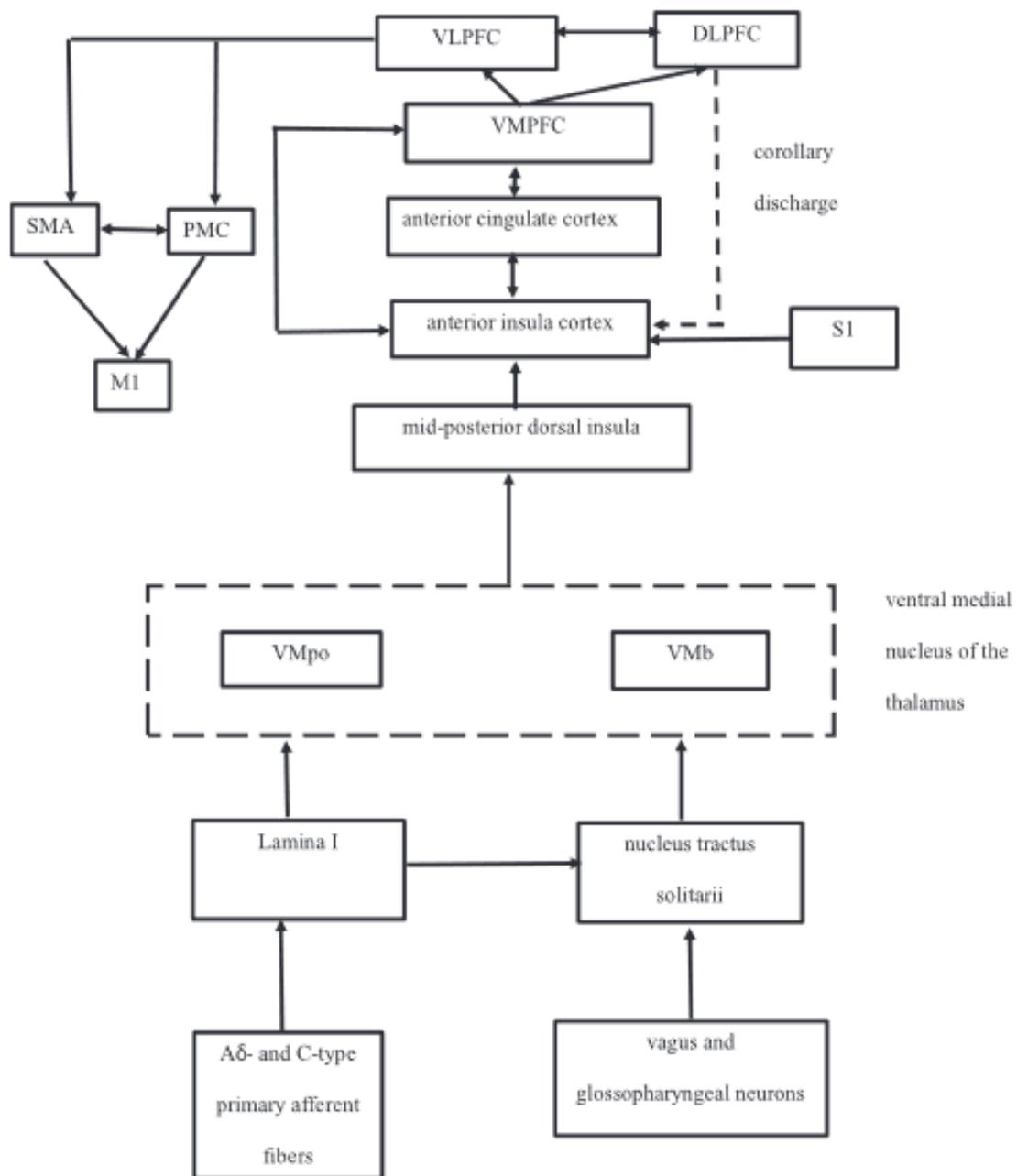


Figure 2.3. Schematic illustrating connections between interoceptive pathway and frontal cortex in the regulation of physical activity. The dIPFC is proposed to issue a prediction of the interoceptive consequences of activity, based on prior experience, beliefs about current fitness levels, perceived importance of the task, long-term goals, plus physical and social development factors. The predictions are compared to sensory feedback within the anterior insula cortex (AIC) to create an awareness of the condition of the body, which is forwarded to the anterior cingulate cortex (ACC) and the PFC (including the dIPFC) to update predictions and motivate decisions regarding what action to take. Figure taken from McMorris, Barwood & Corbett (2018). DLPFC: dorsolateral prefrontal cortex; VLPFC: ventrolateral prefrontal cortex; SMA: supplementary motor area; PMC: pre-motor cortex; M1: primary motor cortex; VMPFC: ventromedial prefrontal cortex; S1: somatosensory cortex; VMpo: posterior ventral medial nucleus of the thalamus; VMb: basal ventral medial nucleus of the thalamus.

constellation of the subjective perceptual and affective experiences defining the regulation of physical performance remains, surprisingly, unclear and understudied. In the following sections, the basis of both the perception of effort and core affect - the two most studied psychological constructs within the regulation of physical performance - will be described. Importantly, possible differences and interactions between perceived effort/core affect and the perception of fatigue (i.e. a perceived reduction in capacity) will be discussed, establishing the basis of the experiments conducted within the presented thesis.

2.4. Effort: Conceptualising the Psychological Construct

The concept of effort is a familiar introspective experience. From running a marathon, to performing a difficult sudoku puzzle, or even abstaining from high-calorie food when dieting. Simply the act of deciding between available options, the need to exert effort pervades many aspects of our daily lives. There is an appreciation of the distinct phenomenal experience of effort; that it is typically viewed as costly, difficult and aversive (Kurzban, 2016) resulting in - all things being equal - the avoidance of effortful actions where possible (Hull, 1943; Solomon, 1948; Kool *et al.*, 2010; though see Inzlicht *et al.*, 2018). Due to its omnipresence, we are keenly aware of non-verbal signatures of the exertion of effort (e.g. de Morree & Marcora, 2012; Timme & Brand, 2020; van Boxtel & Jessurun, 1993) that enable us to communicate to, and importantly understand, its presence in others without explicit verbalization (Rejeski & Lowe, 1980). This ability, and importantly our ability to accurately interpret these signatures relative to our own level of effort (Ibbotson *et al.*, 2019), may hold implications for understanding how we both perceive and function within social, cooperative interactions (Székely & Michael, 2018).

Yet, despite its familiarity, the broad spectrum to be considered when describing effort has seen the construct prove difficult to clearly define (Massin, 2017; Steele, 2021). While several intuitive truths about effort may be evident - for example, all effort is goal-directed and that the intensity of an effort is not deterministic of an action's likelihood of success or failure (Massin, 2017) - several outstanding questions remain when attempting to conceptualise effort. Though an extensive discussion of current understanding and philosophical basis of effort is beyond the scope of the present thesis (for the interested reader, please see insightful discussions on the topic presented by Massin, 2017 and Steele, 2021), several themes will briefly be highlighted to provide an introduction to concepts and help contextualise further discussion of effort in this chapter, specifically to help locate effort in relation to the regulation of physical activity and define its relation to the perception of fatigue.

2.4.1.1. The Function of Effort

Functional definitions of effort offer that it represents the cardinal factor determining (relative) performance (Inzlicht *et al.*, 2018; Shenhav *et al.*, 2017). One recent definition proposed that effort reflects “*the set of intervening processes that determine what level of performance will in fact be realized*” (Shenhav *et al.*, 2017). Indeed, for physical endurance performance, the attainment or one's maximal tolerance of perceived effort is proposed to be *the exercise stopper* (Staiano *et al.*, 2018). However, the effort-performance relationship is complicated (Christie & Schrater, 2015; Székely & Michael, 2020). As stated, effort is independent of the success

of the action, which may sometimes be taken as a measure of performance. For example, one may exert all their effort to solve a difficult mathematical equation and can still come to an incorrect answer. As such, effort has been more cautiously offered as a factor that contributes to performance, modifying default responses in order to ‘boost’ likely performance (Székely & Michael, 2020). Alternative definitions propose that effort reflects the mobilisation of ‘resources’²⁹ to carry out instrumental behaviour (Gendolla & Wright, 2009; Silvestrini & Gendolla, 2019). The function of effort is raised here as it is important to emphasise that, though effort and performance are related, they do represent two distinct properties of action – the former reflecting a behavioural input variable and the latter a behavioural output variable (Silvestrini & Gendolla, 2019).

2.4.1.2. The Domain of Effort

Effort, like fatigue ([section 2.2.2.](#)), is also often separated across different ‘subspecies’, typically based on its domain of origin (e.g. physical, cognitive, etc.; Massin, 2017). It is common to consider these subspecies as unique and separate entities. For example, effort expended during physical tasks is defined as physical (or motor) effort and is typically considered to involve very different mechanisms to the effort exerted during cognitive tasks. As such, the type of effort exerted is largely defined *ad hoc* based on the actions performed. In both domains the fundamental cost of effort is principally entwined with our inability to exert effort *ad infinitum*, reflective of some inherent limitations within both motor and cognitive systems. Objectively (see [section 2.4.1.3.](#)), physical effort is typically associated with the (relative) level of muscle recruitment in the momentary production of force, or that to be sustained across time (e.g. Bonnelle *et al.*, 2016; Iodice *et al.*, 2017). The cost associated with physical effort is attributed to the metabolic consequences of performing a given action. In contrast, cognitive effort is reflective of the active engagement of cognition. Early investigations identified cognitive effort with attention and its allocation (James, 1890; Kahneman, 1973). However, consensus has increasingly associated cognitive effort more broadly with the allocation of the limited resources available for controlled information processing, or executive function (Shenhav *et al.*, 2017; Inzlicht *et al.*, 2014; Székely & Michael, 2020). The cost of cognitive effort has been associated with both intrinsic costs (e.g. depletion of energetic resources: Baumeister *et al.*, 2007; neurotoxin accumulation: Holroyd, 2016; structural constraints: Shenhav *et al.*, 2017, c.f. Oberauer *et al.*, 2016; representational constraints: Musslick *et al.*, 2016) and opportunity costs (i.e. the cost of foregoing alternative options; Kurzban *et al.*, 2013) accompanying the utilisation of control resources. A further model combines both biological resources and opportunity costs, with the aversion to cognitive control not indicative of some inherent cost within the exertion of control, but rather a strategic allocation of finite resources (Christie & Schrater, 2015). The basis of cognitive effort remains poorly understood (Shenhav *et al.*, 2017).

Though it may seem obvious to state that the underlying basis of cognition is separable from the execution of a motor action, the value of separating physical from cognitive effort has been considered since many tasks involve

²⁹ The resource concept is complicated, and the cited authors use it in its broadest (and vaguest) sense, i.e. indicating the allocation of performance processes, be that biochemical, psychological, physical in nature, in pursuit of a goal. A specific ‘resource’ or set of ‘resources’ that constitute the basis of effort has not been clearly defined and the view that effort reflects the utilisation or depletion of some finite biological resource has been criticized (e.g. Kurzban *et al.*, 2013; Inzlicht *et al.*, 2014).

elements of both, to varying degrees. For example, several lines of evidence indicate that exertion of cognitive control is an important aspect of our ability to maintain physical tasks over time (see Holgado & Sanabria, 2020). Some therefore view effort as a single, unitary construct (André *et al.*, 2019; Marcora, 2019). For example, ‘physical’ effort has recently been conceptualised as “*the inhibitory [cognitive] control required to resist the ‘urge to quit’ when sustaining a given velocity/power becomes unpleasant due to fatigue, pain, thermal discomfort, or boredom*” (Marcora, 2019). Currently, empirical investigations examining the similarities and differences between physical and cognitive effort are sparse. In the absence of explicit examinations of underlying mechanisms, differentiation of cognitive and physical effort has, to date, largely been inferred through psychobehavioural responses across different tasks. In support of possible independent mechanisms underlying physical and cognitive effort, it has been observed that individuals integrate rewards and effort costs differently across domains (Chong *et al.*, 2017; see also Chong *et al.*, 2018), and that the motivation to exert effort in different domains may correlate with different symptoms (e.g. anhedonia) and/or markers of function in clinical conditions such as depression (Tran *et al.*, 2020). On the other hand, there is evidence that effort in both physical and cognitive domains may be driven by a common motivational mechanism (Schmidt *et al.*, 2012). Individual sensitivity to subjective costs of effort has also been shown to be related across domains, indicating that the cost of effort may in fact influence decisions in a possible trait-like fashion, independent of domain, suggestive of some shared process(es) (Białaszek *et al.*, 2017; Ostaszewski *et al.*, 2013). In further support of this, there is also some evidence that repeated exposure to effortful demands in one domain can cause the evaluation of effort costs in the other to change and converge towards the other (Chong *et al.*, 2018), which may also indicate transferrable effects as a function of a shared or common mechanism. What is not yet clear is whether such changes are mediated through some ancillary process common to both domains (e.g. subjective temporal factors; Potts *et al.*, 2018) or may be representative of a unitary basis of effort as an entire construct. In summary, it remains unclear if the separation of cognitive and physical effort provides a worthwhile distinction, reflective of disparate mechanisms underlying exertion between domains. This may be further exacerbated if it is unclear to what ‘effort’ pertains (see next section). The distinction is raised here to provide a brief introduction of an important topic that helped form the methodological approach of the presented thesis (this is discussed further in [section 2.7.1](#)).

2.4.1.3. Objective vs. Subjective Effort

Finally, (again, similar to fatigue) it is also important to consider to what is being referred to when describing the exertion of effort. Specifically, to distinguish between objective and subjective effort; between what is actually done and the perception of what is (Steele, 2021; Silvestrini & Gendolla, 2019). For the objective exertion of effort, motivation intensity theory positions the level of effort given to a task is directly proportional to task difficulty, given there is a possibility of success and that the level of effort required does not exceed the amount of effort one is willing to exert towards a given objective (Brehm & Self, 1989). Interestingly, though motivational intensity theory operationalises effort objectively, effort is ultimately determined by a subjective appraisal of task demands. The dependency of the objective mobilization of effort on the subjective appraisal of task demands may make us consider what is of most importance when studying effort: is it the actual mobilisation of resources (i.e.

the output) or, in fact, the setting of parameters that dictate the level of effort achieved (i.e. the *subjective* appraisal of task difficulty)?

Cognitive effort has been described as “*a subjective, psychological phenomenon*” (Westbrook & Braver, 2015). However, the subjective perception of effort is believed to transcend domains, functioning as a non-specific, transferable experience which is furnished based on the context of the goal-directed action (Preston & Wegner, 2009). Yet, an issue with the subjective judgement of effort expenditure is that it may be influenced by factors other than the true exertion of effort (Silvestrini & Gendolla, 2019). Nevertheless, the perception of effort is functionally relevant as it is believed to serve as the conscious experience of task demands, used to adjust exertion, while also imbuing one with a sense of agency during intentional action (Preston & Wegner, 2009). Thus, how the demands of a task are perceived, including all moderating factors, may be particularly important in determining if one is to persist with a task, though may not directly depict the actual intensity of an effort. The present thesis will subsequently focus on the perception of effort and how this subjective experience helps shape our decisions and subsequent behaviour, as it is the perception of effort that is believed to be fundamental to how activity is regulated during physically demanding tasks (Noakes, 2012; Marcora, 2009; see [section 2.3.1](#)).

2.4.2. The Perception of Effort during Physical Activity

Conventionally, the perception of effort is assessed through self-reported measures. Within the exercise sciences, the study of the perception of effort during physical tasks has been dominated by the seminal work of Gunnar Borg and colleagues, originating at the end of the 1950s (Borg, 1998). This work has led to the development of several scales used to capture individuals’ perception of physical strain, including the 15-point (6-20) interval RPE scale (Borg, 1970), the category ratio (CR) 10 scale (Borg, 1982) and the later production of the centiMAX scale (CR100) (Borg & Borg, 2002). The RPE scale was designed to increase linearly with exercise intensity, while the CR10 (and the more finely-grained CR100) was generated with a non-linear positively accelerating growth function (Borg, 1998). Borg defined the perceived exertion (effort) as “*the feeling of how heavy and strenuous a physical task is*”, reflecting a gestalt, or configuration, of sensations, including strains, aches, fatigue and tension within the peripheral muscles, cardiovascular and respiratory systems, as well as other sensation arising from the stimulation of the central nervous system (Borg, 1962; Borg, 1998). In addition to these physiological cues, Borg proposed that cognitive factors including motivation, memory and emotions were also important factors which influence how physical effort may be perceived (Borg, 1998). The ubiquity of the RPE scale in the study of perceptions arising from physical activity has forged significant interest in understanding precisely what participants are reporting when rating their perceived level of effort. Recent years has seen increasing scrutiny of the definition of perceived exertion (or effort), the instructions used for the implementation of the scale and the subsequent underlying neuropsychophysiological processes giving rise to its perception (Marcora, 2009; Abbiss *et al.*, 2015; Halperin & Emanuel, 2020).

2.4.2.1. Defining the Perception of Effort

The extensive use of RPE scales has seen the literature replete with definitions of perceived exertion (effort) (see Halperin & Emanuel, 2020). As noted by others (Halperin & Emanuel, 2020; Pageaux, 2016), alongside Borg's original definition, the definition proposed by Noble and Robertson (1996) has also proved popular amongst researchers. Noble and Robertson (1996) defined perceived exertion (effort) as "*the subjective intensity of effort, strain, discomfort and/or fatigue that is experienced during physical exercise*". This definition has been extensively cited and is currently the definition promoted by the American College of Sports Medicine (Utter *et al.*, 2007). In line with Borg's original definition, the authors' definition emphasises the perception of physical strain as a defining characteristic of the perception of effort, but also explicitly introduces both the perception of discomfort and fatigue within the construct. Several authors have however, noted that the inclusion of these terms may be problematic, since evidence indicates that individuals are capable of differentiating between these perceptual constructs (Steele, 2021; Halperin & Emanuel, 2020; Pageaux, 2016). Indeed, as previously described, the perception of fatigue is clearly separable from the perception of effort (e.g. Micklewright *et al.*, 2017; [section 2.2.3](#)). In relation to the distinction between discomfort and effort, a series of studies utilising resistance-based physical tasks have demonstrated that at the point of task failure, individuals' perception of effort is perceived to be maximal. However, the perceived discomfort experienced during the tasks is not only reported to be submaximal, but the intensity of discomfort is sensitive to the characteristics of the task performed (e.g. lower loads generating greater time under tension due to a greater number of repetitions performed were shown to generate increased perceptions of discomfort than higher loads; Fisher *et al.*, 2017; Fisher *et al.*, 2018; Stuart *et al.*, 2018). During aerobic-based physical activity (e.g. cycling), perceptions of discomfort have similarly been disassociated from the perception of effort, with self-reported discomfort increasing during the exercise bout when perceived effort is held constant (Christian *et al.*, 2014)³⁰. Discomfort is closely related to, or may in fact reflect³¹, pain (i.e. "*an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage*"; Raja *et al.*, 2020). Pain has also been shown to be partially dissociable from the experience of effort during physical tasks (e.g. Smith *et al.*, 2020). Together, these studies indicate that a definition of effort that includes the perceived discomfort/pain and the perception of fatigue may lead to potentially erroneous ratings of effort recorded during physical tasks (Halperin & Emanuel, 2020; Pageaux, 2016)³².

³⁰ Recent findings would appear to extend this finding to other modalities such as running (Hobbins *et al.*, 2019) and walking (Hobbins *et al.*, 2021), but interpretation of the results is hindered by the absence of an explicit definition used for the self-reported perception of overall effort (that is, it is unclear in these studies how the perception of effort was differentiated from that of discomfort).

³¹ It is noted that there is some evidence that individuals may be able to discriminate between discomfort (i.e. any sensory experience considered unpleasant) and pain (Hamilton *et al.*, 1996).

³² Though not incorporated within the definitions above, it is pertinent to also point out that the perception of effort may also be conflated with the perception of force or muscle tension. Importantly, the perception of effort and tension may be disassociated under experimental conditions, depending on the instructions provided to participants (McCloskey *et al.*, 1974; Gandevia & McCloskey, 1977). However, this subjective distinction may prove difficult under certain conditions, such as in presence of motor fatigability, where a heightened perception of effort may dominate the perception of force (Jones & Hunter, 1983b). Though our understanding of the underlying neurophysiology of our muscle senses continues to grow (Proske & Allen, 2019), future research is required to clearly separate that relating to the sense of force from the perception of effort, particular the temporal dynamics of each during protracted physical tasks.

2.4.2.2. *The Perception of Effort or the Perception of Exertion?*

Is the perception of exertion the same as the perception of effort? As may be evident already, the terms are often used interchangeably when referencing RPE. Indeed, Borg did not clearly distinguish between the two, with perceived effort offered as one of the many experiences encapsulated within perceived exertion (Borg, 1998). However, Abbiss *et al.* (2015), like others (e.g. Hutchinson & Tenenbaum, 2006) have proposed that the two should be considered distinct, relating to separate neurophysiological processes. Abbiss and colleagues (2015) propose that perceived exertion be defined as per Borg's original definition (i.e. "*the feeling of how heavy and strenuous a physical task is*"), representing the perceived level of physical and/or physiological strain experienced during a given physical task. Conversely, the perception of effort reflects "*the amount of mental or physical energy being given to a task*". This appeals more to psychic factors and is closer aligned to definitions relating to the mobilization of resources towards achieving a particular goal (i.e. striving) adopted within the study of cognitive control. The distinction between the perception of effort and perceived exertion also appears to parallel distinctions between effort across physical and cognitive domains ([section 2.4.1.2.](#)).

Empirical evidence for a distinction during acute physical activity was presented by Swart *et al.* (2012), who demonstrated participants were able to disassociate perceived exertion (defined similarly to Borg's original concept, relating to physical experiences of how heavy or strenuous the task felt, whilst excluding any psychological factors) from the perception of effort (that is, the psychological/psychic effort required to perform the task) during a cycling task. In this study, participants performed two, 100 km time-trials, each interspersed with brief maximal efforts (i.e. sprints): the first was performed at an individual's maximal, self-paced performance, while the second was performed at a constant submaximal intensity, with power output corresponding to 70% of the average power maintained across the first trial. Perceived exertion was recorded using the RPE scale and the authors created a novel task effort and awareness (TEA) scale for the measurement of the perception of effort. The TEA scale sought to capture both the intensity of perceived effort and how aware the individual was of this perception. During the continuous stages of the time-trial, participants perceived exertion (i.e. RPE) was shown to increase across time, with greater perceived exertion reported during the maximal versus submaximal trial ([Figure 2.4.A.](#)). Perceived exertion (i.e. RPE) also increased over the successive repeated sprints ([Figure 2.4.B.](#)). Like perceived exertion, the perception of effort (i.e. TEA) increased during the continuous portion of the time trial and was again greater in the maximal versus the submaximal trial (which was only demonstrated to reach 'consciousness' after completion of the first 10% of the trial) ([Figure 2.4.C.](#)). However, during the interspersed sprints perceived effort (i.e. TEA) was always maximal, unchanging across repetitions ([Figure 2.4.D.](#)). Moreover, though the relationship between perceived exertion and effort was strong during the maximal trial, the relationship was significantly attenuated during the submaximal trial. The results suggest that individuals possess the ability to distinguish between the physical perception of exertion from the psychic factors driving the perception of effort during physical tasks. The authors concluded, that the perception of effort is the principle regulatory variable used to control behaviour, emerging consciously when afferent signals from the periphery deviate from expected states and signal a potential threat to homeostasis (Swart *et al.*, 2012). The ability to distinguish between the perception of effort and the physical signals defining perceived exertion during brief

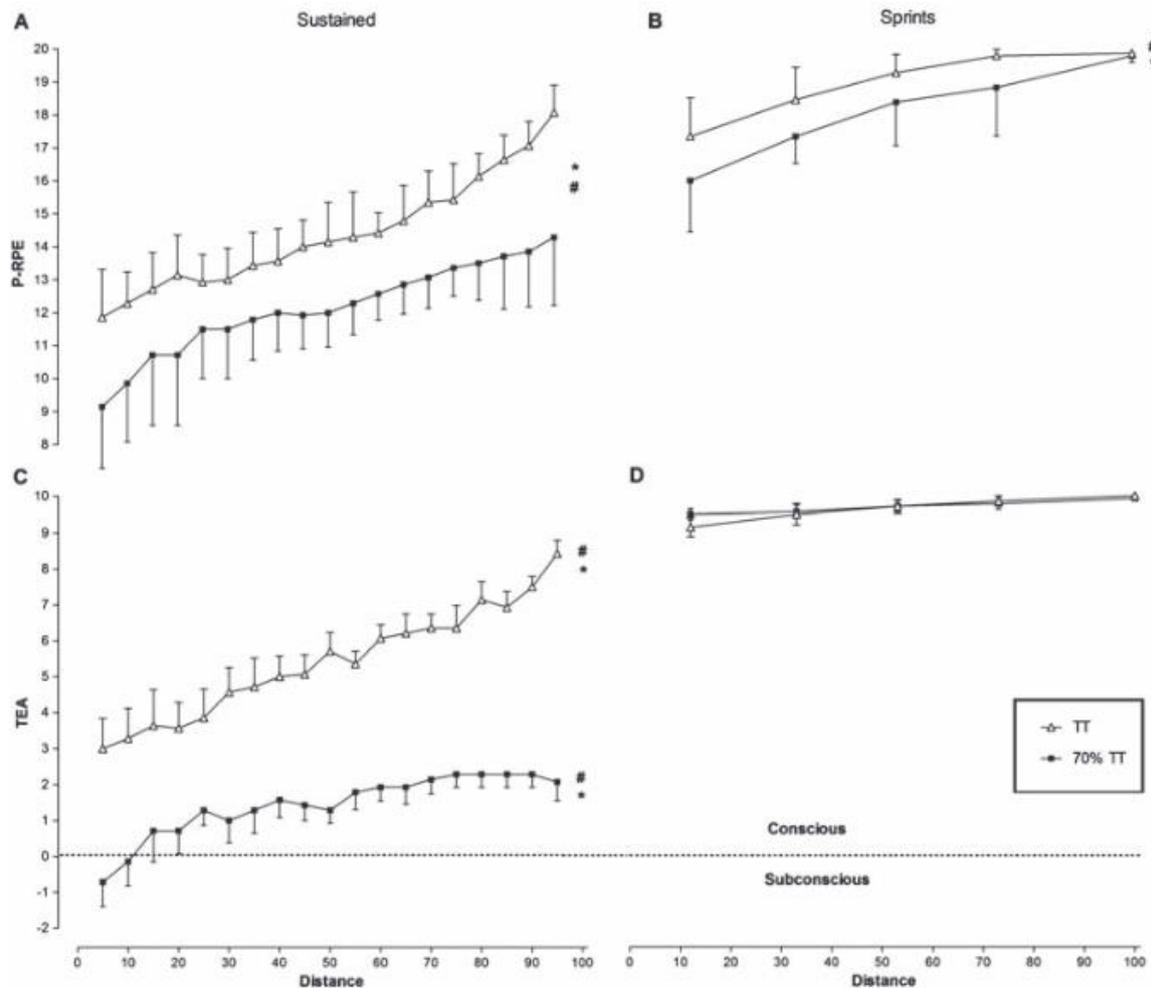


Figure 2.4. Perceived exertion (P-RPE; **A** and **B**) and effort (TEA; **C** and **D**) response to continuous (i.e. sustained; **A** and **C**) and sprint (**B** and **D**) portions of a maximal and submaximal (i.e. 70%) cycling time trial. Participants reported perceptions of physical exertion increased over time/sprints and was different between the maximal and submaximal time trials. The perception of effort increased during the continuous portion of the time trial, again differing between maximal and submaximal performance, with participants indicating that it only just reached consciousness in the latter. However, during the sprint portion of the task, perceived effort was always maximal and did not differ between conditions. Figure taken from Swart *et al.* (2012). *: Significant difference between trials ($p < 0.05$). #: Main effect of time ($p < 0.001$). RPE: ratings of perceived exertion; TEA: Task Effort and Awareness.

maximal efforts (i.e. sprints) has been replicated (Girard *et al.*, 2017), while changing the physiological stress imposed by a physical task, for example, by comparing concentric and eccentric cycling tasks, has also seen a disassociation between the somatic sensation of exertion and the perception of effort (Peñailillo *et al.*, 2018). More recently, exercise at the same relative physiological intensity at increasing altitude was shown to elicit the same perceived physical strain (i.e. exertion), but was associated with a reduction in perceived (mental) effort (Drouin *et al.*, 2021). The authors propose that reduced work capacity arising from hypoxia and thus likely a reduction in central motor drive to the working muscles, could explain the lessening in the perception of effort ([section 2.4.3.2.](#)).

However, there is also several issues related to this proposed distinction. First, in relation to Swart *et al.*'s. (2012) original study, the psychometric properties of the TEA scale have received criticism. This includes the use of the

descriptor ‘unaware’ and also measuring two different constructs (i.e. the perception of effort and awareness) concomitantly on the same rating scale (Jones *et al.*, 2015; Venhorst *et al.*, 2017). Further examination of individuals’ ability to differentiate perceptions of exertion (i.e. RPE) from effort (i.e. TEA) have failed to demonstrate clear separation between constructs during similar time-trial cycling tasks (Jones *et al.*, 2015). Moreover, beliefs in an ability to distinguish between perceived exertion, or physical strain, and the perception of mental effort during physical tasks has seen studies cited in which somatic perceptions reflecting the level of physical discomfort experienced during a task has been separated from the perception of effort (e.g. Christian *et al.*, 2014; Lloyd *et al.*, 2017). This may not accurately reflect the proposed distinction between exertion and effort as (stated previously) discomfort is an affect-laden construct. As such, an explicit separation of perceived physical and mental strain may not be clearly distinguished from the influence of *how* these physiological signals are perceived compared to the mental demands of maintaining activity (Hardy & Rejeski, 1989). Finally, semantic issues surrounding the words ‘exertion’ and ‘effort’ may also limit clear distinction of constructs (Halperin & Emanuel, 2020; Pageaux, 2016; Steele, 2021). Effort and exertion are synonyms, and in many languages the two cannot be easily distinguished since they both translate to the same word (Abbiss *et al.*, 2015; Steele, 2021). This may subsequently lead to confusion in both the application and interpretation of measures of perceived effort. As they are synonyms, Pageaux (2016) has supported the continued use of the terms interchangeably. In contrast, Steele (2021) proposes that effort and exertion should not be used interchangeably so as to remove any ambiguity, suggesting that since exertion is used to reflect *other* subjective aspects of a task other than striving to meet task demands (which is typically ascribed to the perception of effort when the constructs are distinguished), the adoption of another word to represent these aspects (e.g. discomfort³³). In line with this proposition, the present thesis is principally interested in the perception of effort, broadly referencing a feeling of self-mustered energy, labour and difficulty in the performance of goal-directed action (Preston & Wegner, 2009), and independent of somatic feelings of discomfort.

2.4.3. Neurophysiology of the Perception of Effort during Physical Tasks

2.4.3.1. *The Afferent Feedback Model*

The distinction between effort and exertion closely mirrors peripheralist versus centralist views concerning the underlying neurophysiological mechanisms supporting the conscious perception of effort. In the creation of the RPE scale, Borg focussed principally on the physiological condition of the body and the afferent signals relaying this information as the underlying basis of the perception of effort (Borg, 1998). That is, afferent-mediated representation of the physiological conditions of the body in sensory regions form feeling states that are the perceptual counterpart of behavioural motivation, of which the perception of effort is purported to be one (Craig, 2013; the neurophysiology of this afferent-feedback system is discussed in detail in [section 2.5.3.1.](#)). Indeed, the RPE scale was re-scaled from the original concept, starting at a score of 6 (rather than 0), so that a given score could be multiplied by ten to estimate the corresponding heart rate during whole body exercise (Borg, 1998). In line with this view, exercise scientists have demonstrated evidence of strong relationships between RPE and

³³ As stated previously, the use of terms associated with clear affective responses may be problematic. Steele (2021) does state that any ‘contextually appropriate’ term given the task performed may be substituted in.

physiological markers of physical intensity, including heart rate (e.g. Borg, 1973), ventilation and respiratory rate (e.g. Noble *et al.*, 1973) and blood lactate concentration (e.g. Scherr *et al.*, 2013), to name but a few, which have been used to indicate the concurrent validity of the RPE scale (Borg, 1998). However, under experimental manipulation, widespread reports have also indicated that the observed relationships between RPE and physiological sensory cues may be disassociated under certain conditions (e.g. heart rate: Bergstrom *et al.*, 2015; Cochrane, Housh, *et al.*, 2015; ventilation: Allen & Pandolf, 1977; Stamford & Noble, 1974; blood lactate concentration/acid-base balance: Löllgen *et al.*, 1975; Poulus *et al.*, 1974). As such, to date, research has failed to identify a single, cardinal physiological variable that may causally explain the perception of effort during physical tasks (Hampson *et al.*, 2001; Mihevic, 1981). A subsequent interpretation of the literature proposed that the perception of physical strain may not be generated from a single sensory stream, but may emerge from the integration of multiple signals concerning the state of the physiological systems, with the dominant signal for a particular task reflecting the weight afforded to that system given the characteristics of the task (e.g. task type, its intensity, the duration of the bout and the environment; Hampson *et al.*, 2001; Mihevic, 1981)³⁴.

Several authors contend however, that the perception of effort is entirely separate from sensations evoked by increased discharge of small-diameter homeostatic afferents, located in active muscles and viscera, in response to increased metabolic, ionic, thermal and mechanical stress imposed by physical tasks (Marcora, 2009; Pageaux & Gaveau, 2016; Smirmaul, 2012). The main experimental evidence against homeostatic afferent feedback as a primary signal in the generation of the perception of effort comes from the use of anaesthetics, blocking spinal transmission of small-diameter afferents towards the CNS. Several studies have observed that the perception of effort during physical activity is largely unaffected by the blockade of spinal transmission (Barbosa *et al.*, 2016; Fernandes *et al.*, 1990; Friedman *et al.*, 1993; Kjær *et al.*, 1999; Mitchell *et al.*, 1989; Smith *et al.*, 2003). Conversely, Markus Amann and others have reported a change in the perception of effort following spinal injections of a selective μ -opioid receptor agonist (i.e. fentanyl). In the absence of somatosensory feedback, RPE was reported to be lower during both whole-body (Amann *et al.*, 2010; Gagnon *et al.*, 2012) and isolated, small-muscle mass exercise (Broxterman *et al.*, 2017)³⁵. Several limitations prevent full or confident conclusions from being drawn from this collection of studies however, which include (but are not limited to) the very small sample sizes on which these experiments have typically been performed, the difficulty in assessing the proportion of the afferent signals blocked by different anaesthetic interventions and the concomitant effects on muscle force production. Another particularly important limitation is also the lack of a clear and precise presentation of the definitions and instructions used in the implementation of the scales to assess the perception of effort within many of these studies. For example, Amann *et al.* (2010) saw a -13% reduction in participants 'limb RPE' during cycling exercise performed at a high power output (325 ± 19 W; 80% W_{peak}) following the administration of intrathecal fentanyl. The authors referred to the change in 'limb RPE' as a reduction in "*the rating of limb discomfort*". As

³⁴ In line with this, Pandolf (1978; 1982) proposed a hierarchical model of subjective experiences during physical tasks, proposing that the uppermost, global perception of effort represented a superordinate level of reporting that may only be indistinctly related to the underlying physiological condition of the body.

³⁵ In another study, Broxterman *et al.* (2018) reported that an afferent block (i.e. fentanyl) reduced the perception of effort (assessed based on Borg's definition of perceived exertion) by ~60% during the final contraction of an intermittent 'all-out' contraction task. However, since this protocol consisted of repeated maximal voluntary contractions, which by definition, requires maximal effort, it would appear that participants were attentive to somatosensory signals other than those supporting the perception of effort during ratings.

highlighted in [section 2.4.2.1.](#), discomfort is heavily affective, which may be disassociated from the perception of effort ([section 2.5.](#)), thus reference to such constructs in the description of the perception of effort may hinder interpretation (Marcora, 2011).

Presently, empirical support for homeostatic afferent feedback as the underlying basis of the perception of effort during physical activity is relatively modest, and principally based on correlational analysis. Like Borg, Samuele Marcora defines the perception of effort during physical tasks as “*the conscious sensation of how hard, heavy, and strenuous a task is*”³⁶ (Marcora, 2010). However, he rejects the idea that effort is in any way related to signals arising from the muscles and viscera, instead contending that the perception of effort is derived centrally, based on the processing of signals (i.e. copies of motor command) related to the intentional performance of a task (Marcora, 2009).

2.4.3.2. *The Corollary Discharge Model*

The study of the proprioceptive senses (i.e. the perception of the position and movement of the body, as well as the sense of balance, arising from action³⁷) have long held the prevailing view that the perception of effort is, principally, central in origin (Proske & Gandevia, 2012). Sperry (1950) first established the concept of corollary discharge in reference to neural signals that emerge as a direct result of motor commands and serve to influence sensory perception³⁸. This may occur by modulating the processing of incoming sensory inputs or evoke perception in its own right, through the transmission of this motor-related signal to sensory areas of the brain (McCloskey, 1981). The latter (i.e. ‘sensations of innervation’; McCloskey, 1981) is believed to be the basis of the perception of effort during physical tasks (see de Morree & Marcora, 2015). Many putative circuits supporting the modification of sensory processing through motor corollary discharge have been identified within the animal kingdom (Poulet & Hedwig, 2007). However, direct assessment of these circuits is not possible in humans, so

³⁶ This, like Borg’s original definition has however received criticism (Halperin & Emanuel, 2020; Steele, 2021). The main contentions centres on two points: 1) the use of the term ‘heavy’ and 2) the absence of any reference to perceived maximal capacity. In relation to the first, it is argued that the term heavy may be confusing, particularly during resistance-based tasks involving lifting weights. The worry is that in such contexts participants may erroneously rate their perceived level of effort based on the physical properties of the apparatus (i.e. the weight), rather than the perceived level of effort required to perform that task. This is important, as there may be instances where this does not correspond (e.g. in response to motor fatigability). In relation to the second point, it is offered that perceived task demands relative to the perceived capacity to meet those demands determines how we perceive the level of effort exerted. Subsequent definitions offered for the perception of effort include: “*the process of investing a given amount of one’s perceived physical or mental resources out of the perceived maximum to perform a specific task*” (Halperin & Emanuel, 2020), and “*the perception of that which must be done in attempting to achieve a particular demand, or set of demands, and which is determined by the perception of current task demands relative to the perception of capacity to meet those demands, though cannot exceed that current perception of capacity*” (Steele, 2021).

³⁷ Which may be defined separately from kinaesthesia - used in reference to the sense of limb position of movement - which can arise when passive, thus excluding motor commands within these perceptions (Proske & Gandevia, 2012).

³⁸ At the same time von Holst and Mittelstaedt (1950) developed the concept of efference copy; representing an internal signal that is an exact copy of an efferent motor command sent to sensory regions. Due to their similarity the two terms have often been used interchangeably. However, important differences between the original concepts have been highlighted. Namely, while efference copy reflects a subtractive signal used in cancelling out reafference inputs caused by one’s own action, corollary discharge on the other hand refers to a more general signal that can inhibit, facilitate and modulate sensory processing (corollary discharge thus includes efference copy and the effects of all other motor-related signals on sensory processing; Fukutomi & Carlson, 2020; Poulet & Hedwig, 2007). Like others (e.g. Gandevia, 1996), the use of the term ‘corollary discharge’ is used throughout this thesis to avoid confusion based on the nuances of the original definitions.

evidence of corollary discharge on sensory processing are inferred from behavioural and neurophysiological responses to psychophysical tasks.

Several lines of evidence indicate that central, feedforward signals underpin the perception of effort. For example, classic weight-matching tasks have been used to demonstrate that in muscles which are weakened, for example, by inducing ‘muscle fatigue’ through repeated or prolonged actions or through partial paralysis, the increased motor command necessary to compensate for force deficits leads weights to feel heavier, or to be perceived as requiring more effort to hold (McCloskey *et al.*, 1974; Gandevia & McCloskey, 1977; Jones & Hunter, 1983a). Importantly, these studies indicate that this over-compensation is independent of sensory feedback (McCloskey *et al.*, 1974; Gandevia & McCloskey, 1977). In the same vein, (large-diameter) deafferented individuals are also capable of performing force-matching tasks between limbs like healthy controls (Lafargue *et al.*, 2003) and similarly experience an increased perception of heaviness that is, strikingly, proportional to the force deficit induced by experimental manipulation (Luu *et al.*, 2011). Further paradigms designed to modulate descending motor commands, for example, by utilising the effect of prior contraction history on force production (i.e. depression or elevation in isometric force following active shortening or lengthening contractions, respectively) have also shown an association between neuromuscular activation of muscle³⁹ and the perception of effort (Kozlowski *et al.*, 2021).

Deficits in contraction force necessitate an increased efferent motor command to compensate and maintain a given action. Pre-induced muscle fatigability utilising eccentric contractions to induce motor fatigability whilst minimizing metabolic perturbations (e.g. Nielsen *et al.*, 2005) have been shown to evoke a heightened perceived effort during subsequent physical activity (de Morree *et al.*, 2012; Marcora *et al.*, 2008)⁴⁰. Neuroimaging, electrophysiological and neurophysiological evidence identifies the resulting perception of effort with the processing of central signals. That is, motor-related cortical potentials over premotor/motor cortex have been shown to be associated with self-reported perceived effort recorded during the performance of submaximal contractions (de Morree *et al.*, 2012; de Morree *et al.*, 2014; Slobounov *et al.*, 2004). However, the perception of effort does not appear to be proportional to the total activation of the primary motor cortex during voluntary physical tasks. For example, simultaneous contractions at the same relative intensity performed between limbs does not lead to a doubling in the perception of effort (Luu *et al.*, 2016). Accordingly, it is postulated that corollary discharge may emerge from areas upstream of primary motor cortex (M1). Indeed, disruption of the supplementary motor area (SMA) through repeated transcranial magnetic stimulation (TMS) has been shown to reduce indices of perceived effort (Zénon *et al.*, 2015) and alter its associated effects (Sharples *et al.*, 2016). Another cortical region of interest is the dorsal anterior cingulate cortex (dACC) as a primary region involved in signalling the type and intensity of control required to maximize rewarding outcomes (see Shenhav *et al.*, 2017).

³⁹ Neuromuscular activation here (and more typically with the exercise sciences) was assessed through surface electromyography (sEMG) and taken as a marker or proxy of the descending central motor command. However, the use sEMG amplitude as a means of quantifying central motor command is subject to scepticism since peripheral components, beyond the neuromuscular junction, are also known to contribute to the amplitude of the observed response (Dimitrov *et al.*, 2008).

⁴⁰ The work of Taguchi *et al.* (2005) is cited in these studies in an attempt to further exclude activation of group III/IV afferents within observed effects. Taguchi and colleagues demonstrated that eccentric contractions do not increase the sensitivity of thin fibre muscle afferents to thermal or metabolic stimuli. They did however, demonstrate an increased sensitivity of these fibres to mechanical stimuli (Taguchi *et al.*, 2005) which means that a role of these fibres in the resulting effects on the perception of effort cannot be entirely excluded.

Under hypnotic suggestion, changes in RPE with perceived uphill (i.e. increased perception of effort) and downhill (i.e. decreased perception of effort) cycling exercise were associated with altered activation of the thalamus, ACC and insula cortex (Williamson *et al.*, 2001). Finally, in the absence of proprioceptive feedback, the activity of premotor cortex (PMC) has been shown to interact and modulate activation of somatosensory cortex during willed, voluntary movements (Christensen *et al.*, 2007). Collectively, the findings indicate that the feeling of labour and task difficulty, reflective of the perception of effort, is intrinsically coupled with the motor commands generating action, and that centres upstream of M1, involved in the planning of motor actions and control, are the signal genesis of this perception.

However, several recent studies have challenged the exclusivity of central-generated signals under the corollary discharge hypothesis as a complete account of the perception of effort in healthy participants (Brooks *et al.*, 2013; Luu *et al.*, 2011; Monjo *et al.*, 2018; Scotland *et al.*, 2014). Reducing the force-production capacity of the thumb flexors to 40% of maximum using both a high-force contraction and a low-force contraction with vibration, Luu and colleagues (2011) reported participants felt weights to be lighter during a bilateral weight-matching task, contrary to the corollary discharge hypothesis, in which one would expect weights to feel heavier in response to greater drive required to compensate for force deficits. Similar effects were also demonstrated by Brooks *et al.* (2013). The authors speculated that in response to these specific fatiguing tasks (and in contrast to a low-force contraction without simultaneous vibration), reafferent signals associated with efferent motor commands may be reduced (Luu *et al.*, 2011), implicating peripheral signals as a dominant source of information in the perception of effort⁴¹. These findings have increased attention on proprioceptive feedback in the perception of effort and challenged the classic distinction between central and peripheral origins, advancing the notion that perception of centrally generated motor signals may traverse both efferent and afferent pathways. Monjo *et al.* (2018) questioned whether conventional bilateral weight-matching tasks used to study the origins of the perception of effort may obscure evaluation of the interactions between efferent and (re)afferent signals. The premise was thus: if the perception of effort arises from combined efferent and reafferent signals, manipulations (e.g. paralysis or muscle fatigue) designed to decouple outflow (i.e. central commands) from inflow (i.e. afferent signals) must mean that matching this signal to the sense within an intact limb is practically impossible, which may force participants to focus on one source of information during the task. As such the authors examined the same question, using a bilateral weight-matching task in conjunction with a more general and ‘simplistic’ unilateral task, in which participants were simply asked to rate their perceived effort level during a contraction. Both tasks were performed before and after two vibration interventions (one delivered to the muscle at rest and the other in an active state, during a weak contraction) designed to selectively desensitize specific proprioceptors. The authors demonstrated divergent effects of the proprioceptive manipulations between bilateral and unilateral tasks, with corollary discharge dominant in the generation of the perception of effort in the bilateral task, and reafferent signals in driving perception during ‘simple’ unilateral, isometric contractions. The authors concluded that the weighting

⁴¹ Luu *et al.* (2011) examined this proposition further in another experiment. Reducing contraction force again, but this time through a non-depolarising neuromuscular blockade, which effects the recovery dynamics of extrafusal and intrafusal fibres differently (recovery from paralysis delayed in intrafusal fibres compared to extrafusal fibres), the authors observed perception of weight again to be lighter, attributing the effect to a less than expected reafferent signal from muscle spindles, such that this signal consequently dominates the formation of perception.

placed on the central or peripheral sources of information in relation to the perception of effort is not fixed, but context dependent (Monjo *et al.*, 2018).

The highlighted studies have considerably expanded our understanding of the proprioceptive senses, providing evidence of a coupling between efferent signals arising upstream of M1 (i.e. involved in the planned execution of motor actions) and (re)afferent feedback in our subjective experience voluntary muscle contractions. The interaction between efferent and afferent signals may be particularly pertinent to the conscious perception of willed action (Lafargue *et al.*, 2003), within which the subjective experience of effort is included. Furthermore, the influence of each component signal appears sensitive to the context of the voluntary action performed. Though some form of exchange between efferent and afferent signals in the perception of voluntary movement has long been speculated (McCloskey *et al.*, 1974; Cafarelli, 1982), how these signals interact and its implementation within the CNS has not been clearly defined. More recent proposals turned to the simulation of actions across internal models as one potential conceptual framework to understand the neural basis of the perception of effort (Luu *et al.*, 2011; Kuppuswamy, 2017; Monjo *et al.*, 2018). Internal models⁴² enable modelling of the behaviour of the body within the CNS in order to predict the consequences of action or future states of the body and as such have emerged as an important concept across all aspects of sensorimotor control (Wolpert & Miall, 1996; Wolpert & Flanagan, 2001; Friston, 2011). Importantly, this predictive process may also be used in the generation of the perception of effort (Franklin & Wolpert, 2011). In this regard, the experience of effort is determined by the correspondence between our expectations of sensory states arising from action and the actual feedback received, weighted based on the reliability of each signal (Monjo *et al.*, 2018; Kuppuswamy, 2021). Kuppuswamy (2017) proposed that the perception of effort may be understood as a perceptual inference, representing a failure to adequately cancel, or attenuate, reafferent sensory feedback (i.e. the mismatch or error arising from imperfect descending efferent motor predictions) within the sensorimotor control system. From an information-theoretic perspective, the costliness of effort may be inherent within the discrepancy itself, reflecting the information cost of processing the resulting error signal and updating model predictions in light of the brain's capacity limitations, metabolic constraints and/or resulting opportunity costs (Zénon *et al.*, 2019).

2.4.4. Homeostatic Perturbations and the Interaction between the Perception of Fatigue and the Perception of Effort.

The weight of current evidence favours corollary discharge and reafferent processing ([section 2.4.3.2.](#)), over homeostatic afferent feedback ([section 2.4.3.1.](#)), as the primary basis of the perception of effort. This, however, does not preclude an indirect effect of somatovisceral inputs via the modulation of these signals (i.e. both efferent and afferent pathways). Small-diameter afferents are implicated with diverse (albeit seemingly complementary) homeostatic and motor functions during protracted physical activity. Physiologically, they form an essential component of cardiovascular (i.e. the exercise pressor reflex; see Grotle *et al.*, 2020) and respiratory coupling (see

⁴² The theoretical implementation of predictions through internal models is diverse. For example, forward/inverse models used within optimal control theory differ from the generative models underlying the active inference framework (Friston, 2011). Discussion concerning the intricacies of each perspective is beyond the scope of the present thesis. Accordingly, in this chapter, internal models will be broadly referred to as the mechanism through which to understand how the brain makes use of predictions without specifically relating to any one specific implementation.

Dempsey *et al.*, 2014) to the metabolic demands evoked by physical exercise in order to maintain adequate oxygen supply to the working muscles. Moreover, they have been reported to play an important role in the control of metabolic perturbations within working muscles and the maintenance of the economy of muscle contractions through effects on motoneuronal activation (Blain, Mangum, *et al.*, 2016; Broxterman *et al.*, 2017; Broxterman *et al.*, 2018). Group III and IV (A- δ and C-) muscle afferent fibres may exert effects on CNS-function through projections to various sites within the motor pathway (see Laurin *et al.*, 2015), and are thus linked with motor fatigability (see Amann *et al.*, 2015; Taylor *et al.*, 2016). Within the spinal cord, group III/IV afferents connect at a presynaptic level with large diameter muscle afferents (i.e. group Ia) and/or display monosynaptic projections onto α -motoneurons (Della Torre *et al.*, 1996; Panneton *et al.*, 2005). Accordingly, group III/IV muscle afferents have been associated with an inhibitory effect on muscle spindles in the development of motor fatigability (Brunetti *et al.*, 2003; Pettorossi *et al.*, 1999). The effects of these fibres on the excitability of the corticospinal tract during exercise in humans is also subject to much study, but findings have varied widely. Predominantly, these effects have been studied using post-exercise circulatory occlusion, maintaining the metabolic perturbations evoked through exercise and the discharge of group III/IV muscle afferents⁴³, which has shown both inhibitory and null effects (Butler *et al.*, 2003; Martin *et al.*, 2006; Taylor *et al.*, 2000). A possible cause of these disparate findings was elucidated by Martin *et al.* (2006), who demonstrated that flexor and extensor muscles of the human arm are not uniformly affected by group III/IV muscle afferent feedback, with extensor motoneurons inhibited but flexor motoneurons unchanged or facilitated, in broad alignment with findings in cats (Kniffki *et al.*, 1981)⁴⁴. Moreover, the physical toll of the performed task also influences effects on corticospinal excitability. During whole-body, non-exhaustive cycling exercise, blockade of afferent feedback from group III/IV fibres (i.e. fentanyl) has shown that these fibres inhibit spinal motoneurons innervating the knee extensors but facilitate the excitability of motor cortical cells (Sidhu *et al.*, 2017). However, during exhaustive cycling exercise spinal motoneurons appear unaffected, but the excitability of motor cortical cells was inhibited. The results indicate that the effects of group III/IV muscle afferents on the corticospinal excitability change in the presence of motor fatigability (Sidhu *et al.*, 2017). Methodological approaches to the stimulation of muscle afferents (e.g. blood-flow occlusion, neuromuscular blockade) may also be a source of variability in interpreting responses across studies (Amann *et al.*, 2015)⁴⁵. More consistent findings concerning the effect of group III/IV muscle afferents on motor output have been observed at the supraspinal level. Specifically, supraspinal projections of group III/IV muscle afferents have been shown to inhibit descending neural drive, upstream of M1 (Gandevia *et al.*, 1996; Sidhu *et al.*, 2014; Sidhu *et al.*, 2017; Sidhu *et al.*, 2018). A group III/IV muscle afferent-mediated activation of inhibitory intracortical interneurons have been identified as one possible mechanism for this inhibitory effect (Sidhu *et al.*, 2018; Hilty *et al.*, 2011).

⁴³ Predominantly group IV (Hayes *et al.*, 2006).

⁴⁴ This may result from these muscle afferents facilitating the effects of group Ib and group II muscle afferents, and also other skin and joint afferents, which converge on common multisensory interneurons (Schomburg *et al.*, 1999).

⁴⁵ Amann *et al.* (2015) argue that differences in the recruited sub-type of group III/IV muscle afferents depend upon the method of manipulation which may mean that some experimental procedures (e.g. post-exercise circulatory occlusion), based on a greater activation of metabo-nociceptors, may not be reflective of the responses evoked during normal physical activity. It is also important to point out, that the effects of experimental procedures utilising pain in order to assess group III/IV muscle afferent effects on muscle spindle activity (see Lima *et al.*, 2021) and broader motor responses (see Sanderson *et al.*, 2021) have proved highly variable. This may indicate the potential of these experimental procedures to obscure the influence these muscle afferents exert on motor functions during exercise.

Taken together, these findings indicate that feedback from group III/IV muscle afferents, signalling the metabolic, thermal and mechanical conditions of the muscles, have the potential to alter efferent and reafferent motor pathways, with current evidence implicating these fibres most clearly in the modulation of descending efferent commands. Accordingly, the perception of effort may be modulated by signals informing the brain as to the physiological condition of the periphery (e.g. Carson *et al.*, 2002). In the study of motor control and forward models, it has been postulated that feedback from group III/IV muscle afferents may exacerbate a mismatch between sensory predictions and the sensory feedback of mechanical output (Monjo *et al.*, 2015). The precise mechanism(s) through which the integration of homeostatic feedback may alter the perception of effort has not been established. One possibility is that the perception of fatigue, which is closely related to the processing of homeostatic sensory information (e.g. Harrison *et al.*, 2009; see [section 2.3.2.](#)), modulates the processes involved in generating the perception of effort. RPE is known to be sensitive to multiple psychological factors (see McCormick *et al.*, 2015; Morgan, 1994). What is more, RPE has been shown to be particularly sensitive to contextual expectations (e.g. Azevedo *et al.*, 2021). Thus, the aversive, affective experience of fatigue could influence effort perception, possibly by altering the anticipated outcomes of action. However, as the perception of fatigue and effort have extensively been used synonymously ([section 2.2.3.](#)), empirical support for this position is limited and can be only inferred indirectly. In relation to physical activity, partial evidence may be drawn from a body of work demonstrating the performance of prior demanding cognitive activity to evoke a perception of fatigue and subsequently a heightened perception of effort was observed during subsequent exercise (e.g. Marcora *et al.*, 2009; Pageaux *et al.*, 2013; Brownsberger *et al.*, 2013; though see [section 2.7.1.](#)). However, a causal relationship has not been established, with the association principally based on correlational analysis (Harris & Bray, 2019). In line with evidence outlined in [section 2.3.2.](#), portions of the frontal cortex have been implicated in instantiating the perception of fatigue during physical activity. Interestingly, greater self-reported effort has been associated with increased activation of prefrontal cortex during motor preparation across intermittent sub-maximal contractions (Berchicci *et al.*, 2013). This may see an integration of an accumulating perceived fatigue state influence the processing of effort costs (Müller *et al.*, 2021). Research is required to establish the association between the perception of fatigue and the perception of effort during acute physical activity.

2.5. Affective Regulation of Physical Performance.

Though scant in relation to the work on the perception of effort, affective states⁴⁶ arising during prolonged physical activity have also been offered an important role in the regulation of physical performance. Affective states have been identified as an important factor determining prolonged physical behaviour (Hartman *et al.*, 2019; Jones *et al.*, 2015; Renfree *et al.*, 2012). Indeed, the feeling of pleasure/displeasure, the basic substrate of affective states, is posited to act as a ‘common currency’ through which various considerations (e.g. preservation of homeostasis, outcome reward, etc.) informing decisions concerning muscular work may be weighed against each other (Cabanac, 2006). Accordingly, it has been proposed that it may be *how* rather than *what* (i.e. perceived effort) one

⁴⁶ Affect in this instance, is used to refer to a psychological state that is emotional.

feels that may be most pertinent for understanding how the brain regulates physical activity (Hardy & Rejeski, 1989).

As previously highlighted, Gunnar Borg proposed that RPE may be influenced by emotional context (Borg, 1998; [section 2.4.2.](#)). Indeed, Baden *et al.* (2005) showed an influence of affective state on RPE through deception concerning the duration participants believed they would be exercising for. In one trial, participants were led to believe that they would be required to run at 75% of their maximum running speed for 10 minutes. However, at the 10th minute they were told that they would be required to run for a further 10 minutes. Between the 10th and 11th minute, RPE was shown to increase and remained elevated until the end of the running task compared to ratings provided when a run was performed at the same intensity and for the same total duration (i.e. 20 minutes), but the duration was fully known at the start of the task. Concurrent declines in feelings of pleasure were thus inferred to support affective factors influencing individuals' ratings of perceived physical strain (Baden *et al.*, 2005)⁴⁷. More direct evidence of this effect has been demonstrated using subliminal visual affective cues, in which happy- and sad-related cues (i.e. faces) were shown to modulate how effortful a cycling time-trial task was perceived to be (Blanchfield *et al.*, 2014). More recently, music-videos with embedded subliminal, positively-valenced affective words have similarly been shown to reduce RPE and improve affective feeling states during physical activity (Pottratz *et al.*, 2021).

Hartman *et al.* (2019) posited that the homeostatic perturbations imposed by high exercise intensities may see affect (i.e. affective valence) and the feeling of physical strain (i.e. RPE) merge into a single construct and that “*what has commonly been termed ‘perceived exertion’ is, in fact, displeasure*” (p. 8). In support of this view, RPE and affect have been shown to be inversely correlated, with this relationship particularly evident at higher exercise intensities (Hardy & Rejeski, 1989). However, it may be pertinent to reinforce the point that this association may be dependent upon the supported conceptualisation and definition of effort (i.e. the terms used in defining ‘effort’ versus ‘exertion’; [section 2.4.2.2.](#)). Though related to objective effort rather than its subjective experience, similar perspectives within the literature pertaining to cognitive control also offer that affect reflects an inherent component of effort (i.e. linked to the aversiveness of effort). Affect may be integral to various processes including conflict monitoring and cost/benefit evaluations which dictate the mobilisation of cognitive control resources (i.e. effort; Silvestrini & Gendolla, 2019). This may occur directly (i.e. mood effects on behaviour) or implicitly, based on the emotional associations of particular cues or primes, which help inform the subjective appraisal of task difficulty (Silvestrini & Gendolla, 2019). For example, compared to negatively-valenced affective primes (i.e. faces), positively-valenced affective primes have been shown to augment the cardiac post-ejection period (i.e. a marker of objective effort mobilisation) during a demanding vigilance/memory task – but only when affect could inform task appraisal (Framorando & Gendolla, 2019). In line with the propositions of motivational intensity theory (Brehm & Self, 1989), the findings were taken to indicate that positive affective associations alter perceived task difficulty (i.e. perceived as high, but success still feasible) such that it facilitates effort investment, while

⁴⁷ This finding was replicated by Eston *et al.* (2012) during a running task, but affect was disassociated from RPE when the task was performed in a cycling modality. That is, affect was reported to decline when the deception was revealed but RPE remained stable. The authors speculate that this may be due to the type of exercise and its influence on the physiological stress of exercising.

negative affective associations lead to the perception of excessively difficult task demands, resulting in the removal of effort (Framorando & Gendolla, 2019).

However, despite the putative association offered within various research domains, several experimental manipulations including, for example, placebo effects (Brown *et al.*, 2021), hydration strategies (Backhouse *et al.*, 2007), ergogenic supplements (Astorino *et al.*, 2012), taxation of cognitive control resources (Ávila-Gandía *et al.*, 2020; Vera *et al.*, 2018) and social factors (e.g. presence of a competitor; do Carmo *et al.*, 2020) have seen a disassociation between feelings of pleasure-displeasure and RPE during physical activity. Though most of these studies are limited to moderate-intensity, submaximal exercise, and it may be that the higher physiological stress at the limits of exercise tolerance may see it difficult to consciously discern affect from perceived effort, this is yet to be clearly established. Thus, current evidence does not lend clear support to propositions that the conscious feelings of pleasure-displeasure and the perception of effort reflect the same construct. Accordingly, better understanding of how constructs interact during physical activity and the influences modulating their experience is therefore required.

2.5.1. Emotion, Core Affect and Interoception

The study of emotion has a long and varied history, yet, though definitions vary widely, there is a general consensus that all emotions encompass behavioural, experiential and visceral changes (Gendron & Barrett, 2009). Emotions have been described as “*a programmed neural response evolved to serve an adaptive function by mobilizing specific neural activity in both the brain and periphery and by favoring certain behaviors*” (Pace-Schott *et al.*, 2019) rendering them intentional and implicating them in the coordinated control of biological imperatives. Within the study of emotion, several perspectives distinguish between ‘emotion’ and ‘affect’. Modern constructionist perspectives propose that core affect⁴⁸ is a persistent feature of consciousness⁴⁹ and represents a fundamental psychological ‘building block’ through which the experience of a specific emotional episode is constructed based on held emotional concepts⁵⁰ (Russell & Barrett, 1999; Russell, 2003; Barrett *et al.*, 2007; Barrett, 2017). That is, these perspectives propose the presence of a hierarchy in which our continuously evolving core affect is the feeling substrate through which specific emotions may emerge through cognitive ‘categorization’ in order to provide meaning to the more basic psychological states. Core affect is a non-reflective, free-floating (i.e. object free) feeling of one’s current condition (Russell, 2003) that may be described by a blend of two properties, valence (i.e. feelings of pleasure-displeasure) and arousal (i.e. arousing/subduing) (Barrett & Bliss-Moreau, 2009); the former may be more accessible than the latter to many individuals and thus represents the central feature of emotional experiences (Barrett *et al.*, 2007). Though defined as object-free, core affect has also been described as a psychological primitive, grounded by changes within the body (Barrett & Bliss-Moreau, 2009)

⁴⁸ ‘Core’ is used here to describe affect because it represents a basic knowledge concerning objects and events that is crucial to the conscious experience of the world around us (Barrett & Bliss-Moreau, 2009)

⁴⁹ In this regard, proponents of ‘constructionist’ perspectives do not differentiate emotional from cognitive states (Gendron & Barrett, 2009).

⁵⁰ A prototypical representation of an instance of a specific emotion, including the “*typical ingredients, causal connections and temporal order*” that define the concept, such as core affect, physical (i.e. facial expression) and physiological responses in addition to instrumental behaviour (Russell, 2003).

and related to allostatic functions⁵¹ (Barrett, 2017). Indeed, feelings of pleasure-displeasure are positioned to reflect the usefulness of stimuli referenced to the internal conditions of the body (Cabanac, 1971). This touches on a common theme across several other frameworks for understanding emotion - most of whom share origins which can be traced back to the original proposals of authors such as William James (1894) and Carl Lange (1885) - which hold that the representation of the physiological condition of the body represents a core aspect of feelings and emotional experiences (Damasio & Carvalho, 2013; Critchley *et al.*, 2004; Barrett, 2017; Schachter & Singer, 1962; Craig, 2002; Seth & Critchley, 2013; Damasio *et al.*, 1996). Individual differences in the intensity of subjective emotional experiences has been shown to be associated with ones' sensitivity to somatovisceral signals, which can be evaluated using performance tasks including, for example, heartbeat perception tasks (Herbert, Pollatos, *et al.*, 2007; Critchley *et al.*, 2004; Wiens *et al.*, 2000; Pollatos *et al.*, 2007). These findings lend considerable support to the Jamesian notion that physiological changes within the body, in conjunction with top-down expectations of such changes (Critchley & Garfinkel, 2017; Pace-Schott *et al.*, 2019), are important influences and/or determinants of core affect and emotion.

2.5.2. The Dynamics of Core Affect during Physical Activity

Among others, the work of Ekkekakis and colleagues (see Ekkekakis *et al.*, 2011; Ekkekakis & Brand, 2019 for broad overviews) has transformed our understanding of the (core) affective responses to physical activity across different intensities. Their work sought to question common beliefs concerning exercise and feeling states which had become popular between the 1960's and the 1990's (i.e. universal 'feel-good' effect of exercise) and the prevalent methodological approaches adopted within the study of affective responses to exercise, affording greater nuance to our appreciation of the determinants of changing affect both during and in response to physical activity (Ekkekakis *et al.*, 2005; Ekkekakis & Brand, 2019; Ekkekakis & Petruzzello, 1999). The authors developed the dual-mode theory, a framework in which the (core) affective responses to exercise reflect a continuous interplay between two competing factors: 1) top-down cognitive factors, including individual values, goals and self-perceptions, and 2) bottom-up interoceptive cues concerning the physiological state of the body (Ekkekakis, 2003; Ekkekakis *et al.*, 2005). Specifically, cognitive factors are presumed to be the dominant factor determining affect responses during moderate (i.e. below the ventilatory threshold) and heavy (i.e. between the ventilatory threshold and respiratory compensation point) intensity exercise, as at these intensities maintaining physiological steady states is possible and the threat to homeostasis is low. The relative impact of cognitive factors is believed to differ between moderate and heavy exercise intensities however, imparting greater influence during 'heavy' exercise as greater reliance on cognitive factors (e.g. self-efficacy) may be a necessary response to an increased physical challenge, in turn evoking a greater heterogeneity in experienced feeling states (Ekkekakis *et al.*, 2008; Dierkes *et al.*, 2021). Indeed, self-efficacy has been shown to have an inverse association with affect during physical activity (McAuley & Courneya, 1992) and the association between perceived competence and affect is strongest at the transition to heavy intensity exercise (Dierkes *et al.*, 2021). In contrast, the severe exercise intensity domain (i.e. above respiratory compensation point), where intensity exceeds the capacity of physiological systems to

⁵¹ The anticipatory or predictive regulation of the internal milieu (Sterling, 2012).

maintain steady states, sees the dominant factor determining affect shift towards the immediate condition of the body and thus interoceptive cues are afforded greater salience. Affect is universally less pleasurable in this instance, which is believed to be a response emerging through evolutionary and adaptive pressures that serves to signal the potential risks posed to homeostasis (Ekkekakis *et al.*, 2005). A number of studies support the proposition that affect becomes less pleasurable when exercise intensity exceeds that denoting a shift in aerobic-anaerobic metabolism (Sheppard & Parfitt, 2008a; Sheppard & Parfitt, 2008b; Welch *et al.*, 2007; Ekkekakis *et al.*, 2004; Ekkekakis *et al.*, 2010; Ekkekakis *et al.*, 2008). More recently, research has sought to extend the application of dual-model theory from continuous exercise to high-intensity, intermittent exercise, where decreasing affect was shown to track changes in oxygen uptake during repeated cycling bouts, providing a ‘read-out’ of the homeostatic condition of the body (Roloffa *et al.*, 2020)⁵².

2.5.3. Neurobiology of Affect and Emotion

Identification of the representation of emotion and affect within the brain remains a pertinent question within affective neuroscience. Increasing use of more sophisticated meta-analytic techniques and ‘big data’ to investigate this basis has offered the “*most formidable advancement in affective neuroscience*” (Pace-Schott *et al.*, 2019; p. 273). However, interpretation of the neuroscientific evidence is still driven by competing theoretical positions (for a brief historical overview on the issue please see: Barrett & Satpute, 2019), contrasting locationist views (i.e. that discrete emotion categories are consistently and specifically localized to discrete brain regions or anatomical networks) (Vytal & Hamann, 2010; Kirby & Robinson, 2017) with constructionist perspectives (i.e. the view that emotion are not defined by the activation of particular regions of the brain, but emerge from more basic psychological processes) (Lindquist *et al.*, 2012).

Expanding upon the constructionist perspective, in a subsequent analysis, Lindquist *et al.* (2016) examined the evidence for how the brain represents (affective) valence using three different hypotheses: a ‘bipolarity’ hypothesis (i.e. affect is represented by a set of brain regions which change monotonically to changes in valence), a ‘bivalence’ hypothesis (i.e. that positive and negative affective valence are represented across two independent networks) and the ‘affective workspace/affective neural reference space’ (Barrett & Bliss-Moreau, 2009) hypothesis (i.e. there is a set of neurons that are probabilistically involved in realizing positive/negative valence, but this is implemented flexibly across the ‘workspace’; that is, no single region uniquely represents valence). The authors concluded that the evidence offered little to no support for the bipolarity or bivalence hypotheses, favouring the ‘affective neural reference space’ hypothesis (Lindquist *et al.*, 2016).

The ‘affective neural reference space’ identifies the involvement of multiple brain regions, including the amygdala, ventral striatum, thalamus, the AIC, the ventromedial prefrontal cortex (vmPFC) and anterior cingulate cortex (ACC) (Lindquist *et al.*, 2016; see Barrett & Bliss-Moreau, 2009). Traditional emotive brain regions such as the amygdala (see Šimić *et al.*, 2021) and vmPFC (see Hiser & Koenigs, 2018) have a longstanding history in

⁵² However, additional factors (e.g. presence of intervals, total energy expenditure) may also influence the dominant factor driving affect during such exercise, which may signify some differences (or challenges) between the propositions of dual-mode theory for continuous and intermittent exercise that must be considered (Dierkes *et al.*, 2021).

the development of theories of emotion. However, in contrast to views perpetuating their function in instantiating particular discrete emotions (e.g. the amygdala and fear; see Feinstein *et al.*, 2011), in the generation of affective valence under the constructivist perspective they are believed to be part of a distributed network which aids the creation of a neural representation of the threat or reward carried by an object based on its impact on internal homeostasis (Barrett *et al.*, 2007)⁵³. Central to the experience of core affect is therefore the representation of changes within the body (Lindquist *et al.*, 2012; Barrett & Bliss-Moreau, 2009). The neuroanatomical circuits supporting interoception and transmission of peripheral signals from the body have previously been described (Cameron, 2009; Craig, 2002; Craig, 2003; Critchley & Harrison, 2013; Damasio & Carvalho, 2013), so only a brief overview is presented here.

2.5.3.1. Neuroanatomical Interoceptive Pathways

Interoceptive information is conveyed to the brain via cranial (e.g. vagus and glossopharyngeal nerves, via a medullothalamic pathway) and spinal afferent fibres, as well as through humoral processes (e.g. within circumventricular organs or directly within certain brain regions), signalling the thermal, mechanical and chemical status of tissues of the body (e.g. skin, muscle, joints and viscera) (Critchley & Harrison, 2013). For example, in skeletal muscle, activation of free-nerve endings⁵⁴ (group III/IV muscle afferents) and paciniform corpuscles⁵⁵ (group III muscle afferents) (Stacey, 1969) by such stimuli evokes increased discharge of these afferent neurons (Adreani *et al.*, 1997; Jankowski *et al.*, 2013; Kaufman *et al.*, 1984; Mense, 1977). A small proportion of these neurons appear to be multimodal, though the majority are chemosensitive (Jankowski *et al.*, 2013), through which the effects of various metabolites appears to work synergistically in augmenting the afferent response (Light *et al.*, 2008; Pollak *et al.*, 2014). *In vitro* studies of muscle afferent activation have identified the presence of two sub-populations of chemosensitive muscle afferents: those that discharge at low-metabolite concentrations (the so-called ergo- or metabo-ceptors) and those that discharge at high-metabolite concentrations (the so-called metabo-nociceptors) (Light *et al.*, 2008; Jankowski *et al.*, 2013). This sophisticated afferent response thus enables the provision of highly detailed information on the status of the muscle across the physiological range and the subsequent implications for homeostasis.

Through their synaptic terminations on lamina I neurons within the superficial dorsal horn of the spinal cord (Panneton *et al.*, 2005; Jankowski *et al.*, 2013), spinal afferents reach the brain through the lateral spinothalamic tract (Craig, 2002; Craig, 2003) ([Figure 2.3.](#)). This tract ultimately projects to the thalamus, but has various intermediate projections within the brainstem and midbrain (Craig, 1995). Cranial and spinal afferents may initially converge within autonomic centres, including the nucleus of the solitary tract (NTS), the parabrachial nucleus (PB) and the periaqueductal gray (PAG) (Saper, 2002). The integration of afferent signals within higher centres (e.g. PB and PAG) may enable first-order maps of bodily states to be formed, which could be seen as the first potential neural basis for affect and could speak to the early evolutionary history of feelings (Damasio &

⁵³ This perspective shares many commonalities with the proposals of the somatic marker hypothesis (Damasio *et al.*, 1996).

⁵⁴ Terminations of sensory neurons that contain ionotropic and metabotropic receptors.

⁵⁵ A mechanoreceptor found at the terminations of group III muscle afferents, that responds to dynamic changing mechanical stimuli.

Carvalho, 2013). Indeed, connection of these centres to forebrain regions (i.e. amygdala, AIC and orbitofrontal cortex [OFC]), may see them well placed as an important substrate of emotional feelings and behaviour (see Critchley & Harrison, 2013). Homeostatic afferent inputs reach the cortex predominately via (direct or indirect) projections to thalamic relay nuclei (Craig, 2002; Craig, 2003). In primates, a portion of the projections from lamina I neurons reach the posterior part of the ventromedial nucleus (VMpo) of the thalamus directly, circumventing the brainstem (Blomqvist *et al.*, 2000; Craig *et al.*, 1994). Cranial afferents arrive at the basal part of the ventromedial nucleus (VMb) via direct projections from the NTS in primates, alongside the integrated spinal and cranial inputs arriving via the PB (Beckstead *et al.*, 1980). Inputs to the VMpo and VMb are organised orthogonally to the exteroceptive and proprioceptive sensory representations in the ventroposterior nucleus (VP) (Craig, 2002), and principally project, topographically, to the posterior-to-mid portion of the insula cortex, the primary interoceptive cortex (Craig, 2009; Craig, 2011).

Functionally, the insula cortex acts as a processing area for all modalities of sensory input (Flynn, 1999). Forming the floor of the lateral sulcus, the insula cortex is situated at the intersection of the frontal, temporal, and parietal lobes. The insula is roughly divided into three sections based on its cytoarchitecture: a posterior granular section (posterior insula), a middle dysgranular portion (mid insula) and an anterior agranular portion (AIC) (Flynn, 1999; Nieuwenhuys, 2012). Each section of the insula cortex has its own specific connections and function, which enables the integration of multiple neural systems (e.g. Simmons *et al.*, 2013), though a gradation of connectivity is described, with greater connectivity between the anterior portions of the insula and the frontal lobe and greater connectivity between posterior regions and the parietal lobe (Flynn, 1999; Gasquoin, 2014) ([Figure 2.5.](#)). Based on the combined anatomical and neuroimaging evidence, Craig (2009) proposed that the AIC is the hub of human awareness. In this model, the re-representation of homeostatic inputs to the posterior insula (i.e. feelings from the body) within the mid- and then AIC enables a progressive integration of increasingly complex and abstract inputs from other cortical regions (e.g. OFC, vmPFC and dlPFC) relating to the external, motivational, hedonic and social environment, establishing an emotional awareness at an given instance in time (Craig, 2009; Craig, 2011) ([Figure 2.6.](#)). Experimental evidence obtained from various physiological signal detection tasks supports the assertion that the AIC is the seat of interoceptive attention and awareness (Critchley *et al.*, 2004; Wang *et al.*, 2019; Zaki *et al.*, 2012)⁵⁶.

Coactivation of the AIC and ACC (situated in the medial frontal lobe) is a common observation in many neuroimaging studies of emotional processing (e.g. empathy: Gu *et al.*, 2013; see also Craig, 2009). In primates, projections of lamina I neurons are also detailed to the ACC through an ancillary tract via the ventral caudal portion of the medial dorsal nucleus (MDvc) of the thalamus, which has been attributed to the instantiation of the separate motivational component of feeling states (Craig, 2002). Though the insula and cingulate cortex share extensive connections (Taylor *et al.*, 2009), they can be considered functional dissociable. Indeed, the AIC, not

⁵⁶ Others propose it holds a more evaluative role and is responsible for the instantiation of emotion rather than the attention of internal signals, *per se* (Schulz, 2016). More recently, evidence implicates the AIC with a broader function; the gatekeeper of conscious access and processing in high-order systems (Huang *et al.*, 2021).

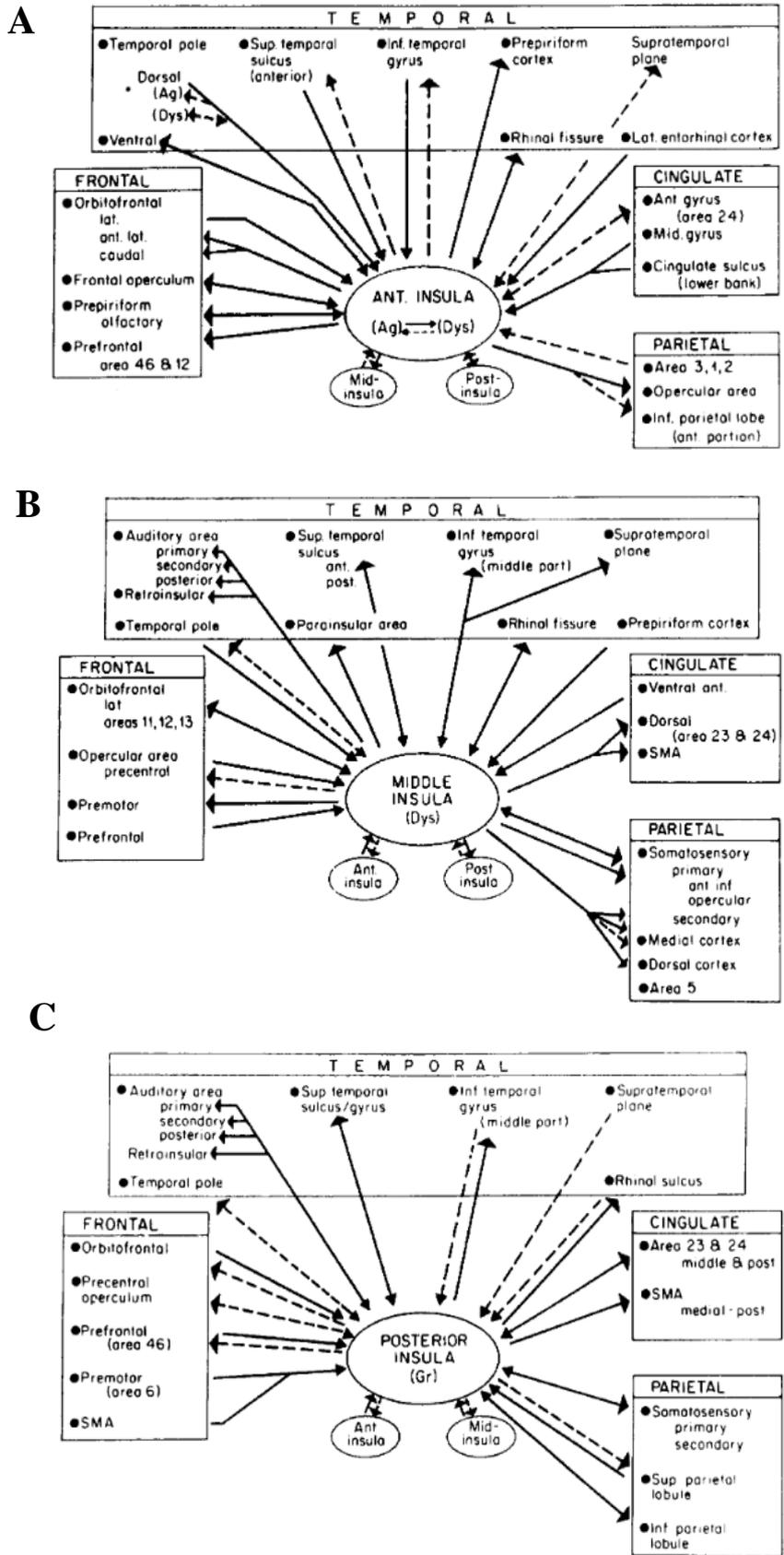


Figure 2.5. Graphical representation of the major cortical connections of the anterior insula (A), mid insula (B) and posterior insula cortex (C). Figures taken from Flynn (1999). Agr: agranular, Dys: dysgranular, Gr: granular.

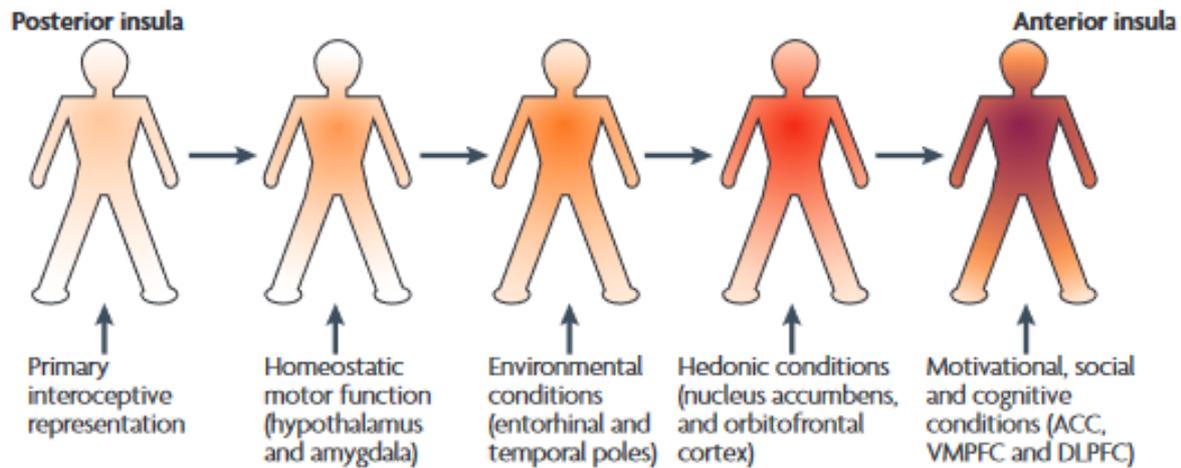


Figure 2.6. A cartoon illustration of the integration of salient activity across the insula cortex, progressing from the posterior insula (left) to the anterior insula (right). Primary interoceptive representations provide a somatotopic foundation of feeling states. Progressive integration includes the successive inclusion of homeostatic environmental, hedonic, motivational, social and cognitive activity to produce “a ‘global emotional moment’, which represents the sentient self at one moment of time” (Craig, 2009; p. 67). Figure adapted from Craig (2009).

the ACC, correlates with explicit awareness of bodily states (Critchley *et al.*, 2004). Accordingly, the consistent coactivation of the AIC and ACC has been proposed to reflect a coordinated response in the system underpinning self-awareness, in which the integrated representations of bodily states within the AIC (inputs) are re-represented in the ACC in order to select responses to internal and external events (outputs) (Craig, 2009; Medford & Critchley, 2010; Gu *et al.*, 2013). In addition to the AIC and ACC, somatosensory cortex has also been implicated in generating feelings of the body (e.g. Harrison *et al.*, 2010; see Khalsa *et al.*, 2009). Recently, awareness of interoceptive signals was shown to involve dynamic changes in the connectivity between AIC and primary somatosensory cortex and reduced connectivity to visual areas, which was believed to be determined by top-down biases emerging from AIC (Wang *et al.*, 2019). As such, the AIC, ACC and somatosensory cortex are key nodes in the representation of bodily states within the brain and thus represent primary candidate hubs in neural networks related to core affect (Kleckner & Quigley, 2015).

2.5.3.2. Furnishing the Constructive Perspective of Emotional Episodes

The described interoceptive pathways detail the afferent connections through which internal events may be transmitted to the brain. It does not however, explain how core affect is formed into a discrete emotional episode. Contemporary perspectives contend that the brain makes use of internal models and the prediction of sensory inputs in order to perceive and understand the meaning of the sensory stimuli it encounters from the world based on past experience (Bubic *et al.*, 2010). Interactions between ascending and descending factors have been discussed in relation to individual differences in interoceptive ability (Ainley *et al.*, 2016) and more broadly, for example, for the purpose of allostatic adaptation (Kleckner *et al.*, 2017; Barrett, 2017). Efforts have sought to identify the structures supporting top-down and bottom-up influences on the perception of our bodies, with the AIC again identified as a key intersection (Dobrushina *et al.*, 2021). Indeed, during physical activity, it has been posited that the AIC integrates top-down expectations of interoceptive states, issued from frontal centres such as

the dlPFC, with the ascending somatovisceral feedback to generate a current felt state which is used to determine whether or not to continue activity (McMorris, Barwood, *et al.*, 2018; [Figure 2.3.](#); [section 2.3.2.](#)). Though empirical evidence is limited, theoretical perspectives suggest that the flow of information follows a laminar differentiation gradient within the cytoarchitectural structure of cortical regions, with top-down signals flowing from regions of less laminar differentiation (i.e. the visceromotor regions: AIC, ACC, posterior vmPFC and posterior OFC [and the amygdala]) to greater differentiation (e.g. primary interoceptive cortex: mid-to-posterior insula cortex) (Barrett & Simmons, 2015; Kleckner *et al.*, 2017). These top-down signals not only drive allostatic processes through their projections to autonomic centres, controlling the deployment of physiological resources (e.g. Shoemaker & Goswami, 2015), but also interoception (Barrett & Simmons, 2015). That is, feeling states are principally based on the predicted state of the body and the anticipated consequence of an object or an event in terms of its impact on allostasis based on prior experiential evidence. The extensive reach of the integrated allostasis-interoceptive network (incorporating two core intrinsic networks: the default and salience networks) is thus seen as the ‘neural backbone’ of information integration across the whole brain, infusing the consequences for allostasis (and thus core affect) within all other psychological phenomena performed by the brain (Kleckner *et al.*, 2017). Indeed, the AIC and ACC (as well as the PMC and SMA; see [section 2.4.3.2.](#) and similar propositions outlined in the perception of effort in the motor domain) have been identified as key nodes within a domain-general network that supports predictive processing across various sensory modalities (Siman-Tov *et al.*, 2019; Ficco *et al.*, 2021). Returning to emotion, the experience of a particular emotion is thus believed to be constructed based on the congruence between internal and external signals and the top-down predictions of an emotional concept, which once reconciled enables an inferential experience of emotion (Barrett, 2017; Barrett & Satpute, 2019). Essentially, the emergence of emotion works through answering the question, what emotional concept is my current state most similar too? Interestingly, under this predictive scheme (Barrett, 2017), the predictions defined by emotional concepts may reciprocally represent important determinants of how we perceive the internal signals arising from our bodies (i.e. interoception) and therefore the experience of affect. This appeals to a cause of the variation of core affect being the contents of consciousness (Russell, 2003) and also shares many similarities to the proposal of dual-mode theory ([section 2.5.2.](#)), detailing how predictions (i.e. cognition) and somatovisceral information interact in forming affect and emotion.

2.5.4. Fatigue, Interoception and the Experience of Affect

As described previously ([sections 2.2.4.](#) and [2.3.2.](#)), the subjective experience of fatigue has been variously described and conceptualised. Hartman *et al.* (2019) attributed exertional fatigue to a “*primordial affective response*”, which may be evidenced as a decline in experienced affective valence in response to exertion-induced perturbations to homeostasis. Processing of interoceptive inputs signalling a challenge to homeostatic control is certainly an important component of fatigue perception and the regulation of physical activity (St Clair Gibson *et al.*, 2003; [section 2.3.2.](#)). However, there is some evidence that the perception of fatigue (i.e. the specific categorisation of the emotion) and affective valence may be disassociated during physical exertion. For example, manipulation of aerobic fitness self-efficacy in a sample of college females led to a differential experience of fatigue (i.e. greater fatigue when self-efficacy was reduced and lower fatigue when self-efficacy was enhanced),

but did not alter affective valence during a subsequent stair climbing exercise task (McAuley *et al.*, 1999). How does this reconcile? If fatigue is represented by a decline in affective valence, how can one report a greater experience of fatigue without respective changes in affective valence? Under constructivist perspectives, this may speak to the separation of core affect from discrete emotional episodes (Russell & Barrett, 1999; Russell, 2003; Barrett, 2017).

Fatigue has been defined as an emotion (Noakes, 2012; Hockey, 2013). Robert Hockey (2013) argued that fatigue has all the hallmarks of an emotion, possibly even a basic emotion⁵⁷, but is often not considered or evaluated as such. As an emotion, fatigue is posited to hold a generalized function which serves to “*alert the organism to both the costs of persisting with effortful, unrewarding activities and the benefits of engaging with more rewarding ones*” (Hockey, 2013; p.114). As described ([sections 2.5.1.](#) and [2.5.3.](#)), under the constructionist perspective, the instantiation of an emotional experience of fatigue is believed to be defined by an emotional concept of fatigue. Alongside core affect, various metacognitive judgements (e.g. a sense of urgency, uncertainty) arising from the perceptual-cognitive processing of an object also aid in categorising the felt state (Russell, 2003). This is an important distinction between the experience of the emotion of fatigue, *per se*, and fatigue-associated reductions in affective valence. Specific changes in affective valence (i.e. declines) are not unique to the emotion of fatigue (Barrett & Satpute, 2019). An apparent limitation of Hartman and colleagues (2019) proposition reflects this, as a decline in affective valence does not easily distinguish between fatigue and other aversive emotions or feeling states that may arise in response to physical exertion (e.g. discomfort, or boredom if the exercise intensity is relatively low). Some authors suggest that this point may be irrelevant, as the related-feeling states (e.g. discomfort, boredom, fatigue) all contribute to the same ‘fatigue process’ (Hockey, 2013), ultimately resulting in an interruption to goal pursuit. However, as outlined in [section 2.2.4.1.](#), there is evidence that fatigue is distinct from such states, thus it is important to understand it’s specific function. A reduction in conscious affective valence in response to strong interoceptive sensation during physical activity is certainly a feature of perceived fatigue, thus any disagreements may appear more semantic than theoretical (i.e. fatigue may just be the terminology used to describe the decline in affective valence). However, as highlighted by the results of McAuley *et al.* (1999), it is not its sole determinant, with the experience of fatigue defined also by the processing (i.e. attribution and appraisal; Russell, 2003) of one’s perceived capacity to cope or perform effectively.

Though dissociable, the obvious relationship between fatigue as an emotional concept and affective valence may be reciprocal. Under nascent predictive processing accounts (Barrett, 2017), the emergence of an emotion through categorisation, or meta-experience, may also subsequently drive how we perceive internal cues from the body, influencing interoceptive processing and core affect. This is because emotional concepts generate expectations or predictions of internal states, all in the service of allostasis (Kleckner *et al.*, 2017). Experimental evidence indicates that categorisation reflects an important top-down process that shapes perceptual intensity and affective evaluations of interoceptive stimuli, particularly under conditions of uncertainty (Petersen *et al.*, 2014; Zacharioudakisa *et al.*, 2020). This may change the balance afforded to the predictions of internal states and the sensory evidence received, altering conscious perception and behaviour during physical activity (Wallman-Jones

⁵⁷ Basic emotions have been defined as emotions that have been “*characterized as having evolutionarily old neurobiological substrates, as well as an evolved feeling component and capacity for expressive and other behavioral actions of evolutionary origin*” (Izard, 2007; p. 261).

et al., 2021). The interactions between conceptual predictions and sensory evidence, and the integration of interoception and allostasis across all functions of the brain (Kleckner *et al.*, 2017; Barrett, 2017) may further obfuscate boundaries between the classic dichotomy of cognition and emotion (Duncan & Barrett, 2007; Pessoa, 2008). As such, the cognitive categorisation defining the perception of being in a state of fatigue, much like a fit of rage, or joyous state of happiness, may instantiate or change expectations that shape interpretation of interoceptive states, core affect and the subsequent regulation of physical activity. In line with this, cognitive emotion regulation strategies (i.e. strategies used to alter the emotional category one finds oneself in; Russell, 2003), such as cognitive reappraisal, have been shown to influence the experience of affective valence and RPE during endurance performance (Giles *et al.*, 2018; Grandjean da Costa *et al.*, 2021). This may suggest that the predictions associated with a perceived state of fatigue may, in part, define the affective response to exercise. However, at present, examinations of the associations and interactions between the perception of fatigue and core affect (i.e. affective valence) during exercise is lacking.

2.6. Interpretation of the Perception of Fatigue within the Context of the Regulation of Physical Activity

A significant proportion of this chapter has been dedicated to literature pertaining to the neurophysiology of the perception of effort and core affect. In the description of both phenomena, recent positions on the underlying substrates indicate that interactions between bottom-up and top-down inputs are fundamental to our subjective experiences. Interestingly, [sections 2.4.](#) and [2.5.](#) highlight evidence indicating that the perception of fatigue may be experimentally disassociated from both the perception of effort and core affect during physical activity, suggesting an independency of percepts. However, interpretation of the literature suggests that a perceived state of fatigue, seemingly reflecting an (meta)awareness of a perceived reduction in capacity to perform or cope with the demands of the task, may be a top-down input that modulates features of the regulation physical performance. That is, the perception of fatigue may exert influence on core perceptual and affective responses central to regulation of performance. This indicates that the perception of fatigue may hold a definable function in the regulation of physical performance, which has presently been understudied. Accordingly, this presents the basis of the presented thesis.

Another theme evident within the literature is that regulation of physical activity is closely aligned to a volitional decision-making processes (Pageaux, 2014; Renfree *et al.*, 2014; Robertson & Marino, 2016; St Clair Gibson *et al.*, 2018). Fatigue may therefore indirectly modulate the motivation to engage in activity by altering the subjective costs (e.g. effort) and/or benefits determining choice behaviour (see Massar *et al.*, 2018). Multiple behavioural paradigms have been translated from work performed in animals (e.g. Walton *et al.*, 2006) to objectively capture motivation and effort-based decision-making in humans (Crosson *et al.*, 2009; Prévost *et al.*, 2010; Kurniawan *et al.*, 2010; Treadway *et al.*, 2009; Klein-Flügge *et al.*, 2015; Chong *et al.*, 2017; Bonnelle *et al.*, 2015; see Pessiglione *et al.*, 2018; Chong *et al.*, 2016). Interestingly, few studies have sought to examine the effect of fatigue on decision-making directly. In fact, many studies have attempted to control for its putative effect (e.g. Klein-Flügge *et al.*, 2015). Emerging evidence suggests that ‘fatigue’ may be an important factor influencing how the costs attributed to effort are appraised (Iodice *et al.*, 2017). Whether this effect is attributable to a conscious awareness of the perception of fatigue and associated self-evaluations concerning ones’ capacity to perform

actions, however, cannot yet be determined based on the current literature and therefore requires empirical investigation. To isolate the subjective experience of fatigue from performance fatigability necessitates careful consideration of the adopted methodological approach.

2.7. Disassociation of the Dimensions of Fatigue

As outlined in [section 2.2.3.](#), fatigue may be defined based on interacting dimensions defining its physical manifestation (i.e. performance fatigability) and its subjective experience. If we are to precisely evaluate the specific effects of one dimension of fatigue it may necessitate the control of the other. This is particularly important when attempting to establish the influence of the subjective perception of fatigue on, for example, physical performance and the perception of effort, which are sensitive to compensatory changes in descending central motor drive in response to fatigue-associated declines in the force-generating capacity of the muscles. Over the past two decades, there has been a growing body of work, involving both cognitive and physical paradigms, that may help accomplish this aim. The literature pertaining to the effect of cognitive exertion on physical performance is first presented to rule out this approach as the experimental framework of the presented thesis, before presenting the literature pertaining to prior physical tasks in different parts of the body as an alternative solution.

2.7.1. Prior Cognitive Activity

The deleterious effects of engaging in prior, demanding cognitive activity on ones' ability to effectively perform a subsequent cognitive task has been well documented (Boksem *et al.*, 2006; Gergelyfi *et al.*, 2015; Hopstaken *et al.*, 2015). Studies have also indicated that this negative effect may transcend physical and cognitive domains, with demanding cognitive tasks also impairing subsequent performance of physical tasks too (see Pageaux & Lepers, 2018; Van Cutsem *et al.*, 2017). Behavioural reports posit that prior cognitive activity may impair physical performance by altering shared processes between domains that are involved in how effortful tasks are perceived to be (Pageaux & Lepers, 2016; [section 2.4.1.2.](#)) and/or more general motivational functions (Martin *et al.*, 2018). This has previously been attributed mechanistically, to a build-up extracellular adenosine during to the neural activity underpinning cognition performance, which may interfere with the release of neurochemicals (i.e. dopamine) in key brain regions, including the ACC (Martin *et al.*, 2018). However, McMorris (2020) recently argued that this proposition may be unlikely due to the type of adenosine release (i.e. tonic vs. phasic) required to evoke sufficient accumulation of extracellular adenosine in the brain and the expected timescale such changes would follow. Alternatively, it is suggested that 'cognitive fatigue' ([section 2.2.2.3.](#)) may impair physical performance by altering the anticipated sensory consequences of action, such that the perception of reduced resources (i.e. fatigue) impacts the perception of task demands in a way that they are deemed to be more demanding or effortful (McMorris, 2020). Importantly, the effect of prior cognitive activity on the perception of effort during a physical task is independent of changes to the neuromuscular system and its capacity to produce force (Pageaux *et al.*, 2013; Pageaux *et al.*, 2015; Rozand *et al.*, 2014), supporting the separation of the perception of fatigue from physical changes.

Due to the popularity of this research topic, over recent years several meta-analyses have emerged summarising the evidence for a deleterious effect of prior cognitive activity on physical task performance (McMorris, Barwood, *et al.*, 2018; Giboin & Wolff, 2019; Brown *et al.*, 2020; Holgado, Sanabria, *et al.*, 2020). In the most extensive analysis to date, Brown *et al.* (2020) concluded that prior cognitive activity exerts a small-to-medium effect across a broad range of physical tasks. The size of this effect was shown to be dependent upon the type of physical task performed, with the largest effects seen during dynamic or isometric resistance exercises (Brown *et al.*, 2020; see also Giboin & Wolff, 2019). However, several issues are present in the interpretation of this effect. First, random error (McMorris, Barwood, *et al.*, 2018) and publication bias (Holgado *et al.*, 2020; Brown *et al.* 2020) present significant confounds to interpretation. Indeed, Brown *et al.* (2020) indicated some evidence of publication bias. When accounting for this error or bias, the effect on performance may be closer-to-null (McMorris, Barwood, *et al.*, 2018; Holgado, Sanabria, *et al.*, 2020). Second, the attribution of this effect to fatigue, at least the perception of fatigue, may also be questionable. In their narrative review, Van Cutsem *et al.* (2017) reported that only 6 of the 11 studies reviewed evidenced a change in the subjective experience of fatigue after the cognitive task. Even in the studies demonstrating a change in the perception of fatigue, recent evidence casts doubts whether the aversive state may be wholly ascribed to the subjective experience of fatigue itself. Thompson and colleagues (2020) reported that the modified Stroop task, a task often used to induce a state of ‘cognitive fatigue’ (e.g. Smith *et al.*, 2016), may incur simultaneous feelings of boredom. This may be due to the monotony of the task and the low level of arousal presumably evoked ([section 2.2.4.1](#)). Moreover, neural evidence suggests that protracted engagement in cognitive control results in fatigability, or a downregulation, of the lateral PFC resulting in a shift in the cost/benefits of exerting further control during temporal choices towards immediate gratitude (Blain, Hollard, *et al.*, 2016). However, this effects only emerges after several hours of extended use (Blain, Hollard, *et al.*, 2016); a timescale far beyond the tasks typically adopted to induce a state of ‘cognitive fatigue’. Together, this highlights the uncertainty to what ‘fatigue’ pertains too when induced in studies examining the detrimental effects of prior cognitive activity on physical performance. Accordingly, it may be pertinent to view studies attributing performance fatigability a result of a perceived state of fatigue evoked by demanding prior cognitive activity with due caution.

In keeping with the recent emergence of replication studies examining the main evidence for ‘cognitive fatigue’ within the literature (Holgado, Troya, *et al.*, 2020), our laboratory attempted to conceptually replicate the effect the detrimental impact of prior cognitive activity on a sustained isometric contraction (Greenhouse-Tucknott *et al.*, 2021). Like other replication studies on the topic (Holgado, Troya, *et al.*, 2020), we demonstrated a small increase in the perception of fatigue accompanying the performance of the protracted cognitive task, but failed to observe a detrimental effect on performance (Greenhouse-Tucknott *et al.*, 2021). As such, the current evidence suggests that the effect of prior cognitive activity on both physical performance and the perception of fatigue is in need of further study and the present lack of clarity, particularly in relation to the effect of the perception of fatigue, may preclude it as a suitable means of investigating how the subjective experience of fatigue shapes the regulation of physical performance.

2.7.2. Prior Motor Activity

2.7.2.1. *Effects of Prior Motor Activity on Force Production and Neuromuscular Function*

An alternative method to prior cognitive activity may be to induce a perceived state of fatigue through physical activity in one part of the body and subsequently measure the regulation of performance in another. This however necessitates an examination of the functional consequences of remote physical activity across other parts of the body. The term non-local muscle fatigue (NLMF) - or crossover (muscle) fatigue when referencing effects in the contralateral limb specifically (Rathey *et al.*, 2006) - has been used to denote the occurrence of a transient impairment to force production in a non-active muscle or muscle group following demanding motor activity in another part of the body (Halperin *et al.*, 2015). Accordingly, there is a suggestion that motor fatigability may not pertain solely to a localised event within active or working muscle, but rather, reflect a global consequence of activity. Acute challenges to the neuromuscular function of homologous muscle following contralateral activity have been observed in both the upper (Doix *et al.*, 2013; Kavanagh *et al.*, 2016; Post *et al.*, 2008; Ye *et al.*, 2018) and lower limbs (Halperin, Copithorne, *et al.*, 2014; Kawamoto *et al.*, 2014; Martin & Rathey, 2007). For example, under isometric conditions, Halperin, Copithorne, *et al.* (2014) reported an 8% reduction in maximal voluntary contraction (MVC) force of the non-dominant knee extensors (KE) following a 100 s MVC of the dominant KE. Ye *et al.* (2018) similarly reported a 7% reduction in MVC force of the non-exercised elbow flexors (EF) following six sets of 30 s MVCs (each separated by 30 s rest) performed by the contralateral limb. A reduction in rested EF MVC was also shown by Doix *et al.* (2013) following the second of two 100 s MVC of the contralateral muscle, while finger abduction force was reduced by 31% when preceded by activity in the contralateral homologous muscle that reduced force production by half (Kavanagh *et al.*, 2016).

Beyond transient impairments to contralateral, homologous muscle, functional deficits have also been evidenced in heterologous, remote muscle(s) within both the upper and lower limbs. Indeed, Kennedy *et al.* (2014) demonstrated a ~10% reduction in EF MVC following a 2 minute MVC of the ipsilateral adductor pollicis. Moreover, Kennedy *et al.* (2013) demonstrated that prior bilateral handgrip exercise reduced force production in the plantar flexors, with deficits most evident when applying maximal versus sub-maximal forces in the upper limbs. The effects across the upper and lower body appear to be bi-directional, with prior exertion of the upper limbs impairing force production of the lower limbs (Halperin, Copithorne, *et al.*, 2014; Kennedy *et al.*, 2013) and the opposite (i.e. impaired force production of upper limb muscles) also evident following lower limb activity (Šambaher *et al.*, 2016; Sidhu *et al.*, 2014). In both homologous and heterologous muscle, transient impairments to voluntary force production has been attributed primarily to central factors, impairing the ability of the CNS to activate remote, non-active muscle groups, independent of acute peripheral contractile dysfunction (Doix *et al.*, 2013; Kennedy *et al.*, 2013; Todd *et al.*, 2003).

2.7.2.2. *Mechanisms of Prior Motor Activity on Contralateral, Homologous Muscle*

Neurologically, the mechanisms underpinning these transient activation deficits remain unclear (see Halperin *et al.*, 2015). For contralateral effects, communication between hemispheres may be the primary mechanism. The corpus callosum is the largest white matter structure in the human brain; a commissure connecting homologous cortical areas of the right and left cerebral hemispheres (Bloom & Hynd, 2005). The precise function of the corpus

callosum has yet to be fully uncovered, associated with the transfer of both inhibitory and excitatory functions, the balance of which may be sensitive to the particular demands of the task performed (Bloom & Hynd, 2005; van der Knaap & van der Ham, 2011). Studies utilising transcranial magnetic stimulation (TMS) to investigate contralateral changes in cortical and spinal excitability (Bestmann & Krakauer, 2015; Di Lazzaro & Rothwell, 2014) have shown motor evoked potentials (MEP) in non-active, homologous muscle groups to be facilitated in response to brief contractions of the contralateral limb (Carson *et al.*, 2004; Hortobágyi *et al.*, 2011; Steadman *et al.*, 1998). Interhemispheric interactions via transcallosal pathways may therefore facilitate corticospinal excitability in the ipsilateral hemisphere. However, though excitatory effects to the corticospinal pathway of the non-active hemisphere have been observed during brief contralateral contractions, such effects may differ when exposed to prolonged, intense or demanding contractions. During demanding unilateral motor activity, neuroimaging studies have demonstrated a progressive activation and enhanced connectivity between active M1 and somatosensory and pre-motor regions of the opposite hemisphere, which has been attributed to a compensatory mechanism increasing the total cortical processes devoted to maintaining descending motor output in the face of muscle fatigability (Jiang *et al.*, 2012; Liu *et al.*, 2003; Post *et al.*, 2009). Thus, intrinsic interactions between hemispheres may prove a critical function in the maintenance of gross motor actions in response to fatigability⁵⁸. Yet, fatiguing unilateral activity has also been shown to elicit a prolonged depression of MEP evoked in the contralateral limb (Takahashi *et al.*, 2009; Triscott *et al.*, 2008; Sharples *et al.*, 2016; Shibuya *et al.*, 2011). Moreover, a decrease in intracortical facilitation (ICF) (Bäumer *et al.*, 2002) have also been observed in the contralateral first dorsal interosseous (FDI) muscle following fatiguing pinch grip tasks. Accordingly, inhibition of homologous muscle group may be mediated by interhemispheric transcallosal pathways in response to heavily fatiguing activity in the contralateral limb. To date only one study has directly assessed interhemispheric inhibition from the active-to-non-active hemisphere using paired-pulse TMS, with no evidence of altered interhemispheric inhibition following exhaustive, unilateral motor activity (Edgley & Winter, 2004). Interestingly, interhemispheric inhibition in the opposite direction (non-active-to-active) has also been shown to remain unchanged following demanding unilateral motor activity (Sharples *et al.*, 2016). To further compound this uncertainty, in addition to inhibitory effects on corticospinal excitability, facilitatory effects in contralateral homologous muscles have also been reported following demanding activity (Aboodarda *et al.*, 2016). Conflicting excitatory and inhibitory influences on MEP may, at least in part, have been influenced by the strenuousness of the physical task. For example, Aboodarda *et al.* (2016) used two 100s MVC of the dominant EF to stress the neuromuscular system, resulting in a force deficit of ~33% and facilitated MEP responses during maximal contractions, whereas exercise to task failure has been shown to elicit reductions in corticospinal excitability (Takahashi *et al.*, 2009). In summary, the transcallosal-mediated effects on the ipsilateral corticospinal pathway following prior motor activity remains unclear.

⁵⁸ In a recent pre-print, motor fatigability induced through repeated unilateral (right) handgrip contractions at 50% MVC were shown to facilitate behaviour (i.e. reaction times) in the contralateral (left) hand (Andrushko *et al.*, 2021). This behavioural improvement was accompanied by increased SMA-SMA connectivity between hemispheres as well as increased functional connectivity between the ipsilateral OFC and M1, and associated with a decrease in inhibitory process (i.e. GABA) (Andrushko *et al.*, 2021).

2.7.2.3. Mechanisms of Prior Motor Activity on Heterologous Muscle

Like homologous muscle, increased excitability of the corticospinal motoneurons has been observed following brief contractions in remote heterologous muscle (Takahashi *et al.*, 2011; Tazoe *et al.*, 2009). Moreover, this facilitatory effect has been shown, in some instances, to be maintained during and immediately following more prolonged, remote unilateral motor activity (Matsuura & Ogata, 2015; Tazoe *et al.*, 2009). Increased excitability has been shown to be accompanied by reduced interhemispheric inhibition from the contralateral to ipsilateral hemisphere (Matsuura & Ogata, 2015). Conversely, Takahashi *et al.* (2011) reported a protracted reduction in corticospinal excitability and short interval cortical inhibition (SICI) of the resting right FDI and bicep brachii (BB) following bilateral leg extensions, in keeping with the authors previous results in contralateral homologous muscle (Takahashi *et al.*, 2009). Šambaher *et al.* (2016) reported a reduction in the MEP/CMEP (cervicomedullary evoked potential) ratio in the EF during MVC, following KE exercise, indicating inhibition was attributed to inputs above the level of the spinal motoneurons. Indeed, excitability of spinal motoneurons remains relatively unchanged following prior remote motor activity (Aboodarda *et al.*, 2017; Šambaher *et al.*, 2016; Tazoe *et al.*, 2009). This however, may be direction-dependent (i.e. evident in the upper limbs following lower body activity as well), since increased motoneuron excitability was observed in the KE following prior activity in the EF (Aboodarda *et al.*, 2015).

Current hypotheses for the observed, widespread cortical inhibition of heterologous muscle following prior, remote motor activity may include changes in inputs upstream of M1 (Takahashi *et al.*, 2011). Indeed, the upper and lower body representations have been shown to display bi-directional neural coupling (e.g. Huang & Ferris, 2009), which may be served by common, higher cortical inputs. Additionally, the activation of group III/IV muscle afferents in active muscles are also implicated the inhibition of corticospinal projections of remote, heterologous muscles (Sidhu *et al.*, 2014). Pharmacological blockade of the spinal receptors of small-diameter afferents with the μ -opioid agonist fentanyl, abolished activity-induced (i.e. prolonged bi-legged cycling) inhibition of corticospinal excitability and maintained activation of the non-active EF (Sidhu *et al.*, 2014). Similarly, blood flow occlusion following demanding activity of intrinsic hand muscles was shown to exacerbate fatigability and further reduce voluntary activation of the ipsilateral EF, in keeping with the notion that the activation of homeostatic muscle afferent fibres serves an inhibitory function (Kennedy *et al.*, 2014). However, blood flow occlusion had no effect on contralateral, homologous muscle in the lower limbs (Kennedy *et al.*, 2015). The absence of afferent-mediated effects in this latter study may indicate different, or at least the balance of the different processes, influencing corticospinal excitability and voluntary activation between homologous and heterologous muscles groups. For homologous muscle, the effects of ascending sensory feedback and transcallosal-mediated interhemispheric connections may act more in opposition of each other during demanding activity. Also, as stated in [section 2.5.3.](#), it must be noted that blood flow occlusion may preferentially activate putative metabo-nociceptors, which may evoke a different activation to that typically elicited through normal physical activity (Amann *et al.*, 2015).

2.7.2.4. Critical Methodological Appraisal of Non-local Effects on Force and Neuromuscular Function

As outlined above, the neurological processes modulating activation and excitability of remote, non-active muscle groups remains uncertain. It does appear however, that any effects are principally observed above the level of the spinal motoneurons. However, both excitatory and inhibitory effects have been observed in homologous and heterologous muscles. Divergent effects may be highly sensitive to both intensity of stimulator output for recordings of stimulation-evoked electrical responses (i.e. MEPs and SICI) and the different prior motor activity protocols adopted. For example, Aboodarda *et al.* (2017) reported opposing influences on cortical and corticospinal excitability following prior motor activity, with excitation demonstrated in maximal contractions and inhibition reported during weak contractions (i.e. 5% MVC). These methodological differences may differentially activate high- and low-threshold motoneurons, which may account for the varying corticospinal responses observed (Aboodarda *et al.*, 2017).

Several key limitations are also readily apparent within the literature. For example, Post *et al.* (2008) reported force recordings of 11% and 28% of MVC for the 'non-exercised muscles' during sub-maximal and maximal contralateral contractions. A significant decline in potentiated twitch force (-20%) in the 'non-exercised' muscle group was also observed, but the activation of the target, 'non-exercised' muscle during the initial task precludes attribution to cross-over effects specifically. Failing to record the activation of non-active, test muscle represents a considerable threat to the internal validity of the paradigm. Moreover, several studies reporting statistical effects fail to incorporate appropriate control measures (e.g. Doix *et al.*, 2013; Post *et al.*, 2008; Ye *et al.*, 2018). Further extraneous influences, including muscle specificity and sex, may also obscure findings. For example, Halperin, Copithorne, *et al.* (2014) demonstrated remote effects in the non-dominant KE compared to passive rest following both contralateral KE ($\Delta 6\%$) and dominant EF activity ($\Delta 8\%$), but reported no effect ($\Delta < 3\%$) in the non-dominant EF following the same tasks. Though it is suggested that the effect is bi-directional, this may suggest that the lower limbs may be more susceptible to global fatigability effects. In addition, sex has been shown to modulate the transfer of inhibitory influences, with males shown to be more susceptible to cross-over effects (Martin & Rattey, 2007; Ye *et al.*, 2018), though again, these findings are not consistent (Doix *et al.*, 2018).

Unsurprisingly perhaps, a number of studies also report null findings, with no transient deficits in the MVC of non-active homologous and heterologous muscles of both the lower (Aboodarda *et al.*, 2015; Aboodarda *et al.*, 2017; Doix *et al.*, 2018; Hamilton & Behm, 2017; Kennedy *et al.*, 2015; Rattey *et al.*, 2006) and upper body reported (Aboodarda *et al.*, 2016; Halperin, Copithorne, *et al.*, 2014; Triscott *et al.*, 2008). Acute inhibition of contralateral muscle has similarly not been evidenced during more dynamic contractions (Elmer *et al.*, 2014; Grabiner & Owings, 1999), nor in remote muscles following prolonged aerobic activity (Decorte *et al.*, 2012; Matsuura *et al.*, 2018; Millet *et al.*, 2003; Place *et al.*, 2004; Ross *et al.*, 2010). Evidence of a transient impairment to maximal force production in remote muscle is therefore equivocal, which raises the question whether the transient decrease in force production in non-active muscle can be considered a true effect. Indeed, a recent meta-analysis reported that current evidence supports, at best, trivial non-local effects on force and power indices (Behm *et al.*, 2021).

Interestingly, Halperin, Aboodarda, *et al.* (2014) reported no change in the MVC force of the EF assessed immediately upon the termination of a bilateral KE task. However, significant reductions in force (~5%) were

evident across the final five contractions of an intermittent contraction task performed afterwards (Halperin, Aboodarda, *et al.*, 2014). Li *et al.* (2019) similarly did not observe any change in single force assessments of the non-dominant index finger abductors (IFA) or EF following activity in the dominant IFA. However, the authors demonstrated a ~10% reduction from the initial assessment to the first contraction of a subsequent intermittent contraction protocol following 30 s rest. This initial decrement was attributed to teleoanticipation, with the participants modulating effort investment in order to successfully complete the intermittent task (Li *et al.*, 2019). This raises the possibility that the effect of prior motor activity of force capacity may not represent a direct, physiological challenge to the motor system to produce force, but reflect a reduction in motor performance of a rested muscle through processes involved in regulating the allocation of resources for the performance of protracted physical activity.

2.7.2.5. Prior Motor Activity and Subsequent Endurance Performance

Compared to the investigation of the effects on brief, maximal force production and neuromuscular function of remote, non-active muscle, fewer studies have investigated the effect of prior motor activity on the impairment of muscular endurance. However, the small number of findings suggest an apparent and consistent reduction in the endurance of remote, non-active muscle or muscle groups following prior motor activity (Amann *et al.*, 2013; Bangsbo *et al.*, 1996; Johnson *et al.*, 2015; Morgan *et al.*, 2019; Nordsborg *et al.*, 2003; Aboodarda *et al.*, 2020). Though in total, the meta-analysis conducted by Behm *et al.* (2021) concluded that the non-local effect on performance may be trivial, the authors conclude that moderate effects may be observed on endurance-based tasks and that this effect was statistically larger than that seen for force- or power-based outcome measures. Select studies investigating this effect are presented in [Table 2.2](#).

Like the putative effects of ‘cognitive fatigue’, the decline in endurance performance following prior remote motor activity has been attributed to altered perceptions (i.e. effort) during subsequent performance (Pageaux & Lepers, 2016; Halperin *et al.*, 2015). For example, Amann *et al.* (2013) demonstrated a 49% reduction in the duration of a repeated KE contraction protocol following the same exercise performed in the contralateral limb. Neuromuscular functionality of the tested limb was not affected by prior activity, nor was the activation of the tested limb during initial portion of the contraction task. However, the perception of effort was heightened from the start of the task (Amann *et al.*, 2013). Similarly, Johnson *et al.* (2015) reported arm cycling impaired tolerance of subsequent legged-cycling exercise. Again, neuromuscular function of the KE was unaffected by the prior activity, however both RPE and perceived dyspnoea were elevated following prior motor activity. The heightened perceptions of effort were correlated with the duration of legged-cycling performance (Johnson *et al.*, 2015). Aboodarda *et al.* (2020) evidenced that beyond RPE, prior, single-legged cycling also heightened perceptions of fatigue and pain during the performance of the same task in the contralateral limb. Impairment of endurance performance was attributed to the combined effects of these perceptual changes leading continued exercise to feel increasingly unattractive (Gandevia, 2001). However, how these constructs potentially interacted with each other in the achievement of this goal was not explored.

Table 2.2. Selected studies examining the effect of prior motor activity on subsequent endurance performance in another part of the body.

Reference	Participants	Prior Physical Activity	Neuromuscular Function and Corticospinal Responses		Subsequent Physical Endurance Task	Control Condition	Cardiorespiratory, Haematological and Metabolic Responses to Endurance Performance	Performance and Perceptual Responses to Endurance Performance
			Muscle Group Involved in Activity	Muscle Group Not Involved in Activity				
Aboodarda <i>et al.</i> (2020) ^a	12 active males	Single-legged cycling (left leg) at 80% of leg-specific peak power output and a cadence between 75 – 85 rpm.	Not measured	↔ MVC ↓ Q _w ↔ VA ↔ MEP ↓ CSP during MVC in VL and RF	Single-legged cycling (right leg) at 80% of leg-specific peak power output and cadence of 75-85 rpm	Single-legged cycling (right leg) at 80% of leg-specific peak power output and cadence of 75-85 rpm (without prior activity)	↔ $\dot{V}O_2$, \dot{V}_E , HR and StO ₂ at task failure ↑ b[La] at task failure	↓ TTF ↑ RPE, perceived fatigue and pain during task ↔ RPE and perceived fatigue at task failure
Amann <i>et al.</i> (2013)	8 active males	Single-leg knee extensions at 80% leg-specific peak power and cadence of 60 rpm	↓ MVC ↓ Q _w ↓ MRFD ↓ MRR ↔ VA	↔ MVC ↔ Q _w ↔ VA	Single-leg knee extensions in the contralateral limb at 80% leg-specific peak power and cadence of 60 rpm	Single-leg knee extensions in the contralateral limb at 80% leg-specific peak power and cadence of 60 rpm (without prior activity)	↑ $\dot{V}O_2$, \dot{V}_E , $\dot{V}_E/\dot{V}CO_2$, HR and CO during task ↑ MAP during first two minutes ↔ $\dot{V}O_2$, \dot{V}_E , $\dot{V}_E/\dot{V}CO_2$, HR, CO and MAP at task failure ↔ femoral blood flow during task (except at the first minute) and task failure	↓ TTF ↑ RPE during task ↔ RPE at task failure ↔ EMG during task ↓ EMG at task failure

Reference	Participants	Prior Physical Activity	Neuromuscular Function and Corticospinal Responses		Subsequent Physical Endurance Task	Control Condition	Cardiorespiratory, Haematological and Metabolic Responses to Endurance Performance	Performance and Perceptual Responses to Endurance Performance
			Muscle Group Involved in Activity	Muscle Group Not Involved in Activity				
Bangsbo <i>et al.</i> (1996)	7 active males	Intermittent bouts of arm cycling exercise at 137 ± 3 W and 60 rpm	Not measured	Not measured	Single-legged supine cycling at ~ 61 W and 60 rpm	Single-legged supine cycling at ~ 61 W and 60 rpm (without prior activity)	<p>\leftrightarrow femoral blood flow and $\dot{V}O_2$ during the task and at task failure</p> <p>\leftrightarrow [ATP], [IMP], [La⁻], arterial and venous [K⁺]</p> <p>\leftrightarrow muscle glycogen utilisation, arterial glucose concentration, adrenaline and insulin</p> <p>\downarrow [PCr], arterial and venous [K⁺]</p> <p>\uparrow b[La⁻] and noradrenaline</p>	\downarrow TTF
Johnson <i>et al.</i> (2014)	7 moderately trained males	8×1 min arm-cycling bouts, interspersed with 30 s rest, at a fixed work-rate of 1.5-2.0 W \cdot kg ⁻¹ body mass. Cadence was 90 – 100 rpm	Not measured	Not measured	Incremental cycling test and constant load cycling task for the determination of CP and W'	Incremental cycling test and constant load cycling task for the determination of CP and W' (without prior activity)	<p>\uparrow cardiorespiratory response at start of task</p> <p>\leftrightarrow S_pO₂ at start of task</p> <p>\downarrow $\dot{V}O_{2peak}$ during incremental task</p> <p>\uparrow HR at task failure in incremental task</p> <p>\leftrightarrow S_pO₂ at task failure in the incremental task. $\dot{V}O_2$, HR and S_pO₂ at task failure in the constant load tasks</p> <p>Extensive changes in ionic and metabolic response to cycling exercise</p>	<p>\downarrow TTF and W_{peak} during incremental task</p> <p>\downarrow TTF during constant load tasks</p> <p>\leftrightarrow CP</p> <p>\downarrow W'</p>

Reference	Participants	Prior Physical Activity	Neuromuscular Function and Corticospinal Responses		Subsequent Physical Endurance Task	Control Condition	Cardiorespiratory, Haematological and Metabolic Responses to Endurance Performance	Performance and Perceptual Responses to Endurance Performance
			Muscle Group Involved in Activity	Muscle Group Not Involved in Activity				
Johnson <i>et al.</i> (2015)	8 moderately trained males	8 × 1 min arm-cycling bouts, interspersed with 30 s rest, at a fixed work-rate of 1.0-1.5 W·kg ⁻¹ body mass. Cadence was 90 – 110 rpm	Not measured	↔ MVC ↔ Q _{tw} ↔ VA	Bi-legged cycling at 85% peak power output and a cadence between 80 – 100 rpm	Bi-legged cycling at 85% peak power output and a cadence between 80 – 100 rpm (without prior activity)	↑ HR at the start and during task ↑ b[La ⁻] at the start of the task	↓ TTF ↔ EMG during task ↓ EMG task failure ↑ RPE and dyspnoea during task ↔ RPE and dyspnoea at task failure
Morgan <i>et al.</i> (2019) ^b	14 active males	Single-leg knee extensions (left leg) at an intensity evoking task failure between 5-8 mins and cadence of 40 rpm	Not measured	Not measured	Single-leg knee extensions (right leg) at an intensity evoking task failure between 5-8 mins and cadence of 40 rpm	Single-leg knee extensions (right leg) at an intensity evoking task failure between 5-8 mins cadence of 40 rpm (without prior activity)	↑ [P _i] and [ADP] at start of task ↓ [PCr] at start of task ↓ [P _i] at task failure ↔ [ADP], [PCr] and pH at task failure	↓ TTF ↑ EMG at start of task ↑ RPE at start of task
Nordsborg <i>et al.</i> (2003)	6 active males	Intermittent bouts of arm cycling exercise at ~140 W and 60 rpm	Not measured	Not measured	Single-leg knee extensions at ~63% leg-specific peak power and 60 rpm	Single-leg knee extensions at ~63% leg-specific peak power and 60 rpm (without prior activity)	↔ [K ⁺] at rest ↑ [K ⁺] during task and at task failure	↓ TTF
Triscott <i>et al.</i> (2008)	24 healthy adults (3 females) split into three groups: sedentary controls, endurance-trained, and resistance-trained	Bicep curls (5.5 kg) of dominant arm	↓ MVC	↔ MVC	Bicep curls (4.5. kg) of non-dominant arm	Bicep curls (4.5. kg) of non-dominant arm (without prior activity)	Not measured	↓ TTF (for controls and resistance-trained)

Reference	Participants	Prior Physical Activity	Neuromuscular Function and Corticospinal Responses		Subsequent Physical Endurance Task	Control Condition	Cardiorespiratory, Haematological and Metabolic Responses to Endurance Performance	Performance and Perceptual Responses to Endurance Performance
			Muscle Group Involved in Activity	Muscle Group Not Involved in Activity				
Zijdewind <i>et al.</i> (1998)	7 healthy adults (4 females)	Sustained abduction of the right index finger at 30% MVC, interspersed with brief MVCs	↓ MVC ↑ SIT	↔ MVC	Sustained abduction of the left index finger at 30% MVC, interspersed with brief MVCs	No control	Not measured	↔ Effort ↔ TTF

MVC: maximal voluntary contraction; Q_{tw} : twitch force; VA: voluntary activation; SIT: superimposed twitch; MRFD: maximal rate of force development; MRR: Maximal rate of relaxation; MEP: motor evoked potential; CSP: cortical silent period; VL: *vastus lateralis*; RF: *rectus femoris*; $\dot{V}O_2$: oxygen uptake; $\dot{V}E$: minute ventilation; $\dot{V}E/\dot{V}CO_2$: ventilatory equivalent of carbon dioxide; HR: heart rate; CO: cardiac output; MAP: mean arterial blood pressure; S_tO_2 : local tissue saturation; S_pO_2 : oxygen saturation; $b[La^-]$: blood lactate concentration; $[La^-]$: muscle lactate concentration; ATP: adenosine triphosphate; ADP: adenosine diphosphate; IMP: inosine monophosphate; P_i : inorganic phosphate; PCr: creatine phosphate; K^+ : interstitial potassium ion; RPE: rating of perceived exertion; EMG: electromyography; W_{peak} : peak power output; CP: critical power; W' : power-duration curvature constant; TTF: time to task failure.

^a In this study a third condition was conducted which examined the effect of pain in the contralateral leg (evoked through blood flow occlusion) on force, neuromuscular and endurance indices. The comparisons presented here exclude this trial and represent just the comparison between the prior activity and control conditions.

^b In this study the effects of the analgesic, acetaminophen, was investigated in a placebo-controlled design. The results reported here represent the effect of the placebo (maltodextrin) intervention only, though there were no differences reported between acetaminophen and the placebo intervention on the effect of prior motor activity (Morgan *et al.*, 2019).

(continued)

Modified perceptual responses to exercise following remote physical activity have typically been attributed to altered total activation of sensory afferents across the whole body (Aboodarda *et al.*, 2020; Amann *et al.*, 2013). For example, Morgan *et al.* (2019) demonstrated that prior activity reduced physical performance and heightened perceptions of effort during the task. In this study, prior activity was shown to increase baseline $[P_i]$ (and $[ADP]$) and reduce the attained peak $[P_i]$ at the point of task failure during protracted activity in the contralateral limb. Activation of sensory muscle afferents have been shown to be particularly sensitive to $[P_i]$, constraining perturbation through a negative feedback loop (Blain, Mangum, *et al.*, 2016; Broxterman *et al.*, 2017; Broxterman *et al.*, 2018). Increased discharge of sensory afferents following prior motor activity, which may play some role in altering the perception of task demands ([section 2.4.2.1.](#) and [2.4.4.](#)), may thus account for the ergolytic effect on subsequent performance (Morgan *et al.*, 2019). However, rather than simply an increased discharge of homeostatic afferent fibres, processing of these homeostatic signals and the formation of a perceived state of fatigue may ultimately account for this effect. This effect may also be observed independently from acute challenges to neuromuscular functionality of the tested muscle group (Aboodarda *et al.*, 2020; Amann *et al.*, 2013; Johnson *et al.*, 2015). Thus, prior physical activity may enable one to dissociate perceptual factors (i.e. subjective fatigue in the present work) from fatigability; enabling an examination of the physical performance within an intact neuromuscular system placed under an induced state of fatigue. This paradigm may therefore help us understand the role of the perception of fatigue in the regulation of performance.

2.8. Concluding Remarks

Central to all fatigue research, within health and disease, is the continued effort to understand the causes and consequences of the subjective experience. Over the past two decades, perspectives on the limits of performance within the exercise have increasingly emphasised the dynamic role of the brain and central regulation in control of behaviour, which due to many prominent models, has increased attention on the subjective perception of fatigue. Yet, for too long, the perception of fatigue has been understudied and often conflated with other perceptual constructs, such as effort, and unclearly related to components of core affect; psychological phenomena that may be disassociated from the perception of fatigue under particular circumstances. Accordingly, our lack of understanding of the effects of a perceived state of fatigue, *per se*, may be considered a key limitation within the understanding of exercise regulation. Clear conceptualisation of distinct percepts alongside the emergence of behavioural paradigms facilitating the isolation of perceptual changes from fatigability may thus provide an opportunity to address this issue.

2.9. Aims and Hypotheses

In consideration of the review of the literature, four experimental studies were conducted which are presented over the experimental chapters of the thesis. The studies sought to examine several key gaps in the literature; first, in relation to the effect of prior motor activity on the neuromuscular function of a remote muscle group, before subsequently examining the effect of a perceived state of fatigue on the central regulation of physical endurance

performance and effort-based choice. The specific title, aims and hypotheses of each individual experimental chapter are detailed below:

CHAPTER 4 – PRIOR HANDGRIP EXERCISE EXERTS LIMITED EFFECTS ON NEUROMUSCULAR FUNCTION OF THE RESTED KNEE EXTENSORS

Aim(s): The aim of this study was to examine whether prior motor activity in the upper body modulated the neuromuscular function of the non-active, dominant knee extensors.

Hypothesis: It was hypothesised that force production, cortical voluntary activation and corticospinal excitability of the knee extensors would be unchanged following prior hand grip activity.

CHAPTER 5 – PRIOR PHYSICAL ACTIVITY IMPAIRS SUBSEQUENT ENDURANCE PERFORMANCE THROUGH ALTERED INTERACTIONS BETWEEN PERCEPTUAL AND AFFECTIVE RESPONSES.

Aim(s): The aim of this study was to investigate the perceptual, affective and behavioural (i.e. performance) response during a sustained contraction of the dominant knee extensors following prior motor activity in the upper body.

Hypothesis: It was hypothesized that prior hand-grip activity would increase the symptom of fatigue, perception of effort and increase negative affect, resulting in impaired performance during the subsequent knee extensor task. Exploratory analyses examining the relationships between perceptual, affective and performance variables were also conducted.

CHAPTER 6 – EFFECT OF THE SUBJECTIVE INTENSITY OF FATIGUE AND INTEROCEPTION ON PERCEPTUAL REGULATION AND PERFORMANCE DURING SUSTAINED PHYSICAL ACTIVITY

Aim(s): The aim of the study was to examine how differing subjective intensities of a perceived state of fatigue, pre-induced through prior motor activity in the upper body, influenced the perceptual, affective and behavioural (i.e. performance) responses during a sustained contraction of the dominant knee extensors. A secondary aim was to explore the moderating effect of interoceptive awareness on the relationship between perceived fatigue and both perceived effort and affective valence.

Hypothesis: It was hypothesized that lower-body endurance performance would be impaired when the intensity of the perceived state of fatigue was greater, with a more severe perceived state of fatigue associated with greater effort and more negative affective valence. In addition, it was hypothesized that individuals' awareness of interoceptive cues would moderate the relationship between the perception of fatigue and the perception of effort and affect reported during the subsequent task.

CHAPTER 7 – EFFECT OF A PHYSICALLY-INDUCED, PERCEIVED STATE OF FATIGUE ON EFFORT-BASED DECISION MAKING

Aim(s): The aim of the study was to examine how a global perceived state of fatigue, evoked by protracted, physically demanding activity in the upper body, influenced the decision to exert effort in the rested knee extensors during a forced choice task.

It was hypothesized that a perceived state of fatigue would influence the evaluation of the costs (e.g. effort) and benefits of action and thus lead to a reduced preference for effortful action during the forced-choice task. This would be accompanied by a reduced confidence in ones' ability to meet effort demands.

CHAPTER 3 - GENERAL METHODS

3.1. Introduction

The following chapter describes the procedures, material, and equipment common to the experimental studies presented within the thesis. Any specific additions, changes and/or modifications may be found in each chapter's respective methods section.

3.2. Ethical Approval

The research presented within this thesis was conducted abiding to the general principles set out by the Declaration of Helsinki, developed by the World Medical Association (WMA) in 1964 and its latest revisions (2013), except for pre-registration within a public database. All research described within this thesis was approved by the University of Brighton Research Ethics Committee, in accordance with institutional policy, prior to participant recruitment.

3.3. Health and Safety Procedures

All experimental procedures described herein conformed to institutional health and safety, and standard operating procedures. Full risk assessments and medical questionnaires ([section 3.5.2.](#)) were completed prior to the start of each research study in order to minimise risk of injury and/or ill-health to both participants and researchers through the use of appropriate control measures. These control measures were agreed upon by the institution's Ethics Committee.

For all experiments conducted, the principal investigator had appropriate training for use of facilities. During sessions, experimentation was immediately terminated if participants requested or displayed signs of disproportionate discomfort or pain, unexpected complaints (e.g. chest pain or muscular injury), nausea or syncope. In such events, participants were closely monitored until symptoms abated, with medical advice sought where appropriate. Participants were fully aware that they could terminate experimentation whenever they so chose without providing a reason.

3.4. Privacy, Confidentiality and Data Management

The research conducted within the present thesis conformed to the Data Protection Act 2018, applying the European Union's (EU's) General Data Protection Regulation (GDPR) law detailing data processing was lawful, fair and transparent. The lawful basis of data processing was 'task in the public interest', operating under the University Charter (Education Reform Act, Universities Scotland Act). The privacy, confidentiality, rights and dignity of participants was respected at all times.

During experimental sessions, the privacy of participants was maintained with screens positioned in front of windows and blinds drawn to obscure views into the laboratory. Signs on doors, indicating testing procedures were in progress, restricted access to the laboratory during experimentation.

The anonymity of participants was ensured through the assignment of a numerical pseudonym. Identifying details were stored separately to anonymised data in accordance with institutional policy. Accordingly, only the principal investigator was aware of an individual's data. Data was stored on an institutional computer, secured by passwords known only to the principal investigator. In addition, back-up copies of data were stored on an external cloud-based service (Microsoft OneDrive), compliant with GDPR, using an institutional account. Paper documentation (e.g. medical questionnaires; written informed consent) was stored in a locked drawer of the principal investigator's office (with restricted access). Collected data is to be stored for a minimum of ten years before being destroyed as confidential waste, as per institutional policy.

All participants were explicitly informed that any data collected would only be used for the intended research purposes and that they were able to view their personal data at any point upon request. All participants consented to the potential use of any collected data for the intended research purposes, even in the event of withdrawal (see informed consent; [section 3.5.3](#)). If following the completion of individual medical questionnaires and informed consent, participants did not meet inclusion criteria or participants withdrew before collection of data for the intended research purpose, personal data was immediately destroyed.

3.5. Participants

3.5.1. Recruitment

Individuals were recruited from the local student body and the wider general population of the surrounding area. All studies were advertised through posters and/or email, both providing a brief description of the aims and/or purpose of the study, along with the principal investigators contact details. Individuals were not obligated to respond and did so voluntarily. Individuals registering interest in the study, were issued with a study-specific participant information sheet, providing a full lay description of the rationale, procedures, requirements (including inclusion and exclusion criteria; [section 3.5.2](#)), and the risks and benefits of participation. Accompanying the participant information sheet, copies of study-specific medical questionnaires were also issued for participants to fully consider their involvement. All interested parties were afforded a minimum of 24 hours to fully consider whether they would like to volunteer within the presented research study. Additionally, the contact details of a senior researcher, who was not directly involved in the research project, was provided to all prospective participants offering impartial advice if sought.

No undue coercion, inducement, pressure or influence was exerted to force participation. Where reimbursement was provided (see [chapter 7](#)), the total amount paid was standardised, calculated to recompense participants' time. That is, the total was derived from the estimated study duration and the current UK national minimum wage (for over 25-year-olds). Payment was provided in the form of gift vouchers, redeemable at various stores online and across the UK (One4all: www.one4all.com). Where appropriate, participants were aware that they would receive a monetary reward with their involvement, though details about the specific amount was not specified. Payment

structure was presented to and agreed by the Ethics Committee. Advertisement of prospective payments for participation conformed to the NHS Health Research Authority (HRA) ethical guidelines.

3.5.2. Inclusion and Exclusion Criteria

All volunteers were screened for study-specific participation eligibility. Common inclusion criteria across the presented research studies included:

- Male;
- Aged between 18-50 years old.

Volunteers were presented with study-specific medical questionnaires which assessed health contraindication to participation. Volunteer's responses to the questions on the issued medical questionnaire and informed consent forms determined participant exclusion. Common exclusion criteria included:

- The volunteer did not provide consent to one or more of the questions outlined on the informed consent form;
- The volunteer answered 'yes' to a questionnaire on the general medical questionnaire. Physical (including blood carried infections, obesity, haematological, cardiac, respiratory, neurological and musculoskeletal disorders) and mental health were assessed;
- The volunteer had a diagnosed learning disability which may have prevented full comprehension and/or fulfilment of the task requirements and procedures;
- The volunteer was currently participating in another study or remained in the wash-out period following participation.

For specific procedures, individuals were screened for contraindications based on recommended guidelines. For example, in [chapter 4](#), contraindications to TMS additionally determined exclusion, with volunteers omitted if they answered 'yes' to one or more of the following questions, devised by international consensus guidelines for repetitive TMS (rTMS) candidates (Rossi *et al.*, 2009; Rossi *et al.*, 2011):

- Do you have epilepsy, or have you ever had a convulsion or a seizure?
- Have you ever had a fainting spell or syncope? If yes, please describe on which occasion(s)?
- Have you ever had a head trauma that was diagnosed as a concussion or was associated with loss of consciousness?
- Do you have any hearing problems or ringing in your ears?

- Do you have cochlear implants?
- Are you pregnant or is there any chance that you might be?
- Do you have metal in the brain, skull or elsewhere in your body (e.g. splinters, fragments, clips, etc.)? If so, specify the type of metal?
- Do you have an implanted neurostimulator (e.g. DBS, epidural/subdural, VNS)?
- Do you have a cardiac pacemaker or intracardiac lines?
- Do you have a medication infusion device?
- Are you taking any medication? (Please list)
- Have you ever undergone TMS in the past? If so, were there any problems?
- Have you ever had an MRI scan in the past? If so, were there any problems?

3.5.3. Informed Consent

Following the issuing of the participant information sheet and medical questionnaire, prospective participants were provided the opportunity to discuss any outstanding questions relating to the study and their involvement with the principal investigator prior to enrolment. Participants were explicitly informed that all data collected would only be used for the intended research purposes and that it was their right to withdraw from the study at any point, without need to provide a reason and without penalisation. For students, it was explicitly stated that participation and/or withdrawal would have no impact upon their standing within the University. Once satisfied, prospective participants were asked to provide written consent stating they agree to the procedures outlined to them. At this point, individuals were enrolled onto the respective study and became participants.

3.6. Deception

Where necessary, aspects of part of the studies were withheld from the participant (see [chapter 7](#)). However, participants were never deliberately deceived about the overall purpose of a research study. Deception was only used when integral to answering the proposed research question. Instances of deception were used only when there was minimal risk of participants becoming distressed through deception discovery, with protection of the dignity and autonomy of the participant paramount at all times. Participants were fully debriefed about the use of any deception at the end of the respective period of experimentation. Deception protocols were submitted to the appropriate Tier 2 (CREC) institutional ethic review, with all procedures agreed by the Ethics Committee.

3.7. Location of Data Collection

Data collection was conducted at the Welkin Laboratories at the University of Brighton (Eastbourne, UK). Experimentation was performed at various periods throughout a calendar year but was generally conducted during the summer months (June-September).

3.8. Pilot Work

Pilot work was principally used to establish appropriate parameters for specific procedures and/or measures (e.g. contraction intensity) used within the described studies, where required. It also provided an opportunity for the principal investigator and research assistants to become familiar with the procedures used, including individual roles and the sequential and temporal properties of the experimental protocol as a whole. Participants partaking in pilot work were subject to the same enrolment procedures described in the previous sections of this chapter.

3.9. Experimental Controls

Experimental controls were implemented for each of the presented studies in order to minimize extraneous influences upon recorded measurements. Participants were asked to abstain from any generic, habitual supplementation throughout the duration of their involvement with a particular study. Participants were also asked to attend the laboratory in a rested state following at least 6 hours sleep and 2 hours postprandial. They were also asked to refrain from strenuous exercise and the consumption of both caffeine (Bowtell *et al.*, 2018; Graham, 2001) and alcohol (El-Sayed *et al.*, 2005) in the 24 hours prior to attending the laboratories. The half-life of single doses of caffeine (4 mg/kg) have been shown to average between approximately 2.5-5 hours, with the half-lives of caffeine's metabolites (e.g. theophylline, theobromine) slightly longer (~6-7 hours) (Arnaud, 2011). The average metabolism of alcohol has been estimated to be 7g/hr^{-1} (Cerderbaum, 2012). Participants were asked to replicate dietary habits during the 24 hours preceding each experimental visit. Each individual's experimental sessions were also performed at the same time of day (± 2 hours) to control for potential diurnal variation on cortical and spinal excitability (Tamm *et al.*, 2009), maximal force production (isometric knee extension: Guette *et al.*, 2005; K  usmaa *et al.*, 2015; Edwards *et al.*, 2013; handgrip: Reilly *et al.*, 2007; Souissi *et al.*, 2010), cortical inhibition (Doeltegen & Ridding, 2010; Lang *et al.*, 2011), subjective fatigue (Micklewright, St Clair Gibson, *et al.*, 2017) and other psychophysiological responses (perceived exertion/effort: Ezagouri *et al.*, 2019; Thosar *et al.*, 2018; affective valence: Eaton & Funder, 2001). In addition, performance fatigability may be subject to the influence of diurnal variations, associated with acrophases of (muscle) cellular functions (see Chtourou *et al.*, 2013). All participants were instructed to wear shorts and a short-sleeved top during experimental sessions. All laboratories contained programmable air conditioning, with ambient temperature set to be maintained at 18°C with a constant air flow direction. Relative humidity was not controlled but typically measured between 40-50%.

3.10. Familiarisation

All presented studies were preceded by a preliminary familiarisation session, to accustom participants to procedures and measures used within the experimental sessions and minimize the potential influence of learning effects. Typically, the familiarisation sessions mirrored the study-specific control protocol. Data collected during this session was not used within the analysis of the respective study unless stated otherwise.

3.11. The Perception of Fatigue

Subjective experiences of (state) fatigue were assessed using the 11-point rating of fatigue (RoF) scale (Micklewright, St Clair Gibson, *et al.*, 2017). The definition of fatigue used in the creation of this scale was a “*feeling of diminishing capacity to cope with physical or mental stressors, either imagined or real*” (Micklewright, St Clair Gibson, *et al.*, 2017). The scale was used to evaluate subjective, global feelings of fatigue at a given moment in time. The scale ranged from 0 (*‘not fatigued at all’*) to 10 (*‘total fatigue & exhaustion – nothing left’*). Descriptors and diagrams anchored rating bands (i.e. 2-3: *‘a little fatigued’*; 4-6: *‘moderately fatigued’*; 7-8: *‘very fatigued’*). The scale has been shown to have good face validity and high divergent validity from other related, but distinct, perceptual constructs (e.g. perceived effort) (Micklewright, St Clair Gibson, *et al.*, 2017). Standardised instructions were presented to participants as per the authors recommendations (Micklewright, St Clair Gibson, *et al.*, 2017), except for rating examples that referenced feelings associated with sleepiness or experiences upon waking, to clearly distinguish perceived fatigue from feelings associated with sleepiness (Pigeon *et al.*, 2003). These were replaced with examples relating to physical exhaustion. Further instructions were provided to the participants that described the difference between the feeling of fatigue and the perception of effort.

3.12. The Perception of Effort

Effort was defined as “*the conscious sensation of how hard, heavy and strenuous exercise is*” (Marcora, 2010). Effort perception was assessed using a category-ratio scale (Borg CR10; Borg, 1982). Experiential anchors were used to anchor the scale, with 0 representing *no effort* and 10 the strongest KE contraction previously experienced (*max effort*). Participants were provided general and complementary instructions as per the recommendations of the scales’ creators prior to its administration in experimental sessions (Borg, 1998). Participants were able to provide decimal responses if they so required. Previously, the test-retest reliability of the CR10 has been shown to be excellent (ICC >0.8; Ljunggren & Johansson, 1988; Bove *et al.*, 2016; Shariat *et al.*, 2018) The instructions provided explicitly stated that ratings of perceived effort should be independent of other somatic sensations, including feelings of pain, which may emerge from distinct neural processes (Marcora, 2009; Smirmaul, 2012). Effort ratings were collected at various stages throughout the performance tasks in order to capture changes in perceptual responses to investigated motor tasks.

3.13. Affective Valence

Changes in mood hedonicity were assessed using the Feeling Scale (FS; Rejeski *et al.*, 1987; Hardy & Rejeski, 1989). The FS is an 11-point (+5 to -5) scale which captures the degree of pleasurable (positive integers) and unpleasurable mood states (negative integers), either side of neutral affect (0). Descriptors are provided at all odd integers. Standard instructions were provided to all participants prior to experimentation, as described by Hardy and Rejeski (1989). Extreme ends of the scale were anchored based on experiential factors. The FS was administered at various points during the motor performance tasks to assess fluctuations in affective valence in response to physical exertion. Little data is currently available illustrating the test-retest reliability of the FS across multiple sessions. However, the average response to the FS recorded during moderate-intensity, submaximal exercise has been indicated to be good (ICC = 0.76) (Unick *et al.*, 2015).

3.14. Motor Performance Tasks

3.14.1. Isometric Knee Extension Endurance Task

In *chapters 5-7*, motor performance of the lower limbs was assessed through a sustained contraction of the dominant knee extensors (KE) at 20% MVC (Neyroud *et al.*, 2012; Pageaux *et al.*, 2013). The task was performed until volitional exhaustion (i.e. self-termination) or an inability to reach the required force level for longer than 3s. Participants were completely naïve to the criteria of task failure and the elapsed time. Moreover, no verbal encouragement was provided during the task. Intersession reliability of this performance measure has previously been reported to be moderate-to-good (ICC = 0.64 – 0.96) (Clark *et al.*, 2007; Mathur *et al.*, 2005; Rochette *et al.*, 2003).

3.14.2. Handgrip Task

The handgrip (HG) task was adopted as an intervention in *chapters 4-7* and thus was not specifically assessed for the analysis of performance primarily. The protocol was adapted from that first described by Gruet *et al.* (2014) in the KE. The HG task was performed bilaterally, consistent with Kennedy *et al.* (2013), and consisted of repeated sequences of submaximal and maximal grip contractions. Each sequence contained a sustained sub-maximal contraction, held at 30% MVC for 15 s, followed immediately (i.e. no rest) by a MVC held for 5 s. Termination criteria was determined by the specific study's purpose.

3.15. Force production

All quantification of force data was recorded using a commercial data acquisition system (PowerLab 15T and 26T, ADInstruments, Oxfordshire, UK) and associated analysis software (LabChart v7.0, ADInstruments). Visual feedback of specific functional features (e.g. force) were provided on a 19" LCD computer monitor positioned directly in front of the participant.

3.15.1. Handgrip Force

Grip force was recorded using a pre-calibrated HG transducer (MLT004/ST, ADInstruments, Colorado, USA). The transducer has a linear response across a range of 0-800 Newtons (N). Participants held the transducer with a standardised grip posture: with fingers wrapped around the front of the transducer and the thumb placed above the rested fingers. Participants' forearms were strapped across the forearm and wrist, in a supinated position, to a custom table positioned directly in front of the participants ([Figure 3.1.](#)).

Force measurements prior to experimental intervention (i.e. pre-assessments) were preceded by a standardised warm-up, consisting of four bilateral handgrip contractions at 25%, 50% and 75% of perceived maximal force (Kennedy *et al.*, 2013). Fifteen seconds of rest separated contractions of a given intensity, with 1 minute of rest separating each level of force.

3.15.2. Knee-Extensor Force

Voluntary and evoked force of the lower-limb was recorded using a calibrated load cell ([chapters 4-5](#): Model 615, Vishay Precision Group, Basingstoke, UK; [chapters 6-7](#): Model 151/152 S-Beam, Honeywell, Minnesota, USA). The S-Beam load cell has an accuracy of $\pm 0.03\%$ across the full scale. Calibration of loads cells consisted of applying known weights of <1 – 85-90 kg, with regression analysis used to convert the raw voltage signal to N. Load cells were connected to a single channel bridge amp ([chapters 4-5](#): Type 132-C, Datum Electronics, Isle of Wight, UK; [chapters 6-7](#): FE221, ADInstruments). The load cell was attached to a custom-built, adjustable chair, and secured to the lower leg via a cuff fastened slightly superior (2-4 cm) of the lateral malleoli. The position of the load cell was adjusted both vertically and horizontally to align it directly behind the line of force production.

Participants sat upright on the high-back chair, with hip and knee angles set at 90° (0° = full extension). The upper torso was secured to the back of the chair via two noncompliant cross-over shoulder straps, minimizing extraneous movement of the upper body, while a cervical neck brace was used to constrain movements of the head ([Figure 3.1.](#)).

All experimental force recordings were preceded by the same standardised warm-up described in [section 3.15.1.](#) but replicated in the lower limbs, with the warm-up protocol for the KE always performed after the HG warm-up.

3.15.3. Electromyography

Surface electromyography (EMG) was recorded from specific muscles of the *quadriceps femoris* within [chapters 4-6](#). Pairs of self-adhesive hydrogel surface Ag/AgCl electrodes (33 x 22 cm; H59P, Kendall Massachusetts, USA) were positioned in a bipolar recording configuration over the specified muscle belly, as per SENIAM guidelines (Hermens *et al.*, 2000). Minor adjustments were permitted based on visual inspection of the raw EMG signal. For repeated measures, measurement positions were recorded and replicated exactly during each subsequent session. Interelectrode distance was ~ 2 cm. A reference electrode was positioned on an electrically inactive site (e.g. the ipsilateral patella). The skin-electrode interface was prepared by shaving the area, lightly abrading and cleansing

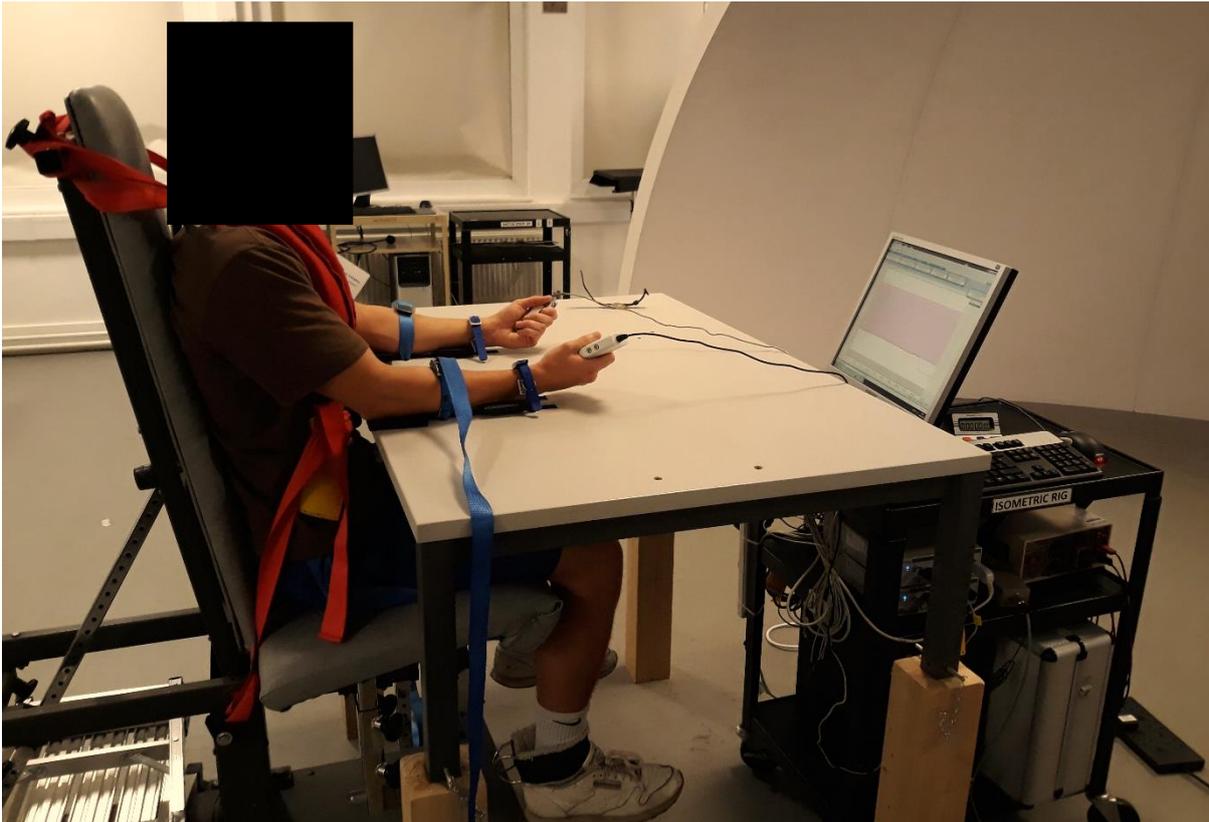


Figure 3.1. Example of experimental set-up during force recordings.

with isopropyl alcohol to minimize electrical resistance (Hermens *et al.*, 2000). Noise generating equipment were turned off where appropriate and located as far away from the electrodes, cables and amplifier as possible. Cables were secured to minimize movement artefacts. EMG signals were sampled at 4 kHz, amplified (gain x1000) and filtered using a digital band-pass filter (20-2000 Hz). The high-pass frequency was set at 20 Hz based on established recommendations, particularly for isometric contractions (Stegeman & Hermens, 1998; De Luca *et al.*, 2010). Surface EMG was used to record neural activation, frequency shifts and the amplitude of magnetically and electrically evoked potentials.

3.16. Perceptual and Psychological Confounds

When evaluating the subjective feeling of fatigue and its influence on behaviour, participants were also screened for potentially confounding perceptual and psychological factors ([chapters 6-7](#)). Identified confounds included sleepiness, depression, anxiety, and stress. These confounds were assessed at the beginning of the experiments (for trait variables) or at the beginning of individual experimental sessions (for state variables), using the following instruments.

3.16.1. Sleepiness

State sleepiness, defined here as the present propensity to sleep, was assessed using the Karolinska sleepiness scale (KSS) (Åkerstedt & Gillberg, 1990). The KSS is a 9-point scale, with responses (1-9) describing participants' current state of sleepiness. Anchors ranged from '*extremely alert*' (1) to '*extremely sleepy – fighting sleep*' (9), with additional descriptors presented at every other integer. The KSS has been shown to be highly correlated with both behavioural and electroencephalographic (EEG) indicators of sleepiness (Åkerstedt & Gillberg, 1990; Kaida *et al.*, 2006). Due to the sensitivity of ratings to preceding contextual factors, including time of previous sleep, duration of sleep, social interaction, physical activity and even light (see Åkerstedt *et al.*, 2014), establishing the test-retest reliability of the KSS has proven difficult (Shahid *et al.*, 2012). Here, sleepiness was recorded prior to and upon completing the experimental procedures within a session.

3.16.2. Depression, Anxiety and Stress

The short-form of the depression, anxiety and stress scale (DASS) was used to assess symptoms experienced by participants over the last week (Lovibond & Lovibond, 1995). The short-form of the DASS is a 21-item instrument, with each item rated using a 4-point scale (0 = '*Did not apply to me at all*', 1 = '*Applied to me to some degree, or some of the time*', 2 = '*Applied to me a considerable degree, or a good part of the time*', and 3 = '*Applied to me very much, or most of the time*'). Depression, anxiety and stress scores were obtained by through the summing the responses provided for the 7 items of that construct. Principal component analysis has demonstrated the DASS is capable of distinguishing the different constructs, with three factors emerging from the analysis, while confirmatory factor analysis demonstrated improved model fit when using a three factor model in a healthy population (Lovibond & Lovibond, 1995). Further analysis supports the contention that the DASS (short-form) holds stable reliability and good discriminant and nomological validity (e.g. Lee, 2019). Importantly, the short-form of the DASS has been shown to be a valid and reliable measure of depression, anxiety and stress in non-clinical populations (Henry & Crawford, 2005).

3.17. Anthropometry

Body mass was measured to the nearest 0.1 kg using a mechanical physician scale with a maximal capacity of 140 kg (Detecto, Missouri, USA). Participants were measured unshod, with minimal clothing. Stature (cm) was also measured, using an attached stadiometer, to the nearest 0.5 cm (Detecto, Missouri, USA). Participants were asked to stand fully erect, with the soles of their feet on the base of the stadiometer. The height rod was then lowered to sit on the vertex of the skull, compressing the hair.

3.18. Hand and Leg Dominance

Handedness and leg dominance was determined prior to experimentation using the Edinburgh handedness inventory (Oldfield, 1971). Participants were asked to indicate their hand preference on 10 manual tasks.

Participants could indicate a strong preference for one hand or an indifference for one hand for any given task. Leg dominance was determined through participants' response to one item, evaluating which "foot the participant prefers to kick (e.g. a football) with?" (Oldfield, 1971).

3.19. Statistical Analysis

Statistical procedures were performed using Statistical Package for the Social Sciences (SPSS Inc., v.25, Chicago, IL) ([chapter 4-5](#)) and jamovi (The jamovi project, 2020) ([chapters 6-7](#)), unless stated otherwise. The main statistical analysis procedures used within the thesis are briefly described within this section. More specific descriptions of the statistical analysis performed within each individual study is present in each respective chapter.

3.19.1. Power Analysis

A priori sample size calculations were performed for each study. Sample size calculations were performed based on $\alpha = 0.05$ (representing the probability of committing a type I error, i.e. falsely rejecting a true null hypothesis) and $1-\beta = 0.8$ (with β representing the probability of making a type II error, i.e. falsely accepting a false null hypothesis) as per recommended guidelines (Prajapati *et al.*, 2010).

3.19.2. Descriptive Statistics

3.19.2.1. Central Tendency

For parametric analyses, the centre of a frequency distribution was modelled using the mean. This represents the average score. The mean was calculated using *equation 3.1*.

$$\bar{X} = \frac{\sum_{i=1}^n X_i}{N}$$

(3.1.)

For non-parametric analyses, the central tendency was modelled using the median (*Mdn*) – the middle score of the data set.

3.19.2.2. Dispersion of Data Sets

The variance in recordings within data sets is the average error between the mean and the observations. Standard deviation (*SD*) is the square root of the average squared deviances (variance) within each data set. *SD* was used to describe the variation in parametric analyses.

$$SD = \sqrt{\frac{\sum_{i=1}^n (X_i - \bar{X})^2}{N - 1}} \quad (3.2.)$$

For non-parametric analyses, the variation was described through the interquartile range (*IQR*) of the dataset, detailing the range in which the middle 50% (i.e. first quartile subtracted from the third quartile) of an ordered set of observations falls.

3.19.3. Statistical Tests of Differences

3.19.3.1. Paired-samples *t*-test

Statistical comparison of the means of two datasets was performed using a *t*-test. Due to the repeated measures experimental designs of the presented thesis, paired-samples *t*-tests were performed. This compares the mean difference between sample datasets (\bar{D}) against the difference expected between population means (μ_D), while accounting for the standard error of the differences (s_D/\sqrt{N}). If the null hypothesis is true, the difference between the population means is expected to be 0 ($\mu_D = 0$):

$$t = \frac{\bar{D} - \mu_D}{s_D/\sqrt{N}} \quad (3.3.)$$

Where data violated the assumption of normality ([section 3.19.6.](#)), Wilcoxon signed-rank test was used to examine differences between the two-sample means. The Wilcoxon signed-rank test is a non-parametric equivalent of the paired-samples *t*-test, which compares the location of a sample based on the summed total rank-scores.

3.19.3.2. Repeated Measures Analysis of Variance (ANOVA)

Comparison between the means of more than two within-participant datasets was performed using an analysis of variance (ANOVA). The effect of multiple independent variables on a single dependent variable was specifically assessed using a factorial repeated measures ANOVA (specific model parameters are presented in each specific

experimental chapter). ANOVA compares the ratio of the systematic variance (i.e. explained by the general linear model fitted to the effects/groups investigated) to the unsystematic variance (i.e. error), known as the *F*-ratio. Significant main effects or interactions in factorial designs were followed up with pairwise comparisons adjusted using Bonferroni corrections to minimize the inflation in familywise error rate with multiple comparisons.

ANOVAs do not deal well with missing and/or unbalanced data. Alternative options (i.e. linear mixed-effects models and generalised linear mixed-effects models) were thus sought in such circumstances present within the thesis (see [chapters 6-7](#)).

3.19.4. Statistical Tests of Relationships

Bivariate Pearson correlation coefficients (*r*) were computed to assess the strength of relationship between two variables. The correlation coefficient reflects the averaged sum of combined deviations (i.e. covariance) of two (*x*, *y*) variables divided by their combined *SD*, expressed in standardised units:

$$r = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{(N-1)SD_x SD_y} \quad (3.4.)$$

When assumptions of normality were violated ([section 3.19.6](#)), the non-parametric Spearman's correlation coefficient (*r_s*) based on ranked data was used. Coefficient statistics range between 1 and -1, with strong positive associations between two variables being closer to 1 and strong negative associations being closer to -1. Weak relationships between variables are expressed when the *r*-statistic is close to zero.

Repeated measures correlations were also used in the present thesis ([chapters 5](#) and [6](#)). Incorporation of repeated measures correlation enabled the evaluation of the association between paired variables recorded on multiple occasions, whilst preventing a violation of the assumption of independence (Bakdash & Marusich, 2017; Bland & Altman, 1995). The implemented analysis of the repeated measures correlation is estimated from an atypical form of analysis of covariance (ANCOVA), controlling for the effect of the categorical variable (i.e. the between-participant variance), rather than the effect of a second, nuisance continuous variable (Bakdash & Marusich, 2017).

3.19.5. Statistical Moderation and Mediation

Moderation ([chapter 6](#)) and mediation ([chapter 8](#)) were examined in the present thesis. Moderation analysis evaluates whether the combined effects of two variables impacts another (i.e. an interaction effect). That is, whether a moderator (B) variable influences the relationship between a predictor (A) and an outcome variable.

$$\text{outcome variable} = (b_0 + b_1A_i + b_2B_i + b_3AB_i) + \varepsilon_i$$

(3.5.)

Mediation analysis examines whether the relationship between a predictor and outcome variable can be explained through their relationships with a third variable. Mediation is generally indicated if the strength of the relationship between the predictor and outcome variable is reduced when including the mediating variable.

3.19.6. Assumptions of Tests

The assumption of normality was formally assessed using the Shapiro-Wilk test (Shapiro & Wilk, 1965). Histograms were also visually inspected, and $Q-Q$ plots considered. For repeated-measures ANOVA, the assumption of sphericity (i.e. that variances of the differences between conditions are equal) for three or more conditions was assessed using Mauchly's test of sphericity (Mauchly, 1940). When the test statistic was significant at $p < 0.05$, a correction was applied. For estimates of sphericity < 0.75 the Greenhouse-Geisser method was applied (Greenhouse & Geisser, 1959). Above 0.75, the Huynh-Feldt estimate was applied (Huynh & Feldt, 1976).

3.19.7. Effect Sizes

Effect sizes were calculated and reported within the present thesis in order to provide a standardised measure of the magnitudes of reported effects. For pairwise comparisons, Cohen's d_{av} (Lakens, 2013) was used to describe the standardised mean difference of the effect of parametric analyses. For non-parametric analyses, the effect was converted to its r -equivalent:

$$r = \frac{z}{\sqrt{N}}$$

(3.6.)

The size of the main and interaction effects calculated through ANOVA are presented as partial eta squared (η_p^2).

CHAPTER 4 - HANDGRIP EXERCISE EXERTS LIMITED EFFECTS ON NEUROMUSCULAR FUNCTION OF THE RESTED KNEE EXTENSORS

4.1. Abstract

The ability of a muscle or muscle group to produce force is impaired in response to the performance of demanding physical activity. Beyond a local event within the active muscle(s), there is evidence that impairment to force production may also occur within non-active muscle(s) across the body, though this effect is currently equivocal. The aim of present study chapter was to evaluate whether demanding motor activity in the upper body influenced neuromuscular function and corticospinal excitability in the lower limbs. Fifteen healthy males completed a control task (i.e. passive rest) and an intermittent handgrip (HG) task, performed in a non-randomized order. Before and after each intervention, voluntary force and evoked responses to transcranial magnetic stimulation (TMS) and electrical femoral nerve stimulation (FNS) were recorded to assess neuromuscular function of the dominant knee extensors (KE). The change in maximal voluntary force (MVC), cortical voluntary activation (VA_{TMS}) and twitch force (Q_{tw}) was not different between the control and HG tasks. However, tests of equivalence indicated that changes exceeded predefined bounds. Small condition-based effects indicated that MVC, VA_{TMS} and Q_{tw} were reduced in the HG condition compared to the control condition. However, differences between conditions were evident pre-intervention (MVC and Q_{tw}) and these differences were within previously reported error for these measures (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). This suggested that the HG task itself was unlikely to be responsible for these effects. Corticospinal excitability of the KE was also unaffected by the HG task. In sum, the findings are cautiously interpreted to indicate that remote upper body physical activity exerts little effect on the neuromuscular function and corticospinal excitability of the non-active lower limbs. The findings suggest that prior remote physical activity may provide a paradigm to assess the effect of an activity-induced state of perceived fatigue within an intact neuromuscular system.

4.2. Introduction

In response to sustained or repeated physical activity, a progressive decline in the capacity of the active muscle or muscle groups to produce force is observed (Place *et al.*, 2010; Taylor *et al.*, 2016). The decline in force production may be attributed to factors of peripheral and/or central origin (Bigland-Ritchie & Woods, 1984; Gandevia, 2001; [section 2.2.2.4.](#)). Task demands are also perceived as more effortful, which is often posited to be *the* principal feature of the subjective experience of fatigue (Enoka & Stuart, 1992; Marcora, 2019). A heightened perception of effort in response to motor fatigability is believed to be evoked by an increased corollary discharge of motor commands processed by the somatosensory cortex in compensation for progressively less responsive or weaker muscles (Marcora *et al.*, 2008; [section 2.4.3.2.](#)). Accordingly, there is a coupling between fatigability and perceptual changes to ‘fatiguing’ physical activity. To identify how a perceived state of fatigue specifically influences sensory processing and performance during sustained physical tasks - the aim of the present thesis - there is therefore a need to try and disassociate subjective changes from activity-induced motor fatigability. Using prior physical activity in one part of the body to examine the effects of a perceived state of fatigue on another, in which neuromuscular function may be left unaffected (Aboodarda *et al.*, 2020; Amann *et al.*, 2013; Johnson *et al.*, 2015), presents a potential paradigm that may achieve this aim. However, there remains uncertainty regarding whether demanding physical activity generates not just local effects within the active muscle, but systemic effects, indicating a transfer of fatigability across non-active muscle groups (Halperin *et al.*, 2015; [section 2.7.2.4.](#)).

Presently, the mechanism(s) supporting potential systemic effects are not well understood ([sections 2.7.2.2.](#) and [2.7.2.3.](#)). While transcallosal-mediated interhemispheric inhibition is proposed to mediate effects across contralateral, homologous muscles (Bäumer *et al.*, 2002; Takahashi *et al.*, 2009), the mechanisms of transfer between heterologous muscle representations of the upper and lower body is less clear. Neural coupling between the upper and lower extremities (Huang & Ferris, 2009) suggests a common neural circuitry which may facilitate fatigability across the upper and lower body. Indeed, stimulation of metabo-sensitive afferent receptors by activity performed in one part of the body (e.g. within the lower limbs) may activate inhibitory circuits upstream of M1, initiating a cascade of inhibitory processes that serves to limit motor output in another (e.g. in the upper body) (Sidhu *et al.*, 2014). Alternatively, spread of inhibitory processes across the motor cortex itself has also been postulated as another possible explanation (Takahashi *et al.*, 2011). However, evidence of activity-induced reductions in maximal force in both contralateral homologous (Aboodarda *et al.*, 2016; Doix *et al.*, 2013; Doix *et al.*, 2018; Rattay *et al.*, 2006; Triscott *et al.*, 2008) and heterologous muscle groups (Aboodarda *et al.*, 2015; Aboodarda *et al.*, 2017; Halperin, Copithorne, *et al.*, 2014; Šambaher *et al.*, 2016; Sidhu *et al.*, 2014) is currently equivocal. Moreover, contrasting excitatory and inhibitory influences on the excitability of corticospinal tract have also been reported (e.g. Aboodarda *et al.*, 2017; Šambaher *et al.*, 2016). Thus, examination of this effect requires further endeavour.

This study chapter therefore examined whether remote activity in the upper body modulated neuromuscular function in the rested dominant knee extensors (KE). The study was performed in male participants; thus, the studied muscle (i.e. within the lower limbs) plus the selected population were chosen to limit potential confounding factors previously identified and provide optimal conditions to observe an effect (Halperin *et al.*, 2014; Ye *et al.*, 2018; [section 2.7.2.4.](#)). Though effects of locomotor muscle activity on the corticospinal responses

in the upper body have been assessed previously (Aboodarda *et al.*, 2017; Šambaher *et al.*, 2016; Sidhu *et al.*, 2014), the same effects in the lower body following upper body activity have not. This therefore provided an opportunity to examine an important gap in the current literature. It was hypothesised that force production, cortical voluntary activation and corticospinal excitability of the non-active KE would be unchanged following HG activity.

4.3. Method

4.3.1. Sample Size Calculation

Commercial methods for calculating sample size estimates for factorial repeated measures ANOVA are sparse. Accordingly, a simulated power analysis was performed using the Superpower Shiny app (see Caldwell *et al.*, 2019). A 2 x 2 within-subjects design was defined with factors condition (HG, control) and time (pre-, post-intervention). There is also a dearth of studies investigating NLMF in the desired direction (i.e. from upper to lower body) and/or providing sufficient data, making deriving appropriate estimates difficult. The power analysis was performed based on the findings of Kennedy *et al.* (2013), who examined the effect of bilateral HG activity on plantar flexor force production, comparing the impact of sub-maximal and maximal force production (observed effect size: $\eta_p^2 = 0.417$). The authors report the relative (i.e. percentage) change in force production from pre-intervention assessments. The interaction between condition and time on force production was the main effect of interest. Assuming a conservative correlation among within-participant factors of 0.5, 2000 Monte Carlo simulations were run to assess power. To achieve a $1-\beta > 0.80$ for the interaction effect and follow-up Bonferonni-adjusted pairwise comparison post-exercise required a minimum sample size of 7. However, given the estimated effects were based on force expressed relative, it was assumed that power would be lower when using absolute values. Accordingly, the minimum participant recruitment goal was roughly doubled to potentially account for this fact and possible participant drop-out.

4.3.2. Participants

Ethical approval ([section 3.2.](#)) was granted in conjunction to the application submitted for [chapter 5](#) (Ref: SSCREC18-09). The two chapters were conducted in concert, with the sample recruited for this experiment representing a sub-sample of those who volunteered to take part in [chapter 5](#). Fifteen healthy participants (25 ± 4 years; weight: 81.1 ± 9.9 kg; height: 1.82 ± 0.07 m; 13 right-handed, 12 right-legged) agreed to take part in the present experiment. All participants provided written informed consent ([section 3.5.3.](#)) and screened negative for contraindications to transcranial magnetic stimulation (TMS) (Rossi *et al.*, 2011; [section 3.5.2.](#)).

4.3.3. Experimental Design

Experimental controls were implemented as described in [section 3.9](#). Participants were familiarised to the measures, equipment and protocols during a familiarisation session common to both the present experiment and

[chapter 5 \(section 3.10.\)](#). The main experiment comprised of a single trial, conducted at the same time of day (\pm 2 hours) as individual trials performed in [chapter 5](#). At the beginning of the trial, a standardised warm-up and assessment of maximal voluntary force for both the HG and KE was performed as described in [sections 3.15.1.](#) and [3.15.2.](#)

Assessment of neuromuscular function and corticospinal excitability was performed on the dominant KE before and after (10s) a control condition (i.e. passive rest) and the HG task ([section 3.14.2.](#)). To standardise the duration between the HG task and the control condition, participants performed the HG task for the same number of successfully completed contraction sequences achieved during the preliminary familiarisation session. In the familiarisation session, the HG task was performed until task failure (voluntary force below 30% MVC for >2 s) in the dominant hand (mean duration: 308.0 ± 96.0 s; range: 140–470 s; 11 ± 3 repetitions). Participants were unaware of the exact number of contraction sequences to be performed during the experimental HG task. The two conditions were performed in a constant order for all participants, with the control condition preceding the HG task. A visual schematic of the experimental design is presented in [Figure 4.1.A](#). Strong verbal encouragement was provided throughout, with participants strictly instructed to relax their legs throughout the HG task (average VL EMG <0.03 mV). Visual feedback of force production was presented on a computer monitor positioned directly in front of the participants.

4.3.4. Knee Extensor Neuromuscular Function Assessment

A neuromuscular fatigue assessment (NMFA) protocol was conducted before and after the control condition and the HG task ([Figure 4.1.B](#)). The quantification of force ([sections 3.15.1.](#) and [3.15.2.](#)) and recording of EMG in the *vastus lateralis* (VL) and *biceps femoris* (BF) ([sections 3.15.3.](#)) are described in detail in [chapter 3](#). The NMFA began with a 30-s KE contraction performed at an absolute force output of 20% of baseline MVC ($20\%_B$). This equated to 126.5 ± 18.6 N. Six TMS pulses were delivered during this sustained contraction, one every 4s. In addition, a single femoral nerve stimulation was applied at the end of the contraction. Following a brief rest (5s), two series of six contractions were then performed, each comprising: 1) an MVC with superimposed TMS; 2) an MVC with FNS superimposed and applied immediately after the contraction (~ 2 s delay); 3) four submaximal contractions performed sequentially at 50%, 87.5%, 62.5% and 75% of MVC, each with superimposed TMS (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). MVCs were followed by 20 s of rest. Thereafter each submaximal contraction was separated by 15 s. Target force levels were derived from the first MVC of the neuromuscular assessment protocol and displayed visually as guidelines, with participants asked to attempt to surpass the guideline during each subsequent MVC.

4.3.4.1. Femoral Nerve Stimulation (FNS)

Evoked force responses from supramaximal electrical stimulation of the parent axons of the peripheral (femoral) nerve was used to evaluate muscle contraction properties, independent of changes within the CNS. These

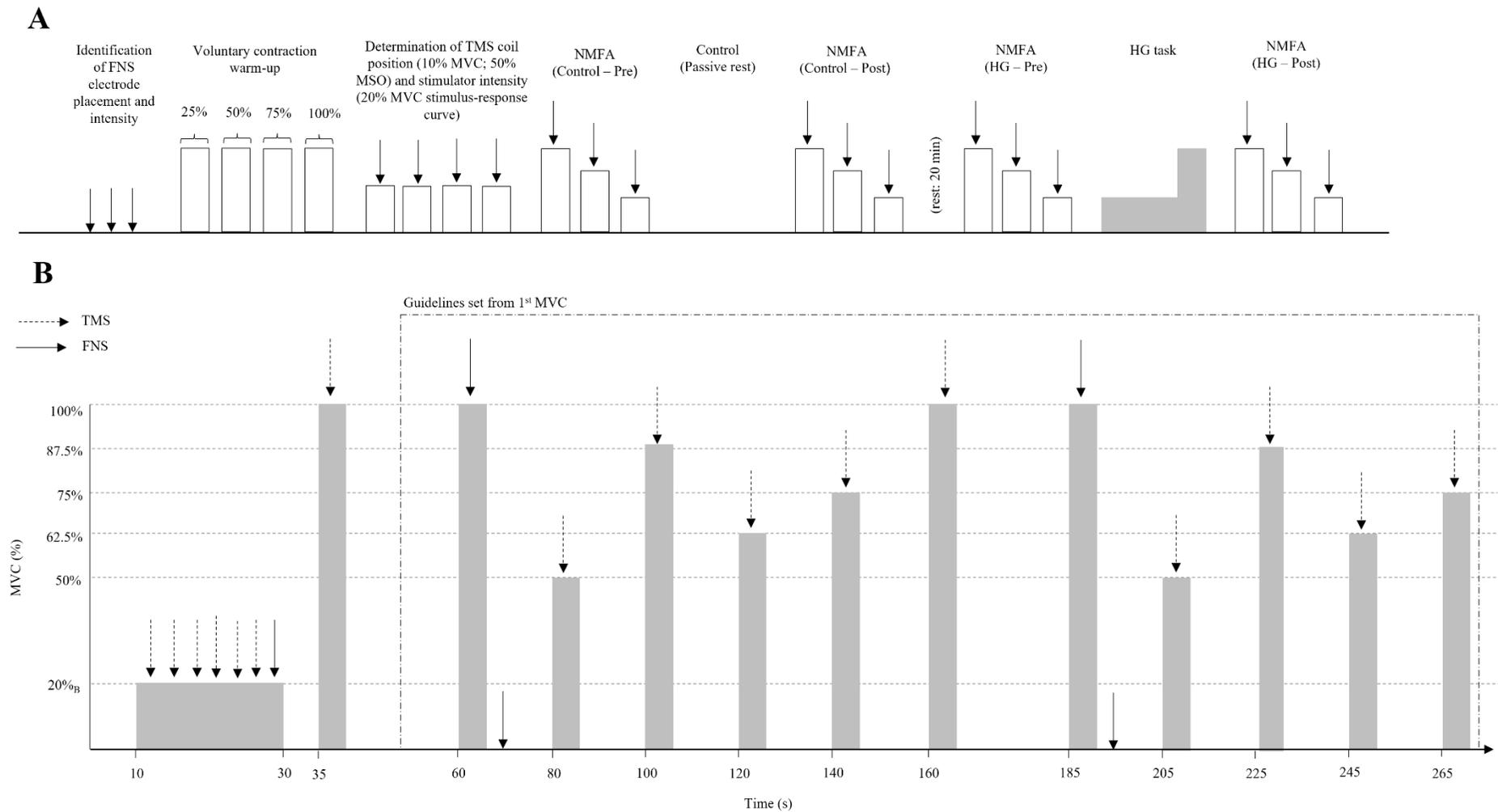


Figure 4.1. Schematic overview of the experimental design of *chapter 4*. (A) and neuromuscular assessment protocol (B). KE: Knee extensors; FNS: Femoral nerve stimulation; TMS: Transcranial magnetic stimulation; MVC: Maximal voluntary contraction; MSO: Maximal stimulator output; NMFA: Neuromuscular fatigue assessment; HG: Intermittent handgrip task.

properties included the assessment of twitch force (Q_{tw}) and the maximal compound muscle action potential (M_{wave}). Single percutaneous electrical stimuli (duration: 200 μ s) were delivered to the femoral nerve of the dominant leg via a pair of square (5 x 5 cm) self-adhesive neuro-stimulation electrodes (Valutrode CF5050; Axelgaard Manufacturing Co., Ltd., California, USA), attached to a high-voltage (maximal voltage: 400 V) constant-current stimulator (Model DS7AH, Digitimer Ltd., Hertfordshire, UK). The cathode was placed high in the femoral triangle, directly over the femoral nerve, with the anode positioned midway between the ipsilateral greater trochanter and iliac crest (Sidhu *et al.*, 2009a). Precise location of cathode placement was determined through systematic adjustments of the electrode until the greatest amplitude for Q_{tw} and M_{wave} in the VL was achieved for a given sub-maximal current (~70 – 90 mA) (Johnson *et al.*, 2015). Optimal stimulation intensity was defined as the intensity at which a plateau in both Q_{tw} and M_{wave} was attained in response to a progressive increment in stimulator current (+20 mA). Stimulator current started at 10 mA, with two stimuli delivered at each intensity. Final stimulation intensity was increased by a further 30% in order to ensure full spatial recruitment of motor units (Rodriguez-Falces *et al.*, 2013) and to account for activity-dependent changes in the excitability of motor axons (Burke *et al.*, 2001). Stimulation intensity was 140 ± 40 mA, established at the beginning of the experimentation and remained constant throughout the session.

4.3.4.2. Transcranial Magnetic Stimulation (TMS)

Assessment of cortical voluntary activation (VA_{TMS}) of the dominant quadriceps and excitability of the corticospinal tract was obtained using TMS. Single, monophasic magnetic stimuli (duration: 1 ms) were manually delivered over the contralateral primary motor cortex to the dominant KE, powered by a magnetic stimulator (Magstim²⁰⁰, The Magstim Company Ltd., Whitland, UK). The maximal stimulator output (MSO) was 1.4 tesla. Stimuli were delivered using a concave (110 mm) double-cone coil, orientated to induce a posterior-anterior intracranial current flow within the cortex. A posterior-anterior cortical current flow was adopted in keeping with previous evaluations in this muscle group (e.g. Sidhu *et al.*, 2017). A concave double-cone coil was used to target the KE representations of the motor cortex, situated deep within the interhemispheric fissure, in an attempt to optimize the focality-field depth trade-off (Deng *et al.*, 2013; c.f. Kesar *et al.*, 2018).

Optimal coil position for the activation of the KE was first determined through establishing vertex; the intersection of the midsagittal and inter-aural lines, measured from theinion (i.e. prominent projection of the occipital bone) to the nasion (i.e. the anterior point of the frontonasal suture), and between tragions (i.e. the notch just above the tragus of the ear), respectively. Points were then marked at vertex, 1 cm and 2 cm posterior to vertex and 1 cm contralateral to each mark along the midline (i.e. 6 marks in total) in order to define a grid through which the optimal representation of the KE could be determined (Souron *et al.*, 2018). Two-to-three stimulations were delivered at each site in a pseudo-randomised order. The site eliciting the largest motor evoked potential (MEP) amplitude and superimposed twitch (SIT) force, whilst minimizing MEP amplitude in the antagonist BF, during a 10% MVC KE contraction at 50% maximal stimulator output (MSO) was chosen as the optimal coil position. If peak amplitude and SIT force were not evoked at the same site, MEP amplitude was prioritised due to the

influence of co-activation on SIT responses (Todd *et al.*, 2016). The coil position was marked with indelible ink directly onto the participants scalp in order to facilitate replication of coil position during the session.

Stimulus intensity was determined through SIT and MEP stimulus-response curves during brief (3 s) contractions of the KE at 20% MVC (Souron *et al.*, 2018; Temesi *et al.*, 2014). An example curve from one participant is presented in [Figure 4.2](#). Four MEPs were evoked across 4 separate contractions (separated by 10s passive rest) using each of the following stimulator intensities: 20%, 30%, 40%, 50%, 60%, 70% and 80% MSO. Stimulator intensities were presented in a randomized order with 10 s between each intensity set. If plateaus in SIT and MEP amplitudes were not evident, higher stimulator intensities were investigated (Temesi *et al.*, 2014). A plateau in the stimulator-response curve was defined as the lowest intensity resulting in an increase <5% of MEP amplitude with an increase in intensity (Temesi *et al.*, 2014). Antagonist MEP amplitude was monitored throughout in order to ensure co-activation was minimized. Stimulator intensity was $65 \pm 13\%$ MSO and remained constant across both the assessment of VA_{TMS} and corticospinal excitability (c.f. Bachasson *et al.*, 2016).

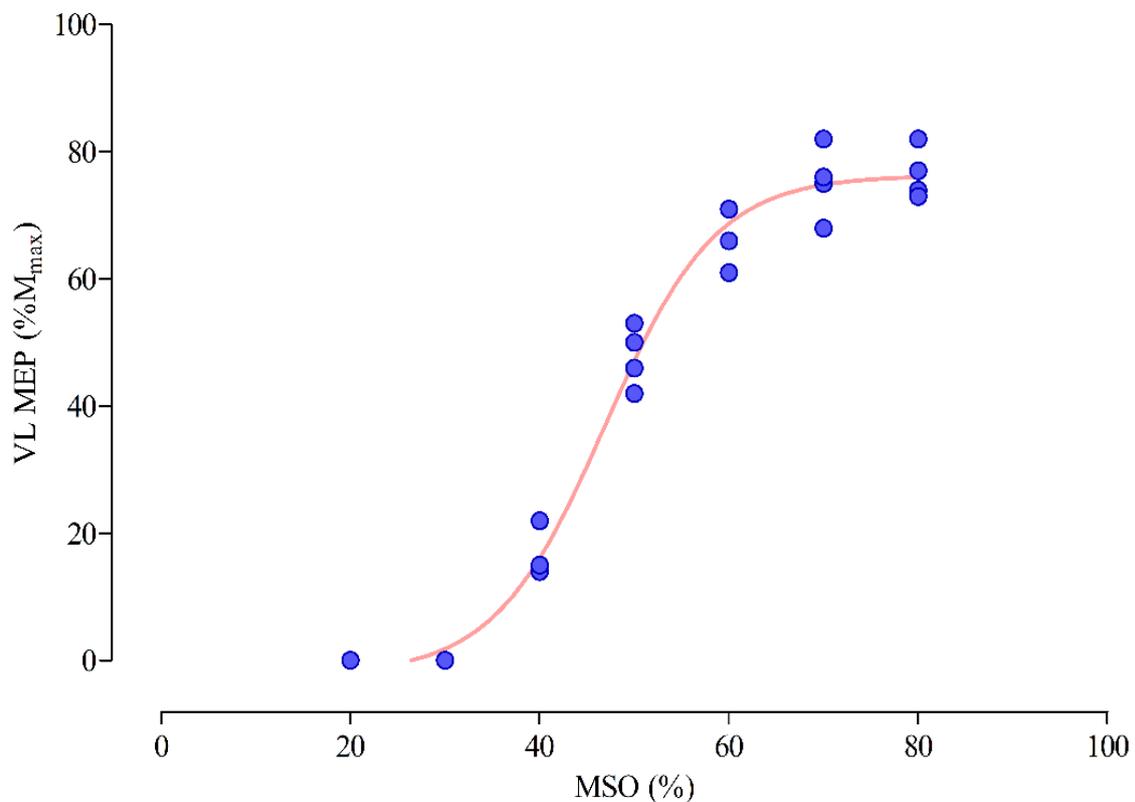


Figure 4.2. MEP stimulus-response curve recorded in the *vastus lateralis* (VL) for the determination of stimulation intensity in one participant. Optimal TMS intensity was defined as that eliciting a plateau in VL MEPs, without a marked increase in antagonist MEP response (data not shown). Four MEPs were evoked at each stimulator intensity. Red line represents Boltzmann sigmoidal modelling of stimulus-response curve.

4.3.5. Data Analysis

4.3.5.1. Voluntary Force Production

MVC force of the dominant KE during the NMFA was defined as the greatest 500-ms force response prior to either electrical or magnetic stimulation, while for the HG it was the greatest 500-ms response across the whole MVC. Identification of MVC force was performed using a programmed macroinstruction within LabChart. Excellent reliability of KE MVC force has been shown previously by our laboratory (Dekerle, Ansdell, *et al.*, 2019; Dekerle, Greenhouse-Tucknott, *et al.*, 2019). Submaximal KE forces were also determined immediately prior to any stimulation, again using a 500-ms window and macroinstruction. The percentage change in HG MVC force was quantified across the HG task from the initial MVC (i.e. following the warm-up) to the last MVC of the task.

4.3.5.2. Quadriceps twitch force (Q_{tw})

Analysis of the force response was performed using a custom macroinstruction. The amplitude of the evoked twitch response was determined as the maximal force response minus the baseline force response, within an 800-ms window around the stimulation artefact. Electrical stimulation was applied ~2s after the termination of voluntary effort. Absolute and relative reliability of Q_{tw} has again been shown to be excellent within our laboratory (Dekerle, Ansdell, *et al.*, 2019; Dekerle, Greenhouse-Tucknott, *et al.*, 2019).

4.3.5.3. Superimposed Twitch Force (SIT)

The response to TMS during voluntary contractions can evoke an additional force response on top of the background voluntary force, termed the superimposed twitch (SIT). The SIT response was determined across all voluntary force levels using a custom macroinstruction, subtracting the maximum evoked force response obtained from a discrete window (500 ms) after the stimulation artefact, from the voluntary force recorded at the point of stimulation.

4.3.5.4. Cortical Voluntary Activation (VA_{TMS})

Cortical voluntary activation (VA_{TMS}) was used to assess the level of descending voluntary drive to the dominant KE based on the principles of the interpolated twitch technique (ITT) (Merton, 1954). VA_{TMS} was determined by the relative expression of the SIT evoked at MVC to the estimated resting twitch (ERT). Force responses evoked directly through TMS applied to the targeted muscle in a state of rest are not appropriate for normalising SIT responses since cortical and motoneuron excitability is much lower in the relaxed muscle. Accordingly, ERT was established through linear regression analysis of SIT responses at maximal and sub-maximal voluntary contraction levels, with the y-intercept representing ERT. Traditionally, protocols have adopted three levels of voluntary contraction above 50% of MVC (i.e. 50%, 75% and 100%), since motor evoked responses plateau above 50% MVC indicating activation of a similar proportion of the motoneuron pool with increasing voluntary effort within

this range (Goodall *et al.*, 2009; Todd *et al.*, 2003; Todd *et al.*, 2004). As little as three points may be used in modelling of the linear relationship between SIT and voluntary force (Mira *et al.*, 2017; Thomas *et al.*, 2016; Todd *et al.*, 2004). However, our laboratory has demonstrated a six-fold increase in the accuracy of the ERT when adopting a minimum of 5 points within the linear model (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). Accordingly, ERT was established from a linear regression containing 10 points (50%, 62.5%, 75%, 87.5% and 100% MVC) obtained from the two series of contractions described in [section 4.3.3](#). ([Figure 4.3](#)). VA_{TMS} was calculated from [equation 4.1](#).

$$VA_{TMS} = 1 - \left(\frac{SIT}{ERT} \right) \cdot 100$$

(4.1.)

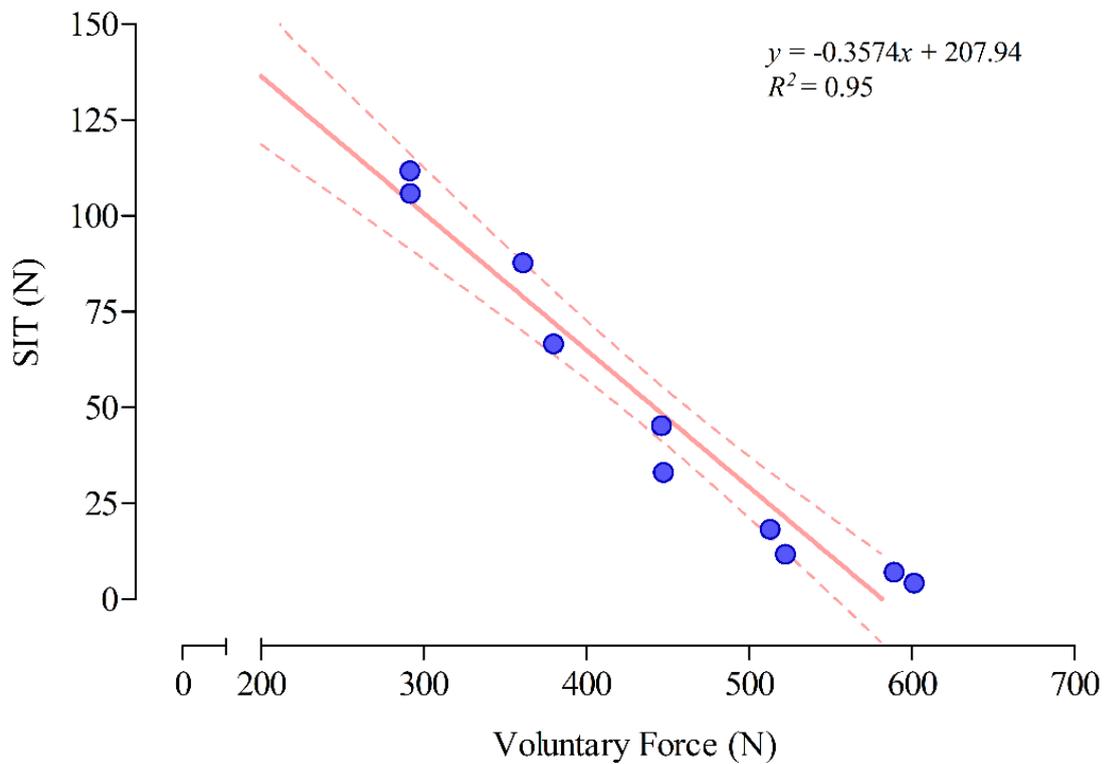


Figure 4.3. Relationship between voluntary contraction force and TMS-evoked superimposed twitch (SIT) force for a representative participant (Pre). Estimated resting twitch (ERT) was derived through extrapolation of the regression line to the y-intercept.

All regression analyses used in the estimation of ERT and the calculation of VA_{TMS} were statistically significant ($p < 0.01$) and demonstrated a strong linear relationship: (R^2) 0.89 ± 0.04 , 0.89 ± 0.07 , 0.90 ± 0.06 and 0.89 ± 0.08 pre- and post-control and pre- and post-HG task, respectively.

4.3.5.5. Electromyography (EMG)

During voluntary contractions, raw EMG signals recorded across the same window used to quantify force were rectified and smoothed using root mean square (RMS). The amplitude of the RMS EMG was used as an indirect, non-invasive measure of changes in neural drive (though for issues with this interpretation see Dimitrova & Dimitrov, 2003; Farina *et al.*, 2004). Sub-maximal responses were normalised to the RMS EMG obtained during the nearest MVC (RMS_{max}).

Motor-evoked potentials (MEP) evoked through TMS and M_{wave} evoked by FNS were used to assess state-changes in the excitability of the corticospinal tract and sarcolemmal membrane, respectively (Bestmann & Krakauer, 2015; Rodriguez-Falces & Place, 2018). The peak-to-peak amplitude of evoked bi-phasic waveforms were analysed as the difference between the lowest deflection and highest inflection using a custom macroinstruction within LabChart. MEP responses evoked in the VL were normalised to the nearest maximal M_{wave} (M_{max}) to account for peripheral excitability changes when interpreting state changes in the corticospinal tract. M_{max} was assessed in the VL only, while MEPs were evaluated in both the VL and the antagonist BF. MEPs evoked in the BF were not normalised to M_{max} (Todd *et al.*, 2016) and were instead presented as raw amplitudes. Examples of MEP, M_{max} and $SIT_{100\%}$ responses from a representative participant are presented in [Figure 4.4](#).

4.3.6. Statistical Analysis

Statistical procedures were performed using SPSS unless otherwise stated ([section 3.19](#)). Voluntary and evoked responses were analysed with a two-way (2 x 2) repeated-measures ANOVA, with factors condition (Control; HG) and time (Pre; Post). Assumptions of the test were evaluated as outlined in [section 3.19.6](#). Data that violated the assumption of normality (i.e. M_{max} , BF MEP) were $\log(10)$ transformed. Significant main effects of time and interaction effects were followed up with Bonferonni-adjusted pairwise comparisons. Due to the hypothesis that neuromuscular function and corticospinal excitability would remain unchanged following the HG task, tests of equivalence were performed using jamovi (v1.0, The jamovi project, 2019) using the TOSTER R package (Lakens, 2017; R Core Team, 2018), to assess the equivalence of the effects induced between conditions. The smallest effects of interest (SESOI) were derived from the test-retest effect size calculated from absolute pre-activity reliability of neuromuscular measures previously assessed within our laboratory (Dekerle, Ansdell, *et al.*, 2019; Dekerle, Greenhouse-Tucknott, *et al.*, 2019). The SESOI was used to set upper and lower equivalence bounds, providing the basis of two composite null hypothesis tests: H_{01} : effect \leq lower bound and H_{02} : effect \geq upper bound. If both hypotheses could be rejected, it was concluded that the effect is close enough to zero to be defined as equivalent. However, if at least one hypothesis could not be rejected, the observed effect was potentially larger than zero. For efficiency, only the one-sided test with the largest p value is reported (Lakens, 2017). For all analyses, the null hypothesis was rejected at an α -level of 0.05.

4.4. Results

The HG task induced significant reductions in MVC force within both the dominant ($-52.2 \pm 11.3\%$) and non-dominant hand ($-44.8 \pm 16.0\%$). An important note, repetitions and duration of the HG task performed were similar

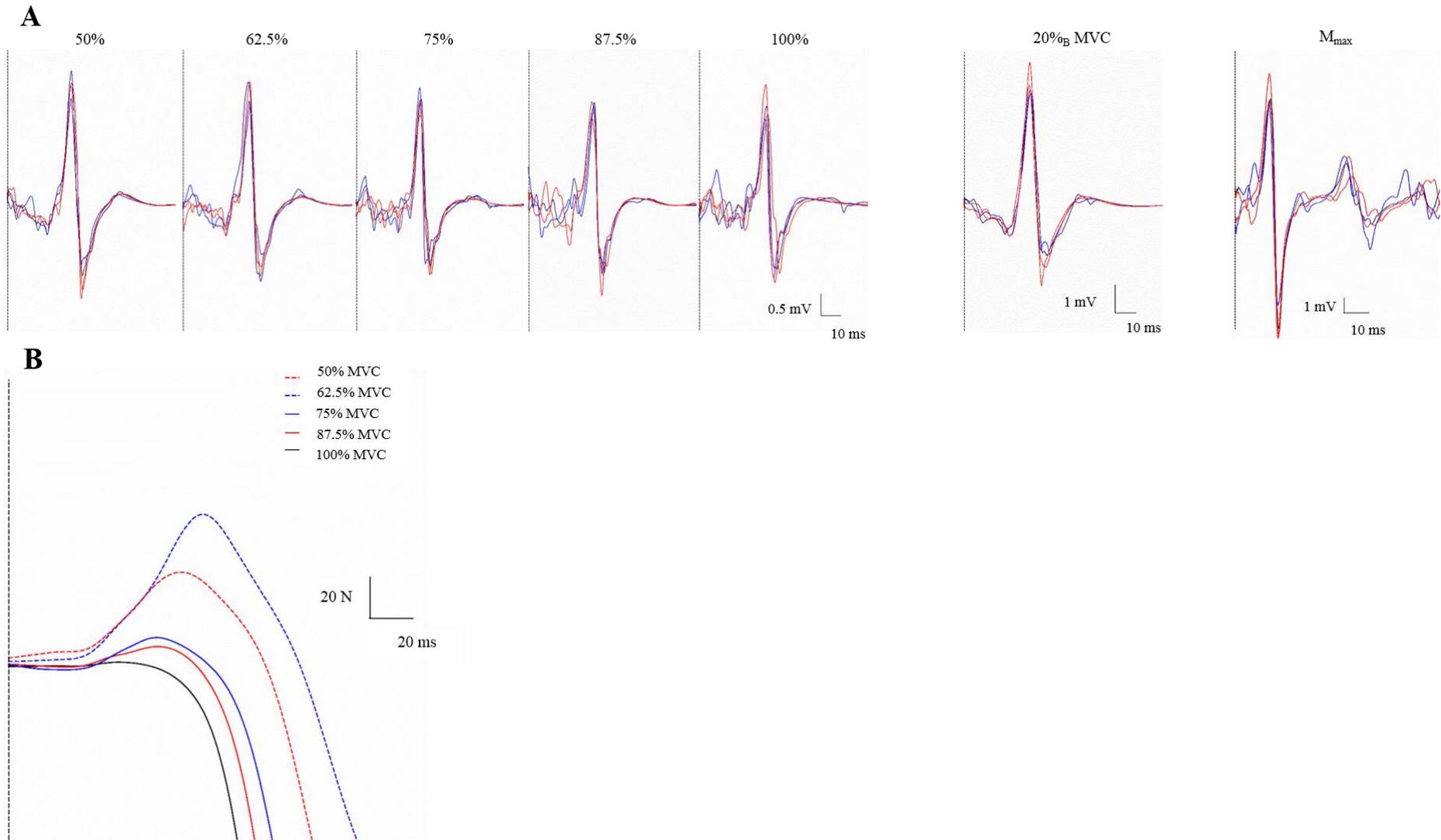


Figure 4.4. Traces of motor evoked potentials (MEP), M_{max} and superimposed twitch (SIT) forces for a representative participant. MEP and M_{max} traces (A): Blue line: Control – pre, dark blue line: Control – post, red line: HG – pre, dark red line: HG – post. SIT responses (B). Dotted black line represents the point of magnetic or electrical stimulation.

to that performed by the full sample outlined in [chapter 5](#) (11 ± 3 reps [range: 6-16 reps]; 310.0 ± 89.0 s [range: 170-470 s]). No difference was evident in the percentage change in HG MVC force of either the dominant ($t_{(14)} = 1.50$, $p = 0.156$, $d_{av} = -0.44$) or the non-dominant ($t_{(14)} = 0.56$, $p = 0.582$, $d_{av} = -0.18$) hand between the whole sample ([chapter 5](#)) and the sub-sample of the present study.

4.4.1. Maximal Voluntary Force and Evoked Twitch Force

Voluntary and evoked neuromuscular responses in the KE may be found in [Table 4.1](#). Small reductions (-2.3%) in voluntary force led to a main effect of time, indicating MVC was reduced between pre and post assessments ($F_{(1,14)} = 11.82$, $p = 0.004$, $\eta_p^2 = 0.458$). Moreover, MVC force was significantly greater in the control compared to the HG condition ($F_{(1,14)} = 13.47$, $p = 0.003$, $\eta_p^2 = 0.490$; Control: 555.5 ± 84.7 N; HG: 532.8 ± 79.0 N). However, there was no interaction between condition and time ($F_{(1,14)} = 0.06$, $p = 0.808$, $\eta_p^2 = 0.004$). To better understand the observed main effect of condition, a paired sample *t*-test was performed to evaluate whether there was a difference between conditions pre-intervention. The outcome of this analysis demonstrated lower KE MVC force before the HG task compared to the control condition ($t_{(14)} = 2.87$, $p = 0.012$, $d_{av} = -0.27$). A test of equivalence was performed on the pre-to-post change in MVC force between conditions. The two one sided test (TOST) procedure indicated that the observed effect ($d_z = 0.06$; 90% raw CI: -16.0 – 21.2 N) was not significantly within the prescribed bounds of equivalence ($d_z = -0.39$ [raw value: -15.9 N] and $d_z = 0.39$ [raw value: 15.9 N]; $t_{(14)} = -1.26$, $p = 0.113$).

Q_{tw} decreased across time ($F_{(1,14)} = 16.43$, $p = 0.001$, $\eta_p^2 = 0.540$; Pre: 147.3 ± 22.0 N vs. Post: 142.8 ± 21.4 N) and, like MVC, was shown to be greater across the control condition ($F_{(1,14)} = 18.09$, $p = 0.001$, $\eta_p^2 = 0.564$; Control: 149.8 ± 18.8 N; HG: 140.2 ± 23.5 N). Again, this could be attributed to differences between conditions prior to the interventions ($t_{(14)} = 3.66$, $p = 0.003$, $d_{av} = -0.43$). However, there was no interaction effect between condition and time on Q_{tw} ($F_{(1,14)} = 0.04$, $p = 0.846$, $\eta_p^2 = 0.003$). The TOST procedure indicated that the observed change in Q_{tw} between conditions ($d_z = 0.05$; 90% raw CI: -3.84 – 4.78 N) was not significantly within the prescribed bounds of equivalence ($d_z = -0.05$ [raw value: -0.47 N] and $d_z = 0.05$ [raw value: 0.47 N]; $t_{(14)} = -0.003$, $p = 0.499$).

4.4.2. Muscle Compound Action Potential

No condition ($F_{(1,14)} = 2.91$, $p = 0.110$, $\eta_p^2 = 0.172$), time ($F_{(1,14)} = 0.18$, $p = 0.674$, $\eta_p^2 = 0.013$) or interaction effects ($F_{(1,14)} = 0.04$, $p = 0.837$, $\eta_p^2 = 0.003$) were observed for M_{max} responses. Similar results were evident for the M_{wave} responses obtained on the muscle at rest (data not shown).

Table 4.1. Parameters of neuromuscular function of the knee extensors (KE) evoked before and after handgrip exercise (HG) and time-matched passive rest (Control).

	Control			HG			ANOVA		
	Pre	Post	%Pre	Pre	Post	%Pre	Condition	Time	Interaction
MVC (N)	561.1 ± 84.3	549.8 ± 87.6	98.0 ± 4.8%	539.8 ± 75.7	525.9 ± 84.2	97.2 ± 4.2%	0.003	0.004	0.808
VA _{TMS} (%)	95.8 ± 2.7	96.0 ± 3.3	N.A.	95.1 ± 2.8	93.0 ± 4.2	N.A.	0.006	0.127	0.067
SIT _{100%} (%MVC)	1.09 ± 0.84	0.92 ± 0.78	N.A.	1.02 ± 0.60	1.49 ± 1.06	N.A.	0.035	0.193	0.054
ERT (N)	136.9 ± 38.5	118.3 ± 37.7*	86.4 ± 12.8%	110.4 ± 31.7	107.3 ± 30.6	98.0 ± 15.1%	0.007	<0.001	0.015
Q _{tw} (N)	152.0 ± 20.0	147.7 ± 18.0	97.4 ± 4.4%	142.6 ± 23.6	137.9 ± 24.0	96.6 ± 4.9%	0.001	0.001	0.846
M _{max} (mV)	9.20 ± 3.00	9.14 ± 2.54	100.7 ± 9.1%	8.76 ± 2.80	8.84 ± 2.85	101.3 ± 8.7%	0.110	0.674	0.837
	(0.95 ± 0.12)	(0.95 ± 0.11)	(100.4 ± 4.1%)	(0.92 ± 0.13)	(0.93 ± 0.12)	(100.6 ± 4.1%)			

Data presented as mean ± SD. MVC: maximal voluntary contraction; VA_{TMS}: voluntary activation; SIT_{100%}: superimposed twitch during MVC; Q_{tw}: twitch force; M_{max}: M-wave during MVC. Values in parentheses represent descriptive statistics for log(10) transformed variables. *: Significantly different from pre values ($p < 0.05$); †: Significantly different from respective Control value ($p < 0.05$).

4.4.3. Cortical Voluntary Activation, Superimposed Twitch Force and Estimated Resting Twitch

An effect across time was not evident for VA_{TMS} ($F_{(1,14)} = 2.64, p = 0.127, \eta_p^2 = 0.159$) but voluntary activation was slightly lower in the HG condition ($F_{(1,14)} = 10.46, p = 0.006, \eta_p^2 = 0.428$; Control: $95.9 \pm 2.9\%$, HG: $94.1 \pm 3.7\%$). No interaction effect was found for VA_{TMS} ($F_{(1,14)} = 3.93, p = 0.067, \eta_p^2 = 0.219$). There was no statistical difference between conditions at the start of each condition ($t_{(14)} = 1.12, p = 0.280, d_{av} = 0.28$). The TOST procedure demonstrated that the effect between conditions in the change in VA_{TMS} ($d_z = 0.51$; 90% raw CI: 0.24 – 4.09%) was not significantly within the bounds of equivalence ($d_z = -0.26$ [raw value: -1.10%] and $d_z = 0.26$ [raw value: -1.10%]; $t_{(14)} = 0.977, p = 0.827$).

Greater SIT_{100%} force was evident in the HG condition ($F_{(1,14)} = 5.42, p = 0.035, \eta_p^2 = 0.279$; Control: $1.00 \pm 0.80\%_{MVC}$; HG: $1.25 \pm 0.88\%_{MVC}$), but no time ($F_{(1,14)} = 1.87, p = 0.193, \eta_p^2 = 0.118$) or interaction effects were evident ($F_{(1,14)} = 4.44, p = 0.054, \eta_p^2 = 0.241$). SIT_{100%} force was not statistically different between conditions pre-intervention ($t_{(14)} = 0.49, p = 0.633, d_{av} = 0.10$). The effect for the change in SIT_{100%} between conditions ($d_z = -0.55$; 90% raw CI: -1.19 – -0.11 N) was not significantly within the bounds of equivalence ($d_z = -0.38$ [raw value: -0.45 N] and $d_z = 0.38$ [raw value: 0.45 N]; $t_{(14)} = -0.636, p = 0.732$).

For the ERT, there was found a main effect of time ($F_{(1,14)} = 9.89, p = 0.007, \eta_p^2 = 0.414$), condition ($F_{(1,14)} = 21.27, p < 0.001, \eta_p^2 = 0.603$), and interaction between condition and time ($F_{(1,14)} = 7.65, p = 0.015, \eta_p^2 = 0.353$). A significant reduction in ERT in the control condition was evident pre-to-post intervention (136.9 ± 38.5 N vs. 118.3 ± 37.7 N; $p = 0.001; d_{av} = -0.49$), but this was not evident in the HG condition (110.4 ± 31.7 N vs. 107.3 ± 30.6 N; $p = 0.479; d_{av} = -0.10$). There was a large, statistically significant difference between the ERT calculated at the beginning of each condition ($t_{(14)} = 5.44, p < 0.001, d_{av} = 0.75$). The observed effect ($d_z = -0.71$; 90% raw CI: -25.4 – -5.63 N) was not significantly within the prescribed bounds of equivalence ($d_z = -0.36$ [raw value: -7.82 N] and $d_z = 0.36$ [raw value: 7.82 N]; $t_{(14)} = -1.37, p = 0.904$).

Table 4.2. Motor evoked potentials (MEPs; %M_{max}) recorded in the *vastus lateralis* (VL) at both relative and absolute force levels.

Force	Control		HG		ANOVA		
	Pre	Post	Pre	Post	Condition	Time	Interaction
100%	40.9 ± 7.8	38.0 ± 11.3	38.9 ± 9.5	39.2 ± 13.7	0.811	0.512	0.255
87.5%	40.7 ± 12.8	40.5 ± 10.3	39.8 ± 10.6	41.9 ± 10.4	0.853	0.611	0.546
75%	43.7 ± 10.2	42.5 ± 11.6	40.9 ± 11.1	40.2 ± 10.5	0.263	0.656	0.860
62.5%	45.0 ± 10.5	43.5 ± 11.3	42.4 ± 10.2	45.2 ± 9.7	0.747	0.750	0.110
50%	46.1 ± 10.9	40.8 ± 10.0	42.5 ± 11.2	42.8 ± 12.0	0.479	0.095	0.068
20% _B	49.6 ± 13.2	44.3 ± 14.8	46.4 ± 11.8	49.3 ± 14.2	0.549	0.208	0.060

Data presented as mean ± SD. 20%_B: Absolute force value (126.5 ± 18.6 N) equating to 20% of preliminary maximal force production.

4.4.4. Corticospinal Excitability

Background EMG RMS, recorded immediately prior to stimulation, demonstrated no effect of condition ($F = 0.04$ - 3.53 , all $p > 0.05$, $\eta_p^2 = 0.003$ - 0.202) or time ($F = 0.07$ - 4.11 , all $p > 0.05$, $\eta_p^2 = 0.005$ - 0.227) across relative force intensities. There was no effect of time ($F_{(1,14)} = 1.13$, $p = 0.306$, $\eta_p^2 = 0.075$) for background EMG RMS at 20%B, but there was a main effect of condition ($F_{(1,14)} = 12.29$, $p = 0.003$, $\eta_p^2 = 0.468$), with EMG RMS greater in the HG condition compared to the control condition (Control: 0.013 ± 0.005 mV vs. HG: 0.015 ± 0.005 mV).

Agonist MEP amplitudes (%M_{max}) evoked in the KE are presented in [Table 4.2](#). Irrespective of absolute or relative contraction intensities, corticospinal excitability was unchanged in both conditions ($F = 0.04$ - 1.36 , all $p > 0.05$, $\eta_p^2 = 0.003$ - 0.089) and time ($F = 0.11$ - 3.21 , all $p > 0.05$, $\eta_p^2 = 0.008$ - 0.187). No interaction effects between condition and time were also observed ($F = 0.03$ - 3.90 , all $p > 0.05$, $\eta_p^2 = 0.002$ - 0.230). The TOST procedure demonstrated that the observed effect between conditions for the change in MEP responses were not within the prescribed bounds of equivalence ($t_{(14)} = -0.59$ - 1.57 , all $p > 0.05$). Antagonist MEP responses at both absolute and relative force intensities ([Table 4.3](#)) were not influenced by condition ($F < 0.01$ - 0.73 , all $p > 0.05$, $\eta_p^2 < 0.001$ - 0.049) or time ($F < 0.01$ - 1.18 , all $p > 0.05$, $\eta_p^2 < 0.001$ - 0.083).

Table 4.3. Motor evoked potentials (MEPs; mV) recorded in the antagonist *biceps femoris* (BF) across relative force intensities.

Force	Control		HG		ANOVA		
	Pre	Post	Pre	Post	Condition	Time	Interaction
100%	1.10 ± 0.98	1.12 ± 0.91	0.95 ± 0.58	1.08 ± 0.86	0.636	0.303	0.850
	(-0.08 ± 0.32)	(-0.06 ± 0.29)	(-0.10 ± 0.27)	(-0.07 ± 0.29)			
87.5%	0.87 ± 0.56	0.83 ± 0.49	0.85 ± 0.57	0.94 ± 0.64	0.792	0.810	0.467
	(-0.13 ± 0.25)	(-0.15 ± 0.25)	(-0.14 ± 0.26)	(-0.12 ± 0.29)			
75%*	0.76 ± 0.50	0.82 ± 0.52	0.77 ± 0.53	0.82 ± 0.58	0.974	0.298	0.629
	(-0.19 ± 0.24)	(-0.15 ± 0.25)	(-0.18 ± 0.24)	(-0.16 ± 0.25)			
62.5%*	0.68 ± 0.44	0.74 ± 0.49	0.71 ± 0.40	0.71 ± 0.44	0.538	0.615	0.161
	(-0.24 ± 0.26)	(-0.21 ± 0.27)	(-0.20 ± 0.22)	(-0.22 ± 0.26)			
50%	0.68 ± 0.60	0.69 ± 0.55	0.66 ± 0.39	0.69 ± 0.51	0.464	0.996	0.615
	(-0.27 ± 0.29)	(-0.26 ± 0.29)	(-0.24 ± 0.24)	(-0.25 ± 0.28)			

Data presented as mean ± SD. Values in parentheses represent descriptive statistics for log(10) transformed variables. * Due to technical issues descriptive statistics and analysis of BF MEPs at 75% and 62.5% were conducted on n = 14.

4.5. Discussion

The purpose of the present study chapter was to determine whether remote physical activity in the upper body impacts the neuromuscular function and corticospinal excitability of a rested muscle group of the lower limbs. The results of the study are mixed. On the one hand, the present study failed to observe significant interaction effects for maximal force production, Q_{tw} , VA_{TMS} and MEPs which would be indicative of an effect of the HG task (specifically) on parameters of neuromuscular function and corticospinal excitability. However, on the other hand, small condition effects were observed, while the change in indices of neuromuscular function exceeded the predefined bounds of equivalence, suggesting effects between conditions may not be equivalent to zero. In relation to the observed main effects of condition, it was demonstrated that differences between the two conditions before the interventions could potentially account for this while, on average, the observed changes resided within the documented absolute error ([Appendix A](#)) established for these measures at rest and when ‘fatigued’ (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). Therefore, on balance, the results are cautiously interpreted in favour of minimal effects of the HG task on neuromuscular function and corticospinal excitability of the dominant KE. The study represents the first attempt to quantify changes in corticospinal excitability and supra-spinal contributions to voluntary activation of the lower limb muscles following activity in the upper body.

Transfer of motor fatigability across remote non-active muscles has previously been attributed to central factors arising independent of acute challenges to peripheral contractile function (Kennedy *et al.*, 2013; Martin & Rattey, 2007; Rattey *et al.*, 2006). In the present study, the HG task was associated with a small change in $SIT_{100\%}$, but this did not translate to a decline in the VA_{TMS} of the rested KE. The results would appear to suggest that, following remote exercise in the upper body, cortical motor output may be maintained during brief contractions of the dominant KE. This supports a growing number of observations indicating null effects on force production across heterologous muscles of the upper and lower body following whole-body (Decorte *et al.*, 2012; Matsuura *et al.*, 2018; Millet *et al.*, 2003; Place *et al.*, 2004; Ross *et al.*, 2007) and single-limb exercise (Aboodarda *et al.*, 2015; Aboodarda *et al.*, 2017).

Compared to the substantial reductions in force within the activated muscle groups (e.g. -30%; Amann *et al.*, 2013), when observed, effects observed within non-active muscle groups are typically more modest (~5-10%; e.g. Halperin, Copithorne, *et al.*, 2014; Sidhu *et al.*, 2014; Šambaher *et al.*, 2016; Ye *et al.*, 2018). Accordingly, it is possible that rather than a true effect, force deficits may be more attributable to methodological issues and/or an artefact of measurement error (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). In the present study, two identified methodological influences, muscle specificity (Halperin, Copithorne, *et al.*, 2014) and participant sex (Ye *et al.*, 2018), were controlled for, in order to offer the greatest potential to observe the transfer of inhibitory effects, yet the observed effects still appeared nominal. Thus, the present study provides little support for the development of systemic fatigability across the body incurred through demanding physical activity⁵⁹. Beyond the acute loss of force observed immediately after remote physical activity, force deficits in non-active muscle have interestingly been evidenced in preparation of (Li *et al.*, 2019) or during protracted or repeated bouts of subsequent activity

⁵⁹ In support of this conclusion, a meta-analysis published after the conduction of the present study concluded that only trivial effects are observed in the present literature regarding for acute force responses in non-active muscle groups, with substantial heterogeneity evidenced between studies (Behm *et al.*, 2021).

(Halperin, Aboodarda, *et al.*, 2014; Hamilton & Behm, 2017). It is here proposed that these force deficits are more likely to reflect changes to motivational and decision-making processes determining the allocation of voluntary force (Meyniel *et al.*, 2013). Indeed, when participants are aware of the duration they are expected to exert effort for in a non-active muscle following prior remote activity, observed deficits are notably ameliorated (Hamilton & Behm, 2017). This may indicate that any effect of remote activity on force production in non-active muscle(s) may be based on the interpretation of the condition of the whole body and strategic allocation of resources based on this interpretation and perceived task demands, rather than any direct inhibitory effect impinging on the output of M1, *per se*.

MEPs in the KE were also shown to be unchanged following the HG task. The present study represents the first quantification of MEPs in the lower limbs following prior motor activity in the upper limbs. Conflicting responses have been reported in the elbow flexors following lower body activity (Aboodarda *et al.*, 2017; Šambaher *et al.*, 2016; Sidhu *et al.*, 2014). This may be potentially attributed to the level of force under which responses were recorded. Aboodarda *et al.* (2017) demonstrated that effects on the supra-spinal excitability of the elbow flexors to be force-dependent, with an increase in the ratio of evoked corticospinal to spinal motoneuron responses evident at 100% MVC, no change evident at 50% MVC and a decrease observed at 5% MVC. A force-dependency was not observed within the present study, with no difference observed across conditions at both absolute and relative force intensities. The discrepancy between results may be attributed to various methodological differences. Indeed, greater stimulator intensities were adopted within the present study than used in the study of Aboodarda *et al.* (2017), resulting in a larger proportion of the motoneuron pool recruited (indicated by the proportional size of the MEP to M_{\max}). Stimulation intensity has been shown to significantly affect neurophysiological responses, particularly the assessment of corticospinal excitability (Bachasson *et al.*, 2016). At lower stimulation intensities, small (low-threshold) motoneurons, which are most active during sub-maximal contractions, are preferentially activated (McNeil *et al.*, 2011). During demanding activity within the lower limbs, repeated activation of these small motoneurons may evoke intrinsic changes to their properties which serves to reduce motoneuron excitability (Finn *et al.*, 2018). It is possible that changing inputs to M1 may cause these intrinsic changes to spread within the brain, specifically reducing responsiveness of low-threshold neurones in other motor representations, which may explain previous observations of a decrease in supraspinal excitability at low contraction intensities but not stronger contractions which recruit higher-threshold cortical motor cells (Aboodarda *et al.*, 2017). The use of higher stimulation intensities in the present study may have possibly proved insensitive to such changes, recruiting a larger portion of the available motoneuron pool and therefore evoking responses within a region of saturation within the stimulus-response relationship (McNeil *et al.*, 2011). This requires further evaluation to establish.

Background EMG remained unchanged across the relative force levels, suggesting that descending neural drive was unaffected by the HG task. In contrast, background EMG displayed a small increase at an absolute force level between conditions, which may be attributed to a compensatory output to account for the loss of force evident prior to the HG task. This did not elicit significant change in MEP which may further support the proposition that observed condition effects were at best minimal. The absence of changes in corticospinal excitability in the KE after upper body activity contrasts with changes observed in the upper limbs following lower body activity (Aboodarda *et al.*, 2017). The observed differences may be, at least in part, attributed to differences between upper

and lower limb neurophysiology. Stronger connectivity between PMC and M1 have previously been reported during activity of the upper limbs compared to the lower limbs (Volz *et al.*, 2015). Increased activation of pre-motor areas during prior activity, which is presumed to aid in facilitating motor output in response to motor fatigability (Jiang *et al.*, 2012; Liu *et al.*, 2003; van Duinen *et al.*, 2007), may therefore account for greater facilitation of MEP responses within the upper compared to lower limbs. The present study did not measure the excitability of the spinal motoneuron pool so could not distinguish the effect on supra-spinal and spinal circuits, however supra-spinal circuits have previously been identified as the primary site altered by remote activity (Aboodarda *et al.*, 2017; Šambaher *et al.*, 2016). Yet, increased motoneuron excitability of the KE has been reported following sustained maximal contractions of the elbow flexors (Aboodarda *et al.*, 2015). As the total excitability of the corticospinal tract is the product of both supra-spinal and spinal influences, the possibility that supra-spinal excitability of the KE motoneurons may have in fact been reduced in the present study cannot be discounted. Future research is required to further quantify the supra-spinal excitability of the lower limbs following prior upper body motor activity.

It is important to acknowledge some limitations of the present study. Main effects of condition for voluntary and evoked contractions were evident. These observed effects may suggest that HG activity did in fact exert functional effects upon the neuromuscular function of the non-active KE, particularly central factors (e.g. VA_{TMS}). However, in the case of MVC force and Q_{tw}, exploratory paired comparisons demonstrated that deficits were evident between conditions prior to the respective interventions. This would appear to suggest that the observed differences are unlikely to represent effects of the HG task specifically. With conditions performed in a non-randomized order to enable the experiment to be performed in a single trial, it would appear more likely that these effects represent an influence of condition order and the total duration of the session. This may be exemplified by the only interaction effect observed - the ERT response - which declined during the control condition, but not in response to the HG task. The condition effect observed for VA_{TMS} (and SIT_{100%}) could not be attributed to differences between conditions pre-intervention. However, it is important to note that the observed differences between conditions were within the typical error associated with these measures at rest (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). Importantly, all interaction effects were not significant suggesting that the change in indices of neuromuscular function in response to the interventions specifically were not different in response to the HG and control conditions. Finally, at least 6 stimulations are recommended for the reliable assessment of corticospinal excitability (Lewis *et al.*, 2014). Two and four MEPs were used to quantify the corticospinal responses at relative and absolute force intensities, respectively, in an attempt to balance accuracy and the duration of neuromuscular assessment which may have influenced the recovery of (and therefore the ability of the present study to detect) central effects (see Gruet *et al.*, 2014). This issue appears to be a common problem within the assessment of corticospinal excitability in non-active muscles (e.g. Aboodarda *et al.*, 2017) which may limit current interpretation of the literature.

4.6. Conclusion

In conclusion, the present study indicates that the performance of demanding HG activity exerted little influence on the capacity of the non-active, dominant KE to produce force and associated indices of neuromuscular function

and corticospinal excitability. The findings add to the growing evidence indicating that systemic motor fatigability is limited across the body following demanding physical activity. In relation to the aims of the present thesis, the findings suggest that a paradigm adopting prior remote physical activity to induce a change in individuals' subjective experience of fatigue may enable an evaluation of the effects of this change in perception, whilst controlling for the typical concomitant motor fatigability, allowing comparisons to be made within an intact system.

CHAPTER 5 - PRIOR PHYSICAL ACTIVITY IMPAIRS SUBSEQUENT ENDURANCE PERFORMANCE THROUGH ALTERED INTERACTIONS BETWEEN PERCEPTUAL AND AFFECTIVE RESPONSES.

5.1. Abstract

Though feeling states are acknowledged as central to the regulation of physical endurance performance, appreciation of the dynamics between psychological constructs in the control of behaviour remains limited. The present study chapter sought to address this by examining the interactions between different perceptual and affective constructs in the central regulatory control of a physical endurance task. The behavioural, perceptual and affective responses to an exhaustive, sub-maximal contraction (20% MVC) of the dominant knee extensors (KE) were assessed following an intermittent handgrip (HG) task and time matched control (passive rest). Twenty healthy male participants reported their perceived effort and affective valence during the KE contraction, while ratings of fatigue were obtained before the HG task, immediately before the start of the KE contraction and upon task termination. Following the HG task, time to task failure (TTF) during the KE endurance task was significantly reduced compared to the control condition. The prior HG task served to heighten perceptions of effort and reduce affective valence during the KE contraction, with both effort and affect correlated with performance across conditions. The subjective experience of fatigue was elevated immediately after the HG task, before the start of the KE contraction, but this was not correlated with subsequent endurance performance. Instead, fatigue was correlated with the perceived effort and affective response to the KE task. The findings indicate that physical endurance performance is regulated by complex, cognitive-emotional interactions. The subjective symptom of fatigue is implicated as an important factor within an overarching control of the psychophysiological regulation of physical performance.

5.2. Introduction

The subjective experience of fatigue is believed to be a central feature of a control strategy set-out by the brain in order to regulate behaviour during prolonged and demanding physical tasks (Noakes, 2012; Marcora, 2008). However, present understanding of the precise features of this central regulation of goal-directed behaviour, specifically the conscious experiences defining it, remain unclear ([section 2.3.2.](#)). This may be attributable to the persistent adoption of a narrow conceptualisation of the psychophysiological constructs used in the description of the psychophysical regulatory processes, based on an overreliance on single-item measures to capture this complex, dynamic process (Venhorst *et al.*, 2018c; [section 2.3.2.](#)). Accordingly, in support of recent calls, greater eclecticism in measurement tools used to further understanding of the central regulation of performance and the consequences of fatigue are required (Venhorst *et al.*, 2018c).

Various changes in perceptual and affective states arise in response to demanding physical activity as ‘fatigue’ develops. The perception of effort, defining the conscious perception of how hard, heavy or strenuous action is (Marcora, 2010), represents a central tenant of many models of fatigue across diverse research domains (Hockey, 2011; Kuppaswamy, 2017; Noakes, 2012; Marcora, 2008). Indeed, an elevated perception of effort is offered as a defining perceptual feature of the subjective experience of fatigue during muscular work (Enoka & Stuart, 1992), and has been titled the cardinal regulatory variable during physical performance (Staiano *et al.*, 2018). Neurophysiologically, the perception of effort is considered to originate centrally, through efferent and reafferent pathways ([section 2.4.3.2.](#)). The subjective experience of effort however, has also been shown to be sensitive to various cognitive factors including ones’ perceived ability to effectively perform tasks (Hutchinson *et al.*, 2008), emotional appraisals (Giles *et al.*, 2018) and outcome expectations (Azevedo *et al.*, 2021). This suggests that higher inputs, reflecting contextual features of the internal and external environment and their relation to ones’ self, also represent important influences on processing of this effort signal. As such, the aversive experience of fatigue may be an important modulating factor of perceived effort ([section 2.4.4.](#)). Importantly, though often used synonymously, evidence indicates that the perception of fatigue (which may be defined in relation to one’s perceived capacity to meet or cope with task demands; Steele, 2021; Micklewright *et al.*, 2017) and effort should be considered independent constructs that can be experienced separately (Micklewright *et al.*, 2017; [section 2.2.3.](#)). This may suggest the two may hold independent functions within the central regulation of goal-directed behaviour. Yet, due to an over-reliance on the perception of effort in attempts to qualify the central regulation of behaviour, relatively little is known regarding the relationship between the perception of fatigue and physical performance, *per se*. In a recent study, a perceived state of fatigue induced by demanding cognitive activity was shown to positively correlate with the level of effort perceived during a subsequent cycling task, but the perception of fatigue was not itself seen to be related to the self-selected intensity of the exercise bout (Harris & Bray, 2019). This suggests that the perception of fatigue may not represent a variable that directly inhibits endurance performance but may possibly exert influence indirectly through modulation of the perception of effort. The interplay between these perceptual constructs has yet to be clearly established.

Afferent feedback of homeostatic perturbations incurred during physical activity are not believed to represent a signal processed in the generation of the perception of effort (Marcora, 2009; Pageaux & Gaveau, 2016); though this is still debated (Broxterman *et al.*, 2017; Broxterman *et al.*, 2018; [section 2.4.3.1.](#)). However, sensed

homeostatic perturbations represent a core feature of affective states (Craig, 2002; Damasio & Carvalho, 2013). During exercise, though effort and affective valence (i.e. feelings of pleasure/displeasure) are related, individuals retain an ability to distinguish between the two, i.e. the *what* from *how* one feels (Hardy & Rejeski, 1989), which may indicate disparate consequences for behaviour ([section 2.5.](#)). Furthermore, though the subjective experience of fatigue has been defined as an emotion (Hockey, 2013; Noakes, 2012), or referenced to declines in affective valence in response to demanding physical activity (Hartman *et al.*, 2019), affective valence and the perception of fatigue have also been shown to be dissociable during physical activity (McAuley *et al.*, 1999). This may similarly indicate that the two constructs are not synonymous and may also hold separable functions within the central regulation of behaviour ([section 2.5.4.](#)).

Accordingly, the aim of this study was to investigate the perceptual, affective and behavioural (i.e. endurance performance) responses during a sustained contraction of the dominant KE following prior physical activity in the upper body (i.e. HG). In response to the findings of [chapter 4](#), the adopted paradigm offered the potential to examine the perceptual and affective changes induced through demanding physical activity within fully functioning neuromuscular system, in keeping with previous reports (Aboodarda *et al.*, 2020; Amann *et al.*, 2013; Johnson *et al.*, 2015). Thus, physical endurance performance could be compared within an intact system. It was hypothesized that prior HG exercise would increase the perception of fatigue, perception of effort and negative affect, resulting in impaired performance during the subsequent KE task. Exploratory analyses examining the relationships between perceptual, affective and performance variables were subsequently conducted.

5.3. Method

5.3.1. Sample Size Calculation

Required sample size estimation was conducted based on effects derived from previous studies demonstrating a deleterious influence of prior physical activity on the subsequent endurance capacity during single limb exercise (Amann *et al.*, 2013; Morgan *et al.*, 2019). Morgan *et al.* (2019) reported the smallest of these effects (Cohen's $d = 0.76$), which was subsequently used to estimate the required sample size to adequately power the planned paired sample t -test (i.e. comparison between conditions for endurance performance) within the present study. With an $\alpha = 0.05$ and $1 - \beta = 0.80$ ([section 3.19.1.](#)) the minimum estimated sample size was 16.

5.3.2. Participants

As previously described in [chapter 4](#), ethical approval and written informed consent were obtained as detailed in [section 3.2.](#) and [section 3.5.3.](#), respectively (Ref: 2019-2375). Following this, 20 healthy males (mean \pm SD; age: 25 ± 4 years; weight: 81.2 ± 9.0 kg; height: 1.82 ± 0.07 m) were recruited to participate in the study. All were medication free and had no history of cardiovascular, neurological or musculoskeletal disorders. Hand (16 right) and leg (15 right) dominance ([section 3.18.](#)) and anthropometric measures ([section 3.17.](#)) were determined upon enrolment into the study.

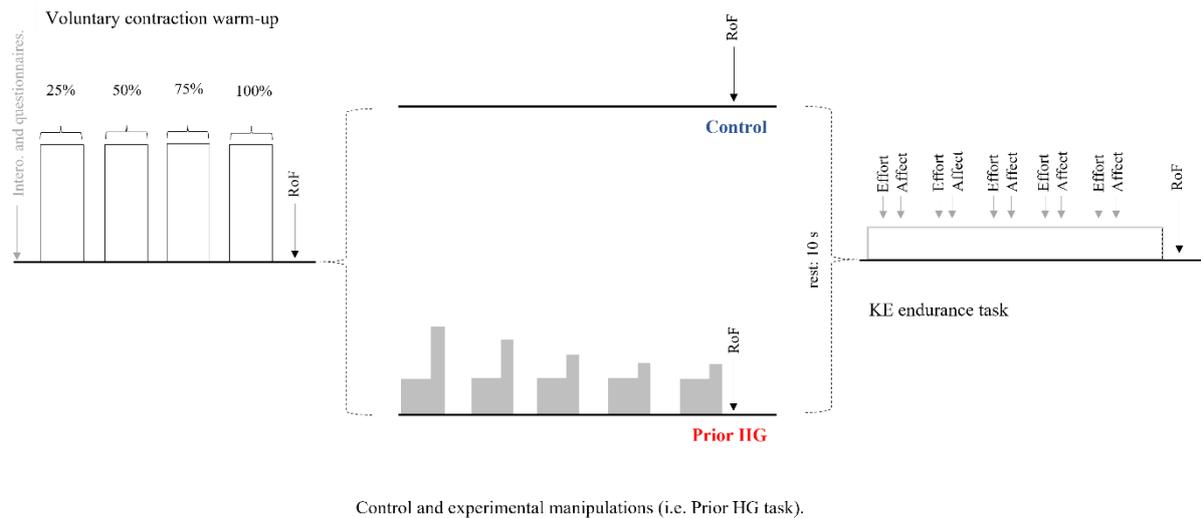


Figure 5.1. Schematic overview of the experimental design of *chapter 5*. The effect of prior activity in upper body (i.e. Prior HG) on endurance performance undertaken in the lower body (i.e. sustained submaximal KE contraction) was compared to a control condition (i.e. no activity). Perception of effort and affective valence were recorded intermittently throughout the endurance task. KE: Knee extensor; Prior HG: prior handgrip task; RoF: Ratings of fatigue.

5.3.3. Experimental Design

Experimental controls were implemented as described in [section 3.9](#). Participants attended three sessions, each separated by a minimum of 48 hours. All sessions started with a standardised warm-up ([section 3.15.1](#) and [3.15.2](#)) followed by the assessment of MVC force for both HG and KE. In the preliminary session, participants were familiarised with all measures ([section 3.10](#)) and maximal HG and KE force was determined. A schematic representation of the main experimental trials is presented in [Figure 5.1](#). In the two experimental sessions, endurance performance was assessed during a sustained submaximal (20% MVC) contraction of the dominant KE ([section 3.14.1](#)), performed immediately (10 s) after a bilateral, intermittent HG contraction task ([section 3.14.2](#)) and time-matched control condition (passive rest). As in [chapter 4](#), to standardize task duration across both the control and prior HG conditions, participants performed only the number of successfully completed contraction sequences achieved during the preliminary familiarisation session, which equated to the number of contractions required to reach task failure (voluntary force below 30% MVC for > 2 s). Target submaximal forces were derived for both the HG and KE tasks from force recorded during the preliminary session (maximal force production did not differ between the preliminary session and experimental trials; all $p > 0.05$). During the KE endurance task, the perception of effort ([section 3.12](#)) and affective valence ([section 3.13](#)) were assessed every 30 s, with scales presented in pseudorandomized order. Participants were also asked to rate their subjective perception of fatigue ([section 3.11](#)) at three time points: before the HG/control task (i.e. baseline), immediately before the KE endurance task and immediately after the KE endurance task. Surface EMG activity of the VL was recorded throughout the KE task ([section 3.15.3](#)).

Participants were positioned in accordance with the set-up for the measurement of force in both the HG and KE outlined in [section 3.15](#). Strong verbal encouragement was provided throughout the HG but not the KE task, so

as to prevent the present investigator from exerting undue influence on endurance performance. Participants were strictly instructed to relax their legs during the HG task (average VL RMS EMG <0.03 mV). Visual feedback of force production was presented on a monitor, with participants naïve to both elapsed time and task failure criteria ([section 3.14.1](#)). Session order was randomised (block randomisation) and counterbalanced across paired participants.

5.3.4. Data Analysis

KE endurance performance was quantified as time to task failure (TTF), defined in [section 3.14.1](#). The percentage change in HG MVC force was quantified across the HG task from the initial MVC (i.e. following the warm-up) to the last MVC of the task. Maximal RMS and mean power frequency (MPF) of the VL EMG signal were obtained during initial MVCs performed at the beginning of each session, across a 500-ms window centred on the highest recorded KE force value. These values were used to normalise the RMS and MPF calculated over consecutive 15s sampling intervals during the KE performance task. Ratings of the perception of effort and affective valence recorded at task failure represent the final recordings achieved for each individual during each respective KE endurance task. In addition to ratings at each designated time interval, the rate of change in effort ($\Delta\text{Effort}/\text{time}$) and affect ($\Delta\text{Affect}/\text{time}$) was also calculated, based on the change from the first to the last recorded response as a function of time.

5.3.5. Statistical Analysis

Statistical procedures were performed using SPSS unless otherwise stated ([section 3.19](#)). Assumptions of statistical tests were assessed prior to performance ([section 3.19.6](#)). Time to task failure (TTF) violated the assumptions of normality and was thus analysed using the non-parametric Wilcoxon signed-rank test. Effort and affective responses were analysed at each time point up to sample iso-time (i.e. time from the beginning of the KE performance task to the penultimate measurement before task failure recorded for the shortest performance across the sample); in this instance, responses obtained up to 60 s. This was performed using a two-way (2 x 2) repeated measures ANOVA across condition (Control; Prior HG) and time (30 s; 60 s). Sphericity was assessed using Mauchly's test, with Greenhouse-Geisser correction applied as appropriate ([section 3.19.6](#)). Effort and affective valence at task failure were not included in this general linear model due to observed ceiling and floor effects, respectively. Instead, effort and affect at task failure were assessed separately using Wilcoxon signed-rank tests, due to violations to the assumption of normality. RoF was assessed using a two-way repeated measures (2 x 3) ANOVA, with factors of condition and time (Baseline, Pre KE, Post KE). The effect of prior HG exercise on VL RMS and MPF were analysed with a two-way (2 x 7) repeated measures ANOVA. Due to technical issues with the acquisition and processing of data, analysis for the RMS and MPF was performed on $n = 19$ and $n = 18$, respectively. The factor of time comprised 7 levels detailing the duration from the start of the task to sample iso-time. EMG parameters at task failure were analysed using paired-sample t -tests. Exploratory Spearman's rank correlation coefficients assessed the relationships between TTF and select perceptual and affective variables with the false discovery rate (FDR) applied to adjust α in response to multiple comparisons (Benjamini & Yosef, 2000; Pike, 2011). Repeated measures correlations were used to assess the association between the perception of fatigue

and both the perception of effort and affective valence across both conditions ([section 3.19.4](#)). For all analyses, the null hypothesis was rejected at an α -level of 0.05.

5.4. Results

5.4.1. Handgrip Task and Time to Task Failure during the Knee Extensor Endurance Task

Mean HG task duration was 308.0 ± 96.0 s (range: 140 – 470 s; 11 ± 3 repetitions). The HG task induced substantial reductions in maximal force production in both the dominant ($-47.0 \pm 10.1\%$; range: $-28.0 - 68.1\%$) and non-dominant hand ($-45.2 \pm 10.4\%$; range: $-23.3 - 63.2\%$), with no difference between hands ($t_{(19)} = -1.17$, $p = 0.258$, $d_{av} = 0.18$). Importantly, Prior HG significantly impaired KE performance (Prior HG: *Mdn*: 230.5 s [191 – 332 s], Control: *Mdn*: 257 s [197 – 363 s]; $Z = -2.24$, $p = 0.025$, $r = 0.35$). Reductions were evidenced in 15 of 20 participants and resulted in a mean reduction in duration of $11.1 \pm 20.8\%$ ([Figure 5.2](#)). The observed effect appeared to be attributable to the intervention and not simply the order of the trials, with no difference

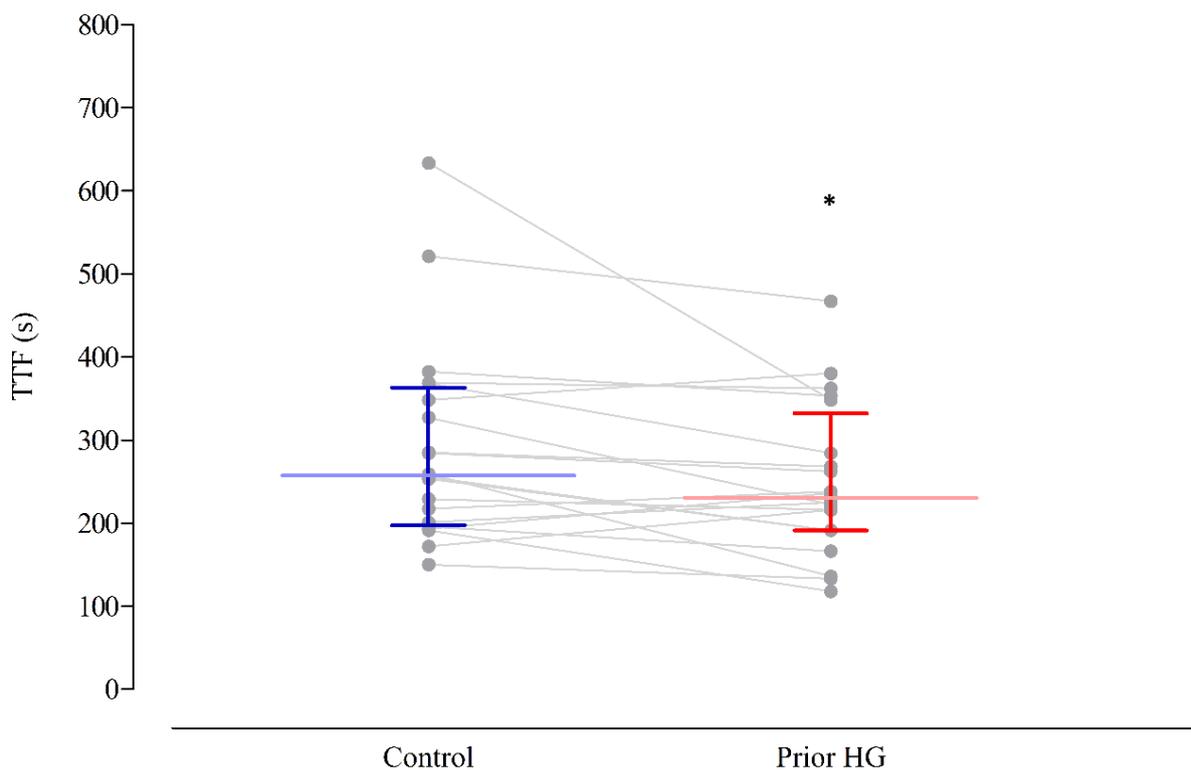


Figure 5.2. Effect of prior handgrip (HG) activity on time to task failure (TTF) in the knee extensor (KE) endurance task. Connected grey points represent paired performance times for each participant. Coloured bars represent the median (*Mdn*) and interquartile range (*IQR*). *: Significantly different to control ($p < 0.05$).

evident between the first and second trial performed, irrespective of condition (trial 1: 244 s [216 – 300 s], trial 2: 248 s [191 – 357 s]; $Z = 0.06, p = 0.955, r = 0.01$).

5.4.2. Perception of Effort, Affect and Ratings of Fatigue during the Knee Extensor Endurance Task

Effort and affective responses are presented in [Table 5.1](#). A heightened effort perception was observed in the Prior HG condition ($F_{(1,19)} = 4.46, p = 0.048, \eta_p^2 = 0.518$) and across time ($F_{(1,19)} = 30.92, p < 0.001, \eta_p^2 = 0.619$), but no interaction between condition and time was observed ($F_{(1,19)} = 3.26, p = 0.087, \eta_p^2 = 0.146$). Effort at task failure was maximal (or near maximal) in both the Prior HG and control condition ($Z = 0.56, p = 0.577, r = 0.09$). Similarly, affective valence was reduced in Prior HG compared to the control condition ($F_{(1,19)} = 9.80, p = 0.006, \eta_p^2 = 0.340$), and declined across time ($F_{(1,19)} = 8.00, p = 0.011, \eta_p^2 = 0.296$). There was no interaction between condition and time ($F_{(1,19)} = 1.09, p = 0.309, \eta_p^2 = 0.054$) and there was no difference in affective valence at task failure between conditions ($Z = -0.54, p = 0.589, r = -0.09$).

Table 5.1. Perceived effort and affective valence ratings across the KE endurance task.

		Time		
		30 s	60 s	TTF
Effort	<i>Control</i>	3 ± 1	4 ± 1	10 [9 – 10]
	<i>Prior HG</i>	4 ± 2	5 ± 2	10 [9 – 10]
Affective Valence	<i>Control</i>	2 ± 2	1 ± 1	-4 [-5 – -2]
	<i>Prior HG</i>	1 ± 2	0 ± 1	-4 [-5 – -3]

Data presented as mean ± SD for variables analysed with parametric models and median and IQR for variables assessed using non-parametric analysis.

A main effect of condition ($F_{(1,19)} = 50.63, p < 0.001, \eta_p^2 = 0.727$), time ($F_{(1,22,23,11)} = 61.05, p < 0.001, \eta_p^2 = 0.763$) and interaction ($F_{(1,535,29,161)} = 72.84, p < 0.001, \eta_p^2 = 0.793$) was observed for RoF. Pairwise comparisons showed that RoF was elevated by the HG task ($t_{(19)} = -12.07, p < 0.001, d_{av} = 3.01$) and was increased further by the completion of the KE task ($t_{(19)} = -2.79, p = 0.035, d_{av} = 0.49$). In contrast, there was a small decrease in RoF following the control intervention ($t_{(19)} = 2.99, p = 0.023, d_{av} = -0.27$), but RoF was increased by the KE task ($t_{(19)} = -6.64, p < 0.001, d_{av} = 2.33$). There was no difference between conditions at baseline ($t_{(19)} = 0.96, p = 0.349, d_{av} = -0.18$), but RoF was greater in Prior HG compared to the control condition immediately before the KE task ($t_{(19)} = -9.53, p < 0.001, d_{av} = 2.88$) and remained greater after the KE task ($t_{(19)} = -8.15, p < 0.001, d_{av} = 0.69$) ([Figure 5.3](#)).

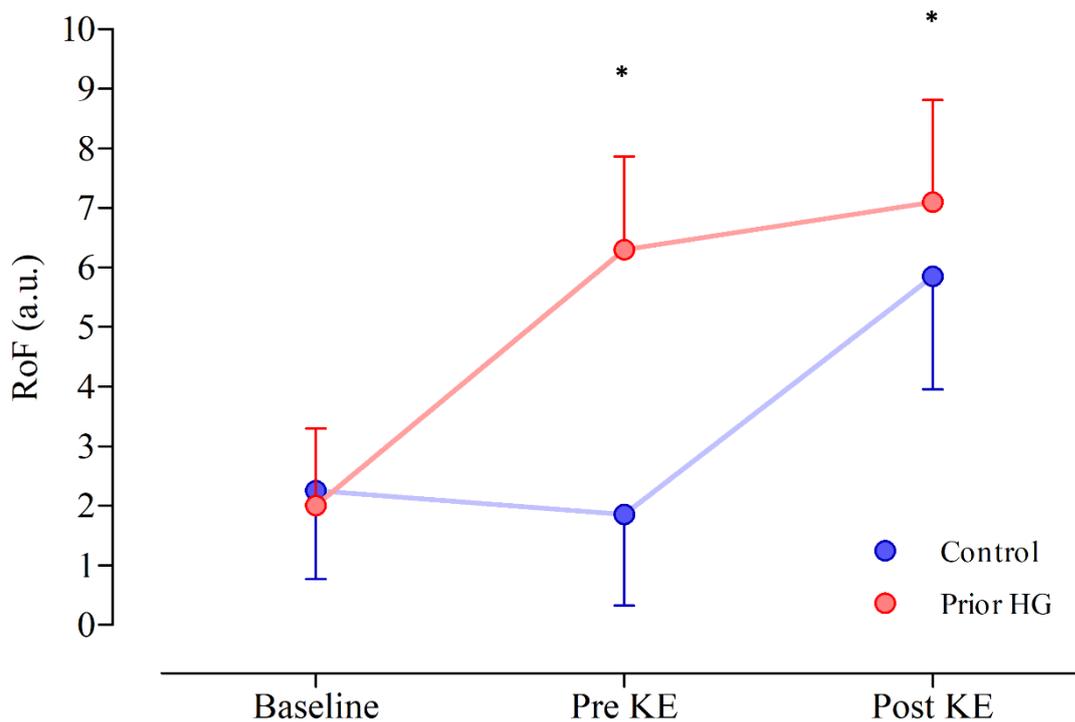


Figure 5.3. Ratings of fatigue (RoF) across stages of the experimental protocol in both the prior handgrip (HG; red circles) and a control (blue circles) condition. Ratings were collected at baseline (i.e. prior to the HG and control task), pre KE (i.e. immediately before the knee extensor endurance task) and post KE (i.e. immediately after the knee extensor endurance task). *: Significantly different from control ($p < 0.05$).

5.4.3. Relationships between Ratings of Fatigue, Perceived Effort, Affective Valence and Task Performance

Exploratory relationships between TTF and perceptual and affective variables (i.e. effort and valence at 60s, rate of change in effort and valence, RoF pre KE) were consistent across conditions ([Figure 5.4](#)). TTF was negatively correlated with effort responses at 60 s (Control: $r_s = -0.72$, FDR-adjusted $p = 0.001$; Prior HG: $r_s = -0.61$, $p = 0.006$) and positively correlated with affective valence at 60 s (Control: $r_s = 0.68$, $p = 0.002$; Prior HG: $r_s = 0.46$, $p = 0.042$). Rate of change in effort perception was also negatively associated with TTF (Control: $r_s = -0.78$, $p < 0.001$; Prior HG: $r_s = -0.59$, $p = 0.008$). However, both the rate of change in affect (Control: $r_s = -0.26$, $p = 0.233$; Prior HG: $r_s = -0.03$, $p = 0.535$) and RoF immediately preceding the start of the KE task (Control: $r_s = 0.12$, $p = 0.439$; Prior HG: $r_s = 0.11$, $p = 0.439$) were not correlated with TTF.

The relationships between RoF and subsequent perceptual and affective responses recorded during the endurance task were also explored. Due to the small range of fatigue scores recorded before the KE task in each condition, repeated measures correlations (Bakdash & Marusich, 2017; Bland & Altman, 1995) were used to examine the association between RoF recorded before the KE endurance task and initial perceptions of effort and affective valence across a wider scope, using the *rmcorr* package (Bakdash & Marusich, 2017) in R (R core team, 2017). The analysis demonstrated RoF displayed a positive ($r_m = 0.60$ [bootstrapped 95% CI: 0.25 – 0.80], $p = 0.004$) and negative ($r_m = -0.68$ [bootstrapped 95% CI: -0.51 – -0.87], $p < 0.001$) relationship with the perception of effort and affective valence, respectively ([Figure 5.5](#)).

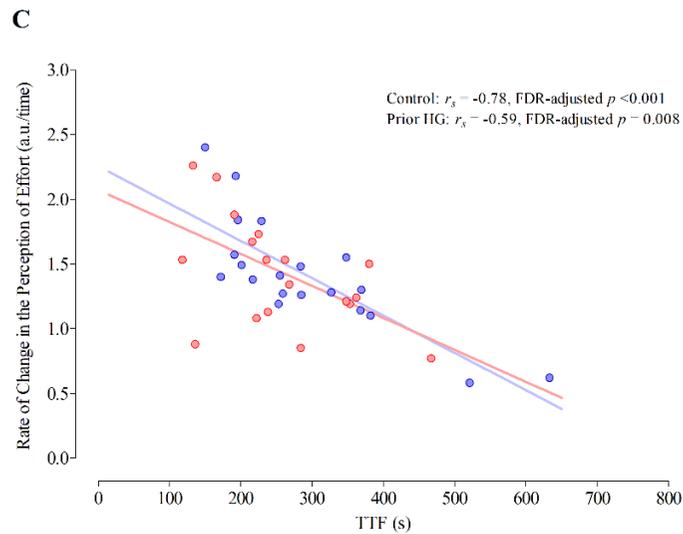
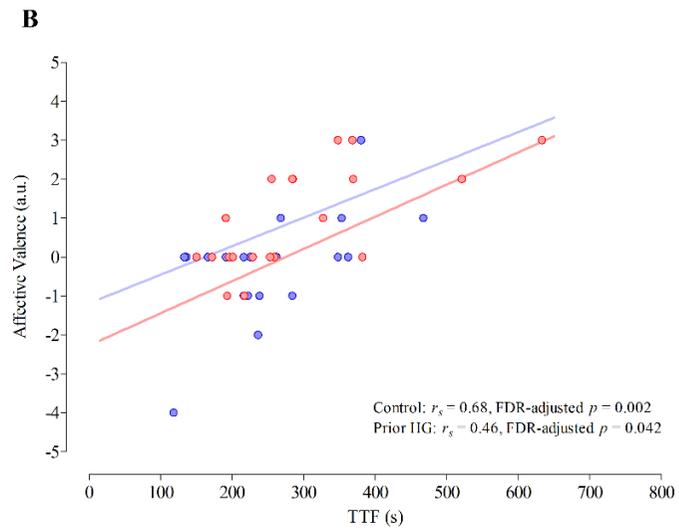
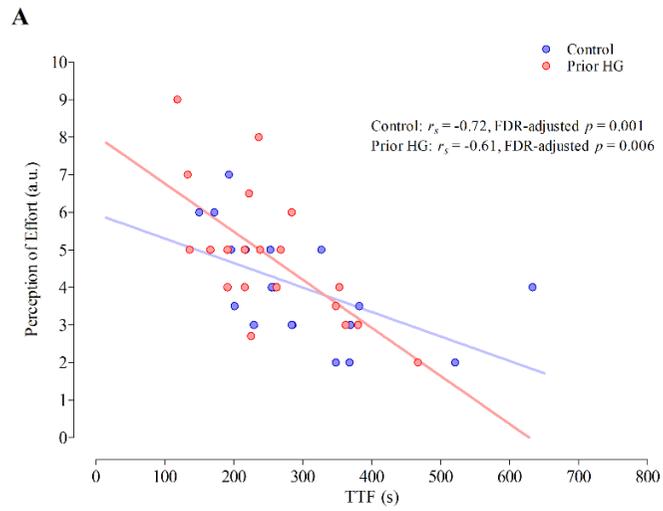


Figure 5.4. Correlations between time to task failure (TTF) for the knee extensor (KE) endurance task and initial ratings of perceived effort (A), initial ratings of affective valence (B) and the rate of change in the perception of effort (C). Correlation coefficients are fitted for both the prior handgrip (HG; red circles) and control (blue circles) condition.

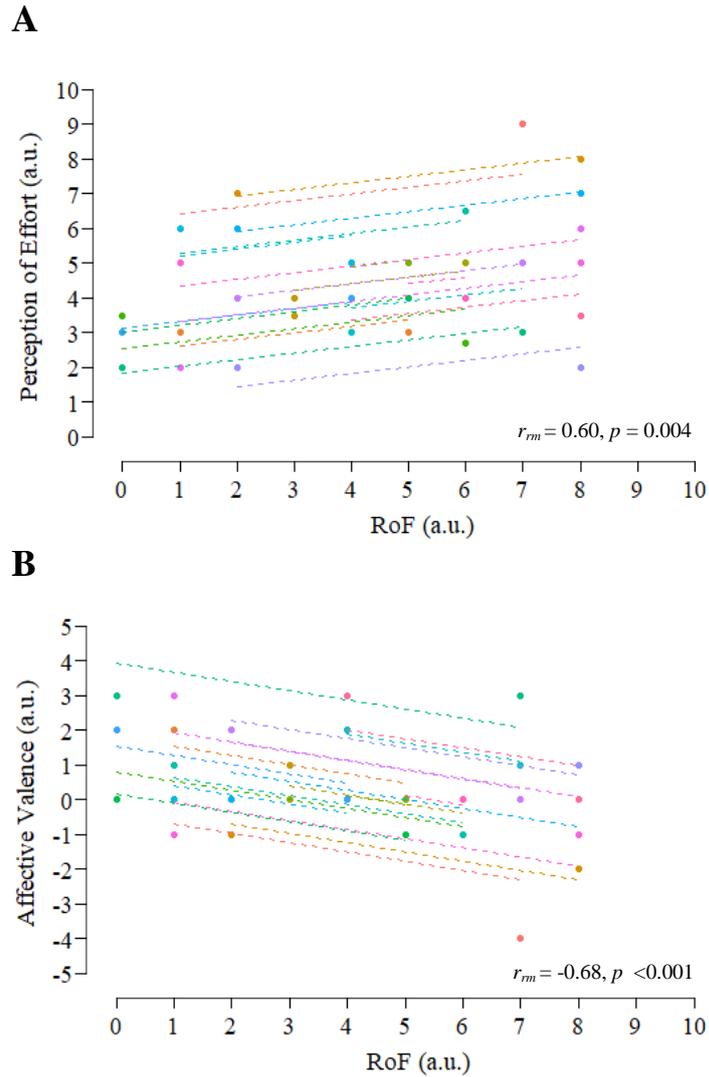


Figure 5.5. Repeated measures correlations between ratings of fatigue (RoF) recorded before the knee extensor (KE) endurance task and both initial (i.e. at 60 s) responses concerning the perception of effort (**A**) and affective valence (**B**). Observations from the same participant are represented by points of the same colour. Corresponding dashed coloured lines represent the repeated measures correlation fit for each participant.

5.4.4. EMG during the Knee Extensor Endurance Task

RMS increased and MPF decreased over time (RMS: $F_{(2.7,48.8)} = 21.94, p < 0.001, \eta_p^2 = 0.549$; MPF: $F_{(3.5,59.1)} = 33.82, p < 0.001, \eta_p^2 = 0.665$) during the KE endurance task. However, there was no main effect of condition (RMS: $F_{(1,18)} = 2.96, p = 0.103, \eta_p^2 = 0.141$; MPF: $F_{(1,17)} = 0.32, p = 0.578, \eta_p^2 = 0.019$) nor interaction across iso-time (RMS: $F_{(2.7,48.5)} = 0.60, p = 0.603, \eta_p^2 = 0.032$; MPF: $F_{(3.0,50.6)} = 0.52, p = 0.666, \eta_p^2 = 0.030$). RMS and MPF were not different between conditions at task termination (RMS: $t_{(18)} = 0.46, p = 0.653, d_{av} = -0.03$; MPF: $t_{(17)} = -1.57, p = 0.134, d_{av} = 0.23$) ([Figure 5.6](#)).

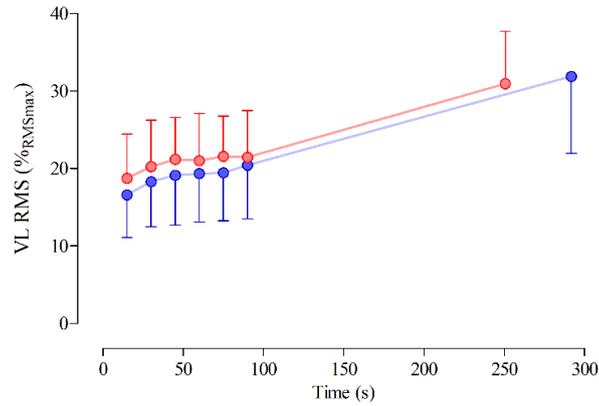
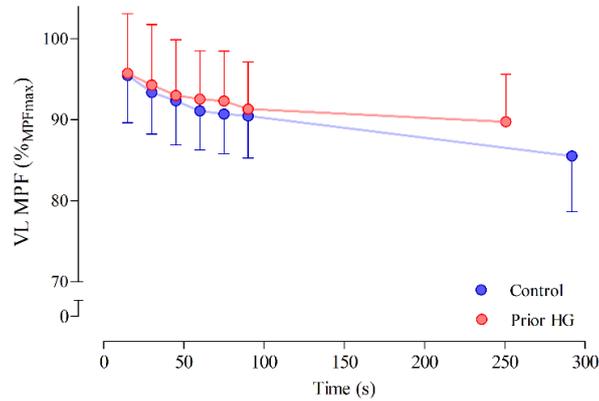
A**B**

Figure 5.6. Effect of prior handgrip (HG) task on the root mean square (RMS) (**A**) and mean power frequency (MPF) (**B**) of the EMG signal recorded in the *vastus lateralis* (VL) during the KE endurance task. Values recorded in the Prior HG (red circles) and a control (blue circles) condition are expressed relative to responses recorded during maximal contractions performed at the start of each trial.

5.5. Discussion

Prior physical activity was used in the present study to examine the interactions between perceptual and affective processes in the central regulation of a physical endurance task. As hypothesized, impaired endurance performance during the KE task was associated with a heightened perception of effort and lower affective valence following the performance of a demanding HG task. Subjective experiences of fatigue were also elevated by the HG task. Though RoF was not correlated with endurance performance directly, RoF was associated with reported effort and valence across the initial stages of the endurance task in both conditions. Accordingly, the results of the present study indicate that sustained physical activity following remote physical activity is limited by changes in cognitive-emotional interactions, with the perception of fatigue implicated as a top-down influence on the experience of task effort and core affective processes.

The results of the present study add to an increasing body of evidence describing impaired physical endurance in one part of the body following motor activity in another. However, the average recorded impairment was relatively modest (-11%) compared to previous reports; though consistent, with three quarters of the sample demonstrating a detrimental effect of the prior HG task. More substantial effects on endurance performance have been reported across homologous muscles of the lower limbs following dynamic contralateral activity (43 – 49%; Aboodarda *et al.*, 2020; Amann *et al.*, 2013), and during unilateral (26 – 33%; Bangsbo *et al.*, 1996; Nordsborg *et al.*, 2003) and bilateral legged-cycling (38%; Johnson *et al.*, 2015) following arm-cycling exercise. The difference in the size of the observed effects may be attributed to various factors relating to the studied populations and adopted tasks, including the training status of the sample (Triscott *et al.*, 2008) and the greater potential influence of central cardiovascular factors evoked during larger muscle mass, aerobic-based protocols (Rossman *et al.*, 2012). Indeed, changes in heart rate imposed by the intermittent HG task were presumably of much lower magnitude (e.g. Lind & McNicol, 1967; Byström & Fransson-Hall, 1994; Toska, 2010) than more dynamic aerobic tasks (e.g. Amann *et al.*, 2013), which may contribute to the different sized effects based on the total level of sensory processing.

In line with previous findings (Amann *et al.*, 2013; Johnson *et al.*, 2015; Morgan *et al.*, 2019; Aboodarda *et al.*, 2020), impaired performance on the KE endurance task was associated with a heightened perception of effort and less positive affective valence following prior performance of the HG task. Termination of performance has been associated with the attainment of a maximal perceived effort, which has been related to either the immediacy or severity of homeostatic threats (Noakes, 2012), and/or general motivational processes (Pageaux, 2014). The observed correlations between time to task failure and the rate of change in the perception of effort across both conditions indicates that the elicited elevation in effort perception by the HG task caused a faster attainment of a maximal perceived effort and supports the perception of effort as a principal variable used in the regulation of physical performance (Staiano *et al.*, 2018). Though representing a crude measure of central motor drive (Dimitrova & Dimitrov, 2003; Farina *et al.*, 2004), EMG indices were unchanged during the KE endurance task following prior performance of the HG task. This may therefore indicate that motor output was not altered during task performance following the HG task, supporting the conclusions of [chapter 4](#) in indicating that neuromuscular function was seemingly left intact. Accordingly, the change in effort perception does not appear to be a result of an increased corollary discharge due to decreasing responsiveness of the KE, instead suggesting prior activity caused changes that consequently altered the processing of effort during the KE endurance task (Pageaux & Lepers, 2016).

Affective valence during the KE endurance task was also reduced by prior HG activity. Moreover, affective valence was shown to be related to task performance across conditions. The data would therefore seem to indicate that both the perception of effort and affective valence are important to the central regulation of physical activity. Challenges to homeostasis are interoceptively sensed and intrinsically affective (Craig, 2002; Damasio & Carvalho, 2013). The integration of interoceptive networks within the putative 'affective workspace' associated with valence (Lindquist *et al.*, 2016; [section 2.5.3.](#)) indicates the propensity for homeostatic challenges to evoke emotional changes and disrupt current goal-related processes in response to threats to biological integrity (i.e. preservation of homeostasis). Accordingly, affective valence has previously been associated with the distribution of energy during self-paced endurance performance (Jones *et al.*, 2015; Renfree *et al.*, 2012) and ultimately the volitional termination of exercise (Hartman *et al.*, 2019). Hartman *et al.* (2019) proposed that the perception of

effort is intrinsically affective, such that during intense and demanding physical exertion the two constructs merge, with the experience of intense displeasure ultimately leading to an ‘instinctive’ decision to terminate current activity. In support of their proposition, the authors demonstrated that the rate of decline in affective valence was associated with task failure during a constant-load cycling task (Hartman *et al.*, 2019). Here, the initial experience of affective valence was related to task performance however, unlike the perception of effort, the change in valence across time was not. This may suggest that the perception of effort may be of (relatively) greater relevance to the regulation of physical activity than affective valence and indicate a partial disassociation between the perception of effort and affective valence. The greater sensitivity to the perception of effort over time may, in part, be representative of its involvement in emotional regulation during the KE task. That is, a progressive increase in the perception of effort may represent the deployment of (presumably explicit) control strategies in response to affective homeostatic perturbations (Braunstein *et al.*, 2017). Accordingly, the change in effort perception may, in part, reflect the increasing resources devoted to the control of emotional states in pursuit of a goal as homeostasis is challenged, and task disengagement may be sensitive to appraisals of implemented (effortful) control strategies, emerging when they no longer holding sufficient value (Etkin *et al.*, 2015). Therefore, rather than merging, affective valence and effort may represent distinct, but interdependent components of a regulation strategy designed to balance goal pursuit and the maintenance of homeostasis. Further studies are required to delineate the behavioural effects of the perception of effort and affective valence, and the relationship between these psychological constructs, in response to physical activity.

The precise mechanism(s) resulting in a heightened perception of effort and less positive affective valence, following prior engagement with the HG task remains unclear. Comparable effects observed after the performance of demanding cognitive tasks have previously been attributed to physiological factors including the extracellular cerebral accumulation of adenosine in active regions of the brain shared by the sequential tasks (Martin *et al.*, 2018; Pageaux *et al.*, 2014), though this has been questioned (McMorris, 2020; [section 2.7.1.](#)). Alternatively, the perception of effort and affective responses have been shown to be sensitive cognitive factors (e.g. self-efficacy; Hutchinson *et al.*, 2008; Treasure & Newbery, 1998). The performance of the HG task evoked a heightened state of perceived fatigue immediately before the start of the KE endurance task. Though not correlated with endurance performance itself, RoF was shown to be positively and negatively associated with initial effort and affective responses during the KE task, respectively. This may indicate that a perceived state of fatigue modified the processing and interpretation of the signals supporting the perception of effort and affective valence. Clear disassociation between fatigue, effort and affect is inherently difficult since they may all reflect outcomes of the same integrated control process (Hockey, 2011). For example, as RoF does not capture the hedonic properties of fatigue (Micklewright, St Clair Gibson, *et al.*, 2017), it is possible that the association between valence and fatigue simply reflects the emotional component of the symptom of fatigue (St Clair Gibson *et al.*, 2003; Hartman *et al.*, 2019). Yet, fatigue can be disassociated from effort (Micklewright, St Clair Gibson, *et al.*, 2017; Milyavskaya *et al.*, 2021) and affective valence (McAuley *et al.*, 1999). Here, two lines of evidence would suggest fatigue perception was at the very least partially disassociated from both the perception of effort and affective valence in the present study. First, while effort and valence were maximal (or near maximal) at task failure in both conditions, perceptions of fatigue were distinctly sub-maximal and differed between conditions ([Figure 5.3.](#)). Second, the

perception of effort and affective valence were associated with different consequences for behaviour compared to the perception of fatigue (i.e. not related to TTF).

To understand how a perceived state of fatigue may influence effort perception and affect, emerging theoretical accounts of pathological fatigue within the neuroscience literature are drawn upon, in which fatigue is associated with negative beliefs concerning one's ability to control (or predict) bodily states, i.e. reduced allostatic self-efficacy (Manjaly *et al.*, 2019; Stephan *et al.*, 2016). In this framework, the development of fatigue is associated with the monitoring and detection of a persistent mismatch between what the brain predicts the sensory state of the body to be and the actual sensory inputs received, which casts doubt in internal models used to understand the world around us (Stephan *et al.*, 2016). As the perception of effort (Kuppuswamy, 2017) and emotion (Barrett, 2017) have both been attributed to this mismatch between sensory predictions and sensory feedback, declines in one's confidence (or precision) in the predictions of internal sensory states arising with the development of fatigue may in turn generate greater prediction errors and thus augment perceptual consequences of action, such as a heightened perception of task effort and reduced affective valence (this will be discussed in greater detail in [section 8.4.](#)).

A few limitations of the present study must be acknowledged. First, the perceptual and affective ratings were analysed as continuous variables, rather than ordinal (e.g. Bishop & Herron, 2015), adopting parametric factorial analyses. It is suggested that, due to the length of the scales used, such an approach may be justified (Harpe, 2015). However, as debate concerning the most appropriate statistical analysis for this form of data continue (Knapp, 1990; Carifio & Perla, 2008), interested parties are urged to reanalyse the data of the present study as they see fit (<https://osf.io/kbzvn/>). Next, it is important to acknowledge that RoF were always assessed at rest, while effort and affective valence were measured in an active state during the KE task. Though this does not invalidate measurements of the perception of fatigue (Micklewright, St Clair Gibson, *et al.*, 2017), like it may do for the perception of effort (that is, the perception of effort is goal-directed, therefore in the absence of goal-directed action the perception of effort cannot be experienced), disassociation of behavioural functions between fatigue and effort/valence may have been influenced by the absence of ongoing motor activity when assessing fatigue.

5.6. Conclusion

When preceded by demanding activity in the upper limbs, lower body endurance performance is limited through changes in the complex, cognitive-emotional interactions involved in the central regulation of performance. The subjective perception of fatigue is an important input influencing the subjective perception of task effort and affective response to task demands. The results thus indicate that the perception of fatigue holds a distinct role in the central regulation and control of physical endurance performance. As the conclusions drawn here are predominantly based on correlational analysis, attempts to establish these associations more causally are required.

CHAPTER 6 - EFFECT OF THE SUBJECTIVE INTENSITY OF FATIGUE AND INTEROCEPTION ON PERCEPTUAL REGULATION AND PERFORMANCE DURING SUSTAINED PHYSICAL ACTIVITY

6.1. Abstract

Evidence of a deleterious effect of the subjective perception of fatigue on an individual's ability to sustain physical tasks has largely been concluded based on correlation analysis. The aim of the present study chapter attempted to better understand causal effects through examining whether the subjective intensity of a perceived state of fatigue, pre-induced through prior upper body activity, differentially impacted the central regulation of performance during a sustained, isometric contraction performed in the lower body. The study also explored relationships between (cardiac) interoception and perceptual and affective experiences during physical activity. Thirty male participants completed three experimental conditions, with the intensity of a pre-induced state of fatigue manipulated to evoke moderate (MOD), severe (SEV) and minimal (control; CON) intensity perceptions prior to performance of the sustained contraction. Performance of the sustained contraction was significantly impaired under a perceived state of fatigue, in both the MOD and SEV conditions. This was accompanied by greater perceived effort and less positive affective valence reported during the endurance task. However, statistical differences were limited to comparisons to CON, with no differences evident between the two experimental trials (i.e. MOD vs. SEV). Individuals' metacognitive awareness of the accuracy of cardioceptive judgments was shown to predict the subjective intensity of fatigue experienced during the endurance task. However, interoception did not moderate the relationship between fatigue and both perceived effort and affective valence. In conclusion, the results demonstrate a perceived state of fatigue limits physical endurance performance, influencing both how effortful activity is perceived to be and the affective response to physical activity. Though awareness of interoceptive representations of bodily states is identified as a potential component of the subjective experience of fatigue, interoception does not modulate the relationships between perceived fatigue and other perceptual (i.e. effort) and affective constructs.

6.2. Introduction

The perception of fatigue has been proposed to define a reflective phenomenological experience associated with a feeling of reduced capacity to cope with experienced demands (Aaronson *et al.*, 1999; Micklewright, St Clair Gibson, *et al.*, 2017; Steele, 2021; André *et al.*, 2019; [section 2.2.4.](#)). The perception of fatigue has therefore been identified with individuals' perception of their capacity to effectively exert control through action; that is, ones' self-efficacy (Steele, 2021; Stephan *et al.*, 2016; [section 2.3.2.](#)). It is well documented that manipulations of self-efficacy influence endurance performance (Halper & Vancouver, 2016; Hutchinson *et al.*, 2008; Weinberg *et al.*, 1979; Weinberg *et al.*, 1981), modulating both the perception of effort (Halper & Vancouver, 2016; Hutchinson *et al.*, 2008; though see Motl *et al.*, 2006) and affective experiences (McAuley *et al.*, 1999; Hutchinson *et al.*, 2008). As evidenced in [chapter 5](#), the development of a perceived state of fatigue may similarly limit physical endurance performance by also influencing sensory processing. The perception of fatigue was identified as a top-down input, biasing perceptual (i.e. effort) and affective responses used in the regulation of physical endurance performance, as evidenced by the relationships observed between constructs. Supporting this proposition, comparable relationships have been reported following the inducement of a perceived state of fatigue through demanding cognitive activity in healthy populations (Benoit *et al.*, 2019; Harris & Bray, 2019). However, causal interpretation of the effects of a perceived state of fatigue on the central regulation of performance are precluded based on this limited, principally correlation-based analysis. Observed effects on physical performance cannot be attributed specifically to the developed perceived state of fatigue over some other latent variable(s) concomitantly changed by the experimental intervention. Attempts to establish causal associations would require explicit manipulation of the perception of fatigue - ideally across multiple levels - and the subsequent examination of its effects.

The perception of fatigue is often quantified as a continuous variable in which perception increases across a range of subjective intensities (e.g. Micklewright, St Clair Gibson, *et al.*, 2017). Currently, it is unclear what the relationship between the intensity of perceived fatigue and its putative perceptual, affective and performance effects should be. That is, it is unclear whether responses to a greater intensity in perceived fatigue are continuous or categorical in nature. It is possible that incremental increases in the perception of fatigue may evoke proportional changes in central regulatory responses (e.g. the perception of effort and affective valence) and task performance (e.g. time to task failure). Alternatively, the instantiation of the perception of fatigue may evoke some change in these regulatory responses, but further increments in its subjective intensity elicit no further changes⁶⁰. Examination of the self-efficacy–endurance performance relationship has indicated that performance may be differentially affected across low, moderate and high perceptions of performance ability, particularly during performance of novel tasks (Ede *et al.*, 2017). Applied to the perception of fatigue, this may suggest that the experienced, subjective intensity of fatigue may exert different influences on perceptual and affective responses, which subsequently impact performance outcomes.

Interoception is a fundamental component of adaptive, allostatic behaviour (Critchley & Harrison, 2013). Interoception is assumed to play an important role in the central regulation of physical endurance performance (McMorris, Barwood, & Corbett, 2018; Robertson & Marino, 2016), though few studies have directly investigated

⁶⁰ Of note, similar considerations have recently been posed of the effort-value relationship (Inzlicht *et al.*, 2018).

this relationship. One of the most commonly adopted methods of quantifying individuals' interoceptive ability is the behavioural assessment of ones' perception of their own heartbeats (e.g. Katkin *et al.*, 1983; Schandry, 1981). Indeed, individuals who display greater accuracy in detecting resting heartbeats have been reported to cycle at lower work rates during self-paced cycling exercise than those of poorer accuracy, despite reporting the same intensity of fatigue in response to the task (Herbert, Ulbrich, *et al.*, 2007). Interoceptive processing can be decomposed across three dimensions relating to an individual's accuracy (objective precision in monitoring internal bodily sensations), confidence (subjective ability to detect interoceptive sensations) and awareness (a metacognitive measure of the correspondence between objective and subjective assessments) in monitoring interoceptive stimuli (Garfinkel & Critchley, 2013; Garfinkel *et al.*, 2015). In a heightened perceived state of fatigue, greater attention may be afforded to (unexpected) ascending interoceptive signals (Stephan *et al.*, 2016), which may reflect salient information used in forming momentary perceptions of task demands (e.g. effort; Iodice *et al.*, 2019). Accordingly, it may be reasonable to assume that an individual's interoceptive ability may influence subjective responses to physical activity and the associations between constructs. Specifically, interoceptive awareness may influence the relationship between perceived fatigue and indices of the central regulation of performance because both the perception of fatigue (Hockey, 2011; Stephan *et al.*, 2016) and performance regulation (Brick *et al.*, 2016) may involve compatible, higher-order (meta)cognitions.

The aim of the present study chapter was to examine the effect of the subjective intensity of fatigue on markers of the central regulation and subsequent performance. As in [chapter 5](#), a prior exercise paradigm was adopted, in which a perceived state of fatigue was pre-induced by an intermittent, upper body exercise prior to the evaluation of its effects during an endurance task performed in the lower body. This also enabled an examination of the replicability of the effects observed in the previous study chapter. It was hypothesized that lower-body endurance performance would be impaired when the intensity of the perceived state of fatigue was greater, with a severe perceived state of fatigue associated with greater effort and more negative affective valence than moderate and control conditions. A secondary aim of the present study was to explore the moderating effect of interoceptive awareness on the relationship between perceived fatigue and both perceived effort and affective valence. It was hypothesized that individuals' characteristic awareness of interoceptive cues would moderate the relationship between the perception of fatigue and the perception of effort and affective valence reported during the KE endurance task.

6.3. Method

6.3.1. Sample Size Calculation

The size of the effect reported in [chapter 5](#) was used to establish a lower bound sample estimate for the present investigation ($n = 20$). A sequential sampling rule was then adopted to determine the sample size for the present investigation using the composite open adaptive sequential test (Frick, 1998). Once $n = 20$, endurance performance was compared between each condition using paired samples t -tests. If the comparison fell between $0.01 < p < 0.36$, further participants were recruited. However, if p fell < 0.01 or > 0.36 for all comparisons, no further

participants were recruited (Frick, 1998). If further participants were recruited the procedure was performed again after the recruitment of an additional 10 participants.

6.3.2. Participants

Ethical approval (Ref: 2019-2679; [section 3.2.](#)) and written informed consent ([section 3.5.3.](#)) were obtained prior to participant enrolment. All participants were screened based on their medical history and reported no cardiovascular, neurological or musculoskeletal disorders, before providing written informed consent. In total, 30 healthy males (mean \pm *SD*; age: 25 ± 7 years, weight: 75.4 ± 11.7 kg, height: 1.78 ± 0.06 m) volunteered to participate in the experiment. Participants were naïve to the true purpose of the study, believing that they were simply taking part in an investigation examining the effect of different durations of prior motor activity on endurance performance in a remote muscle group. The cohort were active (4155 ± 2501 MET min.week⁻¹) based on self-reported activity using the International Physical Activity Questionnaire (Craig *et al.*, 2003). All participants were instructed to refrain from caffeine, alcohol, and strenuous exercise for 24 hours prior to each testing session. Hand ($n = 26$ right) and leg ($n = 25$ right) dominance was determined as per [section 3.18.](#)

6.3.3. Experimental Design

Experimental controls were implemented as described in [section 3.9.](#) The study comprised one familiarisation session ([section 3.10.](#)) and three experimental trials. The experimental trials involved two experimental manipulations of the perceived state of fatigue and one control (CON) trial. The experimental sessions were presented in a randomised (block randomisation) and counterbalanced order. A schematic representation of the experimental design is presented in [Figure 6.1.](#) For the experimental manipulations, two intensities of a perceived state of fatigue were pre-induced through the intermittent bilateral HG task ([section 3.14.2.](#)). The two intensities corresponded to moderate (MOD) and severe (SEV) perceptions of fatigue. During the rest periods of the intermittent HG task, participants scored their RoF ([section 3.11.](#)). The HG task was terminated when a specific numerical response on the RoF scale was provided in each condition. In the development of the RoF scale, descriptors and visual diagrams were orientated in respect to numerical ‘bands’, designed to demarcate progressive symptoms across the full perceptual range (Micklewright, St Clair Gibson, *et al.*, 2017). Moderate perceptions of fatigue correspond to numerical ratings of 4-6, where severe perceptions of fatigue correspond to numerical ratings of 7-8. To ensure adequate differentiation between moderate and severe intensities, numerical ratings of 5 and 8 were used to separate MOD and SEV conditions, respectively. Once the requisite RoF was achieved the HG task was stopped, with participants naïve to the precise stopping criteria. In CON, participants sat quietly for a duration equivalent to the TTF of the HG task performed in the preliminary session (i.e. force below 30% MVC in the dominant hand for > 2 s) and provided a RoF at the end of this period. To prevent the potential outcome of the HG task being terminated after a single contraction, particularly in the MOD condition, and thus ensure a state of fatigue was likely to have developed in response to performing the HG task, unbeknownst to the participants, all were required to perform a minimum of three contraction sequences in each of the two experimental manipulations (i.e. MOD and SEV).

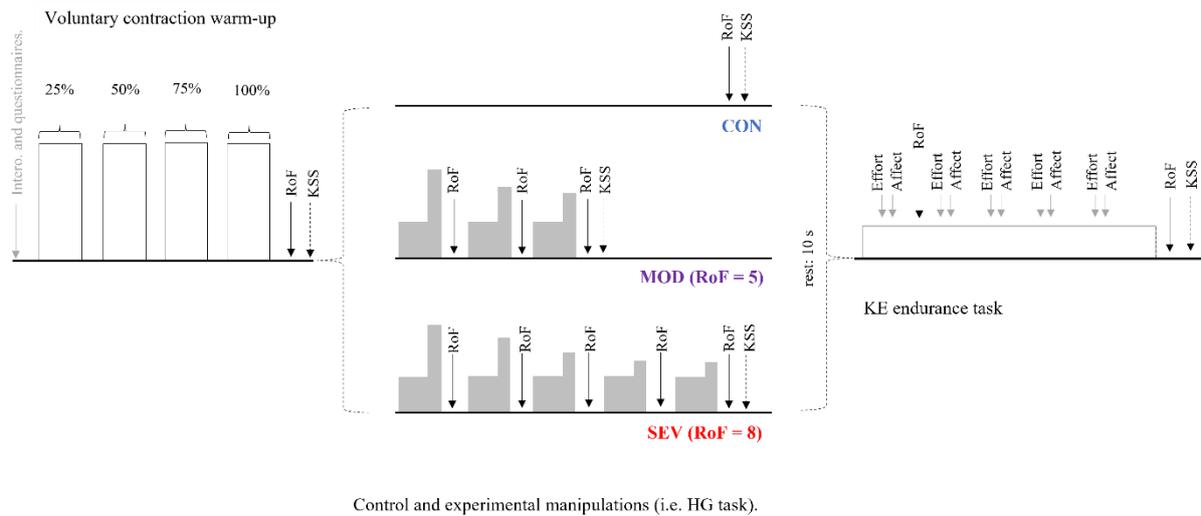


Figure 6.1. Schematic representation of the experimental design of *chapter 6*. Participants completed three separate conditions. The experimental manipulation comprised two separate sessions which involved the performance of an intermittent handgrip (HG) task until ratings of fatigue (RoF) were perceived as moderate (MOD; RoF = 5) and severe (SEV; RoF = 8). The other condition was a control task (CON) in which no prior exercise was performed. Endurance performance was assessed during a sustained, sub-maximal isometric contraction of the dominant knee extensors (KE), where the perception of effort and affective valence were recorded intermittently throughout. RoF: Ratings of fatigue; DASS: Depression, Anxiety and Stress scale; KSS: Karolinska Sleepiness Scale; MVC: Maximal voluntary contraction.

Immediately (10 s) after the interventions adopted in CON, MOD and SEV conditions, endurance performance was assessed in the dominant KE through a sustained isometric contraction ([section 3.14.1](#)). During the KE endurance task, participants were asked to rate their perception of effort ([section 3.12](#)) and affective valence ([section 3.13](#)) every 30 s, with scales presented in a pseudorandomised order. RoF was assessed at baseline, immediately before the start of the KE endurance task, 1-minute into the KE endurance task and upon task failure of the endurance task. EMG activity ([section 3.15.3](#)) was assessed from three muscles of the quadriceps (i.e. VL; *vastus medialis*, VM; *rectus femoris*, RF) throughout the KE endurance task.

Participants were seated on a custom-built rig for the quantification of force in both the HG and KE ([section 3.15](#)). Each trial began with performance of the same voluntary contraction warm-up ([section 3.15.1](#) and [3.15.2](#)) and determination of MVC force for both HGs and the dominant KE. Target forces were determined for both the HG task and KE endurance task based on the highest values recorded during the familiarisation session. During the HG task, participants were strictly instructed to relax their legs (average RMS amplitude across both muscles and experimental manipulation ranged between 2.1-3.1% RMS_{max}). Strong verbal encouragement was provided throughout the HG, but not the KE endurance task to minimize any potential researcher bias from influencing the primary performance measure. Visual feedback of force production was presented on a monitor, with participants naïve to elapsed time.

6.3.3.1. Potential Extraneous Influences on the Perception of Fatigue

To facilitate interpretation of both the development and consequences of fatigue, potentially confounding perceptual and psychological factors were also recorded during each condition. This included the retrospective

recall of depressive, anxiety and stress-related symptoms in the week before each condition, which was examined at the start of each trial ([section 3.16.2](#)). In addition, perceptions of sleepiness ([section 3.16.1](#)) were recorded at various points throughout each condition, to examine whether the perception of fatigue was clearly disassociated from that of sleepiness during the experiment. Participants were asked to respond to the KSS concomitantly with their RoF at baseline, immediately before the KE endurance task and immediately after the KE endurance task ([Figure 6.1](#)).

6.3.3.2. Interoception

Interoception was assessed using a heartbeat discrimination (HBD) task (Katkin *et al.*, 1983) during the preliminary, familiarisation session. The HBD is an interoceptive-exteroceptive discrimination task in which participants are asked to judge whether a series of audio tones (440 Hz; 100 ms) are played synchronously or asynchronously with their own heartbeat. Heartbeats were measured through pulse oximetry of the non-dominant index finger (8000s and Xpod, Nonin, Minnesota, USA). Under asynchronous conditions, a 300 ms delay was inserted resulting in tones played approximately 250 ms and 550 ms after the estimated R-wave in the synchronous and asynchronous trials, respectively. The two intervals correspond to the maximum and minimum durations enabling judgements of synchronicity (Wiens & Palmer, 2001). Each trial consisted of 10 audio tones. Participants were provided with 3 practice trials, before completing 40 test trials, split evenly between synchronous and asynchronous conditions. An accumulation of 40 trials has been recommended as the minimum number of trials required for the HBD task, since reliability and power may be compromised with lower trial numbers (Kleckner *et al.*, 2015). After each single trial, participants were asked to rate how confident they were with their response on a 10-cm VAS, between extremes labelled ‘0 = total guess/no heartbeat awareness’ and ‘10 = complete confidence/full perception of heartbeat’. During the HBD task, participants sat quietly, with their arms and hands supported by cushions on a table directly in front of them, in supinated position. The HBD task was run using a custom script created in MATLAB (MathsWorks, Natick, Massachusetts, USA). Participants were instructed to concentrate on the ‘feeling’ of their heartbeat wherever they can in their body.

6.3.4. Data Analysis

KE endurance performance was quantified as time to task failure (TTF), defined in [section 3.14.1](#). MVC force was defined as the greatest 500 ms average recorded during maximal contractions. The percentage change in HG MVC force during the HG task was quantified from baseline MVC (i.e. performed after the warm-up) to the last MVC of the HG task. RMS_{max} was obtained for each quadriceps muscle using a 500 ms windowed centred around the highest recorded KE MVC force at baseline. During the KE endurance task, RMS was calculated using consecutive 15 s sampling windows and normalised to RMS_{max} . During the HG and KE tasks, rate of change in the perception of effort and affective valence was derived from the difference between the first and the last response over KE performance time. To compare the average rate of change in the perception of fatigue across the HG task in the MOD and SEV conditions, an estimate of perceived fatigue accumulated per contraction sequence was derived from the difference between the baseline rating and the rating at the end of each HG task, divided by the number of contraction sequences completed.

Interoception was assessed based on the three-dimension model proposed by Garfinkel *et al.* (Garfinkel *et al.*, 2015; Garfinkel & Critchley, 2013). Interoceptive awareness was determined using receiver operating characteristic (ROC) curve analysis (Green & Swets, 1966), indicating how well interoceptive accuracy (i.e. proportion of correct judgements) during the HBD task is predicted by an individual's interoceptive confidence (assessed via VAS). The association between hit rate (i.e. the proportion of correct heartbeat identifications) and false alarm rate (i.e. the proportion of incorrect heartbeat identifications) were plotted for each detection threshold, with the area under the curve providing a measure of interoception (meta)awareness (Garfinkel *et al.*, 2015).

6.3.5. Statistical Analysis

Statistical analysis was performed using jamovi (v. 1.6.6) (The jamovi project, 2020), unless stated otherwise. Assumptions of statistical analyses were evaluated as per [section 3.19.6](#). A one-way repeated measures ANOVA was used to assess MVC force between conditions at the beginning of each condition (CON; MOD; SEV). Within the HG task, the relative (%) change in MVC force was assessed between hands (dominant; non-dominant) and experimental manipulation (MOD; SEV) using a two-way (2 x 2) repeated measures ANOVA. The effect of condition (CON; MOD; SEV) on KE endurance performance (i.e. TTF) was assessed using a one-way repeated measures ANOVA. Analysis of RoF was split across each experimental trial: (1) RoF at the beginning of each session was compared between conditions using a Friedman's ANOVA; (2) the difference between recorded and targeted RoF was then tested using one-sample Wilcoxon signed rank tests; (3) the response to the KE endurance task was tested using a two-way (3 x 2) repeated measures ANOVA to assess effects of condition (CON; MOD; SEV) and time (During KE; Post KE). DASS and KSS were compared between conditions at each respective point of assessment using a Friedman's ANOVA.

A linear mixed model (LMM) was fitted to assess the change in the perception of effort and affective valence reported across the endurance task between conditions using the *GAMLj* module in jamovi (Gallucci, 2019). LMM enables effective handling of missing or unbalance data ([section 3.19.3.2](#)), which was evident in the present study due to differences in endurance performance between individuals. Recorded perceptions of effort and affective valence were included as dependent variables in separate models. The effects of condition, time and their interaction were entered into the model as fixed effects. The model residuals for affective valence violated the assumptions of the LMM. This was largely driven by one participant who consistently reported the same numerical response throughout the SEV trial which extended >300 s. Analysis with this participant removed is reported (n = 29), which rectified the violated assumption. The conclusions drawn from the best model (see below) largely hold when the whole sample is included (despite the violation to the assumption of normality). The modelling of random effects was initially compared across two models: one in which random intercepts (grand mean) were included across participants and one in which random intercepts and random slopes for the effect of time varied across participants. Using the Akaike Information Criterion to assess model quality, modelling of effort was best reflected by the inclusion of random intercepts only (random intercepts: 1739.700; random intercepts + random slopes for time: 1774.698), while affective valence was best modelled including both random intercepts and random slopes for the effect of time (random intercepts: 2020.738; random intercepts + random slopes for time: 1910.484). As our purpose was to assess the effect of our experimental manipulation on the perception of effort

and affective valence experienced during the KE endurance task, the model was generated only from time points in which recordings in all three experimental conditions were obtained. This led to the exclusion of 12 data points (0.019% of total data recorded) which were taken from the CON and MOD conditions across six participants. *F*-tests were computed for the fixed effects using Satterthwaite approximation of the degrees of freedom. Analysis of the fixed effect of condition was coded using a Helmert contrast, in which two effects were examined: 1) the difference between CON and the mean across MOD and SEV, 2) the difference between means in MOD and SEV. The effect of time was assessed using a polynomial contrast. Due to issues with the signal-to-noise ratio, five participants were excluded from each of the analyses performed on the EMG response across the different KE muscles. Residuals of the EMG response demonstrated a right-ward skew and thus deviation from the assumption of normality. Therefore a robust approach to the estimation of the mixed effects was performed (Koller, 2016) in *R* (R Core Team, 2018). This robust approach attempts to place limits (or bounds) on the influence of sources of error within the random effects structure (Koller, 2016). The outcome of this analysis is presented in full in [Appendix B \(Table B.4.\)](#).

Within-participant, repeated measures correlations ([section 3.19.4.](#)) were used to assess the relationships between perceptual and affective responses recorded during the endurance task and between perceptual/affective constructs and time to task failure using the *rmcorr* package in *R* (Bakdash & Marusich, 2017). Following the exploratory evaluation of relationships in the previous study chapter ([chapter 5](#)) a more conservative Bonferroni-adjustment to control for multiple comparisons was applied in the present study.

Finally, exploratory analyses were performed to assess the influence of interoception on perceptual and affective constructs. First, LMM were used to examine whether interoceptive dimensions predicted RoF, the perception of effort and affective valence during the initial stages (i.e. at 1 minute) of the endurance task across conditions, with intercepts entered as random effects across participants. Next, the moderating effects (i.e. interaction effects) of different dimensions of interoception were examined on the ability of RoF to predict the perception of effort and affective valence. This again was performed using a LMM with the intercept entered as a random effect across participants. For all analyses, the null hypothesis was rejected at an α -level of 0.05.

6.4. Results

6.4.1. Maximum Force Generating Capacity and Negative Emotional States

Initial assessments were performed to ascertain whether participants differed in both their functional (i.e. MVC force) and emotional state (i.e. depression, anxiety and stress) at the start of each session. The average responses for force and emotional states are presented in [Appendix B](#). The results demonstrated no statistical difference in MVC force (all $p > 0.05$; [Table B.1.](#)) or retrospective recall of depressive, anxiety and stress-related symptoms preceding each session (all $p > 0.05$; [Table B.2.](#)).

Table 6.1. RoF at the beginning of each session and responses to the HG task performed in the experimental manipulations (MOD; SEV).

	Condition		
	CON	MOD	SEV
RoF (a.u.)	1.57 ± 1.04 (1.0, 1.75)	1.53 ± 1.17 (1.5, 1.0)	1.37 ± 0.89 (1.0, 1.0)
HG Task Performance			
<i>Number of contractions sequences</i>		4.50 ± 1.61 (4.5, 2.75)	8.43 ± 2.65 * (8.0, 3.75)
<i>Relative change in dominant HG force (%)</i>		-38.6 ± 8.72	-47.5 ± 12.6 *
<i>Relative change in non-dominant HG force (%)</i>		-37.5 ± 10.1	-48.2 ± 10.2 *
<i>Average rate of change in RoF per contraction (a.u.contraction⁻¹)</i>		0.92 ± 0.32	0.86 ± 0.25

Data presented as mean ± SD. *Mdn* and *IQR* reported for select variables in parentheses. CON: Control; MOD: Moderate RoF; SEV: Severe RoF. *: Significantly differences between MOD and SEV ($p < 0.05$).

6.4.2. Handgrip Task Performance and the Perception of Fatigue

A greater number of contraction sequences were required to induce a RoF of 8 (SEV) vs. 5 (MOD) (Table 6.1.; $p < 0.001$). This was accompanied by a greater relative reduction in HG MVC force ($-47.8 \pm 11.4\%$) in SEV compared to MOD ($-38.1 \pm 9.4\%$; $F_{(1,29)} = 29.62$, $p < 0.001$, $\eta_p^2 = 0.505$). The reduction in MVC force did not differ between the dominant and non-dominant hand ($F_{(1,29)} = 0.03$, $p = 0.861$, $\eta_p^2 = 0.001$) and there was no significant condition by hand interaction ($F_{(1,29)} = 1.22$, $p = 0.278$, $\eta_p^2 = 0.040$).

Mean RoF at the beginning of each session was low (RoF < 2; < “a little fatigued”) and was not statistically different between conditions (Table 6.1.; $\chi^2_{(2)} = 0.756$, $p = 0.685$). During the HG task, RoF increased progressively with the number of contraction sequences performed however, the average rate of change in RoF was not statistically different between MOD and SEV (Table 6.1.; $t_{(29)} = 1.35$, $p = 0.187$, $d_{av} = 0.21$). In SEV, final ratings (mean = 8.0, *Mdn* = 8, range = 8-9) were not different from the target value (RoF = 8; $p > 0.999$). All participants, except one (who reported an RoF of 9), had the HG test terminated after reporting an RoF of 8. Conversely, the RoF in MOD (mean = 5.4, *Mdn* = 5, range = 5-6) did differ from the target value (RoF = 5; $p = 0.001$). Eleven participants reported an RoF of 6 at the end of the HG. Despite some exceeding the specified value, the RoF did not exceed the moderate intensity band (>RoF 6; $p > 0.999$). In CON, RoF remained low (mean = 1.4, *Mdn* = 1, range = 0-3) and did not exceed a RoF of 3 ($p > 0.999$). The change in RoF with experimental manipulation was not accompanied by changes in perceived sleepiness at the end of the HG task (Table B.2.) demonstrating participants’ ability to clearly distinguish between constructs.

6.4.3. Time to Task Failure during the Knee Extensor Endurance Task

Participants' ability to sustain the KE endurance task was significantly impaired by the experimental manipulations (Figure 6.2.); $F_{(2,58)} = 11.1, p < 0.001, \eta_p^2 = 0.278$ ⁶¹, with reduced performance in MOD (219 ± 68 s, $-9.5 \pm 19.1\%$; $t_{(29)} = 3.11, p = 0.013, d_{av} = 0.37$) and SEV (206 ± 59 s, $-13.7 \pm 17.2\%$; $t_{(29)} = 4.29, p < 0.001, d_{av} = 0.57$) compared to CON (246 ± 79 s). Endurance performance between MOD and SEV was not statistically different ($t_{(29)} = 1.62, p = 0.348, d_{av} = 0.20$).

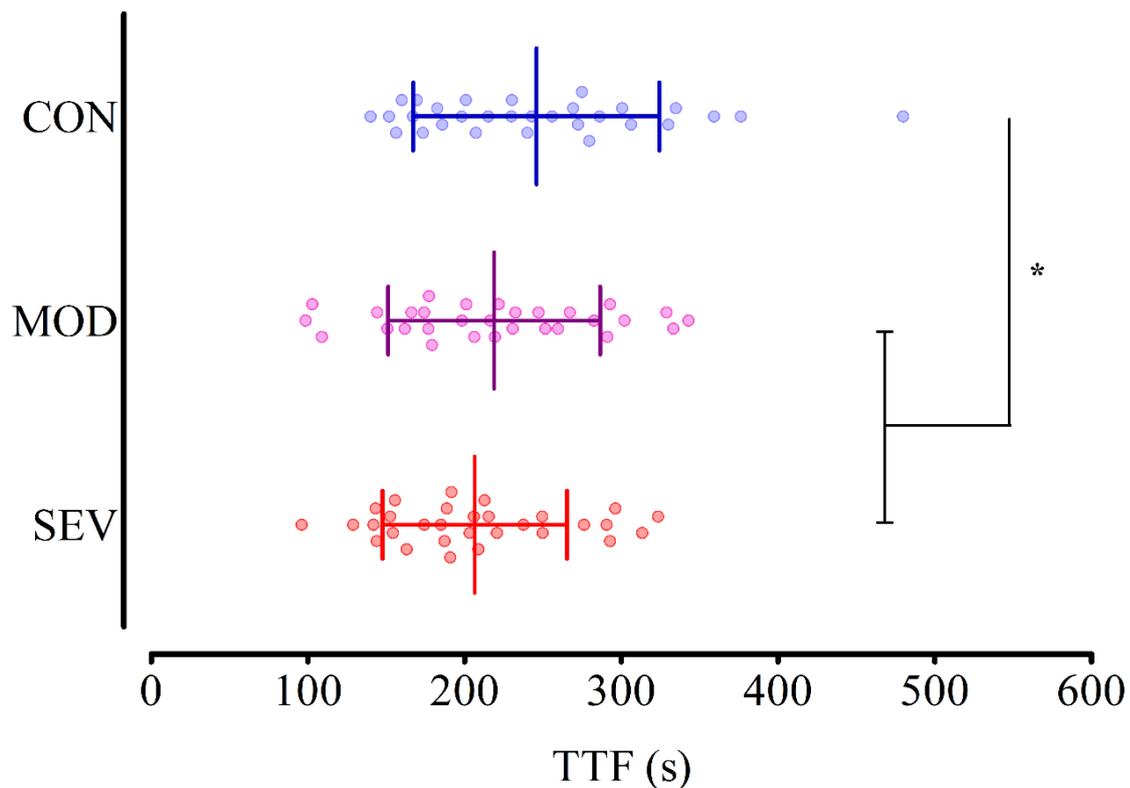


Figure 6.2. The effect of different subjective intensities of a pre-induced state of fatigue on time to task failure (TTF). Knee extensor endurance performance is presented for the control (CON; blue), moderate RoF (MOD; purple) and severe RoF conditions (SEV; red). Lines and error bars indicate condition means and standard deviations, respectively. *: Time to task failure (TTF) significantly different in MOD and SEV compared to CON ($p < 0.01$).

⁶¹ Evident in Figure 6.2., was the possible identification of an outlier in the control condition. Formal evaluation demonstrated that this value had a z-score of 2.98. This participant was however retained for the main analysis as removal did not change the outcome of the statistical analysis ($F_{(2,56)} = 9.69, p < 0.001, \eta_p^2 = 0.257$).

6.4.4. Perceptual and Affective Response to the KE Endurance Task

RoF recorded during and after the KE endurance task are presented in [Figure 6.3](#). Significant main effects for condition ($F_{(2,58)} = 18.14, p < 0.001, \eta_p^2 = 0.385$) and time ($F_{(1,29)} = 176.64, p < 0.001, \eta_p^2 = 0.859$) were found, with a significant interaction between condition and time evident ($F_{(2,58)} = 9.51, p < 0.001, \eta_p^2 = 0.247$). Follow-up analysis of the interaction effect demonstrated RoF during the initial minute of the KE endurance task was elevated in MOD ($t_{(29)} = -5.71, p < 0.001, d_{av} = 1.05$) and SEV ($t_{(29)} = -5.28, p < 0.001, d_{av} = 1.18$) compared to CON. However, at this point, RoF between the two experimental manipulations was not statistically different ($t_{(29)} < 0.01, p > 0.999, d_{av} < 0.01$). In MOD, the average response remained comparable to the intensity of fatigue induced by the HG task (Mean: 5.4; *Mdn*: 5) however, in SEV, RoF appeared to systematically decrease from the RoF reported at the end of the HG task (Mean: 5.4; *Mdn*: 5). Both sets display substantial variation around their mean (MOD: $SD \pm 1.7, \text{range}=2-9$; SEV: $SD \pm 1.4, \text{range}=3-8$). At task failure, there was no statistical difference in RoF between conditions (CON: 7.6 ± 1.2 ; MOD: 8.0 ± 1.0 ; SEV: 8.3 ± 1.2 ; CON vs. MOD: $t_{(29)} = -1.72, p > 0.999, d_{av} = 0.32$; CON vs. SEV: $t_{(29)} = -2.75, p = 0.152, d_{av} = 0.60$; MOD vs. SEV: $t_{(29)} = -1.51, p > 0.999, d_{av} = 0.27$). A main effect of condition was indicated for perceived sleepiness at the end of the KE endurance task ([Table B.2.](#)), however follow-up pairwise comparisons failed to demonstrate significant effects between conditions (all $p > 0.05$).

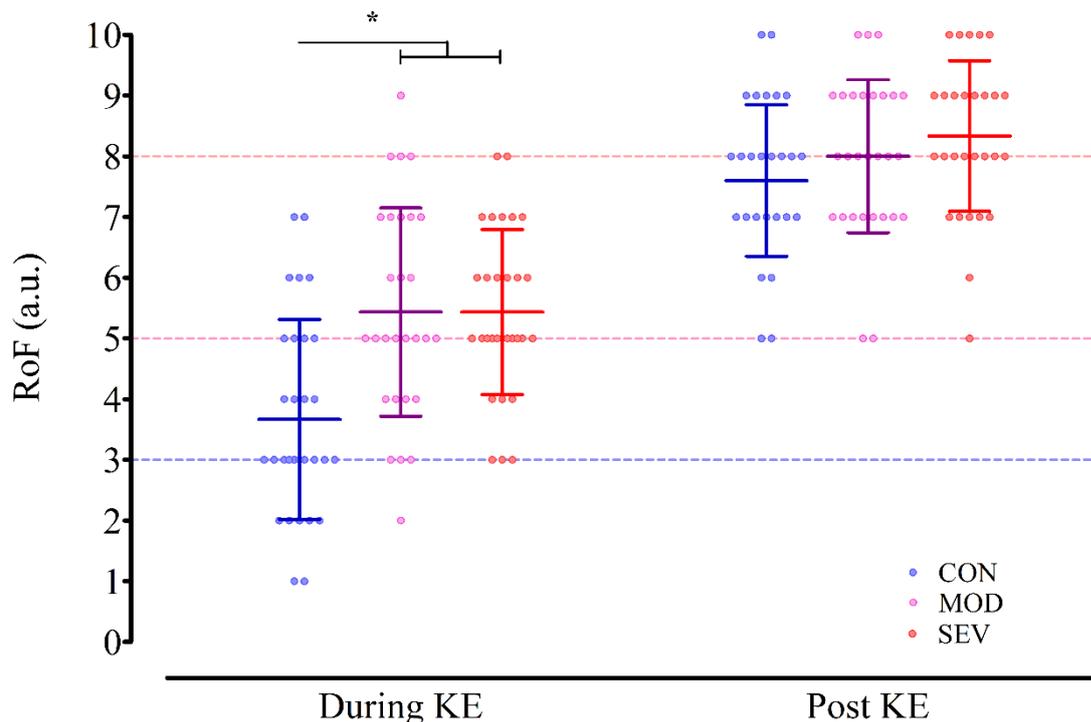


Figure 6.3. Ratings of fatigue (RoF) during and immediately after the knee extensor (KE) endurance task. Data is presented for the control (CON; blue), moderate RoF (MOD; purple) and severe RoF conditions (SEV; red). Circles represent individual ratings in each condition. Lines and error bars indicate condition means and *SD*, respectively. Dashed guidelines represent the target RoF in the handgrip (HG) task within each condition. *: RoF significantly different in MOD and SEV compared to CON ($p < 0.01$).

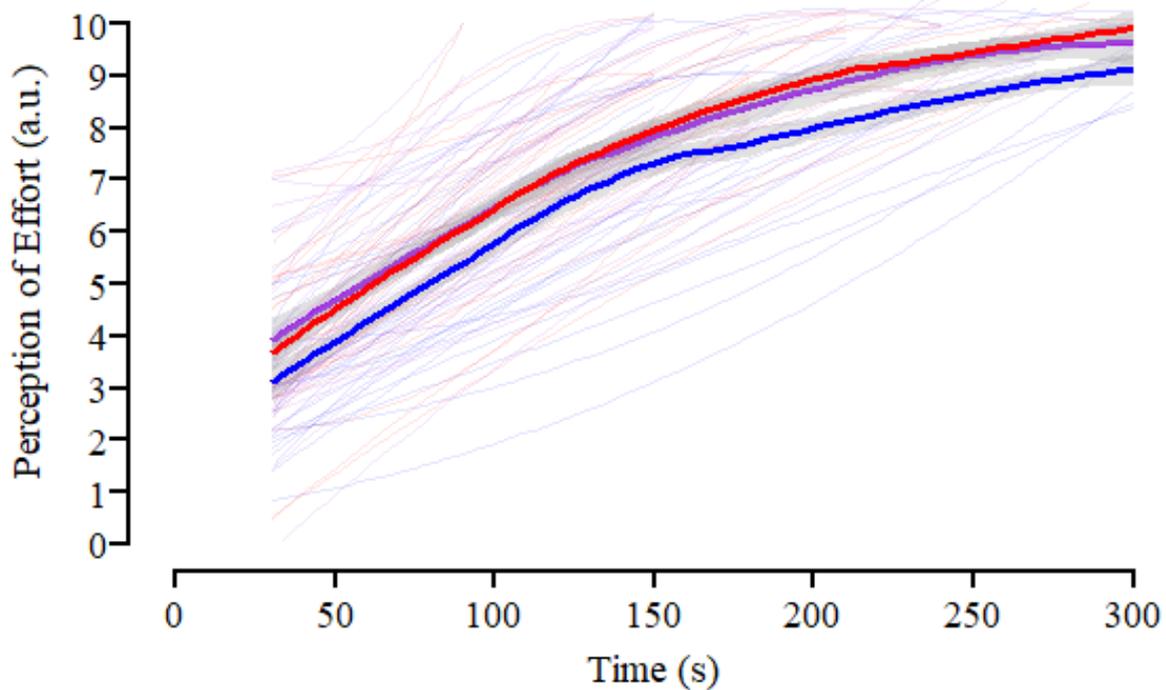


Figure 6.4. Effect of experimental conditions on the perception of effort recorded during the knee extensor (KE) endurance task. Individual responses across time are displayed by smoothed thin lines within each condition, with thick lines representing the change in mean scores over time (with grey boarders representing 95% confidence intervals) for the control (CON; blue), moderate RoF (MOD; purple) and severe RoF conditions (SEV; red).

Description of the estimated fixed and random effects in the analysis of the perception of effort and affective valence during the KE endurance task are presented in [Appendix B \(Table B.3.\)](#). Individual and mean responses for the perception of effort and affective valence recorded in each condition are presented in [Figure 6.4.](#) and [6.5.](#), respectively. Main effects of condition ($F_{(2, 556)} = 48.62, p < 0.001, \eta_p^2 = 0.149$) and time ($F_{(9, 557)} = 357.12, p < 0.001, \eta_p^2 = 0.852$) were evident for the perception of effort during the KE endurance task however, the interaction between condition and time was not statistically significant ($F_{(2, 556)} = 0.55, p = 0.935, \eta_p^2 = 0.002$). There was a linear trend for the effect of time, which flattened out towards the end of the task (quadratic trend). Contrasts between conditions indicated that the average effort response in the combined experimental manipulations (MOD, SEV) was greater than that recorded in CON. The difference between the MOD and SEV however, was not statistically significant. Affective valence decreased over time during the KE endurance task ($F_{(9, 67.2)} = 28.20, p < 0.001, \eta_p^2 = 0.791$). Similar to the perception of effort, there was a trend for a linear decrease which tended to flatten out across time (quadratic trend). There was also a main effect of condition ($F_{(2, 388.2)} = 19.06, p < 0.001, \eta_p^2 = 0.089$). Contrasts between conditions demonstrated greater affective valence during CON compared to the average response over the combined experimental manipulations (MOD, SEV). Affective valence was not different between the MOD and SEV conditions. The interaction between condition and time was also not statistically significant ($F_{(18, 455.5)} = 0.70, p = 0.813, \eta_p^2 = 0.027$).

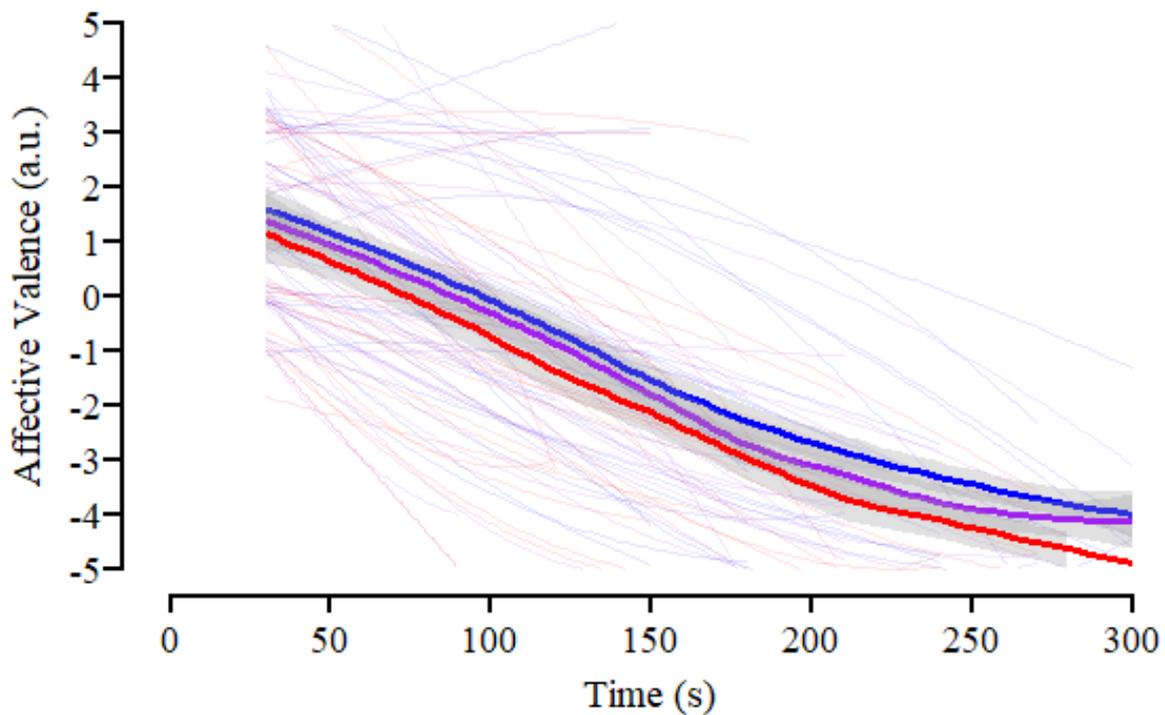


Figure 6.5. Effect of experimental conditions on affective valence recorded during the knee extensor (KE) endurance task. Individual responses across time are displayed by smoothed thin lines within each condition, with thick lines representing the change in mean scores over time (with grey borders representing 95% confidence intervals) for the control (CON; blue), moderate RoF (MOD; purple) and severe RoF conditions (SEV; red).

6.4.5. Relationships between Time to Task Failure and the Perceptual and Affective Responses Recorded during the KE Endurance Task

Correlations were evident between time to task failure and initial (i.e. 60 s) ratings of the perception of effort ($r_{rm} = -0.46$ [bootstrapped 95% CI: $-0.64 - -0.23$], Bonferroni-adjusted $p < 0.001$), the rate of change in the perception of effort ($r_{rm} = -0.41$ [bootstrapped 95% CI: $-0.60 - -0.17$], $p = 0.005$), the rate of change in affective valence ($r_{rm} = 0.38$ [bootstrapped 95% CI: $0.13 - 0.58$], $p = 0.014$) and RoF recorded in the first minute of the task ($r_{rm} = -0.54$ [bootstrapped 95% CI: $-0.70 - -0.32$], $p < 0.001$). Time to task failure was not related to initial recordings of affective valence across conditions ($r_{rm} = 0.20$ [bootstrapped 95% CI: $-0.06 - 0.44$], $p = 0.166$).

6.4.6. Influence of Interoception on Perceptual and Affective Responses of KE Endurance Performance

Finally, the potential influence of interoceptive sensitivity on perceptual and affective responses to the endurance task and its potential moderating effect on the relationships between constructs was explored. First, it was examined whether individual's trait level of interoception predicted perceptual and affective responses recorded during the endurance task. Interoceptive awareness was shown to predict RoF reported during (i.e. at 60 s) the KE endurance task (estimate = -4.18 , [95% CI: $-8.08 - -0.28$], $p = 0.048$) however, interoceptive accuracy (estimate = 1.57 , [95% CI: $-1.66 - 4.81$], $p = 0.348$) and confidence (estimate = -0.02 , [95% CI: $-0.34 - 0.31$], $p = 0.920$) did not. That is, individuals with greater awareness of resting heartbeats reported lower RoF during the endurance

Table 6.2. Moderating effect of the dimensions of interoception on the relationship between the perception of fatigue and the perception of effort.

Fixed Effects	Interoceptive Accuracy					Interoceptive Confidence					Interoceptive Awareness				
	Estimates	95% CI		<i>t</i>	<i>p</i>	Estimates	95% CI		<i>t</i>	<i>p</i>	Estimates	95% CI		<i>t</i>	<i>p</i>
		Lower	Upper				Lower	Upper				Lower	Upper		
<i>Intercept</i>	4.58	4.16	5.01	21.14	<0.001	4.60	4.17	5.02	21.35	<0.001	4.59	4.18	5.00	21.89	<0.001
<i>RoF</i>	0.34	0.23	0.44	6.21	<0.001	0.35	0.24	0.46	6.36	<0.001	0.33	0.23	0.44	6.11	<0.001
<i>Interoceptive Dimension</i>	1.26	-1.86	4.38	0.79	0.436	0.12	-0.19	0.42	0.76	0.456	-2.99	-6.82	0.84	-1.53	0.137
<i>Interaction</i>	0.40	-0.45	1.24	0.92	0.359	0.05	-0.04	0.14	1.03	0.307	-0.08	-1.10	0.94	-0.15	0.879
Random Effect	<i>Participant (Intercept)</i>														
σ^2	0.47			0.47			0.48								
$\tau_{00\text{participant}}$	1.25			1.24			1.14								
<i>ICC</i>	0.73			0.73			0.71								

Interaction: the interaction effect between RoF and the respective interoceptive dimension, RoF: Rating of Fatigue, σ^2 : residual variance, $\tau_{00\text{participant}}$: individual variance, ICC: intraclass correlation coefficient.

Table 6.3. Moderating effect of the dimensions of interoception on the relationship between the perception of fatigue and affective valence.

Fixed Effects	Interoceptive Accuracy					Interoceptive Confidence					Interoceptive Awareness				
	Estimates	95% CI		<i>t</i>	<i>p</i>	Estimates	95% CI		<i>t</i>	<i>p</i>	Estimates	95% CI		<i>t</i>	<i>p</i>
		Lower	Upper				Lower	Upper				Lower	Upper		
<i>Intercept</i>	0.79	0.22	1.37	2.69	0.012	0.80	0.20	1.40	2.61	0.015	0.84	0.25	1.41	2.82	0.009
<i>RoF</i>	-0.29	-0.44	-0.13	-3.64	<0.001	-0.31	-0.46	-0.15	-3.82	<0.001	-0.29	-0.44	-0.13	-3.60	<0.001
<i>Interoceptive Dimension</i>	-2.13	-6.38	2.11	-0.99	0.333	-0.06	-0.49	0.37	-0.26	0.796	1.64	-3.77	7.05	0.60	0.557
<i>Interaction</i>	0.29	-0.94	1.53	0.46	0.646	-0.07	-0.21	0.06	-1.12	0.266	0.72	-0.77	2.21	0.95	0.346
Random Effect	<i>Participant (Intercept)</i>														
σ^2	1.02			0.99			1.02								
$\tau_{00\text{participant}}$	2.24			2.47			2.26								
<i>ICC</i>	0.69			0.71			0.69								

Interaction: the interaction effect between RoF and the respective interoceptive dimension, RoF: Rating of Fatigue, σ^2 : residual variance, $\tau_{00\text{participant}}$: individual variance, ICC: intraclass correlation coefficient.

task. None of the dimensions of interoception predicted the perception of effort or affective valence recorded at the same time point during the KE endurance task ([Tables 6.2.](#) and [6.3.](#)).

It was hypothesized that individuals' meta-awareness of interoceptive signals may be particularly important to the relationship between the perception of fatigue and the degree of effort and affect experienced during the KE endurance task. However, there was no significant interaction effect between RoF and interoceptive awareness on the prediction of the perception of effort ([Table 6.2.](#)). This was the same when both interoceptive accuracy and interoceptive confidence were used as the moderator variable ([Table 6.2.](#)). Moreover, the same effects also extended to the prediction of affective valence ([Table 6.3.](#)).

6.5. Discussion

The present study chapter demonstrated that a perceived state of fatigue, experienced at both moderate and severe intensities, impairs physical endurance performance, exacerbating the perception of effort and reducing affective valence experienced during activity - a replication of the findings reported in [chapter 5](#). However, these effects did not appear to scale with the intensity of the perceived state, as evidenced by the absence of differences between the two experimental manipulations (i.e. MOD vs. SEV). A secondary aim of the study was to explore the potential influence of interoception on the perceptual and affective responses to physical activity and the relationships between constructs. Interoceptive awareness was the only interoceptive dimension shown to predict perceptual and affective responses during physical activity, associated specifically with the perception of fatigue recorded during the endurance task. The perception of fatigue therefore was shown to be an important factor defining the central regulation of physical performance and associated with higher-order (i.e. metacognitive) representations of internal bodily states. Interoception did not influence relationships between fatigue and either the perception of effort or affective valence, suggesting that relationships between constructs may be independent of intermediary sensory processing.

A heightened perceived state of fatigue induced through prior physical activity (i.e. HG) impaired subsequent endurance performance in a remote muscle group (i.e. KE), associated with an increased perceived effort and reduced affective valence reported during the task. The results therefore replicate the findings reported in [chapter 5](#), with the effects observed of comparable magnitude (i.e. [chapter 6](#): -10% and -14% vs. [chapter 5](#): -11%). Several mechanisms accounting for the deleterious effect of prior physical activity on subsequent endurance performance in a remote muscle group have been proposed, including neural (e.g. inhibition of descending drive to non-activated muscles), biochemical (e.g. migration of accumulated metabolites) and cognitive factors, though the precise mechanisms remain unclear (Halperin *et al.*, 2015). The present findings appeal to the latter, indicating that higher-order cognitions related to fatigue may exert influence on lower sensory processes independent of overt functional changes ([chapter 4](#)). Here, the present results suggest that this top-down effect appears relatively potent and may emerge when only moderate subjective symptoms of fatigue are present.

However, though effort was elevated, affective valence reduced and performance impaired through elevating the state perception of fatigue, no statistical differences between the moderate- and severe-intensity manipulations were observed, despite a small effect on performance in the severe-intensity trial compared to moderate-intensity

trial (i.e. -3%). On the face of it, the results suggest that the relationship between the perception of fatigue and performance may be categorical in nature; one experiences a state of (perceived) fatigue beyond some (undetermined) threshold, in which performance is impaired and perception of task demands altered. Further changes in the intensity of the perceived state of fatigue elicits no further perceptual or performance effects beyond this point. However, on closer inspection, it was evident that individual RoF displayed different response profiles between the two experimental manipulations during the endurance task. That is, RoF decreased in the SEV condition from the end of the HG task to the initial minute of the KE task, while RoF was maintained in the MOD condition, leading to no statistical difference observed between experimental manipulations across the beginning of the KE endurance task. This may have implications for the interpretation of the current findings. On the one hand, it may aid in strengthening the association between the perception of fatigue, effort and affective valence; that is, given the proposed relationship between the perception of fatigue and effort/affective valence, a similar RoF between the experimental manipulations may explain why effort, affective valence and performance were also comparable. However, this may come at the expense of limiting interpretation of the perceived fatigue-performance relationship.

According to the motivational control theory of fatigue (Hockey, 2011; 2013), the aversive perceptual response to sustained activity - referred to holistically as 'fatigue' - signals the engagement of compensatory, effortful control processes in order to maintain task performance. The purpose of the subjective experience of fatigue is the interruption of goal-related cognitions, enabling one to re-evaluate the utility of activity engaging effortful processes (Hockey, 2013). Changing tasks to one of lesser demand (e.g. reduced taxation of executive functions) may thus attenuate this signal and enable performance recovery. Accordingly, the reduction in RoF at the beginning of KE task in the SEV condition may not be entirely surprising. However, the perception of fatigue also persists for a period of time after the performance of demanding physical (Micklewright, St Clair Gibson, *et al.*, 2017) and cognitive tasks (Jacquet *et al.*, 2021; Smith *et al.*, 2019), as it serves to deter repeated utilisation of the same task-related processes immediately after extended use (Hockey, 2013). The present results indicate a potential balance of both functions. The perception of fatigue was elevated in both the MOD and SEV condition above the control condition, signalling an existing aversion to the KE endurance performance incurred through the prior HG task. However, the KE task offered some relief following the more demanding conditions encountered during SEV, possibly because demands were lessened with the engagement of the new task. Yet, assuming that the required utilisation of compensatory processes are proportional to the subjective experience of fatigue, it might still be expected that residual fatigue should have been elevated following SEV compared to MOD due to a greater utilisation of these processes. That this was not the case requires new explanations. These explanations may include: 1) the performance of a new task, or simply the removal of the aversive stimulus, in a state of high fatigue may energise the deployment of additional resources during the new task, which may in turn transiently alleviate symptoms. This allocation of additional resources has been speculated to account for differences in physical performance immediately following the performance of cognitively demanding task compared worse performance observed later in recovery (Jacquet *et al.*, 2021)⁶²; 2) the perception of fatigue may increase disproportionately to the utilisation of resources or impairment to physical capacity. The perception of

⁶² Importantly, the authors did not demonstrate that markers of performance were accompanied by corresponding changes in the subjective perception of fatigue, indicating that additional resources alleviated only the subjective symptom of fatigue.

fatigue may therefore reflect a conservative, risk-averse signal of *anticipated* adverse consequences should action continue (Benoit *et al.*, 2019) and as such the disparity between the physical and the perceived challenge may become realigned once the stressor is removed or a new task starts; 3) the challenge to ones' perceived capacity and the need to exert control in pursuit of a goal may involve multiple goal states that extend over different temporal scales (Pezzulo *et al.*, 2018), which may see the physiological condition of the body evaluated in relation to new goals introduced by engaging in a new task. The present study cannot provide sufficient evidence to support any of the above-mentioned possibilities. As such, future research is required to better understand the dynamics of perceived fatigue with the engagement of new tasks and re-examine the relationship between the subjective intensity of perceived fatigue and subsequent performance whilst accounting for such changes.

In contrast to [chapter 5](#), a significant relationship between the perception of fatigue and task performance was found. In the previous chapter, it was proposed that the perception of fatigue may curtail performance indirectly through effects on variables used directly in the central regulation of performance such as the perception of effort and affective valence. This was also taken as indirect evidence of a differentiation of fatigue from the other studied perceptual (i.e. effort) and affective constructs ([section 5.5](#)). The observed relationship between the experience of fatigue and task performance in the present study suggests that perceived fatigue may be more directly involved in the central regulation of performance than previously postulated, forming alongside effort and affect, part of the sensory experience that ultimately signals that the consequences of continuing activity are increasingly unattractive (Gandevia, 2001; Hureau *et al.*, 2016). This does not definitively preclude an indirect effect through changing sensory processing however, and pathway analysis is required to better understand the subtle interactions between perceptual and affective experiences in the regulation of physical behaviour. Conforming to the results of the previous study chapter, there was evidence of relationships between psychological constructs, with the perception of fatigue shown to predict how effortful and how pleasurable activity is experienced to be. Accordingly, like self-efficacy, perceived fatigue may reflect a cognitive input related to beliefs concerning capacity (Steele, 2021), that shapes how much effort is invested into a task and the aversiveness of ensuing actions (McAuley *et al.*, 1999; Hutchinson *et al.*, 2008), which serves to influence physical tolerance.

The possibility that one's interoceptive sensitivity influenced perceptual and affective experiences during sustained physical activity and moderated the relationships between constructs was also explored in the present study. Interoceptive awareness, a measure of an individual's meta-awareness of interoceptive signals⁶³, predicted RoF during the endurance task. Specifically, the greater one's interoceptive awareness, the lower the subjective experience of fatigue reported during the endurance task across all three trials. This may indicate that those with greater insight into internal representations of the body may more accurately predict and/or place greater confidence in top-down factors (i.e. prior beliefs) over ascending the sensory inputs received when trying to understand the condition of the body. This may attenuate the development of fatigue by attenuating the perception of a mismatch or error between expectations and sensory evidence (Stephan *et al.*, 2016). This interpretation is discussed in more detail in [section 8.4](#). Neither the perception of effort nor affective valence were related to any dimension of interoception. This conforms with previous studies examining cardiac interoception on the

⁶³ The measure of interoceptive awareness used in the present study is cited as a stable representation of 'error awareness', that may be generalisable across interoceptive axes (Garfinkel *et al.*, 2016), indicating the potential generalizability of the findings.

perception of effort (da Silva Machado *et al.*, 2019) and affective valence (Köteles *et al.*, 2020) during physical activity. Though (unlike [chapter 5](#)) it was not possible to disassociate constructs based on their relationships to performance, the findings discussed here indicate that the studied perceptual and affective constructs may involve different circuitry, with metacognition associated with the experience of fatigue, specifically. Again, this is discussed in further detail in [sections 8.3.2.](#) and [8.4.](#)

Though no statistically significant effects for baseline interoception were found on the perception of effort and affective valence, it was speculated that interoception (and particularly interoceptive awareness) may moderate the relationships between perceived fatigue, effort and valence. The expectation was that meta-awareness would be particularly important for the interpretation of effort and affective valence under a state of fatigue. Interoceptive awareness has previously been associated with perceptual and affective experiences associated with some form of ‘error’ emergence ([section 8.4.](#)), including symptoms of anxiety (Garfinkel *et al.*, 2016) and susceptibility to exteroceptive manipulation of self-location (Bekrater-Bodmann *et al.*, 2020). In the case of anxiety, there is some evidence that the affective response may be sustained by maladaptive metacognitive beliefs about worry (Ryum *et al.*, 2017). No moderating effect of any dimension of interoception was observed on the relationships between the perception of fatigue and both the perception of effort and affective valence. This suggests that these relationships do not appear to dependent upon intermediary sensory processing. The relationships between constructs may instead emerge from reciprocal interactions within some form of hierarchical processing ([section 8.4.](#)).

Some limitations of the present study must be highlighted. Associations between perceptual responses and endurance performance remain limited to correlational analysis. As already mentioned, further study of the structure of these relationships within the central regulation of performance requires more formal analysis, such as mediation analysis. The study also assessed the impact of the subjective intensity of the perception of fatigue across three separate levels, which were assumed to correspond to distinct intensity boundaries. Even if this assumption is true, the investigated levels may not have been sufficient to interpret the full (perceived) fatigue-performance relationship. Furthermore, at odds with [chapter 5](#) and the others (Amann *et al.*, 2013; Johnson *et al.*, 2015), there appeared to be some evidence of an effect of condition on the EMG response in the KE muscles ([Appendix B; Table B.4.](#)). This may suggest that motor unit activation may have differed between conditions, meaning that the endurance tasks were not necessarily performed in equivalent physical conditions. This may have contributed to altered perception beyond the proposed top-down (meta)cognitive influences (de Morree & Marcora, 2015). However, it is acknowledged that inferences drawn on central drive from bipolar surface EMG is problematic (Dimitrov *et al.*, 2008), and large variation between individuals and only moderate explanation of the variance from the model was observed. As such, it is believed that interpretation of the present EMG data is difficult, and this effect needs to be investigated further.

6.6. Conclusion

The primary aim of the present study chapter was to examine whether the subjective intensity of a pre-induced state of perceived fatigue differentially affected physical endurance performance and altered perceptual/affective

processes. The results demonstrated that both moderate and severe perceptions of fatigue impair subsequent physical endurance performance and affects how effortful and pleasurable the task is perceived to be. The findings presented in [chapter 5](#) were thus replicated. The perception of fatigue itself was however, shown to be sensitive to changing tasks, which hindered understanding of the precise (perceived) fatigue-performance relationship. Nevertheless, higher-order representations of the interoceptive state were shown to predict the perception of fatigue during physical activity, implicating metacognitive appraisals as an important component of this subjective experience. Awareness of internal representations did not moderate the relationship between perceived fatigue and other perceptual (i.e. effort) and affective responses arising through engaging in physical activity, indicating the absence of intermediary sensory processing in the effect of fatigue on the regulation of physical performance.

CHAPTER 7 - EFFECT OF A PHYSICALLY INDUCED, PERCEIVED STATE OF FATIGUE ON EFFORT-BASED DECISION MAKING

7.1. Abstract

Protracted physical activity causes the development of fatigue. The development of fatigue has previously been associated with an increase in the subjective costs associated with further effort, subsequently influencing decisions concerning whether or not to engage in future physical activity. However, whether fatigue-associated changes to effort-based decisions are reflective of a global aversion to effort in response to fatiguing physical exertion is unclear. To investigate this, the study chapter tested whether effort-based decision making was altered by a perceived state of fatigue, pre-induced through physical activity performed in a different part of the body. Twenty-two healthy male participants made a series of choices between two rewarded actions, which varied in both the level of effort required (i.e. relative duration of a submaximal contraction of the dominant knee extensors) and the reward on offer (i.e. monetary incentives), under two conditions: 1) a pre-induced state of fatigue and 2) a rested (control) state. Across conditions, participants' choice behaviour demonstrated the anticipated interaction between an aversion to increasing effort demands and inclination towards greater rewards. However, though prior physical activity increased the perception of fatigue, prolonged choice selection-time and reduced self-reported confidence in ones' ability to perform chosen effort-demanding actions, participants choice behaviour did not significantly differ between the two conditions. The findings indicate that a subjective state of fatigue was not associated with an increase in the general cost of exerting effort, subsequently influencing individuals' decision to exert effort. However, a perceived state of fatigue is associated with greater uncertainty in one's capacity to meet task demands, which may be indicative of changes to evaluative processes that precede changes in the outcome of cost/benefit computations.

7.2. Introduction

In [chapters 5](#) and [6](#), the perception of fatigue has been implicated as a top-down cognitive factor, influencing the perception of effort and affective valence experienced during physical endurance performance. That is, in a perceived state of fatigue, sustained tasks are felt to be more effortful and less pleasurable, which in turn is associated with impaired performance. However, attribution of perceptual and affective changes to detrimental behavioural effects have been limited to correlation-based analysis, which may be problematic, not least, because what is perceived to be driving perception may not always match what is identified to be driving behaviour (Meyniel *et al.*, 2014). The regulation of physical endurance performance is often aligned to theories of decision-making (Renfree *et al.*, 2014; Robertson & Marino, 2016; St Clair Gibson *et al.*, 2018), with the control of behaviour reflective of an integration of various internal and external factors within cost/benefit evaluations determining the most appropriate course of action based on outcome value. Accordingly, explicit examination of altered perceptual influences on choice behaviour may provide further insight into how the brain regulates physical performance.

Recent years have witnessed a growing interest in defining how the effort required to obtain a rewarding outcome shapes our motivation to engage in action (Westbrook & Braver, 2015; Chong *et al.*, 2016; Pessiglione *et al.*, 2018). Effort is typically considered to be costly or aversive (Hull, 1943; Kurzban, 2016; though see Inzlicht *et al.*, 2018; [section 2.4](#)). As such, the level of effort required by a task is proposed to reduce the ‘net value’ of expected outcomes when deciding whether to engage in physical (Bonnelle *et al.*, 2015; Chong *et al.*, 2017; Croxson *et al.*, 2009; Hartmann *et al.*, 2013; Klein-Flügge *et al.*, 2015; Prévost *et al.*, 2010) or cognitive tasks (Apps *et al.*, 2015; Chong *et al.*, 2017; Massar *et al.*, 2015; Massar *et al.*, 2016). Why precisely exerting effort is costly remains unclear, but appears linked to inherent limitations of the brain (and effectors, e.g. the muscles; [section 2.4.1.2](#)), and is associated with a reluctance to engage in actions that tax finite resources close to maximally and/or incur opportunity costs (Shenhav *et al.*, 2017; Kurzban *et al.*, 2013). Effort is thus only exerted when the value of future outcomes is deemed sufficiently ‘worth it’. However, repeated exertion of effort reduces functional, or perceived, capacity (the latter perhaps associated with simply a reduction in ones’ willingness; Inzlicht *et al.*, 2014) to exert further effort, suggesting that effort-based decisions may not be stable and subject to dynamic influences, such as the development of fatigue (Müller & Apps, 2019).

When fatigued, the costs associated with effort are believed to be increased ([chapters 5](#) and [6](#)), resulting in a reduced willingness to engage in actions that were previously deemed of sufficient value (Müller & Apps, 2019). Few studies have however, presently investigated the influence of fatigue on effort-based choice (Massar *et al.*, 2018), particularly in relation to physical tasks⁶⁴. Harris and Bray (2019; 2021) reported mixed results for an effect of fatigue on the decision to engage in physical activity. Performance of a demanding cognitive task increased the subjective perception of fatigue but did not directly influence participants’ choice behaviour when presented with the single, simple decision: to engage in a subsequent physical task or not. However, an elevated perception of fatigue was indirectly implicated in determining choice, mediated by its negative effect on self-reported evaluations of the respective costs and benefits of the task (Harris & Bray, 2019; 2021). Beyond self-reported

⁶⁴ In fact, the development of fatigue is typically controlled for in many studies interested in modelling of effort-discounting during cost-benefit decisions in order to exclude its confounding effects on the interpretation of effects (e.g. Klein-Flügge *et al.*, 2015).

evaluations, Iodice *et al.* (2017) implemented an explicit behavioural evaluation of the changes to costs/benefits of effort based decisions, utilising a forced-choice task to evaluate participants motivation to exert effort after engaging in prolonged and physically demanding cycling exercise. The authors reported a systematic increase in the aversion to high effort demands after performing demanding cycling exercise, in which both effort (i.e. duration of a subsequent cycling bout) and reward were varied across multiple levels. Though the authors attributed this increased effort-discounting of rewarded outcomes to fatigue, interestingly no index of its development, either subjectively or objectively ([section 2.2.2.2.](#)), was recorded. It is therefore unclear to exactly what this fatigue-associated change in decision-making reported by Iodice *et al.* (2017) may be attributed to. It is well established that prolonged physical activity evokes functional impairments within the motor system, in which peripheral and central factors impair the ability of active muscles from producing the force they once could (e.g. Sidhu *et al.*, 2009; Weavil *et al.*, 2016). Increased sensitivity to effort costs in response to fatiguing physical tasks may thus reflect this physical effect, representing the need for a greater relative motor output to perform a task as compensation for activity-induced neuromuscular deficits ([section 2.4.3.2.](#)). Alternatively, a global, perceived state of fatigue may evoke intrinsic changes within evaluation systems responsible for choosing whether or not to exert effort (Müller & Apps, 2019). In support of this latter possibility, it has been proposed that the effects of fatigue on the motivation to exert effort are represented within domain-general network (Müller & Apps, 2019), which may provide a common account for effects reported in response to both cognitive and physical activity (Iodice *et al.*, 2017; Harris & Bray, 2019). As the perceived likelihood of obtaining a reward through effortful control may represent an important factor integrated within the decision process (Frömer *et al.*, 2021), changes associated with a global, perceived state of fatigue may be associated with a lower perceived ability to effectively exert control over task performance and obtain rewarding outcomes, increasing the subjective cost of effort.

The present study chapter sought to address the second of the two possible effects of fatigue induced through physical activity on effort-based decision-making, examining the effects of a global, perceived state of fatigue on effort-based choice, independent of functional changes in neuromuscular function. That is, if a perceived state of fatigue arising through extended physical exertion brings about a change in how the cost of effort is evaluated, greater effort-discounting of reward may be expected even when the functional status of the performing muscle remains intact. Based on the effects reported in [chapter 4](#), a perceived state of fatigue was therefore pre-induced through demanding activity performed in the upper body, before participants made decisions as to whether to exert effort in the lower body to obtain monetary rewards. It was hypothesized that a perceived state of fatigue would increase effort discounting of rewarded action. This would be accompanied by a reduced confidence in participants' ability to meet effort demands.

7.3. Methods

7.3.1. Sample Size Calculation

The present study was performed in conjunction with [chapter 6](#). The studied sample therefore reflected a sub-sample of the volunteers that agreed to participate in the present study and the previous study chapter. No formal

a priori power analysis was performed for the present study. Instead a minimum recruitment goal ($n = 20$) was based on the work of Iodice *et al.* (2017) who investigated similar effects.

7.3.2. Participants

Ethical approval was granted in accordance with [section 3.2](#), (Ref: 2019-2679). In total, 22 healthy males (mean \pm *SD*; age: 25 ± 7 years, weight: 75.0 ± 12.2 kg, height: 1.78 ± 0.06 m) recruited from the local student population and general public volunteered to take part in the study. Participants reported no history of cardiovascular, neurological, or musculoskeletal disorders and all provided written informed consent prior to enrolment ([section 3.5.3](#)). Hand (18 right) and leg (17 right) dominance was determined as per [section 3.18](#).

7.3.3. Experimental Design

Experimental controls were implemented as per [section 3.9](#). Participants undertook three sessions, comprising a preliminary, familiarisation session ([section 3.10](#)) and two experimental conditions. Experimental sessions were designed to last approximately the same duration. Participants were seated on a custom-built rig for the quantification of force in both the HG and KE ([section 3.15](#)). All sessions started with a standardised warm-up for the HG ([section 3.15.1](#)) and dominant KE ([section 3.15.2](#)), before the determination of maximal force production in each muscle group.

In the experimental sessions, participants performed a forced choice task, which evaluated individuals' motivation to engage in rewarded, effortful contractions of the lower limbs, in both a rested state (control) and a pre-induced state of fatigue (fatigue). The order of the experimental conditions was randomized (block randomisation) and counterbalanced across participants. In the fatigue condition, a perceived state of fatigue was pre-induced by a demanding physical task performed in the upper body ([section 3.14.2](#)), leaving the neuromuscular function of the lower body intact ([chapter 4](#)). A schematic representation of the experimental design is presented in [Figure 7.1](#).

7.3.3.1. Effort-based Choice Task

The effort-based choice task was adapted from that designed by Iodice *et al.* (2017). The choice task required participants to make a series of choices between two options, which differed both in the magnitude of the reward offered and the level of effort required to obtain it. Effort was quantified, objectively, as the duration that a sub-maximal contraction (20% MVC) of the dominant KE was to be held for. Durations were individualised to each participant, representing percentiles of the maximum duration each participant could hold the contraction based on individual's best performance recorded in [chapter 6](#). This procedure enabled the normalisation of effort demands across both participants and conditions (Chong *et al.*, 2015). Participants were always presented with the same effort-based decision and asked to select their preference between the two options offered: (1) an option to exert no effort (i.e. perform no contraction; 'No Effort') and receive a fixed reward (£5), or (2) an option in which effort could be exerted for higher monetary rewards. In the 'Effort' option, both effort (20%, 40%, 60%,

80%, 100% of best performance) and reward (£6, £7, £8, £9, £10) were varied, which together led to 25 permutations. Each permutation was presented to participants six times, distributed over two blocks (75 choices per block). The task lasted ~40 minutes in total, with a 1-minute interval between blocks ([Figure 7.1.](#)).

The choice task was coded using Python in PsychoPy 3 (Peirce *et al.*, 2019) and presented on a 19" LCD monitor positioned ~60 cm in front of the participants. An initial set of instructions presented to participants detailed the task protocol. Participants then completed 4 example choices. Initiation of each choice was indicated by presentation of a central white fixation cross on a black screen for 2000ms ([Figure 7.1.](#)). Description of the two choice options was then presented as written text at the top of the screen, with the 'No Effort' option always presented above the 'Effort' option. Two boxes at the bottom of the screen, one on each side, displayed the 'No Effort' (left) and 'Effort' (right) selection. Choice options were presented for 5000ms, but the boxes remained until a choice was made. Participants were instructed to make their choice as quickly as possible through keyboard responses (i.e. 'No Effort' = A; 'Effort' = L), with the position of the boxes corresponding to the side of the associated keyboard response. Keyboard responses were fixed throughout the task. Choice selection time (s) was recorded from the presentation of the choice to the selection of one option. Selection of the 'Effort' option was followed by presentation of a visual analogue scale (VAS) asking participants to rate their level of confidence that they could successfully complete the chosen contraction. The extremes of the VAS were labelled 'Not at all' confident (0) and 'Completely' confident (100). Participants slid the marker along the scale to select an appropriate numerical response ([Figure 7.1.](#)). Presentation of the marker always began at the centre of the scale.

Prior to experimentation, participants were explicitly informed that at the end of the task in each condition, one of their choices would be selected at random and they would be required to perform the chosen contraction. The selected choice would determine participants' pay-out. The participants believed the total pay-out would therefore be the sum of the choices selected across the two conditions. In reality, the selected choice in each condition was not random but represented participants' median selection across the three lowest effort levels (i.e. 20%, 40%, and 60%). This procedure was implemented for two reasons: first, the deception was designed to make participants believe that every choice had a real-world consequence, determining how much they may get paid and how difficult it would be to gain the reward (Chong *et al.*, 2017). Second, the two higher effort levels (i.e. 80% and 100%) were excluded from selection to prevent the possibility of failure to successfully complete the contraction in the first experimental session altering choice behaviour in the next session. Participants were unaware of the elapsed time during the performance of the selected choice contractions, however all successfully completed the selected contractions performed at the end of each condition. At the end of the experiment, participants were debriefed about the deception and received a £30 gift voucher (www.one4all.com) for their participation.

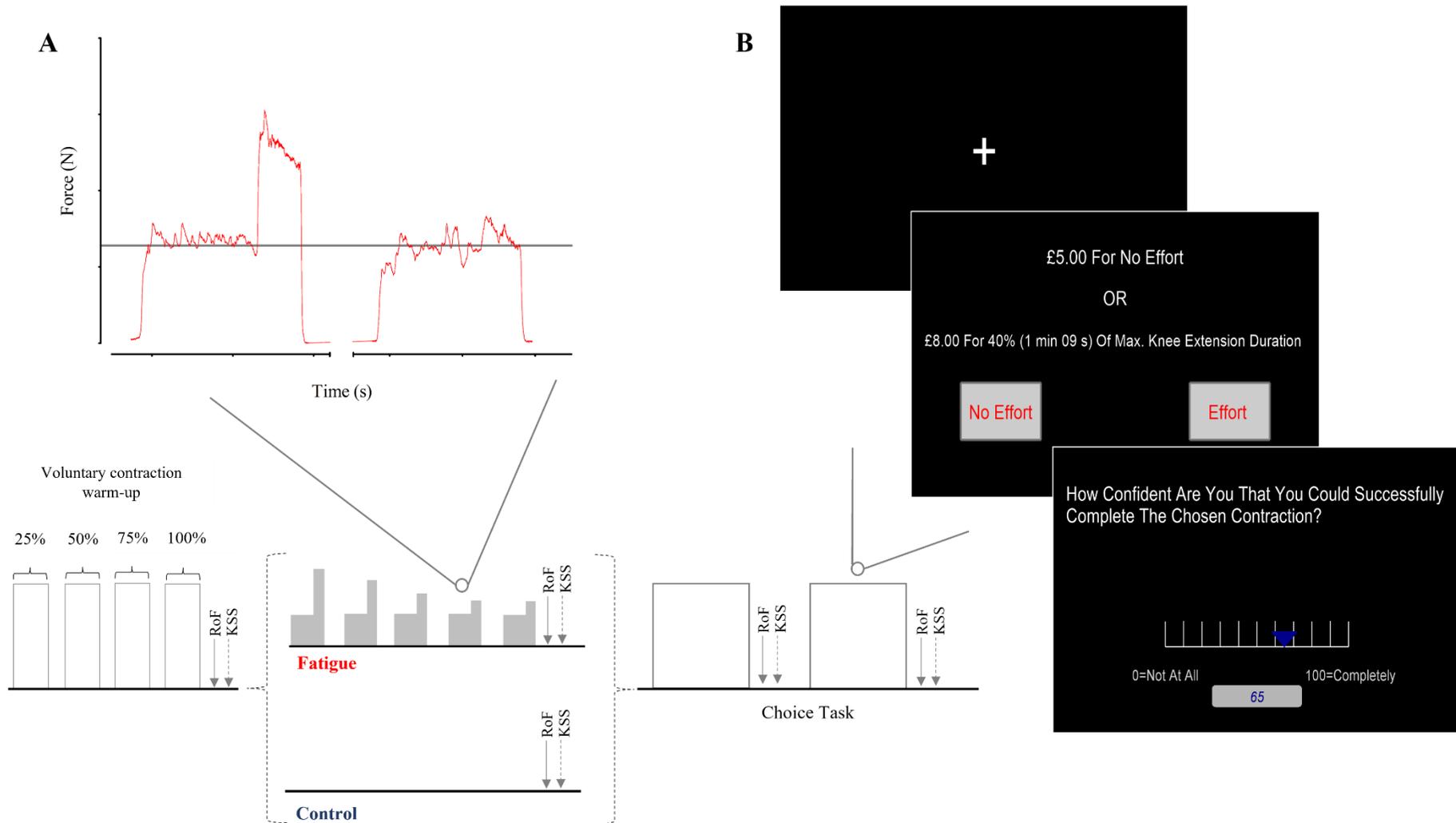


Figure 7.1. Schematic description of the experimental design of *chapter 7*. Participants first completed a standardised set of warm-ups (isometric) contractions performed using the dominant knee extensors (KE) and handgrips (HG) before responding to the rating of fatigue scale (RoF) and Karolinska sleepiness scale (KSS). Responses were recorded again after the completion of the fatigue and control manipulation (**A**: An example of the first and last full contraction sequence completed during the HG task by one representative participant). Following this, participants performed the effort-based choice task, consisting of 150 choices split equally across two blocks. Participants made a series of choice between a fixed reward/no effort option and a variable option in which both level of reward and effort were varied (**B**). RoF and KSS were further scored between blocks and on completion of the choice task.

7.3.3.2. Perceptual Responses

Perceptual responses were recorded at the beginning of each condition, immediately after experimental manipulations (but before the start of the choice task), mid-way through the choice task (in the interval between the two blocks) and on completion of the choice task. During these periods, participants rated their perception of fatigue ([section 3.11.](#)) and perceived sleepiness ([section 3.16.1.](#)). In addition, at the beginning of each experimental condition, participants completed the short form of the DASS, to retrospectively assess depressive, stress and anxiety symptoms experienced over the last week ([section 3.16.2.](#)).

7.3.4. Statistical Analysis

All analyses were performed using jamovi (v. 1.6.6; The jamovi project, 2020), unless otherwise stated. Relevant assumptions of adopted statistical tests were assessed ([section 3.19.6.](#)). Maximal force generating capacity of the dominant and non-dominant HG was assessed between conditions (Fatigue; Control) using a paired sample *t*-test. In analysing maximal force generating capacity of the KE and retrospective emotional state symptoms, the assumption of normality appeared to be violated based on model residuals. As such, Wilcoxon signed rank tests were used in testing the hypotheses that variables differed between conditions. Responses to the RoF and KSS were assessed between conditions and across the various stages within each experimental session. Model residuals of each variable were also shown to deviate from a normal distribution. Therefore, a Friedman's ANOVA was performed with each recording point (Baseline; Pre choice task; Mid choice task; Post choice task) within each condition (Fatigue; Control) entered to identify differences in responses across the multiple recordings. Follow-up Wilcoxon signed rank tests, with Bonferroni adjustments, were used to compare individual recording points between conditions.

The intention was to model the mathematical function that best described effort-discounting of reward within choice behaviour and compare this parameter between conditions, as previously performed (e.g. Iodice *et al.*, 2017). However, initial analysis of the data indicated that many participants did not display the necessary variation in choice between the offered reward/effort combinations enabling the estimation indifference points (i.e. the monetary reward, for each effort level, required to select the 'No Effort' and 'Effort' option with equal probability). This is not uncommon (see Benoit *et al.*, 2019; Bonnelle *et al.*, 2015). Accordingly, a generalized linear mixed-effect model (GLMM), using the *GAMLj* module (Gallucci, 2019) was selected *post hoc*, to assess the experimental effects on the probability of selecting the effort option. The model assumed a binomial distribution with logit link function, with fixed effects of reward, effort, condition and all interactions. The model also included random intercepts for each participant. Fixed effects of reward and effort were coded using a reverse Helmert contrast, through which the mean of each level (bar the first) was compared against the mean of all previous levels. This generated four contrasts within the assessment of both reward and effort. The effect of condition was evaluated using a simple contrast between the control and fatigue condition. A similar GLMM was used to assess choice selection time, due to data being skewed (Lo & Andrews, 2015). Several models were initially evaluated to describe the data, with the best fitting model corresponding to an inverse gaussian distribution with inverse link function ([Appendix C; Table C.1.](#)). Lastly, a LMM was fit to confidence ratings following the 'Effort' option selection. *F*-tests were computed for the fixed effects using Satterthwaite approximation of the degrees of

freedom. For the GLMM performed on choice selection time and the LMM for confidence ratings reward, effort, and condition (plus all interactions) were entered as fixed effects, while intercepts were allowed to vary across participants (random effect). Coding of fixed effects were the same as that outlined for the analysis of choice behaviour. Select significant interaction effects were followed up through examination of simple effects across each level of the variables, with false discovery rate (FDR) adopted for multiple comparisons (Benjamini & Yosef, 2000; Pike, 2011). Full specification of all mixed-effects models can be found in [Appendix C](#). For all analyses, the null hypothesis was rejected at an α -level of 0.05.

7.4. Results

7.4.1. Preliminary Analysis

Force and emotional state recorded at the beginning of each condition are presented in [Table 7.1](#). Maximal force-generating capacity was not statistically different between conditions for KE ($Z = -1.74$, $p = 0.082$, $r = 0.38$), dominant HG ($t_{(21)} = 0.04$, $p = 0.971$, $d_{av} < 0.01$) or non-dominant HG ($t_{(21)} = -0.07$, $p = 0.945$, $d_{av} = 0.01$). Recall of symptoms of depression, anxiety and stress indicated little or negligible experience of symptoms in the sample. Between conditions, there was no difference in anxiety ($Z = 0.54$, $p = 0.588$, $r = 0.20$) and stress-associated symptoms ($Z = 1.54$, $p = 0.124$, $r = 0.41$). Depressive symptoms were however reported to be slightly lower prior to the fatigue condition compared to control ($Z = 2.56$, $p = 0.010$, $r = 0.91$).

Table 7.1. Maximal force and emotional states at the start of each condition.

	Condition	
	Control	Fatigue
MVC Force (N)		
<i>KE</i>	655 ± 161 (656, 218)	668 ± 174 (654, 211)
<i>Dominant HG</i>	467 ± 89	466 ± 92
<i>Non-dominant HG</i>	442 ± 90	442 ± 96
Emotional State Symptoms (DASS; a.u.)		
<i>Depression</i>	2.1 ± 2.7 (2.0, 2.0)	1.1 ± 2.5 (0.0, 1.5)*
<i>Anxiety</i>	1.3 ± 3.2 (0.0, 1.5)	1.0 ± 3.4 (0.0, 0.0)
<i>Stress</i>	5.0 ± 6.3 (2.0, 7.5)	3.7 ± 4.9 (0.0, 7.5)

Data presented as mean ± SD with *Mdn* and *IQR* presented in parentheses. MVC: maximal voluntary contraction; DASS: Depression, Anxiety and Stress Scale. KE: knee extensors; HG: handgrip. *: Significantly different from the control condition ($p < 0.05$).

7.4.2. Subjective State Responses

Differences were present in recorded RoF within and between conditions ($\chi^2_{(7)} = 98.6, p < 0.001$; [Figure 7.2.](#)). In the control condition, RoF remained stable across the entire experimental session (*Mdn*: 1 - 2, *IQR*: 1 - 2.5; all $p > 0.05$). Conversely, the HG task served to increase RoF (*Mdn*, *IQR*: 10, 1) above baseline (*Mdn*, *IQR*: 2, 1: $Z = -4.14, p = 0.001, r = 0.88$), with RoF remaining elevated throughout the choice task (baseline *vs.* mid choice task (*Mdn*, *IQR*: 4, 3): $Z = -3.78, p = 0.004, r = 0.81$; *vs.* post choice task (*Mdn*, *IQR*: 3, 2): $Z = -3.42, p = 0.017, r = 0.83$), though some recovery was evident during the choice task (pre choice task *vs.* mid choice task: $Z = 4.11, p = 0.001, r = 0.88$; *vs.* post choice task: $Z = 4.10, p = 0.001, r = 0.87$). Accordingly, with no difference in RoF between conditions at baseline ($Z = 1.02, p > 0.999, r = 0.31$), the different response profiles saw RoF elevated in the fatigue condition above that recorded in the control condition immediately prior to the choice task (pre choice task: $Z = -4.12, p = 0.001, r = 0.88$), and perceptions remained elevated mid task ($Z = -3.76, p = 0.005, r = 0.86$). RoF was greater in the fatigue condition at the end of the choice task, but the difference between conditions was not significant after correcting for multiple comparisons ($Z = -2.91, p = 0.101, r = 0.69$). Though KSS responses indicated an effect of experimental manipulations ($\chi^2_{(7)} = 35.5, p < 0.001$), KSS was not significantly different between conditions at any point within each session (*Mdn*: 2 - 4, *IQR*: 1 - 4; all $p > 0.05$). KSS was also relatively

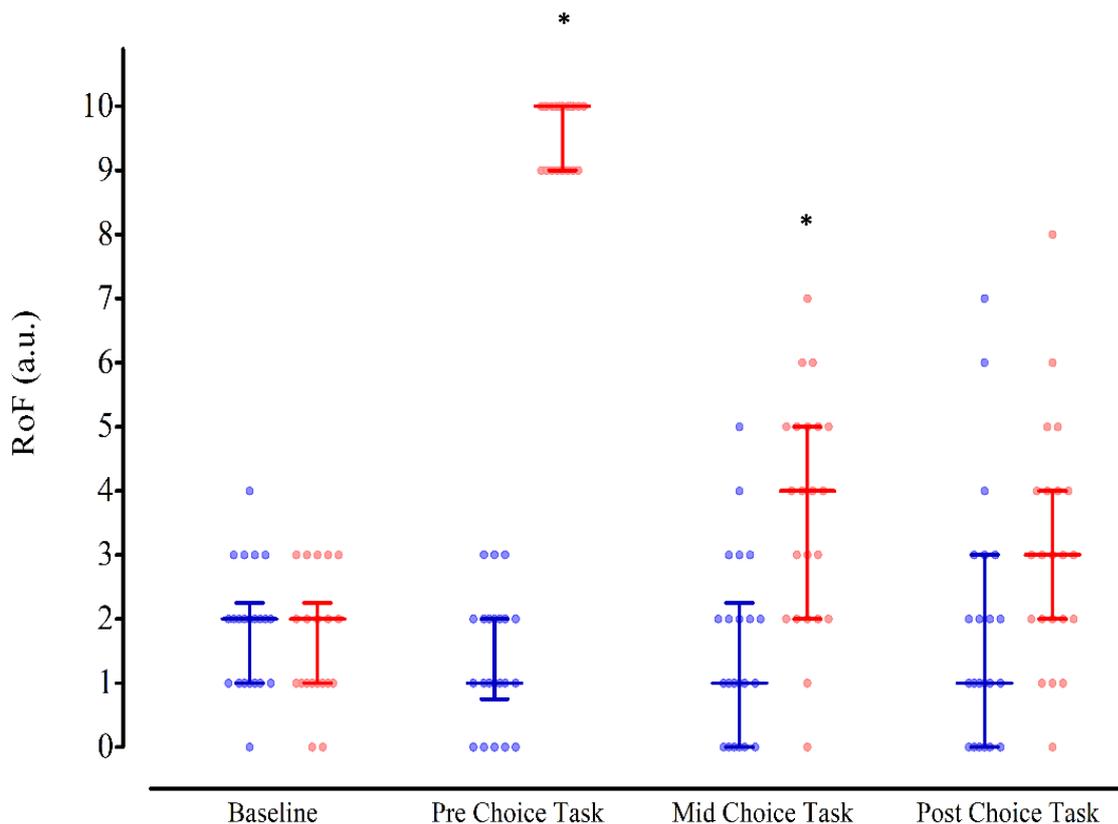


Figure 7.2. Subjective ratings of fatigue (RoF) across control (blue lines and dots) and fatigue (red lines and dots) conditions. Individual responses presented plus *Mdn* and *IQR* at a group level. *: Significantly different from control ($p < 0.05$).

unchanged throughout each condition, except for a small increase evident in the fatigue condition at the end of the choice task (post choice task: *Mdn, IQR*: 4, 4 vs. pre choice task: *Mdn, IQR*: 2, 1; $Z = -3.18$, $p = 0.041$, $r = 0.88$). All other comparisons were non-significant (all $p > 0.05$). Thus, it appeared that participants were able to effectively differentiate between the perception of fatigue and sleepiness.

Table 7.2. Simple effects of effort, moderated by reward level, on parameter estimates of choice probability derived from logistic regression.

Moderator		Contrast	Estimate	SE	exp(B)	95% exp(B) CI		p
Reward						Lower	Upper	
£6	Effort C1		-2.12	0.29	1.198e-01	6.738e-02	2.130e-01	< .001
	Effort C2		-2.82	0.23	5.979e-02	3.786e-02	9.443e-02	< .001
	Effort C3		-4.05	0.24	1.737e-02	1.085e-02	2.780e-02	< .001
	Effort C4		-4.71	0.31	9.010e-03	4.870e-03	1.667e-02	< .001
£7	Effort C1		-1.18	0.36	3.080e-01	1.518e-01	6.249e-01	0.002
	Effort C2		-2.86	0.26	5.744e-02	3.479e-02	9.483e-02	< .001
	Effort C3		-4.21	0.24	1.485e-02	9.290e-03	2.373e-02	< .001
	Effort C4		-5.07	0.27	6.310e-03	3.710e-03	1.075e-02	< .001
£8	Effort C1		-8.56	7.05	1.920e-04	1.910e-10	1.919e+02	0.250
	Effort C2		-6.42	3.53	1.620e-03	1.60e-06	1.644e+00	0.086
	Effort C3		-7.30	2.36	6.760e-04	6.63e-06	6.885e-02	0.003
	Effort C4		-6.79	1.78	1.120e-03	3.46e-05	3.643e-02	< .001
£9	Effort C1		-0.36	8.55	6.948e-01	3.64e-08	1.330e+07	0.966
	Effort C2		-10.28	3.29	3.430e-05	5.42e-08	2.168e-02	0.003
	Effort C3		-10.23	2.20	3.590e-05	4.83e-07	2.670e-03	< .001
	Effort C4		-9.15	1.66	1.060e-04	4.13e-06	2.720e-03	< .001
£10	Effort C1		-14.38	12.41	5.670e-07	1.550e-17	2.072e+04	0.259
	Effort C2		-9.84	6.24	5.340e-05	2.610e-10	1.094e+01	0.135
	Effort C3		-9.62	4.16	6.640e-05	1.91e-08	2.313e-01	0.028
	Effort C4		-9.18	3.12	1.030e-04	2.26e-07	4.701e-02	0.005

SE: standard error; CI: confidence interval; exp(B): exponential of B coefficient (odds ratio); Effort contrast coded using a reverse Helmert contrast: Effort C1 = 40% - (20%), Effort C2 = 60% - (40%, 20%), Effort C3 = 80% - (60%, 40%, 20%), Effort C4 = 100% - (80%, 60%, 40%, 20%). Alpha level adjusted for multiple comparisons using false detection rate (FDR).

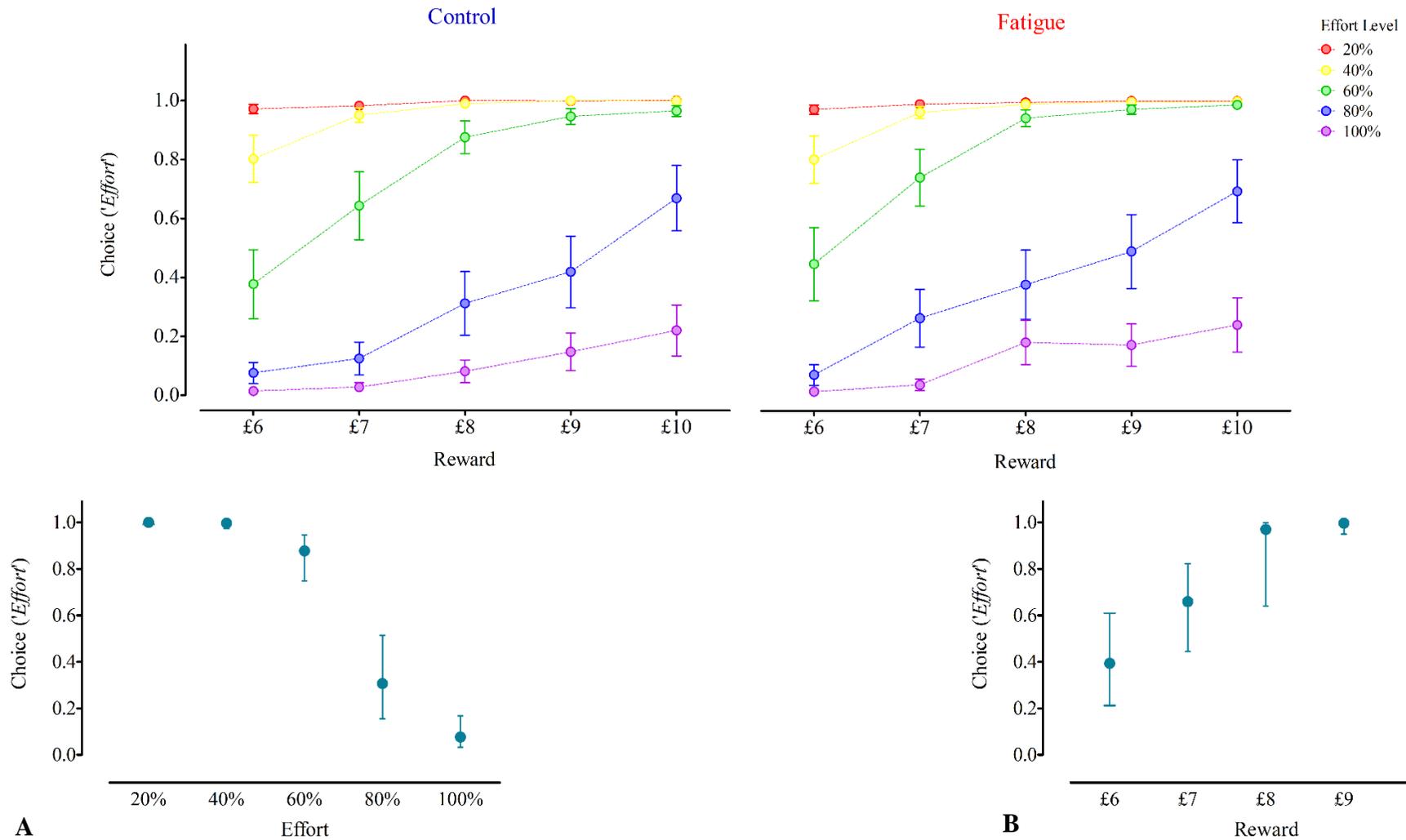


Figure 7.3. The probability of choosing the ‘effort’ option. The top panel displays the change across reward levels for each level of effort, averaged across participants, in both the control (left) and fatigue conditions (right). Data presented as estimated marginal mean \pm standard error (*SE*). In the bottom panel, main effects of effort (**A**: collapsed across condition and reward level) and reward (**B**: collapsed across condition and effort) are presented. Data presented as estimated marginal mean \pm 95% *CI*.

7.4.3. Effort-based Choice Task

Descriptive statistics of the raw data for choice behaviour is presented in [Appendix C \(Table C.2.\)](#). Main effects of reward ($\chi^2_{(4)} = 93.51, p < 0.001$), effort ($\chi^2_{(4)} = 817.57, p < 0.001$) and an interaction between effort and reward ($\chi^2_{(16)} = 37.58, p = 0.002$) were found for the probability of choosing the effort option ([Figure 7.3.](#)). Evaluation of the simple effect of effort level, moderated by reward level, demonstrated that generally, higher effort levels were associated with a reduced probability of selecting the effort option across all reward levels. However, when greater rewards were on offer (i.e. £8 - £10), there was no difference in the probability of choosing the effortful option between lower-level effort contrasts (i.e. <60%; [Table 7.2.](#)). That is, higher levels of reward offset effort-discounting, but only when the effort demands were relatively low. Importantly, a pre-induced state of fatigue did not influence the probability of selecting the effort option, as demonstrated by the absence of a main effect of condition and interaction effects including condition (all $p > 0.05$).

Table 7.3. Simple effects of effort, moderated by reward level, on parameter estimates of choice selection time.

Moderator	Contrast	Estimate	SE	95% CI		p
				Lower	Upper	
£6	Effort C1	-0.060	0.020	-0.099	-0.021	0.002
	Effort C2	-0.030	0.017	-0.063	0.002	0.042
	Effort C3	0.004	0.016	-0.028	0.035	0.333
	Effort C4	0.069	0.017	0.036	0.101	< .001
£7	Effort C1	-0.062	0.020	-0.101	-0.023	0.001
	Effort C2	-0.072	0.016	-0.103	-0.040	< .001
	Effort C3	-0.019	0.016	-0.049	0.012	0.124
	Effort C4	0.026	0.016	-0.005	0.057	0.058
£8	Effort C1	-0.062	0.021	-0.103	-0.021	< .001
	Effort C2	-0.103	0.017	-0.135	-0.071	0.002
	Effort C3	-0.056	0.016	-0.086	-0.025	< .001
	Effort C4	0.014	0.016	-0.017	0.045	0.172
£9	Effort C1	-0.073	0.022	-0.115	-0.030	0.001
	Effort C2	-0.103	0.018	-0.138	-0.069	< .001
	Effort C3	-0.110	0.016	-0.140	-0.079	< .001
	Effort C4	-0.005	0.016	-0.036	0.027	0.333
£10	Effort C1	-0.025	0.022	-0.068	0.018	0.124
	Effort C2	-0.083	0.018	-0.118	-0.049	< .001
	Effort C3	-0.108	0.016	-0.139	-0.078	< .001
	Effort C4	-0.003	0.016	-0.035	0.028	0.333

SE: standard error; CI: confidence interval; Effort contrast coded using a reverse Helmert contrast: Effort C1 = 40% - (20%), Effort C2 = 60% - (40%, 20%), Effort C3 = 80% - (60%, 40%, 20%), Effort C4 = 100% - (80%, 60%, 40%, 20%). Alpha level adjusted for multiple comparisons using false detection rate (FDR).

Analysis of choice selection time indicated a significant main effect for reward ($\chi^2_{(4)} = 33.00, p < 0.001$), effort ($\chi^2_{(4)} = 207.78, p < 0.001$) and an interaction between effort and reward ($\chi^2_{(16)} = 69.11, p < 0.001$). Simple effects of effort for each level of reward are presented in [Table 7.3](#). Broadly speaking, faster selection times tended to be observed when effort requirements were greater, but this was not consistent, particularly when including the highest effort level (i.e. 100%). There was also a significant main effect of condition evident for selection time ($\chi^2_{(1)} = 6.40, p = 0.011$), with the estimated fixed effect demonstrating faster selection times, on average, when in a non-fatigued state (Control: 1.88 s, 95% CI: 1.62 s, 2.22 s; Fatigue: 1.93 s, 95% CI: 1.66 s, 2.30 s; $b = -0.015$, 95% CI: -0.026, -0.003). The effect of condition did not influence the effect of reward, effort, or their interaction on choice selection time, as evidenced by the non-significant two- and three-way interactions including condition (all $p > 0.05$).

Participants' confidence in being able to perform selected effortful contractions was influenced by the level of effort required ($F_{(4, 4148)} = 652.44, p < 0.001, \eta_p^2 = 0.39$) and was different between conditions ($F_{(1, 4150)} = 139.24, p < 0.001, \eta_p^2 = 0.03$). There were also significant interactions between condition and reward ($F_{(4, 4147)} = 8.44, p < 0.001, \eta_p^2 = 0.01$), condition and effort ($F_{(4, 4148)} = 32.83, p < 0.001, \eta_p^2 = 0.03$), reward and effort ($F_{(16, 4147)} = 1.91, p = 0.016, \eta_p^2 = 0.007$), and a three-way interaction between condition, effort and reward ($F_{(16, 4147)} = 2.53, p < 0.001, \eta_p^2 = 0.01$). Simple effects of condition were examined across effort and reward levels ([Table 7.4](#)). Within each reward level, there was a significant reduction in individuals' confidence in their ability to perform the two highest effort levels (i.e. 80-100% of previous best performance) when choices were made under a pre-induced state of perceived fatigue. This was universally observed except for the highest reward level (i.e. £10) in which reduced confidence was only seen at the second highest effort level (i.e. 80%; [Table 7.4](#); [Figure 7.4](#)). Descriptive statistics of the raw data for confidence ratings is presented in [Appendix C \(Table C.5\)](#).

7.5. Discussion

The present study chapter examined whether a perceived state of fatigue, pre-induced through physical activity performed in one part of the body, changed choice preferences during effort-based decisions concerning the performance of exercise in another, rested part of the body. Contrary to the primary hypothesis, no effect of a perceived state of fatigue was observed on effort-discounting of prospective reward. However, participants' reflection on the selection of effortful actions indicated lower confidence in perceived ability to carry out highly effortful actions when the decision was made under a perceived state of fatigue.

Engaging in physically effortful action reduces the attractiveness of outcome rewards (Bonnelle *et al.*, 2015; Chong *et al.*, 2017; Croxson *et al.*, 2009; Hartmann *et al.*, 2013; Klein-Flügge *et al.*, 2015; Prévost *et al.*, 2010). In the present study, this was most evident when effort demands approached individuals' 'maximal' performance, where even the prospect of greater rewards could not fully offset participants' aversion to effort ([Figure 7.3](#)). Importantly, the subjective cost of effort (and the attractiveness of reward) appeared to be unaffected by a state

Table 7.4. Simple effects of condition on subjective confidence ratings, moderated by reward and effort level.

Moderator Variables		Contrast	Estimate	SE	95% CI		t	p
Reward	Effort				Lower	Upper		
£6	20%	Fatigue - Control	0.59	1.38	-2.11	3.29	0.43	0.632
	40%	Fatigue - Control	-2.45	1.58	-5.55	0.66	-1.55	0.232
	60%	Fatigue - Control	-2.07	1.95	-5.90	1.75	-1.06	0.392
	80%	Fatigue - Control	-13.88	3.05	-19.86	-7.90	-4.55	< .001
	100%	Fatigue - Control	-20.03	5.33	-30.48	-9.59	-3.76	< .001
£7	20%	Fatigue - Control	-0.01	1.35	-2.65	2.62	-0.01	0.754
	40%	Fatigue - Control	-0.85	1.40	-3.60	1.90	-0.61	0.575
	60%	Fatigue - Control	-1.44	1.68	-4.73	1.86	-0.86	0.497
	80%	Fatigue - Control	-13.28	2.41	-18.00	-8.56	-5.51	< .001
	100%	Fatigue - Control	-26.55	4.05	-34.48	-18.61	-6.56	< .001
£8	20%	Fatigue - Control	0.46	1.32	-2.12	3.04	0.35	0.632
	40%	Fatigue - Control	-1.46	1.34	-4.08	1.16	-1.09	0.392
	60%	Fatigue - Control	-1.89	1.47	-4.78	0.99	-1.29	0.341
	80%	Fatigue - Control	-6.70	2.04	-10.70	-2.71	-3.29	0.002
	100%	Fatigue - Control	-16.24	2.68	-21.51	-10.98	-6.05	< .001
£9	20%	Fatigue - Control	0.38	1.31	-2.18	2.95	0.29	0.635
	40%	Fatigue - Control	-0.60	1.31	-3.17	1.97	-0.46	0.632
	60%	Fatigue - Control	-1.11	1.40	-3.85	1.63	-0.79	0.505
	80%	Fatigue - Control	-5.01	1.90	-8.74	-1.28	-2.63	0.018
	100%	Fatigue - Control	-9.41	2.46	-14.24	-4.58	-3.82	< .001
£10	20%	Fatigue - Control	0.45	1.31	-2.11	3.01	0.34	0.632
	40%	Fatigue - Control	0.26	1.31	-2.31	2.83	0.20	0.668
	60%	Fatigue - Control	-1.03	1.37	-3.70	1.65	-0.75	0.505
	80%	Fatigue - Control	-7.31	1.69	-10.62	-3.99	-4.32	< .001
	100%	Fatigue - Control	-2.39	2.25	-6.79	2.02	-1.06	0.392

SE: standard error; CI: confidence interval; t: t-statistic. Alpha level adjusted for multiple comparisons using false detection rate (FDR).

experience of fatigue. The findings of the present study are in direct contrast to those reported by Iodice et al. (2017), in which a prior bout of demanding cycling increased effort-discounting of monetary incentives that could be obtained through further cycling exercise. As demonstrated in [chapter 4](#), the functional capacity of the KE remains largely intact following the adopted HG task intervention used here to induce a perceived state of fatigue, therefore potentially precluding influence from activity-induced central and peripheral factors that limit the physical capacity of the active locomotor muscles (Sidhu et al., 2009b; Weavil et al., 2016). This may represent the pivotal difference between the present study and the work of Iodice and colleagues (2017), which taken together may indicate that the effect of fatigue emerging from demanding physical activity on the subjective cost of effort during subsequent physical tasks may be particularly sensitive to the current physical state of the motor system and specifically, the target effectors that will carry out the future effort (i.e. the active muscles).

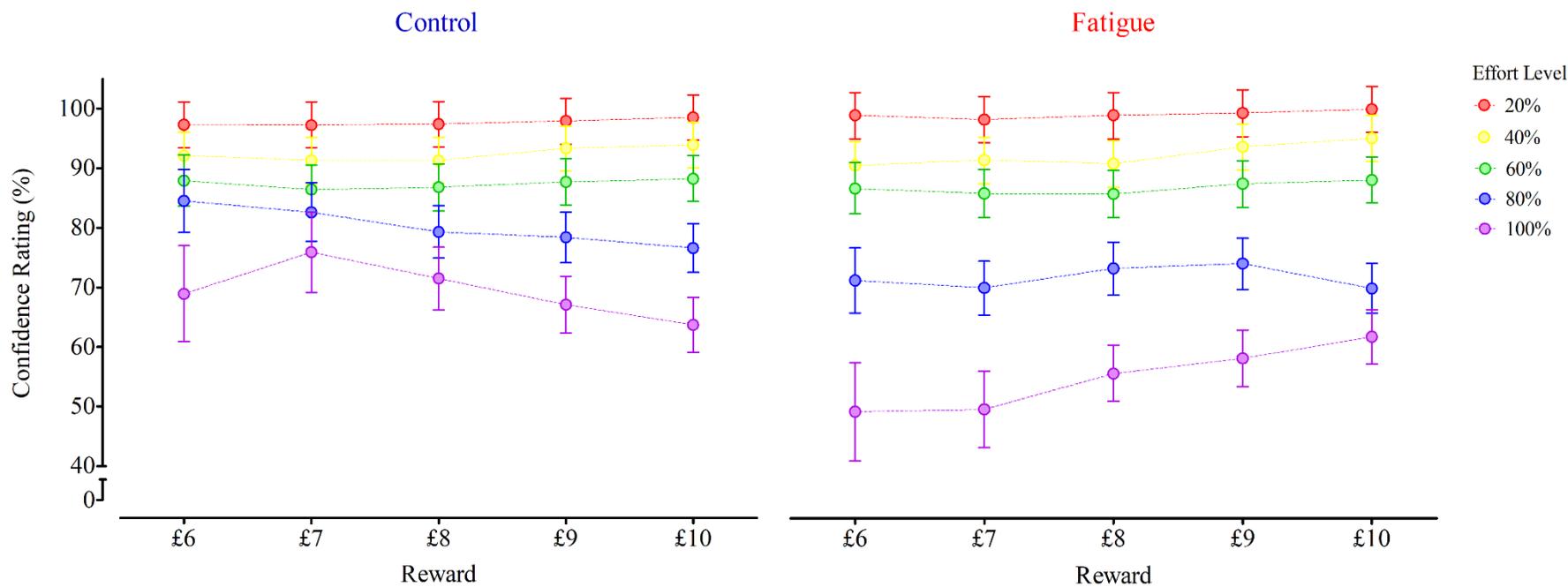


Figure 7.4. Subjective confidence ratings of participants' perceived ability to successfully perform chosen effortful contractions. Separate lines represent the change across reward levels for each level of effort in both the control (left) and fatigue (right) conditions. Data presented as estimated marginal mean \pm standard error (SE).

The cost of effort in the present study was based on physical force production but principally, the need to exert some degree of (cognitive) control to maintain output over time, touching on the unification of effort between domains ([section 2.4.1.2.](#)). In line with the presented findings, voluntary decisions to exert cognitive effort for monetary rewards has also been reported to be unchanged following the development of a perceived state of fatigue through the performance of a separate cognitive task (Benoit *et al.*, 2019). Together, the results appear to suggest that a perceived state of fatigue may exert limited influence on evaluation of the cost/benefits of exerting cognitive control. Both physical (Blain *et al.*, 2019) and cognitive exertion (Blain, Hollard, *et al.*, 2016) have been shown to elicit a fatigue-associated downregulation of the cognitive control system, leading to an increasing preference for more immediate gratification during inter-temporal economic choice tasks. However, these effects were only evident following interventions far exceeding the typical durations of interventions used to examine the effects of exertional fatigue, such as the present study. This may indicate that the (effort) costs of cognitive control are relatively robust and resistant to acute effects of ‘fatigue’, and may suggest that a primary driver of increased aversion to physical effort during forced-choice tasks following physical exertion (Iodice *et al.*, 2017) may reflect the functional capacity of the motor system. The functional capacity of the motor system may represent an important stream of information incorporated into the decision process used to contextualise the likely value of cognitive control during physical tasks. In keeping, physical costs represented across sensorimotor regions have been shown to be encoded early after stimulus presentation during effort-based decisions, before later representation of its subjective value (Harris & Lim, 2016).

Since the completion of the present study, several interesting studies have been published on the topic of fatigue and effort-based decision-making that are relevant to the proposed interpretation of the present results. These will briefly be reviewed. First, Müller *et al.* (2021) provide further insight into the effect of ‘fatigue’ on physical effort-based decisions. The authors demonstrated that the sensitivity to effort costs changed across time during a physical task. The authors constructed a parabolic model to describe this effort-discounting, in which the effects of ‘fatigue’ were modelled as comprising two components: 1) a transient, element that is recoverable through choosing to rest, and 2) a slower nonrecoverable element, which was aligned to ‘executive fatigue’, that is not easily restored through rest. The full model (i.e. containing both fatigue components) was identified as the best predictor of choice behaviour⁶⁵. The two components of fatigue were ascribed to distinct regions of the frontal cortex (i.e. recoverable: posterior rostral cingulate zone; unrecoverable: medial frontal gyrus and anterior rostral cingulate zone), independent of the evaluation of the subjective value of effort. Accordingly, the authors demonstrate that evaluation of effort-based costs are dynamic and may be altered on a moment-to-moment basis based on factors including fatigue. Similarly, Hogan *et al.* (2020) reported an increased aversion to risky effortful choices in response to fatiguing handgrip contractions, with increased costs of effort correlated with declines in the physical capacity to meet force requirements. Interestingly, the authors identified that premotor and motor regions were depressed when ‘fatigued’ during decisions, but the individuals who demonstrated the greatest sensitivity to effort costs were those who demonstrated the smallest change in PMC activity. It was therefore proposed that a failure to adequately alter motor cortical activity to align to activity-induced changes in physical capacity leads to an increased subjective cost of effort. Interestingly, van As *et al.* (2021) compared the effects of ‘physical fatigue’

⁶⁵ And the subjective perception of ‘tiredness’, suggesting choice behaviour may be linked to the momentary perceptions.

and ‘cognitive fatigue’ on the subsequent decision to exert physical effort. The authors report that effort discounting was affected by the ‘physical fatigue’ condition, but found no effect was observed in the ‘cognitive fatigue’ condition. Though the authors note difficulties in clearly attributing effects to fatigue based on participants subjective experiences within each condition, the findings demonstrate that exertion of physical, rather than cognitive effort, alters the appraisal of the cost-benefits of exerting future effort during physical tasks involving the same muscle group (van As *et al.*, 2021). Finally, Jurgelis *et al.* (2021) presented collated findings across three effort-based decision-making studies, correlating the effort discounting function modelled during a force choice task to self-reported perceptions of fatigue. Contrary to the results presented here, the authors observed a significant positive correlation with subjective perceptions of fatigue and effort-based choice (Jurgelis *et al.*, 2021). Taken as a collective, the studies indicate the importance of representation of the condition of the motor system, relevant to the specific task to be performed, in instantiating the effect of fatigue on (physical) effort-based decisions. Though Müller *et al.* (2021) suggest that perceptions may coincide with changes in choice behaviour, the present findings indicate that simply feeling fatigued may not necessarily be sufficient to evoke changes in physical effort-based decisions. Though this may appear in conflict with the results presented by Jurgelis *et al.* (2021), divergent observations may possibly be attributed to the conceptualisation of fatigue as a state (i.e. the present study) or trait (i.e. Jurgelis *et al.*, 2021) measure. The presented results suggest that a state perception of fatigue does not significantly alter processes of effort-based decision making.

The difference between objective behavioural indices (here, the lack of change in the preference of effortful action) and subjective perception of fatigue highlights a common misassumption that subjective and behavioural measures of fatigue are related and deterministic (Leavitt & DeLuca, 2010). The subjective dimension of fatigue has been described as an anticipatory process that may emerge prior to overt behavioural change, signalling future adverse consequences if action is continued (Benoit *et al.*, 2019). Here, in a perceived state of fatigue, participants’ confidence in their ability to perform selected effortful actions was reduced. This was evident only at the highest effort levels ([Figure 7.4](#)), suggesting that participants were increasingly aware of issues that may limit their ability to sustain the motor action across longer durations in a perceived state of fatigue. It was also demonstrated that the fatigue condition increased choice selection time, which may similarly indicate that a degree of uncertainty pervaded all decisions under a state of fatigue. This conforms to the proposition that fatigue is inherently associated with self-perceived confidence to carry out actions (Steele, 2021; Stephan *et al.*, 2016). Neural representations of ‘confidence-related information’ (e.g. in the vmPFC) have been identified as an early and separable signal preceding choice during perceptual decisions (Gherman & Philiastides, 2018). It also forms an important input to metacognitive centres supporting retrospective evaluation of confidence, evidenced by a strengthening of connection by regions representing this early signal and frontal areas (e.g. dlPFC) (Gherman & Philiastides, 2018). Accordingly, a perceived state of fatigue and its associated uncertainty may help shape, but may not necessarily define, the decision-making process, with changes in confidence preceding changes in choice behaviour. Increased uncertainty under a state of fatigue may eventually influence future action selection (Friston *et al.*, 2014), changing the potential of alternative outcome probabilities and associated control policies that may vie for action selection in the future to destabilize choice behaviour (Mullette-Gillman *et al.*, 2015). However, in the absence of behavioural effects, establishing temporal relationships between the perception of fatigue and

changes in choice behaviour could not be performed. It cannot be discounted that fatigue-associated declines in perceived task self-efficacy do not affect, and are thus separable from, the motivation to exert future effort.

A clear limitation of the present study was the recovery of the perception of fatigue across the choice task ([Figure 7.2](#)). Accordingly, participants may have been making choices in a similar state (i.e. unfatigued) towards the end of the choice task and thus the effect of fatigue may have been lost. The presented study did not permit an evaluation of the effect of the intervention on choice behaviour across the two blocks, to observe whether changing perceptions coincided with changes in task behaviour. Future studies are therefore required to reinvestigate this effect whilst maintaining a stable perception of fatigue across the duration of the choice task. The adopted choice task was adapted from that used by Iodice *et al.* (2017). Like the authors, in the present study, one trial was selected from participants choices to be performed at the end of each session. It may, however, be argued that the participants may have factored in the recovery of fatigue when eventually faced with the prospect of performing the KE contraction when forming their decisions about whether they would be willing to exert effort in the future. This may potentially confound understanding the effects of subjective state perceptions on choice behaviour and may also account for differences from studies utilising immediate consequences of choice (e.g. Müller *et al.*, 2021). The conceptualisation of effort as the production of force across time also raises the possibility that other costs were weighed within the decision process, such that decisions were not exclusively attributable to the subjective valuation of effort. This includes temporal-discounting and possibly reward uncertainty (i.e. risk). Disentangling the effect of fatigue on effort costs over other cost factors is therefore required by future investigations. Finally, the present study was unable to fit mathematical functions to describe effort-discounting (Massar *et al.*, 2018; Pessiglione *et al.*, 2018), as choice preferences demonstrated limited variation across effort and reward levels in some individuals. This may be because the range of rewards were too limited to provide sufficient incentive for the exertion of effort. The effect of reward on decisions appeared to be weaker and more variable than the effect of effort ([Figure 7.3](#)). Titration of effort/reward options may help better distinguish individuals' subjective assessment of equivalence between low effort and high effort options (Westbrook & Braver, 2015).

7.6. Conclusion

The present study chapter demonstrates that a perceived state of fatigue, pre-induced through demanding physical activity, was not associated with reduced motivation to exert effort in a rested part of the body. The results indicate that a perceived state of fatigue did not increase the global aversion to effort. However, decisions to engage in demanding and effortful physical actions under a perceived state of fatigue is associated with lower confidence in ones' ability to perform selected actions. The subjective feeling of fatigue may be associated with changes in monitoring and evaluative processes that precede overt changes in effort-based decisions, however future studies are required to examine this proposal, comparing the effects of a perceived state of fatigue on effort-based choice relating to rested and active muscle groups.

CHAPTER 8 - GENERAL DISCUSSION

8.1. Introduction

The aim of the present thesis was to examine how a perceived state of fatigue influenced the psychophysical responses defining the central regulation of endurance performance. The research was based on a need to define the specific function of a perceived state of fatigue within the control of exercise behaviour. To this end, a perception of fatigue was pre-induced through physically demanding activity in the upper body before examining its subsequent effects during an endurance task performed in the lower body. Four experiments based on this paradigm were conducted to address the aims of the thesis. The first ([chapter 4](#)) examined whether the adopted paradigm dissociated the perception of fatigue from motor fatigability in order to enable an examination of the specific effects of the subjective component on performance within an intact neuromuscular system. The latter three studies ([chapters 5-7](#)) examined the effect of a perceived state of fatigue on perceptual and affective responses to prolonged physical activity, and decisions relating to the engagement of such activity. This chapter will provide an overarching discussion of the findings of these studies. Specifically, [section 8.2](#) initially reviews the principal findings of [chapters 4-7](#). [Section 8.3](#) situates the present findings within the broader literature. [Section 8.4](#) outlines a theoretical framework that may account for the observed findings and aid understanding of the development of the acute, exertion-related perception of fatigue. [Section 8.5](#) presents additional analysis of data collated across [chapters 5](#) and [6](#) in an evaluation of the decision-making processes defining the limits of endurance performance. The chapter ends with [section 8.6](#), in which the limitations of the presented research and future directions are discussed.

8.2. Summary of the Principal Findings of the Thesis

The fundamental premise of the present thesis was that the perception of fatigue, that is a feeling of a reduced capacity to effectively cope with demands ([section 2.2.5](#)), reflects an important input defining the regulation of physical endurance performance. To establish this, a paradigm was sought that enabled the manipulation of perceived states independent of motor fatigability, which could preclude clear comparison of performance effects between the control and intervention conditions. Based on previous observations (Aboodarda *et al.*, 2020; Amann *et al.*, 2013; Johnson *et al.*, 2015; [section 2.7.2.5](#)), it was believed that activity in one part of the body (i.e. upper body) may evoke a change in the global perceived state (i.e. fatigue), without incurring a concomitant transfer of fatigability to other parts of the body (i.e. the lower limbs), enabling comparison of performance in the latter. The first experimental study chapter ([chapter 4](#)) explicitly examined whether the performance of a bilateral HG task altered the force-generating capacity and corticospinal excitability of the dominant KE so as to establish the veracity of the paradigm adopted in later study chapters. Changes in peripheral and central mechanisms impacting on acute neuromuscular function of the KE were determined using FNS and TMS, respectively. The study represented the first attempt to quantify supra-spinal effects impacting lower-body motor responses following prior activity in the upper body. The results of the study provided mixed support for the primary hypothesis; that voluntary and electrically evoked force production, cortical voluntary activation and corticospinal excitability of the non-active KE would be unchanged following HG activity. Contrary to this hypothesis, effects between

conditions (i.e. HG task vs. control task) were shown to reside outside of the prescribed bounds of equivalence as defined by effect sizes derived from a previous study examining the intersession reliability of indices of neuromuscular function (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). The results therefore did not support the conclusion that effects observed within each condition were equivalent. Furthermore, main effects of condition were observed for MVC, Q_{TW} and VA_{TMS} . However, exploration of this effect indicated that the participants were not in the same neurophysiological state at the start of each condition (i.e. differences observed in some indices at the pre-neuromuscular assessment), suggesting that the observed main effects were not necessarily incurred due to the performance of the HG task, *per se*. Indeed, the absence of interactions effects between condition and time suggested that fatigability of the KE, from pre- to post-assessment, was not different following the performance of the HG and the control interventions. Accordingly, methodological issues, including those relating to the presented order of the conditions and the total duration of the session may account for these effects. It is also important to note that the average effects were also relatively small and within the documented error of such measures (Dekerle *et al.*, 2019; [Appendix A](#)). Accordingly, on balance, the results were cautiously interpreted in favour of demanding activity in the upper body exerting limited impact on the neuromuscular function of a non-active muscle group of the lower body.

Considering these findings, the aforementioned paradigm was believed to offer an opportunity to examine the subjective component of fatigue evoked by physical activity - independent of concomitant fatigability - in the central regulation of performance during physical endurance tasks. [Chapter 5](#) examined how performance of the HG task, evoking a perceived state of fatigue, influenced individuals' ability to sustain a submaximal contraction of the dominant KE and the perceptual and affective responses defining the central regulation of performance. [Chapter 6](#) examined how explicit manipulation of the intensity of the pre-induced state of fatigue modulated performance and psychophysiological responses during the KE endurance task, therefore attempting to both replicate and extend the results of the previous chapter. In both studies, a perceived state of fatigue was associated with impaired performance on the KE endurance task (i.e. -14 – -10% in TTF) in response to the contraction being perceived as more effortful and less pleasurable. The perception of fatigue was thus established within the thesis as a top-down factor modulating the perceptual and affective processes fundamental to the central regulation of performance. Indeed, [chapter 6](#) reflects the first attempt to establish the causal relation between the perception of fatigue and the regulation of physical performance, beyond other latent variables that may be modulated by the HG task in isolation (i.e. [chapter 5](#)). The study demonstrated no difference in both performance and psychological responses to activity between moderate and severe intensities of fatigue suggesting, on the face of it, that the relationship between a perceived state of fatigue and performance regulation may be categorical; with set performance decrements arising following the attainment of a particular subjective intensity of fatigue. However, due to the observed sensitivity of the perception of fatigue to the termination of one task and the start of a different task, evidenced by a rapid reduction in the intensity of perceptions in the severe condition in response to the start of the KE contraction ([Figure 6.3.](#)), full interpretation was confounded.

Evidence of an ability to disassociate between psychological constructs was observed in [chapters 5](#) and [6](#), supporting the separation of the perception of fatigue from the perception of effort and affective valence within the thesis. In [chapter 5](#), the intensity of responses and relationships with performance indicated that a perceived state of fatigue at rest was separable to the perceptual (i.e. effort) and affective indices of central regulation. It

was thus proposed that the perception of fatigue exerts an indirect effect on the control of performance, through modulating the perception of effort and affect, in keeping with previous observations (e.g. Harris & Bray, 2019). However, contrary to this, [chapter 6](#) indicated that behavioural correlates were similar between constructs (i.e. fatigue, effort and valence) when recorded during the endurance task, suggesting a more direct role for the perception of fatigue within the regulation of performance. Nevertheless, support of a disassociation between constructs was evident through exploratory analysis of the association between interoceptive ability and subjective experiences. It was demonstrated that the perception of fatigue reported during the KE endurance task was negatively associated with individuals' meta-awareness of the accuracy of resting interoceptive judgements. Neither the perception of effort nor affective valence was associated with any dimension of interoception ([Tables 6.2.](#) and [6.3.](#)). Interoceptive dimensions also did not moderate the relationships between markers of central regulation (i.e. the perception of effort and affective valence) and the perception of fatigue. Accordingly, the thesis provides an initial indication that an acute, perceived state of fatigue evoked through demanding physical activity involves higher-order reflections upon the internal conditions of the body.

Finally, [chapter 7](#) examined the impact of a perceived state of fatigue on decision-making processes believed to ultimately define behaviour and exercise tolerance. Contrary to the primary hypothesis - that the subjective cost associated with effort would be increased under a perceived state of fatigue leading to an increased discounting of rewarded action - choice behaviour was not different between the fatigue and the control conditions ([Figure 7.3.](#)). However, when in a perceived state of fatigue, the decision to engage in effortful action was done so with reduced confidence in ones' ability to effectively carry out the chosen action, particularly when actions were associated with high effort demands ([Figure 7.4.](#)). In line with the results of [chapter 6](#), the findings again associate the perception of fatigue with metacognitive judgements of performance capacity. Accordingly, while the perception of fatigue was not shown to be associated with reduced motivation to engage in physical activity, it does appear to undermine confidence in ones' ability to perform actions.

8.3. The Perception of Fatigue and Interactions with other Activity Induced Perceptions

8.3.1. Relationships between Psychological Constructs in the Regulation of Physical Activity

The results of the presented thesis make an important and novel contribution in detailing the interactions between perceptual and affective responses arising from demanding physical activity and their relation to the control of behavioural outputs, addressing an issue that has long precluded full appreciation of the complicated psychophysical processes that define the regulation of performance (Venhorst *et al.*, 2017; [section 2.3.2.](#)). [Chapters 5](#) and [6](#) indicate that the perception of fatigue arising in response to demanding physical activity is a modulating input influencing identified constructs associated with the central regulation of performance (i.e. the perception of effort and affective valence). Task demands were perceived as more effortful and less pleasurable when fatigued. The replication of the initial findings presented in [chapter 5](#) across both experimental manipulations (i.e. MOD and SEV) in [chapter 6](#) indicate that this effect was both potent and robust. Despite a dearth of equivalent paradigms through which to directly compare these findings, the conclusions of [chapters 5](#) and [6](#) concur with themes evident within the broader fatigue literature. For example, a state perception of fatigue has been shown to be associated with the perception of effort during HG contractions in healthy females (van der

Schaaf *et al.*, 2018). Additionally, the physical and cognitive impact of fatigue has recently been shown to be associated with how effortful simple, discrete motor tasks, such as reaching, are perceived to be (Goh *et al.*, 2022). An elevated perception of effort may subsequently affect the decision to engage in such tasks (Morel *et al.*, 2017).

As previously described ([section 2.7.1.](#)), one burgeoning line of research focuses on the effects of ‘cognitive fatigue’. A perceived state of fatigue induced through cognitive activity has been associated with increased effort experienced during another cognitive task (e.g. Benoit *et al.*, 2019) and importantly, subsequent physical activity (e.g. Harris & Bray, 2019). The deleterious effects of this evoked state has been associated with a perception of low or reduced resources available for task performance, leading task demands to be perceived as more effortful (McMorris, 2020) and/or reducing the value associated with action (Müller & Apps, 2019). However, as highlighted in [section 2.7.1.](#), whether these effects may be specifically attributed to the perception of fatigue or other aversive states (e.g. boredom) arising from engaging in protracted cognitive tasks remains to be clearly established. Moreover, the detrimental behavioural effect on physical performance is also subject to debate (Holgado, Sanabria, *et al.*, 2020; [section 2.7.1.](#)). Our laboratory has previously demonstrated that prior cognitive activity, despite evoking a small increase in the perception of fatigue, did not evoke changes in the perception of effort and affective valence, nor physical endurance performance, at a group level (Greenhouse-Tucknott *et al.*, 2021). Relationships between the perception of fatigue and markers of the central regulation of performance were evident at an individual level, however (Greenhouse-Tucknott *et al.*, 2021). Following the assumption that ‘physical’ and ‘cognitive fatigue’ are unitary, reflecting a single construct (Kuppuswamy, 2017; Müller & Apps, 2019), the results of this study and those presented within this thesis may appear conflicting. However, [chapter 6](#) may provide valuable insight into the reason why the effect of fatigue is not consistently observed following cognitive activity. An interesting, but potentially overlooked observation within many evaluations of the effect of prior cognitive activity on subsequent physical performance is that the average change in the reported subjective state of fatigue evoked by cognitive interventions often represents a relatively small change on the adopted measurement instruments (e.g. Greenhouse-Tucknott *et al.*, 2021; Marcora *et al.*, 2009; Pageaux *et al.*, 2013). That is, the interventions are not typically perceived to be highly fatiguing. One interpretation of the findings presented in [chapter 6](#), supports the relationship between the perception of fatigue and behavioural effects on physical performance to potentially be categorical: emerging after the attainment of some threshold intensity. It is possible that, in many cases, the magnitude of the effect of ‘cognitive fatigue’ resides close to this postulated value and possibly remains ‘sub-threshold’, thus the effects of fatigue are not observed at a group level. This interpretation would appeal to the relative robustness of executive functions to protracted use (Blain, Hollard, *et al.*, 2016). However, due to the demonstrated sensitivity of the perception of fatigue to changing environmental contexts ([chapter 6](#); [Figure 6.3.](#)), clear interpretation of the effect of the subjective intensity of a perceived state of fatigue is precluded. Nevertheless, the study represents an interesting initial attempt to understand the effects across the continuum of acute subjective experience of fatigue which future research should now explicitly delineate.

Comparable relationships observed between the perception of fatigue and markers of performance regulation (e.g. the perception of effort) may also be inferred from examination of responses to physical activity in many disease states reporting fatigue (Gibson *et al.*, 1993; Wallman *et al.*, 2004; Wallman & Sacco, 2007; Fernandez *et al.*, 2020; De Doncker *et al.*, 2020; also evident in the cognitive domain: Bruijell *et al.*, 2022). For example, a recent

analysis of the available literature indicated a clear heightened experience of effort during aerobic exercise in people with ME/CFS and fibromyalgia versus healthy matched controls (Barhorst *et al.*, 2020). However, several questions remain that may hinder clear interpretation of such findings. For example, whether such effects are attributable to the subjective perception of fatigue, *per se*, and not concomitant disease effects on physical or neurological function may often be unclear (e.g. Thickbroom *et al.*, 2006). Moreover, whether the effect is related to the present experience of fatigue (i.e. state fatigue) or expectations of (i.e. perceived) fatigability (i.e. trait fatigue) (Enoka *et al.*, 2021), is still to be firmly established within large-scale studies across diseases. It has been proposed that heightened perceptions of effort reported by patients are the product of interactions with state perceptions of fatigue during physical tasks, reflecting an “*adding on*” of state perceptions of fatigue to appraisal of task demands (Gibson *et al.*, 1993). Conversely, trait but not state perceptions of fatigue have been shown to be associated with implicit measures of perceived effort in poststroke fatigue (De Doncker *et al.*, 2020), which may implicate additional factors in the relationship between fatigue and effort in disease (e.g. Malloy *et al.*, 2021). Notwithstanding these outstanding points, the results of [chapters 5](#) and [6](#) add to an ever growing body of research establishing that a perceived state of fatigue appears to be an important factor determining how effortful (and pleasurable) physical tasks are perceived to be, and initiates an appreciation of such relationships during the regulation of acute physical performance in healthy individuals.

8.3.2. The Basis of the Perception of Fatigue During Physical Activity

Relationships between constructs are intelligible when the distinction between said constructs is made clear. The perception of fatigue, the perception of effort and affective valence have all been conflated with one another at various points in the description of the regulation of physical performance, thus observed relationships between measured indices in the present thesis may be considered unsurprising. However, [chapters 6](#) and [7](#) provide new insight into the basis of the perception of fatigue arising in response to demanding physical activity. First, [chapter 6](#) explored the relationships between the perception of fatigue and multidimensions of (cardiac) interoception (i.e. accuracy, confidence and awareness; [section 6.3.4.](#)). The perception of fatigue during the endurance task was associated with the dimension of interoceptive awareness, an index of metacognitive insight into representations of bodily states (Garfinkel & Critchley, 2013; Garfinkel *et al.*, 2015). The same was not evident for both the perception of effort ([Table 6.2.](#)) and affective valence ([Table 6.3.](#)), suggesting that the perception of fatigue, exclusively, is associated with higher-order awareness of judgements concerning the conditions of the body. Specifically, those with greater insight into their interoceptive judgements reported experiencing less fatigue during the endurance task. Comparably, in [chapter 7](#), a perceived state of fatigue was associated with reduced subjective confidence in ones’ capacity to perform chosen effortful actions ([Figure 7.4.](#)). Together, both studies implicate the perception of fatigue with high-order cognitive processes relating to an awareness of held representations of oneself. Greater concurrence between actual performance and the subjective experience of performance appears to offset the development of fatigue ([chapter 6](#)), which is a state reflective of inherent uncertainty concerning ones’ present physical capacity ([chapter 7](#)). The apparent dependence on the correspondence between performance and subjective experiences implicates the development of fatigue with the presence of ‘error’, which has a natural association with developing uncertainty.

The findings provide a new take on the development of the subjective experience of the perception of fatigue during acute physical activity in health. Support for metacognitive processes as a key element of fatigue development in pathology has already attracted interest. For example, recent evidence links metacognitive beliefs regarding reduced performance capabilities in individuals suffering from CFS/ME, with the maintenance of fatigue symptoms in patients (i.e. reduced effort investment) (van der Schaaf *et al.*, 2018). This supports recent theoretical proposals offering poor or low allostatic self-efficacy as the basis of fatigue (Stephan *et al.*, 2016).

Indeed, recent years have witnessed several concerted attempts to provide a clear mechanistic account of pathological fatigue (Kuppuswamy, 2021). A prominent characteristic of many of these proposals is the detailed consideration of how precisely the brain constructs perception. This contrasts with many perspectives on the transient symptoms of fatigue arising in response to acute, protracted exertion in health. Accordingly, drawing upon one of these emerging frameworks within the study of pathological fatigue (Stephan *et al.*, 2016), the discussion of the results of [chapters 5](#) and [6](#) introduced an extension of this framework as an account of the development of fatigue and its subsequent effects during acute physical endurance performance. The proposal is founded on the principle of predictive processing⁶⁶, which is positioned as a core principle of brain function (Bubic *et al.*, 2010; Clark, 2013; Friston, 2009; Hohwy, 2014). The following section offers a more detailed explanation of this proposal (see Greenhouse-Tucknott *et al.*, 2022 for a full presentation).

8.4. A Predictive Processing Account of the Perception of Fatigue in Response to Acute Demanding Physical Activity

8.4.1. Hierarchical Predictive Processing: A Neurobiologically Plausible Theory of the Brain

To understand the outlined description of fatigue development presented in the following sections, the basic premise of predictive processing must first be introduced. Contemporary perspectives on how the brain functions contend that our ability to perceive, act, attend and learn may all be accounted for by viewing the brain as a self-evidencing inference machine (Dayan *et al.*, 1995; Friston, 2005). Explanations of sensory states are not simply extracted from the streams of sensory inputs, like classic views of the brain as some form of *stimulus-response* organ, but instead are inferred through utilising learned causal structures that enable prior expectations to be formed concerning the probabilities of these sensory inputs. This builds upon early propositions that the brain does not deal with veridical sensory information and instead must comprehend its environment through unconscious, knowledge-driven inference (Helmholtz, 1860). Accordingly, the general concept of predictive processing sees the brain formalised as a *statistical* organ that continuously seeks to render internal and external environments predictable. This is achieved through forming and testing hypotheses of (generative) internal models (i.e. models that explain how sensory inputs are generated, probabilistically by latent states of the world) against incoming sensory evidence (Clark, 2013). By inverting generative models (i.e. computing the probability of the states of the world, given the sensory inputs), perception may be described as a form of statistical inference achieved through minimizing the discrepancy (i.e. prediction error) arising between predictions (or perceptual hypotheses) and current sensory evidence (Stephan *et al.*, 2016). That is, through the minimization of prediction

⁶⁶ Predictive processing is used to define a broad, unconstrained framework in which prediction is central to brain function and cognition, which may encompass more specific frameworks such as active inference

error, perception represents the winning, most parsimonious explanation of the data. Perception is thus highly ingrained and contextualised by our beliefs⁶⁷ about the statistical nature of the world (Clark, 2015).

The most prominent predictive processing models are conceptualised as hierarchical, multilevel connections in the brain that implement a form of Bayesian inference (Knill & Pouget, 2004). This inferential process is achieved through a predictive coding strategy (Friston, 2005; Rao & Ballard, 1999); a neurobiologically plausible (e.g. Shipp, 2016; Shipp *et al.*, 2013) and efficient encoding scheme, facilitating the transfer of information across neural connections. Broadly, predictive coding under Bayesian inference proposes that prior beliefs are used to predict the neural activity of the level below, which sees the transfer of predictions and prediction error emerge across a series of recurrent ‘loops’ ([Figure 8.1](#)). Probabilistic predictions (or priors/beliefs) are passed, top-down to the next level below, where it is compared to the sensory inputs. What is transmitted back up the hierarchy through forward connections is the mismatch or prediction error(s) (i.e. the unexplained data). Aligned to Karl Friston’s free energy principle (Friston, 2009; Friston, 2010) – the proposal that all self-organising, biological systems strive to minimize their free energy⁶⁸ in an attempt to avoid the natural tendency of disorder – the ultimate function of predictive processing is the resolution of prediction error in order to provide a deep understanding of the world through causal explanations of sensory data (Hohwy, 2014). Primarily, prediction error may be minimized in two ways: 1) predictions may be updated to better explain sensory inputs (i.e. perceptual inference; described above), optimizing posterior probabilities which subsequently form new empirical priors; 2) sensory evidence that conforms to prior expectations may be selectively sampled through action. Accordingly, within the motor system, motor commands are recast as proprioceptive predictions concerning the sensory consequences of action across various timescales, which are ultimately enacted through closed-loop reflexes at the lowest level of the hierarchy (Adams *et al.*, 2013). Under the framework of active inference, perception and action are positioned as an intimately coordinated response designed to minimize the experience of prediction error (Adams *et al.*, 2013; Friston *et al.*, 2016).

Based on its Bayesian formulation predictions and prediction error are represented probabilistically. Thus predictions and prediction errors do not refer to single, categorical state estimates, but reflect a range of possible states which incorporates the level of variability believed to be inherent in the environment (Knill & Pouget, 2004). Inferential computations must therefore predict not only the sensory inputs (first-order predictions), but also the reliability, or precision, of this signal (second-order predictions) to make informed judgments on which to base perception and engage action (Kanai *et al.*, 2015). The relative precision (i.e. inverse variance; reflecting the uncertainty, or more informally, confidence in the sensory signal) of prediction and prediction error determines

⁶⁷ The probabilistic representation of the causes of sensory data prior to observing the data.

⁶⁸ Free energy is an information theory measure of the bounds of the surprise of outcomes (which over time reflects the level of entropy), given a generative model (Friston, 2010).

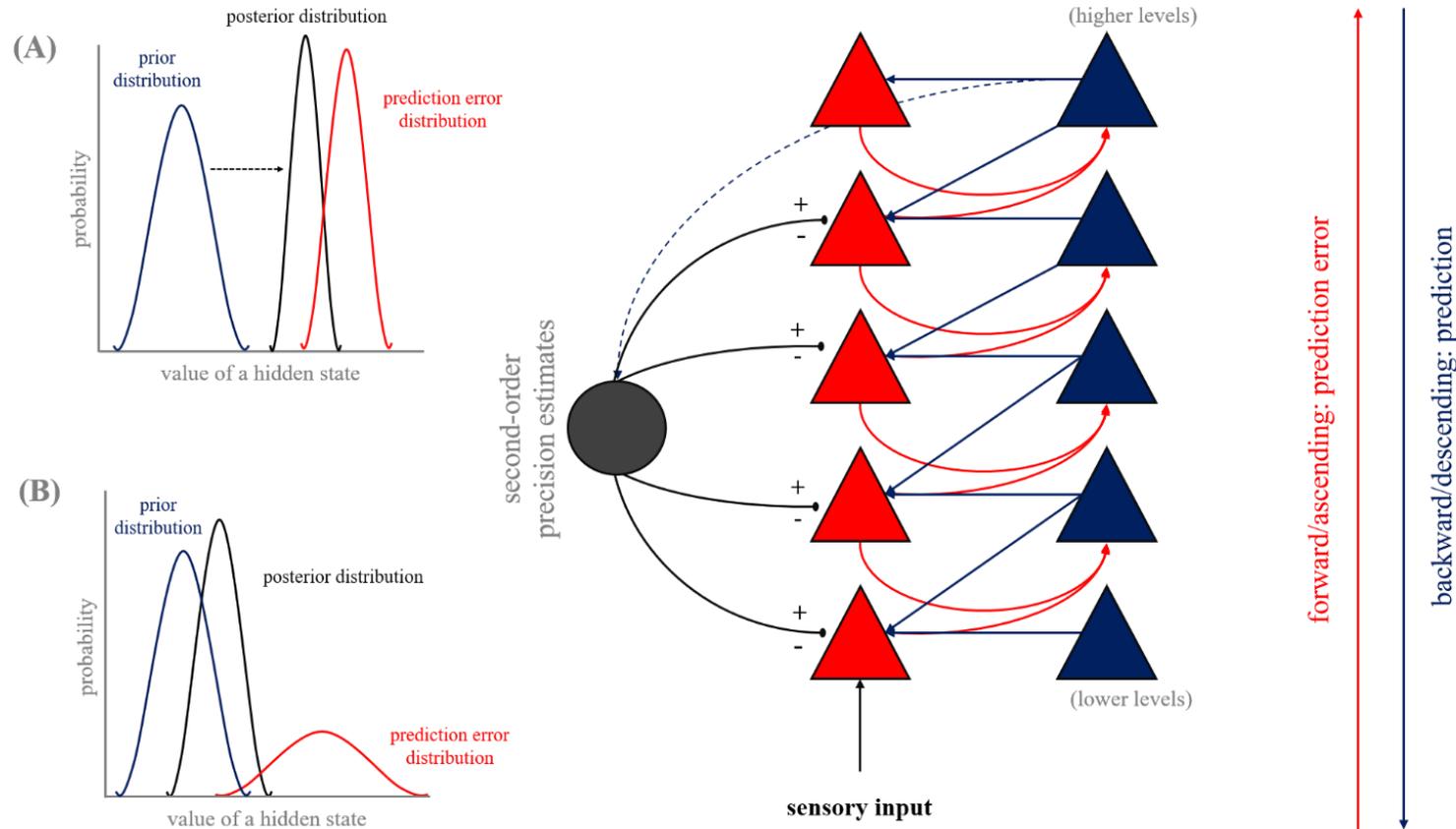


Figure 8.1. A schematic of the neuronal architecture underpinning hierarchical predictive processing. The main figure on the right depicts a simple hierarchy that is assumed to incorporate a predictive coding strategy. The system is split into 5 separate levels in which descending predictions (blue arrows) are transferred within the same level and to the level below. Our prior predictions are not always accurate – thus generating a prediction error. These computed prediction errors are represented by red arrows and are transferred within and between layers, ascending to the level above. The system is self-organising enabling the minimization of prediction error through active sampling of sensory information or updates to beliefs (i.e. posterior probability), which subsequently form new predictions passed on to the level below (i.e. empirical priors). This facilitates deep explanations of sensory inputs. Precision (i.e. inverse variance), akin to a measure of the signal-to-noise properties of an input, informs of the uncertainty or ‘confidence’ placed in the sensory evidence. Precision determines the influence of prior beliefs relative to sensory inputs on prior updates. For example, the two depictions on the left of the figure illustrate how posterior distributions (black curves) of the value of a hidden state may be influenced by the relative precision of the prior (blue curves) and prediction error distributions (red curves). The width of the distributions indicates their variance, with precision the inverse of this variance. Precise prediction errors increase the influence of sensory evidence on updates to model predictions (i.e. posterior) (A). Conversely, when prediction errors are relatively imprecise, they have little impact on the posterior belief (B). Precision itself must be estimated (second-order predictions; system not shown explicitly here) and is established by descending predictions (blue dashed line). The relative precision of prediction errors at every level of the system is believed to be controlled by neuromodulatory actions that gate or control the gain of error carrying neuronal units (grey arrows). Schematic adapted from combined works of: Ainley et al. (2016); Seth and Friston (2016). Taken from Greenhouse-Tucknott *et al.* (2022).

their respective influence on posterior beliefs ([Figure 8.1](#), A and B; see Friston, 2009). Predictions with a high relative precision will dominate inferential processes (e.g. action), even in the presence of conflicting sensory evidence. Conversely, predictions of low precision afford greater weighting to sensory inputs which may force us to re-evaluate and update model predictions (Friston, 2009, 2010). Attention has been proposed as one process of precision inference, through which estimates of precision may be optimized (Feldman & Friston, 2010; Hohwy, 2012)⁶⁹. Therefore attention, alongside action and perception, represents a natural component of error minimization within predictive processing. The estimation of expected precision within uncertain environments may correspond to higher-order beliefs concerning the reliability of the sensory evidence ([Figure 8.1](#); Clark et al., 2018). Beliefs about beliefs, or more specifically, beliefs about the estimated precision of predictions (hyperpriors), may provide a formalised description of metacognition (Friston et al., 2013). Within predictive processing, metacognition has been described as a high-level form of inference associated with the overall performance of prediction error minimization (Petzschner *et al.*, 2017; Stephan *et al.*, 2016).

8.4.2. Inferred Dyshomeostasis: Allostasis, Metacognition and Fatigue.

As well as inferring the ambiguous states of our external environment, our brains must also infer the cause of hidden states of the body (Seth & Critchley, 2013). Several accounts have applied predictive processing within the domain of interoception to explain how dynamically changing visceral, metabolic, autonomic, immunological and hormonal conditions may be integrated and understood (Ainley *et al.*, 2016; Allen & Friston, 2018; Barrett & Simmons, 2015; Barrett, 2017; Gu *et al.*, 2013; Owens *et al.*, 2018; Seth *et al.*, 2012; Seth & Critchley, 2013; Seth & Friston, 2016). To maintain internal states within set bounds (homeostasis) and minimize the entropy of experienced sensory states (Friston, 2010), self-fulfilling interoceptive inference provides a means for the brain to respond to the anticipated future needs of the body (allostasis; Sterling, 2012). Allostasis and the representation of interoceptive consequences of action is a fundamental principle of all basic psychological functions (Kleckner *et al.*, 2017), including our emotional experiences (Critchley & Garfinkel, 2017; Barrett, 2017) and the conscious appreciation and recognition of ones' self (Apps & Tsakiris, 2014; Seth *et al.*, 2012; Seth & Friston, 2016). For a more in-depth discussion on the formulations of homeostatic and allostatic function within current predictive processing frameworks, see Corcoran and Hohwy (2019).

In relation to fatigue, Stephan *et al* (2016) provide a compelling computational account of pathological fatigue, based on allostasis, metacognition and predictive processing. In this model, changes at a somatic level and/or within the hierarchical system's circuitry in response to disease disrupts computational functions such that dyshomeostasis (i.e. error within the interoceptive model) is persistently experienced. The authors propose a novel element to the allostatic control circuitry, outlining a metacognitive mechanism which evaluates the continuing efficacy of internal model predictions in the control of bodily states. The detection of persistent prediction error over time forges an (meta-)awareness of a lack of control (i.e. inability to predict) over bodily states which in turn, is posited to form the conscious perception of fatigue. Importantly, in pathological fatigue, these disruptions affect the system in such a way that the resolution of dyshomeostasis is not solved even through rest (Stephan *et al.*, 2016). Therefore, mastery over body states is not easily restored and the perception of fatigue endures. This is

⁶⁹ Precision may also depend on the effect of neuromodulators (e.g. Friston *et al.*, 2012).

believed to formally distinguish pathological fatigue from the acute, transient exertional fatigue experienced in health (referred to by the authors as ‘tiredness’⁷⁰) which, through rest, sees the gradient of the level of ‘surprise’ turn negative, thus agency is experienced during recovery and fatigue is alleviated (Stephan *et al.*, 2016). However, Stephan and colleague’s description of acute symptoms of fatigue does not explore the dynamics of the inference-control loop during the homeostatic challenges imposed by prolonged physical exertion (e.g. Jeukendrup *et al.*, 2000; Joyner & Coyle, 2008; Gabriel & Zierath, 2017). Thus, an explicit account of how the acute, transient symptoms of fatigue emerge in relation to protracted physical exertion remains absent. What is outlined below (see Greenhouse-Tucknott *et al.*, 2022) conforms to the proposition forwarded by Stephan *et al.* (2016) – that fatigue arises from the metacognitive detection of persistent prediction error which reduces perceived capability (i.e. reduced self-efficacy) of exerting effective control over the body – and extends the metacognitive theory of dyshomeostasis as an account of exertional fatigue.

8.4.3. Transient Exertional Fatigue: A Predictive Processing Model

According to Stephan and colleagues (2016), fatigue may initially reflect an adaptive process, promoting rest and the conservation of energetic resources when effective actions to restore homeostasis are not perceived to be present. All physical behaviour involves energetic expenditure, providing an ever-changing homeostatic context which must be incorporated within predictions across various time scales (Pezzulo *et al.*, 2015). Once the decision to engage with exercise has been made, the brain must predict not only the proprioceptive consequences of action, interactions with the social and physical environment, but also the homeostatic consequences of the transition towards the intended goal state in order to maintain biological integrity. This is obviously challenging, since protracted whole-body exercise incurs a vast array of ever-changing perturbations across a range of biological systems (Hawley *et al.*, 2014), the strength of which may exceed the control capable by simple reflexes at the lowest level of the system and therefore competes for attention and higher-level control ([Figure 8.2.](#)). Integration of this salient, motivational information (i.e. the condition of the body) informs inferential processes that influence the selection of control policies (e.g. how fast one runs or cycles) in the pursuit of goal states (Pezzulo *et al.*, 2018). For action to continue in any given form, high-precision must be afforded to current control (i.e. action) predictions and prediction error attenuated, so that current predictions can dominate posterior beliefs, maintain attention and enable action (Pezzulo *et al.*, 2015). In response to the changing internal conditions arising during exercise, this may be achieved through attentional processes⁷¹ or belief updates at levels lower than those driving the current goal intention, changing the perceived context in which exercise is performed. A problem however is that this may come at the expense of even greater prediction errors that will need to be contextualised within a subsequent inferential cycle. The process of attenuating prediction error is equivalent to its detection and may indicate to metacognitive mechanisms that initial predictions did not provide a good fit of the sensory data. It is proposed that the detection of prediction error is subject to the same metacognitive appraisal as described in the conceptualisation of pathological fatigue. The persistent experience of error, like pathological fatigue (Stephan *et al.*, 2016), may indicate that current model predictions do not accurately depict the state transitions during physical

⁷⁰ The problem with this terminology in respect to the acute, subjective experience of fatigue arising in response to demanding physical activity is discussed in [section 2.2.4.1.](#)

⁷¹ It is acknowledged that the current understanding of volitional control of endogenous attention within predictive coding frameworks is not entirely clear (Metzinger, 2017).

activity, leading to a decline in allostatic control self-efficacy and a developing phenomenological experience of fatigue.

Metacognition within predictive processing frameworks may be ascribed, computationally, to beliefs about the precision of priors (Friston *et al.*, 2013). The developing perception of fatigue may therefore be associated with an increasing uncertainty held in model predictions, reflecting low beliefs concerning the precision of predictions, which cascade through the hierarchy from high levels to low. Low precision afforded to higher, temporally distal, and more abstract levels of prediction in the system may generate a progressive inability to suitably contextualise ascending prediction error at lower levels. Eventually over time, this decline in precision beliefs may be such that there is a shift in the dominant control of behaviour towards lower levels, which attempt to resolve the more immediate differences between predictions and prediction errors (Pezzulo *et al.*, 2015; [Figure 8.2.](#)). A shift to lower-level ‘controllers’ may reflect an adaptive process attempting to restore confidence in model predictions by minimizing the experience of prediction error on more immediate timescales (Pezzulo *et al.*, 2015) which, once achieved may propagate back through the system. That is, during physical activity we are forced to slow down or stop altogether. Importantly, minimization of interoceptive prediction errors may not be immediate (e.g. replenishment of resting muscle glycogen stores can take many hours following exercise; e.g. Casey *et al.*, 1995), therefore proprioceptive predictions⁷² may potentially be used as proxies for predicting the states which will eventually see interoceptive prediction error minimized (Pezzulo *et al.*, 2018; Critchley & Garfinkel, 2017). By slowing down or stopping, the minimization of prediction errors signals conditions that will (eventually) see the restoration of homeostasis indicates a level of control over bodily states, restoring self-efficacy and alleviating the experience of fatigue. However, the restoration of allostatic control self-efficacy is not immediate. Indeed, predictions used to maintain homeostatic set-points likely function across different biological systems under their own individual time constants (Stephan *et al.*, 2016), which may see the experience of dyshomeostasis elongated after a period of physical exertion. Deficits in the precision afforded to control predictions, the proposed hallmark of a fatigued state, may extend the experience of fatigue during recovery post-exertion even when homeostatic balance has been restored. That is, there may be an increased sensitivity to prediction error during recovery (i.e. rest) due to the loss of precision afforded to control predictions. It is possible that full alleviation of the conscious experience of fatigue may require the detection of a similar series of events to that through which it developed (i.e. protracted experience of accurate predictions related to interoceptive states). If this is the case, the experience of fatigue may cooccur with a change in control policy designed to restore confidence in model predictions and rest may represent the most effective context under which this may occur (Greenhouse-Tucknott *et al.*, 2022).

8.4.3.1. Applying the Model to the Results of the Thesis

It is believed that this account provides a plausible framework through which to interpret the mechanisms of exertional fatigue, though admittedly the association is principally anecdotal. Like others (Treasure & Newbery, 1998; Focht *et al.*, 2007), an association between the perception of fatigue and self-efficacy was established in the

⁷² An extension of the metacognitive theory of dyshomeostasis (Manjaly *et al.*, 2019) proposes that metacognitive monitoring may not be exclusive to interoceptive circuits and may involve the detection of a chronic mismatch between prediction and actual sensory evidence across different systems (e.g. proprioception; exteroception). In addition, interdependency between systems (Pezzulo *et al.*, 2018) may see the persistent detection of error and development of fatigue permeate across different systems.

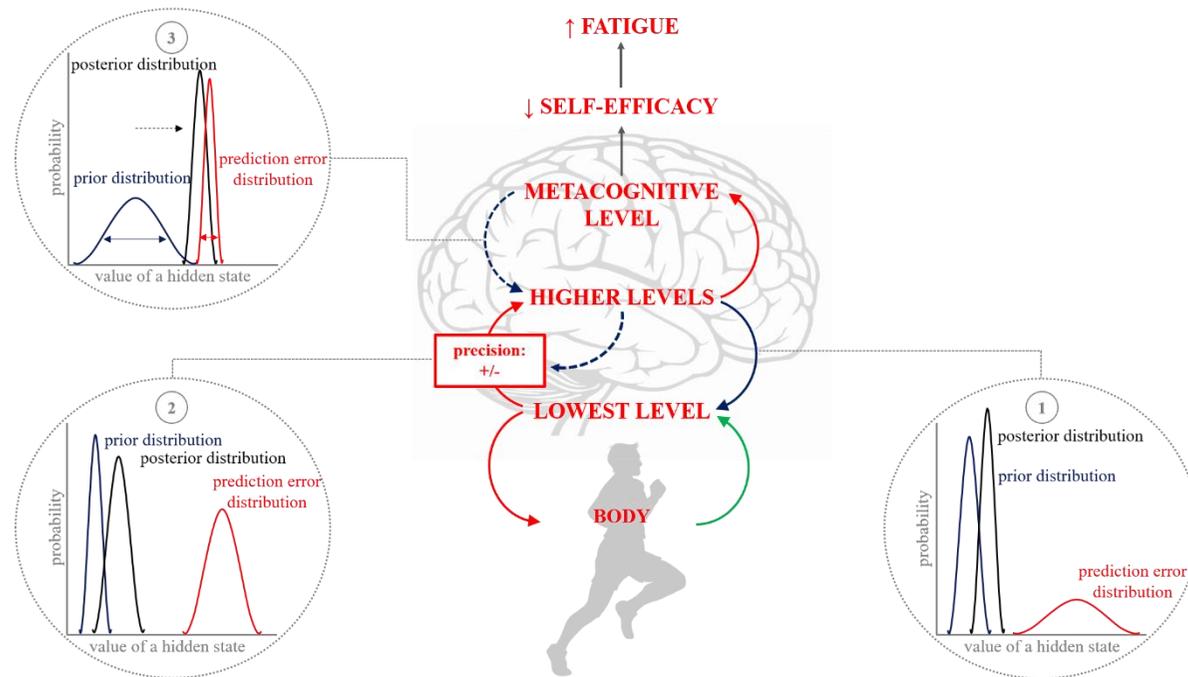


Figure 8.2. A graphical representation of the predictive processing framework underlying the emergence of exertional fatigue. The engagement of protracted physical exertion requires internal models to accurately anticipate the sensory states that will be encountered during transitions towards future goal states, to have the body reside within a (predictable) limited range of states that will sustain its biological integrity (i.e. maintain homeostasis). The subjective perception of fatigue may serve an adaptive function representing the ability of internal models to accurately predict transition states during the pursuit of temporally distal goal states. (1) Under resting conditions or even low-intensity (physical) exertion, evidence of sensory states (green arrow) may be largely predictable (i.e. black posterior distribution dominated by blue prior beliefs). This may see the minimization of prediction error predominated by (autonomic) reflexes at the lowest level of the hierarchy. (2) However, as demands increase and internal conditions become more unstable, physiological perturbations may be associated with greater prediction errors. Increasing strength of the prediction error (i.e. red distribution curve) may force error to ascend further up the levels of the hierarchy, necessitating deeper explanation, increasing its influence on posterior probabilities. This may generate attentional changes or perceptual updates across these lower levels. As pursuit of temporally-distal goal states is driven by increasingly higher-levels, action will continue if the precision of these distal goal beliefs enables it to dominate prior updates and therefore contextualise the levels beneath (i.e. posterior distribution still dominated by prior beliefs). (3) Across time, the performance of the model's overall ability to predict transition states within goal pursuit is monitored by a metacognitive layer. Persistent detection of error within the hierarchy signals an inability to exert effective (allostatic) control of internal states during this pursuit of (longer term) goal states. This signals that the model may provide bad predictions about the present and, importantly, future condition of the body. This perceived lack of control over bodily states undermines allostatic control self-efficacy, which is experienced as the subjective experience of exertional fatigue. Computationally, the emergence of fatigue may be associated with declining precision estimates afforded to predictions driving goal-directed behaviour, signalling increasing uncertainty within the model and weakening prediction's influence on posterior beliefs (dashed black line). The development of exertional fatigue is progressive, thus lower precision beliefs concerning goal-directed predictions result in greater prediction error throughout the levels of the hierarchy, which further undermines control capabilities during goal pursuit. Eventually, changing precision will see prediction error afforded more weight and cause high-level, goal-directed beliefs to be updated (i.e. shift in posterior distribution towards prediction error) which may shift control priorities towards the resolution of more immediate prediction error. This may be achieved through action (i.e. rest). Over time, rest may restore self-efficacy in control over bodily states as through the experience of agency (i.e. accurate predictions) in the restoration of homeostasis. Fatigue is consequently alleviated. However importantly, due to the significant challenge to model evidence encountered, restoration of perceived mastery of the body and homeostasis may be protracted. This is because precision estimates of predictions may be so low that prediction error is exacerbated during the recovery period. Therefore, the detection of accurate allostatic predictions may be bestrewn with prediction error which prolongs the subjective experience of fatigue. *Red arrows represent ascending prediction error, blue arrows represent descending predictions and green arrows represent ascending sensory evidence from the body. Dashed blue line represents effects on precision estimates.* Taken from Greenhouse-Tucknott *et al.* (2022).

presented thesis ([chapter 7](#)). The present thesis did not directly examine the sensitivity of fatigue to deviations from predicted interoceptive states, the principal contention of the described theoretical model, which may be achieved through similar approaches to those recently published (e.g. Iodice *et al.*, 2019). However, [chapter 6](#) provides some indication that a mismatch between what is believed to have occurred (i.e. one's confidence in a judgement) and the reality of that judgement is important to the experience of fatigue. It may be assumed that those who displayed greater interoceptive awareness are better able to both accurately predict internal states of the body and set the relative precision of those predictions versus the sensory evidence, resulting in the detection of less error by metacognitive mechanisms and therefore a reduced experience of fatigue ([chapter 6](#)). The novel implication of metacognitive processing and error detection as a core feature of exertional fatigue identified in the present thesis is described in the outlined proposal.

Furthermore, the proposed decline in precision estimates accompanying the development of fatigue may provide an explanation as to why physical activity is perceived as more effortful and less pleasurable when performed under a perceived state of fatigue ([chapters 5](#) and [6](#)). As fatigue develops, it is proposed here that confidence in the model of the world we hold is shaken, with precision estimates of predictions declining and this propagating, top-down, through the hierarchy. Consequently, higher, multi-modal, abstract predictions that drive goal-directed action on longer timescales (i.e. endurance performance) increasingly lose their ability to adequately anticipate future outcomes and contextualise lower-level transition states, generating greater prediction errors. Persistence with a given course of action may give rise to ever-increasing prediction errors, which are only exacerbated by the developing meta-awareness of prediction failings (i.e. fatigue). Presumably, greater prediction error under a perceived state of fatigue may be responsible for increase perception of effort and reduced affective valence. In support of this contention, core affective responses have been ascribed to lower level interoceptive sensations (Barrett, 2017), with affective valence ascribed to prediction error (Joffily & Coricelli, 2013). Greater mismatches between expected interoceptive states and sensory evidence signals that current states are not compatible with the ultimate goal of reducing the entropy of future states (Friston, 2010). Accordingly, they are experienced as aversive (Joffily & Coricelli, 2013). Similarly, the perception of effort has also been associated with prediction error ([section 2.4.3.2](#)), arising in response to high gain, or insufficient attenuation, of action-associated prediction error (Kuppuswamy, 2017). Zénon *et al.* (2019) applied an information theoretic perspective to the perception of effort, proposing that its emergence is associated with the amount of information required to update prior beliefs, and the limitation it imposes on other processes dependent on the same neural process (i.e. opportunity costs). Predominantly, the need to counteract default control policies and deep priors (the deepest being the fundamental goal of maintaining biological integrity) to maintain beliefs driving action (e.g. a given exercise intensity) is likely the foundation for the perception of effort during physical tasks such as used in the present thesis ([section 3.14.1](#)). This may become more costly under a state of fatigue, where a decline in precision opens the range of action-state probabilities, widening and lowering the spread of priors (Zénon *et al.*, 2019). The proposed framework thus provides a computational account of the interrelationships between the perception of fatigue and markers of the central regulation of performance. Not only that, but it also offers an explanation as to why effortful and unpleasurable actions may be particularly fatiguing, since they are associated with greater deviations away from model predictions (i.e. error).

8.4.3.2. Comparable Concepts within the Description of the Perception of Exertional Fatigue

The proposed framework is briefly contrasted with other established models detailing the development of exertional fatigue. This is felt to be necessary because several of the themes described in the model presented here in [section 8.4.3](#), may appear familiar to those aware of the conceptualisation of the perception of ‘fatigue’ outlined in the central governor model (St Clair Gibson *et al.*, 2003; Tucker, 2009; [section 2.3.1.1](#)). Indeed, a recent description of the perception of fatigue within the central governor framework described fatigue to “*arise secondary to mechanistic inferences of mismatches between predictive coding and error differences using a Bayesian algorithm in the allostatic control of homeostasis*” (Venhorst *et al.*, 2018c; p. 2480). There is no doubt, on the surface, similarities between the basis of fatigue offered under the central governor and that described within the above predictive processing account exist. Both emphasise the importance of anticipatory expectations of sensory states and the integration of these expectations and afferent signalling within the context of maintaining homeostasis⁷³. However, the implementation of these processes is markedly different which has consequences for the interpretation of fatigue. Here it is argued that, though some of the underlying concepts may be similar, the description offered by Venhorst *et al.* (2018c) is in fact an erroneous (possibly revisionary) interpretation of the perception of fatigue within the central governor framework. Understanding of the conscious perception of fatigue within the central governor model is not described based on a predictive coding strategy, does not explicitly describe inference or incorporate a Bayesian algorithm for the generation of perception, and is largely described based on reflexive rather than anticipatory control in the regulation of exercise performance.

According to the central governor model, during physical activity, the ultimate goal of regulation is to return the level of metabolic activity to some pre-defined set-point, typically resting levels (St Clair Gibson *et al.*, 2005). The perception of fatigue reflects the conscious layer within a multilevel regulatory process which functions to achieve this aim (St Clair Gibson & Noakes, 2004). Drawing on the proposal of Parvizi and Damasio (2001), proponents of the central governor model outline how the conscious experience of ‘fatigue’ emerges through changes in the mapped neural patterns representing the moment-to-moment state of the body in response to afferent feedback signalling the exercise-induced perturbations (St Clair Gibson *et al.*, 2003). It is proposed that resting homeostatic set-points across biological systems are stored within a form of neural register and used as an initial first-order reference map. Activity-induced deviations of biological systems away from these set-points are then re-represented as a new first-order map of the state of the body. The difference (aligned to error) between the initial and newly created maps generates a second-order neural representation, in turn generating an awareness of the relationship between this change and action, which is consciously accessible. Through repeated iterations of the formation of second-order representations, the perception of fatigue is believed to emerge (St Clair Gibson *et al.*, 2003). Extensions of this proposal suggest that a forecast ‘template’ of an acceptable level of physical sensations at any given moment during action, incorporating initial (internal and external) environmental, social and motivational factors, as well as characteristics of the task (e.g. duration), is set in anticipation of (and updated throughout) physical activity in order to ensure activity is completed without presenting a threat to homeostasis

⁷³ It is pertinent to note however, that a fundamental difference between the two accounts concerns the particular ‘object’ of interest. For the central governor model, it is the regulation of performance and control of homeostasis. That is, the emphasis is on the outcome. For the proposed model, the focus centres more specifically on the subjective experience of fatigue. That is, the emphasis is on the process. However, in both instances, subjective perceptions and objective actions form complementary parts of an integrative process, and the maintenance of homeostasis is the foundation on which all is based.

(Tucker, 2009). Specifically, a perception of effort⁷⁴ arises when physical sensations deviate (i.e. exceed) from this pre-defined template, serving to instantiate a change in behaviour (Swart *et al.*, 2012).

Proponents of the central governor describe the perception of ‘fatigue’ as an interpretation of afferent feedback in relation to a reference signal, so as to contextualise the state of the body in relation to the goal of maintaining homeostasis (St Clair Gibson *et al.*, 2003; Tucker, 2009). Though the ‘template’ (alternatively termed “anticipatory pacing strategy”) is described as anticipatory, dynamic and hierarchically controlled, what is described is not necessarily predictive. It appears to define what *should*, ideally, be sensed for exercise to be completed without harmful disruption to homeostasis, rather than the sensory states that are *likely* to be encountered when trying to understand both the internal and external environment faced. The perception of ‘fatigue’ is therefore more aligned to an awareness of a homeostatic reflex arc (i.e. the lowest level of [Figure 8.2](#)) and reactive control (see Petzschner *et al.*, 2017). It is acknowledged that it is possible that this interpretation may be a misrepresentation of proposals linked to the central governor, but comprehension is hindered by the fact that the hierarchical structure referenced is not clearly defined (e.g. St Clair Gibson *et al.*, 2005), nor exactly how this anticipatory ‘template’ is dynamically updated or how the ‘template’ is integrated with afferent feedback in the implementation of control. Yet, what is clear is that the description of the neural basis of fatigue within the central governor model does not explicitly describe a predictive processing framework, where the balance between bottom-up sensory signals and top-down predictions, based on the predicted precision of those signals, across the hierarchy determines the construction of perception (see Clark, 2013). Instead it suggests that the perception of fatigue is the detection of a change in some relative state (St Clair Gibson *et al.*, 2003). Moreover, the development of fatigue under the presented predictive processing account defines a very clear mechanistic foundation, based on metacognition and persistent error detection which is not defined within descriptions of fatigue within the central governor model. This also indicates a different object of interest outlined by the two perspectives. Where the central object of the central governor model is internal condition of the body, the principal focus underlying the development of fatigue in the outlined framework is in fact the performance of the internal model used to predict and control homeostasis.

8.5. The Role of Perception and Affect in Centrally Regulated Exercise Behaviour

Many perspectives on the regulation of physical activity ([section 2.3.1](#)) share in the proposition that the end of physical activity coincides with, or is preceded by, the attainment of some sensory or perceptual limit (Gandevia, 2001; Hureau *et al.*, 2016)⁷⁵. The attainment of this threshold is believed to trigger a volitional and deliberative decision to reduce exercise intensity or terminate exercise (Renfree *et al.*, 2014; Pageaux, 2014; McMorris, Barwood, & Corbett, 2018; Robertson & Marino, 2016). Volitional, goal-directed choice is believed to be an economic evaluation of the costs/benefits of available options (Rangel & Hare, 2010)⁷⁶. However, examinations of the decision-making process defining the termination of activity are inexistent. [Chapter 7](#) advances

⁷⁴ Another issue with the conceptualisation of ‘fatigue’ within perspectives based on the central governor model is that it does not (and possibly cannot easily) differentiate between different perceptual and affective constructs, such as fatigue and effort.

⁷⁵ The neurophysiological basis of this perception and the processes defining the upper limit though differ ([section 2.3.1](#)).

⁷⁶ Under predictive processing frameworks, decisions not are defined by the same maximization of utility through consideration of the costs and rewards associated with choices in bounded rational agents, but by the broader goal of minimizing prediction error both in the short- and long-term (Friston *et al.*, 2014).

understanding of the effects of fatigue on effort-based decisions, indicating that the subjective perception of fatigue, specifically, did not alter appraisal of physical effort costs and therefore choice preferences towards rest (for a more contextual discussion of the findings see [section 7.5](#)). This however would appear at odds with the findings presented in [chapters 5](#) and [6](#), where a pre-induced state of fatigue, augmented the perception of effort and reduced affective valence, both of which were closely associated to the limits of task performance. It may be assumed that a pre-induced state of fatigue augmented perceptual and affective constructs used in defining this hypothetical sensory limit, which presumably led to the decision to disengage with the task earlier. The divergence between results may indicate that the decision taken at the limits of exercise tolerance is different to that made in relation to engaging in future activity.

A problem with the causal chain of events proposed based on the findings presented in [chapters 5](#) and [6](#), is that like most of the current literature cited in support of some sensory limit (e.g. Crewe *et al.*, 2008; Hartman *et al.*, 2019), conclusions are based, primarily, on correlation analysis. In an attempt to establish this proposed perception-action sequence more formally, data across [chapters 5](#) and [6](#) were collated ($n = 49$) and a serial mediation model was constructed. The condition effects (independent variable) observed on endurance performance (i.e. TTF; dependent variable) were evaluated, with the perception of fatigue, affective valence and the perception of effort entered as mediating variables within the model (specific methods are presented in [Appendix D](#)). Specifically, it was hypothesized that the detrimental effect of the HG task on performance during the KE endurance task would be mediated by the HG task evoking a greater perceived state of fatigue, which would in turn decrease affective valence, leading to a heightened perception of effort. Affective valence was believed to influence the perception of effort for several reasons: 1) there was indication that effort rather than affect was the variable most related to TTF based on observed relationships of the present thesis (or lack thereof, in the case of affect), particularly in [chapter 5](#), suggesting that the perception of effort may reflect the final destination in this path. This is in keeping with the proposal of Hartman *et al.* (2019), in which affect was suggested to be the channel through which the perception of effort may enter consciousness; 2) it has been proposed that the regulation of emotion may involve effort (Etkin *et al.*, 2015; [section 2.4.](#)) and that affective states can change the appraisal of task demands (Silvestrini & Gendolla, 2019; [section 2.5.](#))⁷⁷; 3) In keeping with the predictive processing model of exertional fatigue outlined in [section 8.4.3.](#), affective valence tracks prediction error (Joffily & Coricelli, 2013), while the perception of effort reflects the cost associated with addressing this error in the pursuit of a higher goal states (Zénon *et al.*, 2019).

A path diagram of the conducted analysis is presented in [Figure 8.3](#). The total effect of the HG intervention on TTF saw performance reduced, on average, by ~30s compared to the control condition (path *c*). Though there was evidence of condition leading to sequential effects on perceptual and affective responses - namely, that performance of the HG task led to a greater perceived state of fatigue, with a greater perception of fatigue resulting in a lower experience of valence during the KE task, which in turn resulted in a greater perception of effort – these

⁷⁷ However, it is also acknowledged that effort itself has an inherent affective component, which may see changes in the perception of effort precede changes in affective valence. Another exploratory model incorporating an indirect path through the perception of fatigue → perception of effort → affective valence was therefore performed, with the results presented in [Appendix D \(Table D.1.\)](#). Broadly, the results for indirect effect were in accordance with those presented below, i.e. that there was no mediation between the condition and TTF, but more limited effects between perceptual and affective variables were observed.

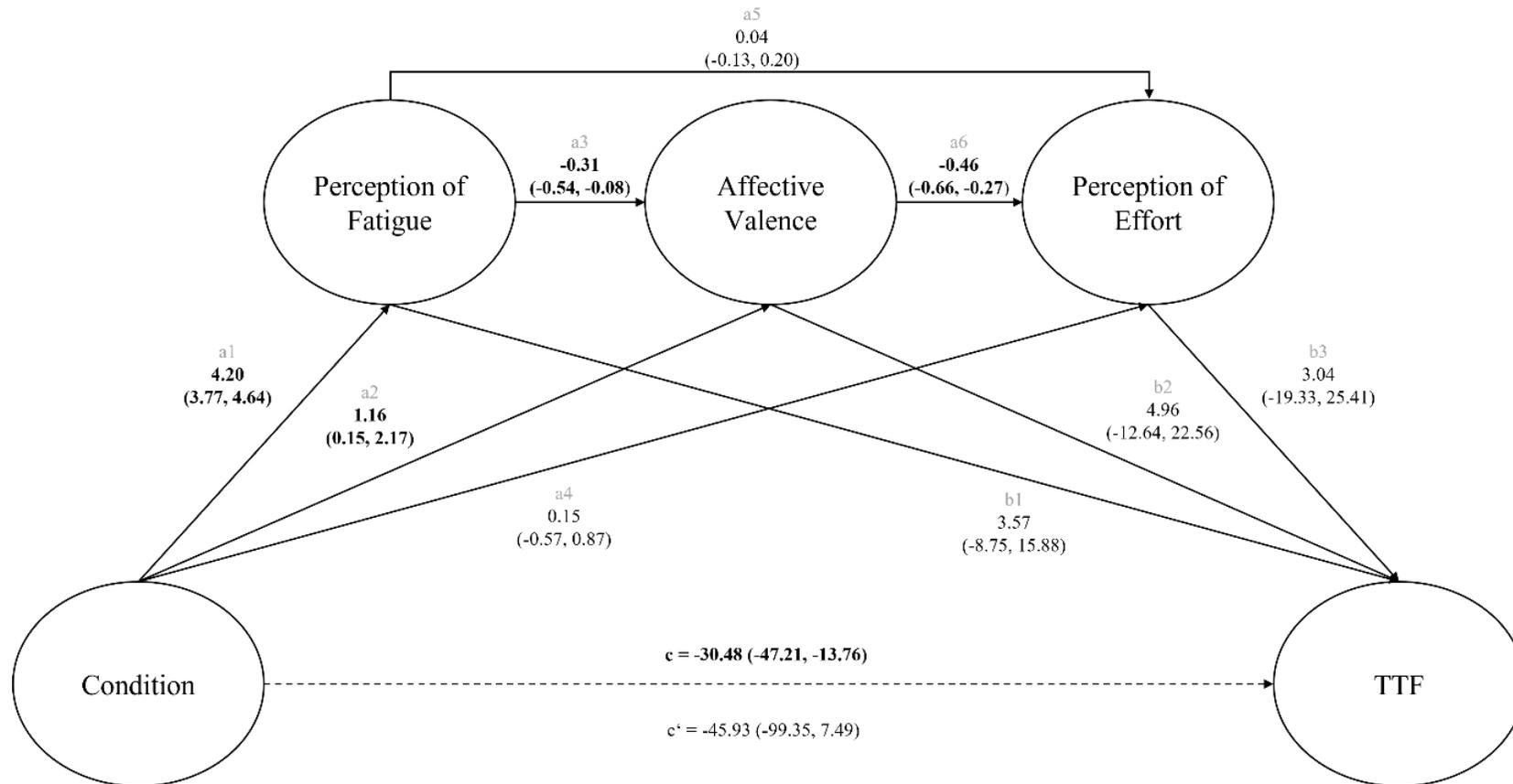


Figure 8.3. Path analysis of condition, perception of fatigue, affective valence, perception of effort and performance (i.e. time to task failure; TTF) based on data synthesised from *chapter 5* and *chapter 6* ($n = 49$). Path estimates presented as standardised estimates plus 95% confidence intervals (CI) in parentheses. Path estimates significantly different from zero are highlighted in bold ($p < 0.05$).

Table 8.1. Indirect path estimates for the mediating effect of the perception of fatigue, affective valence and the perception of effort on the effect of condition on performance (i.e. time to task failure; TTF).

Indirect Effects	Path	Estimate	Bootstrapped <i>SE</i>	Bootstrapped 95% <i>CI</i>	
				Lower	Upper
Perception of Fatigue → TTF	<i>a1b1</i> (4.20)(3.57)	15.00	25.53	-38.74	64.81
Affective Valence → TTF	<i>a2b2</i> (1.16)(4.96)	5.75	10.45	-12.07	29.92
Perception of Effort → TTF	<i>a4b3</i> (0.15)(3.04)	0.46	5.49	-10.25	13.03
Perception of Fatigue → Affective Valence → TTF	<i>a1a3b2</i> (4.20)(-0.31)(4.96)	-6.44	11.73	-33.88	13.26
Perception of Fatigue → Perception of Effort → TTF	<i>a1a5b3</i> (4.20)(0.04)(3.04)	0.48	4.67	-10.03	10.13
Affective Valence → Perception of Effort → TTF	<i>a2a6b3</i> (1.16)(-0.46)(3.04)	-1.64	8.01	-20.19	13.18
Perception of Fatigue → Affective Valence → Perception of Effort → TTF	<i>a1a3a6b3</i> (4.20)(-0.31)(-0.46)(3.04)	1.83	9.05	-14.81	22.57
Total Indirect Effect		15.44	24.59	-35.16	64.20

indirect effects were not shown to mediate the effect on performance ([Table 8.1](#)). However, though the direct effect of condition on TTF (path c') appeared to increase in absolute magnitude after accounting for the mediating variables, this effect also became more uncertain and ultimately, non-significant, as indicated by the size of confidence interval which now ranged across zero. The analysis therefore indicates that though altered cognitive-emotional processing in response to the HG task may not mediate the effect of condition on TTF, perceptual and affective responses may still be an important facet of the latent processes that do.

8.5.1. Implications for the Understanding of the Limits of Exercise Tolerance

The presented analysis does not appear to lend clear support to conceptualisations of the limits of exercise tolerance to be causally associated with some decision taken upon obtainment of a sensory tolerance limit, urging caution in over interpretation of mechanisms based on correlation analysis. Though again, it must be stressed, the above analysis did not explicitly examine the obtainment of this hypothesized threshold, instead examining the observed effects within the present thesis which should have led to its faster attainment, it does raise questions concerning the role of conscious experience in directly defining the termination of exercise. Indeed, Ishii *et al.* (2017) provide evidence of a down-regulation of motor output in response to a subliminal conditioned stimulus, independent of the conscious experience of fatigue, indicating that the mechanisms defining performance fatigability may occur separately to the conscious experience of fatigue-associated percepts. This challenge to the prevailing view of a direct causal association between perception and the limits of exercise tolerance may thus necessitate a re-evaluation of perspectives on the mechanisms defining the termination of exercise.

Dynamic systems approaches have increasingly been applied as a set of general principles that may explain many exercise phenomena (Balagué *et al.*, 2017), including task-disengagement during prolonged physical activity (see Balagué *et al.*, 2020; Venhorst *et al.*, 2018), and may suitably accommodate the presented findings. In reference to the perception of effort, Balagué *et al.* (2020) outline:

“...from a dynamic perspective [perceived effort] is not considered the “exercise stopper” in the sense of a causal agent. Although exhaustion is associated with maximal RPE values, task disengagement is not considered a voluntary decision. In fact, the conscious volition is always oriented toward continuation of the task. From the dynamic perspective, termination emerges as a consequence of the spontaneous loss of intentional or volitional task stability. That is, as a result of the abrupt dissolution of volition to continue the task itself that was maintained through the coupling between psychobiological components. The spontaneous task disengagement may be interpreted as a protective mechanism that temporarily eliminates the very cause of the [perceived effort], that is, the effortful task itself.” (p. 961)

In the dynamical perspective, interactions between hierarchical levels of living systems - from cells to social interactions - are not viewed as invariant, rigid or linear (i.e. context-independent and proportionately). Instead, the system's components are recognised to be multifunctional integrations across different levels of the system, which constantly change over time on different temporal scales. Consequently, through a circular causality between top-down control parameters (i.e. organismic, task, and environmental constraints) and bottom-up factors, behaviour is dependent upon the configuration of sub-system components achieved through a process of self-organisation. Limiting the degrees of freedom available for component reconfigurations through these

interactions may encourage the development of coherent stable, or 'attractor', states to support particular goals (Davids *et al.*, 2003). Attractor states are “*potential states or patterns of change to which a system's behaviour converges to over time*” (Vallacher *et al.*, 2010; p. 265), providing a basis for understanding the formation of concerted activity across the system towards a particular end (e.g. goal pursuit). Importantly, there may exist more than one attractor state at any particular time (e.g. the conflict between the pull to continue or to stop physical activity), which may see non-stationary modes of behaviour based on the simultaneous realization of two competing state points (i.e. multistable and metastable states; Kelso, 2012). The proposition put forward is that the limits of exercise tolerance represents an eventual loss of stability in the intent to continue underpinned by an inability of psychological, biological and environmental components to effectively rearrange and form connections, given the present constraints, thus resulting in an eventual discontinuous change in behaviour toward lower energy expenditure levels or rest; from metastability to monostability (Balagué *et al.*, 2014; Hristovski & Balagué, 2010; Hristovski *et al.*, 2010; Vázquez *et al.*, 2016). The dynamics of the perception of effort is offered as an index of the creation and dissolution of these component couplings - decreasing when new synergies are formed to maintain exercise and increasing when these synergies dissolve due to emerging constraints - but is not defined as a causal determinant of behaviour, which emerges spontaneously (Balagué *et al.*, 2020). Behaviour emerges not because subsequent perceptions and affective states become intolerable and subsequently one consciously decides to stop, but rather the environmental, psychological and biological component configurations in the subsystems underlying the attractor state of goal-pursuit intent become so destabilised that they give way to the spontaneous emergence of a new, competing attractor state (i.e. task termination).

The results of the presented analysis in this section of the thesis indicates that the perception of fatigue may act as a constraint on the emergence of affective valence and the perception of effort, which hold important roles in sustaining task engagement through creating and stabilizing new component synergies (Balagué *et al.*, 2020). Hierarchical implementation of attractors, where higher-level attractors guide the trajectories of lower-level controllers, have been related to generative models (Friston & Kiebel, 2009), which indicates similarities between dynamical perspectives and the proposed model outlined in the previous section (8.4.3.). The proposed shift towards lower level 'controllers' of action when higher-level predictions lose sufficient precision may be reflective, or at least suggestive, of the constraints imposed by an emerging perceived state of fatigue.

8.6. Limitations and Future Directions

The presented work demonstrates evidence of the cognitive, perceptual and affective effects to physical activity when in a perceived state of fatigue. However, the findings must be viewed in light of some of the limitations imposed by the complex and multifaceted nature of fatigue research and broader delimitations adopted within the presented thesis. For example, the study of the effects of a perceived state of fatigue was performed by pre-inducing a state of fatigue through demanding activity performed in one part of the body and evaluating its effects during prolonged activity in another. Interpretation of effects on perceptual and affective responses as a consequence of the performance of the HG task and a direct response to the development of fatigue are comprehensible in the absence of concomitant motor fatigability. It should be emphasised, that explicit examination of such conditions was only cautiously interpreted as providing support for the use of the adopted

paradigm ([chapter 4](#)). Future work is therefore required to confirm the validity of the adopted paradigm, and also the presented effects within other fatigue-inducing paradigms.

The presented work was performed exclusive in healthy, young males. This particular delimitation was adopted as sex has previously been shown to influence the change in force observed within similar paradigms, with females shown to be more resistant to the deleterious global physical effects of demanding physical activity (e.g. Ye *et al.*, 2018). The use of just males was believed to remove this potential confounding effect, enabling evaluation in what had been proposed as the most sensitive cohort (see [chapter 4](#)). There is also some indication that sex differences may determine effort-based decision making (e.g. Treadway *et al.*, 2012), which may have added an additional factor into consideration of the study design of [chapter 7](#). As far as one is aware, it is also yet to be established whether males and females experience the acute, transient perception of fatigue similarly. Potential differences may arise, for example, by differences in perceived performance capabilities, particularly in untrained individuals (e.g. McAuley *et al.*, 1991). Thus, though the present studies attempt to control for potential sources of additional variation, the generalisability of the findings to a wider population are limited. The present work unfortunately perpetuates an under representation of females in biomedical research and sparse understanding of sex-related differences in physical performance (Hunter, 2014).

Additionally, the adopted tasks used both to induce a perceived state of fatigue and measure performance consisted of small muscle mass, single-joint isometric contractions. For the former, this was chosen in order to evaluate the effects of a physically-induced perceived state of fatigue in the presence of modest central physiological perturbations (e.g. Louhevaara *et al.*, 2000), thus clearly emphasising changes in the cognitive processes responsible for generating the perception of fatigue over and above the physical challenge⁷⁸. However, this protocol may fail to adequately describe the strength of subsequent effects during high-intensity, whole-body, dynamic exercise, which may be overwhelmed, or prove smaller, in the face of the vast array of sensory inputs evoked (Ekkekakis & Brand, 2019). Accordingly, future research is required to evaluate the relationship between fatigue and the perceptual and affective response to exercise across a diverse range of physical tasks and studied populations.

Notwithstanding these points however, the presented thesis raises several interesting questions related to the study of the perception of fatigue and the limits of exercise tolerance. In addition to the recommendations made for future research within each experimental chapter, several broader recommendations will now be outlined. Firstly, the main obstacle to any examination of the perception of fatigue remains the lack of clarity in what one is exactly measuring. Dedicated investigations are imperative to gain better understanding of the phenomenological experience of exertional fatigue. The conceptualisation of the perception of fatigue used within the present work ([section 3.11](#); Micklewright *et al.*, 2017) may be seen as resembling definitions of self-efficacy ([section 2.3.2](#); Bandura, 1997) more than what is conventionally defined as the perception of fatigue ([section 2.2.4](#)). As stated, like others (e.g. Focht *et al.*, 2007), the results of [chapter 7](#) indicates an association between a perceived state of fatigue and perceived performance capacity. However, though proposed (Steele, 2021), the relationship between fatigue and self-efficacy is yet to be definitively established. Examination of the dynamics of both constructs during physical activity may provide insight into their association. If the two constructs are in fact separable, they

⁷⁸ A further limitation of the presented work is that indices of cardiorespiratory function were not assessed during the tasks, therefore an evaluation of the physiological impact of the fatiguing task cannot be made.

may thus reflect distinct constraints acting on behaviour across different timescales (see Balagué *et al.*, 2020). This temporal aspect may hold important implications for understanding how perceptions of performance capacity influences engagement in effortful activity.

Secondly, the combined results of [chapters 5-7](#) plus the analysis performed in [section 8.5](#), indicate that further work is required to understand precisely why individuals disengage with effortful physical activity. A limitation of [chapter 7](#) was that decisions were made at rest, which is not reflective of the conditions under which the decision to persist or stop is made at the end of a task. Accordingly, to better understand volitional control in the termination of exercise, it is recommended that similar paradigms are performed during the performance of demanding activity.

Finally, the predictive processing model offers several hypotheses that can be tested in order to examine the proposed basis of the perception of fatigue ([section 8.4.3](#)). Emerging computational models offer a potential means of examining changes in model parameters (i.e. belief precision) at a physiological (Unal *et al.*, 2021) and performance level (Hezemans *et al.*, 2020). However, these may only (currently) capture the lowest level of the hierarchical control system (Unal *et al.*, 2021). However, psychobehavioural interventions designed broadly to manipulate prediction error within the system may be used to understand the conditions responsible for the development of fatigue. For example, false interoceptive feedback can generate an illusion of effort during exercise (Iodice *et al.*, 2019). Further research may use similar paradigms to understand how protracted exposure to prediction error is related to the perception of fatigue and, importantly, how various streams of sensory information (i.e. interoception *vs.* proprioception) interact within the generation of this percept. At the other end of the continuum, sensory categorisation (Zacharioudakisa *et al.*, 2020) or placebo-based effects (Büchel *et al.*, 2014) may similarly aid understanding of how predictions or beliefs shape perception and either exacerbate or ameliorate the development of fatigue. This is important as under the current framework, perception can only be understood when descending beliefs and ascending sensory evidence are considered in conjunction. In keeping with the comparable mechanisms offered in the description of pathological and exertional fatigue development, the framework may provide important insight into interactions between disease and exertion. Comparison between patients and healthy controls may therefore help understand how beliefs shaped by disease determines predictions during acute performance (e.g. van der Schaaf *et al.*, 2018) and potentially how repeated exposure to acute exertion may reshape prior expectations in patients and therefore account for its possible therapeutic implications.

CHAPTER 9 - CONCLUSION

The principal aim of the thesis was to examine the effect of a perceived state of fatigue on the regulation of physical performance. Together the data of this thesis indicate that the perception of fatigue functions as a top-down cognitive influence on the perceptual (i.e. the perception of effort) and affective markers of performance regulation, which were evidenced independently of concomitant neuromuscular disturbances in the working muscle. The thesis establishes the relationships between the studied psychological constructs and provides important insight into the mechanistic basis of exertion-related perceptions. Specifically, the thesis provides a new perspective of the perception of fatigue evoked during acute physical exertion. The perception of fatigue, exclusively, is associated with higher-level processing related to ones' awareness of their selves, including individuals' interoceptive judgements and perceived performance capacity. The thesis also provides an important extension to current understanding of the volitional decisions ultimately defining the limits of exercise tolerance. A state of perceived fatigue, *per se*, did not alter the computations underlying effort-based choice, nor did changes in perception and affect mediate the observed detrimental effects on physical endurance performance. Thus, it is proposed that the perception of fatigue does not directly determine the decision to terminate physical activity but constrains the conditions that enable action to be maintained. Finally, based on the observed findings, a framework on contemporary perspectives of brain function is proposed which sees the perception of fatigue arise in response to a persistent detection of error in predictive models of the world, due to a declining belief in ones' capacity to exert effective control over bodily states. Future research is now required to explore this proposed mechanistic basis of the perception of fatigue.

APPENDICES

Appendix A

Table A.1. Between-session reliability of knee-extensor (KE) neuromuscular function derived from Dekerle, Greenhouse-Tucknott, *et al.* (2019).

	TEM (% of mean)	SDC _{ind} (% of mean)	SDC _{sample} (% of mean)	ICC _{2,1} (95% CI)
<i>Pre-Physical Exertion</i>				
MVC	5.4	14.9	3.3	0.96* (.89-.98)
VA _{TMS}	2.6	7.1	2.3	n.a
SIT _{100%}	40.7	113.0	35.7	.63 ^{n.s.} (-.34-.91)
ERT	10.9	30.2	9.5	.85* (.45-.96)
Q _{tw}	4.9	13.5	3.0	0.89* (.68-.96)
<i>Post-Physical Exertion</i>				
MVC	11.4	31.7	7.1	0.79* (.46-.92)
VA _{TMS}	8.0	22.1	7.0	n.a
SIT _{100%}	34.3	95.1	30.1	.63 ^{n.s.} (-.29-.90)
ERT	20.9	57.8	18.3	.81* (.18-.95)
Q _{tw}	8.8	24.4	5.5	0.78* (.34-.93)

Reliability of neuromuscular parameters were derived between-sessions both before and after the performance of physically demanding KE task (Dekerle, Greenhouse-Tucknott, *et al.*, 2019). The neuromuscular function assessment protocol was similar to that outlined in [section 4.3.4](#). MVC: Maximal voluntary contraction; VA_{TMS}: Voluntary activation assessed through transcranial magnetic stimulation; SIT_{100%}: Super imposed twitch evoked during a maximal contraction; ERT: Estimated resting twitch; Q_{tw}: Twitch force. TEM: Typical error of the mean; SDC_{ind}: Smallest detectable change for an individual participant; SDC_{sample}: Smallest detectable change for the sample; ICC_{2,1}: Intraclass correlation coefficient (two-way random effects, absolute agreement, single rater/measurement); 95% CI: 95% confidence intervals. Calculation of ICC for VA_{TMS} was not applicable due to ceiling effects on VA_{TMS}. * Statistically significant relationship ($p < 0.05$).

Appendix B

Table B.1. Maximum voluntary contraction (MVC) force recorded in the (dominant) knee extensors (KE), and the dominant and non-dominant handgrip (HG) at the beginning of each condition.

	Condition			<i>F</i>	ANOVA	
	CON	MOD	SEV		<i>p</i>	η_p^2
<i>KE</i>	642.5 ± 164.6	648.0 ± 159.3	632.7 ± 168.2	1.80	0.174	0.058
<i>Dominant HG</i>	465.8 ± 94.0	470.1 ± 84.3	469.8 ± 87.5	0.27	0.762	0.009
<i>Non-dominant HG</i>	445.3 ± 102.5	448.3 ± 97.1	443.1 ± 100.8	0.52	0.595	0.018

Data presented as mean ± *SD*.

Table B.2. Emotional states and perceived sleepiness between conditions.

	Condition			Friedman's ANOVA	
	CON	MOD	SEV	χ^2	<i>p</i>
DASS (a.u.)					
<i>Depression</i>	1.73 ± 2.45 (0.0, 1.0)	2.33 ± 3.28 (2.0, 3.5)	1.93 ± 2.95 (0.0, 1.0)	2.50	0.287
<i>Anxiety</i>	1.93 ± 3.17 (0.0, 1.0)	1.93 ± 2.85 (0.0, 1.0)	2.60 ± 4.76 (0.0, 4.0)	1.16	0.559
<i>Stress</i>	4.60 ± 5.20 (4.0, 6.0)	5.00 ± 6.34 (3.0, 8.0)	4.60 ± 5.49 (4.0, 7.5)	0.63	0.732
KSS (a.u.)					
<i>Baseline</i>	2.80 ± 1.79 (2.50, 2.75)	2.77 ± 1.45 (3.0, 3.0)	2.97 ± 1.73 (3.0, 2.75)	0.74	0.691
<i>Pre KE</i>	2.67 ± 1.67 (2.0, 2.75)	2.67 ± 1.37 (3.0, 2.50)	2.70 ± 1.68 (2.5, 3.0)	0.03	0.987
<i>Post KE</i>	2.47 ± 1.43 (2.0, 2.0)	2.80 ± 1.45 (3.0, 1.75)	2.97 ± 1.77 (3.0, 2.75)	6.02	0.049

Data presented as mean ± *SD* with *Mdn* and *IQR* presented in parentheses. DASS: Depression, Anxiety and Stress Scale. KSS: Karolinska Sleepiness Scale

Table B.3. Estimated fixed and random effects from linear mixed analysis of the perception of effort and affective valence recorded during the knee extensor (KE) endurance task.

Fixed Effects	Contrast	Perception of Effort					Affective Valence				
		Estimates	95% CI		<i>t</i>	<i>p</i>	Estimates	95% CI		<i>t</i>	<i>p</i>
			Lower	Upper				Lower	Upper		
Intercept		7.86	7.39	8.32	32.96	<0.001	-1.84	-2.44	-1.23	-5.96	<0.001
Condition	<i>Contrast 1</i>	-0.90	-1.08	-0.72	-9.83	<0.001	0.66	0.45	0.87	6.17	<0.001
	<i>Contrast 2</i>	-0.06	-0.30	0.18	-0.51	0.612	0.17	-0.13	0.48	1.12	0.262
Time	<i>Linear</i>	7.48	7.11	7.85	39.22	<0.001	-5.90	-6.84	-4.96	-12.26	<0.001
	<i>Quadratic</i>	-1.21	-1.55	-0.86	-6.84	<0.001	0.94	0.31	1.58	2.92	0.006
Interaction	<i>Contrast 1*Time (Linear)</i>	-0.51	-1.18	0.16	-1.50	0.134	0.68	-0.13	1.50	1.64	0.102
	<i>Contrast 2*Time (Linear)</i>	-0.47	-1.41	0.47	-0.98	0.329	-0.84	-2.11	0.42	-1.30	0.194
	<i>Contrast 1*Time (Quadratic)</i>	0.07	-0.58	0.72	0.21	0.831	-0.06	-0.86	0.75	-0.14	0.891
	<i>Contrast 2*Time (Quadratic)</i>	0.14	-0.77	1.06	0.30	0.765	-0.99	-2.25	0.27	-1.54	0.126
Random Effects											
	σ^2			0.78					0.86		
	ICC			0.68					0.75		
Model Fit											
	Akaike Information Criterion			1739.700					1910.484		
	R ² marginal			0.67					0.39		
	R ² conditional			0.89					0.88		

Contrast 1 represents the contrast between CON and the combined experimental manipulations (MOD + SEV). Contrast 2 represents the contrast between MOD and SEV. σ^2 : residual variance, ICC: intraclass correlation coefficient, R² marginal: variance explained by the fixed effects over the total (expected) variance of the dependent variable, R² conditional: variance explained by the fixed and random effects over the total (expected) variance of the dependent variable, CON: control; MOD: moderate RoF; SEV: severe RoF. Full fixed and random effects of models not presented for clarity.

Table B.4. Estimated fixed and random effects from robust linear mixed analysis of the relative (%) RMS amplitude in the *vastus lateralis* (VL), *vastus medialis* (VM) and *rectus femoris* (RF) during the knee extensor (KE) endurance task.

Fixed Effects	Contrast	VL			VM			RF		
		Estimate	SE	<i>t</i>	Estimate	SE	<i>t</i>	Estimate	SE	<i>t</i>
Intercept		26.48	0.89	29.85	27.13	1.36	19.95	22.25	1.13	19.75
Condition	<i>Contrast 1</i>	-1.45	0.36	-4.06	-2.17	0.49	-4.41	1.03	0.45	2.29
	<i>Contrast 2</i>	-1.82	0.48	-3.75	-2.94	0.66	-4.47	0.29	0.61	0.48
Time	<i>Linear</i>	28.53	1.11	25.79	29.48	1.53	19.32	2.38	1.40	18.16
	<i>Quadratic</i>	2.01	1.07	1.88	2.55	1.46	1.74	7.16	1.35	5.30
Interaction	<i>Contrast 1*Time (Linear)</i>	-6.22	1.97	-3.16	-5.78	2.76	-2.09	0.33	2.49	0.13
	<i>Contrast 2*Time (Linear)</i>	-1.52	2.82	-0.54	-10.23	3.82	-2.68	-0.85	3.57	-0.24
	<i>Contrast 1*Time (Quadratic)</i>	-1.52	1.97	-0.77	-3.87	2.77	-1.40	-1.21	2.50	-0.48
	<i>Contrast 2*Time (Quadratic)</i>	7.82	2.88	2.72	0.89	3.88	0.23	2.59	3.65	0.71
Random Effect	<i>Participant (Intercept)</i>									
	σ^2		17.80			32.17			28.71	
	$\tau_{00\text{participant}}$		17.75			42.17			28.67	
	ICC		0.50			0.57			0.50	
Model Fit										
	R ² marginal		0.41			0.26			0.23	
	R ² conditional		0.71			0.68			0.62	

Contrast 1 represents the contrast between CON and the combined experimental manipulations (MOD + SEV). Contrast 2 represents the contrast between MOD and SEV. σ^2 : residual variance, $\tau_{00\text{participant}}$: individual variance, ICC_(participant): intraclass correlation coefficient, SE: standard error, R² marginal: variance explained by the fixed effects over the total (expected) variance of the dependent variable, R² conditional: variance explained by the fixed and random effects over the total (expected) variance of the dependent variable. Full fixed effects of models not presented for clarity.

Appendix C

Table C.1. Akaike Information Criterion of model fit comparing different distributions and link function assumptions in the prediction of choice selection time.

Distribution	Link function	Akaike Information Criterion
Gaussian	Identity	23229.95
Inverse Gaussian	Inverse	16962
	Log	16983
	Square	17103
Gamma	Inverse	17477
	Log	17516
	Square	17570

Best fitting model highlighted in bold. LMM: Linear mixed model; GLMM: Generalized linear mixed model.

Table C.2. Proportion of choices in which participants selected the ‘effortful’ option during the effort-based force choice task under experimental conditions.

Reward	Control					Fatigue				
	Effort					Effort				
	20%	40%	60%	80%	100%	20%	40%	60%	80%	100%
£6	0.90 ± 0.28	0.68 ± 0.40	0.43 ± 0.45	0.23 ± 0.41	0.08 ± 0.18	0.90 ± 0.20	0.68 ± 0.39	0.46 ± 0.42	0.18 ± 0.34	0.05 ± 0.18
£7	0.93 ± 0.22	0.86 ± 0.28	0.58 ± 0.40	0.25 ± 0.41	0.10 ± 0.29	0.95 ± 0.13	0.88 ± 0.24	0.64 ± 0.42	0.36 ± 0.44	0.11 ± 0.21
£8	1.00 ± 0.00	0.95 ± 0.15	0.75 ± 0.38	0.39 ± 0.44	0.19 ± 0.36	0.98 ± 0.06	0.95 ± 0.18	0.84 ± 0.35	0.44 ± 0.45	0.30 ± 0.43
£9	1.00 ± 0.00	1.00 ± 0.00	0.85 ± 0.30	0.45 ± 0.44	0.27 ± 0.40	1.00 ± 0.00	0.98 ± 0.05	0.90 ± 0.25	0.49 ± 0.45	0.30 ± 0.40
£10	1.00 ± 0.00	0.99 ± 0.04	0.89 ± 0.25	0.59 ± 0.43	0.36 ± 0.43	1.00 ± 0.00	0.99 ± 0.04	0.95 ± 0.21	0.61 ± 0.44	0.35 ± 0.46

Data presented as means ± *SD*.

Table C.3. Estimated fixed and random effects in the prediction of effort-based choice.

Model							
Type	GLMM						
Distribution	Binomial						
Link function	Logit						
	$P(\text{effort}) / P(\text{no effort})$						
Akaike Information Criterion	3609.37						
R ² marginal	0.852						
R ² conditional	0.935						
		95% exp(B) CI					
Fixed Effects	Estimate	SE	exp(B)	Lower	Upper	p	
(Intercept)	3.099	0.773	2.22e+01	4.87e+00	1.01e+02	< 0.001	
Condition	-0.367	1.214	6.93e-01	6.42e-02	7.47e+00	0.762	
Effort C1	-5.321	3.509	4.89e-03	5.03e0-6	4.75e+00	0.129	
Effort C2	-6.443	1.598	1.59e-03	6.95e0-5	3.64e-02	< 0.001	
Effort C3	-7.083	1.07	8.39e0-4	1.03e0-4	6.83e-03	< 0.001	
Effort C4	-6.980	0.809	9.30e0-4	1.91e0-4	4.54e-03	< 0.001	
Reward C1	1.092	0.139	2.98e+00	2.27e+00	3.91e+00	< 0.001	
Reward C2	3.358	1.414	2.87e+01	1.80e+00	4.59e+02	0.018	
Reward C3	4.430	1.474	8.39e+01	4.67e+00	1.51e+03	0.003	
Reward C4	3.801	2.489	4.47e+01	3.40e-01	5.88e+03	0.127	
Condition * Effort C1	-2.835	5.795	5.87e-02	6.85e0-7	5.03e+03	0.625	
Condition * Effort C2	2.201	3.034	9.03e+00	2.36e-02	3.45e+03	0.468	
Condition * Effort C3	1.124	2.027	3.08e+00	5.79e-02	1.64e+02	0.579	
Condition * Effort C4	0.841	1.529	2.32e+00	1.16e-01	4.64e+01	0.582	
Condition * Reward C1	0.448	0.274	1.56e+00	9.14e-01	2.68e+00	0.103	
Condition * Reward C2	-2.965	2.822	5.15e-02	2.04e0-4	1.30e+01	0.293	
Condition * Reward C3	0.802	3.468	2.23e+00	2.49e-03	1.99e+03	0.817	
Condition * Reward C4	0.770	3.213	2.16e+00	3.98e-03	1.17e+03	0.811	
Effort C1 * Reward C1	0.944	0.463	2.57e+00	1.04e+00	6.37e+00	0.041	
Effort C2 * Reward C1	-0.040	0.334	9.61e-01	4.99e-01	1.85e+00	0.904	
Effort C3 * Reward C1	-0.157	0.315	8.55e-01	4.61e-01	1.58e+00	0.619	
Effort C4 * Reward C1	-0.356	0.391	7.01e-01	3.26e-01	1.51e+00	0.364	
Effort C1 * Reward C2	-6.910	7.053	9.98e0-4	9.89e-10	1.01e+03	0.327	
Effort C2 * Reward C2	-3.587	3.536	2.77e-02	2.71e0-5	2.83e+01	0.310	
Effort C3 * Reward C2	-3.169	2.363	4.21e-02	4.10e0-4	4.32e+00	0.180	
Effort C4 * Reward C2	-1.905	1.785	1.49e-01	4.50e-03	4.92e+00	0.286	
Effort C1 * Reward C3	3.589	9.049	3.62e+01	7.19e0-7	1.82e0+9	0.692	
Effort C2 * Reward C3	-6.248	3.687	1.93e-03	1.41e0-6	2.66e+00	0.090	
Effort C3 * Reward C3	-5.046	2.463	6.43e-03	5.15e0-5	8.03e-01	0.040	
Effort C4 * Reward C3	-3.630	1.856	2.65e-02	6.98e0-4	1.01e+00	0.050	
Effort C1 * Reward C4	-11.326	12.288	1.21e0-5	4.18e-16	3.47e+05	0.357	
Effort C2 * Reward C4	-4.243	6.225	1.44e-02	7.22e0-8	2.86e+03	0.496	
Effort C3 * Reward C4	-3.171	4.152	4.20e-02	1.23e0-5	1.44e+02	0.445	
Effort C4 * Reward C4	-2.750	3.117	6.39e-02	1.42e0-4	2.88e+01	0.378	
Condition * Effort C1 * Reward C1	-0.235	0.923	7.91e-01	1.30e-01	4.83e+00	0.799	
Condition * Effort C2 * Reward C1	-0.213	0.666	8.08e-01	2.19e-01	2.98e+00	0.749	
Condition * Effort C3 * Reward C1	0.681	0.627	1.98e+00	5.78e-01	6.74e+00	0.277	
Condition * Effort C4 * Reward C1	-0.175	0.78	8.40e-01	1.82e-01	3.87e+00	0.823	
Condition * Effort C1 * Reward C2	15.658	14.08	6.31e0+6	6.54e0-6	6.10e+18	0.266	
Condition * Effort C2 * Reward C2	8.429	7.056	4.58e+03	4.51e-03	4.64e0+9	0.232	
Condition * Effort C3 * Reward C2	5.021	4.716	1.52e+02	1.47e-02	1.57e0+6	0.287	
Condition * Effort C4 * Reward C2	4.659	3.562	1.06e+02	9.81e-02	1.14e+05	0.191	
Condition * Effort C1 * Reward C3	-34.588	12.871	9.52e-16	1.06e-26	8.60e0-5	0.007	
Condition * Effort C2 * Reward C3	-1.980	8.664	1.38e-01	5.83e0-9	3.27e0+6	0.819	
Condition * Effort C3 * Reward C3	-1.531	5.784	2.16e-01	2.58e0-6	1.81e+04	0.791	
Condition * Effort C4 * Reward C3	-1.279	4.351	2.78e-01	5.50e0-5	1.41e+03	0.769	
Condition * Effort C1 * Reward C4	3.548	15.76	3.48e+01	1.34e-12	9.04e+14	0.822	
Condition * Effort C2 * Reward C4	-1.482	8.027	2.27e-01	3.34e0-8	1.55e0+6	0.854	
Condition * Effort C3 * Reward C4	-1.683	5.359	1.86e-01	5.10e0-6	6.78e+03	0.754	
Condition * Effort C4 * Reward C4	-1.254	4.033	2.85e-01	1.05e0-4	7.74e+02	0.756	
Random Effects							
σ^2	1.00						
$\tau_{00\text{participant}}$	4.23						

Model Specification: Choice (effort) ~ 1 + Condition + Effort + Reward + Condition*Effort + Condition*Reward + Effort*Reward + Condition*Effort*Reward + (1 | Participant). Differences between conditions compared using a simple difference contrast (Fatigue – Control). Contrasts between effort and reward levels coded using a reverse Helmert contrast: Effort C1 = 40% - (20%), Effort C2 = 60% - (40%, 20%), Effort C3 = 80% - (60%, 40%, 20%), Effort C4 = 100% - (80%, 60%, 40%, 20%); Reward C1 = £7 - (£6), Reward C2 = £8 - (£7, £6), Reward C3 = £9 - (£8, £7, £6), Reward C4 = £10 - (£9, £8, £7, £6) GLMM: Generalized linear mixed model; SE: standard error; CI: confidence interval; exp(B): exponential of B coefficient (odds ratio); σ^2 : residual variance; $\tau_{00\text{participant}}$: individual variance; R² marginal: variance explained by the fixed effects over the total (expected) variance of the dependent variable; R² conditional: variance explained by the fixed and random effects over the total (expected) variance of the dependent variable.

Table C.4. Estimated fixed and random effects in the prediction of choice selection time.

Model						
Type	GLMM					
Distribution	Inverse Gaussian					
Link function	Inverse					
Akaike Information Criterion	16962					
			95% <i>CI</i>			
Fixed Effects	Estimate	<i>SE</i>	Lower	Upper	<i>p</i>	
(Intercept)	0.525	0.042	0.443	0.608	< 0.001	
Condition	-0.015	0.006	-0.026	-0.003	0.011	
Effort C1	-0.056	0.009	-0.075	-0.038	< 0.001	
Effort C2	-0.078	0.008	-0.093	-0.063	< 0.001	
Effort C3	-0.058	0.007	-0.072	-0.044	< 0.001	
Effort C4	0.020	0.007	0.006	0.034	0.005	
Reward C1	-0.019	0.009	-0.036	-0.002	0.029	
Reward C2	0.007	0.008	-0.008	0.022	0.334	
Reward C3	0.028	0.007	0.013	0.042	< 0.001	
Reward C4	0.026	0.007	0.012	0.040	< 0.001	
Condition * Effort C1	-0.013	0.019	-0.049	0.024	0.495	
Condition * Effort C2	0.001	0.015	-0.029	0.030	0.969	
Condition * Effort C3	0.006	0.014	-0.021	0.033	0.665	
Condition * Effort C4	-0.002	0.014	-0.030	0.027	0.907	
Condition * Reward C1	0.006	0.018	-0.028	0.041	0.715	
Condition * Reward C2	-0.015	0.015	-0.045	0.015	0.321	
Condition * Reward C3	0.009	0.015	-0.020	0.038	0.539	
Condition * Reward C4	0.001	0.014	-0.028	0.029	0.971	
Effort C1 * Reward C1	-0.002	0.028	-0.057	0.053	0.945	
Effort C2 * Reward C1	-0.041	0.023	-0.087	0.005	0.078	
Effort C3 * Reward C1	-0.022	0.022	-0.066	0.022	0.319	
Effort C4 * Reward C1	-0.043	0.023	-0.087	0.002	0.059	
Effort C1 * Reward C2	-0.001	0.025	-0.050	0.049	0.981	
Effort C2 * Reward C2	-0.052	0.020	-0.092	-0.012	0.010	
Effort C3 * Reward C2	-0.048	0.019	-0.086	-0.011	0.011	
Effort C4 * Reward C2	-0.033	0.019	-0.071	0.005	0.090	
Effort C1 * Reward C3	-0.011	0.025	-0.060	0.037	0.652	
Effort C2 * Reward C3	-0.035	0.020	-0.074	0.004	0.080	
Effort C3 * Reward C3	-0.086	0.018	-0.121	-0.051	< 0.001	
Effort C4 * Reward C3	-0.041	0.019	-0.077	-0.004	0.029	
Effort C1 * Reward C4	0.039	0.024	-0.008	0.086	0.107	
Effort C2 * Reward C4	-0.006	0.020	-0.045	0.032	0.750	
Effort C3 * Reward C4	-0.063	0.018	-0.098	-0.029	< 0.001	
Effort C4 * Reward C4	-0.029	0.018	-0.065	0.006	0.103	
Condition * Effort C1 * Reward C1	0.033	0.056	-0.077	0.144	0.551	
Condition * Effort C2 * Reward C1	-0.038	0.047	-0.129	0.054	0.418	
Condition * Effort C3 * Reward C1	-0.005	0.045	-0.092	0.083	0.913	
Condition * Effort C4 * Reward C1	-0.033	0.045	-0.122	0.056	0.472	
Condition * Effort C1 * Reward C2	0.014	0.050	-0.085	0.112	0.785	
Condition * Effort C2 * Reward C2	0.021	0.040	-0.058	0.100	0.602	
Condition * Effort C3 * Reward C2	0.018	0.038	-0.057	0.092	0.642	
Condition * Effort C4 * Reward C2	0.028	0.039	-0.048	0.104	0.468	
Condition * Effort C1 * Reward C3	0.018	0.049	-0.079	0.115	0.713	
Condition * Effort C2 * Reward C3	-0.007	0.040	-0.085	0.071	0.866	
Condition * Effort C3 * Reward C3	-0.022	0.036	-0.092	0.049	0.544	
Condition * Effort C4 * Reward C3	-0.028	0.037	-0.101	0.045	0.450	
Condition * Effort C1 * Reward C4	-0.064	0.048	-0.159	0.030	0.182	
Condition * Effort C2 * Reward C4	0.066	0.039	-0.011	0.143	0.091	
Condition * Effort C3 * Reward C4	-0.027	0.035	-0.095	0.042	0.447	
Condition * Effort C4 * Reward C4	-0.010	0.036	-0.080	0.061	0.788	
Random Effects						
σ^2	0.143					
τ_{00} _{participant}	0.007					

Model Specification: Choice selection time (s) $\sim 1 + \text{Condition} + \text{Effort} + \text{Reward} + \text{Condition*Effort} + \text{Condition*Reward} + \text{Effort*Reward} + \text{Condition*Effort*Reward} + (1 | \text{Participant})$. Differences between conditions compared using a simple difference contrast (Fatigue – Control). Contrasts between effort and reward levels coded using a reverse Helmert contrast: Effort C1 = 40% - (20%), Effort C2 = 60% - (40%, 20%), Effort C3 = 80% - (60%, 40%, 20%), Effort C4 = 100% - (80%, 60%, 40%, 20%); Reward C1 = £7 - (£6), Reward C2 = £8 - (£7, £6), Reward C3 = £9 - (£8, £7, £6), Reward C4 = £10 - (£9, £8, £7, £6) GLMM: Generalized linear mixed model; *SE*: standard error; *CI*: confidence interval; σ^2 : residual variance; τ_{00} _{participant}: individual variance; R^2 marginal: variance explained by the fixed effects over the total (expected) variance of the dependent variable; R^2 conditional: variance explained by the fixed and random effects over the total (expected) variance of the dependent variable.

Table C.5. Self-reported confidence (%) in ability to perform selected ‘effortful’ contractions during the effort-based force choice task under experimental conditions.

Reward	Control					Fatigue				
	Effort					Effort				
	20%	40%	60%	80%	100%	20%	40%	60%	80%	100%
£6	97.3 ± 5.5	89.8 ± 17.0	84.1 ± 18.4	81.1 ± 28.2	69.7 ± 28.8	98.1 ± 3.3	88.5 ± 9.6	83.1 ± 14.1	80.7 ± 24.9	60.7 ± 42.9
£7	96.9 ± 5.8	91.5 ± 12.7	83.9 ± 19.6	85.2 ± 14.7	80.7 ± 8.1	97.0 ± 4.8	90.0 ± 10.9	83.9 ± 13.9	72.2 ± 24.8	51.5 ± 29.4
£8	97.4 ± 5.2	91.5 ± 11.8	83.6 ± 17.9	77.1 ± 24.4	75.0 ± 12.9	97.9 ± 3.3	89.9 ± 10.0	85.1 ± 12.5	73.2 ± 22.3	58.8 ± 22.0
£9	97.9 ± 4.2	93.3 ± 9.3	86.0 ± 16.6	75.6 ± 19.4	66.7 ± 24.0	98.3 ± 2.8	92.8 ± 8.2	86.8 ± 12.0	70.1 ± 22.6	59.7 ± 22.5
£10	98.5 ± 3.3	94.0 ± 8.6	86.7 ± 14.1	73.6 ± 22.4	65.5 ± 23.0	98.9 ± 1.7	94.2 ± 6.2	87.5 ± 11.2	68.6 ± 19.6	60.7 ± 19.7

Data presented as estimated mean ± *SD*.

Table C.6. Estimated fixed and random effects in the prediction of effort choice confidence ratings.

Model							
Type	LMM						
Akaike Information Criterion	32048.622						
R ² marginal	0.382						
R ² conditional	0.595						
		95% CI					
Fixed Effects	Estimate	SE	Lower	Upper	t	p	
(Intercept)	82.792	1.654	79.551	86.033	50.062	< 0.001	
Condition	-5.263	0.446	-6.137	-4.389	-11.799	< 0.001	
Effort C1	-5.973	0.431	-6.818	-5.128	-13.853	< 0.001	
Effort C2	-8.199	0.420	-9.022	-7.376	-19.522	< 0.001	
Effort C3	-16.458	0.555	-17.546	-15.370	-29.652	< 0.001	
Effort C4	-26.043	0.829	-27.668	-24.417	-31.404	< 0.001	
Reward C1	0.141	0.864	-1.552	1.834	0.163	0.871	
Reward C2	0.250	0.599	-0.924	1.424	0.417	0.677	
Reward C3	0.791	0.505	-0.199	1.780	1.565	0.118	
Reward C4	0.477	0.449	-0.403	1.357	1.063	0.288	
Condition * Effort C1	-1.393	0.861	-3.082	0.295	-1.618	0.106	
Condition * Effort C2	-1.185	0.832	-2.815	0.445	-1.425	0.154	
Condition * Effort C3	-8.517	1.087	-10.648	-6.386	-7.834	< 0.001	
Condition * Effort C4	-12.076	1.641	-15.292	-8.861	-7.360	< 0.001	
Condition * Reward C1	-0.858	1.723	-4.235	2.518	-0.498	0.618	
Condition * Reward C2	2.828	1.194	0.488	5.168	2.369	0.018	
Condition * Reward C3	3.905	1.006	1.934	5.877	3.883	< 0.001	
Condition * Reward C4	4.075	0.892	2.327	5.823	4.569	< 0.001	
Effort C1 * Reward C1	0.381	1.430	-2.422	3.185	0.267	0.790	
Effort C2 * Reward C1	-0.970	1.472	-3.855	1.915	-0.659	0.510	
Effort C3 * Reward C1	-1.100	2.040	-5.099	2.899	-0.539	0.590	
Effort C4 * Reward C1	4.439	3.407	-2.238	11.116	1.303	0.193	
Effort C1 * Reward C2	-0.499	1.180	-2.813	1.814	-0.423	0.672	
Effort C2 * Reward C2	-0.452	1.142	-2.689	1.786	-0.395	0.693	
Effort C3 * Reward C2	-0.714	1.497	-3.649	2.220	-0.477	0.633	
Effort C4 * Reward C2	2.934	2.202	-1.383	7.250	1.332	0.183	
Effort C1 * Reward C3	1.621	1.088	-0.512	3.753	1.489	0.136	
Effort C2 * Reward C3	-0.393	1.015	-2.382	1.596	-0.387	0.699	
Effort C3 * Reward C3	-1.912	1.286	-4.433	0.608	-1.487	0.137	
Effort C4 * Reward C3	0.000	1.777	-3.483	3.483	0.000	1.000	
Effort C1 * Reward C4	1.598	1.046	-0.451	3.647	1.528	0.126	
Effort C2 * Reward C4	-0.563	0.953	-2.431	1.306	-0.590	0.555	
Effort C3 * Reward C4	-5.110	1.127	-7.319	-2.902	-4.536	< 0.001	
Effort C4 * Reward C4	0.256	1.529	-2.741	3.252	0.167	0.867	
Condition * Effort C1 * Reward C1	2.203	2.859	-3.401	7.806	0.770	0.441	
Condition * Effort C2 * Reward C1	0.137	2.943	-5.632	5.906	0.047	0.963	
Condition * Effort C3 * Reward C1	0.055	4.078	-7.938	8.048	0.013	0.989	
Condition * Effort C4 * Reward C1	-7.067	6.808	-20.411	6.277	-1.038	0.299	
Condition * Effort C1 * Reward C2	0.022	2.359	-4.601	4.645	0.009	0.993	
Condition * Effort C2 * Reward C2	-0.318	2.282	-4.791	4.156	-0.139	0.889	
Condition * Effort C3 * Reward C2	6.800	2.991	0.937	12.663	2.273	0.023	
Condition * Effort C4 * Reward C2	5.276	4.401	-3.350	13.901	1.199	0.231	
Condition * Effort C1 * Reward C3	0.948	2.175	-3.315	5.210	0.436	0.663	
Condition * Effort C2 * Reward C3	0.179	2.028	-3.796	4.153	0.088	0.930	
Condition * Effort C3 * Reward C3	5.705	2.572	0.665	10.745	2.219	0.027	
Condition * Effort C4 * Reward C3	9.533	3.554	2.567	16.498	2.682	0.007	
Condition * Effort C1 * Reward C4	1.506	2.090	-2.591	5.603	0.720	0.471	
Condition * Effort C2 * Reward C4	-0.243	1.904	-3.976	3.489	-0.128	0.898	
Condition * Effort C3 * Reward C4	1.646	2.248	-2.761	6.052	0.732	0.464	
Condition * Effort C4 * Reward C4	14.497	3.058	8.504	20.490	4.741	< 0.001	
Random Effects							
σ^2	112.6						
τ_{00} _{participant}	59.0						
ICC	0.344						

Model Specification: Confidence ratings (%) ~ 1 + Condition + Effort + Reward + Condition*Effort + Condition*Reward + Effort*Reward + Condition*Effort*Reward + (1 | Participant). Differences between conditions compared using a simple difference contrast (Fatigue – Control). Contrasts between effort and reward levels coded using a reverse Helmert contrast: Effort C1 = 40% - (20%), Effort C2 = 60% - (40%, 20%), Effort C3 = 80% - (60%, 40%, 20%), Effort C4 = 100% - (80%, 60%, 40%, 20%); Reward C1 = £7 - (£6), Reward C2 = £8 - (£7, £6), Reward C3 = £9 - (£8, £7, £6), Reward C4 = £10 - (£9, £8, £7, £6) GLMM: Generalized linear mixed model; SE: standard error; CI: confidence interval; σ^2 : residual variance; τ_{00} _{participant}: individual variance; ICC: intraclass correlation coefficient; R² marginal: variance explained by the fixed effects over the total (expected) variance of the dependent variable; R² conditional: variance explained by the fixed and random effects over the total (expected) variance of the dependent variable.

Appendix D

The Serial mediation analysis was performed using the MEMORE (mediation and moderation analysis for repeated measures designs) macro for SPSS (Montoya & Hayes, 2017), which applies a path analytical framework to the original approach of Judd *et al.* (2001) for two-condition, within-participant mediation analysis. Full description of the mathematical basis of this analysis is beyond the scope of the present thesis. In brief however, within-participant mediation examines the degree to which the difference in the dependent variable recorded in two conditions is due to the difference in some other, presumed causal variable recorded in the same conditions (i.e. the mediator), based on an evaluation of the adjustment in the difference in the dependent variable after accounting for the difference in the mediating variable (Judd *et al.*, 2001; Montoya & Hayes, 2017). In this regard, the independent variable (here, the effect of condition) is not explicitly stated in the mediation analysis but is instead carried in the difference scores of the proposed mediating (i.e. perception of fatigue, affective valence, and perception of effort) and dependent variables (i.e. TTF). The MEMORE macro is designed to provide a single estimate of the indirect effect (i.e. pathways *ab*), however the simple reporting of this estimate in the absence of analysis of its constituent paths may inflate the potential of committing a Type I error due to the prepotent influence of large effects for one of the paths on this estimate (Yzerbyt *et al.*, 2018). In the presented analysis, estimated coefficients (and their significance) for all paths between independent, mediating and dependent variables are displayed in addition to indirect estimates, as per recommendations (Yzerbyt *et al.*, 2018). Bootstrapped confidence intervals, derived from 10,000 bootstrap samples, were calculated for indirect path estimates.

In the presented analysis, the perception of fatigue referred to individuals' subjective ratings taken at the end of the HG task, immediately prior to the commencement of the KE endurance tasks, in [chapters 5](#) and [6](#). Affective valence and the perception of effort referenced the average recorded scores obtained across the duration of the KE endurance task, reflecting the observed condition effects observed within the two studies and absence of interaction between condition and time ([sections 5.4.2.](#) and [6.4.4.](#)). Data taken from [chapter 6](#) corresponded to responses obtained during the MOD trial as, even though participants were required to reach a specified target RoF, there was some variation in RoF responses at the end of the HG task. The data of one participant was removed from the sample taken from [chapter 6](#) as he also participated in [chapter 5](#). This led to 49 unique individuals entered into the model across the two study chapters. The analysis was also re-run with indirect path flowing through the perception of fatigue → perception of effort → affective valence. The results of this model are presented in [Table D.1.](#)

Table D.1. Indirect path estimates for the mediating effect of the perception of fatigue, the perception of effort and affective valence on the effect of condition on performance (i.e. time to task failure; TTF).

Indirect Effects	Path	Estimate	Bootstrapped <i>SE</i>	Bootstrapped 95% CI	
				Lower	Upper
Perception of Fatigue → TTF	<i>a1b1</i> (4.20)(3.57)	15.00	25.79	-38.30	64.85
Perception of Effort → TTF	<i>a2b2</i> (1.16)(4.96)	-1.01	7.20	-17.42	13.55
Affective Valence → TTF	<i>a4b3</i> (0.15)(3.04)	4.42	8.63	-9.62	25.73
Perception of Fatigue → Perception of Effort → TTF	<i>a1a3b2</i> (4.20)(-0.31)(4.96)	2.15	10.21	-17.88	24.97
Perception of Fatigue → Affective Valence → TTF	<i>a1a5b3</i> (4.20)(0.04)(3.04)	-3.73	7.42	-22.53	7.45
Perception of Effort → Affective Valence → TTF	<i>a2a6b3</i> (1.16)(-0.46)(3.04)	1.23	4.00	-4.85	11.11
Perception of Fatigue → Perception of Effort → Affective Valence → TTF	<i>a1a3a6b3</i> (4.20)(-0.31)(-0.46)(3.04)	-2.61	5.61	-16.62	6.03
Total Indirect Effect		15.45	24.89	-34.97	64.72

REFERENCES

- Aaronson, L. S., Teel, C. S., Cassmeyer, V., Neuberger, G. B., Pierce, J., Press, A. N., Williams, P. D. and Wingate, A. (1999). Defining and measuring fatigue. *Journal of Nursing Scholarship*, 31: 45–50.
- Abbiss, C. R. and Laursen, P. B. (2005). Models to explain fatigue during prolonged endurance cycling. *Sports Medicine*, 35: 865–898.
- Abbiss, C. R., Peiffer, J. J., Meeusen, R. and Skorski, S. (2015). Role of ratings of perceived exertion during self-paced exercise: What are we actually measuring? *Sports Medicine*, 45: 1235–1243.
- Aboodarda, S. J., Copithorne, D. B., Power, K. E., Drinkwater, E. and Behm, D. G. (2015). Elbow flexor fatigue modulates central excitability of the knee extensors. *Applied Physiology, Nutrition and Metabolism*, 40: 924–930.
- Aboodarda, S. J., Iannetta, D., Emami, N., Varesco, G., Murias, J. M. and Millet, G. Y. (2020). Effects of pre-induced fatigue vs. concurrent pain on exercise tolerance, neuromuscular performance and corticospinal responses of locomotor muscles. *Journal of Physiology*, 598: 285–302.
- Aboodarda, S. J., Šambaher, N. and Behm, D. G. (2016). Unilateral elbow flexion fatigue modulates corticospinal responsiveness in non-fatigued contralateral biceps brachii. *Scandinavian Journal of Medicine and Science in Sports*, 26: 1301–1312.
- Aboodarda, S. J., Šambaher, N., Millet, G. Y. and Behm, D. G. (2017). Knee extensors neuromuscular fatigue changes the corticospinal pathway excitability in biceps brachii muscle. *Neuroscience*, 340: 477–486.
- Adams, R. A., Shipp, S. and Friston, K. J. (2013). Predictions not commands: Active inference in the motor system. *Brain Structure & Function*, 218: 611–643.
- Adreani, C. M., Hill, J. M. and Kaufman, M. P. (1997). Responses of group III and IV muscle afferents to dynamic exercise. *Journal of Applied Physiology*, 82: 1811–1817.
- Agrawal, M., Mattar, M. G., Cohen, J. D. and Daw, N. D. (2021). The temporal dynamics of opportunity costs: A normative account of cognitive fatigue and boredom. *Psychological Review*.
- Ainley, V., Apps, M. A., Fotopoulou, A. and Tsakiris, M. (2016). ‘Bodily precision’: A predictive coding account of individual differences in interoceptive accuracy. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 371: 20160003.
- Åkerstedt, T., Anund, A., Axelsson, J. and Kecklund, G. (2014). Subjective sleepiness is a sensitive indicator of insufficient sleep and impaired waking function. *Journal of Sleep Research*, 23: 242–254.
- Åkerstedt, T. and Gillberg, M. (1990). Subjective and objective sleepiness in the active individual. *International Journal of Neuroscience*, 52: 29–37.
- Allen, D. G., Lamb, G. D. and Westerblad, H. (2008). Skeletal muscle fatigue: Cellular mechanisms. *Physiological Reviews*, 88: 287–332.
- Allen, M. and Friston, K. J. (2018). From cognitivism to autopoiesis: Towards a computational framework for the embodied mind. *Synthese*, 195: 2459–2482.
- Allen, P. D. and Pandolf, K. B. (1977). Perceived exertion associated with breathing hyperoxic mixtures during submaximal work. *Medicine and Science in Sports*, 9: 122–127.
- Amann, M., Blain, G. M., Proctor, L. T., Sebranek, J. J., Pegelow, D. F. and Dempsey, J. A. (2010). Group III and IV muscle afferents contribute to ventilatory and cardiovascular response to rhythmic exercise in humans. *Journal of Applied Physiology*, 109: 966–976.
- Amann, M., Sidhu, S. K., Weavil, J. C., Mangum, T. S. and Venturelli, M. (2015). Autonomic responses to exercise: Group III/IV muscle afferents and fatigue. *Autonomic Neuroscience: Basic and Clinical*, 188: 19–23.
- Amann, M., Venturelli, M., Ives, S., McDaniel, J., Layec, G., Rossman, M. J. and Richardson, R. S. (2013). Peripheral fatigue limits endurance exercise via a sensory feedback-mediated reduction in spinal

- motoneuronal output. *Journal of Applied Physiology*, 115: 355–364.
- Ament, W. and Verkerke, G. (2009). Exercise and fatigue. *Sports Medicine*, 39: 389–422.
- André, N., Audiffren, M. and Baumeister, R. F. (2019). An integrative model of effortful control. *Frontiers in Systems Neuroscience*, 13: 79.
- Andrea, H., Kant, I. J., Beurskens, A. J. H. M., Metsemakers, J. F. M. and van Schayck, C. P. (2003). Associations between fatigue attributions and fatigue, health, and psychosocial work characteristics: A study among employees visiting a physician with fatigue. *Occupational and Environmental Medicine*, 60: i99 LP-i104.
- Andrushko, J. W., Levenstein, J. M., Zich, C., Edmond, E. C., Campbell, J., Clarke, W. T., Emir, U., Farthing, J. P. and Stagg, C. J. (2021). *Fatigue induces behavioural improvements in the unfatigued hand via altered functional connectivity and neurochemicals in cortical motor areas*. Cold Spring Harbor Laboratory.
- Ang, Y. S., Lockwood, P., Apps, M. A., Muhammed, K. and Husain, M. (2017). Distinct subtypes of apathy revealed by the apathy motivation index. *PLoS ONE*, 12: e0169938.
- Ansdell, P., Thomas, K., Howatson, G., Amann, M. and Goodall, S. (2017). Deception improves TT performance in well-trained cyclists without augmented fatigue. *Medicine & Science in Sports & Exercise*, 50: 809–816.
- Apps, M. A. and Tsakiris, M. (2014). The free-energy self: A predictive coding account of self- recognition. *Neuroscience and Biobehavioral Reviews*, 44: 85–97.
- Apps, M., Grima, L. L., Manohar, S. and Husain, M. (2015). The role of cognitive effort in subjective reward devaluation and risky decision-making. *Scientific Reports*, 5: 16880.
- Arnaud, M. J. (2011). Pharmacokinetics and metabolism of natural methylxanthines in animal and man. In: B.B. Fredholm (ed.) *Handbook of Experimental Pharmacology*. London: Springer Heidelberg Dordrecht. pp.33–91.
- van As, S., Beckers, D. G. J., Geurts, S. A. ., Kompier, M. A. J., Husain, M. and Veling, H. (2021). The impact of cognitive and physical effort exertion on physical effort decisions: A pilot experiment. *Frontiers in Psychology*, 12: 4607.
- Astorino, T. A., Cottrell, T., Lazano, A. T., Aburto-Pratt, K. and Duhon, J. (2012). Effect of caffeine on RPE and perceptions of pain, arousal, and pleasure/displeasure during a cycling time trial in endurance trained and active men. *Physiology & Behavior*, 106: 211–217.
- Ávila-Gandía, V., Alarcón, F., Perales, J. C., López-Román, F. J., Luque-Rubia, A. J. and Cárdenas, D. (2020). Dissociable effects of executive load on perceived exertion and emotional valence during submaximal cycling. *International Journal of Environmental Research and Public Health*, 17: 5576.
- Azevedo, P. H., Oliveira, M. G., Tanaka, K., Pereira, P. E., Esteves, G. and Tenan, M. S. (2021). Perceived exertion and performance modulation: Effects of caffeine ingestion and subject expectation. *Journal of Sports Medicine & Physical Fitness*, 61: 1185–1192.
- Bachasson, D., Temesi, J., Gruet, M., Yokoyama, K., Rupp, T., Millet, G. Y. and Verges, S. (2016). Transcranial magnetic stimulation intensity affects exercise-induced changes in corticomotoneuronal excitability and inhibition and voluntary activation. *Neuroscience*, 314: 125–133.
- Backhouse, S. H., Biddle, S. J. H. and Williams, C. (2007). The influence of water ingestion during prolonged exercise on affect. *Appetite*, 48: 193–198.
- Baden, D. A., McLean, T., Tucker, R., Noakes, T. D. and St Clair Gibson, A. (2005). Effect of anticipation during unknown or unexpected exercise duration on rating of perceived exertion, affect, and physiological function. *British Journal of Sports Medicine*, 39: 742–746.
- Bakdash, J. Z. and Marusich, L. R. (2017). Repeated measures correlation. *Frontiers in Psychology*, 8: 456.
- Balagué, N., Hristovski, R. and García-Retortillo, S. (2020). Perceived Exertion. In: G. Tenenbaum & R.C. Eklund (eds) *Handbook of Sport Psychology*.
- Balagué, N., Hristovski, R., Vainoras, A., Vázquez, P. and Aragonés, D. (2014). Psychobiological integration during exercise. In: K. Davids, R. Hristovski, D. Araújo, N. Balagué, C. Button & P. Passos (eds) *Complex Systems in Sport*. London: Routledge. pp.82–102.

- Balagué, N., Torrents, C., Hristovski, R. and Kelso, J. A. S. (2017). Sport science integration: An evolutionary synthesis. *European Journal of Sport Science*, 17: 51–62.
- Bandura, A. (1997). *Self-efficacy: The exercise of control*. New York: W.H. Freeman and Company.
- Bangsbo, J., Madsen, K., Kiens, B. and Richter, E. A. (1996). Effect of muscle acidity on muscle metabolism and fatigue during intense exercise in man. *Journal of Physiology*, 495: 587–596.
- Barbosa, T. C., Vianna, L. C., Fernandes, I. A., Prodel, E., Rocha, H. N. M., Garcia, V. P., Rocha, N. G., Secher, N. H. and Nobrega, A. C. L. (2016). Intrathecal fentanyl abolishes the exaggerated blood pressure response to cycling in hypertensive men. *Journal of Physiology*, 594: 715–725.
- Barhorst, E. E., Andrae, W. E., Rayne, T. J., Falvo, M. J., Cook, D. B. and Lindheimer, J. B. (2020). Elevated perceived exertion in people with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and Fibromyalgia: A meta-analysis. *Medicine & Science in Sports & Exercise*, 52: 2615–2627.
- Baron, B., Moullan, F., Deruelle, F. and Noakes, T. D. (2011). The role of emotions on pacing strategies and performance in middle and long duration sport events. *British Journal of Sports Medicine*, 45: 511–517.
- Barrett, L. F. (2017). The theory of constructed emotion: An active inference account of interoception and categorization. *Social Cognitive and Affective Neuroscience*, 12: 1–23.
- Barrett, L. F. and Bliss-Moreau, E. (2009). Affect as a psychological primitive. *Advances in Experimental Social Psychology*, 41: 167–218.
- Barrett, L. F., Mesquita, B., Ochsner, K. N. and Gross, J. J. (2007). The experience of emotion. *Annual Review of Psychology*, 58: 373–403.
- Barrett, L. F. and Satpute, A. B. (2019). Historical pitfalls and new directions in the neuroscience of emotion. *Neuroscience Letters*, 693: 9–18.
- Barrett, L. F. and Simmons, W. K. (2015). Interoceptive predictions in the brain. *Nature Reviews Neuroscience*, 16: 419–429.
- Bassett Jr, D. R. and Howley, E. T. (2000). Limiting factors for maximum oxygen uptake and determinants of endurance performance. *Medicine & Science in Sports & Exercise*, 32: 70–84.
- Basu, N., Yang, X., Luben, R. N., Whibley, D., Macfarlane, G. J., Wareham, N. J., Khaw, K.-T. and Myint, P. K. (2016). Fatigue is associated with excess mortality in the general population: Results from the EPIC-Norfolk study. *BMC Medicine*, 14.
- Baumeister, R. F., Vohs, K. D. and Tice, D. M. (2007). The strength model of self-control. *Current Directions in Psychological Sciences*, 16: 351–355.
- Bäumer, T., Münchau, A., Weiller, C. and Liepert, J. (2002). Fatigue suppresses ipsilateral intracortical facilitation. *Experimental Brain Research*, 146: 467–473.
- Beckstead, R. M., Morse, J. R. and Norgren, R. (1980). The nucleus of the solitary tract in the monkey: Projections to the thalamus and brain stem nuclei. *Journal of Comparative Neurology*, 190: 259–282.
- Beedie, C. J. and Lane, A. M. (2012). The role of glucose in self-control. *Personality and Social Psychology Review*, 16: 143–153.
- Behm, D. G., Alizadeh, S., Anvar, S. H., Hanlon, C., Ramsay, E., Mahmoud, M. M. I., Whitten, J., Fisher, J. P., Prieske, O., Chaabene, H., Granacher, U. and Steele, J. (2021). Non-local muscle fatigue effects on muscle strength, power, and endurance in healthy individuals: A systematic review and meta-analysis. *Sports Medicine*, 51: 1893–1907.
- Bekrater-Bodmann, R., Azevedo, R. T., Ainley, V. and Tsakiris, M. (2020). Interoceptive awareness is negatively related to the exteroceptive manipulation of bodily self-location. *Frontiers in Psychology*, 11: 562016.
- Benjamini, Y. and Yosef, H. (2000). On the adaptive control of the false discovery rate in multiple testing with independent statistics. *Journal of Educational and Behavioral Statistics*, 25: 60–83.
- Benoit, C. E., Solopchuk, O., Borragán, G., Carbonnelle, A., Van Durme, S. and Zénon, A. (2019). Cognitive task avoidance correlates with fatigue-induced performance decrement but not with subjective fatigue.

Neuropsychologia, 123: 30–40.

- Berchicci, M., Menotti, F., Macaluso, A. and Di Russo, F. (2013). The neurophysiology of central and peripheral fatigue during sub-maximal lower limb isometric contractions. *Frontiers in Human Neuroscience*, 7: 135.
- Bergstrom, H. C., Housh, T. J., Cochrane, K. C., Jenkins, N. D. M., Zuniga, J. M., Buckner, S. L., Goldsmith, J. A., Schmidt, R. J., Johnson, G. O. and Cramer, J. T. (2015). Factors underlying the perception of effort during constant heart rate running above and below the critical heart rate. *European Journal of Applied Physiology*, 115: 2231–2241.
- Bestmann, S. and Krakauer, J. W. (2015). The uses and interpretations of the motor-evoked potential for understanding behaviour. *Experimental Brain Research*, 233: 679–689.
- Białaszek, W., Marcowski, P. and Ostaszewski, P. (2017). Physical and cognitive effort discounting across different reward magnitudes: Tests of discounting models. *PLoS ONE*, 12: e01823353.
- Bigland-Ritchie, B. R., Johansson, R. S., Lippold, O. C. J. and Woods, J. J. (1983). Contractile speed and EMG changes during fatigue of sustained maximal voluntary contractions. *Journal of Neurophysiology*, 50: 313–324.
- Bigland-Ritchie, B. R. and Woods, J. J. (1984). Changes in muscle contractile properties and neural control during human muscular fatigue. *Muscle & Nerve*, 7: 691–699.
- Bishop, P. A. and Herron, R. L. (2015). Use and Misuse of the Likert Item Responses and Other Ordinal Measures. *International journal of exercise science*, 8: 297–302.
- Blain, B., Hollard, G. and Pessiglione, M. (2016). Neural mechanisms underlying the impact of daylong cognitive work on economic decisions. *Proceedings of the National Academy of Sciences of the United States of America*, 113: 6967–6972.
- Blain, B., Schmit, C., Aubry, A., Hausswirth, C., Le Meur, Y. and Pessiglione, M. (2019). Neuro-computational impact of physical training overload on economic decision-making. *Current Biology*, 29: 3289–3297.
- Blain, G. M., Mangum, T. S., Sidhu, S. K., Weavil, J. C., Hureau, T. J., Jessop, J. E., Bledsoe, A. D., Richardson, R. S. and Amann, M. (2016). Group III/IV muscle afferents limit the intramuscular metabolic perturbation during whole body exercise in humans. *Journal of Physiology*, 594: 5303–5315.
- Blanchfield, A., Hardy, J. and Marcora, S. M. (2014). Non-conscious visual cues related to affect and action alter perception of effort and endurance performance. *Frontiers in Human Neuroscience*, 8: 1–16.
- Bland, J. M. and Altman, D. G. (1995). Calculating correlation coefficients with repeated observations: Part 1—correlation within subjects. *BMJ*, 310: 446.
- Blomqvist, A., Zhang, E.-T. and Craig, A. D. (2000). Cytoarchitectonic and immunohistochemical characterization of a specific pain and temperature relay, the posterior portion of the ventral medial nucleus, in the human thalamus. *Brain*, 123: 601–619.
- Bloom, J. S. and Hynd, G. W. (2005). The role of the corpus callosum in interhemispheric transfer of information: Excitation or inhibition? *Neuropsychology Review*, 15: 59–71.
- Bogaty, P., Poirier, P., Boyer, L., Jobin, J. and Dagenais, G. R. (2003). What induces the warm-up ischemia/angina phenomenon: Exercise or myocardial ischemia? *Circulation*, 107: 1858–1863.
- Boksem, M. A. S., Meijman, T. F. and Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, 72: 123–132.
- Boksem, M. A. S. and Tops, M. (2008). Mental fatigue: Costs and benefits. *Brain Research Reviews*, 59: 125–139.
- Bonnelle, V., Manohar, S., Behrens, T. and Husain, M. (2016). Individual differences in premotor brain systems underlie behavioral apathy. *Cerebral Cortex*, 26: 807–819.
- Bonnelle, V., Veromann, K.-R., Burnett Heyes, S., Lo Sterzo, E., Manohar, S. and Husain, M. (2015). Characterization of reward and effort mechanisms in apathy. *Journal of Physiology - Paris*, 109: 16–26.
- Borbély, A. A., Daan, S., Wirz-Justice, A. and Deboer, T. (2016). The two-process model of sleep regulation: A

- reappraisal. *Journal of Sleep Research*, 25: 131–143.
- Borg, E. and Borg, G. (2002). A comparison of AME and CR100 for scaling perceived exertion. *Acta Psychologica*, 109: 157–175.
- Borg, G. (1998). *Borg's perceived exertion and pain scales*. Champaign, IL: Human Kinetics.
- Borg, G. (1973). Perceived exertion: A note on 'history' and methods. *Medicine and Science in Sports*, 5: 90–93.
- Borg, G. (1970). Perceived exertion as an indicator of somatic stress. *Scandinavian Journal of Rehabilitation Medicine*, 2: 92–98.
- Borg, G. (1982). The psychophysical bases of perceived exertion. *Medicine & Science in Sports & Exercise*, 14: 377–381.
- Borg, G. A. V. (1962). *Physical performance and perceived exertion*. Univer. Lund.
- Bouloosa, D. A. and Nakamura, F. Y. (2013). The evolutionary significance of fatigue. *Frontiers in Physiology*, 4: 309.
- Bove, A. M., Lynch, A. D., DePaul, S. M., Terhorst, L., Irrgang, J. J. and Fitzgerald, G. K. (2016). Test-retest reliability of rating of perceived exertion and agreement with 1-repetition maximum in adults. *Journal of Orthopaedic & Sports Physical Therapy*, 46: 768–774.
- Bower, J. E. (2014). Cancer-related fatigue: Mechanisms, risk factors, and treatments. *Nature Reviews. Clinical Oncology*, 11: 597–609.
- Bowtell, J. L., Mohr, M., Fulford, J., Jackman, S. R., Ermidis, G., Krstrup, P. and Mileva, K. N. (2018). Improved exercise tolerance with caffeine is associated with modulation of both peripheral and central neural processes in human participants. *Frontiers in Nutrition*, 5: 6.
- van Boxtel, A. and Jessurun, M. (1993). Amplitude and bilateral coherency of facial and jaw-elevator EMG activity as an index of effort during a two-choice serial reaction task. *Psychophysiology*, 30: 589–604.
- Braunstein, L. M., Gross, J. J. and Ochsner, K. N. (2017). Explicit and implicit emotion regulation: A multi-level framework. *Social Cognitive and Affective Neuroscience*, 12: 1545–1557.
- Brehm, J. W. and Self, E. A. (1989). The intensity of motivation. *Annual Review of Psychology*, 40: 109–131.
- Brick, N. E., MacIntyre, T. E. and Campbell, M. J. (2016). Thinking and action: A cognitive perspective on self-regulation during endurance performance. *Frontiers in Physiology*, 7.
- Brooks, J., Allen, T. J. and Proske, U. (2013). The senses of force and heaviness at the human elbow joint. *Experimental Brain Research*, 226: 617–629.
- Brown, D. M. Y., Graham, J. D., Innes, K. I., Harris, S., Flemington, A. and Bray, S. R. (2020). Effects of prior cognitive exertion on physical performance: A systematic review and meta-analysis. *Sports Medicine*, 50: 497–529.
- Brown, D. R., Cappozzo, F., De Roeck, D., Zariwala, M. G. and Deb, S. K. (2021). Mouth rinsing with a pink non-caloric, artificially-sweetened solution improves self-paced running performance and feelings of pleasure in habitually active individuals. *Frontiers in Nutrition*, 8: 217.
- Brownsberger, J., Edwards, a., Crowther, R. and Cottrell, D. (2013). Impact of mental fatigue on self-paced exercise. *International Journal of Sports Medicine*, 34: 1029–1036.
- Broxterman, R. M., Hureau, T. J., Layec, G., Morgan, D. E., Bledsoe, A. D., Jessop, J. E., Amann, M. and Richardson, R. S. (2018). Influence of group III / IV muscle afferents on small muscle mass exercise performance: A bioenergetics perspective. *Journal of Physiology*, 596: 2301–2314.
- Broxterman, R. M., Layec, G., Hureau, T. J., Morgan, D. E., Bledsoe, A. D., Jessop, J. E., Amann, M. and Richardson, R. S. (2017). Bioenergetics and ATP Synthesis during Exercise: Role of Group III/IV Muscle Afferents. *Medicine & Science in Sports & Exercise*, 49: 2404–2413.
- Bruijel, J., Vermeeren, A., Stapert, S. Z. and van Heugten, C. M. (2022). Mental effort and recovery from task-induced fatigue in people with traumatic brain injury. *Disability and Rehabilitation*: 1–8.

- Brunetti, O., Della Torre, G., Lucchi, M. L., Chiocchetti, R., Bortolami, R. and Pettorossi, V. E. (2003). Inhibition of muscle spindle afferent activity during masseter muscle fatigue in the rat. *Experimental Brain Research*, 152: 251–262.
- Bubic, A., von Cramon, D. Y. and Schubotz, R. I. (2010). Prediction, cognition and the brain. *Frontiers in Human Neuroscience*: 25.
- Büchel, C., Geuter, S., Sprenger, C. and Eippert, F. (2014). Placebo analgesia: A predictive coding perspective. *Neuron*, 81: 1223–1239.
- Bültmann, U., Kant, I., Kasl, S. V., Beurskens, A. J. H. M. and Van Den Brandt, P. A. (2002). Fatigue and psychological distress in the working population psychometrics, prevalence, and correlates. *Journal of Psychosomatic Research*, 52: 445–452.
- Burke, D., Kiernan, M. C. and Bostock, H. (2001). Excitability of human axons. *Clinical Neurophysiology*, 112: 1575–1585.
- Burnley, M. (2010). The limit to exercise tolerance in humans: Validity compromised by failing to account for the power-velocity relationship. *European Journal of Applied Physiology*, 109: 1225–1226.
- Burnley, M. and Jones, A. M. (2018). Power–duration relationship: Physiology, fatigue, and the limits of human performance. *European Journal of Sport Science*, 18: 1–12.
- Butler, J. E., Taylor, J. L. and Gandevia, S. C. (2003). Responses of human motoneurons to corticospinal stimulation during maximal voluntary contractions and ischemia. *Journal of Neuroscience*, 23: 10224–10230.
- Byström, S. and Fransson-Hall, C. (1994). Acceptability of intermittent handgrip contractions based on physiological response. *Human Factors*, 36: 158–171.
- Cabanac, M. (1986). Money versus pain: Experimental study of a conflict in humans. *Journal of the Experimental Analysis of Behavior*, 46: 37–44.
- Cabanac, M. (1971). Physiological role of pleasure. *Science*, 173: 1103–1107.
- Cabanac, M. (2006). Sensory pleasure optimizes muscular work. *Clinical and Investigative Medicine*, 29: 110–116.
- Cafarelli, E. (1982). Peripheral contributions to the perception of effort. *Medicine & Science in Sports & Exercise*, 14: 382–389.
- Cairns, S. P. (2006). Lactic acid and exercise performance - Culprit or friend? *Sports Medicine*, 36: 279–291.
- Caldwell, A. R., Lakens, D., Parlett-Pelleriti, C. M., Prochilo, G. and Aust, F. (2019). *Power analysis with superpower*.
- Cameron, O. G. (2009). Visceral brain-body information transfer. *NeuroImage*, 47: 787–794.
- Cannon, D. T., Coelho, A. C., Cao, R., Cheng, A., Porszasz, J., Casaburi, R. and Rossiter, H. B. (2016). Skeletal muscle power and fatigue at the tolerable limit of ramp-incremental exercise in COPD. *Journal of Applied Physiology*, 121: 1365–1373.
- Carifio, J. and Perla, R. (2008). Resolving the 50-year debate around using and misusing Likert scales. *Medical Education*, 42: 1150–1152.
- do Carmo, E. C., Barroso, R., Renfree, A., da Silva, N. R., Gil, S. and Tricoli, V. (2020). Affective feelings and perceived exertion during a 10-km time trial and head-to-head running race. *International Journal of Sports Physiology and Performance*, 15: 903–906.
- Carson, R. G., Riek, S., Mackey, D. C., Meichenbaum, D. P., Willms, K., Forner, M. and Byblow, W. D. (2004). Excitability changes in human forearm corticospinal projections and spinal reflex pathways during rhythmic voluntary movement of the opposite limb. *Journal of Applied Physiology*, 560: 929–940.
- Carson, R. G., Riek, S. and Shahbazzpour, N. (2002). Central and peripheral mediation of human force sensation following eccentric or concentric contractions. *Journal of Physiology*, 539: 913–925.
- Casey, A., Short, A. H., Hultman, E. and Greenhaff, P. L. (1995). Glycogen resynthesis in human muscle fibre

- types following exercise-induced glycogen depletion. *Journal of Physiology*, 483: 265–271.
- Cerderbaum, A. (2012). Alcohol metabolism. *Clinics in Liver Disease*, 46: 667–685.
- Chaudhuri, A. and Behan, P. O. (2000). Fatigue and basal ganglia. *Journal of the Neurological Sciences*, 179: 34–42.
- Chaudhuri, A. and Behan, P. O. (2004). Fatigue in neurological disorders. *The Lancet*, 363: 978–988.
- Chen, M. K. (1986). The epidemiology of self-perceived fatigue among adults. *Preventive Medicine*, 15: 74–81.
- Chong, T. T.-J., Apps, M. A. J., Giehl, K., Hall, S., Clifton, C. H. and Husain, M. (2018). Computational modelling reveals distinct patterns of cognitive and physical motivation in elite athletes. *Scientific Reports*, 8: 11888.
- Chong, T. T.-J., Apps, M., Giehl, K., Sillence, A., Grima, L. L. and Husain, M. (2017). Neurocomputational mechanisms underlying subjective valuation of effort costs. *PLoS Biology*, 15: e1002598.
- Chong, T. T.-J., Bonnelle, V. and Husain, M. (2016). Quantifying motivation with effort-based decision-making paradigms in health and disease. In: *Progress in Brain Research*. pp.71–100.
- Chong, T. T.-J., Bonnelle, V., Manohar, S., Veromann, K. R., Muhammed, K., Tofaris, G. K., Hu, M. and Husain, M. (2015). Dopamine enhances willingness to exert effort for reward in Parkinson's disease. *Cortex*, 69: 40–46.
- Christensen, M. S., Lundbye-Jensen, J., Geertsen, S. S., Petersen, T. H., Paulson, O. B. and Nielsen, J. B. (2007). Premotor cortex modulates somatosensory cortex during voluntary movements without proprioceptive feedback. *Nature Neuroscience*, 10: 417–419.
- Christian, R. J., Bishop, D. J., Billaut, F. and Girard, O. (2014). The role of sense of effort on self-selected cycling power output. *Frontiers in Physiology*, 5: 115.
- Christie, S. T. and Schrater, P. (2015). Cognitive cost as dynamic allocation of energetic resources. *Frontiers in Neuroscience*, 9: 289.
- Chtourou, H., Hammouda, O., Aloui, A. and Souissi, N. (2013). Effect of time-of-day on muscle fatigue: A review. *Journal of Novel Physiotherapies*, 3: 3.
- Clark, A. (2015). Embodied Prediction. In: T. Metzinger & J. Windt (eds) *Open MIND 7(T)*. Frankfurt am Main: MIND Group.
- Clark, A. (2013). Whatever next? Predictive brains, situated agents, and the future of cognitive science. *Behavioral and Brain Sciences*, 36: 181–204.
- Clark, B. C., Cook, S. B. and Ploutz-Snyder, L. L. (2007). Reliability of techniques to assess human neuromuscular function in vivo. *Journal of Electromyography and Kinesiology*, 17: 90–101.
- Clark, J. E., Watson, S. and Friston, K. J. (2018). What is mood? A computational perspective. *Psychological Medicine*, 48: 2277–2284.
- Coates, K. D., Aboodarda, S. J., Krüger, R. L., Martin, T., Metz, L. M., Jarvis, S. E. and Millet, G. Y. (2020). Multiple sclerosis-related fatigue: The role of impaired corticospinal responses and heightened exercise fatigability. *Journal of Neurophysiology*, 124: 1131–1143.
- Cochrane, G. D., Rizvi, S., Abrantes, A. M., Crabtree, B., Cahill, J. and Friedman, J. H. (2015). The association between fatigue and apathy in patients with either Parkinson's disease or multiple sclerosis. *Parkinsonism and Related Disorders*, 21: 1093–1095.
- Cochrane, K. C., Housh, T. J., Bergstrom, H. C., Jenkins, N. D. M., Johnson, G., Schmidt, R. J. and Cramer, J. T. (2015). Physiological responses during cycle ergometry at a constant perception of effort. *International Journal of Sports Medicine*, 36: 466–473.
- Coelho, A. C., Cannon, D. T., Cao, R., Porszasz, J., Casaburi, R., Knorst, M. M. and Rossiter, H. B. (2015). Instantaneous quantification of skeletal muscle activation, power production, and fatigue during cycle ergometry. *Journal of Applied Physiology*, 118: 646–654.
- Corcoran, A. W. and Hohwy, J. (2019). Allostasis, interoception, and the free energy principle: Feeling our way forward. In: M. Tsarkiris & H. De Preester (eds) *The interoceptive Mind: From homeostasis to awareness*.

- Oxford, UK: Oxford University Press. pp.272–292.
- Corfield, E. C., Martin, N. G. and Nyholt, D. R. (2016). Co-occurrence and symptomatology of fatigue and depression. *Comprehensive Psychiatry*, 71: 1–10.
- Craig, A. D. (2013). An interoceptive neuroanatomical perspective on feelings, energy, and effort. *Behavioral and Brain Sciences*, 36: 685–686.
- Craig, A. D. (1995). Distribution of brainstem projections from spinal lamina I neurons in the cat and the monkey. *The Journal of Comparative Neurology*, 361: 225–48.
- Craig, A. D. (2002). How do you feel? Interoception: The sense of the physiological condition of the body. *Nature Reviews. Neuroscience*, 3: 655–666.
- Craig, A. D. (2009). How do you feel - now? The anterior insula and human awareness. *Nature Reviews. Neuroscience*, 10: 59–70.
- Craig, A. D. (2003). Interoception: The sense of the physiological condition of the body. *Current Opinion in Neurobiology*, 13: 500–505.
- Craig, A. D. (2011). Significance of the insula for the evolution of human awareness of feelings from the body. *Annals of the New York Academy of Sciences*, 1225: 72–82.
- Craig, A. D., Bushnell, M. C., Zhang, E.-T. and Blomqvist, A. (1994). A thalamic nucleus specific for pain and temperature sensation. *Nature*, 372: 770–773.
- Craig, C. L., Marshall, A. L., Sjöström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F. and Oja, P. (2003). International Physical Activity Questionnaire: 12-country reliability and validity. *Medicine & Science in Sports & Exercise*, 35: 1381–1395.
- Crewe, H., Tucker, R. and Noakes, T. D. (2008). The rate of increase in rating of perceived exertion predicts the duration of exercise to fatigue at a fixed power output in different environmental conditions. *European Journal of Applied Physiology*, 103: 569–577.
- Critchley, H. D. and Garfinkel, S. N. (2017). Interoception and emotion. *Current Opinion in Psychology*, 17: 7–14.
- Critchley, H. D. and Harrison, N. A. (2013). Visceral influences on brain and behavior. *Neuron*, 77: 624–638.
- Critchley, H. D., Wiens, S., Rotshtein, P., Öhman, A. and Dolan, R. J. (2004). Neural systems supporting interoceptive awareness. *Nature - Neuroscience*, 7: 189–195.
- Croxson, P. L., Walton, M. E., Reilly, J. X. O., Behrens, T. E. J. and Rushworth, M. F. S. (2009). Effort-based cost-benefit valuation and the human brain. *Brain*, 29: 4531–4541.
- Van Cutsem, J., Marcora, S. M., De Pauw, K., Bailey, S. J., Meeusen, R. and Roelands, B. (2017). The effects of mental fatigue on physical performance: A systematic review. *Sports Medicine*, 47: 1569–1588.
- Damasio, A. and Carvalho, G. B. (2013). The nature of feelings: Evolutionary and neurobiological origins. *Nature Reviews. Neuroscience*, 14: 143–52.
- Damasio, A. R., Everitt, B. J. and Bishop, D. (1996). The somatic marker hypothesis and the possible functions of the prefrontal cortex. *Philosophical Transactions of the Royal Society of London*, 351: 1413–1420.
- Dantzer, R., Heijnen, C. J., Kavelaars, A., Laye, S. and Capuron, L. (2014). The neuroimmune basis of fatigue. *Trends in Neurosciences*, 37: 39–46.
- Dauids, K., Glazier, P., Araújo, D. and Bartlett, R. (2003). Movement systems as dynamical systems. *Sports Medicine*, 33: 245–260.
- Davis, M. P. and Walsh, D. (2010). Mechanisms of fatigue. *The Journal of Supportive Oncology*, 8: 164–174.
- Dayan, P., Hinton, G. E., Neal, R. M. and Zemel, R. S. (1995). The Helmholtz machine. *Neural computation*, 7: 889–904.
- Decorte, N., Lafaix, P. A., Millet, G. Y., Wuyam, B. and Verges, S. (2012). Central and peripheral fatigue kinetics during exhaustive constant-load cycling. *Scandinavian Journal of Medicine and Science in Sports*, 22: 381–

- Dekerle, J., Ansdell, P., Schäfer, L., Greenhouse-Tucknott, A. and Wrightson, J. G. (2019). Methodological issues with the assessment of voluntary activation using transcranial magnetic stimulation in the knee extensors. *European Journal of Applied Physiology*, 119: 991–1005.
- Dekerle, J., Greenhouse-Tucknott, A., Wrightson, J. G., Schäfer, L. and Ansdell, P. (2019). Improving the measurement of TMS-assessed voluntary activation in the knee extensors. *PLoS ONE*, 14: e0216981.
- Dempsey, J. A., Blain, G. M. and Amann, M. (2014). Are type III-IV muscle afferents required for a normal steady-state exercise hyperpnoea in humans? *Journal of Physiology*, 592: 463–74.
- Deng, N., Guyer, R. and Ware Jr, J. E. (2015). Energy, fatigue, or both? A bifactor modeling approach to the conceptualization and measurement of vitality. *Quality of Life Research*, 24: 81–93.
- Deng, Z.-D., Lisanby, S. H. and Peterchev, A. V. (2013). Electric field depth–focality tradeoff in transcranial magnetic stimulation: Simulation comparison of 50 coil designs. *Brain Stimulation*, 6: 1–13.
- Dierkes, K., Mattioni Maturana, F., Rösel, I., Martus, P., Nieß, A. M., Thiel, A. and Sudeck, G. (2021). Different endurance exercise modalities, different affective response: A within-subject study. *Frontiers in Psychology*, 12: 3411.
- Dimitrov, G. V., Arabadzhiev, T. I., Hogrel, J. Y. and Dimitrova, N. A. (2008). Simulation analysis of interference EMG during fatiguing voluntary contractions. Part II - Changes in amplitude and spectral characteristics. *Journal of Electromyography and Kinesiology*, 18: 35–43.
- Dimitrova, N. A. and Dimitrov, G. V. (2003). Interpretation of EMG changes with fatigue: Facts, pitfalls, and fallacies. *Journal of Electromyography and Kinesiology*, 13: 13–36.
- Dittner, A. J., Wessely, S. C. and Brown, R. G. (2004). The assessment of fatigue: A practical guide for clinicians and researchers. *Journal of Psychosomatic Research*, 56: 157–170.
- Dobrushina, O. R., Arina, G. A., Dobrynina, L. A., Novikova, E. S., Gubanova, M. V., Belopasova, A. V., Vorobeva, V. P., Suslina, A. D., Pechenkova, E. V., Perepelkina, O. S., Kremneva, E. I. and Krotenkova, M. V. (2021). Sensory integration in interoception: Interplay between top-down and bottom-up processing. *Cortex*, 144: 185–197.
- Doeltegen, S. H. and Ridding, M. C. (2010). Behavioural exposure and sleep do not modify corticospinal and intracortical excitability in the human motor system. *Clinical Neurophysiology*, 121: 448–452.
- Doix, A.-C. M., Lefèvre, F. and Colson, S. S. (2013). Time course of the cross-over effect of fatigue on the contralateral muscle after unilateral exercise. *PLoS ONE*, 8: e64910.
- Doix, A.-C. M., Wachholz, F., Marterer, N., Immler, L., Insam, K. and Federolf, P. A. (2018). Is the cross-over effect of a unilateral high-intensity leg extension influenced by the sex of the participants? *Biology of Sex Differences*, 9: 29.
- De Doncker, W., Charles, L., Ondobaka, S. and Kuppaswamy, A. (2020). Exploring the relationship between effort perception and poststroke fatigue. *Neurology*, 95: e3321 LP-e3330.
- De Doncker, W., Dantzer, R., Ormstad, H. and Kuppaswamy, A. (2018). Mechanisms of poststroke fatigue. *Journal of Neurology, Neurosurgery and Psychiatry*, 89: 287–293.
- Douven, E., Köhler, S., Schievink, S. H. J., Van Oostenbrugge, R. J., Staals, J., Verhey, F. R. J. and Aalten, P. (2017). Temporal associations between fatigue, depression, and apathy after stroke: Results of the cognition and affect after stroke, a prospective evaluation of risks study. *Cerebrovascular Diseases*, 44: 330–337.
- Driver, H. S. and Taylor, S. R. (2000). Exercise and sleep. *Sleep Medicine Reviews*, 4: 387–402.
- Drouin, P. J., Walsh, J. J., Swart, J., Day, T. A. and Tschakovsky, M. E. (2021). Perceived mental strain dissociates from perceived physical strain during relative intensity submaximal exercise on ascent from low to high altitude. *Physiological Reports*, 9: e14934.
- van Duinen, H., Renken, R., Maurits, N. and Zijdwind, I. (2007). Effects of motor fatigue on human brain activity, an fMRI study. *NeuroImage*, 35: 1438–1449.

- Duncan, S. and Barrett, L. F. (2007). Affect is a form of cognition: A neurobiological analysis. *Cognition & Emotion*, 21: 1184–1211.
- Eaton, L. G. and Funder, D. C. (2001). Emotional experience in daily life: Variance, variability and rate of change. *Emotion*, 1: 413–421.
- Ede, A., Sullivan, P. J. and Feltz, D. L. (2017). Self-doubt: Uncertainty as a motivating factor on effort in an exercise endurance task. *Psychology of Sport & Exercise*, 28: 31–36.
- Edgley, S. A. and Winter, A. P. (2004). Different effects of fatiguing exercise on corticospinal and transcallosal excitability in human hand area motor cortex. *Experimental Brain Research*, 159: 530–536.
- Edwards, A. M. and Polman, R. C. J. (2013). Pacing and awareness: Brain regulation of physical activity. *Sports Medicine*, 43: 1057–1064.
- Edwards, B. J., Pullinger, S. A., Kerry, J. W., Robinson, W. R., Reilly, T. P., Robertson, C. M. and Waterhouse, J. M. (2013). Does raising morning rectal temperature to evening levels offset the diurnal variation in muscle force production? *Chronobiology International*, 30: 486–501.
- Ekkekakis, P. (2003). Pleasure and displeasure from the body: Perspectives from exercise. *Cognition & Emotion*, 17: 213–239.
- Ekkekakis, P. and Brand, R. (2019). Affective responses to and automatic affective valuations of physical activity: Fifty years of progress on the seminal question in exercise psychology. *Psychology of Sport & Exercise*, 42: 130–137.
- Ekkekakis, P., Hall, E. E. and Petruzzello, S. J. (2004). Practical markers of the transition from aerobic to anaerobic metabolism during exercise: Rationale and a case for affect-based exercise prescription. *Preventive Medicine*, 38: 149–159.
- Ekkekakis, P., Hall, E. E. and Petruzzello, S. J. (2008). The relationship between exercise intensity and affective responses demystified: To crack the 40-year-old nut, replace the 40-year-old nutcracker! *Annals of Behavioral Medicine*, 35: 136–149.
- Ekkekakis, P., Hall, E. E. and Petruzzello, S. J. (2005). Variation and homogeneity in affective responses to physical activity of varying intensities: An alternative perspective on dose – response based on evolutionary considerations. *Journal of Sports Sciences*, 23: 477–500.
- Ekkekakis, P., Lind, E. and Vazou, S. (2010). Affective responses to increasing levels of exercise intensity in normal-weight, overweight, and obese middle-aged women. *Obesity*, 18: 79–85.
- Ekkekakis, P., Parfitt, G. and Petruzzello, S. J. (2011). The pleasure and displeasure people feel when they exercise at different intensities - Decennial update and progress towards a tripartite rationale for exercise intensity prescription. *Sports Medicine*, 41: 641–671.
- Ekkekakis, P. and Petruzzello, S. J. (1999). Acute aerobic exercise and affect: Current status, problems, and prospects regarding dose– response. *Sports Medicine*, 28: 337–374.
- El-Sayed, M. S., Ali, N. and Ali, Z. .-S. (2005). Interaction between alcohol and exercise: Physiological and haematological implications. *Sports Medicine*, 35: 257–269.
- Elmer, S. J., Amann, M., McDaniel, J., Martin, D. T. and Martin, J. C. (2014). Fatigue is specific to working muscles: No cross-over with single-leg cycling in trained cyclists. *European Journal of Applied Physiology*, 113: 479–488.
- Enoka, R. M., Almuklass, A. M., Alenazy, M., Alvarez, E. and Duchateau, J. (2021). Distinguishing between fatigue and fatigability in multiple sclerosis. *Neurorehabilitation and Neural Repair*.
- Enoka, R. M. and Duchateau, J. (2016). Translating fatigue to human performance. *Medicine & Science in Sports & Exercise*, 48: 2228–2238.
- Enoka, R. M. and Stuart, D. G. (1992). Neurobiology of muscle fatigue. *Journal of Applied Physiology*, 72: 1631–1648.
- Eston, R., Faulkner, J., St Clair Gibson, A., Noakes, T. D. and Parfitt, G. (2007). The effect of antecedent fatiguing activity on the relationship between perceived exertion and physiological activity during a constant load

- exercise task. *Psychophysiology*, 44: 779–786.
- Eston, R., Stansfield, R., Westoby, P. and Parfitt, G. (2012). Effect of deception and expected exercise duration on psychological and physiological variables during treadmill running and cycling. *Psychophysiology*, 49: 462–469.
- Etkin, A., Büchel, C. and Gross, J. J. (2015). The neural bases of emotion regulation. *Nature Reviews Neuroscience*, 16: 693–700.
- Ezagouri, S., Zwighaft, Z., Sobel, J., Baillieul, S., Doutreleau, S., Ladeux, B., Golik, M., Verges, S. and Asher, G. (2019). Physiological and molecular dissection of daily variance in exercise capacity. *Cell Metabolism*, 30: 1–14.
- Farina, D., Merletti, R. and Enoka, R. M. (2004). The extraction of neural strategies from the surface EMG. *Journal of Applied Physiology*, 96: 1486–1495.
- Faulkner, J., Parfitt, G. and Eston, R. (2008). The rating of perceived exertion during competitive running scales with time. *Psychophysiology*, 45: 977–985.
- Feinstein, J. S., Adolphs, R., Damasio, A. and Tranel, D. (2011). The human amygdala and the induction and experience of fear. *Current Biology*, 21: 34–38.
- Feldman, H. and Friston, K. J. (2010). Attention, uncertainty, and free-energy. *Frontiers in Human Neuroscience*, 4: 215.
- Ferguson, C., Cannon, D. T., Wylde, L. A., Benson, A. P. and Rossiter, H. B. (2016). Power-velocity and power-efficiency implications in the limitation of ramp incremental cycle ergometry: Reply to Morales-Alamo et al. *Journal of Applied Physiology*, 120: 477.
- Ferguson, C., Wylde, L. A., Benson, A. P., Cannon, D. T. and Rossiter, H. B. (2016). No reserve in isokinetic cycling power at intolerance during ramp incremental exercise in endurance-trained men. *Journal of Applied Physiology*, 120: 70–77.
- Fernandes, A., Galbo, H., Kjaer, M., Mitchell, J. H., Secher, N. H. and Thomas, S. N. (1990). Cardiovascular and ventilatory responses to dynamic exercise during epidural anaesthesia in man. *Journal of Physiology*, 420: 281–293.
- Fernandez, C., Firdous, S., Jehangir, W., Behm, B., Mehta, Z., Berger, A. and Davis, M. (2020). Cancer-related fatigue: Perception of effort or task Failure? *American Journal of Hospice and Palliative Care*, 31: 34–40.
- Ficco, L., Mancuso, L., Manuello, J., Teneggi, A., Liloia, D., Duca, S., Costa, T., Kovacs, G. Z. and Cauda, F. (2021). Disentangling predictive processing in the brain: A meta-analytic study in favour of a predictive network. *Scientific Reports*, 11: 16258.
- Finn, H. T., Rouffet, D. M., Kennedy, D. S., Green, S. and Taylor, J. L. (2018). Motoneuron excitability of the quadriceps decreases during a fatiguing submaximal isometric contraction. *Journal of Applied Physiology*, 124: 970–979.
- Fisher, J. P., Ironside, M. and Steele, J. (2017). Heavier and lighter load resistance training to momentary failure produce similar increases in strength with differing degrees of discomfort. *Muscle & Nerve*, 56: 797–803.
- Fisher, J. P., Stuart, C., Steele, J., Gentil, P. and Giessing, J. (2018). Heavier- and lighter-load isolated lumbar extension resistance training produce similar strength increases, but different perceptual responses, in healthy males and females. *PeerJ*, 6: e6001.
- Fleming, S. M. and Dolan, R. J. (2012). The neural basis of metacognitive ability. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 367: 1338–1349.
- Flinn, N. A. and Stube, J. E. (2010). Post-stroke fatigue: Qualitative study of three focus groups. *Occupational Therapy International*, 17: 81–91.
- Flynn, F. G. (1999). Anatomy of the insula functional and clinical correlate. *Aphasiology*, 13: 55–78.
- Focht, B. C., Knapp, D. J., Gavin, T. P., Raedeker, T. D. and Hickner, R. C. (2007). Affective and self-efficacy responses to acute aerobic exercise in sedentary older and younger adults. *Journal of Aging and Physical Activity*, 15: 123–138.

- Framorando, D. and Gendolla, G. H. E. (2019). It's about effort: Impact of implicit affect on cardiovascular response is context dependent. *Psychophysiology*, 56: e13436.
- Franklin, D. W. and Wolpert, D. M. (2011). Computational mechanisms of sensorimotor control. *Neuron*, 72: 425–442.
- Frick, R. W. (1998). A better stopping rule for conventional statistical tests. *Behavior Research Methods, Instruments & Computers*, 30: 690–697.
- Friedman, D. B., Brennum, J., Sztuk, F., Hansen, O. B., Clifford, P. S., Bach, F. W., Arendt-Nielsen, L., Mitchell, J. H. and Secher, N. H. (1993). The effect of epidural anaesthesia with 1% lidocaine on the pressor response to dynamic exercise in man. *Journal of Physiology*, 470: 681–691.
- Friedman, J. H., Brown, R. G., Comella, C., Garber, C. E., Krupp, L. B., Lou, J.-S., Marsh, L., Nail, L., Shulman, L. and Taylor, C. B. (2007). Fatigue in Parkinson's disease: A review. *Movement Disorders*, 22: 297–308.
- Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 360: 815–836.
- Friston, K. (2009). The free-energy principle: A rough guide to the brain? *Trends in Cognitive Sciences*, 13: 293–301.
- Friston, K. (2010). The free-energy principle: A unified brain theory? *Nature Reviews Neuroscience*, 11: 127–138.
- Friston, K. (2011). What is optimal about motor control? *Neuron*, 72: 488–498.
- Friston, K. J., FitzGerald, T., Rigoli, F., Schwartenbeck, P., O'Doherty, J. P. and Pezzulo, G. (2016). Active inference and learning. *Neuroscience and Biobehavioral Reviews*, 68: 862–879.
- Friston, K. J. and Kiebel, S. (2009). Predictive coding under the free-energy principle. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 364: 1211–1221.
- Friston, K. J., Lawson, R. and Frith, C. D. (2013). On hyperpriors and hypopriors: Comment on Pellicano and Burr. *Trends in Cognitive Sciences*, 17: 1.
- Friston, K., Schwartenbeck, P., Fitzgerald, T., Moutoussis, M., Behrens, T. and Dolan, R. J. (2014). The anatomy of choice: dopamine and decision-making. *Philosophical Transactions of the Royal Society B*, 369: 20130481.
- Friston, K., Shiner, T., FitzGerald, T., Galea, J. M., Adams, R., Brown, H., Dolan, R. J., Moran, R., Stephan, K. E. and Bestmann, S. (2012). Dopamine, affordance and active inference. *PLoS Computational Biology*, 8: e1002327.
- Frömer, R., Lin, H., Dean Wolf, C. K., Inzlicht, M. and Shenhav, A. (2021). Expectations of reward and efficacy guide cognitive control allocation. *Nature Communications*, 12: 1030.
- Fukuda, K., Straus, S. E., Hickie, I., Sharpe, M. C., Dobbins, J. G. and Komaroff, A. (1994). The chronic fatigue syndrome: A comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Annals of Internal Medicine*, 121: 953–959.
- Fukutomi, M. and Carlson, B. A. (2020). A history of corollary discharge: Contributions of mormyrid weakly electric fish. *Frontiers in Integrative Neuroscience*, 14: 42.
- Gabriel, B. M. and Zierath, J. R. (2017). The limits of exercise physiology: From performance to health. *Cell Metabolism*, 25: 1000–1011.
- Gagnon, P., Bussièrès, J. S., Ribeiro, F., Gagnon, S. L., Saey, D., Gagné, N., Provencher, S. and Maltais, F. (2012). Influences of spinal anesthesia on exercise tolerance in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, 186: 606–615.
- Gailliot, M. T., Baumeister, R. F., Dewall, C. N., Maner, J. K., Plant, E. A., Tice, D. M., Brewer, L. E. and Schmeichel, B. J. (2007). Self-control relies on glucose as a limited energy source: Will power is more than a metaphor. *Journal of Personality and Social Psychology*, 92: 325–336.
- Gallucci, M. (2019). GAMLj: General analyses for linear models.

- Gandevia, S. C. (1996). Kinesthesia: Roles for afferent signals and motor commands. In: L.B. Rowell & J.T. Shepherd (eds) *Handbook on integration of motor, circulatory, respiratory and metabolic control during exercise*. Bethesda: American Physiological Society. pp.128–172.
- Gandevia, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews*, 81: 1725–1789.
- Gandevia, S. C., Allen, G. M., Butler, J. E. and Taylor, J. L. (1996). Supraspinal factors in human muscle fatigue: Evidence for suboptimal output from the motor cortex. *Journal of Physiology*, 490: 529–536.
- Gandevia, S. C. and McCloskey, D. I. (1977). Changes in motor commands, as shown by changes in perceived heaviness, during partial curarization and peripheral anaesthesia in man. *Journal of Physiology*, 272: 673–689.
- Garfinkel, S. N. and Critchley, H. D. (2013). Interoception, emotion and brain: New insights link internal physiology to social behaviour. Commentary on: “Anterior insular cortex mediates bodily sensibility and social anxiety” by Terasawa et al. (2012). *Social Cognitive and Affective Neuroscience*, 8: 231–234.
- Garfinkel, S. N., Manassei, M. F., Hamilton-Fletcher, G., den Bosch, Y. I., Critchley, H. D. and Engles, M. (2016). Interoceptive dimensions across cardiac and respiratory axes. *Philosophical Transactions of the Royal Society B*, 371: 20160014.
- Garfinkel, S. N., Seth, A. K., Barrett, A. B., Suzuki, K. and Critchley, H. D. (2015). Knowing your own heart: Distinguishing interoceptive accuracy from interoceptive awareness. *Biological Psychology*, 104: 65–74.
- Gasquoine, P. G. (2014). Contributions of the insula to cognition and emotion. *Neuropsychology Review*, 24: 77–87.
- Gendolla, G. H. E. and Wright, R. A. (2009). Effort. In: D. Sander & K.R. Scherer (eds) *The Oxford companion to emotion and the affective science*. New York, NY: Oxford University Press. pp.134–135.
- Gendron, M. and Barrett, L. F. (2009). Reconstructing the past: A century of ideas about emotion in psychology. *Emotional Review*, 4: 316–339.
- Gergelyfi, M., Jacob, B., Olivier, E. and Zénon, A. (2015). Dissociation between mental fatigue and motivational state during prolonged mental activity. *Frontiers in Behavioral Neuroscience*, 9: 176.
- Gherman, S. and Philiastides, M. G. (2018). Human VMPFC encodes early signatures of confidence in perceptual decisions. *eLife*, 7: e38293.
- Giboin, L.-S. and Wolff, W. (2019). The effect of ego depletion or mental fatigue on subsequent physical endurance performance: A meta-analysis. *Performance Enhancement & Health*, 7: 100150.
- Gibson, H., Carroll, N., Clague, J. E. and Edwards, R. H. T. (1993). Exercise performance and fatigability in patients with chronic fatigue syndrome. *Journal of Neurology, Neurosurgery & Psychiatry*, 56: 993–998.
- Giles, G. E., Cantelon, J. A., Eddy, M. D., Brunyé, T. T., Urry, H. L., Taylor, H. A., Mahoney, C. R. and Kanarek, R. B. (2018). Cognitive reappraisal reduces perceived exertion during endurance exercise. *Motivation and Emotion*, 42: 482–496.
- Girard, O., Billaut, F., Christian, R. J., Bradley, P. S. and Bishop, D. J. (2017). Exercise-related sensations contribute to decrease power during repeated cycle sprints with limited influence on neural drive. *European Journal of Applied Physiology*, 117: 2171–2179.
- Goh, H.-T., Stewart, J. C., Becker, K. and Hung, C.-J. (2022). Perceived effort for reaching is associated with self-reported fatigue. *Journal of Motor Behavior*, 54: 14–26.
- Goodall, S., Romer, L. M. and Ross, E. Z. (2009). Voluntary activation of human knee extensors measured using transcranial magnetic stimulation. *Experimental Physiology*, 94: 995–1004.
- Grabiner, M. D. and Owings, T. M. (1999). Effects of eccentrically and concentrically induced unilateral fatigue on the involved and uninvolved limbs. *Journal of Electromyography and Kinesiology*, 9: 185–189.
- Graham, T. E. (2001). Caffeine and exercise: Metabolism, endurance and performance. *Sports Medicine*, 31: 785–807.

- Grandjean da Costa, K., Urry, H. L., Fontes, E. B., Elliott, G., Cantelon, J. A. and Giles, G. E. (2021). Cognitive reappraisal mitigates affective valence declines during exercise at the ventilatory threshold. *International Journal of Sport and Exercise Psychology*, 1–19.
- Green, D. M. and Swets, J. A. (1966). *Signal detection theory and psychophysics*. New York: Wiley.
- Greenhouse-Tucknott, A., Butterworth, J. B., Wrightson, J. G., Smeeton, N. J., Critchley, H. D., Dekerle, J. and Harrison, N. A. (2022). Towards the unity of pathological and exertional fatigue: A predictive processing model. *Cognitive, Affective, & Behavioral Neuroscience*, 22: 215–228.
- Greenhouse-Tucknott, A., Pickering, S., Butterworth, J., Smeeton, N., Wrightson, J. and Dekerle, J. (2021). Prolonged cognitive activity increases perception of fatigue but does not influence perception of effort, affective valence, or performance during subsequent isometric endurance exercise. *Sport, Exercise and Performance Psychology*.
- Greenhouse, G. and Geisser, S. (1959). On methods in the analysis of profile data. *Psychometrika*, 24: 95–112.
- Grotle, A.-K., Macefield, V. G., Farquhar, W. B., O’Leary, D. S. and Stone, A. J. (2020). Recent advances in exercise pressor reflex function in health and disease. *Autonomic Neuroscience: Basic and Clinical*, 228: 102698.
- Gruet, M., Temesi, J., Rupp, T., Levy, P., Verges, S. and Millet, G. Y. (2014). Dynamics of corticospinal changes during and after a high-intensity quadriceps exercise. *Experimental Physiology*, 99: 1053–1064.
- Gu, X., Hof, P. R., Friston, K. J. and Fan, J. (2013). Anterior insular cortex and emotional awareness. *Journal of Comparative Neurology*, 521: 3371–3388.
- Guette, M., Gondin, J. and Martin, A. (2005). Time-of-day effect on the torque and neuromuscular properties of dominant and non-dominant quadriceps femoris. *Chronobiology International*, 22: 541–558.
- Hall, M. M., Rajasekaran, S., Thomsen, T. W. and Peterson, A. R. (2016). Lactate: Friend or foe. *PM & R*, 8: S8–S15.
- Halper, L. R. and Vancouver, J. B. (2016). Self-efficacy’s influence on persistence on a physical task: Moderating effect of performance feedback ambiguity. *Psychology of Sport & Exercise*, 22: 170–177.
- Halperin, I., Aboodarda, S. J. and Behm, D. G. (2014). Knee extension fatigue attenuates repeated force production of the elbow flexors. *European Journal of Sport Science*, 14: 823–829.
- Halperin, I., Chapman, D. W. and Behm, D. G. (2015). Non-local muscle fatigue: Effects and possible mechanisms. *European Journal of Applied Physiology*, 115: 2031–2048.
- Halperin, I., Copithorne, D. B. and Behm, D. G. (2014). Unilateral isometric muscle fatigue decreases force production and activation of contralateral knee extensors but not elbow flexors. *Applied Physiology, Nutrition, and Metabolism*, 39: 1338–1344.
- Halperin, I. and Emanuel, A. (2020). Rating of perceived effort: Methodological concerns and future directions. *Sports Medicine*, 50: 679–687.
- Hamilton, A. L., Killian, K. J., Summers, E. and Jones, N. L. (1996). Quantification of intensity of sensations during muscular work by normal subjects. *Journal of Applied Physiology*, 81: 1156–1161.
- Hamilton, A. R. and Behm, D. G. (2017). The effect of prior knowledge of test endpoint on non-local muscle fatigue. *European Journal of Applied Physiology*, 117: 651–663.
- Hampson, D. B., St Clair Gibson, A., Lambert, M. I. and Noakes, T. D. (2001). The influence of sensory cues on the perception of exertion during exercise and central regulation of exercise performance. *Sports Medicine*, 31: 935–952.
- Hardy, C. J. and Rejeski, W. J. (1989). Not what, but how one feels: The measurement of affect during exercise. *Journal of Sport & Exercise Psychology*, 11: 304–317.
- Harpe, S. E. (2015). How to analyze Likert and other rating scale data. *Currents in Pharmacy Teaching and Learning*, 7: 836–850.
- Harris, A. and Lim, S.-L. (2016). Temporal dynamics of sensorimotor networks in effort-based cost-benefit

- valuation: Early emergence and late net value integration. *Journal of Neuroscience*, 36: 7167–7183.
- Harris, S. and Bray, S. R. (2019). Effects of mental fatigue on exercise decision-making. *Psychology of Sport & Exercise*, 44: 1–8.
- Harris, S. and Bray, S. R. (2021). Mental fatigue, anticipated effort, and subjective valuations of exercising predict choice to exercise or not: A mixed-methods study. *Psychology of Sport & Exercise*, 54: 101924.
- Harrison, N. A., Brydon, L., Walker, C., Gray, M. A., Steptoe, A., Dolan, R. J. and Critchley, H. D. (2009). Neural origins of human sickness in interoceptive responses to inflammation. *Biological Psychiatry*, 66: 415–422.
- Harrison, N. A., Cooper, E., Dowell, N. G., Keramida, G., Voon, V., Critchley, H. D. and Cercignani, M. (2015). Quantitative magnetization transfer imaging as a biomarker for effects of systemic inflammation on the brain. *Biological Psychiatry*, 78: 49–57.
- Harrison, N. A., Gray, M. A., Gianaros, P. J. and Critchley, H. D. (2010). The embodiment of emotional feelings in the brain. *Journal of Neuroscience*, 30: 12878–12884.
- Hartman, M. E., Ekkekakis, P., Dicks, N. D. and Pettitt, R. W. (2019). Dynamics of pleasure-displeasure at the limit of exercise tolerance: Conceptualizing the sense of exertional physical fatigue as an affective response. *Journal of Experimental Biology*, 222: jeb186585.
- Hartmann, M. N., Hager, O. M., Tobler, P. N. and Kaiser, S. (2013). Parabolic discounting of monetary rewards by physical effort. *Behavioural Processes*, 100: 192–196.
- Havlikova, E., van Dijk, J. P., Rosenberger, J., Nagyova, I., Middel, B., Dubayova, T., Gdovinova, Z. and Groothoff, J. W. (2008). Fatigue in Parkinson’s disease is not related to excessive sleepiness or quality of sleep. *Journal of the Neurological Sciences*, 270: 107–113.
- Havlikova, E., Rosenberger, J., Nagyova, I., Middel, B., Dubayova, T., Gdovinova, Z., Van Dijk, J. P. and Groothoff, J. W. (2008). Impact of fatigue on quality of life in patients with Parkinson’s disease. *European Journal of Neurology*, 15: 475–480.
- Hawley, J. A., Hargreaves, M., Joyner, M. J. and Zierath, J. R. (2014). Integrative biology of exercise. *Cell*, 159: 738–749.
- Hayes, S. G., Kindig, A. E. and Kaufman, M. P. (2006). Cyclooxygenase blockade attenuates responses of group III and IV muscle afferents to dynamic exercise in cats. *American Journal of Physiology - Heart and Circulatory Physiology*, 290: H2239–H2246.
- Helmholtz, H. (1860). *Handbuch der Physiologischen Optik*. J.P.C. Southhall (ed.). New York, NY: Dover.
- Henry, J. D. and Crawford, J. R. (2005). The short-form version of the Depression Anxiety Stress Scales (DASS-21): Construct validity and normative data in a large non-clinical sample. *British Journal of Clinical Psychology*, 44: 227–239.
- Herbert, B. M., Pollatos, O. and Schandry, R. (2007). Interoceptive sensitivity and emotion processing: An EEG study. *International Journal of Psychophysiology*, 65: 214–227.
- Herbert, B. M., Ulbrich, P. and Schandry, R. (2007). Interoceptive sensitivity and physical effort: Implications for the self-control of physical load in everyday life. *Psychophysiology*, 44: 194–202.
- Herlofson, K. and Kluger, B. M. (2017). Fatigue in Parkinson’s disease. *Journal of the Neurological Sciences*, 374: 38–41.
- Hermens, H. J., Freriks, B., Disselhorst-Klug, C. and Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *Journal of Electromyography and Kinesiology*, 10: 361–374.
- Heuchert, J. P. and McNair, D. M. (2012). *The Profile of Mood States 2nd Edition (POMS 2)*. North Tonawanda, NY: Multi-Health Systems.
- Hezemans, F. H., Wolpe, N. and Rowe, J. B. (2020). Apathy is associated with reduced precision of prior beliefs about action outcomes. *Journal of Experimental Psychology: General*, 149: 1767–1777.
- Hill, A. B. and Perkins, R. E. (1985). Towards a model of boredom. *British Journal of Psychology*, 76: 235–240.

- Hill, A. V., Long, C. H. N. and Lupton, H. (1924). Muscular exercise, lactic acid and the supply and utilisation of oxygen: Parts VII-VIII. *Proceedings of the Royal Society of London. Series B, Biological Sciences*, 97: 155–176.
- Hill, A. V. and Lupton, H. (1923). Muscular exercise, lactic acid, and the supply and utilization of oxygen. *Quarterly Journal of Medicine*, 16: 135–171.
- Hilty, L., Lutz, K., Maurer, K., Rodenkirch, T., Spengler, C. M., Boutellier, U., Jäncke, L. and Amann, M. (2011). Spinal opioid receptor-sensitive muscle afferents contribute to the fatigue-induced increase in intracortical inhibition in healthy humans. *Experimental Physiology*, 96: 505–517.
- Hiser, J. and Koenigs, M. (2018). The multifaceted role of the ventromedial prefrontal cortex in emotion, decision making, social cognition, and psychopathology. *Biological Psychiatry*, 83: 638–647.
- Hjollund, N. H., Andersen, J. H. and Bech, P. (2007). Assessment of fatigue in chronic disease: A bibliographic study of fatigue measurement scales. *Health and Quality of Life Outcomes*, 5: 12.
- Hobbins, L., Gaoua, N., Hunter, S. and Girard, O. (2019). Psycho-physiological responses to perceptually-regulated interval runs in hypoxia and normoxia. *Physiology & Behavior*, 209: 112611.
- Hobbins, L., Hunter, S., Gaoua, N. and Girard, O. (2021). Short-term perceptually regulated interval-walk training in hypoxia and normoxia in overweight-to-obese adults. *Journal of Sports Science and Medicine*, 20: 45–51.
- Hockey, G. R. J. (2011). A motivational control theory of cognitive fatigue. In: P.L. Ackerman (ed.) *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. Washington, DC: American Psychological Association. pp.167–188.
- Hockey, R. (2013). *The psychology of fatigue: Work, effort and control*. Cambridge University Press.
- Hogan, P. S., Chen, S. X., Teh, W. W. and Chib, V. S. (2020). Neural mechanisms underlying the effects of physical fatigue on effort-based choice. *Nature Communications*, 11: 4026.
- Hohwy, J. (2012). Attention and conscious perception in the hypothesis testing brain. *Frontiers in Psychology*, 3: 1–14.
- Hohwy, J. (2014). The self-evidencing brain. *Noûs*, 50: 259–285.
- Holgado, D. and Sanabria, D. (2020). Does self-paced exercise depend on executive processing? A narrative review of the current evidence. *International Review of Sport and Exercise Psychology*: 1–24.
- Holgado, D., Sanabria, D., Perales, J. C. and Vadillo, M. A. (2020). Mental fatigue might be not so bad for exercise performance after all: A systematic review and bias-sensitive meta-analysis. *Journal of Cognition*, 3: 38.
- Holgado, D., Troya, E., Perales, J. C., Vadillo, M. A. and Sanabria, D. (2020). Does mental fatigue impair physical performance? A replication study. *European Journal of Sport Science*.
- Holroyd, C. B. (2016). The waste disposal problem of effortful control. In: T.S. Braver (ed.) *Motivation and cognitive control*. Routledge/Taylor & Francis Group. pp.235–260.
- von Holst, E. and Mittelstaedt, H. (1950). Das reafferenzprinzip. *Naturwissenschaften*, 37: 464–476.
- Hopstaken, J. F., van der Linden, D., Bakker, A. B. and Kompier, M. A. J. (2015). A multifaceted investigation of the link between mental fatigue and task disengagement. *Psychophysiology*, 52: 305–315.
- Hortobágyi, T., Richardson, S. P., Lomarev, M., Shamim, E. Meunier, S., Russman, H., Dang, N. and Hallett, M. (2011). Interhemispheric plasticity in humans. *Medicine & Science in Sports & Exercise*, 43: 1188–1199.
- Hossain, J. L., Ahmad, P., Reinish, L. W., Kayumov, L., Hossain, N. K. and Shapiro, C. M. (2005). Subjective fatigue and subjective sleepiness: Two independent consequences of sleep disorders? *Journal of Sleep Research*, 14: 245–253.
- Hristovski, R. and Balagué, N. (2010). Fatigue-induced spontaneous termination point—nonequilibrium phase transitions and critical behavior in quasi-isometric exertion. *Human Movement Science*, 29: 483–493.
- Hristovski, R., Venskaityte, E., Vainoras, A., Balagué, N. and Vázquez, P. (2010). Constraints controlled metastable dynamics of exercise-induced psychobiological adaptation. *Medicina*, 46: 447–453.

- Huang, H. J. and Ferris, D. P. (2009). Upper and lower limb muscle activation is bidirectionally and ipsilaterally coupled. *Medicine & Science in Sports & Exercise*, 41: 1778–1789.
- Huang, Z., Tarnal, V., Vlisides, P. E., Janke, E. L., McKinney, A. M., Picton, P., Mashour, G. A. and Hudetz, A. G. (2021). Anterior insula regulates brain network transitions that gate conscious access. *Cell Reports*, 35: 109081.
- Hudson, A. S. R. and Hasan, N. (2022). The dialectical model of fatigue in physical activity. *Fatigue: Biomedicine, Health & Behavior*: 1–13.
- Hull, C. L. (1943). *Principles of behavior*. New York: Appleton-Century.
- Hunter, S. K. (2014). Sex differences in human fatigability: Mechanisms and insight to physiological responses. *Acta Physiologica*, 210: 768–789.
- Hureau, T. J., Romer, L. M. and Amann, M. (2016). The ‘sensory tolerance limit’: A hypothetical construct determining exercise performance? *European Journal of Sport Science*, 7: 1–12.
- Hutchinson, J. C., Sherman, T., Martinovic, N. and Tenenbaum, G. (2008). The effect of manipulated self-efficacy on perceived and sustained effort. *Journal of Applied Sport Psychology*, 20: 457–472.
- Hutchinson, J. C. and Tenenbaum, G. (2006). Perceived effort — Can it be considered gestalt? *Psychology of Sport & Exercise*, 7: 463–476.
- Huynh, H. and Feldt, L. S. (1976). Estimation of the box correction for degrees of freedom from sample data in randomised block and split-plot design. *Educational Statistics*, 1: 69–82.
- Ibbotson, P., Hauert, C. and Walker, R. (2019). Effort perception is made more accurate with more effort and when cooperating with slackers. *Scientific Reports*, 9: 17491.
- Institute of Medicine (2015). *Beyond myalgic encephalomyelitis/chronic fatigue syndrome: Redefining an illness*. Washington, DC: The National Academies Press.
- Inzlicht, M. and Marcora, S. M. (2016). The Central Governor Model of exercise regulation teaches us precious little about the nature of mental fatigue and self-control failure. *Frontiers in Psychology*, 7: 656.
- Inzlicht, M., Schmeichel, B. J. and Macrae, C. N. (2014). Why self-control seems (but may not be) limited. *Trends in Cognitive Sciences*, 18: 127–131.
- Inzlicht, M., Shenhav, A. and Olivola, C. Y. (2018). The effort paradox: Effort is both costly and valued. *Trends in Cognitive Sciences*, 22: 337–349.
- Iodice, P., Calluso, C., Barca, L., Bertollo, M., Ripari, P. and Pezzulo, G. (2017). Fatigue increases the perception of future effort during decision making. *Psychology of Sport & Exercise*.
- Iodice, P., Porciello, G., Bufalari, I., Barca, L. and Pezzulo, G. (2019). An interoceptive illusion of effort induced by false heart-rate feedback. *Proceedings of the National Academy of Sciences of the United States of America*, 116: 13897–13902.
- Ishii, A., Tanaka, M., Yoshikawa, T. and Watanabe, Y. (2017). Evidence for unconscious regulation of performance in fatigue. *Scientific Reports*, 7: 16103.
- Izard, C. E. (2007). Basic emotions, natural kinds, emotion schemas, and a new paradigm. *Perspectives on Psychological Science*, 2: 260–280.
- Jacquet, T., Poulin-Charronnat, B., Bard, P. and Lepers, R. (2021). Persistence of mental fatigue on motor control. *Frontiers in Psychology*, 11: 588523.
- James, W. (1894). Physical basis of emotion. *Psychological Review*, 1: 516–529.
- James, W. (1890). *The Principles of Psychology*. Dover Publications.
- Jankowski, M. P., Rau, K. K., Ekmann, K. M., Anderson, C. E. and Koerber, H. R. (2013). Comprehensive phenotyping of group III and IV muscle afferents in mouse. *Journal of Neurophysiology*, 109: 2374–2381.
- Jason, L. A., Evans, M., Brown, M. and Porter, N. (2010). What is fatigue? Pathological and nonpathological fatigue. *PM & R*, 2: 327–331.

- Jeukendrup, A. E., Craig, N. P. and Hawley, J. A. (2000). The bioenergetics of world class cycling. *Journal of Science and Medicine in Sport*, 3: 414–433.
- Jiang, Z., Wang, X. F., Kisiel-Sajewicz, K., Yan, J. H. and Yue, G. H. (2012). Strengthened functional connectivity in the brain during muscle fatigue. *NeuroImage*, 60: 728–737.
- Joffily, M. and Coricelli, G. (2013). Emotional valence and the free-energy principle. *PLoS Computational Biology*, 9: e1003094.
- Johns, M. W. (1991). A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*, 14: 540–545.
- Johnson, M. A., Mills, D. E., Brown, P. I. and Sharpe, G. R. (2014). Prior upper body exercise reduces cycling work capacity but not critical power. *Medicine & Science in Sports & Exercise*, 46: 802–808.
- Johnson, M. A., Sharpe, G. R., Williams, N. C. and Hannah, R. (2015). Locomotor muscle fatigue is not critically regulated after prior upper body exercise. *Journal of Applied Physiology*, 119: 840–850.
- Jones, H. S., Williams, E. L., Marchant, D., Sparks, S. A., Midgley, A. W., Bridge, C. A. and McNaughton, L. (2015). Distance-dependent association of affect with pacing strategy in cycling time trials. *Medicine & Science in Sports & Exercise*, 47: 825–832.
- Jones, L. A. and Hunter, I. W. (1983a). Effect of fatigue on force sensation. *Experimental Neurology*, 81: 640–650.
- Jones, L. A. and Hunter, I. W. (1983b). Force and EMG correlates of constant effort contractions. *European Journal of Applied Physiology and Occupational Physiology*, 51: 75–83.
- Joyner, M. J. and Coyle, E. F. (2008). Endurance exercise performance: The physiology of champions. *Journal of Physiology*, 586: 35–44.
- Judd, C. M., Kenny, D. A. and McClelland, G. H. (2001). Estimating and testing mediation and moderation in within-subject designs. *Psychological Methods*, 6: 115–134.
- Jurgelis, M., Chong, W. B., Atkins, K. J., Cooper, P. S., Coxon, J. P. and Chong, T. T.-J. (2021). Heightened effort discounting is a common feature of both apathy and fatigue. *Scientific Reports*, 11: 22283.
- Kahneman, D. (1973). *Attention and effort*. Englewood Cliffs, N.J.: Prentice-Hall.
- Kaida, K., Takahashi, M., Åkerstedt, T., Nakata, A., Otsuka, Y., Haratani, T. and Fukasawa, K. (2006). Validation of the Karolinska sleepiness scale against performance and EEG variables. *Clinical Neurophysiology*, 117: 1574–1581.
- Kanai, R., Komura, Y., Shipp, S. and Friston, K. (2015). Cerebral hierarchies: Predictive processing, precision and the pulvinar. *Philosophical Transactions of the Royal Society B*, 370: 20140169.
- Karlsen, K., Larsen, J. P., Tandberg, E. and Jorgensen, K. (1999). Fatigue in patients with Parkinson's disease. *Movement Disorders*, 14: 237–241.
- Karshikoff, B., Sundelin, T. and Lasselin, J. (2017). Role of inflammation in human fatigue: Relevance of multidimensional assessments and potential neuronal mechanisms. *Frontiers in Immunology*, 8: 1–12.
- Katkin, E. S., Reed, S. D. and Deroo, C. (1983). A methodological analysis of 3 techniques for the assessment of individual-differences in heartbeat detection. *Psychophysiology*, 20: 452–452.
- Kaufman, M. P., Waldrop, T. G., Rybycki, K. J., Ordway, G. A. and Mitchell, J. H. (1984). Effects of static and rhythmic twitch contractions on the discharge of group III and IV muscle afferents. *Cardiovascular Research*, 18: 663–668.
- Kavanagh, J. J., Feldman, M. R. and Simmonds, M. J. (2016). Maximal intermittent contractions of the first dorsal interosseous inhibits voluntary activation of the contralateral homologous muscle. *Journal of Neurophysiology*, 116: 2272–2280.
- Kawamoto, J. E., Aboodarda, S. J. and Behm, D. G. (2014). Effect of differing intensities of fatiguing dynamic contractions on contralateral homologous muscle performance. *Journal of Sports Science and Medicine*, 13: 836–845.

- Kayser, B. (2003). Exercise starts and ends in the brain. *European Journal of Applied Physiology*, 90: 411–419.
- Kelso, J. A. S. (2012). Multistability and metastability: Understanding dynamic coordination in the brain. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 367: 906–918.
- Kennedy, A., Hug, F., Sveistrup, H. and Guével, A. (2013). Fatiguing handgrip exercise alters maximal force-generating capacity of plantar-flexors. *European Journal of Applied Physiology*, 113: 559–566.
- Kennedy, D. S., Fitzpatrick, S. C., Gandevia, S. C. and Taylor, J. L. (2015). Fatigue-related firing of muscle nociceptors reduces voluntary activation of ipsilateral but not contralateral lower limb muscles. *Journal of Applied Physiology*, 118: 408–418.
- Kennedy, D. S., McNeil, C. J., Gandevia, S. C. and Taylor, J. L. (2014). Fatigue-related firing of distal muscle nociceptors reduces voluntary activation of proximal muscles of the same limb. *Journal of Applied Physiology*, 116: 385–94.
- Kesar, T. M., Stinear, J. W. and Wolf, S. L. (2018). The use of transcranial magnetic stimulation to evaluate cortical excitability of lower limb musculature: Challenges and opportunities. *Restorative Neurology and Neuroscience*, 36: 333–348.
- Khalsa, S. S., Adolphs, R., Cameron, O. G., Critchley, H. D., Davenport, P. W., Feinstein, J. S., Feusner, J. D., Garfinkel, S. N., Lane, R. D., Mehling, W. E., Meuret, A. E., Nemeroff, C. B., Oppenheimer, S., Petzschner, F. H., Pollatos, O., Rhudy, J. L., Schramm, L. P., Simmons, W. K., Stein, M. B., Stephan, K. E., Van den Bergh, O., Van Diest, I., von Leupoldt, A., Paulus, M. P., Ainley, V., Al Zoubi, O., Aupperle, R., Avery, J., Baxter, L., Benke, C., Berner, L., Bodurka, J., Breese, E., Brown, T., Burrows, K., Cha, Y.-H., Clausen, A., Cosgrove, K., Deville, D., Duncan, L., Duquette, P., Ekhtiari, H., Fine, T., Ford, B., Garcia Cordero, I., Gleghorn, D., Guereca, Y., Harrison, N. A., Hassanpour, M., Hechler, T., Heller, A., Hellman, N., Herbert, B., Jarrahi, B., Kerr, K., Kirlic, N., Klabunde, M., Kraynak, T., Kriegsman, M., Kroll, J., Kuplicki, R., Lapidus, R., Le, T., Hagen, K. L., Mayeli, A., Morris, A., Naqvi, N., Oldroyd, K., Pané-Farré, C., Phillips, R., Poppa, T., Potter, W., Puhl, M., Safron, A., Sala, M., Savitz, J., Saxon, H., Schoenhals, W., Stanwell-Smith, C., Teed, A., Terasawa, Y., Thompson, K., Troups, M., Umeda, S., Upshaw, V., Victor, T., Wierenga, C., Wohlrab, C., Yeh, H., Yoris, A., Zeidan, F., Zotev, V. and Zucker, N. (2018). Interoception and mental health: A roadmap. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 3: 501–513.
- Khalsa, S. S., Rudrauf, D., Feinstein, J. S. and Tranel, D. (2009). The pathways of interoceptive awareness. *Nature Neuroscience*, 12: 1494–1496.
- Kirby, L. A. J. and Robinson, J. L. (2017). Affective mapping: An activation likelihood estimation (ALE) meta-analysis. *Brain and Cognition*, 118: 137–148.
- Kjær, M., Hanel, B., Worm, L., Perko, G., Lewis, S. F., Sahlin, K., Galbo, H. and Secher, N. H. (1999). Cardiovascular and neuroendocrine responses to exercise in hypoxia during impaired neural feedback from muscle. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, 277: R76–R85.
- Kleckner, I. R. and Quigley, K. S. (2015). An approach to mapping the neurophysiological state of the body to affective experience. In: L.F. Barrett & J.A. Russell (eds) *The psychological construction of emotion*. The Guilford Press. pp.265–301.
- Kleckner, I. R., Wormwood, J. B., Simmons, W. K., Barrett, L. F. and Quigley, K. S. (2015). Methodological recommendations for a heartbeat detection-based measure of interoceptive sensitivity. *Psychophysiology*, 52: 1432–1440.
- Kleckner, I. R., Zhang, J., Touroutoglou, A., Chanes, L., Xia, C., Simmons, W. K., Quigley, K. S., Dickerson, B. C. and Barrett, L. F. (2017). Evidence for a large-scale brain system supporting allostasis and interoception in humans. *Nature - Human Behaviour*, 1.
- Klein-Flügge, M. C., Kennerley, S. W., Saraiva, A. C., Penny, W. D. and Bestmann, S. (2015). Behavioral modeling of human choices reveals dissociable effects of physical effort and temporal delay on reward devaluation. *PLoS Computational Biology*, 11: e1004116.
- Kluger, B. M., Krupp, L. B. and Enoka, R. M. (2013). Fatigue and fatigability in neurologic illnesses: Proposal for a unified taxonomy. *Neurology*, 80: 409–416.
- van der Knaap, L. J. and van der Ham, I. J. M. (2011). How does the corpus callosum mediate interhemispheric

- transfer? A review. *Behavioural Brain Research*, 223: 211–221.
- Knapp, T. R. (1990). Treating ordinal scales as interval scales: An attempt to resolve the controversy. *Nursing Research*, 39: 121–123.
- Knicker, A. J., Renshaw, I., Oldham, A. R. H. and Cairns, S. P. (2011). Interactive processes link the multiple symptoms of fatigue in sport competition. *Sports Medicine*, 41: 307–328.
- Kniffki, K.-D., Schomburg, E. D. and Steffens, H. (1981). Synaptic effects from chemically activated fine muscle afferents upon α -motoneurons in decerebrate and spinal cats. *Brain Research*, 206: 361–370.
- Knill, D. C. and Pouget, A. (2004). The Bayesian brain: The role of uncertainty in neural coding and computation. *Trends in Neurosciences*, 27: 712–719.
- Koller, M. (2016). robustlmm: An R package for robust estimation of linear mixed-effects models. *Journal of Statistical Software*, 75: 1–24.
- de Koning, J. J., Foster, C., Bakkum, A., Kloppenburg, S., Thiel, C., Joseph, T., Cohen, J. and Porcari, J. P. (2011). Regulation of pacing strategy during athletic competition. *PLoS ONE*, 6: e15863.
- Kool, W., McGuire, J. T., Rozen, Z. B. and Botvinick, M. M. (2010). Decision making and avoidance of cognitive demand. *Journal of Experimental Psychology: General*, 139: 665–682.
- Köteles, F., Teufel, B., Körmendi, J., Ferentzi, E. and Szemerszky, R. (2020). Cardioceptive accuracy is associated with arousal but not with valence and perceived exertion under physical load. *Psychophysiology*, 57: e13620.
- Kozlowski, B., Pageaux, B., Hubbard, E. F., St. Peters, B., Millar, P. J. and Power, G. A. (2021). Perception of effort during an isometric contraction is influenced by prior muscle lengthening or shortening. *European Journal of Applied Physiology*, 121: 2531–2542.
- Krupp, L. B. and Pollina, D. A. (1996). Mechanisms and management of fatigue in progressive neurological disorders. *Current Opinion in Neurology*, 9: 456–460.
- Krupp, L. B., Serafin, D. J. and Christodoulou, C. (2010). Multiple sclerosis-associated fatigue. *Expert Review of Neurotherapeutics*, 10: 1437–1447.
- Kuppuswamy, A. (2017). The fatigue conundrum. *Brain*, 140: 2240–2245.
- Kuppuswamy, A. (2021). The neurobiology of pathological fatigue: New models, new questions. *The Neuroscientist*: 107385842098544.
- Kurniawan, I. T., Seymour, B., Talmi, D., Yoshida, W., Chater, N. and Dolan, R. J. (2010). Choosing to make an effort: The role of striatum in signaling physical effort of a chosen action. *Journal of Neurophysiology*, 104: 313–321.
- Kurzban, R. (2016). The sense of effort. *Current Opinion in Psychology*, 7: 67–70.
- Kurzban, R., Duckworth, A., Kable, J. W. and Myers, J. (2013). An opportunity cost model of subjective effort and task performance. *Behavioral and Brain Sciences*, 36: 661-679 (Open Peer Commentary 679-726).
- Küüsmaa, M., Sedliak, M. and Häkkinen, K. (2015). Effects of time-of-day on neuromuscular function in untrained men: Specific responses of high morning performers and high evening performers. *Chronobiology International*, 32: 1115–1124.
- Lafargue, G., Paillard, J., Lamarre, Y. and Sirigu, A. (2003). Production and perception of grip force without proprioception: Is there a sense of effort in deafferented subjects? *European Journal of Neuroscience*, 17: 2741–2749.
- Lakens, D. (2013). Calculating and reporting effect sizes to facilitate cumulative science: A practical primer for t-tests and ANOVAs. *Frontiers in Psychology*, 4: 863.
- Lakens, D. (2017). Equivalence tests: A practical primer for t tests, correlations, and meta-analyses. *Social Psychological and Personality Science*, 8: 355–362.
- Lambert, E. V., St Clair Gibson, A. and Noakes, T. D. (2005). Complex systems model of fatigue: Integrative homeostatic control of peripheral physiological systems during exercise in humans. *British Journal of*

Sports Medicine, 39: 52–62.

- Lang, N., Rothkegel, H., Reiber, H., Hasan, A., Sueske, E., Tergau, F., Ehrenreich, H., Wuttke, W. and Paulus, W. (2011). Circadian modulation of GABA-mediated cortical inhibition. *Cerebral Cortex*, 21: 2299–2306.
- Lange, C. (1885). *The Emotions*. Baltimore, MD: Williams & Wilkins.
- Laurin, J., Pertici, V., Dousset, E., Marqueste, T. and Decherchi, P. (2015). Group III and IV muscle afferents: Role on central motor drive and clinical implications. *Neuroscience*, 290: 543–551.
- Di Lazzaro, V. and Rothwell, J. C. (2014). Corticospinal activity evoked and modulated by non-invasive stimulation of the intact human motor cortex. *Journal of Physiology*, 592: 4115–4128.
- Leavitt, V. M. and DeLuca, J. (2010). Central fatigue: Issues related to cognition, mood and behavior, and psychiatric diagnoses. *PM & R*, 2: 332–337.
- Lee, D. (2019). The convergent, discriminant, and nomological validity of the Depression Anxiety Stress Scales-21 (DASS-21). *Journal of Affective Disorders*, 259: 136–142.
- Leproult, R., Van Reeth, O., Byrne, M. M., Sturis, J. and Van Cauter, E. (1997). Sleepiness, performance, and neuroendocrine function during sleep deprivation: Effects of exposure to bright light or exercise. *Journal of Biological Rhythms*, 12: 245–258.
- Lerdal, A., Moum, T., Wahl, A. K., Rustøen, T. and Hanestad, B. R. (2005). Fatigue in the general population: A translation and test of the psychometric properties of the Norwegian version of the fatigue severity scale. *Scandinavian Journal of Public Health*, 33: 123–130.
- Lewis, G. N., Signal, N. and Taylor, D. (2014). Reliability of lower limb motor evoked potentials in stroke and healthy populations: How many responses are needed? *Clinical Neurophysiology*, 125: 748–754.
- Lewis, G. and Wessely, S. (1992). The epidemiology of fatigue: More questions than answers. *Journal of Epidemiology and Community Health*, 46: 92–97.
- Li, Y., Power, K. E., Marchetti, P. H. and Behm, D. G. (2019). The effect of dominant first dorsal interosseous fatigue on the force production of a contralateral homologous and heterologous muscle. *Applied Physiology, Nutrition and Metabolism*, 44: 704–712.
- Lichstein, K. L., Means, M. K., Noe, S. L. and Aguillard, R. N. (1997). Fatigue and sleep disorders. *Behaviour Research and Therapy*, 35: 733–740.
- Light, A. R., Huguen, R. W., Zhang, J., Rainier, J., Liu, Z. and Lee, J. (2008). Dorsal root ganglion neurons innervating skeletal muscle respond to physiological combinations of protons, ATP, and lactate mediated by ASIC, P2X, and TRPV1. *Journal of Neurophysiology*, 100: 1184–1201.
- Lima, C. R., Sahu, P. K., Martins, D. F. and Reed, W. R. (2021). The neurophysiological impact of experimentally-induced pain on direct muscle spindle afferent response: A scoping review. *Frontiers in Cellular Neuroscience*, 15: 649529.
- Lind, A. R. and McNicol, G. W. (1967). Circulatory responses to sustained hand-grip contractions performed during other exercise, both rhythmic and static. *Journal of Physiology*, 192: 595–607.
- Lindquist, K. A., Satpute, A. B., Wager, T. D., Weber, J. and Barrett, L. F. (2016). The brain basis of positive and negative affect: Evidence from a meta-analysis of the human neuroimaging literature. *Cerebral Cortex*, 26: 1910–1922.
- Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E. and Barrett, L. F. (2012). The brain basis of emotion: A meta-analytic review. *Behavioral and Brain Sciences*, 35: 121–202.
- Liu, J. Z., Shan, Z. Y., Zhang, L. D., Sahgal, V., Brown, R. W. and Yue, G. H. (2003). Human brain activation during sustained and intermittent submaximal fatigue muscle contractions: An fMRI study. *Journal of Neurophysiology*, 90: 300–312.
- Ljunggren, G. and Johansson, S. -E. (1988). Use of submaximal measures of perceived exertion during bicycle ergometer exercise as predictors of maximal work capacity. *Journal of Sports Sciences*, 6: 189–203.
- Lloyd, A., Picton, L., Raccuglia, M., Hodder, S. and Havenith, G. (2017). Localized and systemic variations in

- central motor drive at different local skin and muscle temperatures. *American Journal of Physiology - Integrative and Comparative Physiology*, 313: R219–R228.
- Lo, S. and Andrews, S. (2015). To transform or not to transform: Using generalized linear mixed models to analyse reaction time data. *Frontiers in Psychology*, 6: 1171.
- Loge, J. H., Ekeberg, Ø. and Kaasa, S. (1998). Fatigue in the general Norwegian population: Normative data and associations. *Journal of Psychosomatic Research*, 45: 53–65.
- Löllgen, H., Ulmer, H. V., Gross, R., Wilbery, G. and Nieding, G. (1975). Muscle metabolites, force, and perceived exertion bicycling at varying pedal rates. *European Journal of Applied Physiology*, 34: 205–215.
- Louhevaara, V., Smolander, J., Aminoff, T., Korhonen, O. and Shen, N. (2000). Cardiorespiratory responses to fatiguing dynamic and isometric hand-grip exercise. *European Journal of Applied Physiology*, 82: 340–344.
- Lovibond, P. F. and Lovibond, S. H. (1995). The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. *Behaviour Research and Therapy*, 33: 335–343.
- Loy, B. D., Cameron, M. H. and O'Connor, P. J. (2018). Perceived fatigue and energy are independent unipolar states: Supporting evidence. *Medical Hypotheses*, 113: 46–51.
- Loy, B. D., O'Connor, P. J. and Dishman, R. K. (2016). Effect of acute exercise on fatigue in people with ME/CFS/SEID: A meta-analysis. *Medicine & Science in Sports & Exercise*, 48: 2003–2012.
- De Luca, C. J., Gilmore, L. D., Kuznetsov, M. and Roy, S. H. (2010). Filtering the surface EMG signal: Movement artifact and baseline noise contamination. *Journal of Biomechanics*, 43: 1573–1579.
- Luu, B. L., Day, B. L., Cole, J. D. and Fitzpatrick, R. C. (2011). The fusimotor and reafferent origin of the sense of force and weight. *Journal of Physiology*, 589: 3135–3147.
- Luu, B. L., Smith, J. L., Martin, P. G., McBain, R. A., Taylor, J. L. and Butler, J. E. (2016). Feedforward consequences of isometric contractions: Effort and ventilation. *Physiological Reports*, 4: e12882.
- MacMahon, C., Schücker, L., Hagemann, N. and Strauss, B. (2014). Cognitive fatigue effects on physical performance during running. *Journal of Sport & Exercise Psychology*, 36: 375–381.
- Maher-Edwards, L., Fernie, B. A., Murphy, G., Wells, A. and Spada, M. M. (2011). Metacognitions and negative emotions as predictors of symptom severity in chronic fatigue syndrome. *Journal of Psychosomatic Research*, 70: 311–317.
- Mairesse, O. and Neu, D. (2016). Tired of blunt tools? Sharpening the clinical assessment of fatigue and sleepiness. *Psychiatry Research*, 238: 100–108.
- Malloy, S., Genova, H., Chiaravalloti, N., DeLuca, J., Holtzheimer, P. and Wylie, G. R. (2021). Cognitive fatigue in traumatic brain injury: A pilot study comparing state and trait fatigue. *Brain Injury*, 35: 1254–1258.
- Manjaly, Z.-M., Harrison, N. A., Critchley, H. D., Do, C. T., Stefanics, G., Wenderoth, N., Lutterotti, A., Müller, A. and Stephan, K. E. (2019). Pathophysiological and cognitive mechanisms of fatigue in multiple sclerosis. *Journal of Neurology, Neurosurgery & Psychiatry*, 90: 642–651.
- Marcora, S. M. (2008). Do we really need a central governor to explain brain regulation of exercise performance? *European Journal of Applied Physiology*, 104: 929–931.
- Marcora, S. M. (2010). Effort: Perception of. In: E. B. Goldstein (ed.) *Encyclopedia of perception*. Thousand Oaks, CA: Sage. pp.380–383.
- Marcora, S. M. (2009). Perception of effort during exercise is independent of afferent feedback from skeletal muscles, heart, and lungs. *Journal of Applied Physiology*, 106: 2060–2062.
- Marcora, S. M. (2019). Psychobiology of fatigue during endurance exercise. In: C. Meijen (ed.) *Endurance Performance in Sport*. Routledge. pp.15–34.
- Marcora, S. M. (2011). Role of feedback from Group III and IV muscle afferents in perception of effort, muscle pain, and discomfort. *Journal of Applied Physiology*, 110: 1499.
- Marcora, S. M., Bosio, A. B. and de Morree, H. M. (2008). Locomotor muscle fatigue increases cardiorespiratory

- responses and reduces performance during intense cycling exercise independently from metabolic stress. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, 294: R874–R883.
- Marcora, S. M. and Staiano, W. (2010). The limit to exercise tolerance in humans: Mind over muscle? *European Journal of Applied Physiology*, 109: 763–770.
- Marcora, S. M., Staiano, W. and Manning, V. (2009). Mental fatigue impairs physical performance in humans. *Journal of Applied Physiology*, 106: 857–864.
- Marin, R. S. (1991). Apathy: A neuropsychiatric syndrome. *Journal of Neuropsychiatry and Clinical Neurosciences*, 3: 243–254.
- Marino, F. E., Gard, M. and Drinkwater, E. J. (2011). The limits to exercise performance and the future of fatigue research. *British Journal of Sports Medicine*, 45: 65–67.
- Martin, K., Meeusen, R., Thompson, K. G., Keegan, R. and Rattray, B. (2018). Mental fatigue impairs endurance performance: A physiological explanation. *Sports Medicine*, 48: 2041–2051.
- Martin, P. G. and Rattey, J. (2007). Central fatigue explains sex differences in muscle fatigue and contralateral cross-over effects of maximal contractions. *European Journal of Physiology*, 454: 957–969.
- Martin, P. G., Smith, J. L., Butler, J. E., Gandevia, S. C. and Taylor, J. L. (2006). Fatigue-sensitive afferents inhibit extensor but not flexor motoneurons in humans. *Journal of Neuroscience*, 26: 4796–4802.
- Martino, D., Tamburini, T., Zis, P., Rosoklija, G., Abbruzzese, G., Ray-Chaudhuri, K., Pelosin, E. and Avanzino, L. (2016). An objective measure combining physical and cognitive fatigability: Correlation with subjective fatigue in Parkinson's disease. *Parkinsonism and Related Disorders*, 32: 80–86.
- Massar, S. A. A., Csathó, Á. and van der Linden, D. (2018). Quantifying the motivational effects of cognitive fatigue through effort-based decision making. *Frontiers in Psychology*, 9: 843.
- Massar, S. A. A., Libedinsky, C., Weiyang, C., Huettel, S. A. and Chee, M. W. L. (2015). Separate and overlapping brain areas encode subjective value during delay and effort discounting. *NeuroImage*, 120: 104–113.
- Massar, S. A. A., Lim, J., Sasmita, K. and Chee, M. W. L. (2016). Rewards boost sustained attention through higher effort: A value-based decision making approach. *Biological Psychology*, 120: 21–27.
- Massin, O. (2017). Towards a definition of efforts. *Motivation Science*, 3: 230–259.
- Mathur, S., Eng, J. J. and MacIntyre, D. L. (2005). Reliability of surface EMG during sustained contractions of the quadriceps. *Journal of Electromyography and Kinesiology*, 15: 102–110.
- Matsangas, P. and Shattuck, N. L. (2018). Discriminating between fatigue and sleepiness in the naval operational environment. *Behavioral Sleep Medicine*, 16: 427–436.
- Matsumoto, Y., Mishima, K., Satoh, K., Shimizu, T. and Hishikawa, Y. (2002). Physical activity increases the dissociation between subjective sleepiness and objective performance levels during extended wakefulness in human. *Neuroscience Letters*, 326: 133–136.
- Matsuo, T., Ishii, A., Minami, T., Nanjo, H. and Yoshikawa, T. (2022). Neural mechanism by which physical fatigue sensation suppresses physical performance: A magnetoencephalography study. *Experimental Brain Research*, 240: 237–247.
- Matsuura, R., Hirakoba, K. and Takahashi, K. (2018). Effects of submaximal cycling at different exercise intensities on maximal isometric force output of the non-exercised elbow flexor muscles. *Physiology International*, 105: 177–187.
- Matsuura, R. and Ogata, T. (2015). Effects of fatiguing unilateral plantar flexions on corticospinal and transcallosal inhibition in the primary motor hand area. *Journal of Physiological Anthropology*, 34: 4.
- Maulchy, J. W. (1940). Significance test for sphericity of a normal η -variate distribution. *The Annals of Mathematical Statistics*, 11: 204–209.
- McAuley, E. and Courneya, K. S. (1992). Self-efficacy relationships with affective and exertion responses to exercise. *Journal of Applied Social Psychology*, 22: 312–326.
- McAuley, E., Courneya, K. S. and Lettunich, J. (1991). Effects of acute and long-term exercise on self-efficacy

- responses in sedentary, middle-aged males and females. *The Gerontologist*, 31: 534–542.
- McAuley, E., Tablot, H.-M. and Martinez, S. (1999). Manipulating self-efficacy in the exercise environment in women: Influences on affective responses. *Health Psychology*, 18: 288–294.
- McCloskey, D. I. (1981). Corollary discharges: Motor commands and perception. In: V.B. Brooks (ed.) *Handbook of physiology, the nervous system, motor control*. Bethesda: American Physiological Society. pp.1415–1447.
- McCloskey, D. I., Ebeling, P. and Goodwin, G. M. (1974). Estimation of weights and tensions and apparent involvement of a “sense of effort”. *Experimental Neurology*, 42: 220–232.
- McCormick, A., Meijen, C. and Marcora, S. M. (2015). Psychological Determinants of Whole-Body Endurance Performance. *Sports Medicine*, 45: 997–1015.
- McMorris, T. (2020). Cognitive fatigue effects on physical performance: The role of interoception. *Sports Medicine*.
- McMorris, T., Barwood, M., Hale, B. J., Dicks, M. and Corbett, J. (2018). Cognitive fatigue effects on physical performance: A systematic review and meta-analysis. *Physiology & Behavior*, 188: 103–107.
- McMorris, T., Barwood, M. J. and Corbett, J. (2018). Central fatigue theory and endurance exercise: Toward an interoceptive model. *Neuroscience and Biobehavioral Reviews*, 93: 93–107.
- McNeil, C. J., Giesebrecht, S., Gandevia, S. C. and Taylor, J. L. (2011). Behaviour of the motoneurone pool in a fatiguing submaximal contraction. *Journal of Physiology*, 589: 3533–3544.
- Medford, N. and Critchley, H. D. (2010). Conjoint activity of anterior insular and anterior cingulate cortex: Awareness and response. *Brain Structure & Function*, 214: 535–549.
- Melzack, R. and Wall, P. D. (1965). Pain mechanisms: A new theory. *Science*, 150: 971–979.
- Mense, S. (1977). Nervous outflow from skeletal muscle following chemical noxious stimulation. *Journal of Physiology*, 267: 75–88.
- Merton, P. A. (1954). Voluntary strength and fatigue. *Journal of Physiology*, 123: 553–564.
- Metzinger, T. (2017). The problem of mental action - Predictive coding without sensory sheets. In: T. Metzinger & W. Wiese (eds) *Philosophy and Predictive Processing*. Frankfurt am Main: MIND Group. p.19.
- Meyniel, F., Safra, L. and Pessiglione, M. (2014). How the brain decides when to work and when to rest: Dissociation of implicit-reactive from explicit-predictive computational processes. *PLoS Computational Biology*, 10: e1003584.
- Meyniel, F., Sergent, C., Rigoux, L., Daunizeau, J. and Pessiglione, M. (2013). Neurocomputational account of how the human brain decides when to have a break. *Proceedings of the National Academy of Sciences of the United States of America*, 110: 2641–2646.
- Micklewright, D., Kegerreis, S., Raglin, J. and Hettinga, F. (2017). Will the conscious–subconscious pacing quagmire help elucidate the mechanisms of self-paced exercise? New opportunities in dual process theory and process tracing methods. *Sports Medicine*, 47: 1231–1239.
- Micklewright, D. and Parry, D. (2010). The Central Governor Model cannot be adequately tested by observing its components in isolation. *Sports Medicine*, 40: 91–94.
- Micklewright, D., St Clair Gibson, A., Gladwell, V. and Al Salman, A. (2017). Development and validity of the Rating-of-Fatigue scale. *Sports Medicine*, 47: 2375–2393.
- Mihevic, P. M. (1981). Sensory cues for perceived exertion: A review. *Medicine & Science in Sports & Exercise*, 13: 150–163.
- Millet, G. Y. (2011). Can neuromuscular fatigue explain running strategies and performance in ultra-marathons? The flush model. *Sports Medicine*, 41: 489–506.
- Millet, G. Y., Bachasson, D., Temesi, J., Wuyam, B., Féasson, L., Vergès, S. and Lévy, P. (2012). Potential interests and limits of magnetic and electrical stimulation techniques to assess neuromuscular fatigue. *Neuromuscular Disorders*, 22: 181–186.

- Millet, G. Y., Millet, G. P., Lattier, G., Maffiuletti, N. A. and Candau, R. (2003). Alteration of neuromuscular function after a prolonged road cycling race. *International Journal of Sports Medicine*, 24: 190–194.
- Milyavskaya, M., Galla, B. M., Inzlicht, M. and Duckworth, A. (2021). More effort, less fatigue: How interest increases effort and reduces mental fatigue. *Frontiers in Psychology*, 12: 755585.
- Mira, J., Lapole, T., Souron, R., Messonnier, L., Millet, G. Y. and Rupp, T. (2017). Cortical voluntary activation testing methodology impacts central fatigue. *European Journal of Applied Physiology*, 117: 1845–1857.
- Mitchell, J. H., Reeves, D. R., Rogers, H. B. and Secher, N. H. (1989). Epidural anaesthesia and cardiovascular responses to static exercise in man. *Journal of Physiology*, 417: 13–24.
- Mollayeva, T., Kendzerska, T., Mollayeva, S., Shapiro, C. M., Colantonio, A. and Cassidy, J. D. (2014). A systematic review of fatigue in patients with traumatic brain injury: The course, predictors and consequences. *Neuroscience and Biobehavioral Reviews*, 47: 684–716.
- Monjo, F., Shemmell, J. and Forestier, N. (2018). The sensory origin of the sense of effort is context- dependent. *Experimental Brain Research*, 236: 1997–2008.
- Monjo, F., Terrier, R. and Forestier, N. (2015). Muscle fatigue as an investigative tool in motor control: A review with new insights on internal models and posture-movement coordination. *Human Movement Science*, 44: 225–233.
- Montoya, A. K. and Hayes, A. F. (2017). Two-condition within-participant statistical mediation analysis: A path-analytic framework. *Psychological Methods*, 22: 6–27.
- Morales-Alamo, D., Losa-Reyna, J., Torres-Peralta, R., Martin-Rincon, M., Perez-Valera, M., Curtelin, D., Ponce-González, J. G., Santana, A. and Calbet, J. A. L. (2015). What limits performance during whole-body incremental exercise to exhaustion in humans? *Journal of Physiology*, 593: 4631–4648.
- Morales-Alamo, D., Martin-Rincon, M., Perez-Valera, M., Marcora, S. M. and Calbet, J. A. L. (2016). No functional reserve at exhaustion in endurance-trained men? *Journal of Applied Physiology*, 120: 476.
- Morel, P., Ulbrich, P. and Gail, A. (2017). What makes a reach movement effortful? Physical effort discounting supports common minimization principles in decision making and motor control. *PLOS Biology*, 15: e2001323.
- Morgan, P. T., Bailey, S. J., Banks, R. A., Fulford, J., Vanhatalo, A. and Jones, A. M. (2019). Contralateral fatigue during severe-intensity single-leg exercise: Influence of acute acetaminophen ingestion. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, 317: R346–R354.
- Morgan, W. P. (1994). Psychological components of effort sense. *Medicine & Science in Sports & Exercise*, 26: 1071–1077.
- de Morree, H. M., Klein, C. and Marcora, S. M. (2014). Cortical substrates of the effects of caffeine and time-on-task on perception of effort. *Journal of Applied Physiology*, 117: 1514–1523.
- de Morree, H. M., Klein, C. and Marcora, S. M. (2012). Perception of effort reflects central motor command during movement execution. *Psychophysiology*, 49: 1242–1253.
- de Morree, H. M. and Marcora, S. M. (2012). Frowning muscle activity and perception of effort during constant-workload cycling. *European Journal of Applied Physiology*, 112: 1967–1972.
- de Morree, H. M. and Marcora, S. M. (2015). Psychobiology of perceived effort during physical tasks. In: *Handbook of Biobehavioral Approaches to Self-Regulation*. pp.255–270.
- Morris, K. J. (2019). Toward a phenomenology of fatigue. In: E. Dahl, C. Falke & T.E. Eriksen (eds) *Phenomenology of the Broken Body*. New York: Routledge.
- Mosso, A. (1891). *La Fatica*. Milano: Treves.
- Motl, R., Konopack, J. F., Hu, L. and McAuley, E. (2006). Does self-efficacy influence leg muscle pain during cycling exercise? *The Journal of Pain*, 7: 301–307.
- Müller, T. and Apps, M. (2019). Motivational fatigue: A neurocognitive framework for the impact of effortful exertion on subsequent motivation. *Neuropsychologia*, 123: 141–151.

- Müller, T., Klein-Flügge, M. C., Manohar, S., Husain, M. and Apps, M. A. J. (2021). Neural and computational mechanisms of momentary fatigue and persistence in effort-based choice. *Nature Communications*, 12: 4593.
- Mullette-Gillman, O. A., Leong, R. L. F. and Kurnianingsih, Y. A. (2015). Cognitive fatigue destabilizes economic decision making preferences and strategies. *PLoS ONE*, 10: e0132022.
- Musslick, S., Dey, B., Özcimder, K., Patwary, M. M. A., Willke, T. L. and Cohen, J. D. (2016). Controlled vs. automatic processing: A graph-theoretic approach to the analysis of serial vs. parallel processing in neural network architectures. In: *Proceedings of the 38th Annual Conference of the Cognitive Science Society*. Philadelphia, PA. pp.1547–1552.
- Nasiri, M., Rahimian, B., Jahanshahi, M., Fotoukian, Z. and Motamed Omran Chaboki, A. (2016). Study of Fatigue and Associated Factors in Patients with Chronic Heart Failure. *Journal of Critical Care Nursing*, 9: e8124.
- Neu, D., Hoffmann, G., Moutrier, R., Verbanck, P., Linkowski, P. and Le Bon, O. (2008). Are patients with chronic fatigue syndrome just ‘tired’ or also ‘sleepy’? *Journal of Sleep Research*, 17: 427–431.
- Neu, D., Mairesse, O., Hoffmann, G., Valsamis, J. B., Verbanck, P., Linkowski, P. and Le Bon, O. (2010). Do ‘sleepy’ and ‘tired’ go together? Rasch analysis of the relationships between sleepiness, fatigue and nonrestorative sleep complaints in a nonclinical population sample. *Neuroepidemiology*, 35: 1–11.
- Neyroud, D., Maffiuletti, N. A., Kayser, B. and Place, N. (2012). Mechanisms of fatigue and task failure induced by sustained submaximal contractions. *Medicine & Science in Sports & Exercise*, 44: 1243–1251.
- Nielsen, J. S., Madsen, K., Jørgensen, L. V. and Sahlin, K. (2005). Effects of lengthening contraction on calcium kinetics and skeletal muscle contractility in humans. *Acta Physiologica Scandinavica*, 184: 203–214.
- Nieuwenhuys, R. (2012). The insular cortex: A review. *Progress in Brain Research*, 195: 123–163.
- Nijs, J., Van Oosterwijck, J., Meeus, M., Lambrecht, L., Metzger, K., Frémont, M. and Paul, L. (2010). Unravelling the nature of postexertional malaise in myalgic encephalomyelitis/chronic fatigue syndrome: The role of elastase, complement C4a and interleukin-1 β . *Journal of Internal Medicine*, 267: 418–435.
- Nikolaus, S., Bode, C., Taal, E. and Van De Laar, M. A. F. J. (2013). Fatigue and factors related to fatigue in rheumatoid arthritis: A systematic review. *Arthritis Care and Research*, 65: 1128–1146.
- Noakes, T. D. (2012). Fatigue is a brain-derived emotion that regulates the exercise behavior to ensure the protection of whole body homeostasis. *Frontiers in Physiology*, 3: 82.
- Noakes, T. D. (2011). Time to move beyond a brainless exercise physiology: The evidence for complex regulation of human exercise performance. *Applied Physiology, Nutrition, and Metabolism*, 36: 23–35.
- Noakes, T. D., Peltonen, J. E. and Rusko, H. K. (2001). Evidence that a central governor regulates exercise performance during acute hypoxia and hyperoxia. *The Journal of Experimental Biology*, 204: 3225–34.
- Noakes, T. D., St Clair Gibson, A. and Lambert, E. V. (2004). From catastrophe to complexity: A novel model of integrative central neural regulation of effort and fatigue during exercise in humans. *British Journal of Sports Medicine*, 38: 511–514.
- Noakes, T. D., St Clair Gibson, A. and Lambert, E. V. (2005). From catastrophe to complexity: A novel model of integrative central neural regulation of effort and fatigue during exercise in humans - Summary and conclusions. *British Journal of Sports Medicine*, 39: 120–124.
- Noble, B. J., Metz, K. F., Pandolf, K. B. and Cafarelli, E. (1973). Perceptual responses to exercise: A multiple regression study. *Medicine and Science in Sports*, 5: 104–109.
- Noble, B. J. and Robertson, R. J. (1996). *Perceived exertion*. Champaign, IL: Human Kinetics.
- Nordsborg, N., Mohr, M., Pedersen, L. D., Nielsen, J. J., Langberg, H. and Bangsbo, J. (2003). Muscle interstitial potassium kinetics during intense exhaustive exercise: Effect of previous arm exercise. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*, 285: 143–148.
- Oberauer, K., Farrell, S., Jarrold, C. and Lewandowsky, S. (2016). What limits working memory capacity? *Psychological Bulletin*, 142: 758–799.

- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, 9: 97–113.
- Ostaszewski, P., Babel, P. and Swebodziński, B. (2013). Physical and cognitive effort discounting of hypothetical monetary rewards. *Japanese Psychological Research*, 55: 329–337.
- Owens, A. P., Allen, M., Ondobaka, S. and Friston, K. J. (2018). Interoceptive inference: From computational neuroscience to clinic. *Neuroscience & Biobehavioral Reviews*, 90: 174–183.
- Pace-Schott, E. F., Amole, M. C., Aue, T., Balconi, M., Bylsma, L. M., Critchley, H., Demaree, H. A., Friedman, B. H., Gooding, A. E. K., Gosseries, O., Jovanovic, T., Kirby, L. A. J., Kozłowska, K., Laureys, S., Lowe, L., Magee, K., Marin, M.-F., Merner, A. R., Robinson, J. L., Smith, R. C., Spangler, D. P., Van Overveld, M. and VanElzaker, M. B. (2019). Physiological feelings. *Neuroscience & Biobehavioral Reviews*, 103: 267–304.
- Pageaux, B. (2016). Perception of effort in Exercise Science: Definition, measurement and perspectives. *European Journal of Sport Science*, 16: 885–894.
- Pageaux, B. (2014). The Psychobiological Model of endurance performance: An effort-based decision-making theory to explain self-paced endurance performance. *Sports Medicine*, 44: 1319–1320.
- Pageaux, B. and Gaveau, J. (2016). Studies using pharmacological blockade of muscle afferents provide new insights into the neurophysiology of perceived exertion. *Journal of Physiology*, 594: 5049–5051.
- Pageaux, B. and Lepers, R. (2016). Fatigue induced by physical and mental exertion increases perception of effort and impairs subsequent endurance performance. *Frontiers in Physiology*, 7: 587.
- Pageaux, B. and Lepers, R. (2018). The effects of mental fatigue on sport-related performance. In: *Progress in Brain Research* (1st Edition). Elsevier B.V. pp.291–315.
- Pageaux, B., Lepers, R., Dietz, K. C. and Marcora, S. M. (2014). Response inhibition impairs subsequent self-paced endurance performance. *European Journal of Applied Physiology*, 114: 1095–1105.
- Pageaux, B., Marcora, S. M. and Lepers, R. (2013). Prolonged mental exertion does not alter neuromuscular function of the knee extensors. *Medicine & Science in Sports & Exercise*, 45: 2254–2264.
- Pageaux, B., Marcora, S. M., Rozand, V. and Lepers, R. (2015). Mental fatigue induced by prolonged self-regulation does not exacerbate central fatigue during subsequent whole-body endurance exercise. *Frontiers in Human Neuroscience*, 9: 67.
- Pandolf, K. B. (1982). Differentiated ratings of perceived exertion during physical exercise. *Medicine & Science in Sports & Exercise*, 12: 397–405.
- Pandolf, K. B. (1978). Influence of local and central factors in dominating rated perceived exertion during physical work. *Perceptual and Motor Skills*, 46: 683–698.
- Panneton, W. M., Gan, Q. and Juric, R. (2005). The central termination of sensory fibers from nerves to the gastrocnemius muscle of the rat. *Neuroscience*, 134: 175–187.
- Parvizi, J. and Damasio, A. (2001). Consciousness and the brainstem. *Cognition*, 79: 135–160.
- Pattyn, N., Van Cutsem, J., Dessy, E. and Mairesse, O. (2018). Bridging exercise science, cognitive psychology, and medical practice: Is ‘cognitive fatigue’ a remake of ‘the emperor’s new clothes’? *Frontiers in Psychology*, 9: 1246.
- Pattyn, N., Neyt, X., Henderickx, D. and Soetens, E. (2008). Psychophysiological investigation of vigilance decrement: Boredom or cognitive fatigue? *Physiology & Behavior*, 93: 369–378.
- Pawlikowska, T., Chalder, T., Hirsch, S. R., Wallace, P., Wright, D. J. M. and Wessely, S. C. (1994). Population based study of fatigue and psychological distress. *BMJ*, 308: 763–766.
- Peirce, J. W., Gray, J. R., Simpson, S., MacAskill, M., Höchenberger, R., Sogo, H., Kastman, E. and Lindeløv, J. K. (2019). PsychoPy2: Experiments in behavior made easy. *Behavior Research Methods*, 51: 195–203.
- Peñailillo, L., Mackay, K. and Abbiss, C. R. (2018). Rating of perceived exertion during concentric and eccentric cycling: Are we measuring effort or exertion? *International Journal of Sports Physiology and Performance*,

13: 517–523.

- Penner, I. K. and Paul, F. (2017). Fatigue as a symptom or comorbidity of neurological diseases. *Nature Reviews. Neurology*, 13: 662–675.
- Pessiglione, M., Vinckier, F., Bouret, S., Daunizeau, J. and Le Bouc, R. (2018). Why not try harder? Computational approach to motivation deficits in neuro-psychiatric diseases. *Brain*, 141: 629–650.
- Pessoa, L. (2008). On the relationship between emotion and cognition. *Nature Reviews Neuroscience*, 9: 148–158.
- Petersen, S., Schroyen, M., Mölders, C., Zenker, S. and Van den Bergh, O. (2014). Categorical interoception: Perceptual organization of sensations from inside. *Psychological Science*, 25: 1059–1066.
- Pettorossi, V. E., Della Torre, G., Bortolami, R. and Brunetti, O. (1999). The role of capsaicin-sensitive muscle afferents in fatigue-induced modulation of the monosynaptic reflex in the rat. *Journal of Physiology*, 515: 599–607.
- Petzschner, F. H., Weber, L. A. E., Gard, T. and Stephan, K. E. (2017). Computational psychosomatics and computational psychiatry: Toward a joint framework for differential diagnosis. *Biological Psychiatry*, 82: 421–430.
- Pezzulo, G., Rigoli, F. and Friston, K. (2015). Active Inference, homeostatic regulation and adaptive behavioural control. *Progress in Neurobiology*, 134: 17–35.
- Pezzulo, G., Rigoli, F. and Friston, K. J. (2018). Hierarchical active inference: A theory of motivated control. *Trends in Cognitive Sciences*, 22: 294–306.
- Phillips, R. O. (2015). A review of definitions of fatigue - and a step towards a whole definition. *Transportation Research Part F: Traffic Psychology and Behaviour*, 29: 48–56.
- Pigeon, W. R., Sateia, M. J. and Ferguson, R. J. (2003). Distinguishing between excessive daytime sleepiness and fatigue: Toward improved detection and treatment. *Journal of Psychosomatic Research*, 54: 61–69.
- Pike, N. (2011). Using false discovery rates for multiple comparisons in ecology and evolution. *Methods in Ecology and Evolution*, 2: 278–282.
- Pires, F. D. O. (2012). Thomas Kuhn's 'Structure of Scientific Revolutions' applied to exercise science paradigm shifts: Example including the Central Governor Model. *British Journal of Sports Medicine*: 721–722.
- Place, N., Lepers, R., Deley, G. and Millet, G. Y. (2004). Time course of neuromuscular alterations during a prolonged running exercise. *Medicine & Science in Sports & Exercise*, 36: 1347–1356.
- Place, N., Yamada, T., Bruton, J. D. and Westerblad, H. (2010). Muscle fatigue: From observations in humans to underlying mechanisms studied in intact single muscle fibres. *European Journal of Applied Physiology*, 110: 1–15.
- Pollak, K. A., Swenson, J. D., Vanhaitsma, T. A., Hughen, R. W., Jo, D., White, A. T., Light, K. C., Schweinhardt, P., Amann, M. and Light, A. R. (2014). Exogenously applied muscle metabolites synergistically evoke sensations of muscle fatigue and pain in human subjects. *Experimental Physiology*, 99: 368–380.
- Pollatos, O., Herbert, B. M., Matthias, E. and Schandry, R. (2007). Heart rate response after emotional picture presentation is modulated by interoceptive awareness. *International Journal of Psychophysiology*, 63: 117–124.
- Pollo, A., Carlino, E. and Benedetti, F. (2008). The top-down influence of ergogenic placebos on muscle work and fatigue. *European Journal of Neuroscience*, 28: 379–388.
- Post, M., Bayrak, S., Kernell, D. and Zijdwind, I. (2008). Contralateral muscle activity and fatigue in the human first dorsal interosseous muscle. *Journal of Applied Physiology*, 105: 70–82.
- Post, M., Steens, A., Renken, R., Maurits, N. M. and Zijdwind, I. (2009). Voluntary activation and cortical activity during a sustained maximal contraction: An fMRI study. *Human Brain Mapping*, 30: 1014–1027.
- Pottratz, S. T., Hutchinson, J. C., Karageorghis, C. I., Mullin, E. M. and Zenko, Z. (2021). Prime movers: Effects of subliminal primes, music, and music video on psychological responses to exercise. *Annals of Behavioral*

Medicine, 55: 112–122.

- Potts, C. A., Pastel, S. and Rosenbaum, D. A. (2018). How are cognitive and physical difficulty compared? *Attention, Perception and Psychophysics*, 80: 500–511.
- Poulet, J. F. A. and Hedwig, B. (2007). New insights into corollary discharges mediated by identified neural pathways. *Trends in Neurosciences*, 30: 14–21.
- Poulus, A. J., Docter, H. J. and Westra, H. G. (1974). Acid-base balance and subjective feelings of fatigue during physical exercise. *European Journal of Applied Physiology*, 33: 207–213.
- Prajapati, B., Dunne, M. C. M. and Armstrong, R. A. (2010). Sample size estimation and statistical power analyses prajapati. *Optometry Today*: 16/07.
- Prak, R. F., van der Naalt, J. and Zijdwind, I. (2019). Self-reported fatigue after mild traumatic brain injury is not associated with performance fatigability during a sustained maximal contraction. *Frontiers in Physiology*, 9: 1919.
- Preston, J. and Wegner, D. M. (2009). Elbow grease: The experience of effort in action. In: E. Morsella, J.A. Bargh & P.M. Gollwitzer (eds) *Oxford handbook of human action*. New York: Oxford University Press. pp.469–486.
- Prévost, C., Pessiglione, M., Météreau, E., Cléry-Melin, M. L. and Dreher, J. C. (2010). Separate valuation subsystems for delay and effort decision costs. *Journal of Neuroscience*, 30: 14080–14090.
- Proske, U. and Allen, T. (2019). The neural basis of the senses of effort, force and heaviness. *Experimental Brain Research*, 237: 589–599.
- Proske, U. and Gandevia, S. C. (2012). The proprioceptive senses: Their roles in signaling body shape, body position and movement, and muscle force. *Physiological Reviews*, 92: 1651–1697.
- R Core Team (2018). R: A language and environment for statistical computing.
- Raja, S. N., Carr, D. B., Cohen, M., Finnerup, N. B., Flor, H., Gibson, S., Keefe, F. J., Mogil, J. S., Ringkamp, M., Sluka, K. A., Song, X. J., Stevens, B., Sullivan, M. D., Tutelman, P. R., Ushida, T. and Vader, K. (2020). The revised International Association for the Study of Pain definition of pain: Concepts, challenges, and compromises. *PAIN*, 161: 1976–1982.
- Ramírez-Moreno, J. M., Muñoz-Vega, P., Alberca, S. B. and Peral-Pacheco, D. (2019). Health-related quality of life and fatigue after transient ischemic attack and minor stroke. *Journal of Stroke and Cerebrovascular Diseases*, 28: 276–284.
- Rangel, A. and Hare, T. (2010). Neural computations associated with goal-directed choice. *Current Opinion in Neurobiology*, 20: 262–270.
- Rao, R. P. and Ballard, D. H. (1999). Predictive coding in the visual cortex: A functional interpretation of some extra-classical receptive-field effects. *Nature - Neuroscience*, 2: 79–87.
- Rasker, J. J. (2009). The Enigma of Fatigue. *The Journal of Rheumatology*, 36: 2630–2632.
- Rathey, J., Martin, P. G., Kay, D., Cannon, J. and Marino, F. E. (2006). Contralateral muscle fatigue in human quadriceps muscle: Evidence for a centrally mediated fatigue response and cross-over effect. *European Journal of Applied Physiology*, 452: 199–207.
- Rauch, H. G. L., Schönbacher, G. and Noakes, T. D. (2013). Neural correlates of motor vigour and motor urgency during exercise. *Sports Medicine*, 43: 227–241.
- Ream, E. and Richardson, A. (1996). Fatigue: A concept analysis. *International Journal of Nursing Studies*, 33: 519–529.
- Reilly, T., Atkinson, G., Edwards, B., Waterhouse, J., Farrelly, K. and Fairhurst, E. (2007). Diurnal variation in temperature, mental and physical performance, and tasks specifically related to football (soccer). *Chronobiology International*, 24: 507–519.
- Rejeski, W. J., Best, D. L., Griffith, P. and Kenney, E. (1987). Sex-role orientation and the responses of men to exercise stress. *Research Quarterly for Exercise and Sport*, 58: 260–264.

- Rejeski, W. J. and Lowe, C. A. (1980). Nonverbal expression of effort as causally relevant information. *Personality and Social Psychology Bulletin*, 6: 436–440.
- Renfree, A., Martin, L., Micklewright, D. and St Clair Gibson, A. (2014). Application of decision-making theory to the regulation of muscular work rate during self-paced competitive endurance activity. *Sports Medicine*, 44: 147–158.
- Renfree, A., West, J., Corbett, M., Rhoden, C. and St Clair Gibson, A. (2012). Complex interplay between determinants of pacing and performance during 20-km cycle time trials. *International Journal of Sports Physiology and Performance*, 7: 121–129.
- Repping-Wuts, H., Uitterhoeve, R., van Riel, P. and van Achterberg, T. (2008). Fatigue as experienced by patients with rheumatoid arthritis (RA): A qualitative study. *International Journal of Nursing Studies*, 45: 995–1002.
- Ricci, J. A., Chee, E., Lorandeanu, A. L. and Berger, J. (2007). Fatigue in the U.S. workforce: Prevalence and implications for lost productive work time. *Journal of Occupational and Environmental Medicine*, 49: 1–10.
- Riley, W. T., Rothrock, N., Bruce, B., Christodolou, C., Cook, K., Hahn, E. A. and Cella, D. (2010). Patient-reported outcomes measurement information system (PROMIS) domain names and definitions revisions: Further evaluation of content validity in IRT-derived item banks. *Quality of Life Research*, 19: 1311–1321.
- Robergs, R. A. (2017). Lessons from Popper for science, paradigm shifts, scientific revolutions and exercise physiology. *BMJ Open Sport & Exercise Medicine*, 3: e000226.
- Robertson, C. V. and Marino, F. E. (2016). Viewpoint: A role for the prefrontal cortex in exercise tolerance and termination. *Journal of Applied Physiology*, 120: 464–466.
- Rochette, L., Hunter, S. K., Place, N. and Lepers, R. (2003). Activation varies among the knee extensor muscles during a submaximal fatiguing contraction in the seated and supine postures. *Journal of Applied Physiology*, 95: 1515–1522.
- Rodriguez-Falces, J., Maffiuletti, N. A. and Place, N. (2013). Spatial distribution of motor units recruited during electrical stimulation of the quadriceps muscle versus the femoral nerve. *Muscle & Nerve*, 48: 752–761.
- Rodriguez-Falces, J. and Place, N. (2018). Determinants, analysis and interpretation of the muscle compound action potential (M wave) in humans: Implications for the study of muscle fatigue. *European Journal of Applied Physiology*, 118: 501–521.
- Roloffa, Z. A., Dicks, N. D., Krynski, L. M., Hartman, M. E., Ekkekakis, P. and Pettitt, R. W. (2020). Ratings of affective valence closely track changes in oxygen uptake: Application to high-intensity interval exercise. *Performance Enhancement & Health*, 7: 100158.
- Ross, E. Z., Goodall, S., Stevens, A. and Harris, I. (2010). Time course of neuromuscular changes during running in well-trained subjects. *Medicine & Science in Sports & Exercise*, 42: 1184–1190.
- Ross, E. Z., Middleton, N., Shave, R., George, K. and Nowicky, A. (2007). Corticomotor excitability contributes to neuromuscular fatigue following marathon running in man. *Experimental Physiology*, 92: 417–426.
- Rossi, S., Hallett, M., Rossini, P. M. and Pascual-Leone, A. (2011). Screening questionnaire before TMS: An update. *Clinical Neurophysiology*, 122: 1686.
- Rossi, S., Hallett, M., Rossini, P. M., Pascual-Leone, A., Avanzini, G., Bestmann, S., Berardelli, A., Brewer, C., Canli, T., Cantello, R., Chen, R., Classen, J., Demitrack, M., Di Lazzaro, V., Epstein, C. M., George, M. S., Fregni, F., Ilmoniemi, R., Jalinous, R., Karp, B., Lefaucheur, J. P., Lisanby, S., Meunier, S., Miniussi, C., Miranda, P., Padberg, F., Paulus, W., Peterchev, A., Porteri, C., Provost, M., Quartarone, A., Rotenberg, A., Rothwell, J., Ruohonen, J., Siebner, H. R., Thut, G., Valls-Sole, J., Walsh, V., Ugawa, Y., Zangen, A. and Ziemann, U. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, 120: 2008–2039.
- Rossmann, M. J., Venturelli, M., McDaniel, J., Amann, M. and Richardson, R. S. (2012). Muscle mass and peripheral fatigue: A potential role for afferent feedback? *Acta Physiologica*, 206: 242–250.
- Rozand, V., Pageaux, B., Marcora, S. M., Papaxanthis, C. and Lepers, R. (2014). Does mental exertion alter maximal muscle activation? *Frontiers in Human Neuroscience*, 8: 755.

- Ruban, S. D., Hilt, C. C. and Petersen, T. (2021). Quality of life in multiple sclerosis: The differential impact of motor and cognitive fatigue. *Multiple Sclerosis Journal - Experimental, Translational and Clinical*, 7: 2055217321996040.
- Russell, J. A. (2003). Core affect and the psychological construction of emotion. *Psychological Review*, 110: 145–172.
- Russell, J. A. and Barrett, L. F. (1999). Core affect, prototypical emotional episodes, and other things called emotion: Dissecting the elephant. *Journal of Personality and Social Psychology*, 76: 805–819.
- Ryum, T., Kennair, L. E. O., Hjemdal, O., Hagen, R., Halvorsen, J. Ø. and Solem, S. (2017). Worry and metacognitions as predictors of anxiety symptoms: A prospective study. *Frontiers in Psychology*, 8: 924.
- Sáez-Francàs, N., Hernández-Vara, J., Roso, M. C., Martín, J. A. and Brugué, M. C. (2013). The association of apathy with central fatigue perception in patients with Parkinson's disease. *Behavioral Neuroscience*, 127: 237–244.
- Salamone, J. D. and Correa, M. (2012). The mysterious motivational functions of mesolimbic dopamine. *Neuron*, 76: 470–485.
- Šambaher, N., Aboodarda, S. J. and Behm, D. G. (2016). Bilateral knee extensor fatigue modulates force and responsiveness of the corticospinal pathway in the non-fatigued, dominant elbow flexors. *Frontiers in Human Neuroscience*, 10: 18.
- Sanderson, A., Wang, S. F., Elgueta-Cancino, E., Martinez-Valdes, E., Sanchis-Sanchez, E., Liew, B. and Falla, D. (2021). The effect of experimental and clinical musculoskeletal pain on spinal and supraspinal projections to motoneurons and motor unit properties in humans: A systematic review. *European Journal of Pain*, 25: 1668–1701.
- Saper, C. B. (2002). The central autonomic nervous system: Conscious visceral perception and autonomic pattern generation. *Annual Review of Neuroscience*, 25: 433–469.
- van der Schaaf, M. E., Roelofs, K., de Lange, F. P., Geurts, D. E. M., van der Meer, J. W. M., Knoop, H. and Toni, I. (2018). Fatigue is associated with altered monitoring and preparation of physical effort in patients with chronic fatigue syndrome. *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, 3: 392–404.
- Schachter, S. and Singer, J. (1962). Cognitive, social, and physiological determinants of emotional state. *Psychological Review*, 69: 379–399.
- Schandry, R. (1981). Heart beat perception and emotional experience. *Psychophysiology*, 18: 483–488.
- Scherr, J., Wolfarth, B., Christle, J. W., Pressler, A., Wagenpfeil, S. and Halle, M. (2013). Associations between Borg's rating of perceived exertion and physiological measures of exercise intensity. *Journal of Applied Physiology*, 113: 147–155.
- Schijve, J. (2003). Fatigue of structures and materials in the 20th century and the state of the art. *Materials Science*, 39: 307–333.
- Schmidt, L., Lebreton, M., Cléry-Melin, M. L., Daunizeau, J. and Pessiglione, M. (2012). Neural mechanisms underlying motivation of mental versus physical effort. *PLoS Biology*, 10: e1001266.
- Schomburg, E. D., Steffens, H. and Kniffki, K.-D. (1999). Contribution of group III and IV muscle afferents to multisensorial spinal motor control in cats. *Neuroscience Research*, 33: 195–206.
- Schulz, S. M. (2016). Neural correlates of heart-focused interoception: A functional magnetic resonance imaging meta-analysis. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 371: 20160018.
- Scotland, S., Adamo, D. E. and Martin, B. J. (2014). Sense of effort revisited: Relative contributions of sensory feedback and efferent copy. *Neuroscience Letters*, 561: 208–212.
- Scott, J. A., Lasch, K. E., Barsevick, A. M. and Piault-Louis, E. (2011). Patients' experiences with cancer-related fatigue: A review and synthesis of qualitative research. *Oncology Nursing Forum*, 38: E191–E203.
- Seth, A. K. and Critchley, H. D. (2013). Extending predictive processing to the body: Emotion as interoceptive inference. *Behavioral and Brain Sciences*, 36.

- Seth, A. K. and Friston, K. J. (2016). Active interoceptive inference and the emotional brain. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 371: 20160007.
- Seth, A. K., Suzuki, K. and Critchley, H. D. (2012). An interoceptive predictive coding model of conscious presence. *Frontiers in Psychology*, 3: 1–16.
- Shahid, A., Wilkinson, K., Marcu, S. and Shapiro, C. M. (eds) (2012). *STOP, THAT and one hundred other sleep scales*. New York, NY: Springer.
- Shapiro, S. S. S. and Wilk, M. M. B. (1965). An analysis of variance test for normality (complete samples). *Biometrika*, 52: 591–611.
- Shariat, A., Cleland, J. A., Danaee, M., Alizadeh, R., Sangelaji, B., Kargarfard, M., Ansari, N. N., Sepehr, F. H. and Tamrin, S. B. M. (2018). Borg CR-10 scale as a new approach to monitoring office exercise training. *Work: Journal of Prevention, Assessment & Rehabilitation*, 60: 549–554.
- Sharples, S. A., Gould, J. A., Vandenberk, M. S. and Kalmar, J. M. (2016). Cortical mechanisms of central fatigue and sense of effort. *PLoS ONE*, 11: 1–21.
- Shen, J., Barbera, J. and Shapiro, C. M. (2006). Distinguishing sleepiness and fatigue: Focus on definition and measurement. *Sleep Medicine Reviews*, 10: 63–76.
- Shenhav, A., Musslick, S., Lieder, F., Kool, W., Griffiths, T. L., Cohen, J. D. and Botvinick, M. M. (2017). Toward a rational and mechanistic account of mental effort. *Annual Review of Neuroscience*, 40: 99–124.
- Shephard, R. J. (2009). Is it time to retire the ‘Central Governor’? *Sports Medicine*, 39: 709–721.
- Sheppard, K. E. and Parfitt, G. (2008a). Acute affective responses to prescribed and self-selected exercise intensities in young adolescent boys and girls. *Pediatric Exercise Science*, 20: 129–141.
- Sheppard, K. E. and Parfitt, G. (2008b). Patterning of physiological and affective responses during a graded exercise test in sedentary men and boys. *Journal of Exercise Science & Fitness*, 6: 121–129.
- Shipp, S. (2016). Neural elements for predictive coding. *Frontiers in Psychology*, 7: 1792.
- Shipp, S., Adams, R. A. and Friston, K. J. (2013). Reflections on agranular architecture: Predictive coding in the motor cortex. *Trends in Neurosciences*, 36: 706–716.
- Shoemaker, J. K. and Goswami, R. (2015). Forebrain neurocircuitry associated with human reflex cardiovascular control. *Frontiers in Physiology*, 6: 240.
- Siciliano, M., De Micco, R., Trojano, L., Sant’Elia, V., Giordano, A., Russo, A., Passamonti, L., Tedeschi, G., Chiorri, C. and Tessitore, A. (2021). The psychological correlates of fatigue in Parkinson’s disease: Contribution of maladaptive metacognitive beliefs. *Parkinsonism & Related Disorders*, 91: 135–138.
- Sidhu, S. K., Bentley, D. J. and Carroll, T. J. (2009a). Cortical voluntary activation of the human knee extensors can be reliably estimated using transcranial magnetic stimulation. *Muscle & Nerve*, 39: 186–196.
- Sidhu, S. K., Bentley, D. J. and Carroll, T. J. (2009b). Locomotor exercise induces long-lasting impairments in the capacity of the human motor cortex to voluntarily activate knee extensor muscles. *Journal of Applied Physiology*, 106: 556–565.
- Sidhu, S. K., Weavil, J. C., Mangum, T. S., Jessop, J. E., Richardson, R. S., Morgan, D. E. and Amann, M. (2017). Group III/IV locomotor muscle afferents alter motor cortical and corticospinal excitability and promote central fatigue during cycling exercise. *Clinical Neurophysiology*, 128: 44–55.
- Sidhu, S. K., Weavil, J. C., Thurston, T. S., Rosenberger, D., Jessop, J. E., Wang, E., Richardson, R. S., McNeil, C. J. and Amann, M. (2018). Fatigue-related group III/IV muscle afferent feedback facilitates intracortical inhibition during locomotor exercise. *Journal of Physiology*, 596: 4789–4801.
- Sidhu, S. K., Weavil, J. C., Venturelli, M., Garten, R. S., Rossman, M. J., Richardson, R. S., Gmelch, B. S., Morgan, D. E. and Amann, M. (2014). Spinal μ -opioid receptor-sensitive lower limb muscle afferents determine corticospinal responsiveness and promote central fatigue in upper limb muscle. *Journal of Physiology*, 592: 5011–5024.
- da Silva Machado, D. G., de Farias Junior, L. F., do Nascimento, P. H. D., Tavares, M. P. M., da Silva, S. K. A.,

- Agrícola, P. M. D., do Nascimento Neto, L. I., Fonteles, A. I., Elsangedy, H. M., Li, L. M. and Okano, A. H. (2019). Can interoceptive accuracy influence maximal performance, physiological and perceptual responses to exercise? *Physiology & Behavior*, 204: 234–240.
- Silvestrini, N. and Gendolla, G. H. E. (2019). Affect and cognitive control: Insights from research on effort mobilization. *International Journal of Psychophysiology*, 143: 116–125.
- Siman-Tov, T., Granot, R. Y., Shany, O., Singer, N., Hendler, T. and Gordon, C. R. (2019). Is there a prediction network? Meta-analytic evidence for a cortical-subcortical network likely subserving prediction. *Neuroscience & Biobehavioral Reviews*, 105: 262–275.
- Šimić, G., Tkalčić, M., Vukić, V., Mulc, D., Španić, E., Šagud, M., Olucha-Bordonau, F. E., Vukšić, M. and Hof, P. R. (2021). Understanding emotions: Origins and roles of the amygdala. *Biomolecules*, 11: 823.
- Simmons, W. K., Avery, J. A., Barcalow, J. C., Bodurka, J., Drevets, W. C. and Bellgowan, P. (2013). Keeping the body in mind: Insula functional organization and functional connectivity integrate interoceptive, exteroceptive, and emotional awareness. *Human Brain Mapping*, 34: 2944–2958.
- Skau, S., Sundberg, K. and Kuhn, H.-G. (2021). A proposal for a unifying set of definitions of fatigue. *Frontiers in Psychology*, 12: 4680.
- Skorvanek, M., Gdovinova, Z., Rosenberger, J., Ghorbani Saeedian, R., Nagyova, I., Groothoff, J. W. and van Dijk, J. P. (2015). The associations between fatigue, apathy, and depression in Parkinson's disease. *Acta Neurologica Scandinavica*, 131: 80–87.
- Slobounov, S., Hallett, M. and Newell, K. M. (2004). Perceived effort in force production as reflected in motor-related cortical potentials. *Clinical Neurophysiology*, 115: 2391–2402.
- Smets, E. M., Garssen, B., Bonke, B. and De Haes, J. C. (1995). The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research*, 39: 315–325.
- Smirmaul, B. D. P. C. (2012). Sense of effort and other unpleasant sensations during exercise: Clarifying concepts and mechanisms. *British Journal of Sports Medicine*, 46: 308–311.
- Smith, M. R., Chai, R., Nguyen, H. T., Marcora, S. M. and Coutts, A. J. (2019). Comparing the effects of three cognitive tasks on indicators of mental fatigue. *Journal of Psychology*, 153: 759–783.
- Smith, M. R., Coutts, A. J., Merlini, M., Deprez, D., Lenoir, M. and Marcora, S. M. (2016). Mental fatigue impairs soccer-specific physical and technical performance. *Medicine & Science in Sports & Exercise*, 48: 267–276.
- Smith, M. R., Marcora, S. M. and Coutts, A. J. (2014). Mental fatigue impairs intermittent running performance. *Medicine & Science in Sports & Exercise*, 47: 1682–1690.
- Smith, S. A., Micklewright, D., Winter, S. L. and Mauger, A. R. (2020). Muscle pain induced by hypertonic saline in the knee extensors decreases single-limb isometric time to task failure. *European Journal of Applied Physiology*, 120: 2047–2058.
- Smith, S. A., Querry, R. G., Fadel, P. J., Gallagher, K. M., Stromstad, M., Ide, K., Raven, P. B. and Secher, N. H. (2003). Partial blockade of skeletal muscle somatosensory afferents attenuates baroreflex resetting during exercise in humans. *Journal of Physiology*, 551: 1013–1021.
- Smits, B. L. M., Polman, R. C. J., Otten, B., Pepping, G. J. and Hettinga, F. J. (2016). Cycling in the absence of task-related feedback: Effects on pacing and performance. *Frontiers in Physiology*, 7: 1–9.
- Solomon, R. L. (1948). The influence of work on behavior. *Psychological Bulletin*, 45: 1–40.
- Souissi, H., Chaouachi, A., Chamari, K., Dogui, M., Amri, M. and Souissi, N. (2010). Time-of-day effects on short-term exercise performances in 10- to 11-year-old boys. *Pediatric Exercise Science*, 22: 613–623.
- Souron, R., Besson, T., Mcneil, C. J., Lapole, T. and Millet, G. Y. (2018). An acute exposure to muscle vibration decreases knee extensors force production and modulates associated central nervous system excitability. *Applied Physiology, Nutrition and Metabolism*, 43: 427–436.
- Sperry, R. W. (1950). Neural basis of the spontaneous optokinetic response produced by visual inversion. *Journal of Comparative and Physiological Psychology*, 43: 482–489.

- St Clair Gibson, A., Baden, D. A., Lambert, M. I., Lambert, E. V., Harley, Y. X. R., Hampson, D., Russell, V. A. and Noakes, T. D. (2003). The conscious perception of the sensation of fatigue. *Sports Medicine*, 33: 167–176.
- St Clair Gibson, A., Goedecke, J. H., Harley, Y. X., Myers, L. J., Lambert, M. I., Noakes, T. D. and Lambert, E. V. (2005). Metabolic setpoint control mechanisms in different physiological systems at rest and during exercise. *Journal of Theoretical Biology*, 236: 60–72.
- St Clair Gibson, A., Lambert, E. V., Rauch, L. H. G., Tucker, R., Baden, D. A., Foster, C. and Noakes, T. D. (2006). The role of information processing between the brain and peripheral physiological systems in pacing and perception of effort. *Sports Medicine*, 36: 705–722.
- St Clair Gibson, A. and Noakes, T. D. (2004). Evidence for complex system integration and dynamic neural regulation of skeletal muscle recruitment during exercise in humans. *British Journal of Sports Medicine*, 38: 797–806.
- St Clair Gibson, A., Swart, J. and Tucker, R. (2018). The interaction of psychological and physiological homeostatic drives and role of general control principles in the regulation of physiological systems, exercise and the fatigue process – The Integrative Governor theory. *European Journal of Sport Science*, 18: 25–36.
- Stacey, M. J. (1969). Free nerve endings in skeletal muscle of the cat. *Journal of Anatomy*, 105: 231–254.
- Staiano, W., Bosio, A. B., de Morree, H. M., Rampinini, E. and Marcora, S. M. (2018). The cardinal exercise stopper: Muscle fatigue, muscle pain or perception of effort? *Progress in Brain Research*, 240: 175–200.
- Stamford, B. A. and Noble, B. J. (1974). Metabolic cost and perception of effort during bicycle ergometer work performance. *Medicine and Science in Sports*, 6: 226–231.
- Steadman, A., Davey, N. and Ellaway, P. (1998). Facilitation of human first dorsal interosseous muscle responses to transcranial magnetic stimulation during voluntary contraction of the contralateral homonymous muscle. *Muscle & Nerve*, 21: 1033–1039.
- Steele, J. (2021). What is (perception of) effort? Objective and subjective effort during task performance.
- Stegeman, D. F. and Hermens, H. J. (1998). Standards for surface electromyography: the European project (SENIAM). In: H.J. Hermens, G. Rau, C. Disselhorst-Klug & B. Freriks (eds) *Surface Electromyography Application Areas and Parameters. Proceedings of the Third General SENIAM Workshop on surface electromyography*. Aachen, Germany. pp.108–112.
- Stephan, K. E., Manjaly, Z. M., Mathys, C. D., Weber, L. A. E., Paliwal, S., Gard, T., Tittgemeyer, M., Fleming, S. M., Haker, H., Seth, A. K. and Petzschner, F. H. (2016). Allostatic self-efficacy: A metacognitive theory of dyshomeostasis-induced fatigue and depression. *Frontiers in Human Neuroscience*, 10: 550.
- Sterling, P. (2012). Allostasis: A model of predictive regulation. *Physiology & Behavior*, 106: 5–15.
- Stewart, C. C., Wright, R. A., Azor Hui, S. K. and Simmons, A. (2009). Outcome expectancy as a moderator of mental fatigue influence on cardiovascular response. *Psychophysiology*, 46: 1141–1149.
- Stone, M. R., Thomas, K., Wilkinson, M., Jones, A. M., St Clair Gibson, A. and Thompson, K. G. (2012). Effects of deception on exercise performance: Implications for determinants of fatigue in humans. *Medicine & Science in Sports & Exercise*, 44: 534–541.
- Stuart, C., Steele, J., Gentil, P., Giessing, J. and Fisher, J. P. (2018). Fatigue and perceptual responses of heavier- and lighter-load isolated lumbar extension resistance exercise in males and females. *PeerJ*, 6: e4523.
- Swaen, G. M. H. (2003). Fatigue as a risk factor for being injured in an occupational accident: Results from the Maastricht Cohort Study. *Occupational and Environmental Medicine*, 60: i88–i92.
- Swart, J., Lindsay, T. R., Lambert, M. I., Brown, J. C. and Noakes, T. D. (2012). Perceptual cues in the regulation of exercise performance - physical sensations of exercise and awareness of effort interact as separate cues. *British Journal of Sports Medicine*, 46: 42–48.
- Székely, M. and Michael, J. (2018). Investing in commitment: Persistence in a joint action is enhanced by the perception of a partner's effort. *Cognition*, 174: 37–42.
- Székely, M. and Michael, J. (2020). The sense of effort: A cost-benefit theory of the phenomenology of mental

effort. *Review of Philosophy and Psychology*.

- Taguchi, T., Sato, J. and Mizumura, K. (2005). Augmented mechanical response of muscle thin-fiber sensory receptors recorded from rat muscle-nerve preparations in vitro after eccentric contraction. *Journal of Neurophysiology*, 94: 2822–2831.
- Tajima, S., Yamamoto, S., Tanaka, M., Kataoka, Y., Iwase, M., Yoshikawa, E., Okada, H., Onoe, H., Tsukada, H., Kuratsune, H., Ouchi, Y. and Watanabe, Y. (2010). Medial orbitofrontal cortex is associated with fatigue sensation. *Neurology Research International*: 1–6.
- Takahashi, K., Maruyama, A., Hirakoba, K., Maeda, M., Etoh, S., Kawahira, K. and Rothwell, J. C. (2011). Fatiguing intermittent lower limb exercise influences corticospinal and corticocortical excitability in the nonexercised upper limb. *Brain Stimulation*, 4: 90–96.
- Takahashi, K., Maruyama, A., Maeda, M., Etoh, S., Hirakoba, K., Kawahira, K. and Rothwell, J. C. (2009). Unilateral grip fatigue reduces short interval intracortical inhibition in ipsilateral primary motor cortex. *Clinical Neurophysiology*, 120: 198–203.
- Tamm, A. S., Lagerquist, O., Ley, A. L. and Collins, D. F. (2009). Chronotype influences diurnal variations in the excitability of the human motor cortex and the ability to generate torque during a maximum voluntary contraction. *Journal of Biological Rhythms*, 24: 211–224.
- Tanaka, M., Ishii, A. and Watanabe, Y. (2014). Neural effect of mental fatigue on physical fatigue: A magnetoencephalography study. *Brain Research*, 1542: 49–55.
- Tanaka, M., Ishii, A. and Watanabe, Y. (2013). Neural mechanism of central inhibition during physical fatigue: A magnetoencephalography study. *Brain Research*, 1537: 117–124.
- Tanaka, M. and Watanabe, Y. (2012). Supraspinal regulation of physical fatigue. *Neuroscience and Biobehavioral Reviews*, 36: 727–734.
- Taylor, J. L., Amann, M., Duchateau, J., Meeusen, R. and Rice, C. L. (2016). Neural contributions to muscle fatigue: From the brain to the muscle and back again. *Medicine & Science in Sports & Exercise*, 48: 2294–2306.
- Taylor, J. L., Petersen, N., Butler, J. E. and Gandevia, S. C. (2000). Ischaemia after exercise does not reduce responses of human motoneurons to cortical or corticospinal tract stimulation. *Journal of Physiology*, 525: 793–801.
- Taylor, K. S., Seminowicz, D. A. and Davis, K. D. (2009). Two systems of resting state connectivity between the insula and cingulate cortex. *Human Brain Mapping*, 30: 2731–2745.
- Tazoe, T., Sakamoto, M., Nakajima, T., Endoh, T., Shiozawa, S. and Komiyama, T. (2009). Remote facilitation of supraspinal motor excitability depends on the level of effort. *European Journal of Neuroscience*, 30: 1297–1305.
- Temesi, J., Gruet, M., Rupp, T., Verges, S. and Millet, G. Y. (2014). Resting and active motor thresholds versus stimulus-response curves to determine transcranial magnetic stimulation intensity in quadriceps femoris. *Journal of Neuroengineering and Rehabilitation*, 11: 40.
- Tenenbaum, G., Fogarty, G., Stewart, E., Calcagnini, N., Kirker, B., Thorne, G. and Christensen, S. (1999). Perceived discomfort in running: Scale development and theoretical considerations. *Journal of Sports Sciences*, 17: 183–196.
- The jamovi project (2020). jamovi.
- Thickbroom, G. W., Sacco, P., Kermodé, A. G., Archer, S. A., Byrnes, M. L., Guilfoyle, A. and Mastaglia, F. L. (2006). Central motor drive and perception of effort during fatigue in multiple sclerosis. *Journal of Neurology*, 253: 1048–1053.
- Thomas, K., Elmeua, M., Howatson, G. and Goodall, S. (2016). Intensity-dependent contribution of neuromuscular fatigue after constant-load cycling. *Medicine & Science in Sports & Exercise*, 48: 1751–1760.
- Thompson, C., Fransen, J., Beavan, A., Skorski, S., Coutts, A. and Meyer, T. (2020). Understanding the influence of a cognitively demanding task on motor response times and subjective mental fatigue/boredom. *Brazilian*

Journal of Motor Behaviour, 14: 33–45.

- Thosar, S. S., Herzig, M. X., Roberts, S. A., Berman, A. M., Clemons, N. A., McHill, A. W., Bowles, N. P., Morimoto, M., Butler, M. P., Emens, J. S. and Shea, S. A. (2018). Lowest perceived exertion in the late morning due to effects of the endogenous circadian system. *British Journal of Sports Medicine*, 52: 1011–1012.
- Timme, S. and Brand, R. (2020). Affect and exertion during incremental physical exercise: Examining changes using automated facial action analysis and experiential self-report. *PLoS ONE*, 15: e0228739.
- Todd, G., Taylor, J. L. and Gandevia, S. C. (2016). Measurement of voluntary activation based on transcranial magnetic stimulation over the motor cortex. *Journal of Applied Physiology*, 121: 678–686.
- Todd, G., Taylor, J. L. and Gandevia, S. C. (2003). Measurement of voluntary activation of fresh and fatigued human muscles using transcranial magnetic stimulation. *Journal of Physiology*, 551: 661–71.
- Todd, G., Taylor, J. L. and Gandevia, S. C. (2004). Reproducible measurement of voluntary activation of human elbow flexors with motor cortical stimulation. *Journal of Applied Physiology*, 97: 236–242.
- Della Torre, G., Lucchi, M. L., Brunetti, O., Pettorossi, V. E., Clavenzani, P. and Bortolami, R. (1996). Central projections and entries of capsaicin-sensitive muscle afferents. *Brain Research*, 713: 223–231.
- Toska, K. (2010). Handgrip contraction induces a linear increase in arterial pressure by peripheral vasoconstriction, increased heart rate and a decrease in stroke volume. *Acta Physiologica*, 200: 211–221.
- Tran, T., Hagen, A. E. F., Hollenstein, T. and Bowie, C. R. (2020). Physical- and cognitive-effort-based decision-making in depression: Relationships to symptoms and functioning. *Clinical Psychological Science*, 9: 53–67.
- Treadway, M. T., Bossaller, N. A., Shelton, R. C. and Zald, D. H. (2012). Effort-based decision-making in major depressive disorder: A translational model of motivational anhedonia. *Journal of Abnormal Psychology*, 121: 553–558.
- Treadway, M. T., Buckholz, J. W., Schwartzman, A. N., Lambert, W. E. and Zald, D. H. (2009). Worth the ‘EEfRT’? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. *PLoS ONE*, 4: e6598.
- Treasure, D. C. and Newbery, D. M. (1998). Relationship between self-efficacy, exercise intensity, and feeling states in a sedentary population during and following an acute bout of exercise. *Journal of Sport and Exercise Psychology*, 20: 1–11.
- Triscott, S., Gordon, J., Kuppaswamy, A., King, N., Davey, N. and Ellaway, P. (2008). Differential effects of endurance and resistance training on central fatigue. *Journal of Sports Sciences*, 26: 941–951.
- Trojan, D. A. and Cashman, N. R. (2005). Post-poliomyelitis syndrome. *Muscle and Nerve*, 31: 6–19.
- Tseng, B. Y., Billinger, S. A., Gajewski, B. J. and Kluding, P. M. (2010). Exertion fatigue and chronic fatigue are two distinct constructs in people post-stroke. *Stroke*, 41: 2908–2912.
- Tucker, R. (2009). The anticipatory regulation of performance: The physiological basis for pacing strategies and the development of a perception-based model for exercise performance. *British Journal of Sports Medicine*, 43: 392–400.
- Ulmer, H. V. (1996). Concept of an extracellular regulation of muscular metabolic rate during heavy exercise in humans by psychophysiological feedback. *Experientia*, 52: 416–420.
- Unal, O., Eren, O. C., Alkan, G., Petzschnner, F. H., Yao, Y. and Stephan, K. E. (2021). Inference on homeostatic belief precision. *Biological Psychology*, 165: 108190.
- Unick, J. L., Strohacker, K., Papandonatos, G. D., Williams, D., O’Leary, K. C., Dorfman, L., Becofsky, K. and Wing, R. R. (2015). Examination of the consistency in affective response to acute exercise in overweight and obese women. *Journal of Sport & Exercise Psychology*, 37: 534–546.
- Utter, A., Kang, J. and Robertson, R. J. (2007). *Perceived exertion* (on-line).
- Vallacher, R. R., Coleman, P. T., Nowak, A. and Bui-Wrzosinska, L. (2010). Rethinking intractable conflict: The

- perspective of dynamical systems. *American Psychologist*, 65: 262–278.
- Vázquez, P., Hristovski, R. and Balagué, N. (2016). The path to exhaustion: Time-variability properties of coordinative variables during continuous exercise. *Frontiers in Physiology*, 7: 37.
- Venhorst, A., Micklewright, D. and Noakes, T. D. (2018a). Modelling perception-action coupling in the phenomenological experience of “hitting the wall” during long-distance running with exercise-induced muscle damage in highly trained runners. *Sports Medicine - Open*, 4: 30.
- Venhorst, A., Micklewright, D. and Noakes, T. D. (2018b). Modelling the process of falling behind and its psychophysiological consequences. *British Journal of Sports Medicine*, 52: 1523–1528.
- Venhorst, A., Micklewright, D. and Noakes, T. D. (2018c). Perceived fatigability : Utility of a three - dimensional dynamical systems framework to better understand the psychophysiological regulation of goal - directed exercise behaviour. *Sports Medicine*, 48: 2479–2495.
- Venhorst, A., Micklewright, D. and Noakes, T. D. (2017). Towards a three-dimensional framework of centrally regulated and goal-directed exercise behaviour: A narrative review. *British Journal of Sports Medicine: bjsports-2016-096907*.
- Vera, J., Perales, J. C., Jiménez, R. and Cárdenas, D. (2018). A test-retest assessment of the effects of mental load on ratings of affect, arousal and perceived exertion during submaximal cycling. *Journal of Sports Sciences*, 36: 2521–2530.
- Volz, L. J., Eickhoff, S. B., Pool, E.-M., Fink, G. R. and Grefkes, C. (2015). Differential modulation of motor network connectivity during movements of the upper and lower limbs. *NeuroImage*, 119: 44–53.
- Vytal, K. and Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: A voxel-based meta-analysis. *Journal of Cognitive Neuroscience*, 22: 2864–2885.
- Wallman-Jones, A., Perakakis, P., Tsakiris, M. and Schmidt, M. (2021). Physical activity and interoceptive processing: Theoretical considerations for future research. *International Journal of Psychophysiology*, 166: 38–49.
- Wallman, K. E., Morton, A. R., Goodman, C. and Grove, R. (2004). Physiological responses during a submaximal cycle test in chronic fatigue syndrome. *Medicine & Science in Sports & Exercise*, 36: 1682–1688.
- Wallman, K. E. and Sacco, P. (2007). Sense of effort during a fatiguing exercise protocol in chronic fatigue syndrome. *Research in Sports Medicine*, 15: 47–59.
- Walton, M. E., Kennerley, S. W., Bannerman, D. M., Phillips, P. E. . and Rushworth, M. F. . (2006). Weighing up the benefits of work: Behavioral and neural analyses of effort-related decision making. *Neural Networks*, 19: 1302–1314.
- Wang, X., Wu, Q., Egan, L., Gu, X., Liu, P., Gu, H., Yang, Y., Luo, J., Wu, Y., Gao, Z. and Fan, J. (2019). Anterior insular cortex plays a critical role in interoceptive attention. *eLife*, 8: e42265.
- Weavil, J. C., Sidhu, S. K., Mangum, T. S., Richardson, R. S. and Amann, M. (2016). Fatigue diminishes motoneuronal excitability during cycling exercise. *Journal of Neurophysiology*, 116: 1743–1751.
- Weinberg, R. S., Gould, D. and Jackson, A. (1979). Expectations and performance: An empirical test of Bandura’s self-efficacy theory. *Journal of Sport Psychology*, 1: 320–331.
- Weinberg, R. S., Gould, D., Yukelson, D. and Jackson, A. (1981). The effect of preexisting and manipulated self-efficacy on a competitive muscular endurance task. *Journal of Sport Psychology*, 3.
- Weir, J. P., Beck, T. W., Cramer, J. T. and Housh, T. J. (2006). Is fatigue all in your head? A critical review of the central governor model. *British Journal of Sports Medicine*, 40: 573–586; discussion 586.
- Welch, A. S., Hulley, A., Ferguson, C. and Beauchamp, M. R. (2007). Affective responses of inactive women to a maximal incremental exercise test: A test of the dual-mode model. *Psychology of Sport & Exercise*, 8: 401–423.
- Westbrook, A. and Braver, T. S. (2015). Cognitive effort: A neuroeconomic approach. *Cognitive, Affective, & Behavioral Neuroscience*, 15: 395–415.

- Whitehead, L. (2009). The measurement of fatigue in chronic illness: A systematic review of unidimensional and multidimensional fatigue measures. *Journal of Pain and Symptom Management*, 37: 107–128.
- Whittaker, R. L., Sonne, M. W. and Potvin, J. R. (2019). Ratings of perceived fatigue predict fatigue induced declines in muscle strength during tasks with different distributions of effort and recovery. *Journal of Electromyography and Kinesiology*, 47: 88–95.
- Wiens, S., Mezzacappa, E. S. and Katkin, E. S. (2000). Heartbeat detection and the experience of emotions. *Cognition & Emotion*, 14: 417–427.
- Wiens, S. and Palmer, S. N. (2001). Quadratic trend analysis and heartbeat detection. *Biological Psychology*, 58: 159–175.
- Williamson, J. W., McColl, R., Matthews, D., Mitchell, J. H., Raven, P. B. and Morgan, W. P. (2001). Hypnotic manipulation of effort sense during dynamic exercise: Cardiovascular responses and brain activation. *Journal of Applied Physiology*, 90: 1392–1399.
- Wingfield, G., Marino, F. E. and Skein, M. (2018). The influence of knowledge of performance endpoint on pacing strategies, perception of effort, and neural activity during 30-km cycling time trials. *Physiological Reports*, 6: e13892.
- Winter, E. M. and Fowler, N. (2009). Exercise defined and quantified according to the Système International d'Unités. *Journal of Sports Sciences*, 27: 447–460.
- Wolpert, D. M. and Flanagan, J. R. (2001). Motor prediction. *Current Biology*, 11: R729–R732.
- Wolpert, D. M. and Miall, R. C. (1996). Forward models for physiological motor control. *Neural Networks*, 9: 1265–1279.
- Wright, R. A. (2008). Refining the prediction of effort: Brehm's distinction between potential motivation and motivation intensity. *Social and Personality Psychology Compass*, 2: 682–701.
- Wrightson, J. G. and Twomey, R. (2021). Exercise and chronic fatigue. In: Z. Zenko & L. Jones (eds) *Essentials of exercise and sport psychology: An open access textbook*. Society for Transparency, Openness, and Replication in Kinesiology. pp.409–428.
- Ye, X., Beck, T. W., Wages, N. P. and Carr, J. C. (2018). Sex comparisons of non-local muscle fatigue in human elbow flexors and knee extensors. *Journal of Musculoskeletal and Neuronal Interactions*, 18: 92–99.
- Yzerbyt, V., Muller, D., Batailler, C. and Judd, C. M. (2018). New recommendations for testing indirect effects in mediational models: The need to report and test component paths. *Journal of Personality and Social Psychology: Attitudes and Social Cognition*, 115: 929–943.
- Zacharioudakisa, N., Vlemincx, E. and Van den Bergh, O. (2020). Categorical interoception and the role of threat. *International Journal of Psychophysiology*, 148: 25–34.
- Zaki, J., Davis, J. I. and Ochsner, K. N. (2012). Overlapping activity in anterior insula during interoception and emotional experience. *NeuroImage*, 62: 493–499.
- Zénon, A., Sidibé, M. and Olivier, E. (2015). Disrupting the supplementary motor area makes physical effort appear less effortful. *Journal of Neuroscience*, 35: 8737–8744.
- Zénon, A., Solopchuk, O. and Pezzulo, G. (2019). An information-theoretic perspective on the costs of cognition. *Neuropsychologia*, 123: 5–18.
- Zijdewind, I., Zwarts, M. J. and Kernell, D. (1998). Influence of a voluntary fatigue test on the contralateral homologous muscle in humans? *Neuroscience Letters*, 253: 41–44.
- Zwarts, M. J., Bleijenberg, G. and van Engelen, B. G. M. (2008). Clinical neurophysiology of fatigue. *Clinical Neurophysiology*, 119: 2–10.