

**CHARACTERIZING PSYCHOMOTOR PERFORMANCE EFFECTS OF COGNITIVE
FATIGUE**

KATHLEEN PETERS

Thesis submitted to the University of Ottawa
in partial fulfillment of the requirements for the
Doctorate in Philosophy Human Kinetics

School of Human Kinetics
Faculty of Health Sciences
University of Ottawa

© Kathleen Peters, Ottawa, Canada, 2026

Preface

I, Kathleen Peters, was primarily responsible for this research program, including experimental conceptualization and design, participant recruitment, data collection, and analysis. Input and oversight were provided by my thesis committee consisting of Dr. Anthony N. Carlsen (supervisor), Dr. Erin K. Cressman, and Dr. Dana Maslovat. Resources and software for experiments were provided by Dr. Anthony N. Carlsen. Manuscript preparation for all chapters was completed by me, Kathleen J. Peters, with input and/or editorial contributions from Dr. Dana Maslovat and Dr. Anthony N. Carlsen.

Chapter 2 contains content from a published article:

Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>

Reproduced with permission from Springer Nature.

Chapter 3 contains content from a published article:

Peters, K. J., Maslovat, D., & Carlsen, A. N. (2024). Visual perceptual processing is unaffected by cognitive fatigue. *Consciousness and Cognition*, 119, 103666. <https://doi.org/10.1016/j.concog.2024.103666>

Reproduced with permission from Elsevier.

Abstract

Cognitive fatigue (CF) is a state of perceived exhaustion arising from sustained mental effort that is both commonly experienced and consequential. CF negatively affects a broad range of cognitive functions, including working memory, decision making, and attention. It can also impair psychomotor performance, such as the ability to generate timely and accurate goal-directed actions, commonly indexed using reaction time (RT). CF-related psychomotor impairments, including slowed RT, may contribute to the risk of accidents or errors across a range of activities and occupations, including athletics, transportation, construction, and healthcare. Despite this, the mechanisms underlying CF-related psychomotor performance deficits remain poorly understood, and there is limited evidence regarding how these impairments might be mitigated.

This thesis addressed these gaps by systematically investigating the effects of CF on multiple psychomotor processes contributing to RT performance and evaluating a potential intervention to attenuate CF-related deficits. Across four experiments using behavioural and neurophysiological approaches, it was found that stimulus perception, response inhibition, and motor preparation were largely preserved under CF, with the latter showing evidence of compensatory activity. In contrast, response selection was found to be selectively vulnerable to CF, with the degree of disruption depending on the overlap in cognitive demands with recent fatiguing mental work. Taken together, findings suggest that response initiation could play a central role in CF-related RT slowing and may present a key target for future investigation. Finally, a fifth experiment provided promising preliminary evidence supporting further investigation of transcutaneous vagus nerve stimulation as a non-invasive countermeasure for CF-related psychomotor deficits.

Overall, this work advances our understanding of the mechanisms underlying CF-related psychomotor performance impairment by characterizing the effects of CF across multiple stages of psychomotor processing. It also provides preliminary support for tVNS as a potential countermeasure for these deficits. These findings may have particularly relevant implications for safety-critical environments, where even small delays in responding could increase risk.

Acknowledgements

Completion of this doctoral program would not have been possible without the guidance, encouragement, and support I received from several individuals. First and foremost, I would like to thank Dr. Anthony Carlsen, who helped me find my way in a new field with unwavering enthusiasm and support. He has been instrumental in helping me build knowledge, skills, and confidence, providing me countless opportunities to grow, and always keeping me excited about research, for which I am extremely grateful. I am also very thankful for the sincere guidance and encouragement provided by Dr. Dana Maslovat and Dr. Erin Cressman – I appreciate your dedication to my success, your valuable advice, and your constant willingness to help.

I would also like to thank present and past members of the Neuromotor Behaviour Lab. They have been an additional source of support and knowledge and have helped to make the last several years truly enjoyable. Working alongside them has helped me to become a better researcher and mentor, which I truly appreciate.

I must also thank Dr. John Lewis, my undergraduate and master's thesis supervisor, who started me on a path of curiosity and enthusiasm for scientific research and who has continued to provide unwavering support, guidance, and encouragement over all these years.

Finally, I would like to thank my friends and family, without whom I am certain none of this would have been possible. To my brother Colin, thank you for always finding a way to make me laugh, even when I didn't feel like it. To my parents – you have been my rock through every up and down. Thank you for supporting me without fail during the tough times, celebrating with me in the good moments, and for your patience and advice. The heavy things are always lighter when we've talked them through. Lastly, thank you to my grandparents, who I know would be so proud, and to my brother Matthew, who looks out for me constantly. I've got my lucky stone!

Table of Contents

Preface.....	ii
Abstract	iii
Acknowledgements	v
Table of Contents	vi
List of Abbreviations.....	x
List of Tables.....	xi
List of Figures	xiii
Chapter 1: General Introduction	1
1.1 General Overview	1
1.2 Current Understanding of Cognitive Fatigue.....	2
1.3 Psychobiological Basis of Cognitive Fatigue	4
1.4 Studying Cognitive Fatigue	7
1.5 Impacts of Cognitive Fatigue.....	12
1.6 Research Question	15
1.7 Overview of Experiments	17
1.8 References.....	21
Chapter 2. Experiment 1 - Slowed Reaction Times in Cognitive Fatigue Are Not Attributable to Declines in Motor Preparation	38
2.1 Abstract.....	38
2.2 Introduction.....	39
2.3 Materials and Methods.....	44
2.4 Dependent Variables.....	50
2.5 Data Reduction	52
2.6 Statistical Analysis.....	53
2.7 Compliance with Ethical Standards	55

2.8 Results.....	55
2.9 Discussion.....	60
2.10 Conclusion	65
2.11 References.....	67
Chapter 3. Experiment 2 - Visual Perceptual Processing is Unaffected by Cognitive Fatigue	76
3.1 Abstract.....	76
3.2 Introduction.....	76
3.3 Materials and Methods.....	80
3.4 Data Reduction	87
3.5 Statistical Analysis.....	88
3.6 Results.....	91
3.7 Discussion.....	98
3.8 Conclusion	102
3.9 References.....	104
Chapter 4. Experiment 3 - Task-Specific Impacts of Cognitive Fatigue on Subjective Experience and Psychomotor Performance	113
4.1 Abstract.....	113
4.2 Introduction.....	114
4.3 Materials and Methods.....	118
4.4 Data Reduction	121
4.5 Statistical Analysis.....	122
4.6 Results.....	123
4.7 Discussion.....	129
4.8 Conclusion	135
4.9 References.....	136
Chapter 5. Experiment 4 - Corticospinal Excitability During Movement Preparation: Effects of Cognitive Fatigue.....	145
5.1 Abstract.....	145
5.2 Introduction.....	146
5.3 Materials and Methods.....	151
5.4 Data Reduction	157

5.5 Statistical Analysis.....	159
5.6 Results.....	160
5.7 Discussion.....	170
5.8 Conclusion	176
5.9 References.....	178
Chapter 6. Experiment 5 - Preliminary Evidence for Attenuation of Cognitive Fatigue Effects on Psychomotor Performance Following Auricular tVNS: A Sham-Controlled Pilot Study	189
6.1 Abstract.....	189
6.2 Introduction.....	190
6.3 Materials and Methods.....	193
6.4 Data Reduction	200
6.5 Statistical Analysis.....	201
6.6 Results.....	203
6.7 Discussion.....	212
6.8 Conclusion	217
6.9 References.....	218
Chapter 7. General Discussion.....	230
7.1 Summary.....	230
7.2 Psychomotor Impacts of Cognitive Fatigue: Current Insights and Future Directions	232
7.3 Applied Insights: Researching, Screening, and Mitigating Cognitive Fatigue.....	248
7.4 Limitations	250
7.5 Concluding Remarks.....	255
7.6 References.....	257
Appendix A. Supplementary Material for Chapter 2	273
A.1 Supplementary Reaction Time Analysis.....	273
A.2 Supplementary Analysis of Individual Subjective Cognitive Fatigue Measures	275
A.3 Supplementary Bayesian Analysis of SAS Trial Reaction Time.....	279
A.4 Supplementary References.....	280
Appendix B. Supplementary Material for Chapter 4.....	281
B.1 Supplementary Methods.....	281

B.2 Supplementary Data Reduction.....	284
B.3 Supplementary Analyses	286
B.4 Supplementary Results.....	287
B.5 Supplementary Figures.....	290
B.6 Supplementary References	292
Appendix C. Supplementary Material for Chapter 6	294
C.1 Supplementary Methods.....	294
C.2 Supplementary Analyses	294
C.3 Supplementary Results.....	295
C.4 Supplementary References.....	303
Appendix D. Description of Cognitive Intervention Performance	304
D.1 Summary	304
D.2 Tables and Figures	305
Appendix E. Materials Used Across Experiments	316
E.1 Pre-Session Lifestyle Questionnaire.....	316
E.2 Video Descriptions of Cognitive Interventions	317
Appendix F. Trial Counts	318
Appendix G. Certificates of Ethics Approval	326

List of Abbreviations

CF	Cognitive Fatigue
CTL	Control
DB	Time Load Dual-Back Task
ECG	Electrocardiography
ECR	Extensor Carpi Radialis Longus
EEG	Electroencephalography
EMG	Electromyography
ERP	Event-Related Potential
FCR	Flexor Carpi Radialis
FDI	First Dorsal Interosseous
GLMM	Generalized Linear Mixed Effects Model
HRV	Heart Rate Variability
IBI	Inter-Beat Interval
IT	Inspection Time
LMM	Linear Mixed Effects Model
MEP	Motor-Evoked Potential
MM	Math-Memory
NF	Non-Fatiguing
PMC	Premotor Cortex
PVT	Psychomotor Vigilance Task
RMSSD	Root Mean Square of Successive Differences
RMT	Resting Motor Threshold
RT	Reaction Time
SAS	Startling Acoustic Stimulus
SCM	Sternocleidomastoid
SICI	Short-Interval Intracortical Inhibition
ST	Stroop
TMS	Transcranial Magnetic Stimulation
tVNS	Transcutaneous Vagus Nerve Stimulation
VAS	Visual Analog Scale

List of Tables

Table 3.1 Post hoc comparisons of inspection time task performance.....	97
Table 4.1 Description of data set exclusion.....	122
Table 4.2 Post hoc comparisons vs. control for subjective ratings and reaction time.....	127
Table 6.1 Post hoc comparisons by stimulation condition and testing time.....	210
Table C.1 Effect of stimulation condition on reported side-effect prevalence and intensity	302
Table D.1 Descriptive statistics for Math-Memory intervention performance across experiments	305
Table D.2 Descriptive statistics for Modified Stroop (ST) and Time Load Dual-Back (DB) intervention performance in Experiment 3	313
Table F.1 By-subject and condition trial count: mean and range of reaction time (SCM+ and Control) in Experiment 1	318
Table F.2 By-subject and condition trial count: mean and range of reaction time in Experiment 2	318
Table F.3 By-subject and condition trial count: mean and range of reaction time in Experiment 3	319
Table F.4 By-subject and condition trial count: mean and range for cognitive interventions in Experiment 3	320
Table F.5 By-subject and condition trial count: mean and range for response errors in Experiment 3	320
Table F.6 By-subject and condition trial count: mean and range of premotor reaction time in Experiment 4	321

Table F.7 By-subject and condition trial count: mean and range of displacement reaction time in Experiment 4	322
Table F.8 By-subject and condition trial count: mean and range of resting motor-evoked potential amplitude in Experiment 4	322
Table F.9 By-subject and condition trial count: mean and range of preparatory motor-evoked potential amplitude in Experiment 4	323
Table F.10 By-subject and condition trial count: mean and range of premotor reaction time in Experiment 5	324
Table F.11 By-subject and condition trial count: mean and range of displacement reaction time in Experiment 5	324
Table F.12 By-subject and condition trial count: mean and range of EMG burst magnitude (Q100) in Experiment 5	325
Table F.13 By-subject and condition trial count: mean and range of anticipatory responses in Experiment 5	325

List of Figures

Fig. 1.1 Conceptual framework of the thesis	17
Fig. 1.2 Outline of general methodology	17
Fig. 2.1 Experimental timeline	45
Fig. 2.2 Estimated marginal mean subjective cognitive fatigue scores	56
Fig. 2.3 Estimated marginal mean premotor reaction time.....	59
Fig. 3.1 A schematic illustration of the timeline for each trial of the inspection time task	86
Fig. 3.2 Estimated marginal mean subjective cognitive fatigue scores	92
Fig. 3.3 Estimated marginal mean reaction time	94
Fig. 3.4 Model predicted probability of a correct response for each stimulus display duration during the inspection time task	96
Fig. 4.1 Timeline of tasks involved in an experimental session.	121
Fig. 4.2 Model-estimated mean pre- to post-intervention change in subjective rating	124
Fig. 4.3 Model-estimated mean pre- to post-intervention change in reaction time.....	126
Fig. 4.4 Model-estimated mean pre- to post-intervention change in reaction time task error count	129
Fig. 5.1 Experimental timeline	157
Fig. 5.2 Subjective ratings	162
Fig. 5.3 Premotor simple reaction time (ms)	164
Fig. 5.4 Displacement simple reaction time (ms)	166

Fig. 5.5 Resting peak-to-peak motor-evoked potential (MEP) amplitude (mV)	168
Fig. 5.6 Preparatory peak-to-peak motor-evoked potential (MEP) amplitude (mV).....	170
Fig. 6.1 Experimental overview.....	196
Fig. 6.2 Subjective ratings	204
Fig. 6.3 Reaction time.....	206
Fig. 6.4 RT task response EMG burst magnitude (Q100)	207
Fig. 6.5 Probability of an anticipatory response error on the RT task	208
Fig. 6.6 Heart rate measures	209
Fig. 7.1 Schematic timeline of events in a simple reaction time task.....	243
Fig. 7.2 Conceptual model of potential central and peripheral initiation mechanisms underlying cognitive fatigue-related psychomotor performance impairment.....	247
Fig. A.1 Scores for individual subjective cognitive fatigue measures.....	278
Fig. B.1 Model-estimated mean change in tension and difficulty concentrating	290
Fig. B.2 Model predicted probability of an adaptive difficulty reduction (proxy for performance decline) in the cognitive interventions	291
Fig. C.1 Reaction time by testing block	297
Fig. C.2 Math-Memory cognitive task performance metrics	299
Fig. C.3 Average tVNS side-effect ratings (0-10) by stimulation condition (active, sham)	301
Fig. D.1 Histograms of the proportion of math problems correctly completed in the Math- Memory intervention by experiment	306

Fig. D.2 Average proportion of math problems correctly completed in the Math-Memory intervention over time (trial number) by Experiment	307
Fig. D.3 Histograms of the proportion of letters correctly remembered in the Math-Memory intervention by experiment	308
Fig. D.4 Average proportion of letters correctly remembered in the Math-Memory intervention over time (trial number) by Experiment	309
Fig. D.5 Histograms of the letter stimuli display durations in the Math-Memory intervention by experiment.....	310
Fig. D.6 Letter stimuli display durations in the Math-Memory intervention over time (trial number) by experiment	311
Fig. D.7 Average letter display durations in the Math-Memory intervention over time (trial number) by experiment	312
Fig. D.8 Performance on the Time Load Dual-Back (DB) intervention in Experiment 3	314
Fig. D.9 Performance on the Modified Stroop (ST) intervention in Experiment 3	315

Chapter 1: General Introduction

1.1 General Overview

Cognitive fatigue (CF) is a commonly experienced psychobiological state of perceived exhaustion that occurs in response to a sustained mental effort (Leavitt & DeLuca, 2010). Along with a marked reduction in mood states, CF has been linked to a range of mental performance decrements, including impaired working memory, decision making, and attentional focus (Boksem et al., 2005; Farahani et al., 2026; Pessiglione et al., 2025). Importantly, CF also impairs psychomotor performance, or the ability to generate timely and accurate goal-directed actions, often indexed using reaction time (RT) metrics (Habay et al., 2021; Hindmarch, 2015). Given the importance of this ability for safe and effective interaction with our environment, the effect of CF on psychomotor performance is particularly worthy of investigation (Habay et al., 2021; H. Zhou et al., 2025). Indeed, slowed RT in response to CF has been implicated as a risk factor in road accidents for both drivers and cyclists, and as a significant workplace hazard in many occupations (Fazackerley et al., 2025; Mizuno et al., 2020; Petrut et al., 2020; Zeuwts et al., 2021; H. Zhou et al., 2025).

However, despite these serious implications, there is only a limited understanding of the mechanism by which CF impacts psychomotor performance. Psychomotor performance is not unitary but instead is thought to reflect a set of component sensory, cognitive and motor processes (Czyż, 2021; Hindmarch, 2015). Identifying which components are particularly sensitive to CF may be critical in clarifying how CF leads to psychomotor performance decrements. Moreover, despite the costs of CF, knowledge of effective and practical ways to attenuate its effects on psychomotor performance is lacking. As such, this thesis aimed to first characterize the effects of CF on individual psychomotor processes contributing to overall

performance (*Experiments 1-4*), and to subsequently explore an intervention which may mitigate CF-related psychomotor performance decrements (*Experiment 5*).

1.2 Current Understanding of Cognitive Fatigue

Fatigue is a multidimensional phenomenon. It has been described as a subjective experience, such as an “overwhelming sense of tiredness, lack of energy, and a feeling of exhaustion” (Shen et al., 2006, p. 70). It is also sometimes qualified by its behavioural outcomes, as a “reduction in performance with either prolonged or unusual exertion” (DeLuca, 2005, p. 320). Alternatively, it can be viewed as a physiological state of the muscles and/or central nervous system (Job & Dalziel, 2000). Generally, fatigue is a leading reason for which patients seek medical care (Maisel et al., 2021; Nicholson et al., 2015). It can be a debilitating symptom of several medical conditions and a particularly frustrating side effect of certain medications (Chaudhuri & Behan, 2004; Delgado-Alonso et al., 2022; Mozuraityte et al., 2023; Pradeep et al., 2025). Notably, fatigue may also occur in the absence of any specific pathology, such as following sleep deprivation or prolonged mental or physical exertion (“cognitive fatigue” and “physical fatigue”, respectively; DeLuca, 2005; Pessiglione et al., 2025).

Physical fatigue refers to a reduction in the ability to generate muscular force following physical effort and is relatively well understood (Tanaka & Watanabe, 2012). In contrast, the mechanisms underlying cognitive fatigue (CF) are less evident. While the exact definition of CF is often debated (Oliver et al., 2025), it is operationalized here as a psychobiological state of perceived exhaustion triggered by a challenging and sustained mental effort (Ackerman, 2011; Pessiglione et al., 2025). It is characterized by subjective sensations of fatigue and an aversion to continued mental effort, and is sometimes accompanied by reduced ability to meet cognitive, and in some cases physical, task demands (Pessiglione et al., 2025; Van Cutsem et al., 2017).

Notably, CF is considered distinct from fatigue occurring in sleep deprivation, although the resulting sensations of exhaustion may be comparable (Shen et al., 2006). Additionally, CF can be a common yet debilitating symptom of several medical conditions, including multiple sclerosis (Craft et al., 2025), traumatic brain injury (Ezekiel et al., 2021), and post-stroke syndrome (Almhdawi et al., 2021). Even among healthy individuals, CF is difficult to avoid, particularly in modern environments. It results from a myriad of everyday activities, from office work (Brazaitis & Satas, 2023) and studying (A. P. Smith, 2018), to browsing social media (Fortes et al., 2023), playing video games (Faro et al., 2023; Fortes et al., 2023), and participating in virtual meetings (McCabe et al., 2023). It is also prevalent in a variety of professions including transportation (Jaydarifard et al., 2024; Reis & Canhão, 2013), education (Kristiansen et al., 2014), health care (Barker & Nussbaum, 2011; Petrut et al., 2020), and construction (H. Zhou et al., 2025).

Meanwhile, the potential consequences of CF are wide-ranging. It can slow reaction time (RT; Habay et al., 2021; Jaydarifard et al., 2019; Langner et al., 2010; Staiano et al., 2024), impair decision-making (Gantois et al., 2020; Wiehler et al., 2022), and perhaps even impede sensory processing (Jain et al., 2022; van der Linden et al., 2006), among other effects. These impacts can be costly and potentially dangerous, contributing to reduced workplace productivity (Biondi et al., 2021; Ricci et al., 2007), increased medical errors (Rahmani et al., 2025; Thomas et al., 2012), impaired athletic performance (Habay et al., 2021), elevated fall risk (Pitts & Bhatt, 2023), and an increased likelihood of road or workplace accident (Minusa et al., 2021; Mizuno et al., 2020; H. Zhou et al., 2025). Despite this, the biological basis of CF and the mechanisms by which it influences human performance are not well understood.

1.3 Psychobiological Basis of Cognitive Fatigue

While no single account is widely accepted, there has been considerable speculation regarding the neural, metabolic, and psychological mechanisms that might underlie CF development (Pessiglione et al., 2025). According to one outlook (often termed the “functional” or “motivational” perspective), CF reflects a cost-benefit calculation that adaptively shifts behaviour away from effortful tasks toward less demanding or more rewarding alternatives (Boksem & Tops, 2008; Hockey, 2011; Kurzban et al., 2013). This perspective is supported by evidence that rewards or incentives can sometimes restore task performance despite subjective exhaustion, suggesting that performance capacity may not necessarily be depleted, but rather suppressed (Boksem et al., 2006; Herlambang et al., 2019).

However, critics have argued that instead of tracking CF, motivational changes may instead reflect increasing boredom or frustration with prolonged task performance (Pessiglione et al., 2025). Furthermore, the performance benefits of external incentives in CF are sometimes inconsistent (e.g., Gergelyfi et al., 2015, 2021), indicating that motivational factors alone are unlikely to fully explain CF. As such, others have instead advocated for a “biological” or “neuro-metabolic” perspective, where CF is generated by neural and metabolic changes resulting from sustained cognitive control (Pessiglione et al., 2025; Salihu et al., 2022).

A third possibility is that a complementary blend of these two differing perspectives exists. Under this view, CF may *begin* as a sensation - a “biological alarm signal” indicating that cognitive demands are rising toward levels that may eventually become metabolically costly or harmful (Ishii et al., 2014; Pessiglione et al., 2025). Depending on factors like task difficulty and motivation, performance may initially be maintained via a “mental facilitation system” (Ishii et al., 2014). At the same time, fatigue sensations may build due to activation of a corresponding

“mental inhibition system” (Ishii et al., 2014). With continued mental effort, potentially harmful metabolic changes may begin to emerge (Wiehler et al., 2022), which could trigger further enhancement of the inhibition system and/or reduced facilitation (Ishii et al., 2014; Pessiglione et al., 2025). Alongside potential performance decrements, this would theoretically result in rising discomfort and sensations of fatigue, with the goal of encouraging task disengagement to allow metabolic recovery (Ishii et al., 2014). This balance between facilitation and inhibition has been termed a “dual-regulation system”, wherein mental fatigue might arise if i) the facilitation system is insufficiently activated; ii) activity of the mental inhibition system is increased; or iii) both occur simultaneously (Ishii et al., 2014). Notably, other similar integrative accounts have also been proposed, including the metabolico-motivational model of CF (MetaMotiF; Pessiglione et al., 2025).

What exactly might drive each component of this dual-regulation system remains unclear. Although several brain regions have been proposed to be involved (Salihu et al., 2022), regions within the cognitive control network, particularly the anterior cingulate and dorsolateral prefrontal cortices, may help drive the facilitation system (Cole & Schneider, 2007; Lorist et al., 2005; Salihu et al., 2022). The basal ganglia may also contribute, considering their extensive dopaminergic connections with cortical control networks (Boksem & Tops, 2008; Chaudhuri & Behan, 2000; Tanaka et al., 2014). In terms of neurotransmitter involvement in the facilitation system, dopamine has received particular attention (Dobryakova et al., 2013), as dopamine signalling may mediate motivational impacts and promote effort maintenance during CF (Lorist et al., 2009; Meeusen et al., 2021). Involvement of the locus coeruleus – norepinephrine (LC-NE) system has also been proposed, potentially via its role in promoting arousal (van der Linden, 2011).

In contrast, the inhibition system has been linked to the insular cortex and default mode network regions such as the posterior cingulate cortex (Broyd et al., 2009; Gergelyfi et al., 2021; Ishii et al., 2014; Salihu et al., 2022). Activation of this system has been hypothesized to result from depletion of some central resource, such as brain glucose (Gailliot et al., 2007) or glycogen stores (Christie & Schrater, 2015), or due to accumulation of metabolic byproducts with potentially neurotoxic effects, such as adenosine (Holroyd, 2015; Meeusen et al., 2021). Adenosine is an inhibitory neurotransmitter that can accumulate in the brain as a result of substantive ATP breakdown, which may occur with sustained neural activity and be accelerated by intense cognitive effort (Martin et al., 2018; Meeusen et al., 2021). Furthermore, adenosine may be hypogenic – promoting tiredness while suppressing the release of excitatory neurotransmitters like dopamine (Martin et al., 2018; Porkka-Heiskanen, 1999). Thus, elevated adenosine concentrations could dually contribute to CF by both enhancing the inhibition system and suppressing the facilitation system.

More recently, central glutamate accumulation has also been implicated in CF (Wiehler et al., 2022). Excess extracellular glutamate can impair neural signalling or become neurotoxic in extreme cases (Y. Zhou & Danbolt, 2014). Accumulation of glutamate in the lateral prefrontal cortex has been observed following fatiguing day-long mental work and high working memory task demands (Wiehler et al., 2022; Woodcock et al., 2018). In line with this, Wiehler and colleagues (2022) propose that CF plays an adaptive role in avoiding potentially neurotoxic levels of extracellular glutamate, in that sensations of CF may develop in order to discourage continued mental effort and allow metabolic recovery.

Overall, several biological, metabolic, and motivational mechanisms have been proposed to contribute to CF development, none of which are definitive (Pessiglione et al., 2025). It is

possible that several of these mechanisms operate in parallel, but further study is needed to clarify how CF-mechanisms relate to behavioural impacts – including impaired psychomotor performance.

1.4 Studying Cognitive Fatigue

1.4.1 Inducing Cognitive Fatigue

Given the prevalence and impacts of CF, there is considerable interest in investigating this phenomenon experimentally. Laboratory studies typically induce CF using prolonged, mentally demanding tasks. Successful induction is most commonly confirmed by increases in subjective ratings of CF, while performance outcomes are assessed either within the fatiguing task itself or using a separate measure administered before and after the manipulation (Ackerman, 2011; Schamphoeleer et al., 2025).

There is no consensus on the optimal task for CF induction. However, commonly employed interventions include sustained vigilance paradigms (e.g., psychomotor vigilance task, AX-continuous performance test; O’Keeffe et al., 2020; M. R. Smith et al., 2019), working memory tasks (e.g., N-back tasks; Borragán et al., 2016; O’Keeffe et al., 2020), and/or response inhibition tasks (e.g., Stroop Tasks; Pageaux et al., 2015; M. R. Smith et al., 2019). Other interventions that may better reflect real-world fatiguing activities have also been used (Bian et al., 2025), such as mathematical problem solving (G. Li et al., 2020; Ung et al., 2020), video game play or social media use (Bian et al., 2025), transcription tasks (Englert & Bertrams, 2014; Shin et al., 2019), and simulated driving (Guo et al., 2018).

Overall, paradigms that successfully induce CF are thought to share several common characteristics. For instance, the task must be sufficiently challenging and/or performed for a long enough duration to induce CF (Borragán et al., 2017; Pessiglione et al., 2025). More

difficult mental tasks may require less time to induce CF, while less effortful tasks may need to be performed for substantially longer periods to produce a comparable effect (Ackerman et al., 2010; Borragán et al., 2017; O’Keeffe et al., 2020). This may help explain why CF-inducing interventions vary considerably in length, ranging from 10 minutes to over 6 hours, and why CF appears to be induced more efficiently when task difficulty is customized to individual participant ability (Borragán et al., 2017; Habay et al., 2023; O’Keeffe et al., 2020; Wiehler et al., 2022). A lack of breaks or rest periods is also considered an important factor in CF induction; conversely, it is typically recommended that excessive boredom should be avoided (Ackerman, 2011). Although some propose that boredom may actually contribute to CF (Lorist & Faber, 2011; M. R. Smith et al., 2019), the more widely held view is that boredom is a distinct process reflecting a passive “underload” condition. In contrast, CF is considered an active or “overload” state occurring when task demands become unmanageable for the available cognitive resources or capacity (Ackerman et al., 2010; Pattyn et al., 2008).

The *active* form of CF is thought to be best induced, according to Pickering and colleagues (2024, p. 51), by tasks that are “challenging and difficult, but at a level that is engaging”. Accordingly, it has been suggested that CF-inducing interventions should avoid relying on automatic processing and may benefit from combining multiple cognitive requirements (Schampheleer et al., 2025). Time pressure may also enhance induction, along with a low tolerance for errors, such that lapses in attention are costly to performance outcomes (Ackerman et al., 2010). At the same time, interventions should not be *so* challenging that they become discouraging or demotivating, which, like boredom, may confound CF-related effects (Pickering et al., 2024; Schampheleer et al., 2025).

Despite these considerations, no standardized CF-induction protocols exist, which remains a notable challenge for CF research. Recent work has proposed some potential guidelines for CF induction (Schampheleer et al., 2025) and compared the effectiveness of common CF-inducing interventions (O’Keeffe et al., 2020; M. R. Smith et al., 2019). However, further work is still necessary. For instance, it remains unclear how overlapping cognitive demands between CF-inducing tasks and subsequent performance metrics (e.g., reaction time assessments) may influence the observed effects of CF – an aspect which could have important implications for applied CF monitoring and experimental assessment (Brossoit et al., 2023).

1.4.2 Measurement of Cognitive Fatigue

Measuring and confirming CF-induction is an additional challenge. Objective performance metrics are sometimes considered most optimal (Bryant et al., 2004; Hockey, 2011). This includes factors such as response speed, response accuracy, changes to the number of attempts made, or the quality of responses (Ackerman, 2011; M. R. Smith et al., 2019). In some cases, declines in these metrics within the fatigue-inducing task itself have been interpreted as evidence of CF induction. However, an alternative view suggests that CF induction may actually be more likely when CF task performance is *maintained*, as this could reflect more “active” cognitive engagement (Schampheleer et al., 2025). Considering this ambiguity, CF is instead often assessed using a completely separate outcome measure, typically compared before and after a CF-inducing intervention (M. R. Smith et al., 2019; Staiano et al., 2024). This is a viable option given that subjective sensations of CF can remain elevated for up to 60 minutes following a cognitively fatiguing effort, while impairment of objective (motor) performance typically persists for ~20-45 minutes – although notably, this is context dependent (Jacquet et al., 2021; Magnuson et al., 2021; M. R. Smith et al., 2019). For instance, a full workday (~6.5 hours) with a greater

than average workload has been shown to negatively impact central processing speed into the following day (Hernandez et al., 2024).

In addition to performance outcomes, objective CF measures may also include neurophysiological or physiological indices, such as electroencephalography (e.g., ERPs, spectral activity; Ismail & Karwowski, 2020; Tran et al., 2020), eye tracking measures (e.g., blinks, saccades, pupil size; Bafna & Hansen, 2021), and heart rate variability, which appears to increase with time-on-task (Csathó et al., 2024). However, it is notable that interpretation of these (neuro) physiological measures in the context of CF can be challenging; for instance, the degree to which they reflect general cognitive effort or CF specifically is not always well established (Lu et al., 2022; Schamphoeleer et al., 2025).

Alternatively, subjective assessments are also used to confirm CF induction. Subjective reports of fatigue sensations are the most commonly used confirmation metric, and some would argue the most sensitive (Kanfer, 2011; M. R. Smith et al., 2019). These are typically measured using validated questionnaires (e.g., Multidimensional Fatigue Inventory, Piper Fatigue Scale, Fatigue Assessment Scale; Kunasegaran et al., 2023; Michielsen et al., 2003; Reeve et al., 2012). However, these instruments can be long and complex and may include items not applicable to experimental CF assessment. Simpler rating scales (visual analog or Likert scales) are therefore often preferred, as they are quick to administer and simple to interpret (Schamphoeleer et al., 2025; M. R. Smith et al., 2019). These scales may evaluate CF directly (e.g., “How mentally fatigued do you feel?” or “How energetic do you feel?”) and may also be used to capture other related constructs, like stress level, affect, and motivation (Díaz-García et al., 2022; Schamphoeleer et al., 2025).

Broadly considered, subjective assessment is the preferred and most efficient method of confirming CF induction. However, given that little data exists to strongly link subjective and performance measures of CF (Behrens et al., 2023; Christodoulou, 2005), CF assessment using multiple metrics is sometimes recommended (Behrens et al., 2023; Schampheleer et al., 2025). However, this must be balanced with practicality and participant burden, which may already be elevated.

1.4.3 Factors Influencing Cognitive Fatigue

Some determinants of CF, such as task characteristics, task duration, and levels of motivation, have already been discussed. However, individual differences may also play a substantial role. Individuals are known to differ in their susceptibility to CF – or “fatiguability”, defined as the rate at which performance declines under sustained cognitive demand (Bafna & Hansen, 2021; Gao et al., 2025). There is some evidence that this inter-individual variability may have a genetic basis (Lim et al., 2012); however, it may also be influenced by variables such as age, sex assigned at birth, physical fitness level, sleep, diet, and medication use (Behrens et al., 2023; Habay et al., 2023).

Some factors appear to influence CF fairly consistently. Poor sleep quality, insufficient sleep duration, certain psychological or neurological conditions (e.g., burnout, depression, multiple sclerosis), and sedating medications (e.g., antihistamines) have all been linked to increased cognitive fatigability (Ackerman, 2011; Bender et al., 2003; Boolani & Manierre, 2019; Craft et al., 2025; Schampheleer et al., 2025). In contrast, caffeine and prescription stimulants (e.g., methylphenidate) appear to attenuate CF development (Johansson et al., 2015; Rogers et al., 2013; Van Cutsem et al., 2018).

Meanwhile, the effects of other individual factors are less clear. For example, age-related differences are mixed, with some studies showing no differences in CF outcome metrics between younger and older adults (Bouche et al., 2025), and others reporting greater fatiguability in either older (Wascher & Getzmann, 2014) *or* younger adults (Bouche et al., 2025; Gilsoul et al., 2024; Terentjeviene et al., 2018). Similarly, although performance-based measures of CF appear generally unaffected by sex (Jaydari Fard & Lavender, 2019; Kowalski et al., 2022), it is important to consider that females do tend to report general fatigue at higher rates than males (Pereira et al., 2025). The effects of physical fitness or athletic training level are similarly uncertain. On one hand, some studies have demonstrated greater resistance to CF among competitive athletes compared with amateurs or non-athletes (Jaydarifard et al., 2019; Martin et al., 2016), and improvements in CF resistance following endurance training in previously untrained individuals (Filipas et al., 2020). However, others have reported no differences between athletes and non-athletes or suggest that the CF-protective effect of fitness level may depend on the specific type of athletic training undertaken (Coyne et al., 2021; Van Cutsem et al., 2019).

In sum, while individual differences in cognitive fatigability are not fully understood, they are an important consideration for experimental assessments of CF, in both study design and analytical approaches, particularly when comparing across individuals or groups.

1.5 Impacts of Cognitive Fatigue

Cognitive fatigue may have wide-ranging effects on physical performance, sensory processes, and cognitive functions. In particular, CF has been shown to impair many mental/executive processes, including complex planning (Lorist et al., 2000; van der Linden et al., 2003), working memory (Farahani et al., 2026; Jain & Nataraja, 2019), error monitoring and correction (Boksem

et al., 2006; Lorist et al., 2005), inhibition of automatic or incorrect responses (Guo et al., 2018; Kato et al., 2009), emotional regulation (Grillon et al., 2015), adaptation to novel or changing task demands (Petrucio et al., 2018; Plukaard et al., 2015), decision making (Fortes et al., 2023; Wiehler et al., 2022), and selective attention (Boksem et al., 2005; Faber et al., 2012). Practically, these effects may contribute to increased risk of unsafe workplace behaviour in construction and mining (Jia et al., 2022; Zhang et al., 2023), as well as elevated likelihood of surgical error (Chan et al., 2009; Thomas et al., 2012) and missed perioperative nursing care (Rahmani et al., 2025), among other outcomes.

Cognitive fatigue has further been associated with altered physical performance, such as impaired balance control (Pitts & Bhatt, 2023), reduced isometric and dynamic physical endurance (Brown et al., 2020; Pageaux & Lepers, 2018), and impaired physical recovery (Weiler et al., 2025). Altered lower limb biomechanics have also been observed under CF, potentially increasing the risk of falls (Lew & Qu, 2014) and sports-related injury (R. Yang et al., 2025; Zheng et al., 2025).

Several studies have additionally reported sensory effects of CF. These include impaired speech perception in noise (Jain & Nataraja, 2019), altered auditory temporal processing (Jain et al., 2022; Simon et al., 2020), and reduced auditory sensory gating in healthy and clinical populations (Linnhoff et al., 2023; van der Linden et al., 2006). Although fewer studies have examined the impact of CF on sensory processing outside of the auditory domain, CF-related performance changes have been observed in visual search behaviour (Fortes et al., 2025; Zeuwts et al., 2021), as well as reductions in the amplitude of early event-related potentials (ERP) elicited by both auditory and visual stimuli (Boksem et al., 2005; Faber et al., 2012; Moore et al., 2017; B. Yang et al., 2013).

Of particular relevance to the present thesis, CF has also been shown to impact another performance category: psychomotor performance, or the coordination of sensory, cognitive, and motor processes used to generate goal-directed movements in response to environmental stimuli (Habay et al., 2021; Hindmarch, 2015). Experimentally, the effects of CF on psychomotor function are most commonly assessed using reaction time (RT) paradigms, in which participants respond as quickly as possible to an externally presented stimulus with the correctly associated motor response (Dickens et al., 2024; Hindmarch, 2015). These tasks may be implemented in laboratory-based paradigms or in more applied contexts, such as a basketball throwing task or sprint start (Dickens et al., 2024; Englert & Bertrams, 2014; Faro et al., 2023; Habay et al., 2021). In either case, psychomotor performance is typically quantified in terms of response accuracy and / or speed, with the latter being defined as the time from stimulus onset to movement onset (e.g., force onset), to completion of a response (such as a button press, here referred to as displacement RT), or to initial activation of the agonist musculature measured by electromyography (i.e., premotor RT; Czyż, 2021; Schmidt et al., 2019).

Slowed RT is one of the most robustly reported effects of CF and has been used as an objective indicator of CF induction in experimental paradigms and as a workplace safety-related monitoring metric (Brossoit et al., 2023; Habay et al., 2021; Heng et al., 2024; Karim et al., 2024). Although increases in RT resulting from experimentally induced CF can be relatively modest (e.g., on the order of 20-40 ms; Jaydarifard et al., 2019; Staiano et al., 2024), this effect nonetheless may have meaningful consequences in applied settings. CF-related slowing has been implicated in impaired performance and heightened accident or injury risk among aircraft pilots (Fercho et al., 2024; Jahanpour et al., 2020), marine operators (A. Smith, 2011), construction workers (J. Li et al., 2019), drivers (Guo et al., 2018; Wise et al., 2019), military personnel (Head

et al., 2017); and athletes (Habay et al., 2021; Schamphoeleer et al., 2025). Furthermore, symptoms of some neuromotor disorders such as Parkinson's disease and multiple sclerosis include both elevated cognitive fatigability and psychomotor dysfunction (Linnhoff et al., 2019; Lou, 2009). Improved knowledge of the link between these symptoms may contribute to our understanding of the etiology and treatment of these disorders.

1.6 Research Question

Despite the clear impacts of CF described above, there is currently only a limited understanding of the mechanism by which CF acts to impair psychomotor performance. A more targeted investigation of the impact of CF on the central processes that contribute to psychomotor performance may help to address this knowledge gap.

Cognitive fatigue has been shown to affect speed and accuracy across simple RT tasks (which feature only one possible stimulus and response), choice RT tasks (which feature multiple possible stimuli and associated responses), and go / no-go RT tasks (which feature multiple stimuli, only some of which require a response; Guo et al., 2018; M. R. Smith et al., 2019; Xiao et al., 2015). From an information-processing perspective, each of these tasks is thought to involve one or more stages of central processing that may be susceptible to CF (Czyż, 2021; Hindmarch, 2015). These include: i) detection and identification of the imperative stimulus, in which sensory input is analysed and an associated meaning is assigned; ii) response selection, in which an appropriate action must be chosen based on the identified stimulus pattern; iii) motor preparation, involving translation of the abstract idea of the selected movement into an actualizable motor command and modulation of motor system readiness; iv) inhibitory control processes, which may act to prevent anticipatory release of a highly prepared response or to suppress incorrect movements; and v) response initiation at the appropriate time, encompassing

central processes that transition a prepared motor state to descending motor output, followed by peripheral muscle activation (onset of electromyographic activity) and force generation sufficient to produce measurable movement (displacement onset; Czyż, 2021; Rothwell et al., 2021; Schmidt et al., 2019).

Notably, the neural systems and processes involved in translating a stimulus into an appropriate response are undoubtedly more complex and interactive than this simplified serial processing model suggests (e.g., Haazebroek et al., 2017; Turvey & Fonseca, 2009). Nonetheless, this framework is useful for conceptualizing the general psychomotor processes that might be negatively affected by CF. It has been proposed that processes involving higher levels of executive control, such as response selection, inhibition, and planning, may be more sensitive to CF compared to processes requiring more automatic or basic processing demands (such as stimulus detection or response initiation; Boksem et al., 2005; Lorist & Faber, 2011; van der Linden et al., 2003). Yet, CF-related impairments are commonly reported in simple RT tasks, despite the fact that simple RT is typically considered to rely on relatively basic sensorimotor processing (Czyż, 2021; Schmidt et al., 2019). As such, the mechanisms by which CF impairs psychomotor RT performance remain unclear.

Given this uncertainty and the potentially dangerous consequences of slowed responding in real-world settings, the overarching aims of this thesis are as follows: i) to examine how several key psychomotor processes underlying psychomotor RT performance (stimulus processing, response selection, motor preparation, and inhibitory control) are impacted by CF (*Experiments 1-4*); and ii) to investigate a potential intervention to mitigate CF-related psychomotor performance impairments (*Experiment 5*).

1.7 Overview of Experiments

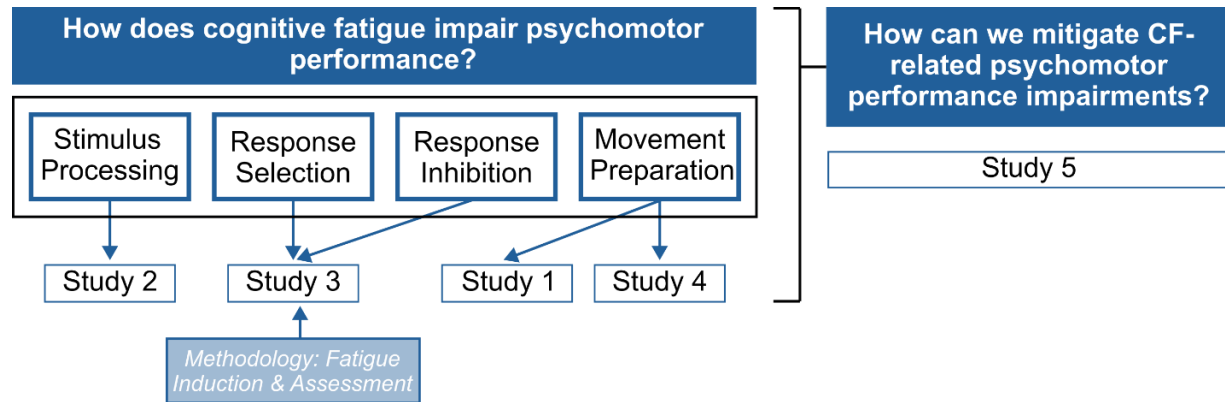


Fig. 1.1 Conceptual framework of the thesis. Experiments 1-4 assess the effects of cognitive fatigue on different psychomotor processes. Experiment 3 additionally helped to refine experimental induction of cognitive fatigue and better understand reaction time as a cognitive fatigue monitoring/assessment tool. Experiment 5 aimed to explore how the effects of cognitive fatigue on psychomotor performance might be mitigated, using non-invasive neurostimulation.

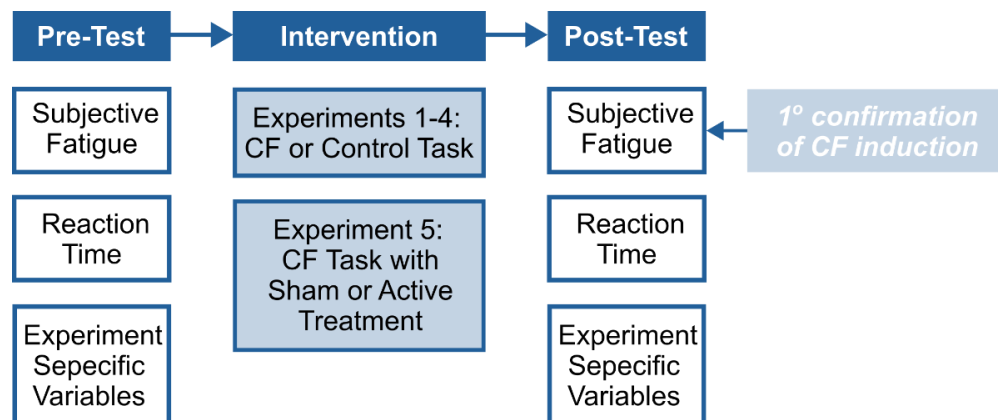


Fig. 1.2 Outline of general methodology. Experiments followed a pre-test – intervention – post-test design. The intervention was an ~60-minute cognitive task or a control task (documentary film viewing). Subjective fatigue / energy level was used throughout as the primary variable to confirm successful cognitive fatigue induction. Specific methods are provided in Chapters 2 through 6.

1.7.1 Experiment 1 (Chapter 2)

Experiment 1 explored the effect of CF on movement preparation in a simple RT task using the StartReact Effect. In this paradigm, a high-intensity (115-130 dB) startling acoustic stimulus (SAS) presented coincidentally with the go-signal is used to provoke a very rapid, involuntary release of a prepared movement (Carlsen & Maslovat, 2026). Preparation level is then inferred from the frequency of SAS-triggered movements as well as the magnitude of RT speeding in response to SAS compared to lower-intensity control stimuli (Maslovat et al., 2021). Thus, it was predicted that if CF impairs movement preparation, we would observe a reduced StartReact Effect (slower and less frequent startle-triggered responses) in CF relative to control conditions.

1.7.2 Experiment 2 (Chapter 3)

CF-related delays in psychomotor RT may be associated with a different component of psychomotor processing, such as perceptual processing of imperative stimuli. In line with this, Experiment 2 used a visual inspection time (IT) task to assess the effect of CF on the display time required to accurately discriminate a visual stimulus (i.e., to accurately determine which of two briefly displayed lines is longest; Vickers & Smith, 1986). We predicted that if CF influences the speed of perceptual processing, then longer display durations would be needed for accurate discrimination of IT task stimuli in CF relative to control conditions.

1.7.3 Experiment 3 (Chapter 4)

Experiment 3 aimed to characterize how CF affects RT performance across tasks with different processing demands, including simple, go/no-go, and choice RT tasks. Simple RT was used to assess basic psychomotor processing stages, while choice RT and go/no-go RT were included to examine response selection and response inhibition processes, respectively (Czyż, 2021).

Experiment 3 additionally explored whether the effects of CF on psychomotor performance

depend on the type of fatigue-inducing mental work. To assess this, simple, go/no-go, and choice RT were measured before and after participants completed one of three differing cognitive interventions or a control intervention. We predicted that CF would produce greater impairments in RT tasks requiring more complex processing (go/no-go, choice), and that these effects may vary depending on the overlapping cognitive demands of the fatigue-inducing intervention (Persson et al., 2007, 2013). This experiment was interpreted from an applied perspective, with emphasis placed on how the findings contribute to understanding psychomotor RT as a CF assessment tool in applied and experimental contexts, and to the design of CF-inducing experimental paradigms.

1.7.4 Experiment 4 (Chapter 5)

While Experiment 1 saw no effects of CF on motor preparation assessed via the StartReact effect, a potential explanation is that StartReact responses may be mediated primarily by subcortical circuits involving the reticulospinal tract (Carlsen & Maslovat, 2019, 2026; Tapia et al., 2022). If CF instead more strongly influences corticospinal mechanisms involved in motor preparation, then the StartReact effect may have been an insensitive metric of fatigue-related preparatory changes. Thus, Experiment 4 explored the effects of CF on motor preparation differently, by examining the effects of CF on corticospinal excitability throughout the preparatory period of a simple RT task, using single-pulse transcranial magnetic stimulation (Bestmann & Duque, 2016; Kennefick et al., 2014). We predicted that CF would lead to changes in corticospinal excitability during the preparatory period relative to the non-fatigued condition, such as reduced early activation and minimized pre-movement suppression of excitability (Bestmann & Duque, 2016; Hannah et al., 2018).

1.7.5 Experiment 5 (Chapter 6)

Few studies have explored how to mitigate the effects of CF on psychomotor performance alongside subjective indications of fatigue. Thus, Experiment 5 assessed whether auricular transcutaneous vagus nerve stimulation (tVNS) might be effective for this purpose, as it has been shown to lead to elevated alertness and arousal and decreased RT latency in other contexts (Chen et al., 2023; Johnson & Wilson, 2018; McIntire et al., 2021). In this pilot experiment, subjective fatigue and simple RT were assessed before and after participants completed a 60-min cognitively fatiguing intervention, with active tVNS throughout the intervention on one day and sham tVNS on another day. We predicted that active tVNS would lead to reduced effects of CF; in other words, better RT performance and reduced subjective fatigue was predicted to follow the cognitive intervention with active stimulation compared to sham.

1.8 References

- Ackerman, P. L. (2011). 100 years without resting. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 11–43). American Psychological Association. <https://doi.org/10.1037/12343-001>
- Ackerman, P. L., Kanfer, R., Shapiro, S. W., Newton, S., & Beier, M. E. (2010). Cognitive Fatigue During Testing: An Examination of Trait, Time-on-Task, and Strategy Influences. *Human Performance*, 23(5), 381–402. <https://doi.org/10.1080/08959285.2010.517720>
- Almhdawi, K. A., Jaber, H. B., Khalil, H. W., Kanaan, S. F., Shyyab, A. A., Mansour, Z. M., & Alazrai, A. H. (2021). Post-stroke fatigue level is significantly associated with mental health component of health-related quality of life: A cross-sectional study. *Quality of Life Research*, 30(4), 1165–1172. <https://doi.org/10.1007/s11136-020-02714-z>
- Bafna, T., & Hansen, J. P. (2021). Mental fatigue measurement using eye metrics: A systematic literature review. *Psychophysiology*, 58(6), e13828. <https://doi.org/10.1111/psyp.13828>
- Barker, L. M., & Nussbaum, M. A. (2011). Fatigue, performance and the work environment: A survey of registered nurses. *Journal of Advanced Nursing*, 67(6), 1370–1382. <https://doi.org/10.1111/j.1365-2648.2010.05597.x>
- Behrens, M., Gube, M., Chaabene, H., Prieske, O., Zenon, A., Broscheid, K.-C., Schega, L., Husmann, F., & Weippert, M. (2023). Fatigue and Human Performance: An Updated Framework. *Sports Medicine*, 53(1), 7–31. <https://doi.org/10.1007/s40279-022-01748-2>
- Bender, B. G., Berning, S., Dudden, R., Milgrom, H., & Tran, Z. V. (2003). Sedation and performance impairment of diphenhydramine and second-generation antihistamines: A meta-analysis. *Journal of Allergy and Clinical Immunology*, 111(4), 770–776. <https://doi.org/10.1067/mai.2003.1408>
- Bestmann, S., & Duque, J. (2016). Transcranial Magnetic Stimulation: Decomposing the Processes Underlying Action Preparation. *The Neuroscientist*, 22(4), 392–405. <https://doi.org/10.1177/1073858415592594>
- Bian, C., Russell, S., Mali, A., Lathouwers, E., De Pauw, K., Habay, J., Bogataj, Š., & Roelands, B. (2025). Methodological Considerations and Effectiveness for Ecologically Valid Mental Fatigue Inducement in Sports: A Systematic Review. *Sports Medicine - Open*, 11(1), 82. <https://doi.org/10.1186/s40798-025-00891-0>
- Biondi, F. N., Cacanindin, A., Douglas, C., & Cort, J. (2021). Overloaded and at Work: Investigating the Effect of Cognitive Workload on Assembly Task Performance. *Human Factors*, 63(5), 813–820. <https://doi.org/10.1177/0018720820929928>
- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2005). Effects of mental fatigue on attention: An ERP study. *Cognitive Brain Research*, 25(1), 107–116. <https://doi.org/10.1016/j.cogbrainres.2005.04.011>

- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, 72(2), 123–132. <https://doi.org/10.1016/j.biopsycho.2005.08.007>
- Boksem, M. A. S., & Tops, M. (2008). Mental fatigue: Costs and benefits. *Brain Research Reviews*, 59(1), 125–139. <https://doi.org/10.1016/j.brainresrev.2008.07.001>
- Boolani, A., & Manierre, M. (2019). An exploratory multivariate study examining correlates of trait mental and physical fatigue and energy. *Fatigue: Biomedicine, Health & Behavior*, 7(1), 29–40. <https://doi.org/10.1080/21641846.2019.1573790>
- Borragán, G., Slama, H., Bartolomei, M., & Peigneux, P. (2017). Cognitive fatigue: A Time-based Resource-sharing account. *Cortex*, 89, 71–84. <https://doi.org/10.1016/j.cortex.2017.01.023>
- Borragán, G., Slama, H., Destrebecqz, A., & Peigneux, P. (2016). Cognitive fatigue facilitates procedural sequence learning. *Frontiers in Human Neuroscience*, 10. <https://doi.org/10.3389/fnhum.2016.00086>
- Bouche, A., Poulin-Charronnat, B., & Lepers, R. (2025). Mental fatigue in older adults: A narrative review of subjective, behavioral, neurophysiological, and physical changes. *Archives of Gerontology and Geriatrics*, 138, 105950. <https://doi.org/10.1016/j.archger.2025.105950>
- Brazaitis, M., & Satas, A. (2023). Regular short-duration breaks do not prevent mental fatigue and decline in cognitive efficiency in healthy young men during an office-like simulated mental working day: An EEG study. *International Journal of Psychophysiology*, 188, 33–46. <https://doi.org/10.1016/j.ijpsycho.2023.03.007>
- Brossoit, R. M., Crain, T. L., Stevens, S. C., Wong, J. R., & Guasta, L. (2023). Alert at Work? Perceptions of Alertness Testing and Recommendations for Practitioners. *Occupational Health Science*, 7(2), 379–396. <https://doi.org/10.1007/s41542-022-00139-3>
- Brown, D. M. Y., Graham, J. D., Innes, K. I., Harris, S., Flemington, A., & Bray, S. R. (2020). Effects of Prior Cognitive Exertion on Physical Performance: A Systematic Review and Meta-analysis. *Sports Medicine*, 50(3), 497–529. <https://doi.org/10.1007/s40279-019-01204-8>
- Broyd, S. J., Demanuele, C., Debener, S., Helps, S. K., James, C. J., & Sonuga-Barke, E. J. S. (2009). Default-mode brain dysfunction in mental disorders: A systematic review. *Neuroscience & Biobehavioral Reviews*, 33(3), 279–296. <https://doi.org/10.1016/j.neubiorev.2008.09.002>
- Bryant, D., Chiaravalloti, N., & Deluca, J. (2004). Objective Measurement of Cognitive Fatigue in Multiple Sclerosis. *Rehabilitation Psychology*, 49(2), 114–122. <https://doi.org/10.1037/0090-5550.49.2.114>

- Carlsen, A. N., & Maslovat, D. (2019). Startle and the StartReact Effect: Physiological Mechanisms. *Journal of Clinical Neurophysiology*, 36(6), 452–459. <https://doi.org/10.1097/WNP.0000000000000582>
- Carlsen, A. N., & Maslovat, D. (2026). What Is the StartReact Effect? *Acta Physiologica*, 242(6), e70235. <https://doi.org/10.1111/apha.70235>
- Chan, M. Y., Cohen, H., & Spiegel, B. M. R. (2009). Fewer Polyps Detected by Colonoscopy as the Day Progresses at a Veteran's Administration Teaching Hospital. *Clinical Gastroenterology and Hepatology*, 7(11), 1217–1223. <https://doi.org/10.1016/j.cgh.2009.07.013>
- Chaudhuri, A., & Behan, P. O. (2000). Fatigue and basal ganglia. *Journal of the Neurological Sciences*, 179(1), 34–42. [https://doi.org/10.1016/S0022-510X\(00\)00411-1](https://doi.org/10.1016/S0022-510X(00)00411-1)
- Chaudhuri, A., & Behan, P. O. (2004). Fatigue in neurological disorders. *The Lancet*, 363(9413), 978–988. [https://doi.org/10.1016/S0140-6736\(04\)15794-2](https://doi.org/10.1016/S0140-6736(04)15794-2)
- Chen, Y., Lu, X., & Hu, L. (2023). Transcutaneous Auricular Vagus Nerve Stimulation Facilitates Cortical Arousal and Alertness. *International Journal of Environmental Research and Public Health*, 20(2), Article 2. <https://doi.org/10.3390/ijerph20021402>
- Christie, S. T., & Schrater, P. (2015). Cognitive cost as dynamic allocation of energetic resources. *Frontiers in Neuroscience*, 9, 289. <https://doi.org/10.3389/fnins.2015.00289>
- Christodoulou, C. (2005). The Assessment and Measurement of Fatigue. In J. DeLuca (Ed.), *Fatigue as a Window to the Brain* (pp. 19–35). MIT Press.
- Cole, M. W., & Schneider, W. (2007). The cognitive control network: Integrated cortical regions with dissociable functions. *NeuroImage*, 37(1), 343–360. <https://doi.org/10.1016/j.neuroimage.2007.03.071>
- Coyne, J. O. C., Coutts, A. J., Newton, R. U., & Haff, G. G. (2021). The Influence of Mental Fatigue on Sessional Ratings of Perceived Exertion in Elite Open and Closed Skill Sports Athletes. *The Journal of Strength & Conditioning Research*, 35(4), 963–969. <https://doi.org/10.1519/JSC.00000000000003980>
- Craft, C. L., Islam, T., Berard, J. A., & Walker, L. A. S. (2025). Subjective cognitive fatigability is associated with worse patient-reported physical disability in multiple sclerosis. *Multiple Sclerosis and Related Disorders*, 103, 106720. <https://doi.org/10.1016/j.msard.2025.106720>
- Csathó, Á., Van der Linden, D., & Matuz, A. (2024). Change in heart rate variability with increasing time-on-task as a marker for mental fatigue: A systematic review. *Biological Psychology*, 185, 108727. <https://doi.org/10.1016/j.biopsycho.2023.108727>

- Czyż, S. H. (2021). Variability of Practice, Information Processing, and Decision Making—How Much Do We Know? *Frontiers in Psychology*, 12, 639131. <https://doi.org/10.3389/fpsyg.2021.639131>
- Delgado-Alonso, C., Cuevas, C., Oliver-Mas, S., Díez-Cirarda, M., Delgado-Álvarez, A., Gil-Moreno, M. J., Matías-Guiu, J., & Matias-Guiu, J. A. (2022). Fatigue and Cognitive Dysfunction Are Associated with Occupational Status in Post-COVID Syndrome. *International Journal of Environmental Research and Public Health*, 19(20), Article 20. <https://doi.org/10.3390/ijerph192013368>
- DeLuca, J. (2005). Fatigue: Its Definition, Its Study, and Its Future. In J. DeLuca (Ed.), *Fatigue as a Window to the Brain* (pp. 319–325). The MIT Press.
- Díaz-García, J., González-Ponce, I., Ponce-Bordón, J. C., López-Gajardo, M. Á., Ramírez-Bravo, I., Rubio-Morales, A., & García-Calvo, T. (2022). Mental Load and Fatigue Assessment Instruments: A Systematic Review. *International Journal of Environmental Research and Public Health*, 19(1), 419. <https://doi.org/10.3390/ijerph19010419>
- Dickens, A., Champion, A. J., & Schenke, K. C. (2024). Fatigue management: A systematic review of objective measurement techniques for cognitive fatigue. *Journal of Clinical and Experimental Neuropsychology*, 46(8), 776–793. <https://doi.org/10.1080/13803395.2024.2415070>
- Dobryakova, E., DeLuca, J., Genova, H. M., & Wylie, G. R. (2013). Neural Correlates of Cognitive Fatigue: Cortico-Striatal Circuitry and Effort–Reward Imbalance. *Journal of the International Neuropsychological Society*, 19(8), 849–853. <https://doi.org/10.1017/S1355617713000684>
- Englert, C., & Bertrams, A. (2014). The Effect of Ego Depletion on Sprint Start Reaction Time. *Journal of Sport and Exercise Psychology*, 36(5), 506–515. <https://doi.org/10.1123/jsep.2014-0029>
- Ezekiel, L., Field, L., Collett, J., Dawes, H., & Boulton, M. (2021). Experiences of fatigue in daily life of people with acquired brain injury: A qualitative study. *Disability and Rehabilitation*, 43(20), 2866–2874. <https://doi.org/10.1080/09638288.2020.1720318>
- Faber, L. G., Maurits, N. M., & Lorist, M. M. (2012). Mental Fatigue Affects Visual Selective Attention. *PLOS ONE*, 7(10), e48073. <https://doi.org/10.1371/journal.pone.0048073>
- Farahani, F. K., Dehkordi, P. S., Khalaji, M., Alboghebeish, S., Kurnaz, M., & Altınkök, M. (2026). Mental and physical fatigue altered working memory consolidation and impaired gaze behavior and perceptual-cognitive skills using video-based and real-situation. *Scientific Reports*, 16(1), 10180. <https://doi.org/10.1038/s41598-026-40994-6>
- Faro, H., Fortes, L. de S., Lima-Junior, de D., Barbosa, B. T., Ferreira, M. E. C., & Almeida, S. S. (2023). Sport-based video game causes mental fatigue and impairs visuomotor skill in male basketball players. *International Journal of Sport and Exercise Psychology*, 21(6), 1125–1139. <https://doi.org/10.1080/1612197X.2022.2109187>

- Fazackerley, L. A., Hickey, J., Johnston, R. D., Tofari, P. J., Timmins, R. G., Roelands, B., Halson, S. L., Tassinon, B., Verschueren, J., & Russell, S. (2025). Practitioner Perspectives on the Association Between Mental Fatigue and Injury Risk in High-Performance Sport: A Mixed Methods Study. *European Journal of Sport Science*, 25(8), e70028. <https://doi.org/10.1002/ejsc.70028>
- Fercho, K. A., Beringer, D. B., & Donovan, C. (2024). Factors that Affect Pilot Response Times to Alerts: Findings From a Literature Review and Aviation Safety Reporting System (ASRS) Reports. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, 68(1), 50–55. <https://doi.org/10.1177/10711813241260286>
- Filipas, L., Martin, K., Northey, J. M., La Torre, A., Keegan, R., & Rattray, B. (2020). A 4-week endurance training program improves tolerance to mental exertion in untrained individuals. *Journal of Science and Medicine in Sport*, 23(12), 1215–1219. <https://doi.org/10.1016/j.jsams.2020.04.020>
- Fortes, L. S., Gantois, P., de Lima-Júnior, D., Barbosa, B. T., Ferreira, M. E. C., Nakamura, F. Y., Albuquerque, M. R., & Fonseca, F. S. (2023). Playing videogames or using social media applications on smartphones causes mental fatigue and impairs decision-making performance in amateur boxers. *Applied Neuropsychology: Adult*, 30(2), 227–238. <https://doi.org/10.1080/23279095.2021.1927036>
- Fortes, L. S., Lima-Junior, D., Barbosa, B. T., Faro, H. K. C., Ferreira, M. E. C., & Almeida, S. S. (2025). Effect of mental fatigue on decision-making skill and visual search behaviour in basketball players: An experimental and randomised study. *International Journal of Sport and Exercise Psychology*, 23(5), xxxx–lix. <https://doi.org/10.1080/1612197X.2022.2058055>
- Gailliot, M. T., Baumeister, R. F., DeWall, C. N., Maner, J. K., Plant, E. A., Tice, D. M., Brewer, L. E., & Schmeichel, B. J. (2007). Self-control relies on glucose as a limited energy source: Willpower is more than a metaphor. *Journal of Personality and Social Psychology*, 92(2), 325–336. <https://doi.org/10.1037/0022-3514.92.2.325>
- Gantois, P., Caputo Ferreira, M. E., Lima-Junior, D. de, Nakamura, F. Y., Batista, G. R., Fonseca, F. S., & Fortes, L. de S. (2020). Effects of mental fatigue on passing decision-making performance in professional soccer athletes. *European Journal of Sport Science*, 20(4), 534–543. <https://doi.org/10.1080/17461391.2019.1656781>
- Gao, L., Xu, M., Qian, L., Zhang, R., Chen, M., Hu, Y., Li, C., & Sun, Y. (2025). Identifying individuals with high susceptibility to mental fatigue: A functional connectivity study. *NeuroImage*, 324, 121623. <https://doi.org/10.1016/j.neuroimage.2025.121623>
- Gergelyfi, M., Jacob, B., Olivier, E., & Zénon, A. (2015). Dissociation between mental fatigue and motivational state during prolonged mental activity. *Frontiers in Behavioral Neuroscience*, 9, 176. <https://doi.org/10.3389/fnbeh.2015.00176>
- Gergelyfi, M., Sanz-Arigita, E. J., Solopchuk, O., Dricot, L., Jacob, B., & Zénon, A. (2021). Mental fatigue correlates with depression of task-related network and augmented DMN

- activity but spares the reward circuit. *NeuroImage*, 243, 118532.
<https://doi.org/10.1016/j.neuroimage.2021.118532>
- Gilsoul, J., Libertiaux, V., Depierreux, F., & Collette, F. (2024). Cognitive Fatigue in Young, Middle-Aged, and Older Adults: A Response Time Distribution Approach. *Journal of Adult Development*, 31(4), 279–292. <https://doi.org/10.1007/s10804-023-09471-6>
- Grillon, C., Quispe-Escudero, D., Mathur, A., & Ernst, M. (2015). Mental fatigue impairs emotion regulation. *Emotion*, 15(3), 383–389.
<https://doi.org/http://dx.doi.org.proxy.bib.uottawa.ca/10.1037/emo0000058>
- Guo, Z., Chen, R., Liu, X., Zhao, G., Zheng, Y., Gong, M., & Zhang, J. (2018). The impairing effects of mental fatigue on response inhibition: An ERP study. *PLOS ONE*, 13(6), e0198206. <https://doi.org/10.1371/journal.pone.0198206>
- Haazebroek, P., Raffone, A., & Hommel, B. (2017). HiTEC: A connectionist model of the interaction between perception and action planning. *Psychological Research*, 81(6), 1085–1109. <https://doi.org/10.1007/s00426-016-0803-0>
- Habay, J., Uylenbroeck, R., Van Droogenbroeck, R., De Wachter, J., Proost, M., Tassignon, B., De Pauw, K., Meeusen, R., Pattyn, N., Van Cutsem, J., & Roelands, B. (2023). Interindividual Variability in Mental Fatigue-Related Impairments in Endurance Performance: A Systematic Review and Multiple Meta-regression. *Sports Medicine - Open*, 9(1), 14. <https://doi.org/10.1186/s40798-023-00559-7>
- Habay, J., Van Cutsem, J., Verschueren, J., De Bock, S., Proost, M., De Wachter, J., Tassignon, B., Meeusen, R., & Roelands, B. (2021). Mental Fatigue and Sport-Specific Psychomotor Performance: A Systematic Review. *Sports Medicine*, 51(7), 1527–1548.
<https://doi.org/10.1007/s40279-021-01429-6>
- Hannah, R., Cavanagh, S. E., Tremblay, S., Simeoni, S., & Rothwell, J. C. (2018). Selective Suppression of Local Interneuron Circuits in Human Motor Cortex Contributes to Movement Preparation. *Journal of Neuroscience*, 38(5), 1264–1276.
<https://doi.org/10.1523/JNEUROSCI.2869-17.2017>
- Head, J., Tenan, M. S., Tweedell, A. J., LaFiandra, M. E., Morelli, F., Wilson, K. M., Ortega, S. V., & Helton, W. S. (2017). Prior Mental Fatigue Impairs Marksmanship Decision Performance. *Frontiers in Physiology*, 8. <https://doi.org/10.3389/fphys.2017.00680>
- Heng, P. P., Yusoff, H. M., & Hod, R. (2024). Individual evaluation of fatigue at work to enhance the safety performance in the construction industry: A systematic review. *PLOS ONE*, 19(2), e0287892. <https://doi.org/10.1371/journal.pone.0287892>
- Herlambang, M. B., Taatgen, N. A., & Cnossen, F. (2019). The Role of Motivation as a Factor in Mental Fatigue. *Human Factors*, 61(7), 1171–1185.
<https://doi.org/10.1177/0018720819828569>

- Hernandez, R., Jin, H., Pyatak, E. A., Roll, S. C., & Schneider, S. (2024). Workers' whole day workload and next day cognitive performance. *Current Psychology*, 43(3), 2005–2018. <https://doi.org/10.1007/s12144-023-04400-y>
- Hindmarch, I. (2015). Psychomotor Performance in Humans. In I. P. Stolerman & L.H. Price (Eds.), *Encyclopedia of Psychopharmacology* (pp. 1383–1388). Springer, Berlin, Heidelberg. https://doi.org/10.1007/978-3-642-36172-2_181
- 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*. (pp. 167–187). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-008>
- Holroyd, C. B. (2015). The Waste Disposal Problem of Effortful Control. In T.S. Braver (Ed.), *Motivation and Cognitive Control* (pp. 235-260). Routledge.
- Ishii, A., Tanaka, M., & Watanabe, Y. (2014). Neural mechanisms of mental fatigue. *Reviews in the Neurosciences*, 25(4), 469–479. <https://doi.org/10.1515/revneuro-2014-0028>
- Ismail, L. E., & Karwowski, W. (2020). Applications of EEG indices for the quantification of human cognitive performance: A systematic review and bibliometric analysis. *PLoS ONE*, 15(12), 1–33. (147380159). <https://doi.org/10.1371/journal.pone.0242857>
- Jacquet, T., Poulin-Charronnat, B., Bard, P., & Lepers, R. (2021). Persistence of Mental Fatigue on Motor Control. *Frontiers in Psychology*, 11. <https://doi.org/10.3389/fpsyg.2020.588253>
- Jahanpour, E. S., Berberian, B., Imbert, J.-P., & Roy, R. N. (2020). Cognitive fatigue assessment in operational settings: A review and UAS implications. *IFAC-PapersOnLine, 3rd IFAC Workshop on Cyber-Physical & Human Systems CPHS 2020*, 53(5), 330–337. <https://doi.org/10.1016/j.ifacol.2021.04.188>
- Jain, S., & Nataraja, N. P. (2019). The Effect of Fatigue on Working Memory and Auditory Perceptual Abilities in Trained Musicians. *American Journal of Audiology*, 28(2S), 483–494. (138310640). https://doi.org/10.1044/2019_AJA-IND50-18-0102
- Jain, S., Nataraja, N. P., & Narne, V. K. (2022). The Effect of Subjective Fatigue on Auditory Processing in Musicians and Nonmusicians. *Music Perception*, 39(3), 309–319. <https://doi.org/10.1525/mp.2022.39.3.309>
- Jaydari Fard, S., & Lavender, A. P. (2019). A comparison of task-based mental fatigue between healthy males and females. *Fatigue: Biomedicine, Health & Behavior*, 7(1), 1–11. <https://doi.org/10.1080/21641846.2019.1562582>
- Jaydarifard, S., Behara, K., Baker, D., & Paz, A. (2024). Driver fatigue in taxi, ride-hailing, and ridesharing services: A systematic review. *Transport Reviews*, 44(3), 572–590. <https://doi.org/10.1080/01441647.2023.2278446>

- Jaydarifard, S., Tahmasebi Boroujeni, S., & Lavender, A. P. (2019). Mental fatigue impairs simple reaction time in non-athletes more than athletes. *Fatigue: Biomedicine, Health & Behavior*, 7(3), 117–126. <https://doi.org/10.1080/21641846.2019.1632614>
- Jia, A., Guo, X., & Tian, S. (2022). Experimental study on the influence of mental fatigue on risk decision-making of miners. *Scientific Reports*, 12(1), 11902. <https://doi.org/10.1038/s41598-022-14045-9>
- Job, R. F. S., & Dalziel, J. (2000). Defining fatigue as a condition of the organism and distinguishing it from habituation, adaptation, and boredom. In P. A. Hancock & P. A. Desmond (Eds.), *Stress, Workload, and Fatigue* (pp. 466–476). Lawrence Erlbaum Associates, Inc.
- Johansson, B., Wentzel, A.-P., Andréll, P., Mannheimer, C., & Rönnbäck, L. (2015). Methylphenidate reduces mental fatigue and improves processing speed in persons suffered a traumatic brain injury. *Brain Injury*, 29(6), 758–765. <https://doi.org/10.3109/02699052.2015.1004747>
- Johnson, R. L., & Wilson, C. G. (2018). A review of vagus nerve stimulation as a therapeutic intervention. *Journal of Inflammation Research*, 11, 203–213. <https://doi.org/10.2147/JIR.S163248>
- Kanfer, R. (2011). Determinants and consequences of subjective cognitive fatigue. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 189–207). American Psychological Association. <https://doi.org/http://dx.doi.org.proxy.bib.uottawa.ca/10.1037/12343-009>
- Karim, E., Pavel, H. R., Nikanfar, S., Hebri, A., Roy, A., Nambiappan, H. R., Jaiswal, A., Wylie, G. R., & Makedon, F. (2024). Examining the Landscape of Cognitive Fatigue Detection: A Comprehensive Survey. *Technologies*, 12(3), 38. <https://doi.org/10.3390/technologies12030038>
- Kato, Y., Endo, H., & Kizuka, T. (2009). Mental fatigue and impaired response processes: Event-related brain potentials in a Go/NoGo task. *International Journal of Psychophysiology*, 72(2), 204–211. <https://doi.org/10.1016/j.ijpsycho.2008.12.008>
- Kennefick, M., Maslovat, D., & Carlsen, A. N. (2014). The Time Course of Corticospinal Excitability during a Simple Reaction Time Task. *PLoS ONE*, 9(11), e113563. <https://doi.org/10.1371/journal.pone.0113563>
- Kowalski, K. L., Tierney, B. C., & Christie, A. D. (2022). Mental fatigue does not substantially alter neuromuscular function in young, healthy males and females. *Physiology & Behavior*, 253, 113855. <https://doi.org/10.1016/j.physbeh.2022.113855>
- Kristiansen, J., Lund, S. P., Persson, R., Shibuya, H., Nielsen, P. M., & Scholz, M. (2014). A study of classroom acoustics and school teachers' noise exposure, voice load and speaking time during teaching, and the effects on vocal and mental fatigue development.

- International Archives of Occupational and Environmental Health*, 87(8), 851–860.
<https://doi.org/10.1007/s00420-014-0927-8>
- Kunasegaran, K., Ismail, A. M. H., Ramasamy, S., Gnanou, J. V., Caszo, B. A., & Chen, P. L. (2023). Understanding mental fatigue and its detection: A comparative analysis of assessments and tools. *PeerJ*, 11, e15744. <https://doi.org/10.7717/peerj.15744>
- Kurzban, R., Duckworth, A., Kable, J. W., & Myers, J. (2013). An opportunity cost model of subjective effort and task performance. *The Behavioral and Brain Sciences*, 36(6), 10.1017/S0140525X12003196. <https://doi.org/10.1017/S0140525X12003196>
- Langner, R., Steinborn, M. B., Chatterjee, A., Sturm, W., & Willmes, K. (2010). Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychologica*, 133(1), 64–72. <https://doi.org/10.1016/j.actpsy.2009.10.001>
- Leavitt, V. M., & DeLuca, J. (2010). Central Fatigue: Issues Related to Cognition, Mood and Behavior, and Psychiatric Diagnoses. *PM&R*, 2(5), 332–337. <https://doi.org/10.1016/j.pmrj.2010.03.027>
- Lew, F. L., & Qu, X. (2014). Effects of mental fatigue on biomechanics of slips. *Ergonomics*, 57(12), 1927–1932. <https://doi.org/10.1080/00140139.2014.937771>
- Li, G., Huang, S., Xu, W., Jiao, W., Jiang, Y., Gao, Z., & Zhang, J. (2020). The impact of mental fatigue on brain activity: A comparative study both in resting state and task state using EEG. *BMC Neuroscience*, 21(20), 1. <https://doi.org/10.1186/s12868-020-00569-1>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835. <https://doi.org/10.1016/j.autcon.2019.102835>
- Lim, J., Ebstein, R., Tse, C.-Y., Monakhov, M., Lai, P. S., Dinges, D. F., & Kwok, K. (2012). Dopaminergic Polymorphisms Associated with Time-on-Task Declines and Fatigue in the Psychomotor Vigilance Test. *PLOS ONE*, 7(3), e33767. <https://doi.org/10.1371/journal.pone.0033767>
- Linnhoff, S., Fiene, M., Heinze, H.-J., & Zaehle, T. (2019). Cognitive Fatigue in Multiple Sclerosis: An Objective Approach to Diagnosis and Treatment by Transcranial Electrical Stimulation. *Brain Sciences*, 9(5), 100. <https://doi.org/10.3390/brainsci9050100>
- Linnhoff, S., Haghighi, A., & Zaehle, T. (2023). Cognitive fatigue-related sensory gating deficits in people with multiple sclerosis. *Neurobiology of Disease*, 176, 105950. <https://doi.org/10.1016/j.nbd.2022.105950>
- Lorist, M. M., Bezdan, E., ten Caat, M., Span, M. M., Roerdink, J. B. T. M., & Maurits, N. M. (2009). The influence of mental fatigue and motivation on neural network dynamics; an EEG coherence study. *Brain Research*, 1270, 95–106. <https://doi.org/10.1016/j.brainres.2009.03.015>

- Lorist, M. M., Boksem, M. A. S., & Ridderinkhof, K. R. (2005). Impaired cognitive control and reduced cingulate activity during mental fatigue. *Cognitive Brain Research*, 24(2), 199–205. <https://doi.org/10.1016/j.cogbrainres.2005.01.018>
- Lorist, M. M., & Faber, L. G. (2011). Consideration of the influence of mental fatigue on controlled and automatic cognitive processes and related neuromodulatory effects. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 105–126). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-005>
- Lorist, M. M., Klein, M., Nieuwenhuis, S., de Jong, R., Mulder, G., & Meijman, T. F. (2000). Mental fatigue and task control: Planning and preparation. *Psychophysiology*, 37(5), 614–625. <https://doi.org/10.1111/1469-8986.3750614>
- Lou, J.-S. (2009). Physical and Mental Fatigue in Parkinson's Disease. *Drugs & Aging*, 26(3), 195–208. <https://doi.org/10.2165/00002512-200926030-00002>
- Lu, K., Sjörs Dahlman, A., Karlsson, J., & Candefjord, S. (2022). Detecting driver fatigue using heart rate variability: A systematic review. *Accident Analysis & Prevention*, 178, 106830. <https://doi.org/10.1016/j.aap.2022.106830>
- Magnuson, J. R., Doesburg, S. M., & McNeil, C. J. (2021). Development and recovery time of mental fatigue and its impact on motor function. *Biological Psychology*, 161, 108076. <https://doi.org/10.1016/j.biopsycho.2021.108076>
- Maisel, P., Baum, E., & Donner-Banzhoff, N. (2021). Fatigue as the Chief Complaint. *Dtsch Arztebl International*, 118(33–34), 566–576.
- Martin, K., Meeusen, R., Thompson, K. G., Keegan, R., & Rattray, B. (2018). Mental Fatigue Impairs Endurance Performance: A Physiological Explanation. *Sports Medicine*, 48(9), 2041–2051. <https://doi.org/10.1007/s40279-018-0946-9>
- Martin, K., Staiano, W., Menaspà, P., Hennessey, T., Marcora, S., Keegan, R., Thompson, K. G., Martin, D., Halson, S., & Rattray, B. (2016). Superior Inhibitory Control and Resistance to Mental Fatigue in Professional Road Cyclists. *PLOS ONE*, 11(7), e0159907. <https://doi.org/10.1371/journal.pone.0159907>
- Maslovat, D., Sadler, C. M., Smith, V., Bui, A., & Carlsen, A. N. (2021). Response triggering by an acoustic stimulus increases with stimulus intensity and is best predicted by startle reflex activation. *Scientific Reports*, 11(1), Article 1. <https://doi.org/10.1038/s41598-021-02825-8>
- McCabe, J. A., Banasik, C. S., Jackson, M. G., Postlethwait, E. M., Steitz, A., & Wenzel, A. R. (2023). Exploring perceptions of cognitive load and mental fatigue in pandemic-era zoom classes. *Scholarship of Teaching and Learning in Psychology*, 11(2). <https://doi.org/10.1037/stl0000347>

- McIntire, L. K., McKinley, R. A., Goodyear, C., McIntire, J. P., & Brown, R. D. (2021). Cervical transcutaneous vagal nerve stimulation (ctVNS) improves human cognitive performance under sleep deprivation stress. *Communications Biology*, 4(1), 634. <https://doi.org/10.1038/s42003-021-02145-7>
- Meeusen, R., Van Cutsem, J., & Roelands, B. (2021). Endurance exercise-induced and mental fatigue and the brain. *Experimental Physiology*, 106(12), 2294–2298. <https://doi.org/10.1113/EP088186>
- Michielsen, H. J., De Vries, J., & Van Heck, G. L. (2003). Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *Journal of Psychosomatic Research*, 54(4), 345–352. [https://doi.org/10.1016/S0022-3999\(02\)00392-6](https://doi.org/10.1016/S0022-3999(02)00392-6)
- Minusa, S., Mizuno, K., Ojiro, D., Tanaka, T., Kuriyama, H., Yamano, E., Kuratsune, H., & Watanabe, Y. (2021). Increase in rear-end collision risk by acute stress-induced fatigue in on-road truck driving. *PLOS ONE*, 16(10), e0258892. <https://doi.org/10.1371/journal.pone.0258892>
- Mizuno, K., Ojiro, D., Tanaka, T., Minusa, S., Kuriyama, H., Yamano, E., Kuratsune, H., & Watanabe, Y. (2020). Relationship between truck driver fatigue and rear-end collision risk. *PLOS ONE*, 15(9), e0238738. <https://doi.org/10.1371/journal.pone.0238738>
- Moore, T. M., Key, A. P., Thelen, A., & Hornsby, B. W. Y. (2017). Neural mechanisms of mental fatigue elicited by sustained auditory processing. *Neuropsychologia*, 106, 371–382. <https://doi.org/10.1016/j.neuropsychologia.2017.10.025>
- Mozuraityte, K., Stanyte, A., Fineberg, N. A., Serretti, A., Gecaite-Stonciene, J., & Burkauskas, J. (2023). Mental fatigue in individuals with psychiatric disorders: A scoping review. *International Journal of Psychiatry in Clinical Practice*, 27(2), 186–195. <https://doi.org/10.1080/13651501.2022.2129069>
- Nicholson, K., Stewart, M., & Thind, A. (2015). Examining the symptom of fatigue in primary care: A comparative study using electronic medical records. *BMJ Health & Care Informatics*, 22(1). <https://doi.org/10.14236/jhi.v22i1.91>
- O’Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics*, 63(1), 1–12. <https://doi.org/10.1080/00140139.2019.1687940>
- Oliver, L., Goodman, S., Sullivan, J., Peake, J., & Kelly, V. (2025). Challenges and perspectives with understanding the concept of mental fatigue. *International Journal of Sports Medicine*, 46(5), 316–323. <https://doi.org/10.1055/a-2514-1195>
- Pageaux, B., & Lepers, R. (2018). Chapter 16—The effects of mental fatigue on sport-related performance. In S. Marcora & M. Sarkar (Eds.), *Progress in Brain Research* (Vol. 240, pp. 291–315). Elsevier. <https://doi.org/10.1016/bs.pbr.2018.10.004>

- Pageaux, B., Marcora, S. M., Rozand, V., & 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. <https://doi.org/10.3389/fnhum.2015.00067>
- Pattyn, N., Neyt, X., Henderickx, D., & Soetens, E. (2008). Psychophysiological investigation of vigilance decrement: Boredom or cognitive fatigue? *Physiology & Behavior*, 93(1), 369–378. <https://doi.org/10.1016/j.physbeh.2007.09.016>
- Pereira, H. M., Bertholf, R. L., dos Santos, M. B., Black, C. D., & Allen, J. O. (2025). Sex differences in the prevalence of fatigue across age groups and associated factors. *Fatigue: Biomedicine, Health & Behavior*, 13(2), 146–159. <https://doi.org/10.1080/21641846.2025.2466401>
- Persson, J., Larsson, A., & Reuter-Lorenz, P. A. (2013). Imaging Fatigue of Interference Control Reveals the Neural Basis of Executive Resource Depletion. *Journal of Cognitive Neuroscience*, 25(3), 338–351. https://doi.org/10.1162/jocn_a_00321
- Persson, J., Welsh, K. M., Jonides, J., & Reuter-Lorenz, P. A. (2007). Cognitive fatigue of executive processes: Interaction between interference resolution tasks. *Neuropsychologia*, 45(7), 1571–1579. <https://doi.org/10.1016/j.neuropsychologia.2006.12.007>
- Pessiglione, M., Blain, B., Wiehler, A., & Naik, S. (2025). Origins and consequences of cognitive fatigue. *Trends in Cognitive Sciences*, 29(8), 730–749. <https://doi.org/10.1016/j.tics.2025.02.005>
- Petruo, V. A., Mückschel, M., & Beste, C. (2018). On the role of the prefrontal cortex in fatigue effects on cognitive flexibility—A system neurophysiological approach. *Scientific Reports*, 8(1), 6395. <https://doi.org/10.1038/s41598-018-24834-w>
- Petrut, B., Berindan-Neagoe, I., Feflea, D. I., Hoge, M., Pasca, S., Bujoreanu, C. E., & Bschleipfer, T. (2020). Mental Fatigue Evaluation of Surgical Teams during a Regular Workday in a High-Volume Tertiary Healthcare Center. *Urologia Internationalis*, 104(3–4), 301–308. <https://doi.org/10.1159/000504988>
- Pickering, T., Wright, B., Schücker, L., & MacMahon, C. (2024). Active or passive? Investigating different types of cognitive fatigue. *Canadian Journal of Experimental Psychology/Revue Canadienne de Psychologie Expérimentale*, 78(1), 50–65. <https://doi.org/10.1037/cep0000312>
- Pitts, J., & Bhatt, T. (2023). Effects of mentally induced fatigue on balance control: A systematic review. *Experimental Brain Research*, 241(1), 13–30. <https://doi.org/10.1007/s00221-022-06464-x>
- Plukaard, S., Huizinga, M., Krabbendam, L., & Jolles, J. (2015). Cognitive flexibility in healthy students is affected by fatigue: An experimental study. *Learning and Individual Differences*, 38, 18–25. <https://doi.org/10.1016/j.lindif.2015.01.003>

- Porkka-Heiskanen, T. (1999). Adenosine in sleep and wakefulness. *Annals of Medicine*, 31(2), 125–129. <https://doi.org/10.3109/07853899908998788>
- Pradeep, R., Singh, J., Gupta, M., Moshtaghi, A., Rocca, N., & Kudelka, A. P. (2025). Analyzing fatigue as a common adverse effect in patients treated with immune checkpoint inhibitors. *Journal of Clinical Oncology*, 43(16), e23190–e23190. https://doi.org/10.1200/JCO.2025.43.16_suppl.e23190
- Rahmani, V., Marsh, V. L., Aliafsari Mamaghani, E., Soleimani, A., Alizadeh, M., Zadi, O., & Aghazadeh, N. (2025). Mental fatigue of operating room nurses and its relationship with missed perioperative nursing care: A descriptive-analytical study. *BMC Research Notes*, 18(1), 302. <https://doi.org/10.1186/s13104-025-07380-3>
- Reeve, B., Stover, A., Alfano, C., Smith, A., Ballard-Barbash, R., Bernstein, L., McTiernan, A., Baumgartner, K., & Piper, B. (2012). The Piper Fatigue Scale-12 (PFS-12): Psychometric findings and item reduction in a cohort of breast cancer survivors. *Breast Cancer Research and Treatment*, 136(1). <https://doi.org/https://doi.org/10.1007/s10549-012-2212-4>
- Reis, C., & Canhão, H. (2013). Prevalence of Fatigue in a Group of Airline Pilots. *Aviation, Space, and Environmental Medicine*, 84, 828–833. <https://doi.org/10.3357/ASEM.3548.2013>
- Ricci, J., Chee, E., Lorandean, A., & 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), 1–10. <https://doi.org/10.1097/01.jom.0000249782.60321.2a>
- Rogers, P. J., Heatherley, S. V., Mullings, E. L., & Smith, J. E. (2013). Faster but not smarter: Effects of caffeine and caffeine withdrawal on alertness and performance. *Psychopharmacology*, 226(2), 229–240. <https://doi.org/10.1007/s00213-012-2889-4>
- Rothwell, J., Antal, A., Burke, D., Carlsen, A., Georgiev, D., Jahanshahi, M., Sternad, D., Valls-Solé, J., & Ziemann, U. (2021). Central nervous system physiology. *Clinical Neurophysiology*, 132(12), 3043–3083. <https://doi.org/10.1016/j.clinph.2021.09.013>
- Salihu, A. T., Hill, K. D., & Jaberzadeh, S. (2022). Neural mechanisms underlying state mental fatigue: A systematic review and activation likelihood estimation meta-analysis. *Reviews in the Neurosciences*, 33(8), 889–917. <https://doi.org/10.1515/revneuro-2022-0023>
- Schamphoeleer, E., Habay, J., Proost, M., Arauz, Y. L. A., Russell, S., Roose, M., Bian, C., Meeusen, R., De Pauw, K., & Roelands, B. (2025). Current Practices for Mental Fatigue Quantification and Induction in Movement Science: Introducing the SPeCIFY Guidelines. *Sports Medicine*, 55(10), 2387–2413. <https://doi.org/10.1007/s40279-025-02286-3>
- Schmidt, R., Lee, T., Winsten, C., Wulf, G., & Zelaznik, H. (2019). *Motor Control and Learning: A Behavioral Emphasis* (6th ed.). Human Kinetics.

- Shen, J., Barbera, J., & Shapiro, C. M. (2006). Distinguishing sleepiness and fatigue: Focus on definition and measurement. *Sleep Medicine Reviews*, 10(1), 63–76.
<https://doi.org/10.1016/j.smr.2005.05.004>
- Shin, M., Kim, Y., & Park, S. (2019). Effects of State Anxiety and Ego Depletion on Performance Change in Golf Putting: A Hierarchical Linear Model Application. *Perceptual and Motor Skills*, 126(5), 904–921.
<https://doi.org/10.1177/0031512519856970>
- Simon, J., Takács, E., Orosz, G., Berki, B., & Winkler, I. (2020). Short-term cognitive fatigue effect on auditory temporal order judgments. *Experimental Brain Research*, 238(2), 305–319. <https://doi.org/10.1007/s00221-019-05712-x>
- Smith, A. (2011). From the brain to the workplace: Studies of cognitive fatigue in the laboratory and aboard ship. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 291–305). American Psychological Association. <https://doi.org/10.1037/12343-014>
- Smith, A. P. (2018). Cognitive fatigue and the well-being and academic attainment of university students. *Journal of Education, Society and Behavioral Science*, 24(2).
<https://doi.org/10.9734/JESBS/2018/39529>
- Smith, M. R., Chai, R., Nguyen, H. T., Marcora, S. M., & Coutts, A. J. (2019). Comparing the Effects of Three Cognitive Tasks on Indicators of Mental Fatigue. *The Journal of Psychology*, 153(8), 759–783. <https://doi.org/10.1080/00223980.2019.1611530>
- Staiano, W., Romagnoli, M., Salazar Bonet, L. R., & Ferri-Caruana, A. (2024). Adaptive cognitive tasks for mental fatigue: An innovative paradigm for cognitive loading in human performance. *Journal of Science and Medicine in Sport*, 27(12), 883–889.
<https://doi.org/10.1016/j.jsams.2024.08.199>
- Tanaka, M., Ishii, A., & Watanabe, Y. (2014). Neural effect of mental fatigue on physical fatigue: A magnetoencephalography study. *Brain Research*, 1542, 49–55.
<https://doi.org/10.1016/j.brainres.2013.10.018>
- Tanaka, M., & Watanabe, Y. (2012). Supraspinal regulation of physical fatigue. *Neuroscience & Biobehavioral Reviews*, 36(1), 727–734. <https://doi.org/10.1016/j.neubiorev.2011.10.004>
- Tapia, J. A., Tohyama, T., Poll, A., & Baker, S. N. (2022). The Existence of the StartReact Effect Implies Reticulospinal, Not Corticospinal, Inputs Dominate Drive to Motoneurons during Voluntary Movement. *Journal of Neuroscience*, 42(40), 7634–7647.
<https://doi.org/10.1523/JNEUROSCI.2473-21.2022>
- Terentjeviene, A., Maciuleviciene, E., Vadopalas, K., Mickeviciene, D., Karanauskiene, D., Valanciene, D., Solianik, R., Emeljanovas, A., Kamandulis, S., & Skurvydas, A. (2018). Prefrontal Cortex Activity Predicts Mental Fatigue in Young and Elderly Men During a 2 h “Go/NoGo” Task. *Frontiers in Neuroscience*, 12.
<https://www.frontiersin.org/articles/10.3389/fnins.2018.00620>

- Thomas, M., Allen, M. S., Wigle, D. A., Shen, K. R., Cassivi, S. D., Nichols, F. C., & Deschamps, C. (2012). Does Surgeon Workload Per Day Affect Outcomes After Pulmonary Lobectomies? *The Annals of Thoracic Surgery*, 94(3), 966–972. <https://doi.org/10.1016/j.athoracsur.2012.04.099>
- Tran, Y., Craig, A., Craig, R., Chai, R., & Nguyen, H. (2020). The influence of mental fatigue on brain activity: Evidence from a systematic review with meta-analyses. *Psychophysiology*, 57(5), e13554. <https://doi.org/10.1111/psyp.13554>
- Turvey, M. T., & Fonseca, S. (2009). Nature of Motor Control: Perspectives and Issues. In D. Sternad (Ed.), *Progress in Motor Control: A Multidisciplinary Perspective* (pp. 93–123). Springer US. https://doi.org/10.1007/978-0-387-77064-2_6
- Ung, W. C., Meriaudeau, F., Kiguchi, M., & Tang, T. B. (2020). Functional Near-Infrared Spectroscopy Adaptive Cognitive Training System (FACTS) for Cognitive Underload and Overload Prevention: A Feasibility Study. *IEEE Access*, 8, 172939–172950. <https://doi.org/10.1109/ACCESS.2020.3024867>
- Van Cutsem, J., De Pauw, K., Marcora, S., Meeusen, R., & Roelands, B. (2018). A caffeine-maltodextrin mouth rinse counters mental fatigue. *Psychopharmacology*, 235(4), 947–958. <https://doi.org/10.1007/s00213-017-4809-0>
- Van Cutsem, J., De Pauw, K., Vandervaeren, C., Marcora, S., Meeusen, R., & Roelands, B. (2019). Mental fatigue impairs visuomotor response time in badminton players and controls. *Psychology of Sport and Exercise*, 45, 101579. <https://doi.org/10.1016/j.psychsport.2019.101579>
- Van Cutsem, J., Marcora, S., De Pauw, K., Bailey, S., Meeusen, R., & Roelands, B. (2017). The Effects of Mental Fatigue on Physical Performance: A Systematic Review. *Sports Medicine*, 47(8), 1569–1588. <https://doi.org/10.1007/s40279-016-0672-0>
- van der Linden, D. (2011). The urge to stop: The cognitive and biological nature of acute mental fatigue. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 149–164). American Psychological Association. <https://doi.org/10.1037/12343-007>
- van der Linden, D., Frese, M., & Meijman, T. F. (2003). Mental fatigue and the control of cognitive processes: Effects on perseveration and planning. *Acta Psychologica*, 113(1), 45–65. [https://doi.org/10.1016/S0001-6918\(02\)00150-6](https://doi.org/10.1016/S0001-6918(02)00150-6)
- van der Linden, D., Massar, S. A. A., Schellekens, A. F. A., Ellenbroek, B. A., & Verkes, R.-J. (2006). Disrupted sensorimotor gating due to mental fatigue: Preliminary evidence. *International Journal of Psychophysiology*, 62(1), 168–174. <https://doi.org/10.1016/j.ijpsycho.2006.04.001>
- Vickers, D., & Smith, P. L. (1986). The rationale for the inspection time index. *Personality and Individual Differences*, 7(5), 609–623. [https://doi.org/10.1016/0191-8869\(86\)90030-9](https://doi.org/10.1016/0191-8869(86)90030-9)

- Wascher, E., & Getzmann, S. (2014). Rapid Mental Fatigue Amplifies Age-Related Attentional Deficits. *Journal of Psychophysiology*, 28(3), 215–224. <https://doi.org/10.1027/0269-8803/a000127>
- Weiler, H., Russell, S., Spielmann, J., & Englert, C. (2025). Mental Fatigue: Is It Real? *Journal of Applied Sport and Exercise Psychology*, 32(1), 14–26. <https://doi.org/10.1026/2941-7597/a000033>
- Wiehler, A., Branzoli, F., Adanyeguh, I., Mochel, F., & Pessiglione, M. (2022). A neuro-metabolic account of why daylong cognitive work alters the control of economic decisions. *Current Biology*, 32(16), 3564–3575.e5. <https://doi.org/10.1016/j.cub.2022.07.010>
- Wise, J. M., Heaton, K., & Patrician, P. (2019). Fatigue in Long-Haul Truck Drivers: A Concept Analysis. *Workplace Health & Safety*, 67(2), 68–77. <https://doi.org/10.1177/2165079918800509>
- Woodcock, E. A., Anand, C., Khatib, D., Diwadkar, V. A., & Stanley, J. A. (2018). Working Memory Modulates Glutamate Levels in the Dorsolateral Prefrontal Cortex during 1H fMRS. *Frontiers in Psychiatry*, 9(66), 1–10. <https://doi.org/10.3389/fpsyt.2018.00066>
- Xiao, Y., Ma, F., Lv, Y., Cai, G., Teng, P., Xu, F., & Chen, S. (2015). Sustained Attention is Associated with Error Processing Impairment: Evidence from Mental Fatigue Study in Four-Choice Reaction Time Task. *PLOS ONE*, 10(3), e0117837. <https://doi.org/10.1371/journal.pone.0117837>
- Yang, B., Xiao, W., Liu, X., Wu, S., & Miao, D. (2013). Mental fatigue impairs pre-attentive processing: A MMN study. *Neuroscience Letters*, 532, 12–16. <https://doi.org/10.1016/j.neulet.2012.08.080>
- Yang, R., Zhang, M., Wang, Z., Zhao, M., & Zhu, X. (2025). Effects of Mental Fatigue on Trunk and Knee Kinetics and Kinematics During Unanticipated Stop-Jump in Amateur Soccer Players. *Orthopaedic Journal of Sports Medicine*, 13(5), 23259671251338239. <https://doi.org/10.1177/23259671251338239>
- Zeuwts, L. H. R. H., Iliano, E., Smith, M., Deconinck, F., & Lenoir, M. (2021). Mental fatigue delays visual search behaviour in young cyclists when negotiating complex traffic situations: A study in virtual reality. *Accident Analysis & Prevention*, 161, 106387. <https://doi.org/10.1016/j.aap.2021.106387>
- Zhang, Z., Xiang, T., Guo, H., Ma, L., Guan, Z., & Fang, Y. (2023). Impact of physical and mental fatigue on construction workers' unsafe behavior based on physiological measurement. *Journal of Safety Research*, 85, 457–468. <https://doi.org/10.1016/j.jsr.2023.04.014>

- Zheng, B., Zhang, Z., Zhang, Z., Sun, Y., Xiao, Y., & Li, M. (2025). Effects of mental fatigue on biomechanical characteristics and risk associated with non-contact anterior cruciate ligament injuries during landing. *Frontiers in Bioengineering and Biotechnology*, 13. <https://doi.org/10.3389/fbioe.2025.1582873>
- Zhou, H., Chan, A. P.-C., Yang, Y., & Yi, W. (2025). A Systematic Review of Mental States and Safety Performance of Construction Workers. *Journal of Construction Engineering and Management*, 151(10), 03125007. <https://doi.org/10.1061/JCEMD4.COENG-15931>
- Zhou, Y., & Danbolt, N. C. (2014). Glutamate as a neurotransmitter in the healthy brain. *Journal of Neural Transmission*, 121(8), 799–817. <https://doi.org/10.1007/s00702-014-1180-8>

Chapter 2. Experiment 1 - Slowed Reaction Times in Cognitive Fatigue Are Not Attributable to Declines in Motor Preparation

A version of this chapter has been published: Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>

2.1 Abstract

Cognitive fatigue (CF) can result from sustained mental effort, is characterized by subjective feelings of exhaustion and cognitive performance deficits, and is associated with slowed simple reaction time (RT). This study determined whether declines in motor preparation underlie this RT effect. Motor preparation level was indexed using simple RT and the StartReact effect, wherein a prepared movement is involuntarily triggered at short latency by a startling acoustic stimulus (SAS). It was predicted that if decreased motor preparation underlies CF-associated RT increases, then an attenuated StartReact effect would be observed following cognitive task completion. Subjective fatigue assessment and a simple RT task were performed before and after a cognitively fatiguing task or non-fatiguing control intervention. On 25% of RT trials, a SAS replaced the go-signal to assess the StartReact effect. CF inducement was verified by significant declines in cognitive performance ($p = .003$), along with increases in subjective CF ($p < .001$) and control RT ($p = .018$) following the cognitive fatigue intervention, but not the control intervention. No significant pre-to-post-test changes in SAS RT were observed, indicating that RT increases resulting from CF are not substantially associated with declines in motor preparation, and instead may be attributable to other stages of processing during a simple RT task.

2.2 Introduction

Fatigue, whether pathological or situational, is a phenomenon that is widely experienced, and is a leading reason for which patients seek medical care (Nicholson et al., 2015; Okkes et al., 2002). Broadly speaking, fatigue can be considered as a performance reduction that occurs following an effortful or prolonged task, whether the task be physical (such as an endurance race) or mental (such as taking a difficult math test; DeLuca, 2005; Phillips, 2015). Although the mechanisms of physical (e.g., muscle) fatigue are well understood (Tanaka & Watanabe, 2012), cognitive fatigue (CF) is a more abstract concept. While no commonly accepted definition of CF exists, it has been postulated to occur following a sustained mental effort, and can be characterized by subjective feelings of exhaustion, sometimes accompanied by an inability to sustain cognitive performance levels (Boksem & Tops, 2008; Leavitt & DeLuca, 2010; Phillips, 2015). Along with a reduction in mood states (van der Linden & Eling, 2006) and a decline in general arousal (Boksem et al., 2005), CF has been associated with a host of mental performance decrements, including reductions in working memory capacity (Jain & Nataraja, 2019; Massar et al., 2010), attentional focus (Boksem et al., 2005; Guo et al., 2016), error correction (Lorist et al., 2005), response inhibition (Kato et al., 2009), and planning (Lorist et al., 2000; van der Linden et al., 2003). Moreover, the effects of CF are not limited to mental tasks; increased levels of CF have been linked to reduced physical endurance (Van Cutsem et al., 2017), declining sports performance (Pageaux & Lepers, 2018), and altered gait control (Behrens et al., 2018; Grobe et al., 2017).

Several studies have indicated that cognitive performance declines attributable to CF are particularly apparent in complex tasks involving high levels of executive control, such as those requiring intricate planning and coordination of responses (van der Linden et al., 2003), adaptation to novel or changing task demands (Massar et al., 2010; Plukaard et al., 2015), goal-

directed attention (Boksem et al., 2005; Csathó et al., 2012; Faber et al., 2012) and online inhibition of incorrect actions (Guo et al., 2018; Kato et al., 2009). Simpler tasks lacking in response variability are considered more resistant to CF, as they are less susceptible to deteriorations in executive control that are thought to drive the behavioural effects of CF (Boksem et al., 2005; Lorist & Faber, 2011; van der Linden et al., 2003). However, some motor tasks requiring little investment of executive control are influenced by CF. Specifically, reaction time (RT), or the time required to respond to a stimulus, is thought to represent basic sensorimotor processing but nevertheless has been demonstrated to be impaired in states of CF (Ferreira Junior et al., 2020; Jaydari Fard et al., 2019; Langner, Steinborn, et al., 2010; Langner, Willmes, et al., 2010; Lisper et al., 1977; M. R. Smith et al., 2019).

An investigation of the effects of CF on RT is particularly important given the common nature of CF and the potentially dangerous impacts of slowed RT. Indeed, studies have demonstrated that slowed RT in response to CF presents a key risk in road accident occurrence (Guo et al., 2018; Zeuwts et al., 2021; Zhao et al., 2012). CF is also a significant workplace hazard; slowed RTs due to CF have been implicated in impaired work performance and heightened accident risk in a variety of occupational roles, including surgical teams (Petrut et al., 2020), aircraft pilots (Jahanpour et al., 2020), marine operators (A. Smith, 2011), construction workers (Li et al., 2019), and truck drivers (Wise et al., 2019). Furthermore, neuromotor disorders including Parkinson's disease (Lou, 2009), multiple sclerosis (Linnhoff et al., 2019), traumatic brain injury (Johansson et al., 2009), and post-stroke syndrome (Chaudhuri & Behan, 2004) are marked by both CF and motor dysfunction. A deeper understanding of the relationship between these two symptoms could inform the etiology and treatment of such conditions.

Despite these noteworthy applications, an understanding of the mechanism by which CF acts to slow RT has yet to be developed.

An examination of the effect of CF on the sub-processes that underlie RT could begin to address this knowledge gap. Reaction time, or more specifically, premotor RT (i.e., the time from imperative stimulus onset to EMG onset in the relevant musculature) in both choice and simple RT tasks can be divided into several components of central processing (Donders, 1969; Spijkers & Walter, 1985; Taylor, 1976). In a choice RT task, where two or more stimuli are presented and multiple responses are possible, premotor RT involves identification of the stimulus type, selection of the appropriately coupled response, preparation of the movement, and response initiation. On the other hand, in a simple RT task, featuring only one stimulus and a single possible response, the imperative stimulus need only be detected rather than identified among two or more possibilities. Moreover, because the required response is certain, the correct motor program can be selected and prepared in advance of the imperative (go) stimulus, following which response initiation can occur (see Klapp & Maslovat, 2020 for review). Although slowed simple RT in the presence of CF has been frequently demonstrated (Ferreira Junior et al., 2020; Jaydari Fard et al., 2019; Langner, Steinborn, et al., 2010; Langner, Willmes, et al., 2010; Lisper et al., 1977; M. R. Smith et al., 2019), it is unknown which stage of central processing (advance preparation, stimulus detection or response initiation) is responsible for the observed effect. Previous studies have indicated that preparatory activities in cognitive tasks are vulnerable to the effects of CF (Lorist et al., 2000; van der Linden et al., 2003), while physical performance decrements in response to CF have also been reported (Behrens et al., 2018; Jacquet et al., 2021; Pageaux & Lepers, 2018; Van Cutsem et al., 2017). As such, it is possible that impairment of

response preparation may underlie CF-related performance decrements in both cognitive and motor tasks, including tests of simple RT.

Several methods can be used to assess the level of motor preparation in advance of a go-signal, including the presentation of a startling acoustic stimulus (SAS; Carlsen & Maslovat, 2019). Specifically, a high intensity (115-130 dB) SAS can be used to probe the state of preparation during the instructed delay phase of a simple RT task (Carlsen et al., 2004b; Valls-Solé et al., 1999). The SAS commonly elicits a startle reflex – a widespread protective response, measured objectively via blink responses (Blumenthal et al., 2005) or early onset of muscle activity in the sternocleidomastoid (SCM) muscle (Carlsen et al., 2011; Valls-Solé et al., 1995). When the SAS is presented at the time of the go-signal in a simple RT task, it can cause an early release of the prepared movement, an effect that is independent from stimulus intensity effects and has been suggested to reflect the bypassing of usual cortical release mechanisms (Carlsen et al., 2007; Carlsen & Maslovat, 2019; V. Smith et al., 2019). This ‘Start-React effect’ can be used to index levels of advance motor preparation, in that highly prepared movements result in StartReact RTs that are well below those achieved in startle-free voluntary RT trials (e.g., <100 ms; Carlsen et al., 2004b; Valls-Solé et al., 1995). Moreover, compared to SAS trial responses in a state of poorer advance preparation (such as in a choice RT or dual task paradigm), highly prepared movements result in an elevated proportion of involuntary response triggering and an increased likelihood of eliciting a startle reflex (Carlsen et al., 2004a; Maslovat et al., 2021; V. Smith et al., 2019). In the context of the current study, if motor preparatory processes are impaired by the inducement of CF, one would expect a diminished StartReact effect; that is, compared to baseline (pre-fatigue) measurements, RT on SAS trials would increase, and the proportion of SAS trials wherein a startle reflex in the SCM muscle is observed would decline

(Maslovat et al., 2012). On the other hand, if CF does not impair the advance preparation of movement, the StartReact effect would appear intact, with both SAS RT and the proportion of startle reflex responses remaining unchanged.

The current study aimed to assess whether declines in motor preparation underlie the increases in simple RT seen with CF. This was accomplished through evaluation of non-startle (control) RT as well as the StartReact effect before and after completion of a sustained cognitively demanding task. Cognitive fatigue was induced using a continuous, effortful Math-Memory task, designed to tax working memory processes and to require consistently high levels of vigilance (Ackerman, 2011; M. R. Smith et al., 2019). Changes in voluntary control RT, subjective reports of fatigue, as well as changes in cognitive task performance were used to confirm inducement of CF following the cognitive task (Christodoulou, 2005), while responses to startle stimuli were used to probe the effects of CF on motor preparation (Carlsen et al., 2004a; Maslovat et al., 2012). Given the hypothesis that declines in motor preparation underlie slowed RT in response to CF, it was predicted that the StartReact effect would be unaffected following completion of a non-fatiguing task (watching a documentary film) but diminished following completion of a challenging cognitive task (i.e., RT latency on SAS trials would be seen to increase following CF task completion, while the proportion of responses demonstrating a startle reflex would decline). Findings of this study will contribute to our understanding of the mechanism by which CF impairs simple RT, an important endeavour given the commonality of CF and the potentially dangerous outcomes of slowed RT.

2.3 Materials and Methods

2.3.1 Participants

An a priori sample size calculation was determined based on the results detailed by Smith, Chai et al. (M. R. Smith et al., 2019), who reported the effect size of cognitive fatigue on simple reaction time (partial $\eta^2 = 0.441$)¹. This analysis determined that a total of 11 participants were required to demonstrate observable effects of mental fatigue on simple reaction time. In the current study, 22 participants (8M, 14F, mean age = 28.9 years, $SD = 9.6$) with no history of neurological, sensory, or motor dysfunctions gave written informed consent to participate in the study. All participants had normal or corrected to normal vision, and were free from any sleep disorders, chronic pain, or fatigue syndromes. Participants took part in both non-fatiguing (NF) and cognitive fatigue (CF) testing session on separate days at times between 9:00 am and 5:00 pm, in counterbalanced order. Each session required approximately two hours to complete. Two participants were unable to attend both sessions and were therefore excluded. An additional 4 participants who did not demonstrate objective increases in CF were excluded from subsequent analysis (see section 2.5 *Data Reduction*) leading to a final sample size of 16 participants (6M, 10F, mean age = 29.4 years, $SD = 9.9$).

2.3.2 General Timeline and Set Up

A schematic timeline for each of the two experimental sessions (days) is shown in Fig. 2.1. Prior to beginning each session, participants completed a pre-session questionnaire (similar to that presented in *Appendix E.1*), which recorded several lifestyle factors that could influence RT or cognitive fatigability, including estimates of caffeine intake and number of hours of sleep in the 24 hours prior to the testing session (Jewett et al., 1999; Knufinke et al., 2018; McLellan et al.,

¹ Additional specifications for power analysis were as follows: alpha = .05, power = .95, correlation among repeated measures = 0 (for a conservative estimate)

2016; Rogers et al., 2013). Directly following completion of this questionnaire, participants were seated in a comfortable chair, 1.5 m directly in front of a 24-inch LCD computer monitor (Asus VG248). All experimental tasks were completed in this position. Experiments began with pre-test measurements of subjective CF and a simple RT task used to assess baseline simple premotor RT and levels of motor preparation (see section 2.3.4 *Pre- and Post-Test*). Following baseline measurements, participants performed either the CF or NF task, depending on the testing day, with each task requiring approximately 1 hour to complete. Following completion of the imperative task, subjective CF and RT measures were reassessed. Data collection, as well as ordering and presentation of pre-tests, post-tests, and the CF task, were controlled by a custom LabVIEW program (National Instruments Inc.).

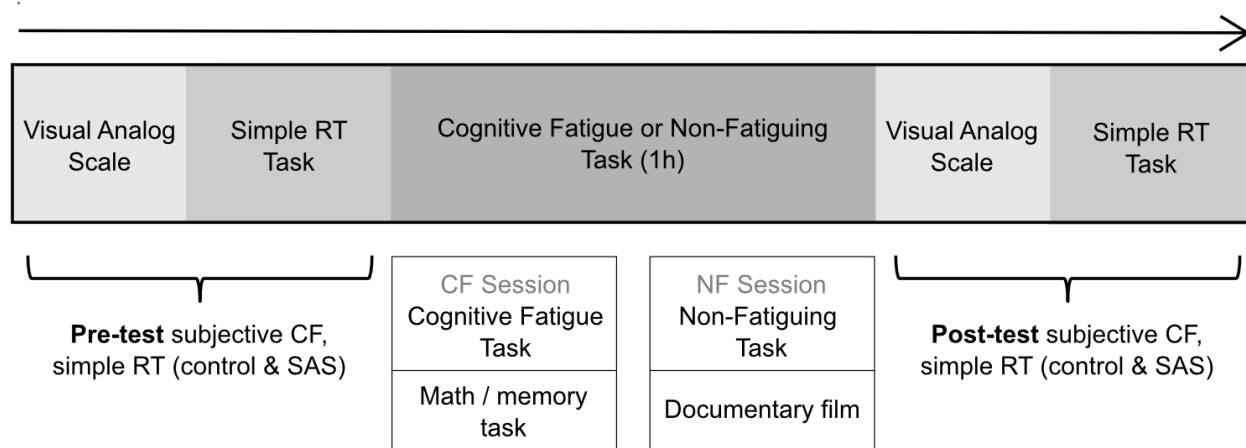


Fig. 2.1 Experimental timeline. Following the pre-test and prior to the post-test, participants completed either the cognitive intervention (in the cognitive fatigue task session) or documentary film viewing intervention (in the non-fatiguing task session). CF = cognitive fatigue, NF = non-fatiguing, RT = reaction time, SAS = startling acoustic stimulus.

2.3.3 Cognitive Fatigue and Control Interventions

In the CF session, participants performed a cognitively demanding Math-Memory dual task designed to optimally induce CF (Ackerman, 2011; M. R. Smith et al., 2019). The CF task was presented on the computer screen using a custom LabVIEW program. To complete the task, participants were provided with a lap desk along with a wireless keyboard and mouse (Logitech MK270). In this task, 7 letters appeared consecutively on the computer screen, for 800 ms each with a pause of 500 ms between letters, in a pre-generated sequence. Participants were told that they should remember these letters, using whatever mental strategy they wish, but without rehearsing the letters out loud. After all letters had been displayed, a series of math problems was presented for 45 seconds. In this component of the task, participants were required to use the computer mouse to select the mathematical operation that correctly completed the math problem presented (e.g., $20 ? 5 = 25$; answer = +). Participants were instructed to correctly complete as many math problems as possible during the 45 second period. To maintain motivation, participants were provided feedback on the number of math problems correctly solved, as well as the accuracy of responses. After 45 seconds had elapsed, participants were presented with 7 blank boxes horizontally aligned in the middle of the computer screen and were instructed to use the keyboard to input the remembered letters into these boxes, in the correct order. Immediately after the final letter was inputted, the words “Get Ready” reappeared on the computer screen, followed 1 second later by 7 new letters, again presented sequentially. The cognitive task continued in this manner repeatedly for 60 math and memory dual-task trials (this phase took approximately 55-65 minutes to complete). Keypress responses and selected math operators were recorded using a custom LabView program. Performance on each trial of the CF task was

measured by the proportion of math problems correctly completed as well as the proportion of letters correctly remembered in the order presented (see section 2.5 *Data Reduction*).

In the NF session, in place of the memory / math task, participants were required to sit quietly and watch a documentary film (*Our Planet*; Pearson, 2019; Stark, 2019) for one hour, using the same computer monitor described above. Both the NF and CF tasks were preceded and followed by subjective fatigue measurement and a simple RT task.

2.3.4 Pre- and Post-Test

Pre- and post- tests were performed prior to and immediately following completion of the cognitively demanding (CF session) and control interventions (NF session). These tests were used to assess three measures: i) subjective CF levels, as a manipulation check to confirm that the CF task led to increased fatigue; ii) control RT, to verify previously documented increases in RT following CF inducement; and iii) SAS RT, to assess the effects of CF on motor preparation.

Subjective CF was assessed using a series of visual analog scales (VAS) presented on the computer monitor (M. R. Smith et al., 2019). Participants provided ratings of several subjective aspects of CF by using a computer mouse to slide a visual marker along a horizontal scale of 0 - 10 (slider length 200 mm). Scales included in the VAS were obtained from the cognitive and sensory subscales of the Piper Fatigue Scale-12 (Reeve et al., 2012). Participants were asked to rate their energy level (0-energetic, 10-unenergetic), stress level (0-relaxed, 10-tense), and ability to concentrate (0-able to concentrate, 10-unable to concentrate). Since it is suggested that changes in motivation are both an important moderator and symptom of CF (Herlambang et al., 2019, 2021; Hockey, 2011), an additional measure to assess motivation was included (0-motivated to succeed in the task, 10-unmotivated to succeed in the task).

Following subjective fatigue assessment, participants performed a simple RT task requiring a 20° targeted wrist extension in response to an auditory go-signal. Participants placed their right arm, abducted to 30° on an armrest parallel to the floor. The right elbow was flexed at approximately 90° and the right palm faced inward. The right hand was placed in the hand support of a custom-made aluminum manipulandum, oriented so that the manipulandum's axis of rotation was in line with the wrist joint. The computer monitor was used to indicate the hand position on a visual dial, which provided a real time approximation of the flexion / extension of the wrist. A line at the central position of the dial indicated the hand starting position, with the wrist located in neutral position (neither flexed nor extended). A visual target line was presented at 20° of wrist extension; the simple RT task required participants to extend the wrist as quickly and accurately as possible to this target position, following an auditory go-signal (82 dB, 25 ms, 1000 Hz sine wave). Each trial began with the words "Get Ready!" appearing on the monitor for 1000 ms, followed by an auditory warning tone (82 dB, 100 ms, 200 Hz). The monitor went blank after the warning signal, followed by random variable foreperiod of 2000-2500 ms before presentation of the go-signal. Following each RT trial, feedback including displacement reaction time (time between the go-signal and the initial manipulandum movement) and accuracy (in degrees error from target position) was presented on the computer monitor for 3500 ms, with points awarded for reaction times faster than 140 ms (1 point per ms below, with a maximum of 25 points awarded). Participants were allowed 5 practice reaction time trials prior to the pre-test to familiarize themselves with the equipment and task. Pre- and post-RT tests consisted of 2 blocks of 20 RT trials each. On 25% of trials, a startling acoustic stimulus (SAS; 120 dB, 25 ms, broadband white noise waveform) replaced the go-signal, resulting in a total of 30 non-SAS RT trials and 10 SAS RT trials presented at each testing time (pre- and post-test) and testing session

(NF and CF). Participants were told that the loudness of the imperative go-signal would vary, and that they should respond in the same manner no matter the stimulus intensity. The trial order was pseudorandomised, with SAS never being presented on the first trial of a block, nor on two consecutive trials within a block. The warning, SAS, and go-signals were generated by digital to analog hardware (National Instruments PCIE-6321). The warning signal was presented through standard computer speakers while the go-signal and SAS were amplified and presented by a loudspeaker located 30 cm from the ear, directly behind the participant's head (MG Electronics M58-H, frequency response 300 Hz-11 kHz, rise time <1 ms). The intensity of all auditory stimuli was confirmed with a precision sound level meter (Cirrus Research model CR:162C, "A" weighting, impulse setting) placed in a location corresponding to the location of the participant's left ear.

2.3.5 Recording Equipment

Bipolar pre-amplified surface EMG electrodes (gain = 10; Delsys Bagnoli DE-2.1) were placed on the skin above the superficial muscle bellies of the right extensor carpi radialis longus (ECR), right flexor carpi radialis (FCR) and right sternocleidomastoid (SCM) muscles and connected to an external amplifier (Delsys Bagnoli-8) by shielded cabling. EMG electrodes were oriented parallel to the muscle fibers and fastened using adhesive strips. A 2-inch square carbon-pad grounding electrode (Easy@Home) was placed on the right medial epicondyle. Prior to EMG and grounding electrode placement, the attachment sites were prepared and cleaned with alcohol to optimize recording quality. Wrist angular displacement was collected using a potentiometer at the pivot point of the manipulandum. Position and band-passed (20-450 Hz) EMG data were digitally sampled at 4 kHz (National Instruments PCIE-6321) using a custom LabVIEW software

program (National Instruments Inc.) and were collected over a 3000 ms period beginning at 1000 ms before go-stimulus onset.

2.4 Dependent Variables

2.4.1 Subjective Cognitive Fatigue

Subjective CF was assessed using responses to the VAS to confirm that CF had been successfully induced by the CF intervention. To determine a global measure of subjective CF, an average score of the four 10-point measures assessed by the VAS (energy, ability to concentrate, motivation, and stress level) was calculated. The resulting value was subtracted from 10, so that higher scores (on a scale of 0-10) indicated greater levels of subjective CF (*Subjective CF score* = $10 - [(Energy\ Score + Concentration\ Score + Motivation\ Score + Stress\ Score) / 4]$).

2.4.2 Cognitive Task Performance

Performance on the cognitive task was used as an objective confirmation of CF. Although the time course of objective performance changes varies greatly depending on task demands (Lorist & Faber, 2011), many studies have noted initial performance plateaus or gains in cognitive task performance, followed by subsequent declines in performance as the effects of CF arise. For complex cognitive tasks, performance declines have been observed following 15-30 min of task performance (Gergelyfi et al., 2015; Mackworth, 1948; Pattyn et al., 2008); as such, the current study assessed cognitive performance over the latter half (i.e., last 30 trials) of the cognitive task.

Cognitive task performance metrics included the number of math problems completed, the proportion of math problems correctly completed, as well as the proportion of letters remembered in the correct order. Overall cognitive task performance was represented by a trial-by-trial average composite score, consisting of the proportion of correct math problems completed and the proportion of letters correctly remembered on each trial of the cognitive task

(*Cognitive performance score* = $[(\text{proportion correct math problems} + \text{proportion correct letters}) / 2]$). The total number of math problems completed was excluded from the overall score, as both graphical and statistical indices suggested that performance in this metric was largely invariable across participants and trials.

Previous studies have observed high inter-subject variability in cognitive task performance under the effects of CF, with subsets of individuals demonstrating CF resistance and failing to show significant signs of performance decline (Breckel et al., 2013; Lim et al., 2012; Qi et al., 2020). As this study is not primarily concerned with manipulation of CF, but rather with the effects resulting from CF, it was necessary to ensure that only participants who demonstrated evidence of CF inducement were included in analyses of RT task measures. As such, participants who displayed trends of increasing cognitive performance scores (i.e., improvements, rather than declines in cognitive task performance; $n = 4$) over the final 30 cognitive task trials were excluded from RT and startle response analyses.

2.4.3 Control and SAS Trial Reaction Time

Premotor RT on control trials was used to confirm previously documented effects of CF on simple RT, while premotor RT on SAS trials was used to assess the unknown effects of CF on advance motor preparation. Premotor RT was defined as the time from go-signal presentation to initial EMG onset measured at the right ECR. EMG onset was defined as the point where rectified and filtered EMG activity rose two standard deviations above baseline EMG activity (i.e., the average EMG activity in the 500 ms window immediately preceding the go-signal / SAS) and remained above baseline activity for a minimum of 20 ms. A custom LabVIEW program was used to mark EMG onsets, which were then visually confirmed by a researcher, who adjusted the onset values in the case of visible errors (see Hodges & Bui, 1996).

2.4.4 Proportion of SAS Trials Resulting in a Startle

Motor preparation was further assessed by the proportion of SAS trials with an observable startle reflex. A startle reflex was said to have occurred on SAS trials where a burst of EMG activity in the SCM muscle was observed within 25-120 ms following presentation of a SAS (Carlsen et al., 2011).

2.5 Data Reduction

Two participants who did not complete both testing sessions and were excluded from all analyses. Four participants who demonstrated resistance to the CF manipulation were removed from analyses of RT and proportion of startle responses. Among the remaining 16 participants, counterbalance of session order delivery was equally maintained. Practice trials were not analysed. Testing RT trials where participants performed the movement incorrectly (e.g., not a smooth ballistic-type response, total = 72 trials, including 68 control trials and 4 SAS trials) or responded in anticipation of the go-signal (RTs ≤ 50 ms; total = 59 trials, including 44 control trials and 15 SAS trials) were excluded from analysis. Outlying RT data points (greater than mean RT ± 2 standard deviations) within each session, stimulus type and testing time were also removed prior to analysis (total = 91 trials, including 70 control trials and 21 SAS trials; please see *Appendix A.1* for analysis with an expanded ± 3 standard deviation outlier removal, which did not alter the conclusions of the study). As a startle reflex was considered requisite to investigate the StartReact effect as an index of advance motor preparation, SAS trials without SCM activation 25-120 ms following SAS presentation were not included in assessments of RT values (total = 213 trials). The final exclusion rate of control trials was 9.5% (182 / 1920 control trials) and for SAS trials was 39.5% (253 / 640 SAS trials), for an overall trial exclusion rate of 17% (total = 435 / 2560 trials).

2.6 Statistical Analysis

Statistical analyses were completed using linear and linear mixed-effect model (LMM) analyses in R statistical software (Bates et al., 2015; R Core Team, 2021). LMM analyses allowed for the retention of all data within the repeated-measures design, without violation of the assumption of independence (Bates et al., 2015). Data were assessed for homoscedasticity and approximate normal distribution of residuals. To best meet these assumptions, an arcsine square root transformation of proportion data was performed. The significance of fixed effects was explored using analysis of variance of each model, with F -tests and p -values using Satterthwaite's method for denominator degrees-of-freedom and F -statistic, applied using the *lmerTest* package (Kuznetsova et al., 2017). In all cases, differences with a probability of .05 or less were considered significant. Where applicable, planned post hoc contrasts with Bonferroni corrections, estimated marginal means, and 95% confidence intervals (CI) for each measure were determined within each analysis using the *emmeans* package (Lenth et al., 2021). Effect sizes (d) for post hoc comparisons were calculated according to methods outlined in (Brysbaert & Stevens, 2018).

2.6.1 Subjective Cognitive Fatigue

Subjective CF scores were assessed with a model including the fixed effect interaction of testing session (NF, CF) and time (pre-test, post-test), with random intercepts specified for the effect of participant. As such the model took the following form: $model = \text{Subjective CF Score} \sim \text{Session} * \text{Time} + (1 \mid \text{Participant})$. While this model assesses an overall score for subjective CF, an analysis of individual subjective fatigue measures (energy, stress level, motivation and ability to concentrate) is available in *Appendix A.2*.

2.6.2 Cognitive Task Performance

Changes in cognitive performance over the last 30 trials of the cognitive task were measured using a model including the fixed effect of trial number and random intercepts specified for the effect of participant: $model = \text{Cognitive Performance Score} \sim \text{Trial Number} + (1 | \text{Participant})$. Generally, high inter-subject variability in cognitive performance over sustained tasks has been demonstrated, with a subset of individuals displaying clear resiliency against CF effects (Breckel et al., 2013; Lim et al., 2012; Qi et al., 2020). To determine which participants demonstrated CF-resistance in the current study, the slope of changes in cognitive performance scores over the latter half of the time-on-task were also assessed for each individual subject, using simple linear regression models.

2.6.3 Control and SAS Trial Reaction Time

A linear mixed effects model was used to assess changes in RT, in response to the fixed effect interaction of stimulus (control, SAS), session type (NF, CF), and time (pre-test, post-test). Random intercepts for the effect of participant and by-participant random slopes for the effect of session (NF, CF) were used in the model to account for variation in overall RT that may exist between subjects, and between testing days within each subject: $model = RT \sim \text{Session} * \text{Time} * \text{Stimulus Type} + (1 + \text{Session} | \text{Participant})$.

The results of the initial RT analysis demonstrated significant pre-test RT differences between testing sessions (see section 2.8.3 *Control and SAS Trial Reaction Time*), therefore follow-up analyses were performed to examine whether lifestyle measures as assessed in the pre-session questionnaire may be contributing to this baseline RT difference. These measures included the approximate number of hours of sleep and mg of caffeine intake in 24 hours prior to the testing session (Jewett et al., 1999; Knufinke et al., 2018; McLellan et al., 2016; Rogers et

al., 2013). Linear mixed effect models were used to assess the relationship of each of these lifestyle measures to the fixed effect of testing session (NF, CF). A term representing by-subject random intercepts was also included in each model: $model = Lifestyle\ Measure \sim Session + (1 | Participant)$.

2.6.4 Proportion of SAS Trials Resulting in a Startle

A final model was used to assess differences in the proportion of SAS trials leading to an overt startle reflex (indicated by activity in the SCM muscle) in response to the fixed effect interaction of testing session (NF, CF) and time (pre-test, post-test): $model = Startle\ Proportion \sim Session * Time + (1 | Participant)$.

2.7 Compliance with Ethical Standards

All stages involved in the completion of this study, including interactions with participants, have been carried out in accordance with the ethical standards in the Declaration of Helsinki and its later amendments. This experiment was approved by the Research Ethics Board at the University of Ottawa. All participants in this study provided informed consent prior to participation. The authors have no conflicts of interest to declare.

2.8 Results

2.8.1 Subjective Cognitive Fatigue

Subjective CF score as a function of time (pre-test, post-test) and session type (NF, CF) is presented in Fig. 2.2. LMM analysis demonstrated significant main effects of both time ($F(1, 57) = 43.96, p < .001$) and session type ($F(1, 57) = 25.54, p < .001$), which were superseded by a significant time x session type interaction ($F(1, 57) = 9.49, p = .003$). Planned post hoc comparisons revealed significantly greater post-test subjective CF scores as compared to pre-test in the CF session (mean difference score = +2.15; $p < .001, d = 1.41$). No significant difference

in subjective CF scores between the NF session pre- and post-tests was observed (mean difference score = +0.79; $p = .060$, $d = 0.62$). Pre-test measures of subjective CF did not differ between the NF and CF sessions (mean difference score = +0.44; $p = .674$, $d = 0.33$), while post-test subjective CF scores were significantly greater in the CF session (mean difference score = +1.80; $p < .001$, $d = 1.22$).

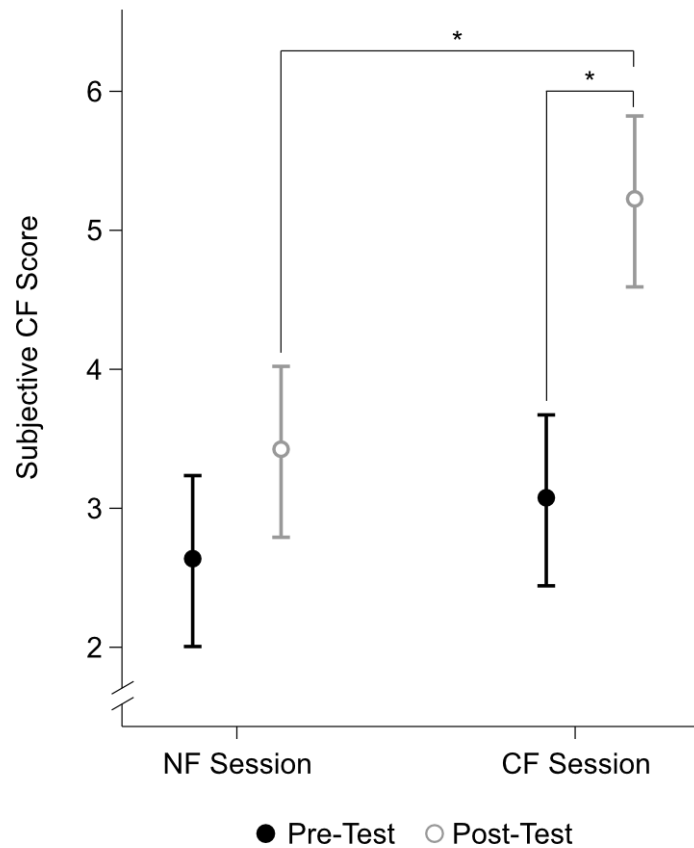


Fig. 2.2 Estimated marginal mean subjective cognitive fatigue scores. Scores are presented as a function of session type (NF, CF) and testing time (pre-test, post-test). Error bars indicate 95% confidence intervals. Asterisks indicate significant comparisons ($p < .05$). CF = cognitive fatigue, NF = non-fatiguing.

2.8.2 Cognitive Task Performance

LMM analysis indicated a significant decline in cognitive task performance scores over time-on-task ($F(1,597) = 8.76, p = .003$). Model estimates indicated an intercept score of 0.891 ($SE = 0.036$) and score decline of 0.002 ($SE < 0.001$) per trial. To determine which participants did not follow this trend (i.e., who did not demonstrate objective increases in CF over the latter half of the time-on-task), changes in cognitive performance score over the last 30 trials were assessed individually for each participant. Positive regression slopes were observed in 4 participants, indicating that CF was not successfully induced in these individuals. As these participants did not demonstrate objective (cognitive task performance) evidence of CF inducement, they were considered resistant to CF in the current task and were removed from analyses of RT and startle responses.

2.8.3 Control and SAS Trial Reaction Time

Control and SAS trial premotor RT as a function of time (pre-test, post-test) and session type (NF, CF) can be seen in Fig. 2.3. RT analysis indicated significant main effects of stimulus ($F(1, 2095) = 298.19, p < .001$) and session type ($F(1, 17) = 6.14, p = .024$), which were superseded by a significant stimulus x session type x time interaction ($F(1, 2089) = 4.69, p = .031$). As expected, SAS trials exhibited shorter RT compared to control trials in all cases ($p < .001$). However, the RT comparison of greatest interest with respect to the proposed hypothesis involved the analysis of RT differences between pre- and post-test. Post hoc analyses confirmed that control trial RT increased significantly from pre- to post-test in the CF session (mean difference = +7.30 ms, $p = .018, d = 0.18$) and decreased significantly from pre- to post-test in the NF session (mean difference = -7.50 ms, $p = .013, d = 0.16$). Conversely, on SAS trials, no significant differences were found between pre- and post-tests in either the NF session (mean

difference = +2.30 ms, $p > .999$, $d = 0.06$) or CF session (mean difference = +0.60 ms, $p > .999$, $d = 0.04$). A post hoc Bayesian analysis confirmed the lack of substantial SAS RT change from pre- to post-test in both sessions, demonstrating substantial evidence in favour of the null hypothesis ($BF_{10} = 0.119 \pm 1.24\%$; see *Appendix A.3* for further details of this analysis; Jeffreys 1961; cited in Wetzels et al. 2011).

Additional analysis indicated a baseline (pre-test) control RT difference whereby participants showed shorter pre-test control RT latencies in the CF versus the NF session (mean difference = -18.10 ms, $p = .016$, $d = 0.41$). No other significant between session comparisons were apparent ($p > .100$ in all cases). As such, follow-up analyses were performed to explore whether any of the lifestyle factors differed between testing days, and thus might have contributed to the pre-test RT difference between sessions. Indeed, approximate hours of sleep (mean difference = +0.07 hrs; $F(1, 2108) = 5.16$, $p = .023$, $d = 0.06$) and approximate caffeine intake (mean difference = +15.10 mg; $F(1, 2108) = 101.59$, $p < .001$, $d = 0.16$) were both significantly greater prior to the CF session compared to the NF session, although the size of each effect was small.

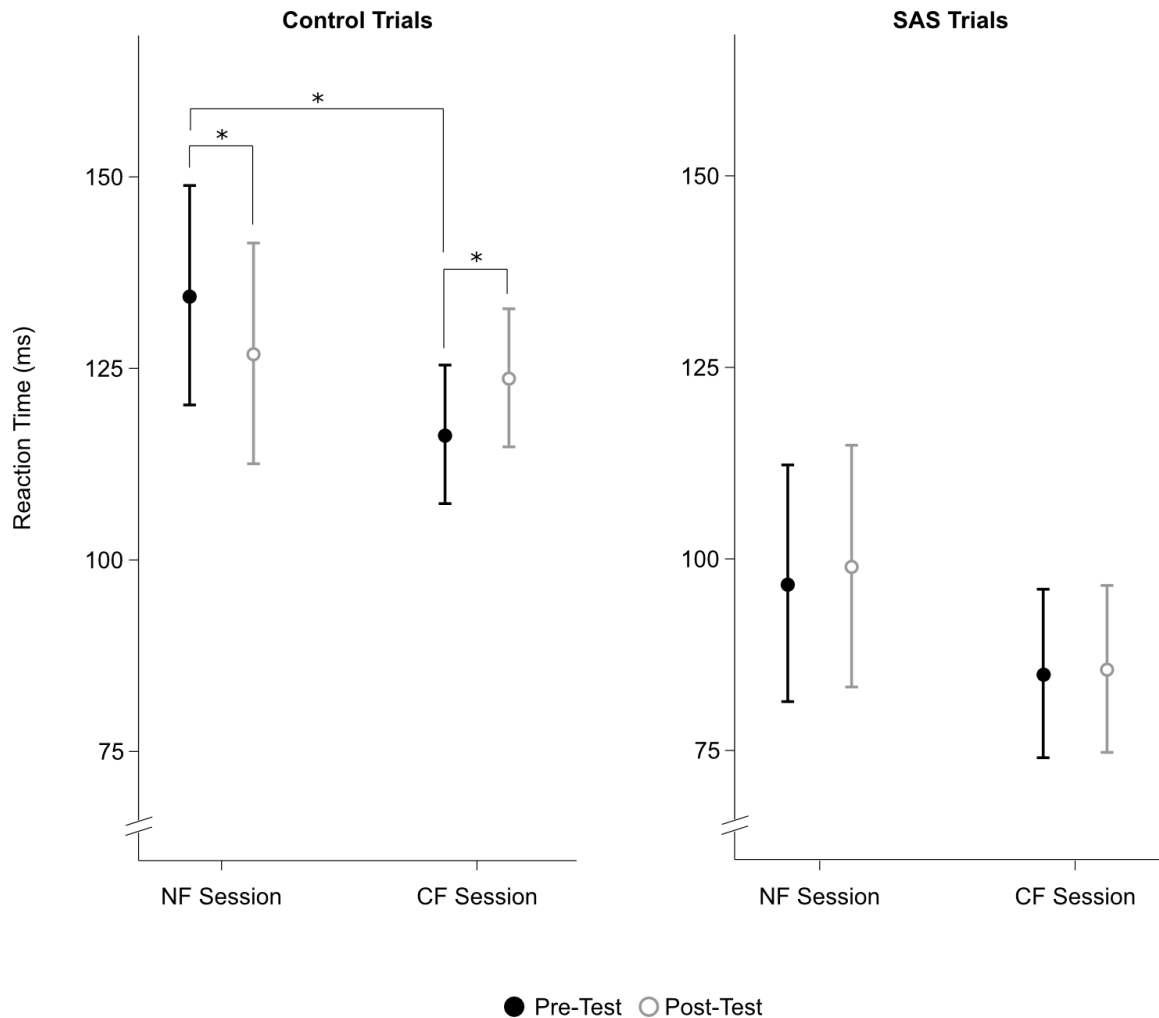


Fig. 2.3 Estimated marginal mean premotor reaction time. Control (left) and SAS (right) trial premotor reaction time (ms) is presented as a function of session type (NF, CF) and testing time (pre-test, post-test). Error bars indicate 95% confidence intervals. Asterisks indicate significant comparisons ($p < .05$). CF = cognitive fatigue, NF = non-fatiguing, SAS = startling acoustic stimulus.

2.8.4 Proportion of SAS Trials Resulting in a Startle

Analysis of the proportion of startle responses in SAS trials as a function of session type (NF, CF) and assessment time (pre-test, post-test) demonstrated no significant main effects of session type (mean proportion difference = 0.01, $F(1, 45) = 0.848$, $p = .362$) or assessment time (mean

proportion difference = 0.036, $F(1, 45) = 1.930$, $p = .172$) on the proportion of startle responses in SAS trials (mean proportion NF session: pre-test = 0.679 (95% CI [0.458, 0.901]), post-test = 0.581 (95% CI [0.360, 0.803])); mean proportion CF session: pre-test = 0.627 (95% CI [0.406, 0.849]), post-test = 0.653 (95% CI [0.432, 0.875])). Additionally, analyses demonstrated no significant session type x assessment time interaction ($F(1, 45) = 2.704$, $p = .107$).

2.9 Discussion

Cognitive fatigue has been shown to result in slowed simple RT (Ferreira Junior et al., 2020; Jaydari Fard et al., 2019; Langner, Steinborn, et al., 2010; Langner, Willmes, et al., 2010; Lisper et al., 1977; M. R. Smith et al., 2019). However, the mechanism underlying this effect has not yet been established. This study aimed to determine whether CF acts to slow simple RT through a reduction in the level of advance motor preparation. Participants attended two separate testing sessions: a CF task session, and a NF task session. Subjective levels of CF, as well as RT latency on control and SAS trials were assessed before and after each intervention. Inducement of CF was confirmed by declines in performance over the last half of the cognitive task and by increases in subjective CF levels (Fig. 2.2). Motor preparation level was inferred using the StartReact effect, that is, the RT latency and proportion of startle reflex responses observed on simple RT task SAS trials. In line with previous studies, cognitive task completion was associated with increases in control trial RT (Fig. 2.3). However, StartReact trials did not show a similar pre- to post-test change in SAS RT (Fig. 2.3), nor any difference in the proportion of startle reflex responses elicited. Overall, results of this study indicate that CF does not meaningfully impact motor preparation level; instead, slowed RT due to CF may be attributable to other stages of sensorimotor processing, such as stimulus perception and / or response initiation.

This study employed both subjective (VAS ratings) and objective (cognitive task performance) metrics to confirm that the CF intervention was successful in eliciting CF. There is ongoing debate around which of these measures represents the most accurate method of CF assessment. Some consider changes in objective performance metrics, such as response time and error rates in a cognitive task, to be the most relevant measure (Bryant et al., 2004; Holtzer et al., 2010). Others propose that subjective reports provide an adequate assessment of CF (M. R. Smith et al., 2019), with suggestions that subjective sensations of fatigue may precede changes in cognitive task performance (Kanfer, 2011; Kurzban et al., 2013). Overall, there is little data strongly linking subjective and objective (performance) measures of fatigue (Christodoulou, 2005; Kanfer, 2011). Here, a consideration of both types of measures was used to confirm the presence of CF in most participants following the CF intervention. Subjective levels of CF measured using the VAS increased significantly following completion of the CF task but remained stable following the NF task (Fig. 2.2), indicating that the CF intervention produced significant sensations of fatigue among participants. In addition, assessment of performance changes (math and memory task performance) over the last half of the CF task indicated that most participants were increasingly unable to maintain cognitive performance as the time-on-task progressed. Although a significant overall decline in task performance was observed, 20% of participants did not reflect this trend, instead showing signs of improved performance (i.e., positive regression slope) over the last half of the CF task. This “resistance” to CF has been observed in other studies, which have reported similarly sized subsets of non-fatigued respondents (Breckel et al., 2013; Qi et al., 2020), with some suggesting that intraindividual variation in cognitive fatigability may have a genetic basis (Lim et al., 2012; Parasuraman, 2009).

In this study, CF was associated with significant increases in control RT following cognitive task completion, supporting what has been demonstrated in previous works (Ferreira Junior et al., 2020; Jaydari Fard et al., 2019; Langner, Steinborn, et al., 2010; Langner, Willmes, et al., 2010; Lisper et al., 1977; M. R. Smith et al., 2019). Contrastingly, in the NF task, control RT *decreased* significantly from pre- to post-test (Fig. 2.3). Although the reason for this is uncertain, one potential explanation is that the NF task, watching a documentary film, was directly implicated in improving RT performance. While no significant changes in subjective mood states (indicated by the VAS) were observed following NF task completion, documentary film viewing could have led to heightened positive affect, which has been associated with faster RT (Irrmischer et al., 2018). However, another possible explanation lies in potential practice effects, which are known to occur in simple RT tasks (Ando et al., 2002; Del Rossi et al., 2014). If practice effects do indeed underlie RT performance improvements over the NF session, they may also have acted to moderate the magnitude of RT slowing following the CF intervention, resulting in a relatively small RT increase (7.30 ms) compared to reports by previous works (approximate mean range of 20-30 ms; Jaydari Fard et al., 2019; Langner, Steinborn, et al., 2010; Lim et al., 2010). Furthermore, if pre- to post-test control trial RT differences are affected by practice, the lack of such temporal changes in SAS trial RT would indicate that practice does not result in higher levels of motor preparation. Instead, practice may be associated with enhanced stimulus detection, a possibility that is supported by the sensitivity of auditory perception to both between and within session practice effects (Atienza et al., 2002; de Souza et al., 2013), with steep improvements observed within 8 minutes of performing an auditory perceptual task (Molloy et al., 2012). A more direct assessment of the role of practice effects in the current experimental paradigm, particularly with respect to temporal changes in stimulus perception,

would be required to confirm this possibility. Finally, in addition to potential practice effects, the SAS may also have counteracted the effects of CF on control RT, perhaps by elevating levels of arousal or alertness. While outside the scope of the current study, a direct assessment of this possibility in a separate experimental paradigm may be informative.

An additional unexpected control RT difference was observed between NF and CF session pre-tests, with faster control RT occurring prior to the CF session (Fig. 2.3). While SAS trial pre-test RT did not vary significantly between the sessions, these trials nevertheless demonstrated a similar trend (-11.80 ms in the CF session pre-test), which may be indicative of higher levels of pre-test preparatory activation on the day of the CF session. Although the reasons underlying this baseline RT difference are uncertain, a potential contribution to this difference involves several of the “lifestyle” factors known to influence RT, which varied significantly, albeit moderately, between testing days. Indeed, as observed in the current study, shorter simple RT has been shown to correlate with greater amounts of sleep, varying with natural within-individual fluctuations in sleep time (Knufinke et al., 2018) and with sleep deprivation manipulations (Jewett et al., 1999). Similarly, there is much evidence supporting the RT-speeding effect of caffeine intake, wherein greater intake is associated with significantly faster RT responses. This was also the case in the current study, wherein greater caffeine intake (mg) was recorded prior to the CF session, compared to the NF session (McLellan et al., 2016; Rogers et al., 2013). While the current study demonstrated only a small magnitude difference in these lifestyle measures between testing days, they may have contributed, perhaps in conjunction with other unknown factors, to the observed between-session baseline RT difference.

Although lifestyle factors may have influenced between-session RT differences, the current study was primarily interested in within session (pre- to post-test) changes in RT, to

assess possible changes in advance motor preparation following CF inducement. While control RT increased following cognitive task completion, no significant changes in the StartReact effect were detected following the NF or CF tasks. That is, no significant pre- to post-test differences were observed in the RT on SAS trials, nor in the proportion of SAS trials demonstrating a startle reflex response for either intervention. These results indicate that in the current study, motor preparation is not substantially influenced by CF, and that motor preparation changes are unlikely to explain why CF is associated with increases in control RT. While it is acknowledged that the results presented here cannot conclusively demonstrate an absence of SAS RT changes associated with CF, they demonstrate substantial evidence in favour of the null hypothesis ($BF_{10} = 0.119 \pm 1.24\%$). This conclusion is affirmed by several studies that have demonstrated significantly longer SAS trial RT conditions where the ability to prepare the response is impaired (e.g., Begeman et al., 2007; Carlsen et al., 2004a; Maslovat et al., 2015; V. Smith et al., 2019). The observed lack of preparatory changes in response to CF is also in line with research exploring cortical activity changes that occur over sustained task performance. These studies have determined that activity in the premotor cortex (PMC), an area integral for movement preparation (Passingham, 1988), does not decline alongside RT with increasing time-on-task (Derosiere et al., 2015). In fact, there is some indication that activity in the PMC actually *increases* along with rising levels of CF, potentially as a compensatory mechanism to maintain sensorimotor task performance under CF (Chuang et al., 2018). Corticospinal activity, considered to be associated with preparation level, has also been shown to increase with time-on-task, even while reaction time slowed (Derosiere et al., 2015). Behaviourally, an absence of preparatory changes has likewise been demonstrated in the variable foreperiod effect, wherein foreperiod length is associated with RT changes that are thought to reflect preparation level.

Langner, Steinborn, et al. (2010) assessed the variable foreperiod effect over time in a sustained simple RT task, showing that while both RT and subjective reports of mental fatigue increased, temporal preparation remained consistent.

The studies described above, along with the results presented here, support the absence of motor preparation decrements under CF, and instead point towards other explanations for the increased RT that is associated with CF. As previously stated, simple RT tasks have been conceptualized as including several information processing stages, such as advance motor preparation, stimulus detection, and response initiation (Donders, 1969; Spijkers & Walter, 1985; Taylor, 1976). If motor preparation is not substantially affected by CF, impaired stimulus detection and / or response initiation processes could underlie increased RT in CF. As of yet, it is unclear which of these remaining processes may drive the effects of CF on simple RT; however, existing evidence lends support to the role of impaired stimulus detection processes. For instance, there are indications that visual perceptual certainty (i.e., confidence in stimulus assessment; Wylie et al., 2021) and sensitivity (Langner et al., 2011) are negatively associated with CF, along with reports of CF-associated declines in pre-attentive auditory perceptual discrimination (Yang et al., 2013), speech perception in noise (Jain & Nataraja, 2019), and temporal order discrimination of auditory stimuli (Simon et al., 2020). Overall, although it seems that stimulus detection processes may present the most likely source of CF induced RT increases, further exploration is required to confirm this, and to determine whether response initiation processes also play a role in this effect.

2.10 Conclusion

This study examined whether CF results in impaired motor preparation in a simple RT task. A challenging, prolonged cognitive task successfully induced CF, as indicated by declines in

cognitive task performance and subjective reports of fatigue. While CF task performance led to increases in RT on non-startle trials, no substantial change in the StartReact effect (indicated by the RT latency on SAS trials and the proportion of startle responses elicited) was observed following CF task completion. The results of this study indicate that motor preparation is not a significant source of slowed RT observed in CF. As such, future studies should assess the impact of CF on other stages of simple RT, including stimulus detection and response initiation. An improved understanding of the mechanism by which CF acts to slow RT could allow the development of future interventions to counteract these effects, with particularly important implications for situations where fast RT is necessary, but CF is unavoidable.

2.11 References

- Ackerman, P. L. (2011). 100 years without resting. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 11–43). American Psychological Association. <https://doi.org/10.1037/12343-001>
- Ando, S., Kida, N., & Oda, S. (2002). Practice effects on reaction time for peripheral and central visual fields. *Perceptual and Motor Skills*, 95(3), 747–751. <https://doi.org/10.2466/pms.2002.95.3.747>
- Atienza, M., Cantero, J. L., & Dominguez-Marin, E. (2002). The Time Course of Neural Changes Underlying Auditory Perceptual Learning. *Learning & Memory*, 9(3), 138–150. <https://doi.org/10.1101/lm.46502>
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, 67, 1–48. <https://doi.org/10.18637/jss.v067.i01>
- Begeman, M., Kumru, H., Leenders, K., & Valls-Sole, J. (2007). Unilateral reaction time task is delayed during contralateral movements. *Experimental Brain Research*, 181(3), 469–475. <https://doi.org/10.1007/s00221-007-0944-x>
- Behrens, M., Mau-Moeller, A., Lischke, A., Katlun, F., Gube, M., Zschorlich, V., Skripitz, R., & Weippert, M. (2018). Mental Fatigue Increases Gait Variability During Dual-task Walking in Old Adults. *The Journals of Gerontology: Series A*, 73(6), 792–797. <https://doi.org/10.1093/gerona/glx210>
- Blumenthal, T. D., Cuthbert, B. N., Filion, D. L., Hackley, S., Lipp, O. V., & Van Boxtel, A. (2005). Committee report: Guidelines for human startle eyeblink electromyographic studies. *Psychophysiology*, 42(1), 1–15. <https://doi.org/10.1111/j.1469-8986.2005.00271.x>
- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2005). Effects of mental fatigue on attention: An ERP study. *Cognitive Brain Research*, 25(1), 107–116. <https://doi.org/10.1016/j.cogbrainres.2005.04.011>
- Boksem, M. A. S., & Tops, M. (2008). Mental fatigue: Costs and benefits. *Brain Research Reviews*, 59(1), 125–139. <https://doi.org/10.1016/j.brainresrev.2008.07.001>
- Breckel, T. P. K., Thiel, C. M., Bullmore, E. T., Zalesky, A., Patel, A. X., & Giessing, C. (2013). Long-Term Effects of Attentional Performance on Functional Brain Network Topology. *PLOS ONE*, 8(9), e74125. <https://doi.org/10.1371/journal.pone.0074125>
- Bryant, D., Chiaravalloti, N., & Deluca, J. (2004). Objective Measurement of Cognitive Fatigue in Multiple Sclerosis. *Rehabilitation Psychology*, 49(2), 114–122. <https://doi.org/10.1037/0090-5550.49.2.114>

- Brysbaert, M., & Stevens, M. (2018). Power Analysis and Effect Size in Mixed Effects Models: A Tutorial. *Journal of Cognition*, 1(1), 9. <https://doi.org/10.5334/joc.10>
- Carlsen, A. N., Chua, R., Inglis, J. T., Sanderson, D. J., & Franks, I. M. (2004a). Can prepared responses be stored subcortically? *Experimental Brain Research*, 159(3), 301–309. <https://doi.org/10.1007/s00221-004-1924-z>
- Carlsen, A. N., Chua, R., Inglis, J. T., Sanderson, D. J., & Franks, I. M. (2004b). Prepared Movements Are Elicited Early by Startle. *Journal of Motor Behavior*, 36(3), 253–264. <https://doi.org/10.3200/JMBR.36.3.253-264>
- Carlsen, A. N., Dakin, C. J., Chua, R., & Franks, I. M. (2007). Startle produces early response latencies that are distinct from stimulus intensity effects. *Experimental Brain Research*, 176(2), 199–205. <https://doi.org/10.1007/s00221-006-0610-8>
- Carlsen, A. N., & Maslovat, D. (2019). Startle and the StartReact Effect: Physiological Mechanisms. *Journal of Clinical Neurophysiology*, 36(6), 452–459. <https://doi.org/10.1097/WNP.0000000000000582>
- Carlsen, A. N., Maslovat, D., Lam, M. Y., Chua, R., & Franks, I. M. (2011). Considerations for the use of a startling acoustic stimulus in studies of motor preparation in humans. *Neuroscience & Biobehavioral Reviews*, 35(3), 366–376. <https://doi.org/10.1016/j.neubiorev.2010.04.009>
- Chaudhuri, A., & Behan, P. O. (2004). Fatigue in neurological disorders. *The Lancet*, 363(9413), 978–988. [https://doi.org/10.1016/S0140-6736\(04\)15794-2](https://doi.org/10.1016/S0140-6736(04)15794-2)
- Christodoulou, C. (2005). The Assessment and Measurement of Fatigue. In J. DeLuca (Ed.), *Fatigue as a Window to the Brain* (pp. 19–35). MIT Press.
- Chuang, C.-H., Cao, Z., King, J.-T., Wu, B.-S., Wang, Y.-K., & Lin, C.-T. (2018). Brain Electrodynamical and Hemodynamic Signatures Against Fatigue During Driving. *Frontiers in Neuroscience*, 12, 181. <https://doi.org/10.3389/fnins.2018.00181>
- Csathó, Á., van der Linden, D., Hernádi, I., Buzás, P., & Kalmár, G. (2012). Effects of mental fatigue on the capacity limits of visual attention. *Journal of Cognitive Psychology*, 24(5), 511–524. <https://doi.org/10.1080/20445911.2012.658039>
- de Souza, A. C. S., Yehia, H. C., Sato, M., & Callan, D. (2013). Brain activity underlying auditory perceptual learning during short period training: Simultaneous fMRI and EEG recording. *BMC Neuroscience*, 14(1), 8. <https://doi.org/10.1186/1471-2202-14-8>
- Del Rossi, G., Malaguti, A., & Del Rossi, S. (2014). Practice Effects Associated With Repeated Assessment of a Clinical Test of Reaction Time. *Journal of Athletic Training*, 49(3), 356–359. <https://doi.org/10.4085/1062-6059-49.2.04>
- DeLuca, J. (2005). Fatigue: Its Definition, Its Study, and Its Future. In J. DeLuca (Ed.), *Fatigue as a Window to the Brain* (pp. 319–325). The MIT Press.

- Derosiere, G., Billot, M., Ward, E. T., & Perrey, S. (2015). Adaptations of Motor Neural Structures' Activity to Lapses in Attention. *Cerebral Cortex*, 25(1), 66–74. <https://doi.org/10.1093/cercor/bht206>
- Donders, F. C. (1969). On the speed of mental processes. *Acta Psychologica*, 30, 412–431. [https://doi.org/10.1016/0001-6918\(69\)90065-1](https://doi.org/10.1016/0001-6918(69)90065-1)
- Faber, L. G., Maurits, N. M., & Lorist, M. M. (2012). Mental Fatigue Affects Visual Selective Attention. *PLOS ONE*, 7(10), e48073. <https://doi.org/10.1371/journal.pone.0048073>
- Ferreira Junior, A., Chierotti, P., Gabardo, J. M., Giovanini, B., Okano, A. H., Buzzachera, C. F., Okazaki, V. H. A., Okuno, N. M., & Altimari, L. R. (2020). Residual Effects of Mental Fatigue on Subjective Fatigue, Reaction Time and Cardiac Responses. *Rev de Psicol Del Deporte (J Sport Psychol)*, 29(2), 27–34.
- Gergelyfi, M., Jacob, B., Olivier, E., & Zénon, A. (2015). Dissociation between mental fatigue and motivational state during prolonged mental activity. *Frontiers in Behavioral Neuroscience*, 9, 176. <https://doi.org/10.3389/fnbeh.2015.00176>
- Grobe, S., Kakar, R. S., Smith, M. L., Mehta, R., Baghurst, T., & Boolani, A. (2017). Impact of cognitive fatigue on gait and sway among older adults: A literature review. *Preventive Medicine Reports*, 6, 88–93. <https://doi.org/10.1016/j.pmedr.2017.02.016>
- Guo, Z., Chen, R., Liu, X., Zhao, G., Zheng, Y., Gong, M., & Zhang, J. (2018). The impairing effects of mental fatigue on response inhibition: An ERP study. *PLOS ONE*, 13(6), e0198206. <https://doi.org/10.1371/journal.pone.0198206>
- Guo, Z., Chen, R., Zhang, K., Pan, Y., & Wu, J. (2016). The Impairing Effect of Mental Fatigue on Visual Sustained Attention under Monotonous Multi-Object Visual Attention Task in Long Durations: An Event-Related Potential Based Study. *PLOS ONE*, 11(9), e0163360. <https://doi.org/10.1371/journal.pone.0163360>
- Herlambang, M. B., Cnossen, F., & Taatgen, N. A. (2021). The effects of intrinsic motivation on mental fatigue. *PLOS ONE*, 16(1), e0243754. <https://doi.org/10.1371/journal.pone.0243754>
- Herlambang, M. B., Taatgen, N. A., & Cnossen, F. (2019). The Role of Motivation as a Factor in Mental Fatigue. *Human Factors*, 61(7), 1171–1185. <https://doi.org/10.1177/0018720819828569>
- 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*. (pp. 167–187). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-008>
- Hodges, P. W., & Bui, B. H. (1996). A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography.

- Electroencephalography and Clinical Neurophysiology*, 101(6), 511–519.
[https://doi.org/10.1016/S0921-884X\(96\)95190-5](https://doi.org/10.1016/S0921-884X(96)95190-5)
- Holtzer, R., Shuman, M., Mahoney, J. R., Lipton, R., & Verghese, J. (2010). Cognitive Fatigue Defined in the Context of Attention Networks. *Aging, Neuropsychology, and Cognition*, 18(1), 108–128. <https://doi.org/10.1080/13825585.2010.517826>
- Irmischer, M., Wal, C. N. van der, Mansvelder, H. D., & Linkenkaer-Hansen, K. (2018). Negative mood and mind wandering increase long-range temporal correlations in attention fluctuations. *PLOS ONE*, 13(5), e0196907.
<https://doi.org/10.1371/journal.pone.0196907>
- Jacquet, T., Poulin-Charronnat, B., Bard, P., & Lepers, R. (2021). Persistence of Mental Fatigue on Motor Control. *Frontiers in Psychology*, 11, 3679.
<https://doi.org/10.3389/fpsyg.2020.588253>
- Jahanpour, E. S., Berberian, B., Imbert, J.-P., & Roy, R. N. (2020). Cognitive fatigue assessment in operational settings: A review and UAS implications. *IFAC-PapersOnLine, 3rd IFAC Workshop on Cyber-Physical & Human Systems CPHS 2020*, 53(5), 330–337.
<https://doi.org/10.1016/j.ifacol.2021.04.188>
- Jain, S., & Nataraja, N. P. (2019). The Effect of Fatigue on Working Memory and Auditory Perceptual Abilities in Trained Musicians. *American Journal of Audiology*, 28(2S), 483–494. https://doi.org/10.1044/2019_AJA-IND50-18-0102
- Jaydari Fard, S., Tahmasebi Boroujeni, S., & Lavender, A. P. (2019). Mental fatigue impairs simple reaction time in non-athletes more than athletes. *Fatigue: Biomedicine, Health & Behavior*, 7(3), 117–126. <https://doi.org/10.1080/21641846.2019.1632614>
- Jewett, M. E., Dijk, D.-J., Kronauer, R. E., & Dinges, D. F. (1999). Dose-response Relationship Between Sleep Duration and Human Psychomotor Vigilance and Subjective Alertness. *Sleep*, 22(2), 171–179. <https://doi.org/10.1093/sleep/22.2.171>
- Johansson, B., Berglund, P., & Rönnbäck, L. (2009). Mental fatigue and impaired information processing after mild and moderate traumatic brain injury. *Brain Injury*, 23(13–14), 1027–1040. <https://doi.org/10.3109/02699050903421099>
- Kanfer, R. (2011). Determinants and consequences of subjective cognitive fatigue. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 189–207). American Psychological Association.
<https://doi.org/http://dx.doi.org.proxy.bib.uottawa.ca/10.1037/12343-009>
- Kato, Y., Endo, H., & Kizuka, T. (2009). Mental fatigue and impaired response processes: Event-related brain potentials in a Go/NoGo task. *International Journal of Psychophysiology*, 72(2), 204–211. <https://doi.org/10.1016/j.ijpsycho.2008.12.008>

- Klapp, S. T., & Maslovat, D. (2020). Programming of action timing cannot be completed until immediately prior to initiation of the response to be controlled. *Psychonomic Bulletin & Review*, 27(5), 821–832. <https://doi.org/10.3758/s13423-020-01740-9>
- Knufinke, M., Nieuwenhuys, A., Maase, K., Moen, M. H., Geurts, S. A. E., Coenen, A. M. L., & Kompier, M. A. J. (2018). Effects of Natural Between-Days Variation in Sleep on Elite Athletes' Psychomotor Vigilance and Sport-Specific Measures of Performance. *Journal of Sports Science & Medicine*, 17(4), 515–524.
- Kurzban, R., Duckworth, A., Kable, J. W., & Myers, J. (2013). An opportunity cost model of subjective effort and task performance. *The Behavioral and Brain Sciences*, 36(6), 10.1017/S0140525X12003196. <https://doi.org/10.1017/S0140525X12003196>
- Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, 82, 1–26. <https://doi.org/10.18637/jss.v082.i13>
- Langner, R., Eickhoff, S. B., & Steinborn, M. B. (2011). Mental Fatigue Modulates Dynamic Adaptation to Perceptual Demand in Speeded Detection. *PLOS ONE*, 6(12), e28399. <https://doi.org/10.1371/journal.pone.0028399>
- Langner, R., Steinborn, M. B., Chatterjee, A., Sturm, W., & Willmes, K. (2010). Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychologica*, 133(1), 64–72. <https://doi.org/10.1016/j.actpsy.2009.10.001>
- Langner, R., Willmes, K., Chatterjee, A., Eickhoff, S. B., & Sturm, W. (2010). Energetic effects of stimulus intensity on prolonged simple reaction-time performance. *Psychological Research*, 74(5), 499–512. <https://doi.org/10.1007/s00426-010-0275-6>
- Leavitt, V. M., & DeLuca, J. (2010). Central Fatigue: Issues Related to Cognition, Mood and Behavior, and Psychiatric Diagnoses. *PM&R*, 2(5), 332–337. <https://doi.org/10.1016/j.pmrj.2010.03.027>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835. <https://doi.org/10.1016/j.autcon.2019.102835>
- Lim, J., Ebstein, R., Tse, C.-Y., Monakhov, M., Lai, P. S., Dinges, D. F., & Kwok, K. (2012). Dopaminergic Polymorphisms Associated with Time-on-Task Declines and Fatigue in the Psychomotor Vigilance Test. *PLOS ONE*, 7(3), e33767. <https://doi.org/10.1371/journal.pone.0033767>

- Lim, J., Wu, W., Wang, J., Detre, J. A., Dinges, D. F., & Rao, H. (2010). Imaging brain fatigue from sustained mental workload: An ASL perfusion study of the time-on-task effect. *NeuroImage*, 49(4), 3426–3435. <https://doi.org/10.1016/j.neuroimage.2009.11.020>
- Linnhoff, S., Fiene, M., Heinze, H.-J., & Zaehle, T. (2019). Cognitive Fatigue in Multiple Sclerosis: An Objective Approach to Diagnosis and Treatment by Transcranial Electrical Stimulation. *Brain Sciences*, 9(5), 100. <https://doi.org/10.3390/brainsci9050100>
- Lisper, H.-O., Melin, L., Sjöden, P.-O., & Fagerström, K.-O. (1977). Temporal uncertainty of auditory signals in a monitoring task: Effects of inter-signal interval length and regularity on increase in reaction time. *Acta Psychologica*, 41(2), 183–190. [https://doi.org/10.1016/0001-6918\(77\)90034-8](https://doi.org/10.1016/0001-6918(77)90034-8)
- Lorist, M. M., Boksem, M. A. S., & Ridderinkhof, K. R. (2005). Impaired cognitive control and reduced cingulate activity during mental fatigue. *Cognitive Brain Research*, 24(2), 199–205. <https://doi.org/10.1016/j.cogbrainres.2005.01.018>
- Lorist, M. M., & Faber, L. G. (2011). Consideration of the influence of mental fatigue on controlled and automatic cognitive processes and related neuromodulatory effects. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 105–126). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-005>
- Lorist, M. M., Klein, M., Nieuwenhuis, S., de Jong, R., Mulder, G., & Meijman, T. F. (2000). Mental fatigue and task control: Planning and preparation. *Psychophysiology*, 37(5), 614–625. <https://doi.org/10.1111/1469-8986.3750614>
- Lou, J.-S. (2009). Physical and Mental Fatigue in Parkinson's Disease. *Drugs & Aging*, 26(3), 195–208. <https://doi.org/10.2165/00002512-200926030-00002>
- Mackworth, N. H. (1948). The Breakdown of Vigilance during Prolonged Visual Search. *Quarterly Journal of Experimental Psychology*, 1(1), 6–21. <https://doi.org/10.1080/17470214808416738>
- Maslovat, D., Carlsen, A. N., & Franks, I. M. (2012). Subcortical motor circuit excitability during simple and choice reaction time. *Behavioral Neuroscience*, 126(3), 499–503. <https://doi.org/http://dx.doi.org/10.1037/a0028285>
- Maslovat, D., Drummond, N. M., Carter, M. J., & Carlsen, A. N. (2015). Reduced motor preparation during dual-task performance: Evidence from startle. *Experimental Brain Research*, 233(9), 2673–2683. <https://doi.org/10.1007/s00221-015-4340-7>
- Maslovat, D., Sadler, C. M., Smith, V., Bui, A., & Carlsen, A. N. (2021). Response triggering by an acoustic stimulus increases with stimulus intensity and is best predicted by startle reflex activation. *Scientific Reports*, 11(1), Article 1. <https://doi.org/10.1038/s41598-021-02825-8>

- Massar, S. A. A., Wester, A. E., Volkerts, E. R., & Kenemans, J. L. (2010). Manipulation specific effects of mental fatigue: Evidence from novelty processing and simulated driving. *Psychophysiology*, 47(6), 1119–1126. <https://doi.org/https://doi.org/10.1111/j.1469-8986.2010.01028.x>
- McLellan, T. M., Caldwell, J. A., & Lieberman, H. R. (2016). A review of caffeine's effects on cognitive, physical and occupational performance. *Neuroscience & Biobehavioral Reviews*, 71, 294–312. <https://doi.org/10.1016/j.neubiorev.2016.09.001>
- Molloy, K., Moore, D. R., Sohoglu, E., & Amitay, S. (2012). Less Is More: Latent Learning Is Maximized by Shorter Training Sessions in Auditory Perceptual Learning. *PLOS ONE*, 7(5), e36929. <https://doi.org/10.1371/journal.pone.0036929>
- Nicholson, K., Stewart, M., & Thind, A. (2015). Examining the symptom of fatigue in primary care: A comparative study using electronic medical records. *BMJ Health & Care Informatics*, 22(1). <https://doi.org/10.14236/jhi.v22i1.91>
- Okkes, I. M., Oskam, S. K., & Lamberts, H. (2002). The probability of specific diagnoses for patients presenting with common symptoms to Dutch Family Physicians. *Journal of Family Practice*, 51(1), 31–37.
- Pageaux, B., & Lepers, R. (2018). Chapter 16—The effects of mental fatigue on sport-related performance. In S. Marcora & M. Sarkar (Eds.), *Progress in Brain Research* (Vol. 240, pp. 291–315). Elsevier. <https://doi.org/10.1016/bs.pbr.2018.10.004>
- Parasuraman, R. (2009). Assaying individual differences in cognition with molecular genetics: Theory and application. *Theoretical Issues in Ergonomics Science*, 10(5), 399–416. <https://doi.org/10.1080/14639220903106403>
- Passingham, R. E. (1988). Premotor cortex and preparation for movement. *Experimental Brain Research*, 70(3), 590–596. <https://doi.org/10.1007/BF00247607>
- Pattyn, N., Neyt, X., Henderickx, D., & Soetens, E. (2008). Psychophysiological investigation of vigilance decrement: Boredom or cognitive fatigue? *Physiology & Behavior*, 93(1), 369–378. <https://doi.org/10.1016/j.physbeh.2007.09.016>
- Pearson, H. (Director). (2019). *The High Seas (TV Episode 2019)* [Video recording]. Netflix. <http://www.imdb.com/title/tt9253878/fullcredits>
- Petrut, B., Berindan-Neagoe, I., Feflea, D. I., Hoge, M., Pasca, S., Bujoreanu, C. E., & Bschleipfer, T. (2020). Mental Fatigue Evaluation of Surgical Teams during a Regular Workday in a High-Volume Tertiary Healthcare Center. *Urologia Internationalis*, 104(3–4), 301–308. <https://doi.org/10.1159/000504988>
- 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. <https://doi.org/10.1016/j.trf.2015.01.003>

- Plukaard, S., Huizinga, M., Krabbendam, L., & Jolles, J. (2015). Cognitive flexibility in healthy students is affected by fatigue: An experimental study. *Learning and Individual Differences*, 38, 18–25. <https://doi.org/10.1016/j.lindif.2015.01.003>
- Qi, P., Hu, H., Zhu, L., Gao, L., Yuan, J., Thakor, N., Bezerianos, A., & Sun, Y. (2020). EEG Functional Connectivity Predicts Individual Behavioural Impairment During Mental Fatigue. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, 28(9), 2080–2089. <https://doi.org/10.1109/TNSRE.2020.3007324>
- R Core Team. (2021). *R: A language and environment for statistical computing*. [Computer software]. R Foundation for Statistical Computing. <https://www.R-project.org/>
- Reeve, B., Stover, A., Alfano, C., Smith, A., Ballard-Barbash, R., Bernstein, L., McTiernan, A., Baumgartner, K., & Piper, B. (2012). The Piper Fatigue Scale-12 (PFS-12): Psychometric findings and item reduction in a cohort of breast cancer survivors. *Breast Cancer Research and Treatment*, 136(1). <https://doi.org/10.1007/s10549-012-2212-4>
- Rogers, P. J., Heatherley, S. V., Mullings, E. L., & Smith, J. E. (2013). Faster but not smarter: Effects of caffeine and caffeine withdrawal on alertness and performance. *Psychopharmacology*, 226(2), 229–240. <https://doi.org/10.1007/s00213-012-2889-4>
- Simon, J., Takács, E., Orosz, G., Berki, B., & Winkler, I. (2020). Short-term cognitive fatigue effect on auditory temporal order judgments. *Experimental Brain Research*, 238(2), 305–319. <https://doi.org/10.1007/s00221-019-05712-x>
- Smith, A. (2011). From the brain to the workplace: Studies of cognitive fatigue in the laboratory and aboard ship. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 291–305). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-014>
- Smith, M. R., Chai, R., Nguyen, H. T., Marcora, S. M., & Coutts, A. J. (2019). Comparing the Effects of Three Cognitive Tasks on Indicators of Mental Fatigue. *The Journal of Psychology*, 153(8), 759–783. <https://doi.org/10.1080/00223980.2019.1611530>
- Smith, V., Maslovat, D., Drummond, N. M., & Carlsen, A. N. (2019). A Timeline of Motor Preparatory State Prior to Response Initiation: Evidence from Startle. *Neuroscience*, 397, 80–93. <https://doi.org/10.1016/j.neuroscience.2018.11.020>
- Spijkers, W. A. C., & Walter, A. (1985). Response processing stages in choice reactions. *Acta Psychologica*, 58(2), 191–204. [https://doi.org/10.1016/0001-6918\(85\)90007-1](https://doi.org/10.1016/0001-6918(85)90007-1)
- Stark, M. (Director). (2019). *Fresh Water (TV Episode 2019)* [Video recording]. Netflix. <http://www.imdb.com/title/tt9253880/fullcredits>
- Tanaka, M., & Watanabe, Y. (2012). Supraspinal regulation of physical fatigue. *Neuroscience & Biobehavioral Reviews*, 36(1), 727–734. <https://doi.org/10.1016/j.neubiorev.2011.10.004>

- Taylor, D. A. (1976). Stage analysis of reaction time. *Psychological Bulletin*, 83(2), 161–191. <https://doi.org/http://dx.doi.org.proxy.bib.uottawa.ca/10.1037/0033-2909.83.2.161>
- Valls-Solé, J., Rothwell, J. C., Goulart, F., Cossu, G., & Muñoz, E. (1999). Patterned ballistic movements triggered by a startle in healthy humans. *The Journal of Physiology*, 516(3), 931–938. <https://doi.org/https://doi.org/10.1111/j.1469-7793.1999.0931u.x>
- Valls-Solé, J., Solé, A., Valldeoriola, F., Muñoz, E., Gonzalez, L. E., & Tolosa, E. S. (1995). Reaction time and acoustic startle in normal human subjects. *Neuroscience Letters*, 195(2), 97–100. [https://doi.org/10.1016/0304-3940\(94\)11790-P](https://doi.org/10.1016/0304-3940(94)11790-P)
- Van Cutsem, J., Marcora, S., De Pauw, K., Bailey, S., Meeusen, R., & Roelands, B. (2017). The Effects of Mental Fatigue on Physical Performance: A Systematic Review. *Sports Medicine*, 47(8), 1569–1588. <https://doi.org/10.1007/s40279-016-0672-0>
- van der Linden, D., & Eling, P. (2006). Mental fatigue disturbs local processing more than global processing. *Psychological Research*, 70(5), 395–402. <https://doi.org/10.1007/s00426-005-0228-7>
- van der Linden, D., Frese, M., & Meijman, T. F. (2003). Mental fatigue and the control of cognitive processes: Effects on perseveration and planning. *Acta Psychologica*, 113(1), 45–65. [https://doi.org/10.1016/S0001-6918\(02\)00150-6](https://doi.org/10.1016/S0001-6918(02)00150-6)
- Wise, J. M., Heaton, K., & Patrician, P. (2019). Fatigue in Long-Haul Truck Drivers: A Concept Analysis. *Workplace Health & Safety*, 67(2), 68–77. <https://doi.org/10.1177/2165079918800509>
- Wylie, G. R., Yao, B., Sandry, J., & DeLuca, J. (2021). Using Signal Detection Theory to Better Understand Cognitive Fatigue. *Frontiers in Psychology*, 11. <https://doi.org/10.3389/fpsyg.2020.579188>
- Yang, B., Xiao, W., Liu, X., Wu, S., & Miao, D. (2013). Mental fatigue impairs pre-attentive processing: A MMN study. *Neuroscience Letters*, 532, 12–16. <https://doi.org/10.1016/j.neulet.2012.08.080>
- Zeuwts, L. H. R. H., Iliano, E., Smith, M., Deconinck, F., & Lenoir, M. (2021). Mental fatigue delays visual search behaviour in young cyclists when negotiating complex traffic situations: A study in virtual reality. *Accident Analysis & Prevention*, 161, 106387. <https://doi.org/10.1016/j.aap.2021.106387>
- Zhao, C., Zhao, M., Liu, J., & Zheng, C. (2012). Electroencephalogram and electrocardiograph assessment of mental fatigue in a driving simulator. *Accident Analysis & Prevention*, 45, 83–90. <https://doi.org/10.1016/j.aap.2011.11.019>

Chapter 3. Experiment 2 - Visual Perceptual Processing is Unaffected by Cognitive Fatigue

A version of this chapter has been published: Peters, K. J., Maslovat, D., & Carlsen, A. N. (2024). Visual perceptual processing is unaffected by cognitive fatigue. *Consciousness and Cognition*, 119, 103666. <https://doi.org/10.1016/j.concog.2024.103666>

3.1 Abstract

Cognitive fatigue (CF) can lead to an increase in the latency of simple reaction time, although the processes involved in this delay are unknown. One potential explanation is that a longer time may be required for sensory processing of relevant stimuli. To investigate this possibility, the current study used a visual inspection time task to measure perceptual processing speed before and after a CF (Math-Memory) or non-fatiguing (documentary film) intervention. Subjective fatigue and simple reaction time significantly increased following the CF, but not the non-fatiguing intervention, confirming that CF was induced. Conversely, there was no effect of CF on inspection time task performance. It was therefore concluded that the speed of perceptual processing is not significantly impacted by CF, and thus is unlikely to underlie CF-related reaction time increases. Instead, increases in simple reaction time latency in CF may be due to delays in response preparation or initiation.

3.2 Introduction

Cognitive fatigue is a psychobiological state that develops gradually with sustained and demanding mental effort, leading to feelings of exhaustion and often an inability to continue to meet challenging cognitive task demands without performance reductions (Boksem & Tops, 2008; Borghini et al., 2014; Phillips, 2015). In healthy populations, cognitive fatigue (CF) is an acute phenomenon, often arising from day-to-day mentally demanding tasks; however, its consequences are multi-dimensional and complex. For instance, CF has been associated with

impaired working memory capacity (Jain & Nataraja, 2019), decision making (Gantois et al., 2020; A. Jia et al., 2022; H. Jia et al., 2022; Wiehler et al., 2022), physical endurance (Dallaway et al., 2022; Van Cutsem et al., 2017), and athletic performance (Cao et al., 2022; Habay et al., 2021; Smith et al., 2018; H. Sun et al., 2021), and it is thought to be a potential risk-factor in road and workplace accidents (Li et al., 2019; Petrut et al., 2020; Williamson et al., 2011; Wise et al., 2019; Zeuwts et al., 2021). Experimentally, CF is frequently characterized by subjective sensations of tiredness, which may be described as a feeling of energy depletion or even a negative shift in mood (O’Keeffe et al., 2020; Phillips, 2015; van der Linden & Eling, 2006). These subjective changes are often (although not always, see DeLuca, 2005) observed alongside mental performance reductions (Hopstaken et al., 2015; Kanfer, 2011). It has been suggested that the mental performance effects of CF are typically most apparent in tasks that place high demands on executive functioning, such as those that require inhibition of automatic or incorrect responses (Guo et al., 2018; Kato et al., 2009), error monitoring and correction (Boksem et al., 2006; Lorist et al., 2005), complex planning (Lorist et al., 2000; van der Linden et al., 2003), or adaptation to novel or evolving task demands (Massar et al., 2010; Plukaard et al., 2015). Meanwhile, performance on simpler tasks with minimal response variability should be more resilient to CF, as they are less affected by the degradation of executive control thought to underlie the behavioural consequences of CF (Boksem et al., 2005; Lorist & Faber, 2011; van der Linden et al., 2003). However, some exceptions to this rationale are apparent. For instance, some studies indicate that CF-related performance decrements may not increase with task complexity (e.g., Borragán et al., 2017; Hopstaken et al., 2015), while tasks thought to require only basic sensorimotor processing, such as tests of simple reaction time (RT), have been shown to be susceptible to the effects of CF. More specifically, simple RT, or the time required to respond to a

known stimulus with a predetermined response, has frequently been observed to be slowed in states of CF (Ferreira Junior et al., 2020; Jaydarifard et al., 2019; Kowalski et al., 2022; Langner, Steinborn, et al., 2010; Langner, Willmes, et al., 2010; Lim et al., 2010; Shen et al., 2019; Smith et al., 2019). Given the prevalence of cognitive fatigue and its multivarious effects, determining *how* exactly CF works to impair RT presents a valuable avenue of investigation.

To address this question, it is useful to consider the sensorimotor processes that are thought to contribute to RT. In a simple RT task, where the required response is held constant and is known in advance (unlike a choice RT task, where multiple stimuli and responses are possible), RT can be thought of in terms of several composite processes: i) response preparation, which can be performed in advance of the imperative (go) stimulus; ii) perceptual processing (i.e., detection and/or identification) of the imperative stimulus; and iii) initiation and execution of the predetermined response (Donders, 1969; Spijkers & Walter, 1985; Taylor, 1976). Although it is noted that this perspective may be an oversimplification (for example, see Henderson & Dittrich, 1998; Pachella, 1974), the impact of CF on simple RT has been well-documented, and the specific stage(s) of central processing (e.g., advance preparation, stimulus processing, or response initiation) that underlie these RT changes in CF are still uncertain. Previous work has begun to explore this uncertainty, demonstrating that the level of advance preparation in a simple RT task appears to be unaffected by CF (Peters et al., 2022). Thus, the locus of RT delays in CF may reside in a different component of sensorimotor processing, such as those required for stimulus perception.

There is indeed some evidence that the perceptual processing stage of RT may be impacted by CF. For instance, decreases in the amplitude of early event-related potentials (ERP, e.g., N1) elicited by both auditory and visual stimuli have been observed with fatiguing mental

workloads (Boksem et al., 2005; Faber et al., 2012; Ghani et al., 2020; Samuel et al., 2019; L. Sun et al., 2022). The amplitudes of these ERPs are thought to reflect neural activity in the early stages of sensory processing involved in discriminating and/or alerting and orienting to a relevant stimulus (Gonçalves et al., 2018; Hopf et al., 2002; Neuhaus et al., 2010; Sokhadze et al., 2017). If these early attentional processes are impaired by CF, they may lead to perceptual processing delays in recognizing the go-signal. However, it is unclear whether this electrophysiological evidence is in fact indicative of delayed sensory processing which could viably contribute to slowed RT in CF. While CF-related performance decrements have been observed in some auditory processing tasks, including tests of auditory temporal resolution and speech perception in noise (Jain et al., 2022; Jain & Nataraja, 2019; Simon et al., 2020), such tasks do not directly assess the speed of perceptual processing in CF, nor how this may contribute to slowed RT in CF. To directly test perceptual processing, a measure is needed which assesses only the sensory processing stages of simple RT independently from the motor stages of simple RT upon which CF may also act. The visual inspection time (IT) task is a perceptual processing measure that meets these requirements.

The visual IT task measures the amount of time required for a participant to accurately discriminate a visual stimulus (Irwin, 1984; Vickers & Smith, 1986). In this task, a “pi-figure,” with two vertical lines (or legs) that differ in length, is presented for a brief time interval. After each stimulus presentation, participants must attempt to accurately identify the side (left or right) of the longest leg. When the stimulus is presented for only a very short duration (e.g., 15 ms), response accuracy approaches chance performance. In this case, perceptual processing speed may not be fast enough to allow for sufficient accumulation of evidence regarding the correct response, necessitating an essentially random response selection (Vickers & Smith, 1986).

However, at increasingly longer stimulus durations, more time becomes available to process the stimulus, greater evidence is accumulated, and response accuracy improves (Vickers & Smith, 1986). It has been suggested that IT task performance relates to the speed at which sensory inputs are encoded during the initial stages of information processing, which may be influenced by attentiveness to the task – processes that would also affect the speed of stimulus perception in an RT paradigm (M. C. Fox et al., 2009; Hill et al., 2011; Jensen, 2006; Kranzler & Jensen, 1989; Nettelbeck, 2001). Importantly, because the IT task does not require participants to respond quickly (as in an RT task), IT task performance offers a measure of perceptual processing that is distinct from other components of a motor response (e.g., response preparation and initiation, speed-accuracy trade-offs) which may also be affected by CF (Gregory et al., 2008; Jensen, 2006).

As such, the present study employed an IT task to explore whether CF acts to delay visual perceptual processing, which may be contributing to the prolongation of simple RT that has been associated with CF. To induce CF, participants completed a sustained, cognitively demanding Math-Memory task. Changes in subjective fatigue levels and simple RT were used to confirm that participants were indeed fatigued by the intervention, while an IT task was used to probe the effect of CF on perceptual processing speed. If CF does lead to impaired perceptual processing, then IT task response accuracy was predicted to decline.

3.3 Materials and Methods

3.3.1 Participants

An a priori sample size calculation was performed based on the results detailed by Hill et al. (2011), who reported the effect size of a significant group (high IQ, low IQ) by stimulus duration interaction on IT task response accuracy (partial $\eta^2 = 0.10$). This analysis determined that a

sample size of 40 participants (20 per condition) is required to detect relevant changes in IT task performance. In the present study, data sets were obtained from 269 different participants between 18 and 60 years of age who gave informed consent to participate in the study. All participants had normal or corrected to normal vision, and reported being free from any motor control dysfunction, sleep disorders, or fatigue syndromes. Participants were given the choice to complete only one or both of two testing sessions, requiring approximately 1.5 hours each. In exchange for their participation, participants received course credit and/or could choose to be entered in a gift card draw. Data from 101 unique participants were retained following initial screening (see section 3.4 *Data Reduction*; 83 participants completed one session, while 18 completed both sessions). The mean age of the retained participants was 19.42 years ($SD = 2.53$), including 71 participants who identified their sex assigned at birth as female (19.38 years, $SD = 2.77$) and 30 participants who identified their sex assigned at birth as male (19.50 years, $SD = 1.91$).

3.3.2 General Experimental Protocol

All stages involved in the completion of this study were in full accordance with the ethical standards in the Declaration of Helsinki and its later amendments. Approval from the Research Ethics Board at the University of Ottawa was obtained for this experiment. Data collection was performed remotely using a custom downloadable application available for Windows and MacOS platforms written using LabVIEW®. All components of the experiment, including completion of consent forms and questionnaires, were completed within this application in either French or English. Participation in the experiment was not supervised by the researchers and was completed on a laptop or desktop computer at the location of the participants choosing. Instructions within the application asked participants to minimize outside distractions while

completing the experiment, to ensure adequate time to complete the testing session without interruption, and to use mental effort only to complete cognitive tasks (e.g., to not use a pen and paper or calculator). Participants were also instructed to delay participation if they had consumed any alcohol or recreational drugs within the prior 6 hours. Participants could choose to complete either one, or both, of two separate testing sessions, which were assigned in random order: a cognitive fatigue (CF) testing session and/or a non-fatiguing (NF) control session. In the case that both sessions were completed, participants were instructed to begin both sessions of the study at approximately the same time of day, separated by a minimum of 24 hours. Responses for all segments of the experiment were time-stamped, to allow identification of instances where instructions were not followed (e.g., when a participant took a break during the experiment). Upon completion of each testing session the data were automatically sent via email from the application to the researchers.

Prior to beginning each session, participants completed a pre-session questionnaire to record several lifestyle factors that could influence task performance, including sex assigned at birth (male or female), age, caffeine intake, and amount of sleep in the 24 hours prior to the testing session (Knufinke et al., 2018; Rogers et al., 2013; Sadler et al., 2022). Participants next completed pre-test assessments, which included an estimation of subjective fatigue level as well as simple reaction time (RT) and inspection time (IT) tasks (described in section 3.3.4 *Pre- and Post-Tests*). Following baseline measurements, participants performed either the CF or NF task, each requiring approximately 1 hour to complete. After completion of the CF or NF task, the subjective fatigue level assessment was repeated, followed by post-test RT and IT tasks. Testing session (NF or CF) as well as IT and RT task order were randomly assigned by the custom LabVIEW® program.

3.3.3 Cognitive Fatigue and Control Interventions

In the CF session, participants performed a cognitively demanding dual-task that has previously been demonstrated to induce CF, as assessed by both subjective and objective measures of fatigue (Peters et al., 2022). In this task, 7 letters appeared consecutively on the study window in a pre-generated sequence, for 800 ms each with a pause of 500 ms between letters. Participants were instructed that they could use any mental strategy to remember these letters, but that they should not rehearse the letters out loud or write them down. After all letters had been displayed, a series of math problems was presented for 45 seconds. Participants used their computer mouse to select the mathematical operation that correctly completed the math problem displayed (e.g.: $20 ? 5 = 25$; answer = +). Written instructions indicated that participants should try to accurately complete as many math problems as possible during the 45 second period. To help keep participants motivated, feedback of the number of math problems correctly solved and the accuracy of responses was provided after each trial at the bottom of the study window. Following each 45 second math segment, participants were presented with 7 blank boxes horizontally aligned in the middle of the study window and were instructed to use their keyboard to input the remembered letters into these boxes, in the correct order. Feedback on the accuracy of memory task responses were provided immediately after each attempt (boxes would turn green for correctly inputted letters, and red for incorrectly inputted letters). Immediately following this, the words “Get Ready” reappeared on the study window, followed 1 second later by 7 new letters. The cognitive task repeated in this manner for 60 minutes. Keypress responses and selected math operators were recorded using the custom LabVIEW® program.

In the NF session, in place of the memory / math task, participants were provided a link to a documentary film that lasted approximately 55 minutes (English: *Uncharted – The Beautiful*

World of the Amazon, Thompson, 2015; French: *Dans le bleu de la Méditerranée*, Espla, 2014) and were instructed to watch this film in its entirety without interruption and while minimizing distractions.

3.3.4 Pre- and Post-Tests

Pre- and post-tests were performed immediately before and after the cognitively demanding (CF session) and control (NF session) interventions. These tests were used to assess 3 measures: i) subjective fatigue level, to confirm that the CF task led to increased feelings of fatigue; ii) simple RT, to confirm that the CF task objectively led to increased cognitive processing time; and iii) inspection time task performance, to assess the effects of CF on the speed of perceptual processing.

Subjective CF was evaluated using a series of four visual analog scales (VAS) presented within the study window. Participants rated their energy level (0-energetic, 10-unenergetic), tension level (0-relaxed, 10-tense), and ability to concentrate (0-able to concentrate, 10-unable to concentrate) using their computer mouse to slide a visual marker along a horizontal scale of 0-10 (slider length 200 mm). These three scales were selected from the cognitive and sensory subscales of the Piper Fatigue Scale-12 (Reeve et al., 2012). Energy level was used to capture the subjective experience of tiredness, while tension level was included as it has been shown to increase with effortful sustained attention (Grier et al., 2003; O’Keeffe et al., 2020; Szalma et al., 2004), and the ability to concentrate was measured since CF has been associated with lapses in attention (Boksem et al., 2005). An additional scale was used to assess motivation (0-motivated to succeed in the task, 10-unmotivated to succeed in the task), as it has been suggested that motivation changes can moderate CF, and also be a result of CF inducement (Herlambang et al., 2019, 2021; Hockey, 2011).

Following subjective fatigue assessment, participants performed either the RT task or the IT task. In the RT task, each trial began with the words “Get Ready” appearing on the screen. After 1000 ms, the text disappeared. Following a variable (500 – 1500 ms) foreperiod, a black circle at the centre of the experimental window illuminated green (go-signal). Participants were instructed to respond as quickly as possible by pressing any keyboard key when this go-signal was presented. Feedback of RT performance was presented at the bottom of the experimental window following each trial. After 2500 ms, the next trial began, again starting with the words “Get Ready” appearing on the screen. Pre-test RT assessments began with 12 practice trials followed by 30 testing trials, whereas post-test RT assessments included only 30 testing trials.

In the IT task, each trial began with the words “Get Ready” appearing on the study window for 1500 ms (Fig. 3.1). The text then disappeared, and 1500 ms later a fixation cross was presented at the centre of the window for 500 ms. The fixation cross then disappeared, and 500 ms later a pi-figure was presented with its centre at the location of the fixation cross. This figure featured two vertical lines (or legs) of differing length (135 px, 115 px) connected at the top by a horizontal line (49 px). Note that the legs would appear to be a slightly different size depending on the resolution and screen size of the user’s computer (e.g., on a 24 in monitor with 1080p resolution, the long leg would appear to be 3.74 cm long and the short leg would appear to be 3.18 cm long, attached at the top by 1.36 cm line). Two variations of the pi-figure were pseudo-randomly presented, with the longest leg either on the left or right side of the figure. The pi-figure was briefly displayed for a duration of 15, 30, 45, 60, 75 or 90 ms, and then backward masked using a “lightning” mask. On each trial, participants were instructed to indicate whether they perceived the longer leg of the figure to be on the left or the right by using their mouse to click an on-screen button labelled “left” or “right”. Following their selection, the next trial began

with the words “Get Ready” re-appearing in the study window. Pre-test IT assessments included 12 practice trials followed by 60 testing trials, whereas post-test IT assessments included only 60 testing trials. In both the pre- and post-test, 10 testing trials of each stimulus duration were delivered, with 5 “left leg longer” stimulus trials and 5 “right leg longer” stimulus trials presented at each stimulus duration.

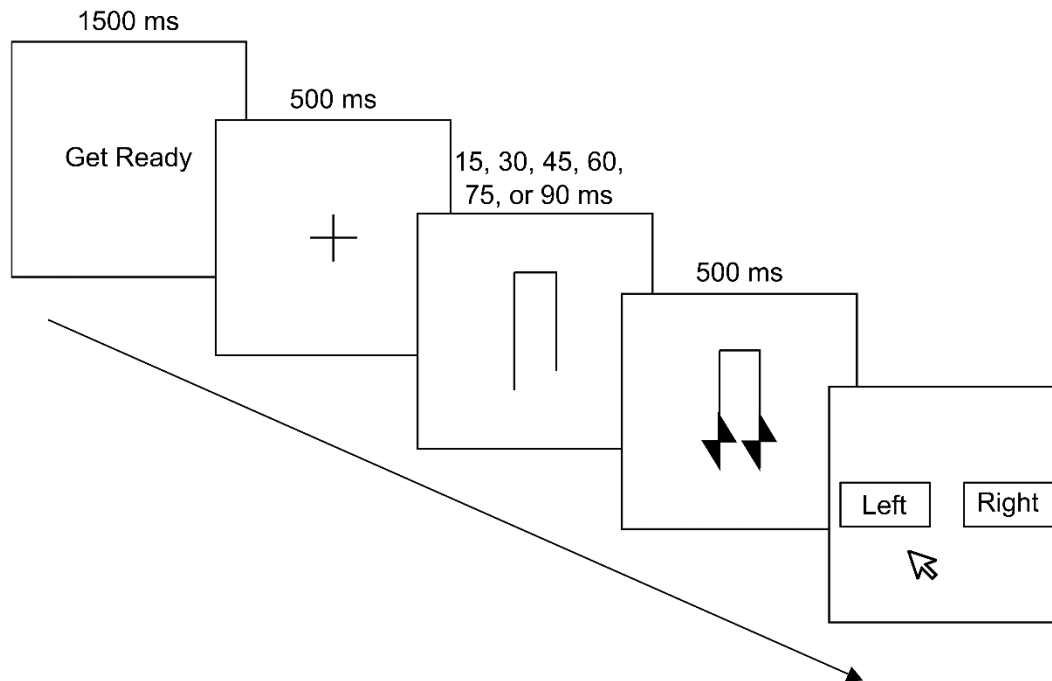


Fig. 3.1 A schematic illustration of the timeline for each trial of the inspection time task. Trials began with the words “Get Ready” displayed on the study window for 1500 ms. A fixation cross was then displayed at the centre of the screen for 500 ms, before the “pi-figure” was displayed for 15, 30, 45, 60, 75 or 90 ms. The pi-figure was then immediately replaced with a backward mask for 500 ms. Participants then used their computer mouse to select a button indicating the perceived side of the longest pi-figure leg and their response accuracy was recorded.

3.4 Data Reduction

A total of 353 data sets were collected, including 190 NF session data sets and 163 CF session data sets. Given that data collection occurred remotely and was unsupervised, data sets were thoroughly screened (using a priori defined criteria) to exclude those that may have included errors such as lapses in attention, overly speedy or slow performance, random responding, or breaks in experiment completion. 222 data sets which did not meet these quality standards were excluded as it could not be assumed that participants followed instructions as requested. Data were removed for not adhering to the following quality checks (note that some data sets failed to meet several standards): NF task length greater than 90 minutes in length [$n = 15$]; NF task duration less than 30 minutes in length [$n = 40$]; CF task duration greater than 70 minutes in length [$n = 9$]; CF task duration less than 50 minutes in length [$n = 10$]; IT task duration greater than 2.5 standard deviations from the mean (> 9.52 minutes) [$n = 33$]; RT task duration greater than 2.5 deviations from the mean (> 2.61 minutes) [$n = 13$]; number of CF task trials attempted less than 2.5 standard deviations from the mean (< 30 trials) [$n = 24$]; mean number of math problems attempted per trial in the CF task less than 2.5 standard deviations from the mean (< 4.58 problems attempted) [$n = 2$]; mean number of correctly remembered letters per trial in the CF task less than 2.5 standard deviations from the mean (< 2.28 letters correctly remembered) [$n = 4$]; total experiment duration less than 50 minutes in the NF session or 70 minutes in the CF session [$n = 39$]; total experiment duration greater than 130 minutes in the NF session or 110 minutes in the CF session [$n = 38$]; less than 12 hours between testing sessions if both the NF and CF task were attempted (only the second session discarded) [$n = 8$]; and an IT task performance with less than 70% correct responses in the pre-test 90 ms stimulus condition [$n = 175$].

A total of 131 data sets (37.1% of total collected) were retained following the above quality checks (71 NF sessions and 60 CF sessions). RT and IT task practice trials were excluded from these data prior to analyses. Further reduction of RT data was performed to remove error trials and outlying data points: 208 trials were removed for anticipation of the go-signal ($RT < 100$ ms; 112 from NF sessions, 96 from CF sessions); 286 trials were removed for slow responding ($RT > 500$ ms), indicating a lapse in attention (170 from NF sessions, 116 from CF sessions); and 92 outlier data points ($> \text{ or } < 3 SD$ from the mean) were removed (CF pre-test: 29, CF post-test: 9, NF pre-test: 28, NF post-test: 26). A total of 93.5% of RT testing trials were retained following this further reduction of RT data. A final reduction was performed to remove a small subset of participants ($n = 6$) who performed the IT task with a different, pilot set of stimulus durations than were delivered to all other participants, resulting in a final total of 119 data sets retained for analysis. While the final data inclusion rate was low (only 33.7% of data collected were retained), extensive data reduction based on a priori defined criteria was necessary to ensure that only data where participants adhered to study instructions were included for analyses.

3.5 Statistical Analysis

Summary data that support the findings of this study are available at [OSF: <https://doi.org/10.17605/OSF.IO/GK7JF>] (Peters et al., 2023). Statistical analyses were completed using linear mixed-effect and logistic mixed-effect model analyses in R statistical software (Bates et al., 2015; R Core Team, 2021). Linear mixed-effect models were assessed for homoscedasticity and approximate normal distribution of residuals. Logistic mixed-effect models were assessed for uniformity of residuals, as well as for the absence of zero-inflation and significant over- or under-dispersion using the *DHARMa* package (Hartig & Lohse, 2022).

Where linear mixed-effect models were used, the significance of fixed effects was explored using analysis of variance of each model, with F-tests and p-values using Satterthwaite's method for denominator degrees-of-freedom and F-statistic, applied using the *lmerTest* package (Kuznetsova et al., 2017). Logistic mixed-effect models were computed using the *glmer* function with an additional term specifying a binomial outcome variable (*family = binomial (link = "logit")*). In this case, the *car* package (function: *Anova*) was used to examine the significance of fixed effects, obtained by Type II Wald Chi-Square testing (J. Fox & Weisberg, 2019). Wald-Chi Square *p*-values were verified against those obtained by likelihood ratio Chi-Square tests of models *with* the effects of interest against a null model *without* the effects of interest.

In all cases, differences with a probability of .05 or less were considered significant. Where applicable, planned post hoc contrasts with Bonferroni corrections, estimated marginal means, and 95% confidence intervals for each measure were determined within each analysis using the *emmeans* package (Lenth et al., 2021). Mixed-effect model analyses were chosen because they are capable of handling unbalanced data sets and missing data, and because they can expressly model within-participant variance across conditions. Furthermore, these analyses have been shown to be superior to other methods in controlling for Type I errors (Barr et al., 2013; Bates et al., 2015; Boisgontier & Cheval, 2016; Judd et al., 2012), and to have greater power to detect significant differences, if they truly exist (Brown, 2021). However, it is important to note that there is no widely established method of calculating standardized effect sizes for individual mixed-effect model factors or for interactions between factors. As such, where possible, unstandardized effect sizes (odds ratios or mean differences and associated 95% confidence intervals determined using the *modelbased* package) are presented (Makowski et al., 2020), as recommended by Pek and Flora (2018).

3.5.1 Subjective Fatigue

An average score of the four 10-point measures assessed by the VAS (energy, ability to concentrate, motivation, and tension level) was calculated to provide an overall subjective fatigue score. This score was subtracted from 10, so that higher scores (on a scale of 0-10) represented greater levels of subjective fatigue ($subjective\ fatigue\ score = 10 - [(Energy\ Score + Concentration\ Score + Motivation\ Score + Tension\ Score) / 4]$). Overall subjective fatigue scores were then assessed with a linear mixed-effect model including the fixed effect interaction of testing session (NF, CF) and time (pre-test, post-test), with random intercepts specified for the effect of participant: $model = Subjective\ Fatigue\ Score \sim Session * Time + (1 | Participant)$.

3.5.2 Simple Reaction Time

A linear mixed-effect model was also used to assess changes in RT, in response to the fixed effect interaction of testing session (NF, CF) and time (pre-test, post-test). For the analysis of RT, model fit was significantly improved by the inclusion of reported sex assigned at birth (male or female) as a main effect without interaction. As such, sex was also included in the RT model², which again included random intercepts for the effect of participant: $model = RT \sim Session * Time + Sex + (1 | Participant)$.

3.5.3 Inspection Time Task Performance

IT task response accuracy on each trial is a binary outcome (0 = incorrect, 1 = correct), so logistic mixed-effect analyses were used to model this data, using random intercepts for the effect of participant: $model = Accuracy \sim Session * Time * Stimulus\ Duration + (1 | Participant)$.

² A likelihood ratio test of three models (no effect of sex, interacting effect of sex, and main effect of sex) indicated that the RT model with sex as a main effect provided the best model fit ($\chi^2(1) = 10.83, p < .001$). The addition of sex as a main or interacting effect did not significantly improve the model fit for subjective fatigue (main effect: $\chi^2(1) = 0.81, p = .369$; interacting effect: $\chi^2(3) = 5.74, p = .125$) nor IT task performance (main effect: $\chi^2(1) = 0.6583, p = .417$; interacting effect: $\chi^2(23) = 34.21, p = .062$), so sex was not included as a factor in these analyses.

An additional term for parameter optimization (“*Bound Optimization by Quadratic Approximation (BOBYQA)*”) was included in this model, with a set maximum of 200,000 iterations (Powell, 2009).

Post hoc testing was pre-planned to assess only the effects of greatest interest. Planned testing included a comparison of response accuracy at each IT task stimulus duration against all others (over all testing times and sessions) to confirm previously demonstrated stimulus duration effects (15 comparisons), as well as relevant comparisons between sessions and/or testing times within each level of the remaining factors (e.g., between test times at each stimulus duration; 12 comparisons).

3.6 Results

3.6.1 Subjective Fatigue

Subjective fatigue score as a function of time (pre-test, post-test) and testing session (NF, CF) is presented in Fig. 3.2. Linear mixed-effect analysis demonstrated significant main effects of both time ($F(1, 147) = 82.21, p < .001$, mean difference score pre to post = +1.49, 95% CI [1.17, 1.82]) and testing session ($F(1, 223) = 35.94, p < .001$, mean difference score between NF and CF = +1.14, 95% CI [0.76, 1.51]), which were superseded by a significant *time x session* interaction ($F(1, 147) = 42.52, p < .001$). Planned post hoc comparisons indicated a significant increase in subjective fatigue score from pre- to post-test in the CF session (mean difference score pre to post = +2.56, 95% CI [2.08, 3.05]; $p < .001$). No significant difference in subjective fatigue score from pre- to post-test in the NF session was observed (mean difference score pre to post = +0.42, 95% CI [-0.02, 0.86]; $p = .244$). Pre-test measures of subjective fatigue did not differ significantly between the NF and CF sessions (mean difference score between NF and CF = +0.07, 95% CI [-0.43, 0.56]; $p > .999$), while post-test subjective fatigue scores were

significantly greater in the CF session (mean difference score between NF and CF = +2.21, 95% CI [1.71, 2.71]; $p < .001$).

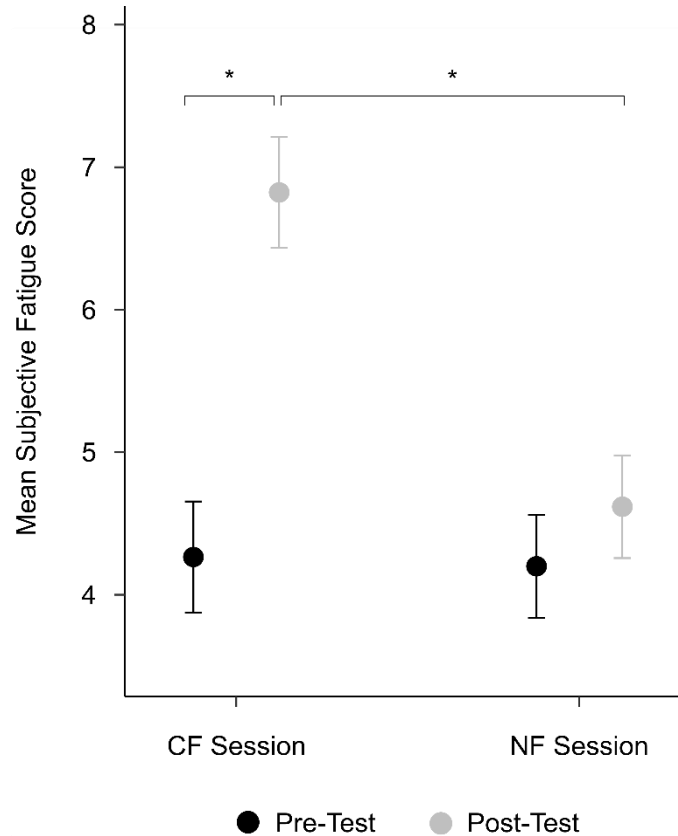


Fig. 3.2 Estimated marginal mean subjective cognitive fatigue scores. Scores are shown for each session (Cognitive Fatigue, CF; Non-Fatiguing, NF) and testing time (Pre-Test, black circles; Post-Test, gray circles). Error bars represent 95% confidence intervals. Asterisks indicate significant comparisons ($p < .050$).

3.6.2 Simple Reaction Time

Simple reaction time as a function of time (pre-test, post-test) and testing session (NF, CF) is presented in Fig. 3.3. RT analysis demonstrated a significant main effect of time ($F(1, 6493) = 17.82, p < .001$, mean difference pre to post = +5.3 ms, 95% CI [2.82, 7.71]) which was superseded by a significant *session x time* interaction ($F(1, 6493) = 12.11, p < .001$). Post hoc

analyses confirmed that RT increased significantly from pre- to post-test in the CF session (mean difference pre to post = +9.6 ms, 95% CI [6.0, 13.2], $p < .001$). No significant change from pre- to post-test in the NF session was observed (mean difference pre to post = +0.92 ms, 95% CI [-2.4, 4.2], $p > .999$). Pre-test measures of RT did not differ significantly between the NF and CF sessions (mean difference between NF and CF = -1.8 ms, 95% CI [-6.6, 3.0], $p > .999$), while post-test RT was significantly longer in the CF session (mean difference between NF and CF = +6.9 ms, 95% CI [2.1, 11.7], $p = .020$). A significant main effect of sex was also observed ($F(1, 99) = 11.20$, $p = .001$), with male participants displaying significantly shorter reaction times than female participants (mean RT male = 278 ms, 95% CI [269, 288]; mean RT female = 297 ms, 95% CI [291, 304]).

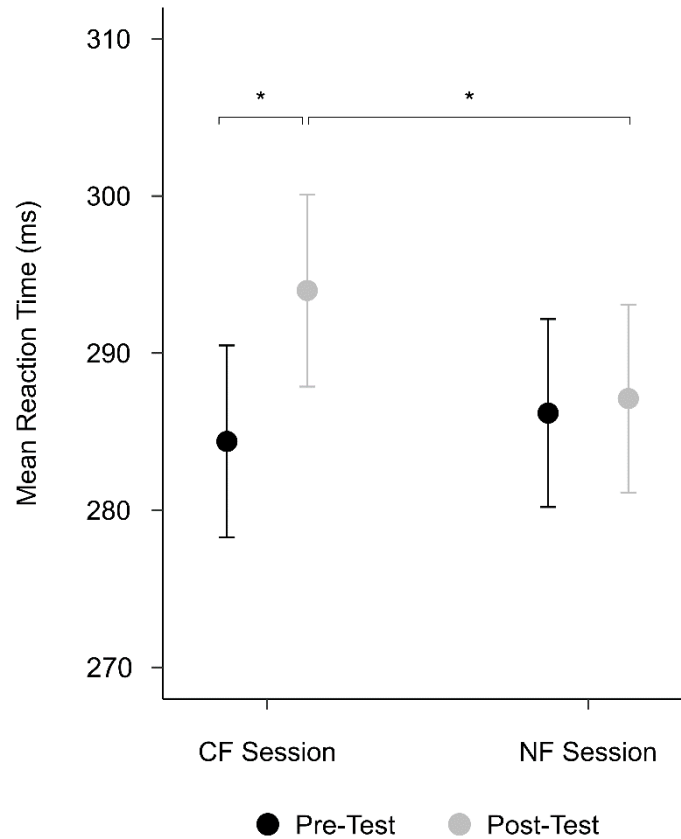


Fig. 3.3 Estimated marginal mean reaction time. Reaction time (ms) is shown for each session (Cognitive Fatigue, CF; Non-Fatiguing, NF) and testing time (Pre-Test, black circles; Post-Test, gray circles). Error bars represent 95% confidence intervals. Asterisks indicate significant comparisons ($p < .050$).

3.6.3 Inspection Time Task Performance

Inspection time task response accuracy (probability of correct response) as a function of stimulus duration, time (pre-test, post-test) and testing session (CF, NF) is shown in Fig. 3.4. As expected, response accuracy significantly increased along with stimulus display duration ($\chi^2(5) = 697.90, p < .001$); but importantly, no significant main effects of testing time (pre-test vs. post-test; $\chi^2(1) = .46, p = .500$) or session (CF vs. NF; $\chi^2(1) = 1.31, p = .252$) were observed. A significant interaction was found between stimulus duration and time ($\chi^2(5) = 21.27, p < .001$), while the

interactions between stimulus duration and session ($\chi^2 (5) = 0.38, p = .996$), between time and session ($\chi^2 (1) = 0.07, p = .791$), and between time, session, and stimulus duration ($\chi^2 (5) = 5.05, p = .410$) were not significant. Post hoc comparisons demonstrated significant improvement in IT task response accuracy with increasing IT stimulus duration, except when comparing the *15 ms* and *30 ms* stimulus durations (Table 3.1). A significant pre- to post-test decrease in the probability of a correct response was apparent only at the 90 ms stimulus duration condition (odds ratio = 1.61 [1.30, 1.99], $p = .002$), while a non-significant trend for improved response accuracy from pre- to post-test was observed at most other stimulus durations (30, 45, 60, and 75 ms). No other significant differences from pre- to post-test were detected (Table 3.1).

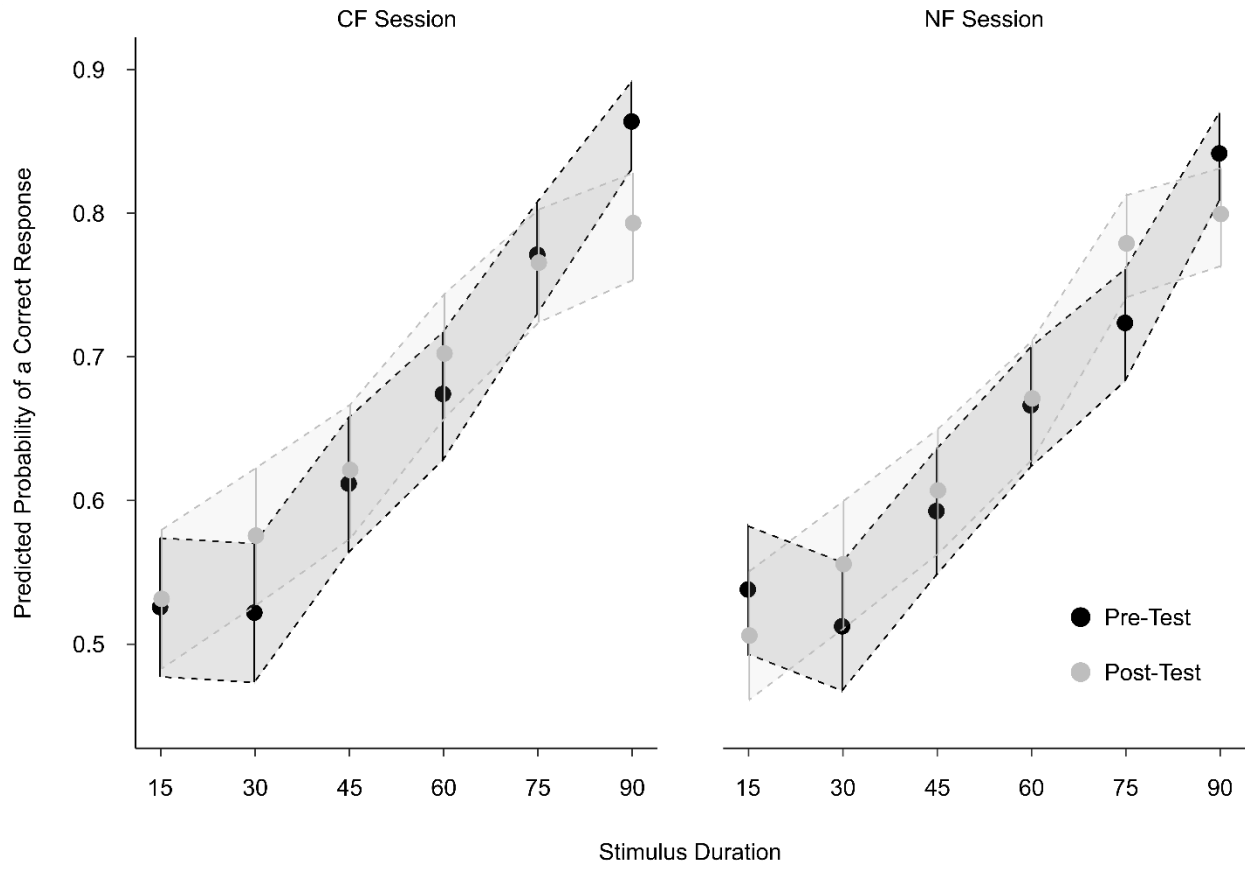


Fig. 3.4 Model predicted probability of a correct response for each stimulus display duration during the inspection time task. Data are presented as a function of session (Cognitive Fatigue, CF; Non-Fatiguing, NF), and testing time (Pre-Test, black circles; Post-Test grey circles). Error bars and shaded regions represent 95% confidence intervals.

Table 3.1 Post hoc comparisons of inspection time task performance. Odds ratios and associated 95% confidence intervals (CI), the difference in the probability of a correct response (Δ prob.), and Bonferroni corrected p -values are presented.

Comparison		Odds Ratio	95% CI	Δ prob.	p -value
Stimulus Duration					
15 ms	30 ms	1.01	0.90, 1.14	0.016	1.000
15 ms	45 ms	0.77	0.69, 0.87	0.080	<.001
15 ms	60 ms	0.57	0.50, 0.64	0.148	<.001
15 ms	75 ms	0.38	0.33, 0.43	0.229	<.001
15 ms	90 ms	0.25	0.22, 0.29	0.295	<.001
30 ms	45 ms	0.82	0.73, 0.93	0.064	<.001
30 ms	60 ms	0.60	0.54, 0.68	0.132	<.001
30 ms	75 ms	0.40	0.35, 0.46	0.213	<.001
30 ms	90 ms	0.27	0.23, 0.31	0.279	<.001
45 ms	60 ms	0.79	0.70, 0.90	0.068	<.001
45 ms	75 ms	0.53	0.47, 0.60	0.149	<.001
45 ms	90 ms	0.35	0.31, 0.40	0.215	<.001
60 ms	75 ms	0.72	0.63, 0.82	0.081	<.001
60 ms	90 ms	0.48	0.42, 0.55	0.147	<.001
75 ms	90 ms	0.72	0.62, 0.83	0.066	<.001
Time x Stimulus Duration					
15 ms Pre	15 ms Post	1.14	0.97, 1.34	-0.013	1.000
30 ms Pre	30 ms Post	0.89	0.75, 1.05	0.047	.122
45 ms Pre	45 ms Post	1.03	0.87, 1.22	0.012	1.000
60 ms Pre	60 ms Post	1.00	0.84, 1.19	0.016	1.000
75 ms Pre	75 ms Post	0.95	0.78, 1.14	0.024	1.000
90 ms Pre	90 ms Post	1.61	1.30, 1.99	-0.057	.002

3.7 Discussion

In the current study, a challenging, sustained cognitive task was successfully employed to induce cognitive fatigue among participants. This was evidenced by significant increases in subjective CF scores (Fig. 3.2) and simple RT latency (Fig. 3.3) following completion of the CF intervention, but not the control (NF) intervention. Results for the IT task were as expected based on what has been documented in previous works (Irwin, 1984; Vickers & Smith, 1986), such that response accuracy significantly increased along with IT stimulus duration for all but one of the comparisons examined. While it was clear that CF and IT manipulations were successful in their respective aims, no meaningful changes to IT task response accuracy could be attributed to CF. It was expected that if the speed of perceptual processing was negatively impacted by CF, then a similar decrease in response accuracy would have been observed across stimulus durations, or at least across those that achieved a baseline response accuracy above the level of chance (50%). This would be reflected in an overall rightward shift of the stimulus duration by response accuracy curve, such that the IT task display duration required to achieve a comparative level of accuracy is generally increased. However, as seen in Fig. 3.4, such a shift did not occur to any measurable degree. While a significant pre- to post-test decrease in response accuracy was observed in the 90 ms stimulus duration condition, this change did not differ between the CF and NF interventions, and therefore is unlikely to be an effect of CF. This is supported by the fact that response accuracy actually appeared to improve (although not significantly so) from pre- to post-test at most other stimulus durations (30, 45, 60, and 75 ms; Table 3.1). Instead, the pre- to post-test reduction in performance at the 90 ms stimulus duration over both sessions may be due to natural response variation or outlying data points that were not captured by the data reduction process.

An alternative potential explanation for the null effect of CF on IT response accuracy is that the experimental manipulation was simply not sensitive enough to detect CF-related changes in IT task performance that may exist. While this is a possibility, the number of participants included in this study was large compared to the number specified by a priori sample size calculations. Despite extensive data exclusion, statistical power was evidently adequate to reliably detect CF-related increases in subjective fatigue, and even increases in RT that may be considered small compared to some other reports (for example, see Jaydarifard et al., 2019; Langner, Steinborn, et al., 2010; Lim et al., 2010). As such, it is likely that changes to IT task performance in CF would also have been detected if they did indeed exist in the current experimental manipulation. Furthermore, although there are few examples of analyses comparing IT task response accuracy between conditions or time points, performance differences of approximately 12-18% have been previously reported (e.g., Hajj et al., 2019). Much smaller magnitude changes between testing conditions were observed here (the overall percent change from pre- to post-test was less than 1%, while the percent difference between the NF and CF sessions was approximately 2.3%). As this is a null result, it cannot be definitively concluded that IT task performance (and therefore speed of perceptual processing) is *not* affected by CF; nevertheless, due to the large sample and relatively small effects observed, the present analysis does provide some evidence in support of this conclusion.

The results observed here are somewhat contradictory to previous studies demonstrating auditory perceptual processing impairments in CF (Jain et al., 2022; Jain & Nataraja, 2019; Simon et al., 2020). These studies examined perceptual processing in the auditory domain using tests of speech perception in noise and temporal processing, while the current study employed a visual discrimination task. Arguably, these tasks are similar in that they assess the early stages of

sensory information processing, and as such, may theoretically respond similarly to fatigue. However, it is possible that the effects of CF on early sensory information processing are dependent on the sensory modality being tested (e.g., Matuz et al., 2019). While modality-specific effects were not addressed in the current analysis, visual processing may be less sensitive to the effects of CF than processing in the auditory domain. This may partly explain why the current analysis demonstrated no significant effects of CF on IT task performance. The present results are also contrary to the results of some studies investigating the effect of CF on electrophysiological indices. In particular, several studies have demonstrated CF-related decreases in the amplitude of early sensory ERPs (i.e., N1; Boksem et al., 2005; Faber et al., 2012; Ghani et al., 2020; Samuel et al., 2019; L. Sun et al., 2022). These N1 amplitude shifts are thought to reflect early sensory processes such as alerting to, orienting to, or discriminating a stimulus (Gonçalves et al., 2018; Hopf et al., 2002; Neuhaus et al., 2010; Sokhadze et al., 2017). However, although the IT task requires participants to alert to the pi-figure and to discriminate between the shorter and longer legs of the stimulus, no apparent CF-related decline in IT task performance was observed in the present analysis. This could suggest that N1 amplitude decreases in CF do not primarily reflect an impairment of early visual processing related to discriminating or alerting to a stimulus, and instead may be more related to impairments in the ability to spatially orient towards a stimulus, which was not a major requirement of the IT task. Alternatively, the resistance of IT task performance to CF may be in accordance with a different hypothesis – that compensatory neural mechanisms can act to mitigate the impairment of sensory processing, such that while the amplitude of early sensory ERPs may decline in CF, efficient perceptual processing is maintained (Samuel et al., 2019). Additional research, ideally with

combined electrophysiological and behavioural measures of sensory processing, would be required to determine whether these possibilities have merit.

This study had several limitations of note. As mentioned previously, the RT decrements observed following the CF intervention were of a smaller magnitude (+9.6 ms) than has been reported in some other cases (approximate mean range of +20-30 ms; see Jaydarifard et al., 2019; Langner, Steinborn, et al., 2010; Lim et al., 2010), but were comparable to what was reported previously when the same CF task was employed (+7.30 ms; Peters et al., 2022). Although standardized effect sizes were not reported due to the nature of the chosen analyses, it may be meaningful to note that according to Brysbaert & Stevens (2018), the effect size of RT changes in cognitive psychology is typically small (i.e., around $d = .10$), and that a minimum of 1600 data points per condition would be required to detect such small changes – a condition that was met by the large sample included here. Accordingly, it is possible that such small (but reliably elicited) RT changes are simply representative for the CF intervention that was used. Future studies may compare this CF intervention with others that have been employed elsewhere (e.g., as in O’Keeffe et al., 2020; Smith et al., 2019) to determine whether there are task demands particular to (or lacking in) this task that might explain the discrepancy in CF-related RT increases.

An additional limitation of this work relates to its virtual deployment. While virtual deployment allowed a greater number of participants to be tested compared to a laboratory-based task, an extensive data reduction process was required to eliminate poor quality data. Even with this process, it is still certainly possible that some factors remained uncontrolled. For instance, while the study window and all stimuli were consistent in size, participants may have been seated at different distances from their computer monitor and could have used computer monitors with

differing resolutions. This may have had some impact on the estimation of IT task performance as the relative size of the pi-figure arms may have been slightly different between participants. However, this effect would likely not have a large overall effect on the results due to the within-participant nature of the study design. Furthermore, although participants were asked to find a quiet, distraction-free place to complete the study, it cannot be confirmed that these instructions were always followed. In this vein, one previously documented finding is that distractibility increases with CF, and the ability to attend to task-relevant stimuli declines (Boksem et al., 2005; Csathó et al., 2012; Herlambang et al., 2019). Given this, it is possible that some participants may have become distracted and strayed from focusing on the task at some point during the experiment, especially as they became increasingly cognitively fatigued (i.e., following the CF intervention). Considering that both RT and IT performance typically depend on attentiveness to task-relevant stimuli, such a reduction in attentional focus could work to impair *both* IT and RT task performance (M. C. Fox et al., 2009; Hill et al., 2011; Prinzmetal et al., 2005). Instead, only a reduction in RT performance (and not IT task performance) was observed following the CF intervention. Overall, the present results seem to indicate that CF has no significant impact on IT task performance, regardless of the mechanism that is considered (i.e., perceptual processing speed or attentiveness to the stimuli).

3.8 Conclusion

The current study employed an IT task to determine whether perceptual processing impairments could underlie RT increases that have been observed in CF. Following the CF intervention, but not the NF intervention, participants demonstrated significantly increased levels of subjective fatigue, as well as modestly increased RT. Nevertheless, no meaningful change in IT response accuracy was observed following CF. As such, perceptual processing impairments appear to be

an unlikely source for slowed RT in CF, which instead may be due to a delay in another stage of sensorimotor processing. For example, while previous work has indicated that the *level* of response preparation is likewise unimpaired in CF, it is unclear whether CF could lead to a delay in the *speed* of response preparation (Peters et al., 2022). Simple RT increases in CF may also be attributable to impaired response initiation processes. Future studies should work to assess these possibilities and would also benefit from considering how the negative effects of CF on RT might be circumvented.

3.9 References

- Barr, D. J., Levy, R., Scheepers, C., & Tily, H. J. (2013). Random effects structure for confirmatory hypothesis testing: Keep it maximal. *Journal of Memory and Language*, 68(3), 10.1016/j.jml.2012.11.001. <https://doi.org/10.1016/j.jml.2012.11.001>
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, 67, 1–48. <https://doi.org/10.18637/jss.v067.i01>
- Boisgontier, M. P., & Cheval, B. (2016). The anova to mixed model transition. *Neuroscience & Biobehavioral Reviews*, 68, 1004–1005. <https://doi.org/10.1016/j.neubiorev.2016.05.034>
- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2005). Effects of mental fatigue on attention: An ERP study. *Cognitive Brain Research*, 25(1), 107–116. <https://doi.org/10.1016/j.cogbrainres.2005.04.011>
- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, 72(2), 123–132. <https://doi.org/10.1016/j.biopsycho.2005.08.007>
- Boksem, M. A. S., & Tops, M. (2008). Mental fatigue: Costs and benefits. *Brain Research Reviews*, 59(1), 125–139. <https://doi.org/10.1016/j.brainresrev.2008.07.001>
- Borghini, G., Astolfi, L., Vecchiato, G., Mattia, D., & Babiloni, F. (2014). Measuring neurophysiological signals in aircraft pilots and car drivers for the assessment of mental workload, fatigue and drowsiness. *Neuroscience & Biobehavioral Reviews*, 44, 58–75. <https://doi.org/10.1016/j.neubiorev.2012.10.003>
- Borragán, G., Slama, H., Bartolomei, M., & Peigneux, P. (2017). Cognitive fatigue: A Time-based Resource-sharing account. *Cortex*, 89, 71–84. <https://doi.org/10.1016/j.cortex.2017.01.023>
- Brown, V. A. (2021). An Introduction to Linear Mixed-Effects Modeling in R. *Advances in Methods and Practices in Psychological Science*, 4(1), 2515245920960351. <https://doi.org/10.1177/2515245920960351>
- Brysbaert, M., & Stevens, M. (2018). Power Analysis and Effect Size in Mixed Effects Models: A Tutorial. *Journal of Cognition*, 1(1), 9. <https://doi.org/10.5334/joc.10>
- Cao, S., Geok, S. K., Roslan, S., Sun, H., Lam, S. K., & Qian, S. (2022). Mental Fatigue and Basketball Performance: A Systematic Review. *Frontiers in Psychology*, 12. <https://www.frontiersin.org/articles/10.3389/fpsyg.2021.819081>
- Csathó, Á., van der Linden, D., Hernádi, I., Buzás, P., & Kalmár, G. (2012). Effects of mental fatigue on the capacity limits of visual attention. *Journal of Cognitive Psychology*, 24(5), 511–524. <https://doi.org/10.1080/20445911.2012.658039>

- Dallaway, N., Lucas, S. J. E., & Ring, C. (2022). Cognitive tasks elicit mental fatigue and impair subsequent physical task endurance: Effects of task duration and type. *Psychophysiology*, 59(12). <https://doi.org/10.1111/psyp.14126>
- DeLuca, J. (2005). Fatigue: Its Definition, Its Study, and Its Future. In J. DeLuca (Ed.), *Fatigue as a Window to the Brain* (pp. 319–325). The MIT Press.
- Donders, F. C. (1969). On the speed of mental processes. *Acta Psychologica*, 30, 412–431. [https://doi.org/10.1016/0001-6918\(69\)90065-1](https://doi.org/10.1016/0001-6918(69)90065-1)
- Espla, J. (Director). (2014). *Dans le bleu de la Méditerranée* [Video recording]. Cosmopolitis Productions.
- Faber, L. G., Maurits, N. M., & Lorist, M. M. (2012). Mental Fatigue Affects Visual Selective Attention. *PLOS ONE*, 7(10), e48073. <https://doi.org/10.1371/journal.pone.0048073>
- Ferreira Junior, A., Chierotti, P., Gabardo, J. M., Giovanini, B., Okano, A. H., Buzzachera, C. F., Okazaki, V. H. A., Okuno, N. M., & Altimari, L. R. (2020). Residual Effects of Mental Fatigue on Subjective Fatigue, Reaction Time and Cardiac Responses. *Rev de Psicol Del Deporte (J Sport Psychol)*, 29(2), 27–34.
- Fox, J., & Weisberg, S. (2019). *An R companion to applied regression* (Third edition). Sage.
- Fox, M. C., Roring, R. W., & Mitchum, A. L. (2009). Reversing the speed–IQ correlation: Intra-individual variability and attentional control in the inspection time paradigm. *Intelligence*, 37(1), 76–80. <https://doi.org/10.1016/j.intell.2008.08.002>
- Gantois, P., Caputo Ferreira, M. E., Lima-Junior, D. de, Nakamura, F. Y., Batista, G. R., Fonseca, F. S., & Fortes, L. de S. (2020). Effects of mental fatigue on passing decision-making performance in professional soccer athletes. *European Journal of Sport Science*, 20(4), 534–543. <https://doi.org/10.1080/17461391.2019.1656781>
- Ghani, U., Signal, N., Niazi, I. K., & Taylor, D. (2020). ERP based measures of cognitive workload: A review. *Neuroscience & Biobehavioral Reviews*, 118, 18–26. <https://doi.org/10.1016/j.neubiorev.2020.07.020>
- Gonçalves, Ó. F., Rêgo, G., Conde, T., Leite, J., Carvalho, S., Lapenta, O. M., & Boggio, P. S. (2018). Mind Wandering and Task-Focused Attention: ERP Correlates. *Scientific Reports*, 8(1), Article 1. <https://doi.org/10.1038/s41598-018-26028-w>
- Gregory, T., Nettelbeck, T., Howard, S., & Wilson, C. (2008). Inspection Time: A biomarker for cognitive decline. *Intelligence*, 36(6), 664–671. <https://doi.org/10.1016/j.intell.2008.03.005>
- Grier, R. A., Warm, J. S., Dember, W. N., Matthews, G., Galinsky, T. L., Szalma, J. L., & Parasuraman, R. (2003). The vigilance decrement reflects limitations in effortful attention, not mindlessness. *Human Factors*, 45(3), 349–360.

- Guo, Z., Chen, R., Liu, X., Zhao, G., Zheng, Y., Gong, M., & Zhang, J. (2018). The impairing effects of mental fatigue on response inhibition: An ERP study. *PLOS ONE*, *13*(6), e0198206. <https://doi.org/10.1371/journal.pone.0198206>
- Habay, J., Van Cutsem, J., Verschueren, J., De Bock, S., Proost, M., De Wachter, J., Tassignon, B., Meeusen, R., & Roelands, B. (2021). Mental Fatigue and Sport-Specific Psychomotor Performance: A Systematic Review. *Sports Medicine*, *51*(7), 1527–1548. <https://doi.org/10.1007/s40279-021-01429-6>
- Hajj, J., Maslovat, D., Cressman, E. K., Germain, L. S., & Carlsen, A. N. (2019). Visual processing is diminished during movement execution. *PLOS ONE*, *14*(3), e0213790. <https://doi.org/10.1371/journal.pone.0213790>
- Hartig, F., & Lohse, L. (2022). *DHARMA: Residual Diagnostics for Hierarchical (Multi-Level / Mixed) Regression Models* (Version 0.4.6) [Computer software]. <https://cran.r-project.org/web/packages/DHARMA/index.html>
- Henderson, L., & Dittrich, W. H. (1998). Preparing to react in the absence of uncertainty: I. New perspectives on simple reaction time. *British Journal of Psychology*, *89*(4), 531–554. <https://doi.org/10.1111/j.2044-8295.1998.tb02702.x>
- Herlambang, M. B., Cnossen, F., & Taatgen, N. A. (2021). The effects of intrinsic motivation on mental fatigue. *PLOS ONE*, *16*(1), e0243754. <https://doi.org/10.1371/journal.pone.0243754>
- Herlambang, M. B., Taatgen, N. A., & Cnossen, F. (2019). The Role of Motivation as a Factor in Mental Fatigue. *Human Factors*, *61*(7), 1171–1185. <https://doi.org/10.1177/0018720819828569>
- Hill, D., Saville, C. W. N., Kiely, S., Roberts, M. V., Boehm, S. G., Haenschel, C., & Klein, C. (2011). Early electro-cortical correlates of inspection time task performance. *Intelligence*, *39*(5), 370–377. <https://doi.org/10.1016/j.intell.2011.06.005>
- 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*. (pp. 167–187). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-008>
- Hopf, J.-M., Vogel, E., Woodman, G., Heinze, H.-J., & Luck, S. J. (2002). Localizing Visual Discrimination Processes in Time and Space. *Journal of Neurophysiology*, *88*(4), 2088–2095. <https://doi.org/10.1152/jn.2002.88.4.2088>
- Hopstaken, J. F., van der Linden, D., Bakker, A. B., & Kompier, M. A. J. (2015). A multifaceted investigation of the link between mental fatigue and task disengagement. *Psychophysiology*, *52*(3), 305–315. <https://doi.org/10.1111/psyp.12339>
- Irwin, R. J. (1984). Inspection time and its relation to intelligence. *Intelligence*, *8*(1), 47–65. [https://doi.org/10.1016/0160-2896\(84\)90006-0](https://doi.org/10.1016/0160-2896(84)90006-0)

- Jain, S., & Nataraja, N. P. (2019). The Effect of Fatigue on Working Memory and Auditory Perceptual Abilities in Trained Musicians. *American Journal of Audiology*, 28(2S), 483–494. https://doi.org/10.1044/2019_AJA-IND50-18-0102
- Jain, S., Nataraja, N. P., & Narne, V. K. (2022). The Effect of Subjective Fatigue on Auditory Processing in Musicians and Nonmusicians. *Music Perception*, 39(3), 309–319. <https://doi.org/10.1525/mp.2022.39.3.309>
- Jaydarifard, S., Tahmasebi Boroujeni, S., & Lavender, A. P. (2019). Mental fatigue impairs simple reaction time in non-athletes more than athletes. *Fatigue: Biomedicine, Health & Behavior*, 7(3), 117–126. <https://doi.org/10.1080/21641846.2019.1632614>
- Jensen, A. R. (2006). Chapter 5—Chronometry of Mental Development. In A. R. Jensen (Ed.), *Clocking the Mind* (pp. 75–94). Elsevier Science Ltd. <https://doi.org/10.1016/B978-008044939-5/50006-9>
- Jia, A., Guo, X., & Tian, S. (2022). Experimental study on the influence of mental fatigue on risk decision-making of miners. *Scientific Reports*, 12(1), 11902. <https://doi.org/10.1038/s41598-022-14045-9>
- Jia, H., Lin, C. J., & Wang, E. M. (2022). Effects of mental fatigue on risk preference and feedback processing in risk decision-making. *Scientific Reports*, 12(1), 10695. <https://doi.org/10.1038/s41598-022-14682-0>
- Judd, C. M., Westfall, J., & Kenny, D. A. (2012). Treating stimuli as a random factor in social psychology: A new and comprehensive solution to a pervasive but largely ignored problem. *Journal of Personality and Social Psychology*, 103(1), 54–69. <https://doi.org/10.1037/a0028347>
- Kanfer, R. (2011). Determinants and consequences of subjective cognitive fatigue. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 189–207). American Psychological Association. <https://doi.org/http://dx.doi.org.proxy.bib.uottawa.ca/10.1037/12343-009>
- Kato, Y., Endo, H., & Kizuka, T. (2009). Mental fatigue and impaired response processes: Event-related brain potentials in a Go/NoGo task. *International Journal of Psychophysiology*, 72(2), 204–211. <https://doi.org/10.1016/j.ijpsycho.2008.12.008>
- Knufinke, M., Nieuwenhuys, A., Maase, K., Moen, M. H., Geurts, S. A. E., Coenen, A. M. L., & Kompier, M. A. J. (2018). Effects of Natural Between-Days Variation in Sleep on Elite Athletes' Psychomotor Vigilance and Sport-Specific Measures of Performance. *Journal of Sports Science & Medicine*, 17(4), 515–524.
- Kowalski, K. L., Tierney, B. C., & Christie, A. D. (2022). Mental fatigue does not substantially alter neuromuscular function in young, healthy males and females. *Physiology & Behavior*, 253, 113855. <https://doi.org/10.1016/j.physbeh.2022.113855>

- Kranzler, J. H., & Jensen, A. R. (1989). Inspection time and intelligence: A meta-analysis. *Intelligence*, 13(4), 329–347. [https://doi.org/10.1016/S0160-2896\(89\)80006-6](https://doi.org/10.1016/S0160-2896(89)80006-6)
- Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, 82, 1–26. <https://doi.org/10.18637/jss.v082.i13>
- Langner, R., Steinborn, M. B., Chatterjee, A., Sturm, W., & Willmes, K. (2010). Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychologica*, 133(1), 64–72. <https://doi.org/10.1016/j.actpsy.2009.10.001>
- Langner, R., Willmes, K., Chatterjee, A., Eickhoff, S. B., & Sturm, W. (2010). Energetic effects of stimulus intensity on prolonged simple reaction-time performance. *Psychological Research*, 74(5), 499–512. <https://doi.org/10.1007/s00426-010-0275-6>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835. <https://doi.org/10.1016/j.autcon.2019.102835>
- Lim, J., Wu, W., Wang, J., Detre, J. A., Dinges, D. F., & Rao, H. (2010). Imaging brain fatigue from sustained mental workload: An ASL perfusion study of the time-on-task effect. *NeuroImage*, 49(4), 3426–3435. <https://doi.org/10.1016/j.neuroimage.2009.11.020>
- Lorist, M. M., Boksem, M. A. S., & Ridderinkhof, K. R. (2005). Impaired cognitive control and reduced cingulate activity during mental fatigue. *Cognitive Brain Research*, 24(2), 199–205. <https://doi.org/10.1016/j.cogbrainres.2005.01.018>
- Lorist, M. M., & Faber, L. G. (2011). Consideration of the influence of mental fatigue on controlled and automatic cognitive processes and related neuromodulatory effects. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 105–126). American Psychological Association. <https://doi.org/http://dx.doi.org/10.1037/12343-005>
- Lorist, M. M., Klein, M., Nieuwenhuis, S., de Jong, R., Mulder, G., & Meijman, T. F. (2000). Mental fatigue and task control: Planning and preparation. *Psychophysiology*, 37(5), 614–625. <https://doi.org/10.1111/1469-8986.3750614>
- Makowski, D., Ben-Shachar, M., Patil, I., & Lüdtke, D. (2020). *Estimation of Model-Based Predictions, Contrasts and Means*. <https://github.com/easystats/modelbased>
- Massar, S. A. A., Wester, A. E., Volkerts, E. R., & Kenemans, J. L. (2010). Manipulation specific effects of mental fatigue: Evidence from novelty processing and simulated driving.

- Psychophysiology*, 47(6), 1119–1126. <https://doi.org/https://doi.org/10.1111/j.1469-8986.2010.01028.x>
- Matuz, A., Van der Linden, D., Topa, K., & Csathó, Á. (2019). Cross-Modal Conflict Increases With Time-on-Task in a Temporal Discrimination Task. *Frontiers in Psychology*, 10. <https://www.frontiersin.org/articles/10.3389/fpsyg.2019.02429>
- Nettelbeck, T. (2001). Correlation between inspection time and psychometric abilities: A personal interpretation. *Intelligence*, 29(6), 459–474. [https://doi.org/10.1016/S0160-2896\(01\)00072-1](https://doi.org/10.1016/S0160-2896(01)00072-1)
- Neuhaus, A. H., Urbanek, C., Opgen-Rhein, C., Hahn, E., Ta, T. M. T., Koehler, S., Gross, M., & Dettling, M. (2010). Event-related potentials associated with Attention Network Test. *International Journal of Psychophysiology: Official Journal of the International Organization of Psychophysiology*, 76(2), 72–79. <https://doi.org/10.1016/j.ijpsycho.2010.02.005>
- O’Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics*, 63(1), 1–12. <https://doi.org/10.1080/00140139.2019.1687940>
- Pachella, R. G. (1974). The Interpretation of Reaction Time in Information-Processing Research 1. In B.H. Kantowitz (Ed.), *Human Information Processing* (pp. 41-82). Routledge. <https://doi.org/10.4324/9781003176688>
- Pek, J., & Flora, D. B. (2018). Reporting effect sizes in original psychological research: A discussion and tutorial. *Psychological Methods*, 23(2), 208–225. <https://doi.org/10.1037/met0000126>
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>
- Peters, K. J., Maslovat, D., & Carlsen, T. (2023). *Investigating the effects of cognitive fatigue on visual perceptual processing* [Dataset]. Open Science Framework. <https://doi.org/https://doi.org/10.17605/OSF.IO/GK7JF>
- Petrut, B., Berindan-Neagoe, I., Feflea, D. I., Hoge, M., Pasca, S., Bujoreanu, C. E., & Bschiepfer, T. (2020). Mental Fatigue Evaluation of Surgical Teams during a Regular Workday in a High-Volume Tertiary Healthcare Center. *Urologia Internationalis*, 104(3–4), 301–308. <https://doi.org/10.1159/000504988>
- 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. <https://doi.org/10.1016/j.trf.2015.01.003>

- Plukaard, S., Huizinga, M., Krabbendam, L., & Jolles, J. (2015). Cognitive flexibility in healthy students is affected by fatigue: An experimental study. *Learning and Individual Differences*, 38, 18–25. <https://doi.org/10.1016/j.lindif.2015.01.003>
- Powell, M. J. D. (2009). *The BOBYQA algorithm for bound constrained optimization without derivatives* (Report DAMTP 2009/NA06). University of Cambridge.
- Prinzmetal, W., McCool, C., & Park, S. (2005). Attention: Reaction Time and Accuracy Reveal Different Mechanisms. *Journal of Experimental Psychology*, 134(1), 73–92. <https://doi.org/10.1037/0096-3445.134.1.73>
- R Core Team. (2021). *R: A language and environment for statistical computing*. [Computer software]. R Foundation for Statistical Computing. <https://www.R-project.org/>
- Reeve, B., Stover, A., Alfano, C., Smith, A., Ballard-Barbash, R., Bernstein, L., McTiernan, A., Baumgartner, K., & Piper, B. (2012). The Piper Fatigue Scale-12 (PFS-12): Psychometric findings and item reduction in a cohort of breast cancer survivors. *Breast Cancer Research and Treatment*, 136(1). <https://doi.org/https://doi.org/10.1007/s10549-012-2212-4>
- Rogers, P. J., Heatherley, S. V., Mullings, E. L., & Smith, J. E. (2013). Faster but not smarter: Effects of caffeine and caffeine withdrawal on alertness and performance. *Psychopharmacology*, 226(2), 229–240. <https://doi.org/10.1007/s00213-012-2889-4>
- Sadler, C. M., Peters, K. J., Santangelo, C. M., Maslovat, D., & Carlsen, A. N. (2022). Retrospective composite analysis of StartReact data indicates sex differences in simple reaction time are not attributable to response preparation. *Behavioural Brain Research*, 426, 113839. <https://doi.org/10.1016/j.bbr.2022.113839>
- Samuel, I. B. H., Wang, C., Burke, S. E., Kluger, B., & Ding, M. (2019). Compensatory Neural Responses to Cognitive Fatigue in Young and Older Adults. *Frontiers in Neural Circuits*, 13. <https://doi.org/10.3389/fncir.2019.00012>
- Shen, R., Weng, D., Chen, S., Guo, J., & Fang, H. (2019). Mental Fatigue of Long-Term Office Tasks in Virtual Environment. *2019 IEEE International Symposium on Mixed and Augmented Reality Adjunct (ISMAR-Adjunct)*, 124–127. <https://doi.org/10.1109/ISMAR-Adjunct.2019.00-65>
- Simon, J., Takács, E., Orosz, G., Berki, B., & Winkler, I. (2020). Short-term cognitive fatigue effect on auditory temporal order judgments. *Experimental Brain Research*, 238(2), 305–319. <https://doi.org/10.1007/s00221-019-05712-x>
- Smith, M. R., Chai, R., Nguyen, H. T., Marcora, S. M., & Coutts, A. J. (2019). Comparing the Effects of Three Cognitive Tasks on Indicators of Mental Fatigue. *The Journal of Psychology*, 153(8), 759–783. <https://doi.org/10.1080/00223980.2019.1611530>

- Smith, M. R., Thompson, C., Marcora, S. M., Skorski, S., Meyer, T., & Coutts, A. J. (2018). Mental Fatigue and Soccer: Current Knowledge and Future Directions. *Sports Medicine*, 48(7), 1525. <https://doi.org/10.1007/s40279-018-0908-2>
- Sokhadze, E. M., Casanova, M. F., Casanova, E. L., Lamina, E., Kelly, D. P., & Khachidze, I. (2017). Event-related Potentials (ERP) in Cognitive Neuroscience Research and Applications. *NeuroRegulation*, 4(1), 14–14. <https://doi.org/10.15540/nr.4.1.14>
- Spijkers, W. A. C., & Walter, A. (1985). Response processing stages in choice reactions. *Acta Psychologica*, 58(2), 191–204. [https://doi.org/10.1016/0001-6918\(85\)90007-1](https://doi.org/10.1016/0001-6918(85)90007-1)
- Sun, H., Soh, K. G., Roslan, S., Wazir, M. R. W. N., & Soh, K. L. (2021). Does mental fatigue affect skilled performance in athletes? A systematic review. *PLOS ONE*, 16(10), e0258307. <https://doi.org/10.1371/journal.pone.0258307>
- Sun, L., Guo, Z., Yuan, X., Wang, X., Su, C., Jiang, J., & Li, X. (2022). An Investigation of the Effects of Brain Fatigue on the Sustained Attention of Intelligent Coal Mine VDT Operators. *International Journal of Environmental Research and Public Health*, 19(17), Article 17. <https://doi.org/10.3390/ijerph191711034>
- Szalma, J. L., Warm, J. S., Matthews, G., Dember, W. N., Weiler, E. M., Meier, A., & Eggemeier, F. T. (2004). Effects of sensory modality and task duration on performance, workload, and stress in sustained attention. *Human Factors*, 46(2), 219–234.
- Taylor, D. A. (1976). Stage analysis of reaction time. *Psychological Bulletin*, 83(2), 161–191. <https://doi.org/http://dx.doi.org.proxy.bib.uottawa.ca/10.1037/0033-2909.83.2.161>
- Thompson, T. (Director). (2015). *Uncharted – The Beautiful World of the Amazon* [Video recording]. Seedling Media.
- Van Cutsem, J., Marcora, S., De Pauw, K., Bailey, S., Meeusen, R., & Roelands, B. (2017). The Effects of Mental Fatigue on Physical Performance: A Systematic Review. *Sports Medicine*, 47(8), 1569–1588. <https://doi.org/10.1007/s40279-016-0672-0>
- van der Linden, D., & Eling, P. (2006). Mental fatigue disturbs local processing more than global processing. *Psychological Research*, 70(5), 395–402. <https://doi.org/10.1007/s00426-005-0228-7>
- van der Linden, D., Frese, M., & Meijman, T. F. (2003). Mental fatigue and the control of cognitive processes: Effects on perseveration and planning. *Acta Psychologica*, 113(1), 45–65. [https://doi.org/10.1016/S0001-6918\(02\)00150-6](https://doi.org/10.1016/S0001-6918(02)00150-6)
- Vickers, D., & Smith, P. L. (1986). The rationale for the inspection time index. *Personality and Individual Differences*, 7(5), 609–623. [https://doi.org/10.1016/0191-8869\(86\)90030-9](https://doi.org/10.1016/0191-8869(86)90030-9)
- Wiehler, A., Branzoli, F., Adanyeguh, I., Mochel, F., & Pessiglione, M. (2022). A neuro-metabolic account of why daylong cognitive work alters the control of economic

- decisions. *Current Biology*, 32(16), 3564-3575.e5.
<https://doi.org/10.1016/j.cub.2022.07.010>
- Williamson, A., Lombardi, D. A., Folkard, S., Stutts, J., Courtney, T. K., & Connor, J. L. (2011). The link between fatigue and safety. *Accident Analysis & Prevention, Advancing Fatigue and Safety Research*, 43(2), 498–515. <https://doi.org/10.1016/j.aap.2009.11.011>
- Wise, J. M., Heaton, K., & Patrician, P. (2019). Fatigue in Long-Haul Truck Drivers: A Concept Analysis. *Workplace Health & Safety*, 67(2), 68–77.
<https://doi.org/10.1177/2165079918800509>
- Zeuwts, L. H. R. H., Iliano, E., Smith, M., Deconinck, F., & Lenoir, M. (2021). Mental fatigue delays visual search behaviour in young cyclists when negotiating complex traffic situations: A study in virtual reality. *Accident Analysis & Prevention*, 161, 106387.
<https://doi.org/10.1016/j.aap.2021.106387>

Chapter 4. Experiment 3 - Task-Specific Impacts of Cognitive Fatigue on Subjective Experience and Psychomotor Performance

4.1 Abstract

Objective: To determine how cognitive fatigue (CF) affects subjective experience and reaction time (RT) performance across tasks with different processing demands (simple, go/no-go, choice), and whether these effects depend on the type of fatigue-inducing mental work.

Background: CF is a psychobiological state of subjective exhaustion from mental effort that can compromise workplace productivity and safety. Although slowed RT is an often-observed consequence of CF, it is unclear how this compares across RT paradigms and fatigue-inducing tasks. **Method:** Using a remotely administered experiment, 402 participants completed a 60-minute CF (Math-Memory, Stroop, Time Load Dual-Back) or control (documentary)

intervention. Subjective ratings (mental fatigue, motivation) and RT performance (simple, go/no-go, choice) were assessed pre- and post-intervention. **Results:** Relative to control, all CF tasks increased subjective fatigue ($p < .001$), while motivation declined following Dual-Back and Stroop ($p \leq .030$) but not Math-Memory. Simple and choice RT slowed significantly following all CF interventions vs control ($p < .010$), with the greatest choice-RT slowing after Stroop ($p \leq .032$). Only Stroop produced significant go/no-go RT slowing ($p = .004$). **Conclusion:** Subjective fatigue and simple RT were broadly sensitive to CF, indicating general psychomotor slowing.

Conversely, motivation and higher-complexity RT measures showed task specific effects, perhaps reflecting overlap between fatigue-inducing and RT task demands. **Application:** Task type is important when considering RT as a fatigue-assessment tool. These findings support multidimensional (subjective and RT) CF assessments and indicate that simple RT may be

effective for rapid, broad fatigue monitoring, whereas complex RT metrics may be useful when exploring task-specific executive processing effects.

4.2 Introduction

Cognitive fatigue (CF) is a transient psychobiological state arising from demanding mental effort, typically characterized by feelings of mental exhaustion (Ackerman, 2011; Behrens et al., 2023). CF is operationalized here as resulting from sustained, effortful, goal-directed activity requiring continuous cognitive control (“overload/active” CF), in contrast to fatigue sensations from low-demand, monotonous conditions (“underload/passive” CF; Desmond & Hancock, 2001; Pattyn et al., 2018). Active CF is widely experienced, including in occupations such as construction (Li et al., 2020; Zhang et al., 2023), transportation (Meng et al., 2015; Reis & Canhão, 2013), healthcare (Barker & Nussbaum, 2011; Petrut et al., 2020), and the military (Frone & Blais, 2019; Rabat et al., 2025). Although often perceived as routine, CF can have significant negative effects, including reduced focus (Boksem et al., 2005), impaired decision making (H. Jia et al., 2022), and slower reaction times (Langner et al., 2010; Peters et al., 2024).

Importantly, these effects translate into real-world consequences. In applied contexts, CF leads to notable productivity losses and economic costs, estimated at \$330 million annually in the US workforce (Keller et al., 2009; Ricci et al., 2007). CF contributes to increased workplace accident risk, including reduced hazard detection (~30-40%), slower responses to hazards (~20%), and riskier decision making in construction and mining (A. Jia et al., 2022; Li et al., 2019, 2020; Zhang et al., 2023). CF has additionally been linked to elevated road accident risk (Minusa et al., 2021; Mizuno et al., 2020) and impaired reaction time among drivers (e.g., slowing by ~17% in one study; Guo et al., 2016). Consistent with this, fatigue is estimated to contribute to 15-20% of serious road crashes, which may be particularly prevalent in professional

drivers where long work hours and high job demands increase exposure to CF (van Schagen, 2021). Further, for surgeons, a 3-4% increase in surgical complications can occur per additional work hour, potentially mediated by accumulating CF (Chan et al., 2009; Thomas et al., 2012).

Given its prevalence and impact, there is a growing interest in how CF can be empirically assessed to optimize detection and inform fatigue screening. Subjective measures, such as visual analog scales, are frequently used but often diverge from cognitive performance metrics and rely on accurate self-judgement (Karim et al., 2024; Kunasegaran et al., 2023), highlighting the need for objective CF indicators. These have included physiological and neurological metrics (e.g., pupillometry, EEG; Bafna & Hansen, 2021; Goodman et al., 2025). However, behavioural indices like reaction time may offer a simple and accessible alternative.

Reaction time (RT), the time between a stimulus onset and motor response, consistently slows under CF (Habay et al., 2021; Langner et al., 2010; Peters et al., 2022, 2024). Accordingly, brief RT-based fatigue assessments have been developed for applied contexts (e.g., healthcare, transportation), including the AlertMeter® (Ferguson et al., 2020; Sherry & Owen, 2022) and the NASA-PVT (Arsintescu et al., 2019). Such tools typically compare RT performance to an individual's baseline to index operator readiness.

Many RT-based assessments (like the PVT) use simple RT, involving a single stimulus-response pairing (Smith et al., 2019; Staiano et al., 2024). Simple RT is thought to reflect the speed of basic psychomotor processing, including stimulus detection, response preparation, and movement initiation (Donders, 1969; Lindemann & Fischer, 2023). CF-related slowing of simple RT suggests that these fundamental processes are sensitive to CF. However, more complex RT paradigms introduce additional cognitive demands: “go/no-go” RT tasks (where one stimulus requires a response, another that the response be withheld) emphasize inhibitory processing,

while choice RT paradigms (with multiple stimulus-response pairings) require added response selection (Eagle et al., 2008; Lindemann & Fischer, 2023; Spijkers & Walter, 1985). These tasks also demand greater cognitive flexibility and conflict monitoring compared to simple RT (Simola et al., 2017; Szmalec et al., 2008).

Because they engage differing executive processes, simple, go/no-go, and choice RT tasks may vary in sensitivity to CF. This presents an important limitation for applied and experimental contexts: although RT is widely used to index CF, it remains unclear how findings generalize across different RT paradigms, and whether they provide comparable or distinct information about fatigue-related performance changes. Accordingly, the first aim of this study is to compare CF effects across these RT tasks to determine whether differential effects exist. If so, this may identify psychomotor processes preferentially impacted by CF and inform the use of RT measures in operational and research settings.

The second aim is to explore how different cognitively demanding tasks – the Modified Incongruent Stroop (Pageaux et al., 2015; Stroop, 1935), Time Load Dual-Back (Borragán et al., 2016, 2017), and Math-Memory tasks (Peters et al., 2022, 2024) – influence subjective and RT-based CF measures. These tasks share overlapping demands such as sustained attention and response selection, but each also emphasizes distinct processes: the Stroop task primarily taxes inhibitory control, cognitive flexibility, and conflict monitoring (Heidlmayr et al., 2020; Tahamtan et al., 2025); the dual-back task requires continuous stimulus comparison and working-memory updating (Borragán et al., 2017; Wan et al., 2020); and the Math-Memory task emphasizes information maintenance and interference control across longer retention intervals while attention is divided (Hensen et al., 2024; Raghubar et al., 2010).

These distinctions allow examination of whether CF-related RT changes are general or depend on the overlap between the cognitive demands of the fatigue-inducing task and the RT paradigm. For example, a Stroop intervention (emphasizing inhibitory control) might preferentially impair performance requiring response inhibition, such as go/no-go RT. This aligns with resource-depletion frameworks, in which performance declines when shared, limited cognitive resources are taxed by simultaneous or successive demands (Parasuraman, 2000; Wickens, 1991). Demonstrating such *task-specific dependence* would indicate that CF does not simply produce general psychomotor slowing but can affect performance through interactions among specific executive functions (Persson et al., 2007, 2013; Van Cutsem et al., 2022).

While prior studies have compared CF interventions using measures such as subjective fatigue, physical endurance, and simple RT (Dallaway et al., 2022; O’Keeffe et al., 2020; Smith et al., 2019), it remains unclear how subjective sensations and multiple psychomotor processes respond to different CF-inducing tasks within the same experimental framework. Addressing this gap, the present study pursued two aims directly relevant to CF assessment: (1) to compare CF effects across RT paradigms reflecting varying psychomotor processes (simple, go/no-go, choice), and (2) to evaluate whether CF-related RT slowing depends on depletion of shared cognitive resources engaged by the preceding mental task. Together, these aims clarify CF’s impact on psychomotor performance, informing experimental and applied RT-based assessments of fatigue and operator readiness. This may be especially informative for safety-critical occupations, where even small RT delays can introduce substantial risk.

4.3 Materials and Methods

4.3.1 Participants

An a priori power analysis (power = .95, partial $\eta^2 = 0.025$) indicated that ~285 participants were needed (Peters et al., 2022, 2024). Data were collected from 500 volunteers to account for anticipated quality-control exclusions and increased variability associated with heterogeneous remote testing environments and varying levels of compliance. After screening, 402 healthy adults (mean age = 21.1 $\pm$ 5.5 years; 270 female) were retained. All participants reported normal or corrected-to-normal vision and no history of motor control disorders or chronic fatigue. This research was conducted in accordance with the Declaration of Helsinki and was approved by the University of Ottawa Research Ethics Board. All participants provided informed consent.

4.3.2 Study Design

This study followed a between-groups pre-test-post-test design. Testing was conducted remotely using a standalone LabVIEW® application. Participants completed a single ~90-minute session on their laptop or desktop computer in a quiet, interruption-free environment. Following eligibility screening and consent, participants completed a questionnaire capturing sex assigned at birth, age, handedness, sleep quantity and quality, caffeine intake (prior 12 hours), and recent mental/physical activity. The experiment then began, including (1) pre-intervention subjective ratings and RT tests; (2) a 60-minute cognitive (groups 1-3) or control (group 4) intervention; and (3) post-intervention subjective ratings and RT tests in identical order to baseline (Fig. 4.1). All responses were time-stamped for quality checks. *Appendix B.1* contains extended methodological details.

4.3.3 Subjective Ratings

Participants used their mouse/trackpad to move digital sliders along horizontal, linear, continuous visual analog scales rating cognitive fatigue level (0 = not at all mentally fatigued, 10 = extremely mentally fatigued) and motivation level (0 = motivated to succeed in the task, 10 = indifferent about the task) before and after the intervention (Michielsens et al., 2003).

4.3.4 Reaction Time Tasks

Participants performed 20 simple, 40 go/no-go, and 40 two-choice RT trials pre- and post-intervention, preceded by 10 baseline practice trials per task (blocked and randomised). Each RT trial began with a warning signal (“Get Ready”) above a black open circle for 1000 ms. This was followed by a 500-1500 ms variable foreperiod before the circle illuminated (imperative stimulus).

In the simple RT task, the circle illuminated blue, signalling a right index finger press of the “L” key. In the go/no-go RT task, the circle either illuminated blue (press “L”) or orange (withhold response). The same pattern was preserved in the choice RT task, except that orange stimuli signalled a left index finger press (“S” key). Go/no-go and choice stimulus options were presented randomly at equal frequency. Participants were instructed to respond as quickly and accurately as possible. Feedback (RT and errors) was displayed for 2500 ms after each trial.

4.3.5 Cognitive Interventions

Participants were randomly assigned to one of four 60-minute interventions: Modified Incongruent Stroop task (ST; Pageaux et al., 2015), Time Load Dual-Back task (DB; Borragán et al., 2016, 2017), Math-Memory dual-task (MM; Peters et al., 2022, 2024), or a “non-fatiguing” control (NF). All began with a ~2-3-minute instruction video (*Appendix E.2*). NF participants viewed a documentary (“Animal Language”, Baus & Farmer, 2005), providing a low-demand

comparison intended to minimise active cognitive control relative to the cognitive interventions. Cognitive interventions were adaptive, such that difficulty (available response time) was individually adjusted to maintain ~85% accuracy, encouraging continuous, high-load cognitive work (O’Keeffe et al., 2020; Staiano et al., 2024).

Math-Memory Dual-Task (MM). Adapted from Peters et al. (2022, 2024), the MM task combines working memory retention and math-based interference. Each trial presented 7 letters in sequence. While attempting to hold these letters in memory, participants completed a 45-second math task requiring selection of correct mathematical operators to complete presented equations, before inputting the letters recalled from the last-displayed letter sequence. The next trial then began with a new letter sequence.

Modified Incongruent Stroop Task (ST). Similar to that employed by Pageaux et al. (2015), this Stroop task targets selective attention and inhibitory control, while also requiring frequent task-set switching. Incongruent color-word stimuli (e.g., “RED” in blue font) were presented. When the font colour was blue, red, or green, participants were to report the font color via keypress. Conversely, when the font was yellow, participants instead selected the response key reflecting the word meaning.

Time Load Dual-Back Task (DB). This version of the dual-back task was based on that of Borragán and colleagues (2016, 2017) and involves frequent updating of working memory with task interference. Numbers and letters were presented alternately. If a number was presented, participants were required to indicate parity via keypress (Odd = “1”, Even = “2”). If a letter was presented, participants were instructed to press the space bar if that letter matched the one previously presented (n-back paradigm).

Table 4.1 Description of data set exclusion. A single data set may be flagged with multiple exclusion criteria; therefore, the number of flagged data sets exceeds the total number of data sets excluded. NF = Control, MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back, RT = reaction time.

Exclusion Criteria	Number of Data Sets Flagged ^a
NF duration outside 30-90 min	22
CF duration outside 50-70 min	42
RT task duration outside of mean ± 2.5 <i>SD</i>	1
MM/ST/DB task trials attempted < mean -2.5 <i>SD</i>	19
MM math attempts per trial < mean -2.5 <i>SD</i>	2
MM correct letters per trial ≤ 1	6
ST/DB accuracy ≤ 0.60	28
Total session duration outside 70-140 min	57
Total Number of Data Sets Excluded	98

4.5 Statistical Analysis

Baseline demographic and lifestyle measures were compared across groups using chi-square or Fisher's exact tests (where counts < 5) for categorical variables and Kruskal-Wallis tests for continuous variables.

Effects of CF on subjective and RT measures were analysed with linear mixed-effect models (LMMs) including fixed effects of timepoint (pre, post), intervention (MM, ST, DB, NF), and their interaction. Generalized LMMs (GLMMs) with a Poisson distribution (*log link*) estimated the log of the model-predicted mean RT error counts as a function of the predictors (same fixed effects as noted above).

To compare CF effects across RT task types (simple, choice, go/no-go), RT *change scores* (post-pre intervention) were analysed in an LMM with fixed effects of RT task type, intervention, and their interaction. The association between subjective fatigue change scores and RT change was tested with a similar LMM, adding subjective fatigue change score and its interactions as predictors.

All models included by-participant random intercepts to account for repeated measures. Fixed-effect significance was assessed using *F*-tests for LMMs and Wald chi-square tests for GLMMs (Fox & Weisberg, 2019; Kuznetsova et al., 2017). Holm-Bonferroni-corrected post hoc comparisons were applied (Lenth et al., 2021). Where possible, approximate Cohen's *d* (d_a) values were derived from model-based standardized mean differences with total model variance used for standardization (Lenth et al., 2021). Unstandardized effect sizes (incidence rate ratios and mean differences $\pm 95\%$ CI) are also reported (Pek & Flora, 2018). Additional analyses are presented in *Appendix B.3*.

4.6 Results

4.6.1 Baseline Demographic and Lifestyle Measures

Demographic and lifestyle measures did not differ between intervention groups in any variables assessed (all $p > .189$), indicating successful randomisation.

4.6.2 Subjective Ratings

Neither subjective fatigue nor motivation differed significantly between interventions at baseline (both $p > .241$). Subjective fatigue showed significant main effects of timepoint ($F(1, 398) = 505.72, p < .001$) and intervention ($F(3, 398) = 9.65, p < .001$) with a significant interaction ($F(3, 398) = 21.32, p < .001$). Subjective fatigue increased more pre- to post-test over the MM, ST, and DB interventions compared to NF (Table 4.2; Fig. 4.2a).

Task indifference (i.e., inverse of motivation) also demonstrated a significant main effect of timepoint ($F(1, 398) = 124.61, p < .001$) and a timepoint x intervention interaction ($F(3, 398) = 4.99, p = .002$). Indifference rose significantly more over ST and DB compared to NF, while no such effect was observed over the MM intervention (Table 4.2; Fig. 4.2b). No significant differences in either subjective measure were observed between cognitive tasks (MM, ST, DB).

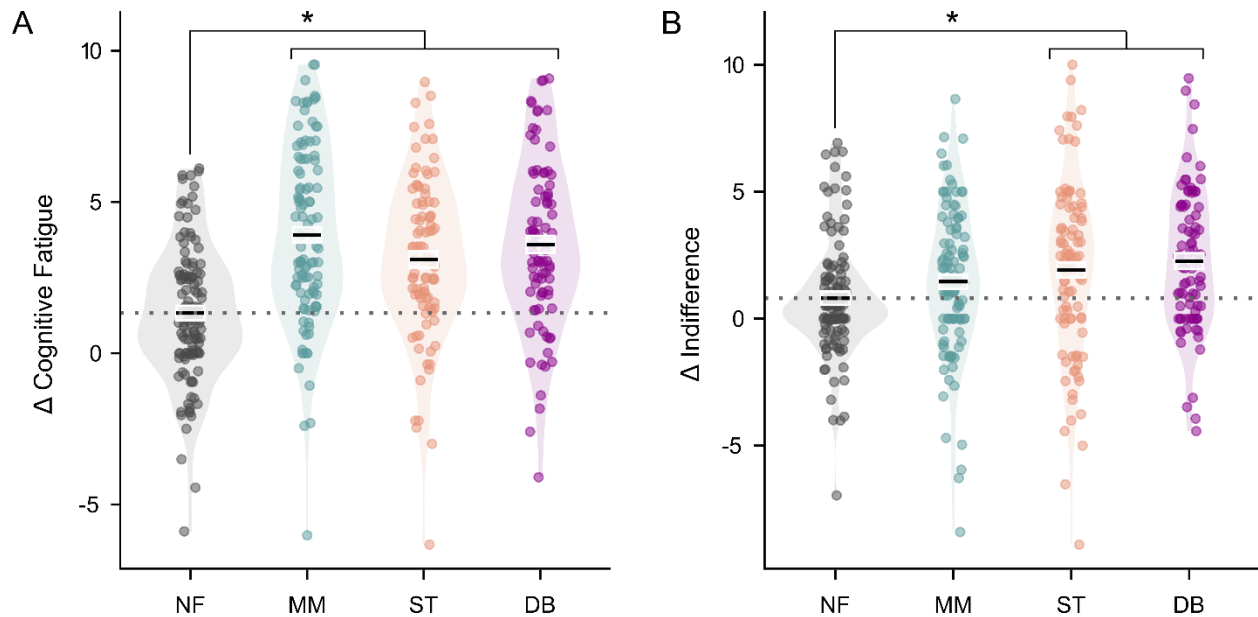


Fig. 4.2 Model-estimated mean pre- to post-intervention change in subjective ratings. Black bars show mean (a) cognitive fatigue and (b) indifference (original scale = 0-10). White areas above and below the black bars show *SE*, dotted line indicates Control (NF) mean, and points show individual data with violin distributions. NF = Control, MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back.

4.6.3 Reaction Time

RT did not differ between interventions at baseline within any RT task (all $p > .943$). For simple RT, a significant main effect of timepoint emerged ($F(1, 13890) = 318.07, p < .001$) alongside a timepoint x intervention interaction ($F(3, 13891) = 5.55, p < .001$). Simple RT slowed more

following the MM, ST, and DB interventions compared to NF (Table 4.2), with no significant differences among the cognitive tasks (Fig. 4.3a).

Go/no-go RT also showed a significant main effect of timepoint ($F(1, 14850) = 92.70, p < .001$) and a timepoint x intervention interaction ($F(3, 14850) = 4.18, p = .006$). Relative to NF, go/no-go RT only slowed significantly following ST (Table 4.2); however, ST changes did not significantly differ from MM and DB (Fig. 4.3b).

Choice RT exhibited a significant main effect of timepoint ($F(1, 28074) = 144.98, p < .001$) and a significant timepoint x intervention interaction ($F(3, 28074) = 26.50, p < .001$). Choice RT slowed significantly more over MM, ST, and DB compared to NF (Table 4.2). Slowing was greater following ST vs. MM ($\Delta = +9.55$ ms, 95% CI [0.67, 18.42], $p = .014, d_a = 0.08$) and DB ($\Delta = +8.42$ ms, 95% CI [-0.82, 17.66], $p = .032, d_a = 0.07$), while MM and DB did not significantly vary (Fig. 4.3c).

Although simple RT demonstrated a slightly greater *absolute* pre- to post-test increase across cognitive interventions (simple: $M = 22.3$ ms, $SD = 38.9$ ms; go/no-go: $M = 18.2$ ms, $SD = 48.5$ ms; choice: $M = 19.5$ ms, $SD = 59.1$ ms), and choice RT the largest increase when considered relative to NF (Table 4.2), RT change scores did not significantly depend on RT task type regardless of the CF intervention (interaction: $F(4, 536) = 0.08, p = .989$). Further, no significant associations were found between subjective fatigue change and RT change (main effect of subjective fatigue change: $F(1, 378) = 0.33, p = .564$; no significant interactions).

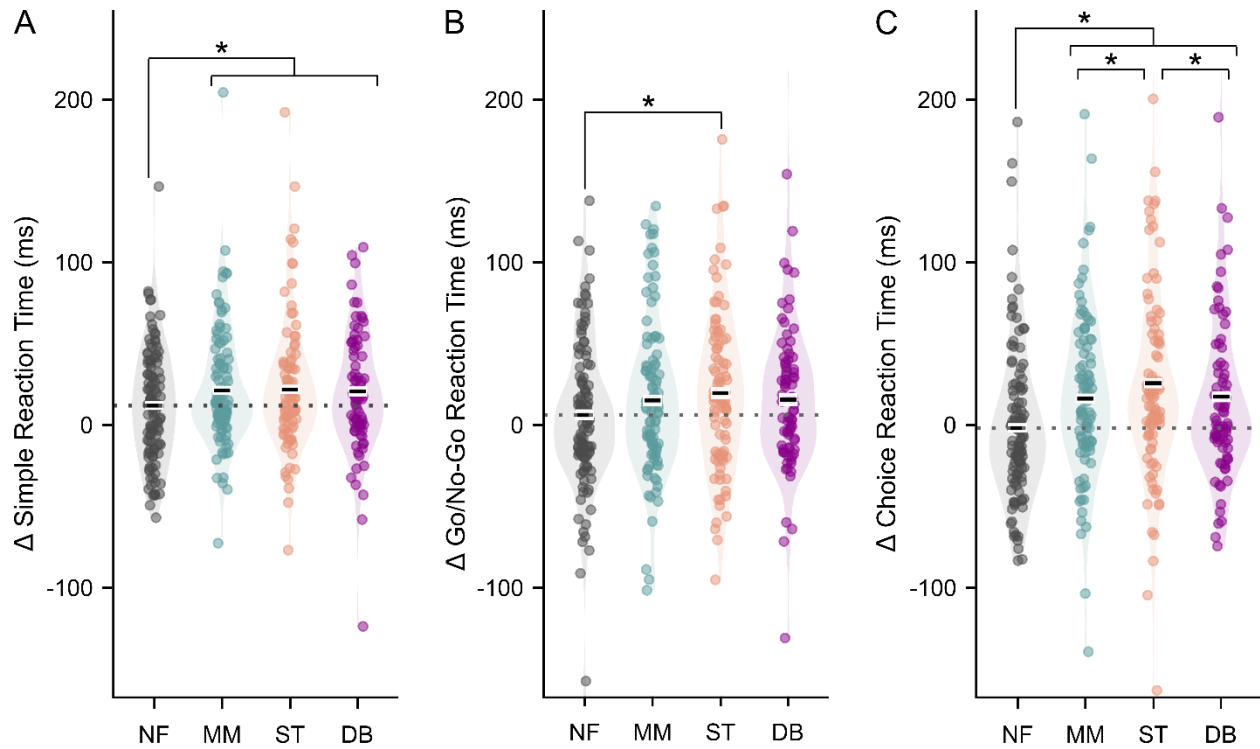


Fig. 4.3 Model-estimated mean pre- to post-intervention change in reaction time. Black bars show mean (a) simple, (b) go/no-go, and (c) choice reaction time (ms). White areas above and below the black bars show *SE*, dotted line indicates Control (NF) mean, and points show individual data with violin distributions. Y-axis is truncated to facilitate visualization (0.78% data points not shown). NF = Control, MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back.

Table 4.2 Post hoc comparisons vs. control for subjective ratings and reaction time. NF = Control, MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back, RT = reaction time; Δ indicates pre- to post-intervention change.

	Difference	95% CI	<i>p</i>	<i>d_a</i>
<i>Subjective Fatigue Ratings</i>				
Δ MM vs. NF	+2.58	[1.64, 3.52]	< .001	1.13
Δ ST vs. NF	+1.77	[0.80, 2.73]	< .001	0.78
Δ DB vs. NF	+2.26	[1.27, 3.26]	< .001	0.99
<i>Task Indifference Ratings</i>				
Δ MM vs. NF	+0.66	[-0.36, 1.67]	.270	0.26
Δ ST vs. NF	+1.11	[0.06, 2.16]	.030	0.44
Δ DB vs. NF	+1.46	[0.38, 2.55]	.002	0.58
<i>Simple Reaction Time (ms)</i>				
Δ MM vs. NF	+9.38	[1.88, 16.88]	.005	0.13
Δ ST vs. NF	+9.94	[2.28, 17.59]	.004	0.14
Δ DB vs. NF	+8.76	[0.87, 16.65]	.014	0.12
<i>Go/No-Go RT Reaction Time (ms)</i>				
Δ MM vs. NF	+8.89	[-1.43, 19.22]	.115	0.08
Δ ST vs. NF	+13.43	[2.93, 23.93]	.004	0.13
Δ DB vs. NF	+9.39	[-1.55, 20.33]	.115	0.09
<i>Choice RT Reaction Time (ms)</i>				
Δ MM vs. NF	+18.03	[9.57, 26.50]	<.001	0.15
Δ ST vs. NF	+27.58	[19.05, 36.12]	<.001	0.23
Δ DB vs. NF	+19.16	[10.32, 28.00]	<.001	0.16

4.6.4 Reaction Time Task Errors

The prevalence of go/no-go commission errors increased significantly pre- to post-test across interventions ($\chi^2(1) = 28.23, p < .001$; ratio post/pre = 1.41, 95% CI [1.24, 1.61]; Fig. 4.4a).

The prevalence of choice errors showed a significant timepoint x intervention interaction ($\chi^2(3) = 33.18, p < .001$). Choice errors increased significantly following MM (ratio post/pre = 1.34, 95% CI [1.16, 1.53], $p < .001$), rose but did not significantly change over DB (ratio post/pre = 1.11, 95% CI [0.92, 1.34], $p = .277$), and decreased following ST (ratio post/pre = 0.78, 95% CI [0.66, 0.93], $p = .004$) and NF (ratio post/pre = 0.83, 95% CI [0.72, 0.95], $p = .007$). Accordingly, choice errors increased more following MM compared to ST (ratio = 1.71, 95% CI [1.27, 2.30], $p < .001$) and NF (ratio = 1.62, 95% CI [1.24, 2.11], $p < .001$), and following DB compared to ST (ratio = 1.42, 95% CI [1.01, 2.00], $p = .026$) and NF (ratio = 1.35, 95% CI [0.98, 1.84], $p = .039$; Fig. 4.4b).

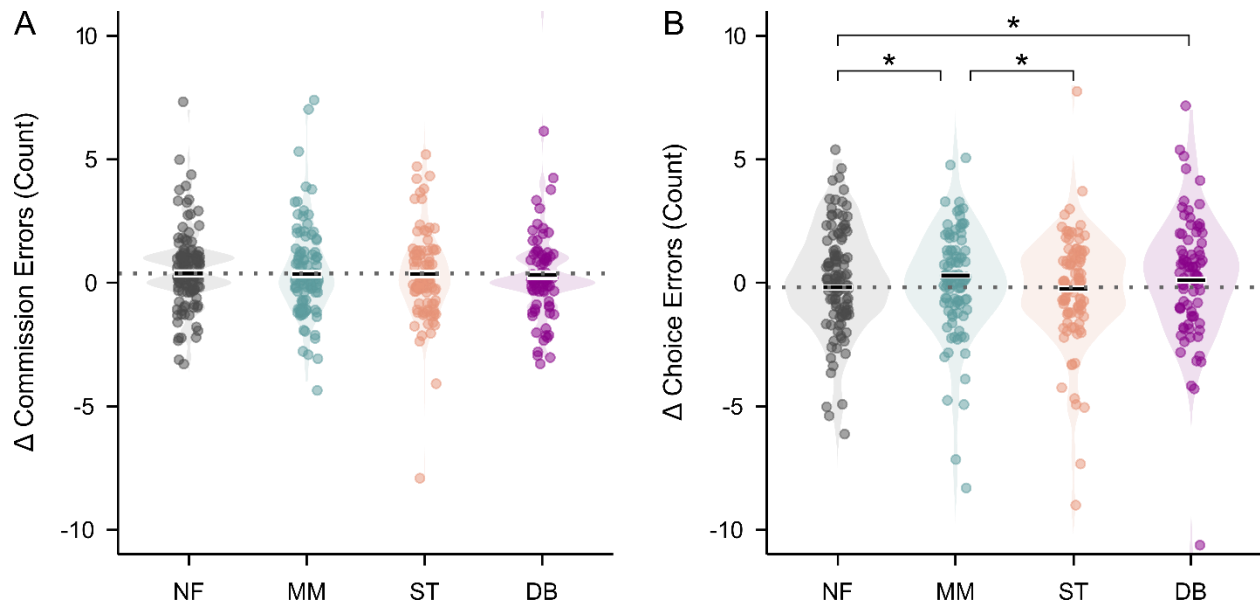


Fig. 4.4 Model-estimated mean pre- to post-intervention change in reaction time task error count.

Black bars show mean count of (a) go/no-go RT commission errors and (b) choice RT errors.

White areas above and below the black bars show *SE*, dotted line indicates Control (NF) mean, and points show individual data with violin distributions. Y-axis is truncated to facilitate visualization (1.89% data points not shown). NF = Control, MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back.

4.7 Discussion

This study investigated the effects of three cognitive interventions (MM, ST, DB) on subjective fatigue-related states and psychomotor performance across RT tasks with varying processing demands (simple, go/no-go, choice). Broadly, CF impacted both subjective and objective measures in task-specific ways: simple RT and subjective fatigue were impacted similarly across cognitive interventions, whereas motivation and choice RT depended on the preceding cognitive task demands. These findings provide insight into CF's effects on psychomotor processing and inform fatigue assessment for experimental and applied contexts.

4.7.1 Task-Specific Effects of CF on RT Performance

RT responses to CF varied by RT task and cognitive intervention. Consistent with prior findings, simple RT slowed across all cognitive interventions ($\sim +21$ ms) relative to control, suggesting generalized fatigue-related slowing of the core sensorimotor processes underlying simple RT, including preparation, stimulus perception, and response initiation (Lindemann & Fischer, 2023). Although modest, this effect was robust across fatiguing tasks (Fig. 4.3a).

In contrast, go/no-go RT increased relative to control only after ST; however, this effect did not differ from increases over MM and DB (Fig. 4.3b). Commission errors increased significantly pre- to post-intervention, but this occurred across *both* CF and control conditions, implying a general time-on-task effect rather than a CF-specific one (Fig. 4.4a). These results, possibly excepting the ST condition, align with prior reports of null go/no-go effects under comparable conditions (Magnuson et al., 2021).

Like simple RT, choice RT slowed following all CF interventions versus control. However, the extent of this slowing varied by intervention, with the largest increase occurring after ST (Fig. 4.3c). Interestingly, post-ST slowing was accompanied by *fewer* choice errors, whereas DB and MM interventions led to slower responses and *more* errors (Fig. 4.4b). Consistent with previous evidence of altered response strategies in CF (Rozand et al., 2015; Salomone et al., 2021; Wiehler et al., 2022), these results suggest a strategy shift unique to ST, toward prioritization of accuracy over speed. This may reflect a compensatory reallocation of reduced cognitive resources to preserve task accuracy (Badarin et al., 2025; C. Wang et al., 2016). Such an effect may be reinforced by the Stroop task's high conflict-monitoring demands, which can upregulate proactive control (Kerns et al., 2004; Ridderinkhof et al., 2004). This upregulation may persist into subsequent tasks with overlapping executive processes and, in the

choice RT task, manifest as increased response thresholds. In turn, this could promote more cautious, accurate responding at the cost of speed (Mattes et al., 2022).

Broadly, these findings suggest that while simple RT was consistently impaired across fatiguing interventions relative to control, choice RT (and to a lesser extent go/no-go RT) showed more task-specific patterns, particularly following ST. Although it is uncertain why task-specific effects were particular to ST (beyond the possible strategic shift described above), one explanation is the extent to which the fatigue-inducing and RT tasks draw on shared cognitive resources (Persson et al., 2007, 2013; Van Cutsem et al., 2022). This interpretation aligns with a resource-depletion framework, where performance declines when limited cognitive resources are recruited by simultaneous or subsequent tasks (Parasuraman, 2000; Wickens, 1991). The ST intervention – which emphasizes inhibitory control, conflict monitoring, and cognitive flexibility – may therefore have produced greater interference with subsequent tasks emphasizing similar requirements, such as go/no-go and (to a greater extent) choice RT. Neuroimaging evidence supports this, showing that go/no-go, choice, and ST tasks activate similar frontoparietal executive regions, including the dorsolateral prefrontal (Friebs et al., 2020; Isfahani et al., 2025) and anterior cingulate cortex (Braver et al., 2001; Heidlmayr et al., 2020).

4.7.2 Subjective Ratings

Subjective fatigue rose similarly across cognitive interventions compared to control (Fig. 4.2) but did not correlate with fatigue-related RT changes. This aligns with previous findings reporting poor or inconsistent associations between self-reported fatigue and objective performance (Matsui et al., 2024; Walker et al., 2012). Some evidence suggests fatigue sensations could precede performance declines, perhaps due to compensatory recruitment of facilitatory frontoparietal networks (Badarin et al., 2025; C. Wang et al., 2016). In other cases, the reverse

has been suggested, including fatigue “perceptual blindness” (i.e., performance decrements without self-reported fatigue) observed in mine workers (Purto et al., 2024).

Notably, while all interventions increased subjective CF, only ST and DB reduced motivation relative to control, whereas MM did not. This suggests that demotivation is not inevitable in CF (Gergelyfi et al., 2015). While beyond the scope of this analysis, identifying which MM task attributes minimize demotivation could be valuable for research, workplace, or rehabilitation contexts where it may be important to sustain motivation despite elevated fatigue sensations.

4.7.3 Practical Implications for Research and Human Factors

The present findings suggest that simple RT may offer advantages as a behavioural index of CF: it is simple and quick to test and appears sensitive to generalized CF effects rather than task-specific influences. Conversely, choice RT introduces interpretive complexity as a fatigue measure due to its sensitivity to the cognitive demands of the preceding, fatigue-inducing task. This suggests that choice RT may be more appropriately used when task-specific executive impacts, rather than general fatigue detection, are of interest. Notably, results also underscore the importance of assessing both objective and subjective CF, as they do not always align and may capture distinct components of the fatigue experience (Behrens et al., 2023).

Moreover, this study indicates that selection of experimental CF-inducing interventions is nuanced. All cognitive interventions induced subjective fatigue, yet most other outcome measures varied. DB and ST reduced motivation relative to control, while MM produced generalized RT slowing and increased subjective fatigue without significant demotivation. Overall, this suggests that the MM intervention may present a balanced method for experimentally eliciting CF while maintaining engagement levels comparable to control.

Compared to DB and ST, MM may also better approximate CF in high-stake operational contexts where motivation is preserved despite accumulating cognitive load (Kim & Beehr, 2018; Whelehan et al., 2021). It is also notable that adaptive difficulty adjustments appeared to enhance CF effects on RT relative to earlier *non-adaptive* implementations of the MM task (~22.3 ms, compared to <10 ms; Peters et al., 2024). This is consistent with evidence that individualized, dynamic task difficulty may more effectively induce experimental CF (O’Keeffe et al., 2020; Staiano et al., 2024).

Practically, these findings are likely most applicable to brief, intermittent fatigue assessments rather than continuous monitoring, which may be impractical or disruptive in safety-critical environments (Brossoit et al., 2023; Ferris et al., 2021). Short RT-based tools (~1.5-5 minutes, e.g., AlertMeter®) are already implemented in applied settings, typically administered pre/post-duty or during breaks, often using smartphone or smartwatch devices (Ferguson et al., 2020; Ferris et al., 2021; Rogers et al., 2023; Sherry & Owen, 2022; Talebi et al., 2026; Weetman et al., 2024). Within this framework, the current findings support simple RT as a feasible, low-burden indicator of CF. However, they also indicate that more complex RT assessment paradigms, while potentially sensitive to task-specific effects, should be validated carefully within the intended operational context. Where feasible, subjective fatigue measures should be included alongside RT to ensure comprehensive CF evaluation. Finally, these results may also inform the development of non-RT based CF indicators, such as predictive models and physiological indices, where RT is a common metric used to validate their success (Guo et al., 2016; Naeeri et al., 2021; H. Wang et al., 2018).

4.7.4 Limitations

This study was conducted virtually and was unsupervised, increasing accessibility and sample size, but reducing experimental control. Participant compliance to instructions could not be technically enforced or verified beyond data screening procedures, and environmental factors (e.g., lighting, ambient noise, device-related variability) were not standardized. In line with this, RT variability was high across participants (Fig. 4.3). Several steps were taken to maximize quality control, including clear in-task instructions, time-stamping and data screening, as well as the use of mixed-effect models with by-participant random intercepts (which improve robustness over traditional ANOVA approaches for unbalanced or noisy data; Yu et al., 2022). However, some uncontrolled variance related to these factors presumably remained.

Further, CF interventions differed by trial structure and stimulus pacing, making it difficult to attribute differences in subjective or behavioural outcomes solely on differing cognitive processes. Also, the control intervention did not fully prevent mild fatigue (Fig. 4.2), consistent with prior studies reporting small increases in subjective fatigue under similar conditions (e.g., Daneshgar-Pironneau et al., 2025; Jacquet et al., 2024). Therefore, while the NF intervention appeared to be an adequate control (as significant effects relative to control were detectable), it may not have been optimal. Developing more effective control paradigms with lower cognitive load remains an open challenge in CF research.

Finally, the sample comprised only healthy young adults. RT has been shown to be slower and more variable in children and older adults (Deary & Der, 2005; Dykiert et al., 2012), and behavioural, subjective, and neural responses to CF may vary with age and clinical status (Aoun Sebaiti et al., 2022; Hu et al., 2025; Samuel et al., 2019). As such, exploring similar questions in more diverse populations is needed to ensure inclusive CF assessment.

4.8 Conclusion

This study demonstrates that CF is multifaceted, impacting both subjective experience and psychomotor performance, often in complex ways. RT was generally slowed in CF – a notable risk factor in contexts where the potential for CF and the risks of slowed responses are high. While basic psychomotor processes captured by simple RT are widely vulnerable to fatigue, more specific CF effects emerge when additional processing demands (e.g., response selection, cognitive flexibility) are introduced and overlap with the preceding fatiguing effort. Thus, both the type of CF-inducing work and the nature of performance measures can critically impact the observed fatigue profile. For human factors applications, results support a multidimensional CF assessment approach, using simple RT when the goal is rapid assessment of overall performance decline, but more complex RT metrics (e.g., choice RT) when the objective is to understand task-specific interactions with specific executive demands. These findings clarify how CF impacts psychomotor processing in both general and task-specific ways, informing approaches to assess CF and mitigate its impact on human performance and safety.

4.9 References

- Ackerman, P. L. (2011). 100 years without resting. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 11–43). American Psychological Association. <https://doi.org/10.1037/12343-001>
- Aoun Sebaiti, M., Hainselin, M., Gounden, Y., Sirbu, C. A., Sekulic, S., Lorusso, L., Nacul, L., & Authier, F. J. (2022). Systematic review and meta-analysis of cognitive impairment in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). *Scientific Reports*, *12*(1), 2157. <https://doi.org/10.1038/s41598-021-04764-w>
- Arsintescu, L., Kato, K. H., Cravalho, P. F., Feick, N. H., Stone, L. S., & Flynn-Evans, E. E. (2019). Validation of a touchscreen psychomotor vigilance task. *Accident Analysis & Prevention*, *126*, 173–176. <https://doi.org/10.1016/j.aap.2017.11.041>
- Badarin, A. A., Antipov, V. M., Grubov, V. V., Andreev, A. V., Pitsik, E. N., Kurkin, S. A., & Hramov, A. E. (2025). Brain Compensatory Mechanisms During the Prolonged Cognitive Task: fNIRS and Eye-Tracking Study. *IEEE Transactions on Cognitive and Developmental Systems*, *17*(2), 303–314. <https://doi.org/10.1109/TCDS.2024.3453590>
- Bafna, T., & Hansen, J. P. (2021). Mental fatigue measurement using eye metrics: A systematic literature review. *Psychophysiology*, *58*(6), e13828. <https://doi.org/10.1111/psyp.13828>
- Barker, L. M., & Nussbaum, M. A. (2011). Fatigue, performance and the work environment: A survey of registered nurses. *Journal of Advanced Nursing*, *67*(6), 1370–1382. <https://doi.org/10.1111/j.1365-2648.2010.05597.x>
- Baus, E., & Farmer, J. (Directors). (2005). “*Animals Like Us*” *Animal Language (TV Episode)*—IMDb [Video recording]. <http://www.imdb.com/title/tt4504660/fullcredits>
- Behrens, M., Gube, M., Chaabene, H., Prieske, O., Zenon, A., Broscheid, K.-C., Schega, L., Husmann, F., & Weippert, M. (2023). Fatigue and Human Performance: An Updated Framework. *Sports Medicine*, *53*(1), 7–31. <https://doi.org/10.1007/s40279-022-01748-2>
- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2005). Effects of mental fatigue on attention: An ERP study. *Cognitive Brain Research*, *25*(1), 107–116. <https://doi.org/10.1016/j.cogbrainres.2005.04.011>
- Borragán, G., Slama, H., Bartolomei, M., & Peigneux, P. (2017). Cognitive fatigue: A Time-based Resource-sharing account. *Cortex*, *89*, 71–84. <https://doi.org/10.1016/j.cortex.2017.01.023>
- Borragán, G., Slama, H., Destrebecqz, A., & Peigneux, P. (2016). Cognitive fatigue facilitates procedural sequence learning. *Frontiers in Human Neuroscience*, *10*. <https://doi.org/10.3389/fnhum.2016.00086>

- Braver, T. S., Barch, D. M., Gray, J. R., Molfese, D. L., & Snyder, A. (2001). Anterior Cingulate Cortex and Response Conflict: Effects of Frequency, Inhibition and Errors. *Cerebral Cortex*, 11(9), 825–836. <https://doi.org/10.1093/cercor/11.9.825>
- Brossoit, R. M., Crain, T. L., Stevens, S. C., Wong, J. R., & Guasta, L. (2023). Alert at Work? Perceptions of Alertness Testing and Recommendations for Practitioners. *Occupational Health Science*, 7(2), 379–396. <https://doi.org/10.1007/s41542-022-00139-3>
- Chan, M. Y., Cohen, H., & Spiegel, B. M. R. (2009). Fewer Polyps Detected by Colonoscopy as the Day Progresses at a Veteran’s Administration Teaching Hospital. *Clinical Gastroenterology and Hepatology*, 7(11), 1217–1223. <https://doi.org/10.1016/j.cgh.2009.07.013>
- Dallaway, N., Lucas, S. J. E., & Ring, C. (2022). Cognitive tasks elicit mental fatigue and impair subsequent physical task endurance: Effects of task duration and type. *Psychophysiology*, 59(12). <https://doi.org/10.1111/psyp.14126>
- Daneshgar-Pironneau, S., Audiffren, M., Benraïss, A., Métais, A., & André, N. (2025). Mental fatigue impairs endurance performance in a time-to-exhaustion handgrip task: Psychophysiological markers of effort engagement dynamics. *Frontiers in Psychology*, 16. <https://doi.org/10.3389/fpsyg.2025.1611135>
- Deary, I. J., & Der, G. (2005). Reaction Time, Age, and Cognitive Ability: Longitudinal Findings from Age 16 to 63 Years in Representative Population Samples. *Aging, Neuropsychology, and Cognition*, 12(2), 187–215. <https://doi.org/10.1080/13825580590969235>
- Desmond, P. A., & Hancock, P. A. (2001). Active and Passive Fatigue States. In P. A. Desmond & P. A. Hancock (Eds.), *Stress, Workload, and Fatigue* (pp. 455–465). CRC Press. <https://doi.org/10.1201/b12791-3.1>
- Donders, F. C. (1969). On the speed of mental processes. *Acta Psychologica*, 30, 412–431. [https://doi.org/10.1016/0001-6918\(69\)90065-1](https://doi.org/10.1016/0001-6918(69)90065-1)
- Dykiert, D., Der, G., Starr, J. M., & Deary, I. J. (2012). Age Differences in Intra-Individual Variability in Simple and Choice Reaction Time: Systematic Review and Meta-Analysis. *PLOS ONE*, 7(10), e45759. <https://doi.org/10.1371/journal.pone.0045759>
- Eagle, D. M., Bari, A., & Robbins, T. W. (2008). The neuropsychopharmacology of action inhibition: Cross-species translation of the stop-signal and go/no-go tasks. *Psychopharmacology*, 199(3), 439–456. <https://doi.org/10.1007/s00213-008-1127-6>
- Ferguson, B. A., Lauriski, D. R., Huecker, M., Wichmann, M., Shreffler, J., & Shoff, H. (2020). Testing Alertness of Emergency Physicians: A Novel Quantitative Measure of Alertness and Implications for Worker and Patient Care. *The Journal of Emergency Medicine*, 58(3), 514–519. <https://doi.org/10.1016/j.jemermed.2019.10.032>
- Ferris, M., Bowles, K.-A., Bray, M., Bosley, E., Rajaratnam, S. M. W., & Wolkow, A. P. (2021). The impact of shift work schedules on PVT performance in naturalistic settings: A

- systematic review. *International Archives of Occupational and Environmental Health*, 94(7), 1475–1494. <https://doi.org/10.1007/s00420-021-01668-0>
- Fox, J., & Weisberg, S. (2019). *An R companion to applied regression* (Third edition). Sage.
- Friebs, M. A., Klaus, J., Singh, T., Frings, C., & Hartwigsen, G. (2020). Perturbation of the right prefrontal cortex disrupts interference control. *NeuroImage*, 222, 117279. <https://doi.org/10.1016/j.neuroimage.2020.117279>
- Frone, M. R., & Blais, A.-R. (2019). Work Fatigue in a Non-Deployed Military Setting: Assessment, Prevalence, Predictors, and Outcomes. *International Journal of Environmental Research and Public Health*, 16(16), Article 16. <https://doi.org/10.3390/ijerph16162892>
- Gergelyfi, M., Jacob, B., Olivier, E., & Zénon, A. (2015). Dissociation between mental fatigue and motivational state during prolonged mental activity. *Frontiers in Behavioral Neuroscience*, 9, 176. <https://doi.org/10.3389/fnbeh.2015.00176>
- Goodman, S. P. J., Collins, B., Shorter, K., Moreland, A. T., Papic, C., Hamlin, A. S., Kassman, B., & Marino, F. E. (2025). Approaches to inducing mental fatigue: A systematic review and meta-analysis of (neuro)physiologic indices. *Behavior Research Methods*, 57(4), 1–29. <https://doi.org/10.3758/s13428-025-02620-7>
- Guo, M., Li, S., Wang, L., Chai, M., Chen, F., & Wei, Y. (2016). Research on the Relationship between Reaction Ability and Mental State for Online Assessment of Driving Fatigue. *International Journal of Environmental Research and Public Health*, 13(12), 1174. <https://doi.org/10.3390/ijerph13121174>
- Habay, J., Van Cutsem, J., Verschueren, J., De Bock, S., Proost, M., De Wachter, J., Tassignon, B., Meeusen, R., & Roelands, B. (2021). Mental Fatigue and Sport-Specific Psychomotor Performance: A Systematic Review. *Sports Medicine*, 51(7), 1527–1548. <https://doi.org/10.1007/s40279-021-01429-6>
- Heidlmayr, K., Kihlstedt, M., & Isel, F. (2020). A review on the electroencephalography markers of Stroop executive control processes. *Brain and Cognition*, 146, 105637. <https://doi.org/10.1016/j.bandc.2020.105637>
- Hensen, S., Koch, I., & Hirsch, P. (2024). Impact of process interference on memory encoding and retrieval processes in dual-task situations. *Memory & Cognition*, 52(6), 1246–1262. <https://doi.org/10.3758/s13421-024-01539-2>
- Hu, T., Wang, F., Duan, Q., Zhao, X., & Yang, F. (2025). Prevalence of fatigue and perceived fatigability in older adults: A systematic review and meta-analysis. *Scientific Reports*, 15(1), 4818. <https://doi.org/10.1038/s41598-025-88961-x>
- Isfahani, S. A., McGurrin, P., Vial, F., & Hallett, M. (2025). Patterns of brain activity in choice or instructed go and no-go tasks. *Experimental Brain Research*, 243(3), 1–10. <https://doi.org/10.1007/s00221-025-07027-6>

- Jacquet, T., Poulin-Charronnat, B., Bard, P., & Lepers, R. (2024). Effect of mental fatigue on hand force production capacities. *PLOS ONE*, 19(4), e0298958. <https://doi.org/10.1371/journal.pone.0298958>
- Jia, A., Guo, X., & Tian, S. (2022). Experimental study on the influence of mental fatigue on risk decision-making of miners. *Scientific Reports*, 12(1), 11902. <https://doi.org/10.1038/s41598-022-14045-9>
- Jia, H., Lin, C. J., & Wang, E. M. (2022). Effects of mental fatigue on risk preference and feedback processing in risk decision-making. *Scientific Reports*, 12(1), 10695. <https://doi.org/10.1038/s41598-022-14682-0>
- Karim, E., Pavel, H. R., Nikanfar, S., Hebri, A., Roy, A., Nambiappan, H. R., Jaiswal, A., Wylie, G. R., & Makedon, F. (2024). Examining the Landscape of Cognitive Fatigue Detection: A Comprehensive Survey. *Technologies*, 12(3), 38. <https://doi.org/10.3390/technologies12030038>
- Keller, S. M., Berryman, P., & Lukes, E. (2009). Effects of Extended Work Shifts and Shift Work on Patient Safety, Productivity, and Employee Health. *AAOHN Journal*, 57(12), 497–504. <https://doi.org/10.1177/216507990905701204>
- Kerns, J. G., Cohen, J. D., MacDonald, A. W., Cho, R. Y., Stenger, V. A., & Carter, C. S. (2004). Anterior Cingulate Conflict Monitoring and Adjustments in Control. *Science*, 303(5660), 1023–1026. <https://doi.org/10.1126/science.1089910>
- Kim, M., & Beehr, T. A. (2018). Challenge and hindrance demands lead to employees' health and behaviours through intrinsic motivation. *Stress & Health*, 34(3), 367–378. (131189828). <https://doi.org/10.1002/smi.2796>
- Kunasegaran, K., Ismail, A. M. H., Ramasamy, S., Gnanou, J. V., Caszo, B. A., & Chen, P. L. (2023). Understanding mental fatigue and its detection: A comparative analysis of assessments and tools. *PeerJ*, 11, e15744. <https://doi.org/10.7717/peerj.15744>
- Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, 82, 1–26. <https://doi.org/10.18637/jss.v082.i13>
- Langner, R., Steinborn, M. B., Chatterjee, A., Sturm, W., & Willmes, K. (2010). Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychologica*, 133(1), 64–72. <https://doi.org/10.1016/j.actpsy.2009.10.001>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Li, J., Li, H., Umer, W., Wang, H., Xing, X., Zhao, S., & Hou, J. (2020). Identification and classification of construction equipment operators' mental fatigue using wearable eye-

- tracking technology. *Automation in Construction*, 109, 103000. <https://doi.org/10.1016/j.autcon.2019.103000>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835. <https://doi.org/10.1016/j.autcon.2019.102835>
- Lindemann, O., & Fischer, M. H. (2023). Chronometric methods: Reaction times and movement times. In A. Felisatti & M.H. Fischer (Eds.), *Experimental Methods in Embodied Cognition* (pp. 37-48). Routledge.
- Magnuson, J. R., Doesburg, S. M., & McNeil, C. J. (2021). Development and recovery time of mental fatigue and its impact on motor function. *Biological Psychology*, 161, 108076. <https://doi.org/10.1016/j.biopsycho.2021.108076>
- Matsui, T., Takahashi, S., Ochi, G., Yoshitake, S., Funabashi, D., Matsuoka, H., Kagesawa, J., Dobashi, S., Yoshimoto, H., Sakairi, Y., & Takagi, H. (2024). Cognitive decline with pupil constriction independent of subjective fatigue during prolonged esports across player expertise levels. *Computers in Human Behavior*, 156, 108219. <https://doi.org/10.1016/j.chb.2024.108219>
- Mattes, A., Porth, E., & Stahl, J. (2022). Linking neurophysiological processes of action monitoring to post-response speed-accuracy adjustments in a neuro-cognitive diffusion model. *NeuroImage*, 247, 118798. <https://doi.org/10.1016/j.neuroimage.2021.118798>
- Meng, F., Li, S., Cao, L., Li, M., Peng, Q., Wang, C., & Zhang, W. (2015). Driving Fatigue in Professional Drivers: A Survey of Truck and Taxi Drivers. *Traffic Injury Prevention*, 16(5), 474–483. <https://doi.org/10.1080/15389588.2014.973945>
- Michielsen, H. J., De Vries, J., & Van Heck, G. L. (2003). Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *Journal of Psychosomatic Research*, 54(4), 345–352. [https://doi.org/10.1016/S0022-3999\(02\)00392-6](https://doi.org/10.1016/S0022-3999(02)00392-6)
- Minusa, S., Mizuno, K., Ojiro, D., Tanaka, T., Kuriyama, H., Yamano, E., Kuratsune, H., & Watanabe, Y. (2021). Increase in rear-end collision risk by acute stress-induced fatigue in on-road truck driving. *PLOS ONE*, 16(10), e0258892. <https://doi.org/10.1371/journal.pone.0258892>
- Mizuno, K., Ojiro, D., Tanaka, T., Minusa, S., Kuriyama, H., Yamano, E., Kuratsune, H., & Watanabe, Y. (2020). Relationship between truck driver fatigue and rear-end collision risk. *PLOS ONE*, 15(9), e0238738. <https://doi.org/10.1371/journal.pone.0238738>
- Naeeri, S., Kang, Z., Mandal, S., & Kim, K. (2021). Multimodal Analysis of Eye Movements and Fatigue in a Simulated Glass Cockpit Environment. *Aerospace*, 8(10), 283. <https://doi.org/10.3390/aerospace8100283>

- O’Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics*, 63(1), 1–12.
<https://doi.org/10.1080/00140139.2019.1687940>
- Pageaux, B., Marcora, S. M., Rozand, V., & 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.
<https://doi.org/10.3389/fnhum.2015.00067>
- Parasuraman, R. (2000). *The Attentive Brain*. MIT Press.
- Pattyn, N., Van Cutsem, J., Dessy, E., & 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.
<https://doi.org/10.3389/fpsyg.2018.01246>
- Pek, J., & Flora, D. B. (2018). Reporting effect sizes in original psychological research: A discussion and tutorial. *Psychological Methods*, 23(2), 208–225.
<https://doi.org/10.1037/met0000126>
- Persson, J., Larsson, A., & Reuter-Lorenz, P. A. (2013). Imaging Fatigue of Interference Control Reveals the Neural Basis of Executive Resource Depletion. *Journal of Cognitive Neuroscience*, 25(3), 338–351. https://doi.org/10.1162/jocn_a_00321
- Persson, J., Welsh, K. M., Jonides, J., & Reuter-Lorenz, P. A. (2007). Cognitive fatigue of executive processes: Interaction between interference resolution tasks. *Neuropsychologia*, 45(7), 1571–1579. <https://doi.org/10.1016/j.neuropsychologia.2006.12.007>
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2024). Visual perceptual processing is unaffected by cognitive fatigue. *Consciousness and Cognition*, 119, 103666.
<https://doi.org/10.1016/j.concog.2024.103666>
- Petrut, B., Berindan-Neagoe, I., Feflea, D. I., Hoge, M., Pasca, S., Bujoreanu, C. E., & Bschleipfer, T. (2020). Mental Fatigue Evaluation of Surgical Teams during a Regular Workday in a High-Volume Tertiary Healthcare Center. *Urologia Internationalis*, 104(3–4), 301–308. <https://doi.org/10.1159/000504988>
- Purto, H., Anabalón, H., Vargas, K., Jara D, C., & de la Vega, R. (2024). Self-perceptual blindness to mental fatigue in mining workers. *Frontiers in Neuroergonomics*, 5.
<https://doi.org/10.3389/fnrgo.2024.1441243>

- Rabat, A., Cutsem, J. V., Marcora, S. M., Lambert, A., Markwald, R., Kubala, A. G., & Friedl, K. E. (2025). Fatigue and management of warfighter mental endurance. *BMJ Military Health*. <https://doi.org/10.1136/military-2025-002963>
- Raghubar, K. P., Barnes, M. A., & Hecht, S. A. (2010). Working memory and mathematics: A review of developmental, individual difference, and cognitive approaches. *Learning and Individual Differences*, 20(2), 110–122. <https://doi.org/10.1016/j.lindif.2009.10.005>
- Reis, C., & Canhão, H. (2013). Prevalence of Fatigue in a Group of Airline Pilots. *Aviation, Space, and Environmental Medicine*, 84, 828–833. <https://doi.org/10.3357/ASEM.3548.2013>
- Ricci, J., Chee, E., Lorandean, A., & 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), 1–10. <https://doi.org/10.1097/01.jom.0000249782.60321.2a>
- Ridderinkhof, K. R., Ullsperger, M., Crone, E. A., & Nieuwenhuis, S. (2004). The Role of the Medial Frontal Cortex in Cognitive Control. *Science*, 306(5695), 443–447. <https://doi.org/10.1126/science.1100301>
- Rogers, W. P., Marques, J., Talebi, E., & Drews, F. A. (2023). IoT-Enabled Wearable Fatigue-Tracking System for Mine Operators. *Minerals*, 13(2), 287. <https://doi.org/10.3390/min13020287>
- Rozand, V., Lebon, F., Papaxanthis, C., & Lepers, R. (2015). Effect of mental fatigue on speed–accuracy trade-off. *Neuroscience*, 297, 219–230. <https://doi.org/10.1016/j.neuroscience.2015.03.066>
- Salomone, M., Burle, B., Fabre, L., & Berberian, B. (2021). An Electromyographic Analysis of the Effects of Cognitive Fatigue on Online and Anticipatory Action Control. *Frontiers in Human Neuroscience*, 14. <https://doi.org/10.3389/fnhum.2020.615046>
- Samuel, I. B. H., Wang, C., Burke, S. E., Kluger, B., & Ding, M. (2019). Compensatory Neural Responses to Cognitive Fatigue in Young and Older Adults. *Frontiers in Neural Circuits*, 13. <https://doi.org/10.3389/fncir.2019.00012>
- Sherry, P., & Owen, J. (2022). Validation of AlertMeter® Mobile Phone Fatigue Assessment Device. In K. Arai (Ed.), *Proceedings of the Future Technologies Conference (FTC) 2021, Volume 1* (pp. 484–501). Springer International Publishing. https://doi.org/10.1007/978-3-030-89906-6_33
- Simola, J., Zhigalov, A., Morales-Muñoz, I., Palva, J. M., & Palva, S. (2017). Critical dynamics of endogenous fluctuations predict cognitive flexibility in the Go/NoGo task. *Scientific Reports*, 7(1), 2909. <https://doi.org/10.1038/s41598-017-02750-9>

- Smith, M. R., Chai, R., Nguyen, H. T., Marcora, S. M., & Coutts, A. J. (2019). Comparing the Effects of Three Cognitive Tasks on Indicators of Mental Fatigue. *The Journal of Psychology*, 153(8), 759–783. <https://doi.org/10.1080/00223980.2019.1611530>
- Spijkers, W. A. C., & Walter, A. (1985). Response processing stages in choice reactions. *Acta Psychologica*, 58(2), 191–204. [https://doi.org/10.1016/0001-6918\(85\)90007-1](https://doi.org/10.1016/0001-6918(85)90007-1)
- Staiano, W., Romagnoli, M., Salazar Bonet, L. R., & Ferri-Caruana, A. (2024). Adaptive cognitive tasks for mental fatigue: An innovative paradigm for cognitive loading in human performance. *Journal of Science and Medicine in Sport*, 27(12), 883–889. <https://doi.org/10.1016/j.jsams.2024.08.199>
- Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, 18(6), 643–662. <https://doi.org/10.1037/h0054651>
- Szmales, A., Verbruggen, F., Vandierendonck, A., De Baene, W., Verguts, T., & Notebaert, W. (2008). Stimulus ambiguity elicits response conflict. *Neuroscience Letters*, 435(2), 158–162. <https://doi.org/10.1016/j.neulet.2008.02.023>
- Tahamtan, Z., Osia, S. A., & Herman, P. (2025). *Neural Mechanisms of Cognitive Flexibility and Interference Control in a Stroop Task Switching Paradigm*. bioRxiv. <https://doi.org/10.1101/2025.05.05.652181>
- Talebi, E., Rogers, W. P., & Drews, F. A. (2026). Predicting Fatigue of Haul Truck Operators Using Reaction Time. *Mining, Metallurgy & Exploration*, 43(2), 1951–1972. <https://doi.org/10.1007/s42461-025-01415-w>
- Thomas, M., Allen, M. S., Wigle, D. A., Shen, K. R., Cassivi, S. D., Nichols, F. C., & Deschamps, C. (2012). Does Surgeon Workload Per Day Affect Outcomes After Pulmonary Lobectomies? *The Annals of Thoracic Surgery*, 94(3), 966–972. <https://doi.org/10.1016/j.athoracsur.2012.04.099>
- Van Cutsem, J., Van Schuerbeek, P., Pattyn, N., Raeymaekers, H., De Mey, J., Meeusen, R., & Roelands, B. (2022). A drop in cognitive performance, whodunit? Subjective mental fatigue, brain deactivation or increased parasympathetic activity? It's complicated! *Cortex*, 155, 30–45. <https://doi.org/10.1016/j.cortex.2022.06.006>
- van Schagen. (2021). *Road Safety Thematic Report—Fatigue* (p. 19). European Road Safety Observatory. https://road-safety.transport.ec.europa.eu/european-road-safety-observatory/data-and-analysis/thematic-reports_en
- Walker, L. A. S., Berard, J. A., Berrigan, L. I., Rees, L. M., & Freedman, M. S. (2012). Detecting cognitive fatigue in multiple sclerosis: Method matters. *Journal of the Neurological Sciences*, 316(1), 86–92. <https://doi.org/10.1016/j.jns.2012.01.021>
- Wan, Q., Cai, Y., Samaha, J., & Postle, B. R. (2020). Tracking stimulus representation across a 2-back visual working memory task. *Royal Society Open Science*, 7(8), 190228. <https://doi.org/10.1098/rsos.190228>

- Wang, C., Trongnetrpunya, A., Samuel, I. B. H., Ding, M., & Kluger, B. M. (2016). Compensatory Neural Activity in Response to Cognitive Fatigue. *Journal of Neuroscience*, 36(14), 3919–3924. <https://doi.org/10.1523/JNEUROSCI.3652-15.2016>
- Wang, H., Dragomir, A., Abbasi, N. I., Li, J., Thakor, N. V., & Bezerianos, A. (2018). A novel real-time driving fatigue detection system based on wireless dry EEG. *Cognitive Neurodynamics*, 12(4), 365–376. <https://doi.org/10.1007/s11571-018-9481-5>
- Weetman, S., Roche, M., Leckie, T., Samuels, T., & Hodgson, L. (2024). Feasibility of application-based psychomotor vigilance testing to assess fatigue in doctors working night shifts and correlation with smartwatch assessed shift intensity. *Occupational and Environmental Medicine*, 81(5), 252–257. <https://doi.org/10.1136/oemed-2023-109311>
- Whelehan, D. F., Brown, D. J., Connelly, T. M., & Ridgway, P. F. (2021). Fatigued surgeons: A thematic analysis of the causes, effects and opportunities for fatigue mitigation in surgery. *International Journal of Surgery Open*, 35, 100382. <https://doi.org/10.1016/j.ijso.2021.100382>
- Wickens, C. D. (1991). Processing resources and attention. In D.L. Damos (Ed.), *Multiple Task Performance* (pp. 3-34). CRC Press.
- Wiehler, A., Branzoli, F., Adanyeguh, I., Mochel, F., & Pessiglione, M. (2022). A neuro-metabolic account of why daylong cognitive work alters the control of economic decisions. *Current Biology*, 32(16), 3564-3575.e5. <https://doi.org/10.1016/j.cub.2022.07.010>
- Yu, Z., Guindani, M., Grieco, S. F., Chen, L., Holmes, T. C., & Xu, X. (2022). Beyond t test and ANOVA: Applications of mixed-effects models for more rigorous statistical analysis in neuroscience research. *Neuron*, 110(1), 21–35. <https://doi.org/10.1016/j.neuron.2021.10.030>
- Zhang, Z., Xiang, T., Guo, H., Ma, L., Guan, Z., & Fang, Y. (2023). Impact of physical and mental fatigue on construction workers' unsafe behavior based on physiological measurement. *Journal of Safety Research*, 85, 457–468. <https://doi.org/10.1016/j.jsr.2023.04.014>

Chapter 5. Experiment 4 - Corticospinal Excitability During Movement Preparation: Effects of Cognitive Fatigue

5.1 Abstract

Cognitive fatigue (CF) is associated with road and workplace hazards, potentially due to disruptions in motor system performance and processing efficiency. While the mechanism driving these motor impacts is uncertain, one possibility is that CF could alter corticospinal excitability during movement preparation. To assess this possibility, we used single pulse transcranial magnetic stimulation to measure corticospinal excitability before and after participants completed a 60-minute CF intervention (Math-Memory task) and a control intervention (CTL; documentary film viewing) on separate days. Corticospinal excitability was indexed via motor evoked potential amplitude of the right first dorsal interosseous both at rest and at three timepoints (500, 150, and 0 ms before the go-signal) during the foreperiod of a simple RT task requiring a right index finger button-press. Subjective fatigue, motivation, resting motor threshold, and premotor and displacement RT were also assessed pre- and post-intervention. Participants ($n = 32$, 16F) reported significant increases in subjective fatigue following CF relative to CTL ($p = .001$). RT showed non-significant increases in CF but was primarily impacted by the timing of TMS delivery. Notably, corticospinal excitability declined over CTL while remaining consistent over CF, leading to a relative elevation of post-intervention excitability in CF across foreperiod timepoints ($p < .001$). Resting MEP amplitude was similarly affected, such that it increased more over CF compared to CTL ($p < .001$). No significant changes in resting motor threshold occurred. Overall, these results are consistent with a broad compensatory elevation in corticospinal excitability in response to CF, perhaps to preserve motor system processing efficiency despite CF-related strain.

5.2 Introduction

Fatigue, broadly defined as a suboptimal psychophysiological state reflected by feelings of tiredness, is a prevalent phenomenon that imposes a high economic burden at both the societal and individual level (Kunasegaran et al., 2023; Mirin et al., 2022; Phillips, 2015; Ricci et al., 2007; Rodriguez Llorian et al., 2022). In a global systematic review, more than 20% of adults reported significant general fatigue (Yoon et al., 2023). However, fatigue is not considered a unitary construct; instead, multiple dimensions have been identified that differ in their source and their performance consequences (Behrens et al., 2023; Phillips, 2015). Fatigue arising from sustained and/or challenging mental effort, characterized by feelings of exhaustion and a desire to disengage from mental work, is commonly referred to as cognitive (or mental) fatigue (Behrens et al., 2023; Salihu et al., 2022). This form of fatigue is one that most individuals have experienced, although it can be particularly prevalent and consequential in certain populations. For instance, individuals in some high-demand or high-pressure occupations have reported elevated cognitive fatigue (Mahdavi et al., 2024; Yoon et al., 2023), such as surgeons (Bourne et al., 2013; Janhofer et al., 2019), students (Kotnik et al., 2024; Sievertsen et al., 2016), athletes (Russell et al., 2019; Weiler et al., 2025), and construction (Xing et al., 2020; Zong et al., 2024) and transportation workers (Jaydarifard et al., 2024; Meng et al., 2015; Reis & Canhão, 2013). Notably, cognitive fatigue has been linked not only to reduced productivity (Chen et al., 2022; Macfarlane et al., 2024; Mahdavi et al., 2024), but also to an increased risk of workplace accidents, errors, and injuries (Chan et al., 2009; Costedoat et al., 2023; Jia et al., 2022; J. Li et al., 2019; Schamphoeleer & Roelands, 2024; Swaen et al., 2003; Zhang et al., 2023). It is also a common and often debilitating symptom of several medical disorders, including multiple sclerosis (Gullo et al., 2019; Islam et al., 2026; Ruban et al., 2021), traumatic brain injury

(Johansson & Rönnbäck, 2017; Palm et al., 2017), Parkinson's disease (Lou, 2009), long-COVID (Bao et al., 2025; Nielsen et al., 2022), and myalgic encephalomyelitis/chronic fatigue syndrome (Azcue et al., 2026; Park et al., 2024), where it can significantly reduce quality of life.

Given its prevalence and significant impact across occupational and clinical contexts, an important question is how cognitive fatigue alters fundamental neural processes that support efficient goal-directed motor behaviour. Many everyday activities, particularly in safety-critical environments, depend on the rapid detection of sensory information, preparation of an appropriate motor response, and execution of that response (Donders, 1969; Lindemann & Fischer, 2023; Taylor, 1976). In line with this, previous research has indicated that the overall speed of these processes (indexed experimentally via reaction time) may be slowed under conditions of reported cognitive fatigue (Habay et al., 2021; Langner et al., 2010; Peters et al., 2022, 2024). This effect has been suggested to contribute to delayed responses to road and workplace hazards (Guo et al., 2018; J. Li et al., 2019; Zeuwts et al., 2021) and have negative impacts to safety and performance in sport and military settings (Barbosa et al., 2025; Habay et al., 2021; Lieberman et al., 2009; Vrijkotte et al., 2016). However, the neural mechanism by which cognitive fatigue influences the efficiency of these motor system processes remains poorly understood.

One possibility is that cognitive fatigue disrupts neural processing related to movement preparation. Supporting this view, cognitive fatigue has been associated with weakened functional connectivity between sensory and motor planning regions, including the premotor cortex and supplementary motor area (Leitner et al., 2024; Yan et al., 2024), as well as reductions in response-locked lateralized readiness potential, reflecting diminished late-stage motor preparation (Kato et al., 2009). Over a prolonged task switching paradigm, cognitive fatigue led

to less efficient use of preparatory intervals, increased error rates, and reduced frontal negativity associated with planning upcoming actions (Lorist et al., 2000). Similar effects have been observed with extended motor imagery practice, which resulted in less distinct preparatory representations for imagined left- versus right-handed movements alongside reduced functional connectivity within motor-related networks (T. Li et al., 2024).

Together, these findings suggest that cognitive fatigue could alter neural activity during movement preparation. If so, such changes should be detectable during the preparatory delay period of a simple reaction time (RT) task, i.e., during the interval between a warning signal and the imperative (go) signal, when the known required response is thought to be actively prepared (Donders, 1969; Lindemann & Fischer, 2023; Taylor, 1976). This possibility has previously been examined using the StartReact effect (Peters et al., 2022), which assesses the extent to which a startling acoustic stimulus triggers a pre-planned movement during the preparatory phase of a simple RT task (Carlsen et al., 2004; Valls-Solé et al., 1999). In this paradigm, earlier and/or more frequent triggering is generally considered as evidence of heightened motor preparation (Carlsen et al., 2011). Contrary to expectations, although a Math-Memory intervention increased RT and subjective fatigue relative to a documentary film-viewing control condition, the StartReact effect was unchanged. A potential explanation is that StartReact responses may be mediated in large part by subcortical circuits involving the reticulospinal tract (Carlsen & Maslovat, 2019, 2026; Tapia et al., 2022). If cognitive fatigue instead primarily affects corticospinal mechanisms involved in motor preparation, then the StartReact effect may have been relatively insensitive to fatigue-related preparatory changes.

An alternative way to probe the preparatory state of the corticospinal system during this window is by assessing corticospinal excitability, or the ease with which the corticospinal

pathway can be activated to transmit descending motor signals from the motor cortex to spinal motoneurons and ultimately the muscle (Bestmann & Duque, 2016; Bestmann & Krakauer, 2015). Single-pulse transcranial magnetic stimulation (TMS) applied over the motor cortex can provide a snapshot of corticospinal excitability at the moment of stimulation, by measuring the amplitude of an evoked response (motor-evoked potential, MEP) in a target muscle with electromyography (Hallett, 2007). Single-pulse TMS has been used previously to characterize the time course of corticospinal excitability during the preparatory delay period of a simple RT task, showing a stereotyped pattern of corticospinal excitability changes in the non-fatigued state (Kennefick et al., 2014). Namely, corticospinal excitability is broadly elevated relative to resting/baseline measurements, showing a gradual and then sustained increase after the warning signal, followed by a period of suppression often referred to as “preparatory inhibition” as the go-signal approaches (i.e., beginning at approximately 150ms prior to the go-signal; Greenhouse et al., 2015; Ibáñez et al., 2020). When the go-signal is then presented, a rapid increase in corticospinal excitability is observed just prior to movement initiation (Greenhouse et al., 2015; Ibáñez et al., 2020; Kennefick et al., 2014).

Alterations in the balance of facilitatory and/or inhibitory network processes due to cognitive fatigue could potentially disrupt this normal preparatory pattern of corticospinal excitability (Ishii et al., 2014; Morris & Christie, 2020; Schumann et al., 2025). For instance, disruptions may appear as a reduced elevation of corticospinal excitability relative to baseline (resting-state). According to a neural accumulator perspective, this reduction could in turn prolong the time required for excitability to reach a threshold level necessary for movement initiation (Carlsen et al., 2012; Hanes & Schall, 1996). Cognitive fatigue-related changes in preparatory inhibition may also be present and could contribute to RT increases. Stronger

suppression of corticospinal excitability near the time of the go-signal has been associated with faster RT (De Doncker et al., 2021; Vassiliadis et al., 2020), potentially by stabilizing the motor system or raising the signal-to-noise ratio to support efficient preparatory processing prior to movement initiation (Greenhouse et al., 2015; Ibáñez et al., 2020). Cognitive fatigue could interfere with these processes, leading to reduced or prolonged preparatory inhibition, potentially observable as changes in the magnitude or timing of MEP suppression late in the preparatory delay period.

To date, only a small number of studies have used TMS to examine the effect of cognitive fatigue on the corticospinal system. However, these studies have typically assessed MEP amplitude only at rest, rather than during active preparation (i.e., during the preparatory delay phase of an RT task) and have yielded inconsistent results. While some have reported reductions in corticospinal excitability with increasing subjective ratings of cognitive fatigue (Bailey et al., 2021; Nakashima et al., 2021), others observed no such changes (Holgado et al., 2023; Kowalski et al., 2022; Rozand et al., 2015). Thus, it is still uncertain whether cognitive fatigue alters not only resting corticospinal excitability, but also the time-course of corticospinal excitability during the preparatory delay period of a simple RT task, where preparatory mechanisms are directly engaged.

Accordingly, the present study used single-pulse TMS to assess corticospinal excitability both at rest and at three different timepoints (500, 150, and 0 ms before the go-signal) during the preparatory delay period of a simple RT task. Resting motor threshold, MEP amplitude at rest and during preparation, displacement and premotor RT, and subjective ratings of fatigue and motivation were obtained before and after participants completed either a control task (watching a documentary film) or a Math-Memory task previously shown to induce subjective cognitive

fatigue and RT slowing (Peters et al., 2022, 2024). We predicted that if cognitive fatigue alters corticospinal contributions to motor preparation, then cognitive task completion would be associated with measurable changes in the pattern of preparatory corticospinal excitability (for instance, a flatter early rise in excitability and/or delayed or reduced preparatory inhibition) relative to the control condition. In testing this prediction, this study aims to clarify a possible neural mechanism underlying psychomotor impairments in cognitive fatigue.

5.3 Materials and Methods

5.3.1 Participants

An a priori power analysis was conducted using the effect size reported by Chiu et al. (2014) for differences in MEP amplitude between task conditions (partial $\eta^2 = 0.31$) as an estimate of the expected effect magnitude. This analysis indicated that twenty-four participants were required to meet a power of 0.95 (G*Power; Faul et al., 2007). Thirty-two healthy volunteers participated in the study; 16 who self-identified as assigned female at birth (mean age = 21.5 ± 4.3 years) and 16 who self-identified as assigned male at birth (mean age = 21.6 ± 3.8 years). Participants reported no motor control disorders, chronic fatigue, or uncorrected visual deficits. All participants completed a TMS safety screening form prior to participation, in line with that proposed by Rossi and colleagues (2009), confirming that they had no contraindications to stimulation.

Each volunteer participated in two testing sessions (cognitive fatigue and control) of approximately 2 hours each, completed on separate days between 8:30 am and 4:30 pm. Testing session order was randomised and counterbalanced. All participants provided written informed consent prior to taking part in each session of the study. All aspects of the study were approved by University of Ottawa's Research Ethics Board (REB approval: H-11-24-10794) and adhered to the guidelines of the Declaration of Helsinki.

5.3.2 Experiment Overview

A summary of the experimental timeline is depicted in Fig. 5.1. Following provision of informed consent and confirmation of eligibility, subjective fatigue and motivation were assessed using computerized visual analog scales. The optimal location for TMS was then determined, followed by measurement of pre-intervention resting motor threshold and resting MEP amplitude.

Participants next performed a simple RT task, during which premotor RT was recorded.

Preparatory MEP amplitude was also measured in this task, within the RT task delay period at 500, 150, and 0 ms prior to the go-signal. Following these pre-intervention measurements, participants completed either a control intervention (CTL), wherein they watched a ~60-minute documentary film, or a cognitively fatiguing intervention (CF), wherein they completed a ~60-minute sustained Math-Memory dual task (Peters et al., 2022, 2024). Post-intervention measures of subjective fatigue, motivation, premotor reaction time, preparatory MEP amplitude, resting MEP amplitude, and resting motor threshold were then obtained to complete each study session.

5.3.3 Participant Set-Up

Participants were seated in a padded, height-adjustable chair approximately 1m in front of a 24-inch computer monitor for the duration of each experimental session. A lap desk with a computer mouse and keyboard were used to complete subjective fatigue and motivation scales and the interactive cognitive intervention. For the reaction time task, participants rested their right arm comfortably on an armrest in a pronated position, with the palm of the hand facing downwards, the shoulder abducted at approximately 30 degrees, and the elbow flexed at approximately 90 degrees. The index finger rested on a telegraph key button (Ameco AM-K4B) that provided a voltage of 0 V when the switch was open and 5 V when the switch was closed. A bipolar pre-amplified surface electromyography (EMG) electrode (Delsys DE-2.1) was applied superficially

above the muscle belly of the right first dorsal interosseous (FDI) muscle to record premotor reaction time and the amplitude of motor-evoked potentials (MEPs). Adhesive strips were used to fasten the EMG electrode parallel to the orientation of muscle fibers following cleansing of electrode sites with alcohol. A carbon-pad grounding electrode (2-inch square, Easy@home) was applied to the medial epicondyle of the right elbow. The EMG electrode was connected via shielded cabling to an external amplifier system (Delsys Bagnoli), and EMG data were band-passed (20-450 Hz) and digitally sampled at 4 kHz (National Instruments PCIe-6321). To guide TMS delivery, a fiducial marker used by TMS optical tracking-based neuronavigation software was placed at the centre of the participant's forehead, and a digitized pointer was used to register the shape and location of the participant's skull in relation to the stimulation coil (ANT Neuro Visor 2, Madison, WI).

5.3.4 Subjective Fatigue Assessment

Participants used the computer mouse to move digital sliders along horizontal linear visual analog scales (length = 20 cm) to provide a rating of cognitive fatigue level (0 = not at all mentally fatigued, 10 = extremely mentally fatigued) and motivation/indifference level (0 = motivated to succeed in the task, 10 = indifferent about the task; Michielsen et al., 2003).

5.3.5 Simple Reaction Time (RT) Task

Each simple RT task trial began with an empty black square (7 cm x 7 cm) appearing at the centre of the computer screen. After 1-second pause, a fixation cross (1 cm) appeared at the centre of the square. After 1 second, the fixation cross disappeared (acting as the “warning signal”), followed by a 1-second fixed foreperiod. The visual go-signal then appeared, consisting of the square illuminating green. Participants were instructed to press the telegraph key with their index finger as quickly as possible following this go-signal, ignoring any sounds or sensations

related to TMS delivery. Performance feedback (time to telegraph key press, anticipation error) was displayed on the screen for 2 seconds during each intertrial interval. In addition to RT task trials, catch trials, which included a warning signal and TMS but no go-signal, were delivered randomly to encourage participants to only make purposeful responses. In the pre-intervention phase, participants performed 10 RT practice trials without any TMS to familiarize themselves with the RT task. Then, in both the pre- and post-intervention phases, participants performed 2 blocks of RT testing, each with 18 RT trials and 1 catch trial. EMG data were collected over a 3-second period during each RT task trial, starting 1 second prior to the warning signal.

5.3.6 Transcranial Magnetic Stimulation

TMS was applied using a Magstim 2002 stimulator with a figure-eight coil (D70 mm; Magstim Company Ltd, UK), over the left primary motor cortex to generate MEPs in the target muscle (right FDI). Before testing, the approximate target location was determined by first measuring the mid-point between the nasion and inion, and the left and right preauricular notches. From this point, a mark was made 5 cm laterally and 1 cm anteriorly using a red grease crayon. With the coil handle pointed backwards at approximately a 45-degree angle, test pulses were then delivered nearby this mark to determine the optimal location for stimulation, i.e., where MEPs with consistently large amplitude could be obtained. When the optimal location was determined, it was marked with a blue grease crayon, and the location was saved via the neuronavigation system (visor2TM, ANT neuro).

Using the neuronavigation system as a positional guide, additional TMS pulses were delivered to determine resting motor threshold (RMT), defined as the stimulation intensity needed to elicit a peak-to-peak (FDI) MEP amplitude of $\geq 50 \mu\text{V}$ in approximately five out of ten pulses to the nearest 1% of simulator output intensity (Rossini et al., 2015). RMT was assessed

before and after each intervention (Fig. 5.1). TMS intensity was set to 120% of pre-test RMT during all subsequent MEP measurement within the same session (except for post-test RMT assessment; Cuypers et al., 2014; Demjan et al., 2023).

Resting MEP amplitude was measured at the FDI 10 times as participants sat quietly, with pulses triggered by the researcher. While participants performed the RT task, preparatory MEP amplitude was measured once per trial during the preparatory delay period (foreperiod), excluding practice trials, with TMS triggered automatically at -500, -150, or 0 ms relative to the go-signal (or at 1000 ms following the warning signal on catch trials). Triggering was precisely timed using custom software (NI LabVIEW). Catch trials were delivered once per RT task block to prevent anticipation of the go-signal and were not analysed for MEP amplitude. All other TMS delivery timepoints (-500, -150, -0 ms relative to go) were each tested six times per RT task block, resulting in 12 pre-intervention and 12 post-intervention measures of MEP amplitude at each TMS timepoint per participant.

5.3.7 Cognitive Fatigue (CF) and Control (CTL) Interventions

For the control intervention (CTL), participants viewed a documentary film (“Animal Language”; Baus & Farmer, 2005) for approximately 60 minutes between the pre- and post-intervention phases. For the cognitive fatigue intervention (CF), participants completed a Math-Memory dual task combining working memory retention and math-based interference (Peters et al., 2022, 2024). Each trial of the Math-Memory task began with seven letters appearing briefly and consecutively in a pre-generated sequence at the centre of the computer monitor. Participants were instructed to remember these letters in the order presented without verbal rehearsal. This was followed by a 45-second math segment, where participants were required to select the mathematical operator to correctly complete a presented equation (e.g., $4 ? 2 = 6$, answer = +)

using marked keyboard keys (+, -, ÷, x). Participants were encouraged to correctly complete as many math problems as possible within the trial interval and were provided ongoing feedback of response accuracy (correct/incorrect indicated by a green check mark or red X). Next, participants were asked to recall the last-displayed letter sequence, inputting the letters into blank boxes, again using the keyboard. Feedback indicating the accuracy of the letter inputs was provided at the end of the trial interval by the box frames turning green if the inputted letter was correct, or red if incorrect.

Math-Memory task difficulty was adaptive, such that difficulty was individually adjusted throughout to maintain a response accuracy of approximately 85%, consistent with evidence that individualizing cognitive task difficulty may enhance mental fatigue induction (O’Keeffe et al., 2020; Staiano et al., 2024). Task difficulty was adapted based on performance by adjusting stimulus display times and the time available to respond. Responses were considered errors if they were incorrect or if the response was not made during the response interval (the length of which was adapted throughout). The display/response time for math problems began at 3000 ms and for letter input boxes at 800 ms for the first four trials of the task. Accuracy was then averaged across both task segments after every 4 subsequent trials (~4 minutes). If performance fell below 85%, task difficulty was decreased by increasing the display/response time within the math and memory segments of the task by 10%. Conversely, if accuracy rose above 85%, task difficulty was increased by reducing the display/response time by 10%.

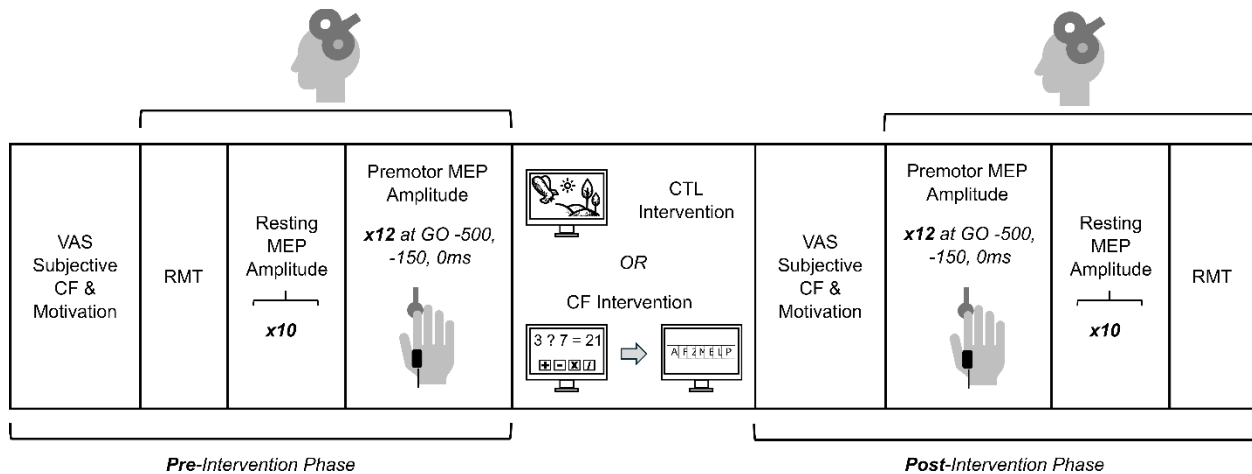


Fig. 5.1 Experimental timeline. Each testing session proceeded in the following order: pre-intervention phase, 60-minute cognitively fatiguing (CF) or control (CTL) intervention, post-intervention phase. Pre- and post-intervention phases included the following assessments, in the order visually depicted: visual analog scale (VAS) measures of subjective cognitive fatigue and motivation; resting motor threshold (RMT) measurement; resting motor evoked potential (MEP) measurement (10 trials); and preparatory MEP measured at three TMS timepoints (500, 150, and 0 ms prior to the go-signal) within the simple RT task (12 trials each + 2 catch; premotor RT of button press measured at right first dorsal interosseus). Ten simple RT practice trials (without TMS) preceded the pre-intervention assessment of preparatory MEP amplitude (not depicted).

5.4 Data Reduction

Displacement onset of the key-press response was defined as the time at which the key moved from the open to the closed position and voltage changed from 0 to 5 V. To quantify premotor RT, EMG burst onsets were identified as the point at which the rectified, filtered EMG activity increased above baseline (i.e., more than 2 standard deviations above mean EMG activity preceding the go-signal). EMG burst onsets were then verified by visually locating and manually adjusting the onset mark to the point at which the activity first increased on the raw EMG trace

(Hodges & Bui, 1996). EMG offsets were marked in a similar fashion (i.e., when EMG activity dropped below 20% of peak), with the activity between EMG onset and EMG offset being defined as a distinct burst. MEP amplitude was measured as the largest peak-to-peak amplitude (mV) recorded in a 30 ms window beginning 15 ms after presentation of each TMS pulse. MEPs were automatically identified by the computer program and visually verified by the researcher.

Resting MEP, preparatory MEP, and RT data sets were processed separately for data reduction and subsequent analyses. For MEP data sets, trials were excluded if MEPs were indistinguishable from movement-related EMG bursts or contaminated by TMS artifacts (resting MEP: 48 trials; preparatory MEP: 294 trials). Additional exclusions were applied to the preparatory MEP data set for trials with excessive background EMG activity (defined as RMS activity $> 3\times$ baseline in the 100 ms preceding TMS onset, 65 trials), movement-related EMG activity occurring prior to the recorded MEP (1 trial), or absence of a movement response (2 non-catch trials). For RT data, trials were removed if no button press and/or EMG response was detected on non-catch trials (30 trials), if responses were anticipatory (RT < 50 ms; 321 trials), or if response errors occurred (e.g., double taps of the telegraph key; 2 trials).

Outliers were identified and removed from resting MEP, preparatory MEP, and RT data sets as values exceeding ± 2 standard deviations of their respective means (resting MEP: 47 trials; preparatory MEP: 194 trials; premotor RT: 195 trials, displacement RT: 197 trials). In total, data reduction resulted in exclusion of 95 trials from the resting MEP data set (7.4%), 556 trials from the preparatory MEP data set (12.0%), 548 trials from the premotor RT data set (11.9%), and 550 trials from the displacement RT data set (11.9%). Practice trials were not analysed.

5.5 Statistical Analysis

Data analysis was performed with R statistical software (version 4.5.3; R Core Team, 2026).

Mixed-effect model analyses were used to assess the effects of intervention condition (CF, CTL), pre/post phase, and TMS timepoint (go-500ms, go-150ms, go-0ms) on each dependent variable (RMT, resting MEP amplitude, preparatory MEP amplitude, premotor RT, displacement RT, and subjective fatigue and motivation). The proportion of responses incorrectly made on catch trials was also assessed.

For each dependent variable, distributions were first inspected to guide selection of mixed-effect model family. Subjective ratings were analysed using a generalized linear mixed-effect model fitted with a Tweedie distribution (*glmmTMB* package), which was chosen to accommodate continuous right-skewed data with several true zero values (Brooks et al., 2017). Catch trials were analysed with a binomial generalized linear mixed-effect model (*lme4* package) as the outcome variable was binary (i.e., response or no response; Bates et al., 2015). The remaining variables (RMT, RT, and resting and preparatory MEP amplitude) were fit to Gaussian mixed-effect models (Bates et al., 2015). Log transformations were applied where required to meet model assumptions. Models were refit using the *BOBYQA* optimizer in cases of convergence difficulty (Powell, 2009). For all models, the maximal random-effects structure justified by the design was initially specified. Models exhibiting singular fits or convergence failures despite optimizer use were simplified. Random-effects variance–covariance structures were assessed, and models showing evidence of overparameterization (e.g., highly correlated random effects or principal components explaining negligible variance) were simplified iteratively to achieve a parsimonious final model (Bates et al., 2018; Matuschek et al., 2017).

The significance of fixed-effects was assessed using Type II Wald χ^2 tests (*Anova()* function from the *car* package) for generalized linear mixed-effect models (Brooks et al., 2017; Fox & Weisberg, 2019), and with Type III F-tests with Satterthwaite's approximation for denominator degrees of freedom (*anova()* function from the *lmerTest* package) for linear mixed-effect models (Bates et al., 2015; Kuznetsova et al., 2017). Estimated marginal means (EMMs) were computed using the *emmeans* package (Lenth et al., 2021). In cases where fixed effects were log transformed, EMMs were back-transformed to the response scale and the reference grid was re-expressed on that scale using the *regrid()* function (Lenth et al., 2021). Pairwise contrasts for significant fixed effects and/or interactions were then calculated on the response scale. Standard errors and confidence intervals for post hoc contrasts were obtained using the delta method; *p*-values were Holm-Bonferroni corrected.

5.6 Results

5.6.1 Subjective Ratings

Subjective ratings of cognitive fatigue (0 = not at all mentally fatigued, 10 = extremely mentally fatigued) were significantly impacted by pre/post phase ($\chi^2(1) = 35.75, p < .001$), intervention condition ($\chi^2(1) = 7.07, p = .008$), and their interaction ($\chi^2(1) = 10.37, p = .001$). Post hoc contrasts showed that subjective fatigue did not differ between the interventions at baseline (CTL-CF = +0.35 points, *SE* = 0.39, *p* = .374) but was significantly higher post-CF intervention (CTL-CF = -2.70 points, *SE* = 0.71, *p* < .001). In accordance, a significant increase in subjective cognitive fatigue was observed from pre- to post-intervention in the CF condition ($\Delta = +3.90$ points, *SE* = 0.70 points, *p* < .001) but not in the CTL condition ($\Delta = +0.85$ points, *SE* = 0.47 points, *p* = .074). Further, the magnitude of pre- to post-intervention change was significantly

greater in the CF condition compared to CTL ($\Delta\text{CTL}-\Delta\text{CF} = -3.05$ points, $SE = 0.82$ points, $p < .001$; Fig. 5.2a and 5.2b).

In contrast, subjective ratings of motivation/indifference (0 = motivated to succeed in the task, 10 = indifferent about the task) only showed significant effects of pre/post phase ($\chi^2(1) = 4.64$, $p = .031$), such that participants became slightly less motivated and more indifferent from pre- to post-intervention regardless of the intervention condition ($\Delta = +0.31$ points overall, $SE = 0.15$ points, $p = .044$; Fig. 5.2c and 5.2d). The main effect of intervention condition (CF, CTL) and the interaction of pre/post phase x intervention condition did not significantly influence subjective ratings of motivation/indifference ($p > .400$).

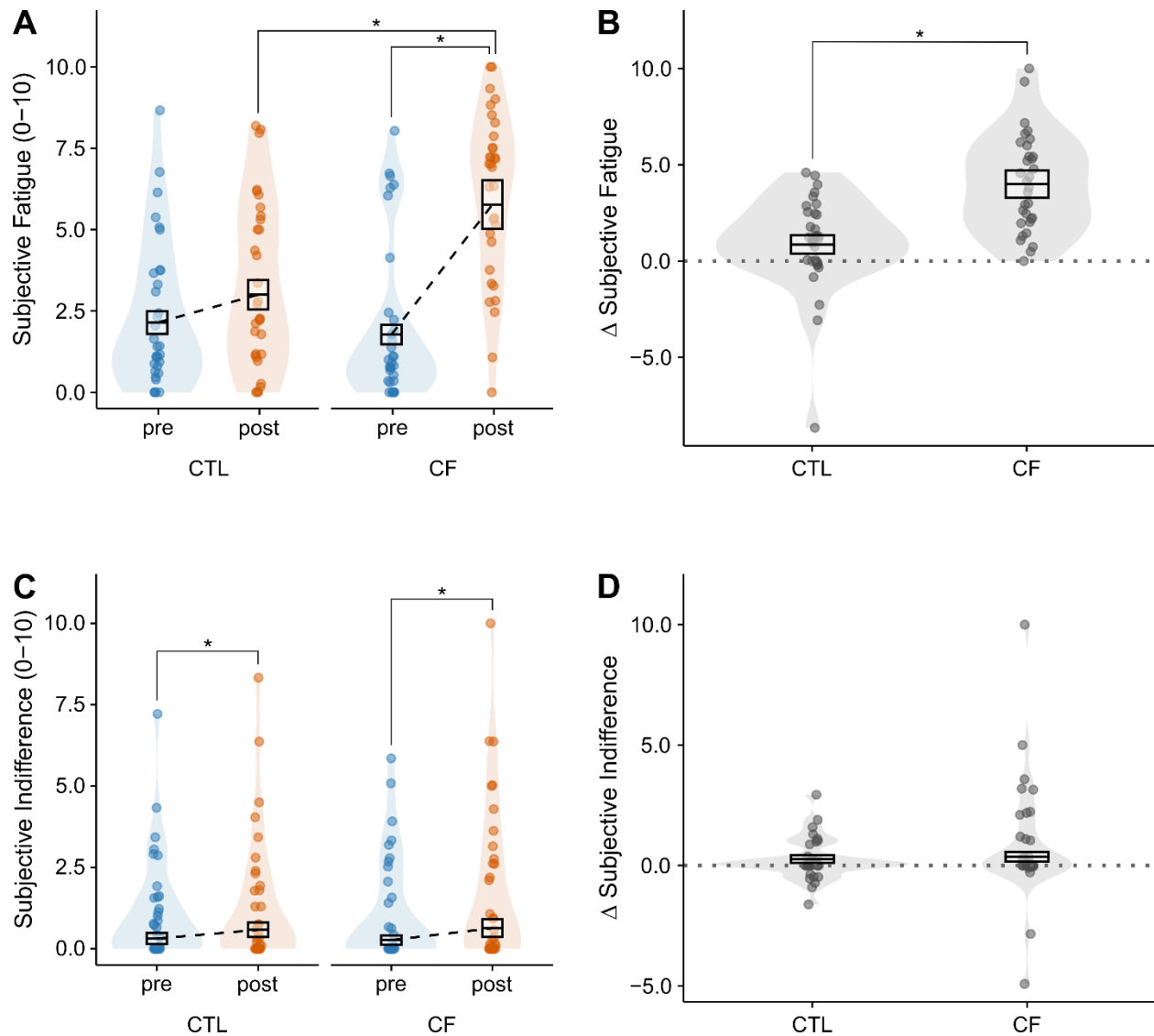


Fig. 5.2 Subjective ratings. (a) Subjective cognitive fatigue rating (0 = not at all mentally fatigued, 10 = extremely mentally fatigued) as a function of intervention condition (CTL, CF) and pre/post phase (pre-intervention, post-intervention). (b) Change in subjective cognitive fatigue rating (post – pre) by intervention condition. (c) Subjective indifference/motivation rating (0 = motivated to succeed in the task, 10 = indifferent about the task) as a function of intervention condition and pre/post phase. (d) Change in subjective indifference/motivation rating (post – pre) by intervention condition. Throughout, violin plots show the distribution of individual values, with points representing individual participants. Black boxes indicate model-

predicted means $\pm SE$. The dotted horizontal line in (b) and (d) indicates no change, such that values below the line indicate a rating decrease from pre- to post-intervention while values above indicate an increase. Asterisks indicate significant differences where $p < .050$. CF = cognitive fatigue intervention, CTL = control intervention.

5.6.2 Premotor Simple Reaction Time

Premotor RT varied significantly across TMS timepoints ($F(2,3924) = 327.91, p < .001$), and there was also a significant interaction between pre/post phase and TMS timepoint ($F(2,3925) = 3.38, p = .034$). Within both the pre- and post-intervention phases, premotor RT increased systematically as TMS delivery approached the go-signal (Fig. 5.3a). Responses were faster when TMS was delivered at go-500ms compared with go-150ms ($\Delta = -9.51$ ms, $SE = 1.44$ ms, $p < .001$), at go-150ms compared to go-0ms ($\Delta = -25.27$ ms, $SE = 1.40$ ms, $p < .001$), and at go-500ms compared to go-0ms ($\Delta = -34.78$ ms, $SE = 1.42$ ms, $p < .001$). Notably, this RT facilitation by early TMS delivery became more pronounced post-intervention, particularly for the go-150ms vs go-0ms comparison ($\Delta_{\text{post}} - \Delta_{\text{pre}} = +\Delta 7.20$ ms, $SE = 2.80$ ms, $p = .030$). The go-500ms vs go-0ms comparison followed a similar trend but did not reach significance ($\Delta_{\text{post}} - \Delta_{\text{pre}} = +\Delta 2.58$ ms, $SE = 2.83$ ms, $p = .363$).

No other significant main effects or interactions were observed (all $p > .170$). However, the above results indicate the timing of the TMS pulse affected premotor RT and likely acted as a temporal pre-cue that facilitated subsequent responses to the go-signal. In order to isolate potential CF-related effects from TMS-related temporal cueing, a follow-up analysis was performed on only the go-0ms TMS timepoint, as this condition would have provided minimal advance cueing. Within go-0ms trials, premotor RT became faster pre- to post-CTL ($\Delta = -2.09$ ms, $SE = 4.72$ ms, $p = .661$) and slower pre- to post-CF ($\Delta = +2.62$ ms, $SE = 5.28$ ms, $p = .623$),

yet neither these differences nor the overall interaction of pre/post phase x intervention condition ($F(1,31) = 0.533, p = .471$) was statistically significant (Fig. 5.3b).

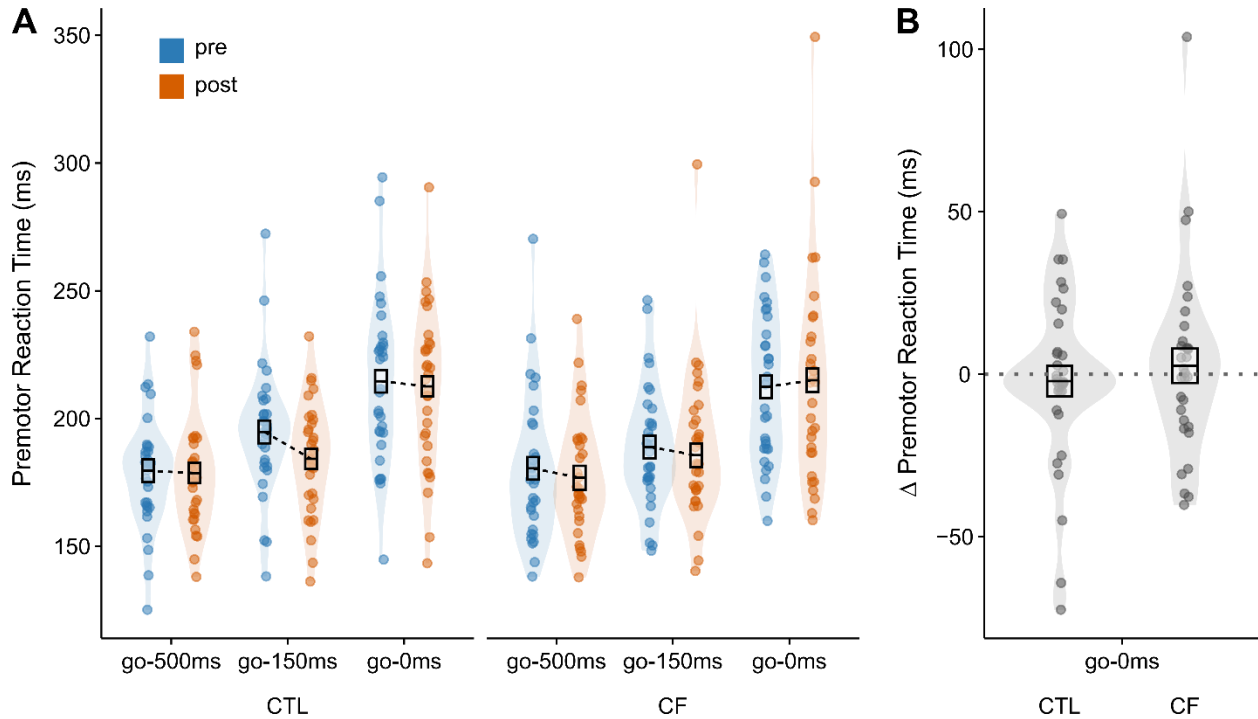


Fig. 5.3 Premotor simple reaction time (ms). (a) Premotor reaction time as a function of intervention condition (CTL, CF), TMS timepoint (go-500ms, go-150ms, go-0ms) and pre/post phase (pre-intervention, post-intervention). Violin plots show the distribution of individual mean values, with points representing individual participants. Black boxes indicate model-predicted means $\pm$ SE. (b) Change in premotor reaction time (post – pre) at the go-0ms TMS timepoint by intervention condition. The dotted horizontal line indicates no change, such that values below the line indicate a decrease in premotor reaction time from pre- to post-intervention while values above indicate an increase. Violin plots show the distribution of individual change scores, with points representing individual participants. Black boxes indicate model-predicted mean change $\pm$ SE. CF = cognitive fatigue intervention, CTL = control intervention.

5.6.3 Displacement Reaction Time

Displacement RT varied significantly by TMS timepoint ($F(2,3927) = 189.08, p < .001$), and by the interaction of pre/post phase x TMS timepoint ($F(2,3929) = 5.78, p = .003$). Similar to premotor RT, displacement RT increased systematically as TMS delivery approached the go-signal (Fig. 5.4a). Specifically, displacement RT was faster when TMS was delivered at go-500ms vs go-150ms ($\Delta = -9.22$ ms, $SE = 1.59$ ms, $p < .001$), at go-150ms vs go-0ms ($\Delta = -20.34$ ms, $SE = 1.55$ ms, $p < .001$), and at go-500ms compared to go-0ms ($\Delta = -29.56$ ms, $SE = 1.57$ ms, $p < .001$). A greater degree of RT facilitation due to early TMS delivery was observed post-intervention, particularly for the go-150ms vs the go-0ms comparison (post-pre = $+\Delta 10.12$ ms, $SE = 3.10$ ms, $p = .003$) and for the go-500ms vs go-0ms comparison (post-pre = $+\Delta 7.45$ ms, $SE = 3.13$, $p = .035$).

No other significant main effects or interactions were observed (all $p > .140$). However, as with premotor RT, these results suggest that the TMS pulse may have acted as a temporal pre-cue for the upcoming go-signal, and as such a follow-up analysis was performed focusing only on the go-0ms TMS delivery timepoint. The interaction of pre/post phase x intervention condition was not significant in this analysis ($F(1,1352) = 1.63, p = .202$). However, exploratory post hoc contrasts showed an increase in displacement RT from pre- to post-CF that neared significance ($\Delta = +9.66$ ms, $SE = 4.86$ ms, $p = .051$), and a smaller non-significant increase from pre- to post-CTL ($\Delta = +2.85$ ms, $SE = 4.79$ ms, $p = .554$; Fig. 5.4b).

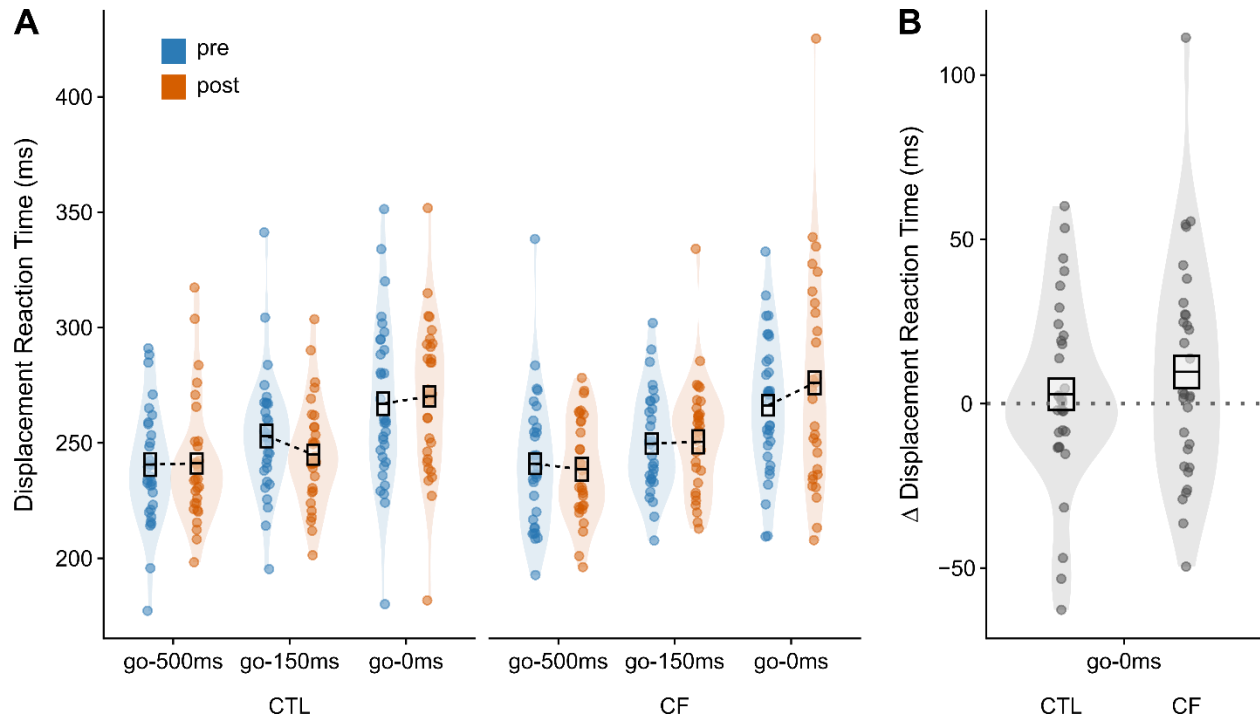


Fig. 5.4 Displacement simple reaction time (ms). (a) Displacement reaction time as a function of intervention condition (CTL, CF), TMS timepoint (go-500ms, go-150ms, go-0ms) and pre/post phase (pre-intervention, post-intervention). Violin plots show the distribution of individual mean values, with points representing individual participants. Black boxes indicate model-predicted means $\pm$ SE. (b) Change in displacement reaction time (post – pre) at the go-0ms TMS timepoint by intervention condition. The dotted horizontal line indicates no change, such that values below the line indicate a decrease in displacement reaction time from pre- to post-intervention while values above indicate an increase. Violin plots show the distribution of individual change scores, with points representing individual participants. Black boxes indicate model-predicted mean change $\pm$ SE. CF = cognitive fatigue intervention, CTL = control intervention.

5.6.4 Catch Trial Performance

Participants incorrectly responded on 17.2% of catch trials. The probability of responding on a catch trial was not significantly impacted by intervention condition, pre/post phase, or their interaction ($p > .160$ in all cases).

5.6.5 Resting Motor Threshold

No significant effect of intervention condition on RMT was observed ($F(1,90) = 0.50, p = .480$). While RMT rose slightly from pre- to post-intervention for both conditions (Δ intensity = +0.82, $SE = 0.75$), this increase was not significant ($F(1,90) = 1.20, p = .277$), nor was the interaction of pre/post phase and intervention condition ($F(1,90) = 0.02, p = .880$).

5.6.6 Resting MEP Amplitude

A significant intervention condition x pre/post phase interaction was observed ($F(1,1117) = 19.05, p < .001$). Post hoc testing showed a tendency for resting MEP amplitude to decrease over CTL ($\Delta = -0.06$ mV, $SE = 0.04$ mV, $p = .090$) but increase over CF ($\Delta = +0.06$ mV, $SE = 0.04$ mV, $p = .158$), resulting in a significant difference in pre-to-post change between conditions ($\Delta_{CTL-\Delta CF} = -0.12$ mV, $SE = 0.03$ mV, $p < .001$; Fig. 5.5b). Further, there was no significant difference in resting MEP amplitude at pre-intervention (CTL-CF = 0.03 mV, $SE = 0.04$ mV, $p = .437$) while the post-intervention contrast approached significance (CTL-CF = -0.08 mV, $SE = 0.05$ mV, $p = .082$; Fig. 5.5a).

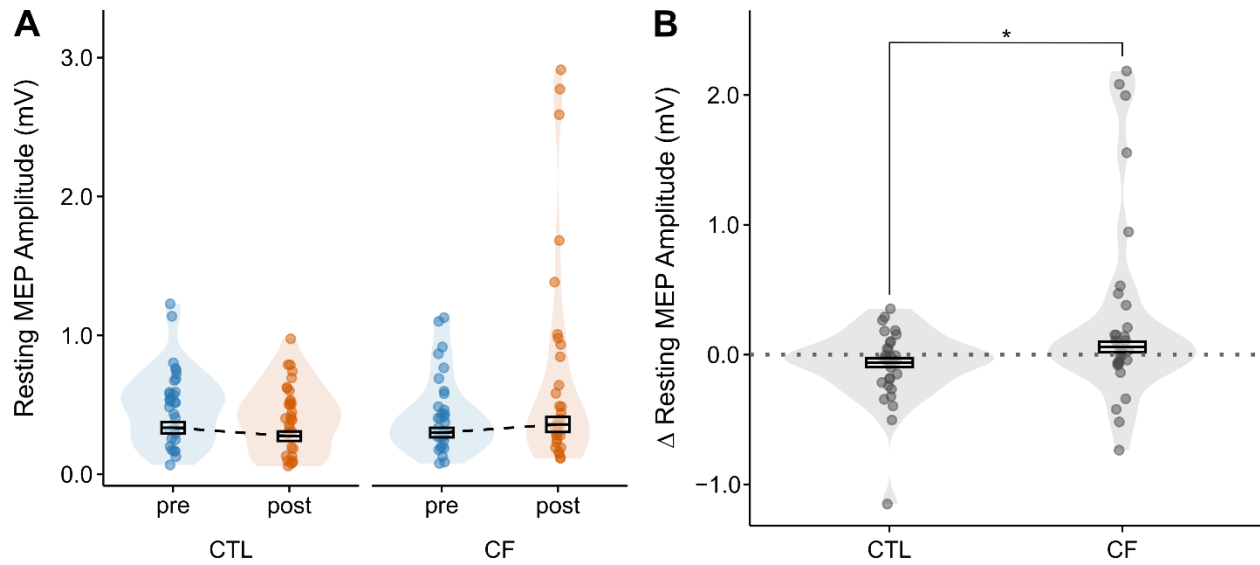


Fig. 5.5 Resting peak-to-peak motor-evoked potential (MEP) amplitude (mV). (a) Resting MEP amplitude as a function of intervention condition (CTL, CF) and pre/post phase (pre-intervention, post-intervention). Violin plots show the distribution of individual mean values, with points representing individual participants. Black boxes indicate model-predicted means $\pm$ SE. (b) Change in resting MEP amplitude (post – pre) by intervention condition. The dotted horizontal line indicates no change, such that values below the line indicate a decline in resting MEP amplitude from pre- to post-intervention while values above indicate an increase. Violin plots show the distribution of individual change scores, with points representing individual participants. Black boxes indicate model-predicted mean change $\pm$ SE. Asterisks indicate significant differences where $p < .050$. CF = cognitive fatigue intervention, CTL = control intervention.

5.6.7 Preparatory MEP Amplitude

MEP amplitude measured during the RT task preparatory delay period was significantly affected by TMS timepoint ($F(2,3963) = 25.59, p < .001$) such that MEP amplitude became progressively smaller as the go-signal approached. Specifically, preparatory MEP amplitude was significantly

smaller at go-150ms compared to go-500ms ($\Delta = -0.05$ mV, $SE = 0.02$ mV, $p = .003$), and was further reduced at go-0ms compared to go-150ms ($\Delta = -0.04$ mV, $SE = 0.01$ mV, $p = .004$) and go-500ms ($\Delta = -0.09$ mV, $SE = 0.02$ mV, $p < .001$; Fig. 5.6).

There was also a significant main effect of pre/post phase on MEP amplitude, $F(1,29) = 4.42$, $p = .044$); however, this was superseded by a significant interaction between pre/post phase and intervention condition, $F(1,3976) = 29.88$, $p < .001$). While MEP amplitude did not significantly differ between intervention conditions at the pre-intervention phase ($\Delta_{CTL-CF} = -0.034$ mV, $SE = 0.09$ mV, $p = .692$) or post-intervention phase ($\Delta_{CTL-CF} = -0.082$ mV, $SE = 0.07$ mV, $p = .265$), the magnitude of the pre- to post-intervention change in MEP amplitude differed by intervention condition ($\Delta_{CTL-\Delta CF} = -0.12$ mV, $SE = 0.03$ mV, $p < .001$). Specifically, MEP amplitude declined significantly between pre- and post phases in the CTL condition ($\Delta = -0.12$ mV, $SE = 0.04$ mV, $p = .005$) but did not significantly change in the CF condition ($\Delta = -0.004$ mV, $SE = 0.03$ mV, $p = .906$; Fig. 5.6).

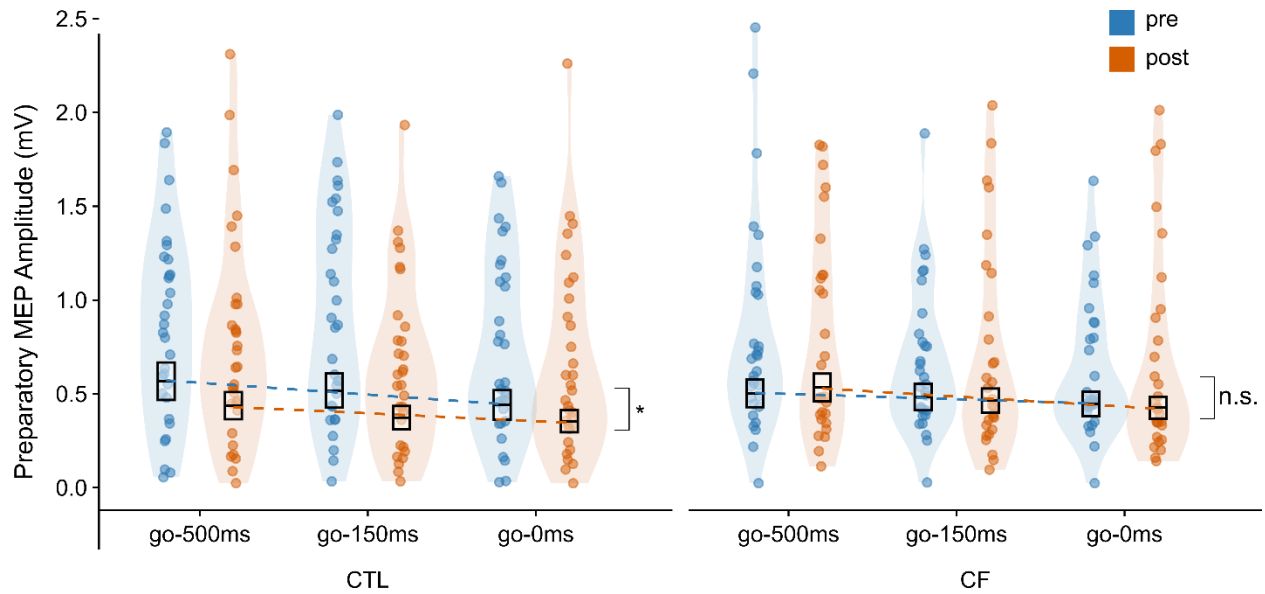


Fig. 5.6 Preparatory peak-to-peak motor-evoked potential (MEP) amplitude (mV). MEP amplitude is shown as a function of intervention condition (CTL, CF), TMS timepoint (go-500ms, go-150ms, go-0ms), and pre/post phase (pre-intervention, post-intervention). Violin plots show the distribution of individual mean values, with points representing individual participants. Black boxes indicate model-predicted means $\pm$ SE. Dashed lines show linear trends fitted to the estimated marginal means. Asterisks indicate significant differences where $p < .050$. CF = cognitive fatigue intervention, CTL = control intervention.

5.7 Discussion

This study examined whether inducing cognitive fatigue (CF) would alter corticospinal excitability at rest and during movement preparation, to explore a potential mechanism for CF-related motor performance decrements. The CF manipulation was successful, shown by robust increases in subjective fatigue without specific effects on motivation, alongside non-significant trends toward slowed RT. Although it was expected that RT would be significantly increased by CF, response latency was influenced by the timing of the TMS pulse, which likely acted as a temporal pre-cue and may have reduced the detectability of CF-related slowing. We predicted

that CF would alter preparatory corticospinal excitability relative to control, potentially reflected as a reduced early rise or diminished suppression of excitability just prior to the go-signal. Importantly, while corticospinal excitability was clearly modulated by the CF manipulation, the observed changes were not in line with our predictions. Instead, corticospinal excitability actually declined between the pre-test and post-intervention testing in the CTL condition, while it was maintained following CF, becoming significantly elevated relative to control in the post-test. This effect of the fatigue manipulation on corticospinal excitability was consistent across the preparatory delay period (i.e., the effect was similar at all TMS delivery timepoints) and a similar pattern was evident at rest. Overall, these results suggest that CF leads to a broad elevation of corticospinal excitability relative to control, potentially reflecting compensatory maintenance of motor system readiness.

5.7.1 Subjective Fatigue and Motivation

In line with previous research, we confirmed that our Math-Memory intervention was successful in inducing cognitive fatigue, as indicated by a significantly greater rise in subjective fatigue ratings following the CF intervention compared to the CTL intervention (Fig. 5.2a and 5.2b) (Peters et al., 2022, 2024). Notably, although subjective fatigue increased, pre- to post-intervention change in motivation did not differ between the intervention conditions (Fig. 5.2c and 5.2d). This latter finding concurs with previous research indicating that the Math-Memory task successfully induces cognitive fatigue without notable demotivation compared to control. This reduces the possibility that differences observed between the intervention conditions are due to varying levels of motivation rather than cognitive fatigue (Peters & Carlsen, 2025).

5.7.2 Premotor and Displacement Reaction Time

Based on previous experiments using the same fatigue manipulation, it was expected that RT would be slowed following CF (Peters et al., 2022, 2024). However, in contrast, CF did not lead to a statistically significant increase in either premotor or displacement RT. Closer inspection suggested that the TMS pulse may have acted as a temporal pre-cue for the upcoming go-signal, as RT became systematically faster the earlier TMS was delivered relative to the go-signal (Fig. 5.3a, Fig. 5.4a). Although foreperiod duration was held constant to allow sampling of comparable stages of preparation across participants and conditions (Kennefick et al., 2014), this consistency may have also allowed the TMS pulse to become a reliable temporal cue relative to the go-signal. This occurred despite variable intertrial intervals and instructions to actively ignore any sounds or sensations from the TMS. As shown elsewhere (Duecker et al., 2013; Duecker & Sack, 2013), the audible TMS “click”, sometimes accompanied by a light tapping sensation, may have primed the timing of the go-signal and facilitated RT, particularly when delivered early in the preparatory delay. Consistent with this explanation, RT was slowest when TMS coincided with the go-signal, when it could not provide advance temporal information. This pre-cueing effect also strengthened from pre- to post-intervention, especially at the -150 ms interval, suggesting that participants became more adept at using the pulse as a temporal cue with practice. Additionally, the unexpectedly high proportion of trials where participants incorrectly made a response on catch trials ($> 17\%$) further supports the interpretation that the pulse acted as an unintended pre-cue, provoking anticipatory responses even when no go-stimulus was delivered.

Generally, these findings suggest that TMS-related pre-cueing influenced RT throughout the experiment. As a result, inferences regarding the direct effects of CF on RT in the current

experiment should be made cautiously. However, several observations do suggest that CF-related RT slowing was nevertheless present, although potentially attenuated by the pre-cuing influence. More specifically, exploratory analyses at the go-0ms TMS delivery timepoint – where the TMS pulse theoretically could not act as a pre-cue – showed directional slowing of premotor RT following CF and slight speeding following CTL, with a similar and larger trend observed for displacement RT. Thus, while temporal cueing introduced by the TMS likely masked CF effects on RT, there is support for subtle CF-related slowing, in line with previous findings using the same Math-Memory intervention (Peters et al., 2022, 2024).

5.7.3 Resting Motor Threshold

Although few prior studies have statistically examined the effects of experimentally induced CF on RMT, several studies have explored this TMS metric in fatigue-prone clinical populations, with mixed results. For example, patients with post-COVID-19 fatigue have been reported to show significantly higher RMT than healthy controls (Ortelli et al., 2022), whereas no such differences were observed in post-stroke fatigue (Kindred et al., 2024). In our study, RMT appeared to increase from pre- to post-intervention in both the CF and CTL conditions, but these changes were not statistically significant. This is perhaps unsurprising, as our analysis may have been underpowered given that a single threshold value per participant and testing time (CF/CTL, pre/post) was recorded. Future work may wish to further examine the effects of CF on resting motor threshold in both healthy and clinical populations using larger samples.

5.7.4 Preserved Corticospinal Excitability in CF Relative to Control

The most notable finding was a divergence in pre-to post-intervention changes in corticospinal excitability between CTL and CF conditions. Corticospinal excitability measured during the preparatory period declined following the CTL intervention but remained stable following the

CF intervention (Fig. 5.6). This pattern was consistent across all stimulation timepoints within the preparatory delay period. Resting corticospinal excitability followed a similar trajectory, appearing to decrease over the CTL intervention while increasing over CF (Fig. 5.5). Although changes in resting corticospinal excitability were not significant within each intervention condition, the magnitude and direction of change differed significantly between CTL and CF. Thus, cognitive fatigue was associated with an overall elevation of corticospinal output relative to control, in a manner that was not specific to any particular phase of motor preparation.

These findings align with some previous studies reporting maintenance of corticospinal excitability following cognitive tasks that produced subjective fatigue, both at rest and during motor imagery (Holgado et al., 2023; Rozand et al., 2015). However, these studies also reported stable corticospinal excitability in control conditions (including in comparable control conditions, i.e., a documentary film; Rozand et al., 2015), whereas we showed a decline in corticospinal excitability over CTL.

Although it is not entirely evident why corticospinal excitability declined over the CTL intervention in this study, one possible explanation is that this reflects increased neural efficiency with repeated task performance. As participants became more practiced at the RT task from pre- to post-intervention, less central drive may have been required to elicit similarly rapid responses, resulting in the reduction in corticospinal excitability observed over the CTL task (Takenaka et al., 2024). In contrast, this practice-related decline was absent following the CF intervention. Instead, under CF, greater central drive may have been necessary to stabilize motor output and preserve performance despite potential fatigue-related reductions in processing efficiency (Ishii et al., 2014; Wang et al., 2016).

Importantly, elevated corticospinal excitability following the CF intervention relative to control was observed both at rest and uniformly across the preparatory delay period, indicating a global impact rather than targeted changes at specific stages of preparation. As expected, preparatory period corticospinal excitability displayed the typical pattern of early elevation followed by suppression (or “preparatory inhibition”) as the go-signal approached (Greenhouse et al., 2015; Hasbroucq et al., 1999); however, this temporal pattern was not altered by CF (Fig. 5.6). The absence of stronger fatigue effects at timepoints nearest the go-signal, when preparatory inhibition is thought to be maximal (Hasbroucq et al., 1999; Ibáñez et al., 2020), argues against a purely inhibition-based explanation for the psychomotor impacts of CF. This interpretation is consistent with our previous behavioural observations showing that go/no-go RT performance (a measure of inhibitory control; Eagle et al., 2008; Menon et al., 2001) seemed less sensitive than choice or simple RT performance to the Math-Memory intervention (Peters & Carlsen, 2025).

Overall, the pattern observed here is most consistent with broad compensatory modulation of corticospinal excitability in CF. Other work supports the idea that preserved performance under CF may involve compensatory neural activity. For example, improved task performance in CF has been associated with deactivation of midbrain regions that typically drive mental rest (Nakagawa et al., 2013) and increased frontoparietal network connectivity (Badarin et al., 2025; Niu et al., 2024). Electroencephalography studies have shown increased anterior frontal evoked potentials that correlate with reduced behavioural decline, even when rising subjective fatigue was reported (Samuel et al., 2019; Wang et al., 2016). In one study, the peak of this neural activity occurred around 60-100 minutes of sustained cognitive effort – approximately the duration of the Math-Memory task used here (Wang et al., 2016). Further, high-density

surface EMG analyses show no CF-related reduction in neural drive to the muscle during isometric contractions (Alix-Fages et al., 2023), and as previously described, the StartReact Effect appears resistant to CF induced by a similar version of the Math-Memory task (Peters et al., 2022).

Together, these findings suggest that higher order/executive neural systems may be recruited to help offset fatigue-related disruptions and stabilize motor output. The results presented in this study support this interpretation, demonstrating preserved (or when compared to control, elevated) corticospinal excitability under cognitive fatigue. Overall, this is consistent with the idea of broad compensatory maintenance of motor readiness in CF, rather than fatigue-induced motor suppression or changes in motor neural activity specific to any preparation phase.

5.8 Conclusion

This study explored the effect of cognitive fatigue on corticospinal excitability at rest and during motor preparation in a simple RT task. The cognitive fatigue intervention (Math-Memory Task) successfully increased subjective fatigue relative to control (documentary film viewing) without meaningfully affecting motivation. Premotor and displacement RT were primarily affected by the timing of TMS delivery, although directional trends consistent with CF-related RT slowing were observed. Contrary to our initial predictions, corticospinal excitability declined over the control condition but was preserved following cognitive fatigue induction, resulting in relatively elevated excitability in CF compared to control. This pattern was evident both at rest and across all measured timepoints within the preparatory delay period.

Overall, these results are consistent with a compensatory, global maintenance of motor readiness in CF. In the context of other prior studies, these findings suggests that higher-order networks may upregulate motor system excitability to stabilize performance in the presence of

CF. Future research should further explore the relationship between preparatory corticospinal excitability and behavioural motor outcomes and assess whether this apparent compensatory maintenance of corticospinal excitability breaks down under longer or more demanding CF paradigms.

5.9 References

- Alix-Fages, C., Jiménez-Martínez, P., de Oliveira, D. S., Möck, S., Balsalobre-Fernández, C., & Del Vecchio, A. (2023). Mental fatigue impairs physical performance but not the neural drive to the muscle: A preliminary analysis. *European Journal of Applied Physiology*, 123(8), 1671–1684. <https://doi.org/10.1007/s00421-023-05189-1>
- Azcue, N., Del Pino, R., Tijero Merino, B., & Gómez Esteban, J. C. (2026). Fatigue in myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): Linking in brain fog. In C. R. Martin, V. R. Preedy, V. B. Patel, & R. Raiendram (Eds.), *The Scientific Basis of Fatigue* (pp. 75–90). Academic Press. <https://doi.org/10.1016/B978-0-443-24080-5.00032-1>
- Badarin, A. A., Antipov, V. M., Grubov, V. V., Andreev, A. V., Pitsik, E. N., Kurkin, S. A., & Hramov, A. E. (2025). Brain Compensatory Mechanisms During the Prolonged Cognitive Task: fNIRS and Eye-Tracking Study. *IEEE Transactions on Cognitive and Developmental Systems*, 17(2), 303–314. <https://doi.org/10.1109/TCDS.2024.3453590>
- Bailey, S. P., Harris, G. K., Lewis, K., Llewellyn, T. A., Watkins, R., Weaver, M. A., Roelands, B., Van Cutsem, J., & Folger, S. F. (2021). Impact of a Carbohydrate Mouth Rinse on Corticomotor Excitability after Mental Fatigue in Healthy College-Aged Subjects. *Brain Sciences*, 11(8), Article 8. <https://doi.org/10.3390/brainsci11080972>
- Bao, W., Chen, S., Hong, N., Ye, G., Li, C., Xie, J., Li, P., Li, H., Wang, Y., Liu, J., Niu, X., & Zhang, Y. (2025). Longitudinal relationships between changes in post-COVID mental fatigue and neuropsychiatric symptoms across distinct recovery trajectories. *Inflammopharmacology*, 33(9), 5471–5481. <https://doi.org/10.1007/s10787-025-01860-5>
- Barbosa, B. T. T., de Lima-Junior, D., Moreira, A., Nakamura, F. Y. Y., Batista, G. R. R., Faro, H. K. C., & Fortes, L. de S. D. S. (2025). Mental fatigue and sleep restriction effects on perceptual-cognitive performance in trained beach volleyball athletes. *Frontiers in Psychology*, 16, 1537482. <https://doi.org/10.3389/fpsyg.2025.1537482>
- Bates, D., Kliegl, R., Vasishth, S., & Baayen, H. (2018). *Parsimonious Mixed Models* (arXiv:1506.04967). arXiv. <https://doi.org/10.48550/arXiv.1506.04967>
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, 67, 1–48. <https://doi.org/10.18637/jss.v067.i01>
- Baus, E., & Farmer, J. (Directors). (2005). “Animals Like Us” *Animal Language (TV Episode)*—IMDb [Video recording]. <http://www.imdb.com/title/tt4504660/fullcredits>
- Behrens, M., Gube, M., Chaabene, H., Prieske, O., Zenon, A., Broscheid, K.-C., Schega, L., Husmann, F., & Weippert, M. (2023). Fatigue and Human Performance: An Updated Framework. *Sports Medicine*, 53(1), 7–31. <https://doi.org/10.1007/s40279-022-01748-2>

- Bestmann, S., & Duque, J. (2016). Transcranial Magnetic Stimulation: Decomposing the Processes Underlying Action Preparation. *The Neuroscientist*, 22(4), 392–405. <https://doi.org/10.1177/1073858415592594>
- Bestmann, S., & Krakauer, J. W. (2015). The uses and interpretations of the motor-evoked potential for understanding behaviour. *Experimental Brain Research*, 233(3), 679–689. <https://doi.org/10.1007/s00221-014-4183-7>
- Bourne, S. K., Walcott, B. P., Sheth, S. A., & Coumans, J.-V. C. E. (2013). Neurological surgery: The influence of physical and mental demands on humans performing complex operations. *Journal of Clinical Neuroscience*, 20(3), 342–348. <https://doi.org/10.1016/j.jocn.2012.09.008>
- Brooks, M. E., Kristensen, K., Benthem, K. J. van, Magnusson, A., Berg, C. W., Nielsen, A., Skaug, H. J., Mächler, M., & Bolker, B. M. (2017). glmmTMB Balances Speed and Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. *The R Journal*, 9(2), 378–400. <https://doi.org/10.32614/RJ-2017-066>
- Carlsen, A. N., Chua, R., Inglis, J. T., Sanderson, D. J., & Franks, I. M. (2004). Prepared Movements Are Elicited Early by Startle. *Journal of Motor Behavior*, 36(3), 253–264. <https://doi.org/10.3200/JMBR.36.3.253-264>
- Carlsen, A. N., & Maslovat, D. (2019). Startle and the StartReact Effect: Physiological Mechanisms. *Journal of Clinical Neurophysiology*, 36(6), 452–459. <https://doi.org/10.1097/WNP.0000000000000582>
- Carlsen, A. N., & Maslovat, D. (2026). What Is the StartReact Effect? *Acta Physiologica*, 242(6), e70235. <https://doi.org/10.1111/apha.70235>
- Carlsen, A. N., Maslovat, D., & Franks, I. M. (2012). Preparation for voluntary movement in healthy and clinical populations: Evidence from startle. *Clinical Neurophysiology*, 123(1), 21–33. <https://doi.org/10.1016/j.clinph.2011.04.028>
- Carlsen, A. N., Maslovat, D., Lam, M. Y., Chua, R., & Franks, I. M. (2011). Considerations for the use of a startling acoustic stimulus in studies of motor preparation in humans. *Neuroscience & Biobehavioral Reviews*, 35(3), 366–376. <https://doi.org/10.1016/j.neubiorev.2010.04.009>
- Chan, M. Y., Cohen, H., & Spiegel, B. M. R. (2009). Fewer Polyps Detected by Colonoscopy as the Day Progresses at a Veteran's Administration Teaching Hospital. *Clinical Gastroenterology and Hepatology*, 7(11), 1217–1223. <https://doi.org/10.1016/j.cgh.2009.07.013>
- Chen, P.-Y., Hsieh, S.-H., Lin, C.-K., Wei, L., Su, Y.-K., Tsai, P.-S., & Chiu, H.-Y. (2022). Mental fatigue mediates the relationship between cognitive functions and return to productive activity following traumatic brain injury: A mediation analysis. *Brain Injury*, 36(1), 32–38. <https://doi.org/10.1080/02699052.2022.2034044>

- Chiu, Y.-C., Cools, R., & Aron, A. R. (2014). Opposing Effects of Appetitive and Aversive Cues on Go/No-go Behavior and Motor Excitability. *Journal of Cognitive Neuroscience*, 26(8), 1851–1860. https://doi.org/10.1162/jocn_a_00585
- Costedoat, G., Chao, A., & Feria, C. S. (2023). The Effects of Physiological and Mental Fatigue on Driving Performance and an Analysis of Countermeasures. *Proceedings of the Human Factors and Ergonomics Society Annual Meeting*, 67(1), 1953–1957. <https://doi.org/10.1177/21695067231192414>
- Cuypers, K., Thijs, H., & Meesen, R. L. J. (2014). Optimization of the Transcranial Magnetic Stimulation Protocol by Defining a Reliable Estimate for Corticospinal Excitability. *PLOS ONE*, 9(1), e86380. <https://doi.org/10.1371/journal.pone.0086380>
- De Doncker, W., Brown, K. E., & Kuppaswamy, A. (2021). Influence of post-stroke fatigue on reaction times and corticospinal excitability during movement preparation. *Clinical Neurophysiology*, 132(1), 191–199. <https://doi.org/10.1016/j.clinph.2020.11.012>
- Demjan, M., Säisänen, L., Reijonen, J., Rissanen, S., Määttä, S., & Julkunen, P. (2023). Near-threshold recruitment characteristics of motor evoked potentials in transcranial magnetic stimulation. *Brain Research*, 1805, 148284. <https://doi.org/10.1016/j.brainres.2023.148284>
- Donders, F. C. (1969). On the speed of mental processes. *Acta Psychologica*, 30, 412–431. [https://doi.org/10.1016/0001-6918\(69\)90065-1](https://doi.org/10.1016/0001-6918(69)90065-1)
- Duecker, F., Graaf, T. A. de, Jacobs, C., & Sack, A. T. (2013). Time- and Task-Dependent Non-Neural Effects of Real and Sham TMS. *PLOS ONE*, 8(9), e73813. <https://doi.org/10.1371/journal.pone.0073813>
- Duecker, F., & Sack, A. T. (2013). Pre-Stimulus Sham TMS Facilitates Target Detection. *PLOS ONE*, 8(3), e57765. <https://doi.org/10.1371/journal.pone.0057765>
- Eagle, D. M., Bari, A., & Robbins, T. W. (2008). The neuropsychopharmacology of action inhibition: Cross-species translation of the stop-signal and go/no-go tasks. *Psychopharmacology*, 199(3), 439–456. <https://doi.org/10.1007/s00213-008-1127-6>
- Faul, F., Erdfelder, E., Lang, A.-G., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39(2), 175–191. <https://doi.org/10.3758/BF03193146>
- Fox, J., & Weisberg, S. (2019). *An R companion to applied regression* (Third edition). Sage.
- Greenhouse, I., Sias, A., Labruna, L., & Ivry, R. B. (2015). Nonspecific Inhibition of the Motor System during Response Preparation. *Journal of Neuroscience*, 35(30), 10675–10684. <https://doi.org/10.1523/JNEUROSCI.1436-15.2015>
- Gullo, H. L., Fleming, J., Bennett, S., & Shum, D. H. K. (2019). Cognitive and physical fatigue are associated with distinct problems in daily functioning, role fulfilment, and quality of

- life in multiple sclerosis. *Multiple Sclerosis and Related Disorders*, 31, 118–123.
<https://doi.org/10.1016/j.msard.2019.03.024>
- Guo, Z., Chen, R., Liu, X., Zhao, G., Zheng, Y., Gong, M., & Zhang, J. (2018). The impairing effects of mental fatigue on response inhibition: An ERP study. *PLOS ONE*, 13(6), e0198206. <https://doi.org/10.1371/journal.pone.0198206>
- Habay, J., Van Cutsem, J., Verschueren, J., De Bock, S., Proost, M., De Wachter, J., Tassignon, B., Meeusen, R., & Roelands, B. (2021). Mental Fatigue and Sport-Specific Psychomotor Performance: A Systematic Review. *Sports Medicine*, 51(7), 1527–1548.
<https://doi.org/10.1007/s40279-021-01429-6>
- Hallett, M. (2007). Transcranial Magnetic Stimulation: A Primer. *Neuron*, 55(2), 187–199.
<https://doi.org/10.1016/j.neuron.2007.06.026>
- Hanes, D. P., & Schall, J. D. (1996). Neural control of voluntary movement initiation. *Science*, 274(5286), 427–431.
- Hasbroucq, T., Osman, A., Possamaï, C.-A., Burle, B., Carron, S., Dépy, D., Latour, S., & Mouret, I. (1999). Cortico-spinal inhibition reflects time but not event preparation: Neural mechanisms of preparation dissociated by transcranial magnetic stimulation. *Acta Psychologica*, 101(2), 243–266. [https://doi.org/10.1016/S0001-6918\(99\)00007-4](https://doi.org/10.1016/S0001-6918(99)00007-4)
- Hodges, P. W., & Bui, B. H. (1996). A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography. *Electroencephalography and Clinical Neurophysiology*, 101(6), 511–519.
[https://doi.org/10.1016/S0921-884X\(96\)95190-5](https://doi.org/10.1016/S0921-884X(96)95190-5)
- Holgado, D., Jolidon, L., Borragán, G., Sanabria, D., & Place, N. (2023). Individualized Mental Fatigue Does Not Impact Neuromuscular Function and Exercise Performance. *Medicine and Science in Sports and Exercise*, 55(10), 1823–1834.
<https://doi.org/10.1249/MSS.0000000000003221>
- Ibáñez, J., Hannah, R., Rocchi, L., & Rothwell, J. C. (2020). Premovement Suppression of Corticospinal Excitability may be a Necessary Part of Movement Preparation. *Cerebral Cortex*, 30(5), 2910–2923. <https://doi.org/10.1093/cercor/bhz283>
- Ishii, A., Tanaka, M., & Watanabe, Y. (2014). Neural mechanisms of mental fatigue. *Reviews in the Neurosciences*, 25(4), 469–479. <https://doi.org/10.1515/revneuro-2014-0028>
- Islam, T., Berard, J. A., & Walker, L. A. S. (2026). Perceived Cognitive Fatigability in Multiple Sclerosis: Input from People with Lived Experience on Unmet Needs. *Canadian Journal of Neurological Sciences*, 1–10. <https://doi.org/10.1017/cjn.2026.10531>
- Janhofer, D. E., Lakhiani, C., & Song, D. H. (2019). Addressing Surgeon Fatigue: Current Understanding and Strategies for Mitigation. *Plastic and Reconstructive Surgery*, 144(4), 693e. <https://doi.org/10.1097/PRS.0000000000006075>

- Jaydarifard, S., Behara, K., Baker, D., & Paz, A. (2024). Driver fatigue in taxi, ride-hailing, and ridesharing services: A systematic review. *Transport Reviews*, 44(3), 572–590. <https://doi.org/10.1080/01441647.2023.2278446>
- Jia, H., Lin, C. J., & Wang, E. M. (2022). Effects of mental fatigue on risk preference and feedback processing in risk decision-making. *Scientific Reports*, 12(1), 10695. <https://doi.org/10.1038/s41598-022-14682-0>
- Johansson, B., & Rönnbäck, L. (2017). Assessment and treatment of mental fatigue after a traumatic brain injury. *Neuropsychological Rehabilitation*, 27(7), 1047–1055. <https://doi.org/10.1080/09602011.2017.1292921>
- Kato, Y., Endo, H., & Kizuka, T. (2009). Mental fatigue and impaired response processes: Event-related brain potentials in a Go/NoGo task. *International Journal of Psychophysiology*, 72(2), 204–211. <https://doi.org/10.1016/j.ijpsycho.2008.12.008>
- Kennefick, M., Maslovat, D., & Carlsen, A. N. (2014). The Time Course of Corticospinal Excitability during a Simple Reaction Time Task. *PLoS ONE*, 9(11), e113563. <https://doi.org/10.1371/journal.pone.0113563>
- Kindred, J. H., Gregory, C. M., Kautz, S. A., & Bowden, M. G. (2024). Interhemispheric Asymmetries in Intracortical Facilitation Correlate With Fatigue Severity in Individuals With Poststroke Fatigue. *Journal of Clinical Neurophysiology*, 41(4), 365. <https://doi.org/10.1097/WNP.0000000000000994>
- Kotnik, P., Roelands, B., & Bogataj, Š. (2024). Prolonged theoretical classes impact students' perceptions: An observational study. *Frontiers in Psychology*, 15, 1278396. <https://doi.org/10.3389/fpsyg.2024.1278396>
- Kowalski, K. L., Tierney, B. C., & Christie, A. D. (2022). Mental fatigue does not substantially alter neuromuscular function in young, healthy males and females. *Physiology & Behavior*, 253, 113855. <https://doi.org/10.1016/j.physbeh.2022.113855>
- Kunasegaran, K., Ismail, A. M. H., Ramasamy, S., Gnanou, J. V., Caszo, B. A., & Chen, P. L. (2023). Understanding mental fatigue and its detection: A comparative analysis of assessments and tools. *PeerJ*, 11, e15744. <https://doi.org/10.7717/peerj.15744>
- Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, 82, 1–26. <https://doi.org/10.18637/jss.v082.i13>
- Langner, R., Steinborn, M. B., Chatterjee, A., Sturm, W., & Willmes, K. (2010). Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychologica*, 133(1), 64–72. <https://doi.org/10.1016/j.actpsy.2009.10.001>
- Leitner, M., Opriessnig, P., Ropele, S., Schmidt, R., Leal-Garcia, M., Fellner, M., & Koini, M. (2024). Changes in thalamic functional connectivity in post-Covid patients with and

- without fatigue. *NeuroImage*, 301, 120888.
<https://doi.org/10.1016/j.neuroimage.2024.120888>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835.
<https://doi.org/10.1016/j.autcon.2019.102835>
- Li, T., Zhang, D., Wang, Y., Cheng, S., Wang, J., Zhang, Y., Xie, P., & Chen, X. (2024). Research on mental fatigue during long-term motor imagery: A pilot study. *Scientific Reports*, 14(1), 18454. <https://doi.org/10.1038/s41598-024-69013-2>
- Lieberman, H. R., Castellani, J. W., & Young, A. J. (2009). Cognitive function and mood during acute cold stress after extended military training and recovery. *Aviation, Space, and Environmental Medicine*, 80(7), 629–636. <https://doi.org/10.3357/ase.2431.2009>
- Lindemann, O., & Fischer, M. H. (2023). Chronometric methods: Reaction times and movement times. In A. Felisatti & M.H. Fischer (Eds.), *Experimental Methods in Embodied Cognition* (pp. 37-48). Routledge.
- Lorist, M. M., Klein, M., Nieuwenhuis, S., de Jong, R., Mulder, G., & Meijman, T. F. (2000). Mental fatigue and task control: Planning and preparation. *Psychophysiology*, 37(5), 614–625. <https://doi.org/10.1111/1469-8986.3750614>
- Lou, J.-S. (2009). Physical and Mental Fatigue in Parkinson's Disease. *Drugs & Aging*, 26(3), 195–208. <https://doi.org/10.2165/00002512-200926030-00002>
- Macfarlane, G. J., D'Angelo, S., Ntani, G., & Walker-Bone, K. (2024). Impact of fatigue on work productivity and health-related job loss. *Occupational Medicine*, 74(6), 423–429. <https://doi.org/10.1093/occmed/kqae056>
- Mahdavi, N., Tapak, L., Darvishi, E., Doosti-Irani, A., & Shafiee Motlagh, M. (2024). Unraveling the interplay between mental workload, occupational fatigue, physiological responses and cognitive performance in office workers. *Scientific Reports*, 14(1), 17866. <https://doi.org/10.1038/s41598-024-68889-4>
- Matuschek, H., Kliegl, R., Vasishth, S., Baayen, H., & Bates, D. (2017). Balancing Type I error and power in linear mixed models. *Journal of Memory and Language*, 94, 305–315. <https://doi.org/10.1016/j.jml.2017.01.001>
- Meng, F., Li, S., Cao, L., Li, M., Peng, Q., Wang, C., & Zhang, W. (2015). Driving Fatigue in Professional Drivers: A Survey of Truck and Taxi Drivers. *Traffic Injury Prevention*, 16(5), 474–483. <https://doi.org/10.1080/15389588.2014.973945>

- Menon, V., Adleman, N. E., White, C. d., Glover, G. h., & Reiss, A. l. (2001). Error-related brain activation during a Go/NoGo response inhibition task. *Human Brain Mapping, 12*(3), 131–143. [https://doi.org/10.1002/1097-0193\(200103\)12:3%3C131::AID-HBM1010%3E3.0.CO;2-C](https://doi.org/10.1002/1097-0193(200103)12:3%3C131::AID-HBM1010%3E3.0.CO;2-C)
- Michielsens, H. J., De Vries, J., & Van Heck, G. L. (2003). Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *Journal of Psychosomatic Research, 54*(4), 345–352. [https://doi.org/10.1016/S0022-3999\(02\)00392-6](https://doi.org/10.1016/S0022-3999(02)00392-6)
- Mirin, A. A., Dimmock, M. E., & Jason, L. A. (2022). Updated ME/CFS prevalence estimates reflecting post-COVID increases and associated economic costs and funding implications. *Fatigue: Biomedicine, Health & Behavior, 10*(2), 83–93. <https://doi.org/10.1080/21641846.2022.2062169>
- Morris, A. J., & Christie, A. D. (2020). The Effect of Mental Fatigue on Neuromuscular Function is Similar in Young and Older Women. *Brain Sciences, 10*(4), 191. <https://doi.org/10.3390/brainsci10040191>
- Nakagawa, S., Sugiura, M., Akitsuki, Y., Hosseini, S. M. H., Kotozaki, Y., Miyauchi, C. M., Yomogida, Y., Yokoyama, R., Takeuchi, H., & Kawashima, R. (2013). Compensatory Effort Parallels Midbrain Deactivation during Mental Fatigue: An fMRI Study. *PLOS ONE, 8*(2), e56606. <https://doi.org/10.1371/journal.pone.0056606>
- Nakashima, A., Moriuchi, T., Matsuda, D., Hasegawa, T., Nakamura, J., Anan, K., Satoh, K., Suzuki, T., Higashi, T., & Sugawara, K. (2021). Corticospinal excitability during motor imagery is diminished by continuous repetition-induced fatigue. *Neural Regeneration Research, 16*(6), 1031. <https://doi.org/10.4103/1673-5374.300448>
- Nielsen, T. B., Leth, S., Pedersen, M., Harbo, H. D., Nielsen, C. V., Laursen, C. H., Schiøttz-Christensen, B., & Oestergaard, L. G. (2022). Mental Fatigue, Activities of Daily Living, Sick Leave and Functional Status among Patients with Long COVID: A Cross-Sectional Study. *International Journal of Environmental Research and Public Health, 19*(22), Article 22. <https://doi.org/10.3390/ijerph192214739>
- Niu, S., Guo, J., Hanson, N. J., Wang, K., Chai, J., & Guo, F. (2024). The effects of mental fatigue on fine motor performance in humans and its neural network connectivity mechanism: A dart throwing study. *Cerebral Cortex, 34*(3), bhae085. <https://doi.org/10.1093/cercor/bhae085>
- O’Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics, 63*(1), 1–12. <https://doi.org/10.1080/00140139.2019.1687940>
- Ortelli, P., Ferrazzoli, D., Sebastianelli, L., Maestri, R., Dezi, S., Spampinato, D., Saltuari, L., Alibardi, A., Engl, M., Kofler, M., Quartarone, A., Koch, G., Oliviero, A., & Versace, V. (2022). Altered motor cortex physiology and dysexecutive syndrome in patients with

- fatigue and cognitive difficulties after mild COVID-19. *European Journal of Neurology*, 29(6), 1652–1662. <https://doi.org/10.1111/ene.15278>
- Palm, S., Rönnbäck, L., & Johansson, B. (2017). Long-term mental fatigue after traumatic brain injury and impact on employment status. *Journal of Rehabilitation Medicine*, 49(3), Article 3. <https://doi.org/10.2340/16501977-2190>
- Park, J.-W., Park, B.-J., Lee, J.-S., Lee, E.-J., Ahn, Y.-C., & Son, C.-G. (2024). Systematic review of fatigue severity in ME/CFS patients: Insights from randomized controlled trials. *Journal of Translational Medicine*, 22(1), 529. <https://doi.org/10.1186/s12967-024-05349-7>
- Peters, K. J., & Carlsen, A. (2025, March). Task-dependent reaction time impairments under cognitive fatigue. *2025 Annual Meeting Abstract Book*. Cognitive Neuroscience Society 32nd Annual Meeting.
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2024). Visual perceptual processing is unaffected by cognitive fatigue. *Consciousness and Cognition*, 119, 103666. <https://doi.org/10.1016/j.concog.2024.103666>
- 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. <https://doi.org/10.1016/j.trf.2015.01.003>
- Powell, M. J. D. (2009). *The BOBYQA algorithm for bound constrained optimization without derivatives* (Report DAMTP 2009/NA06). University of Cambridge.
- R Core Team. (2026). *R: A language and environment for statistical computing*. [Computer software]. R Foundation for Statistical Computing. <https://www.R-project.org/>
- Reis, C., & Canhão, H. (2013). Prevalence of Fatigue in a Group of Airline Pilots. *Aviation, Space, and Environmental Medicine*, 84, 828–833. <https://doi.org/10.3357/ASEM.3548.2013>
- Ricci, J., Chee, E., Lorandean, A., & 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), 1–10. <https://doi.org/10.1097/01.jom.0000249782.60321.2a>
- Rodriguez Llorian, E., Zhang, W., Khakban, A., Patten, S., Traboulsee, A., Oh, J., Kolind, S., Prat, A., Tam, R., & Lynd, L. D. (2022). Productivity loss among people with early multiple sclerosis: A Canadian study. *Multiple Sclerosis Journal*, 28(9), 1414–1423. <https://doi.org/10.1177/13524585211069070>

- Rossi, S., Hallett, M., Rossini, P. M., & Pascual-Leone, A. (2009). Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology*, 120(12), 2008–2039. <https://doi.org/10.1016/j.clinph.2009.08.016>
- Rossini, P. M., Burke, D., Chen, R., Cohen, L. G., Daskalakis, Z., Di Iorio, R., Di Lazzaro, V., Ferreri, F., Fitzgerald, P. B., George, M. S., Hallett, M., Lefaucheur, J. P., Langguth, B., Matsumoto, H., Miniussi, C., Nitsche, M. A., Pascual-Leone, A., Paulus, W., Rossi, S., ... Ziemann, U. (2015). Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. *Clinical Neurophysiology*, 126(6), 1071–1107. <https://doi.org/10.1016/j.clinph.2015.02.001>
- Rozand, V., Lebon, F., Papaxanthis, C., & Lepers, R. (2015). Effect of mental fatigue on speed–accuracy trade-off. *Neuroscience*, 297, 219–230. <https://doi.org/10.1016/j.neuroscience.2015.03.066>
- Ruban, S. D., Hilt, C. C., & Petersen, T. (2021). Quality of life in multiple sclerosis: The differential impact of motor and cognitive fatigue. *Multiple Sclerosis Journal*, 7(1), 2055217321996040. <https://doi.org/10.1177/2055217321996040>
- Russell, S., Jenkins, D., Rynne, S., Halson, S. L., & Kelly, V. (2019). What is mental fatigue in elite sport? Perceptions from athletes and staff. *European Journal of Sport Science*, 19(10), 1367–1376. <https://doi.org/https://doi.org/10.1080/17461391.2019.1618397>
- Salihu, A. T., Hill, K. D., & Jaberzadeh, S. (2022). Neural mechanisms underlying state mental fatigue: A systematic review and activation likelihood estimation meta-analysis. *Reviews in the Neurosciences*, 33(8), 889–917. <https://doi.org/10.1515/revneuro-2022-0023>
- Samuel, I. B. H., Wang, C., Burke, S. E., Kluger, B., & Ding, M. (2019). Compensatory Neural Responses to Cognitive Fatigue in Young and Older Adults. *Frontiers in Neural Circuits*, 13, 12. <https://doi.org/10.3389/fncir.2019.00012>
- Schamphoeleer, E., & Roelands, B. (2024). Mental Fatigue in Sport-From Impaired Performance to Increased Injury Risk. *International Journal of Sports Physiology and Performance*, 19(10), 1158–1166. <https://doi.org/10.1123/ijsp.2023-0527>
- Schumann, A., Di Giuliano, M., Schulz, S., de la Cruz, F., Kreuder, T., Seifert, G., & Bär, K.-J. (2025). Mapping the brain's fatigue network: A transdiagnostic systematic review and meta-analysis on functional correlates of mental fatigue. *Brain Communications*, 7(5), fcac315. <https://doi.org/10.1093/braincomms/fcac315>
- Sievertsen, H. H., Gino, F., & Piovesan, M. (2016). Cognitive fatigue influences students' performance on standardized tests. *Proceedings of the National Academy of Sciences*, 113(10), 2621–2624. <https://doi.org/10.1073/pnas.1516947113>
- Staiano, W., Romagnoli, M., Salazar Bonet, L. R., & Ferri-Caruana, A. (2024). Adaptive cognitive tasks for mental fatigue: An innovative paradigm for cognitive loading in

- human performance. *Journal of Science and Medicine in Sport*, 27(12), 883–889.
<https://doi.org/10.1016/j.jsams.2024.08.199>
- Swaen, G. M. H., Amelsvoort, L. G. P. M. van, Bültmann, U., & Kant, I. J. (2003). Fatigue as a risk factor for being injured in an occupational accident: Results from the Maastricht Cohort Study. *Occupational and Environmental Medicine*, 60(suppl 1), 88–92.
https://doi.org/10.1136/oem.60.suppl_1.i88
- Takenaka, Y., Tomisaki, Y., Hirose, I., & Sugawara, K. (2024). Effects of Motor Learning on Corticospinal Tract Excitability During Motor Imagery. *Perceptual and Motor Skills*, 131(5), 2030–2044. <https://doi.org/10.1177/00315125241275212>
- Tapia, J. A., Tohyama, T., Poll, A., & Baker, S. N. (2022). The Existence of the StartReact Effect Implies Reticulospinal, Not Corticospinal, Inputs Dominate Drive to Motoneurons during Voluntary Movement. *Journal of Neuroscience*, 42(40), 7634–7647.
<https://doi.org/10.1523/JNEUROSCI.2473-21.2022>
- Taylor, D. A. (1976). Stage analysis of reaction time. *Psychological Bulletin*, 83(2), 161–191.
- Valls-Solé, J., Rothwell, J. C., Goulart, F., Cossu, G., & Muñoz, E. (1999). Patterned ballistic movements triggered by a startle in healthy humans. *The Journal of Physiology*, 516(3), 931–938. <https://doi.org/https://doi.org/10.1111/j.1469-7793.1999.0931u.x>
- Vassiliadis, P., Derosiere, G., Grandjean, J., & Duque, J. (2020). Motor training strengthens corticospinal suppression during movement preparation. *Journal of Neurophysiology*, 124(6), 1656–1666. <https://doi.org/10.1152/jn.00378.2020>
- Vrijkotte, S., Roelands, B., Meeusen, R., & Pattyn, N. (2016). Sustained Military Operations and Cognitive Performance. *Aerospace Medicine and Human Performance*, 87(8), 718–727.
<https://doi.org/10.3357/AMHP.4468.2016>
- Wang, C., Trongnetrpunya, A., Samuel, I. B. H., Ding, M., & Kluger, B. M. (2016). Compensatory Neural Activity in Response to Cognitive Fatigue. *Journal of Neuroscience*, 36(14), 3919–3924. <https://doi.org/10.1523/JNEUROSCI.3652-15.2016>
- Weiler, H., Russell, S., Spielmann, J., & Englert, C. (2025). Mental Fatigue: Is It Real? *Journal of Applied Sport and Exercise Psychology*, 32(1), 14–26.
<https://doi.org/https://10.1026/2941-7597/a000033>
- Xing, X., Zhong, B., Luo, H., Rose, T., Li, J., & Antwi-Afari, M. F. (2020). Effects of physical fatigue on the induction of mental fatigue of construction workers: A pilot study based on a neurophysiological approach. *Automation in Construction*, 120, 103381.
<https://doi.org/10.1016/j.autcon.2020.103381>
- Yan, W., He, J., Peng, Y., Ma, H., & Li, C. (2024). Research on brain functional network property analysis and recognition methods targeting brain fatigue. *Scientific Reports*, 14(1), 22556. <https://doi.org/10.1038/s41598-024-73919-2>

- Yoon, J.-H., Park, N.-H., Kang, Y.-E., Ahn, Y.-C., Lee, E.-J., & Son, C.-G. (2023). The demographic features of fatigue in the general population worldwide: A systematic review and meta-analysis. *Frontiers in Public Health*, 11. <https://doi.org/10.3389/fpubh.2023.1192121>
- Zeuwts, L. H. R. H., Iliano, E., Smith, M., Deconinck, F., & Lenoir, M. (2021). Mental fatigue delays visual search behaviour in young cyclists when negotiating complex traffic situations: A study in virtual reality. *Accident Analysis & Prevention*, 161, 106387. <https://doi.org/10.1016/j.aap.2021.106387>
- Zhang, Z., Xiang, T., Guo, H., Ma, L., Guan, Z., & Fang, Y. (2023). Impact of physical and mental fatigue on construction workers' unsafe behavior based on physiological measurement. *Journal of Safety Research*, 85, 457–468. <https://doi.org/10.1016/j.jsr.2023.04.014>
- Zong, H., Yi, W., Antwi-Afari, M. F., & Yu, Y. (2024). Fatigue in construction workers: A systematic review of causes, evaluation methods, and interventions. *Safety Science*, 176, 106529. <https://doi.org/10.1016/j.ssci.2024.106529>

Chapter 6. Experiment 5 - Preliminary Evidence for Attenuation of Cognitive Fatigue Effects on Psychomotor Performance Following Auricular tVNS: A Sham-Controlled Pilot Study

6.1 Abstract

Cognitive fatigue is known to increase subjective feelings of exhaustion and negatively impact psychomotor performance, including reaction time (RT). This pilot study explored whether auricular transcutaneous vagus nerve stimulation (tVNS) can attenuate the subjective, psychomotor, and/or autonomic effects of cognitive fatigue using a randomised, single-blind, sham-controlled design. Simple RT performance, average heart rate, heart rate variability, and subjective sensations of fatigue, motivation loss, and tension were assessed before and after participants ($n = 14$) completed a 60-minute cognitively fatiguing Math-Memory intervention. On separate days, participants received either active auricular tVNS or sham (earlobe) stimulation throughout the Math-Memory intervention. Results suggested that active stimulation may attenuate cognitive fatigue-related increases in subjective fatigue, motivation loss, and tension compared to sham. Active stimulation also tended to reduce the impact of cognitive fatigue on psychomotor outcomes, reflected by smaller pre- to post-intervention increases in premotor and displacement RT, fewer anticipation errors, and higher EMG magnitude compared with sham. Average heart rate appeared unaffected by stimulation condition; however, heart rate variability tended to increase over the cognitive fatigue intervention with sham stimulation, while active stimulation produced the opposite pattern. A side-effect questionnaire indicated that stimulation was well-tolerated. While many of the observed effects remained at the trend level ($.05 < p < .1$) in this exploratory pilot study, these findings strongly support continued investigation of tVNS as a promising non-invasive technique for counteracting cognitive fatigue-

related psychomotor performance deficits, while also highlighting the need for future work clarifying the neurophysiological mechanisms underlying these effects.

6.2 Introduction

Cognitive fatigue, often referred to as mental fatigue, is a common psychobiological state that occurs with demanding or prolonged cognitive effort (Ackerman, 2011; Behrens et al., 2023). It is an acute phenomenon characterized by sensations of exhaustion and a desire to disengage from mental work, considered conceptually distinct from sleep deprivation-related fatigue (Balkin & Wesensten, 2011; Hopstaken et al., 2015). Cognitive fatigue is an inherent part of modern life, arising during activities ranging from office work (Brazaitis & Satas, 2023), virtual meetings (Shockley et al., 2021), and smartphone use (Fortes et al., 2023; Jacquet et al., 2023), to driving (Adachi et al., 2024; M. Guo et al., 2016) and child care (Dettmers et al., 2020).

Despite its commonality, cognitive fatigue can pose substantial risks. It has been shown to lead to slowed reaction times (Habay et al., 2021; Jacquet et al., 2023; Peters et al., 2022, 2024), impaired sustained attention (Z. Guo et al., 2016), reduced physical endurance (Dallaway et al., 2022; Van Cutsem et al., 2017), altered balance control (Pitts & Bhatt, 2023), and disrupted emotional regulation (Grillon et al., 2015) and decision making (Jia et al., 2022). In healthcare settings, it has been associated with increased risk of surgical error (Chan et al., 2009; Thomas et al., 2012) and missed perioperative nursing care (Rahmani et al., 2025). Cognitive fatigue is also a known contributor to fatigue-related road accidents (Jaydarifard et al., 2024; Zeuwts et al., 2021), which account for an estimated total 15-20% of collisions internationally (Transport Canada, 2023). In construction work, cognitive fatigue can impair hazard recognition and slow responses to such hazards (Li et al., 2019, 2020; Z. Zhang et al., 2023), and in sports settings, it has been linked to impaired athletic performance (Habay et al., 2021; Yuan et al.,

2023) and increased risk of injury (Fazackerley et al., 2025; Wirdnam et al., 2024). Cognitive fatigue is also one of the most debilitating symptoms reported in conditions such as traumatic brain injury (Ezekiel et al., 2021), post-stroke syndrome (Almhdawi et al., 2021), and multiple sclerosis (Craft et al., 2025; Islam et al., 2026), where it can substantially reduce quality of life.

Overall, the prevalence of cognitive fatigue and its negative effects on cognitive, physical, and psychomotor performance are well documented. Given this, the development of interventions to counteract cognitive fatigue is of considerable interest (Proost et al., 2022). Several potential countermeasures have been explored, including behavioural interventions (e.g., nature exposure, listening to music, and physical activity), psychological interventions (e.g., mindfulness and extrinsic motivation), and physiological interventions (e.g., caffeine, carbohydrate intake, and odours; Proost et al., 2022; H. Sun et al., 2024). However, findings have been mixed, and many approaches are difficult to implement for real-time mitigation of cognitive fatigue outside controlled laboratory environments (Pan et al., 2024; Proost et al., 2022; H. Sun et al., 2024).

One possible countermeasure that has received comparatively less attention is transcutaneous vagus nerve stimulation (tVNS). The vagus nerve (the tenth cranial nerve) originates in the medulla and projects extensively between the brain and peripheral organs (Johnson & Wilson, 2018). Stimulation of the vagus nerve has been used for more than two decades in the treatment of epilepsy and depression (Johnson & Wilson, 2018). Although early implementations of vagus nerve stimulation required surgical implantation of electrodes, non-invasive options have since been developed. These methods deliver a mild electrical current through the skin, typically via paired electrodes, that activate vagal afferents at either the external ear (auricular branch) or neck (cervical branch; Badran et al., 2019; Butt et al., 2020).

Transcutaneous VNS is considered safe and is typically associated with only limited side effects, such as mild dizziness, headache, or skin irritation at the stimulation site (Badran et al., 2019; Giraudier et al., 2025; A. Y. Kim et al., 2022; Redgrave et al., 2018). As a result, some tVNS devices have been approved for self-administered at-home use (e.g., in the treatment of migraine; A. Y. Kim et al., 2022; Mertens et al., 2018). Overall, the simplicity and safety of tVNS have made it increasingly accessible both to the public and for use in research settings.

Research in healthy participants has associated vagus nerve stimulation with elevated cortical alertness and arousal (Y. Chen et al., 2023), improved associative (Jacobs et al., 2015) and working memory performance (L. Sun et al., 2017), decreased RT latency (Lerman et al., 2022; Marano et al., 2022; McIntire et al., 2021), and other enhanced psychomotor processes such as response selection (Jongkees et al., 2018; Su et al., 2025) and inhibition (Beste et al., 2016; Schevernels et al., 2016). Some of such reported benefits have been suggested to arise from activation the locus coeruleus (LC), a small nucleus in the dorsal pons with widespread projections throughout the brain and spinal cord, and the brain's primary source of norepinephrine (often referred to as the LC-NE system; Chandler, 2016; Poe et al., 2020).

Transcutaneous VNS is thought to activate vagal afferent fibers in the ear, which, via the nucleus tractus solitarius, project to the LC and stimulate secretion of norepinephrine (Butt et al., 2020; Colzato & Beste, 2020). Enhanced levels of norepinephrine with stimulation, potentially alongside modulation of autonomic circuits (Ridgewell et al., 2021), may help explain the improvements in cognitive, memory, and psychomotor performance observed with VNS (McIntire et al., 2021; Ridgewell et al., 2021; H. Zhang et al., 2022).

Given these benefits to cognitive and psychomotor functioning, recent work has begun to explore whether tVNS may also help counteract fatigue-related impairments. Compared to sham

stimulation, tVNS has been shown to improve general cognitive (multi-tasking) performance, reaction time task speed and accuracy, and subjective sensations of fatigue in sleep deprivation (McIntire et al., 2021). There is also evidence that tVNS may improve symptoms of mental fatigue in long-COVID syndrome (Badran et al., 2022; Linnhoff et al., 2023), primary Sjogren's Syndrome (Tarn et al., 2023), and systemic lupus erythematosus (Aranow et al., 2021). However, despite growing evidence that tVNS may enhance cognitive and psychomotor functioning, its potential to counteract the effects of acute *cognitive* fatigue in healthy individuals remains largely unexplored. Therefore, the current pilot study investigated whether tVNS can attenuate subjective sensations of fatigue and/or psychomotor performance declines typically associated with cognitive fatigue, assessed using visual analog scales and a simple reaction time task. Preliminary signs of effectiveness would suggest that this approach could have practical implications for improving safety and wellbeing in contexts where cognitive fatigue is prevalent.

6.3 Materials and Methods

6.3.1 Participants

An a priori power analysis was conducted based on the smallest effect size reported by Borges et al. (2021) for reaction time following transcutaneous vagus nerve stimulation (tVNS). Borges and colleagues reported partial η^2 values of 0.164 for differences between three stimulation locations and 0.147 for differences across three testing sessions. Using the smaller effect size (partial $\eta^2 = 0.147$) to provide a conservative estimate, the analysis indicated that 14 participants were required to achieve 80% power ($\alpha = .05$).

Fourteen participants took part in this pilot experiment, including 11 who self-identified as assigned female at birth (mean age = 21.60 ± 4.52 years) and 3 who self-identified as assigned male at birth (mean age = 21.70 ± 2.89 years). All participants were free from neurological

disorders, chronic fatigue, and uncorrected visual impairments. Consistent with safety recommendations for tVNS application (Badran et al., 2019), individuals were excluded if they had a history of epilepsy or seizures, severe mood or psychiatric disorders (e.g., schizophrenia, bipolar disorder), alcohol dependence, recent illicit drug use, or any cardiovascular conditions. Individuals were also ineligible to participate if they were pregnant, taking medications known to increase seizure risk (e.g., benzodiazepines, antiepileptics), had recently used illicit drugs, or had any implanted electrical devices (e.g., pacemaker, cochlear implant).

All participants provided written informed consent prior to participation and were fully informed of the potential side-effects associated with sham and active tVNS, such as temporary and mild skin irritation from the electrodes, headache, and dizziness (Badran et al., 2019; A. Y. Kim et al., 2022).

6.3.2 Experiment Overview

This pilot experiment followed a randomised, single-blind, sham-controlled, within-participants design. Each participant completed two 2-hour testing sessions scheduled at the same time of day (between 8:30 am and 2:30 pm). Sessions were separated by at least 24 hours and no more than 1 week. Active tVNS was applied during one session and sham stimulation during the other in randomised order. Participants remained blinded to stimulation condition until completion of the study, at which point they were fully debriefed.

An overview of the experimental timeline is depicted in Fig. 6.1a. To begin each session, participants completed a brief lifestyle questionnaire assessing factors that could influence fatigue or motor performance, including recent sleep, caffeine intake, mental work (e.g., studying), or physical activity. Participants were then seated in a comfortable chair ~1.5 m from a 24-inch computer monitor. At this point, tVNS, electromyography (EMG), and

electrocardiography (ECG) electrodes were applied, and tVNS threshold estimation was completed. Next, immediately before and after 60-minute cognitively fatiguing Math-Memory intervention (Peters et al., 2022, 2024; Peters & Carlsen, 2025), participants: 1) provided subjective ratings of cognitive fatigue, tension, and motivation/indifference level, 2) completed a visual simple reaction time task, and 3) underwent a 40-second ECG recording for assessment of heart rate measures (Fig. 6.1).

At the end of each session, participants completed a tVNS side-effect questionnaire (see *Appendix C.1.2* for details; adapted from Jacobs et al., 2015). Participants were fully debriefed regarding the order of stimulation (active, sham) they received following completion of the final session.

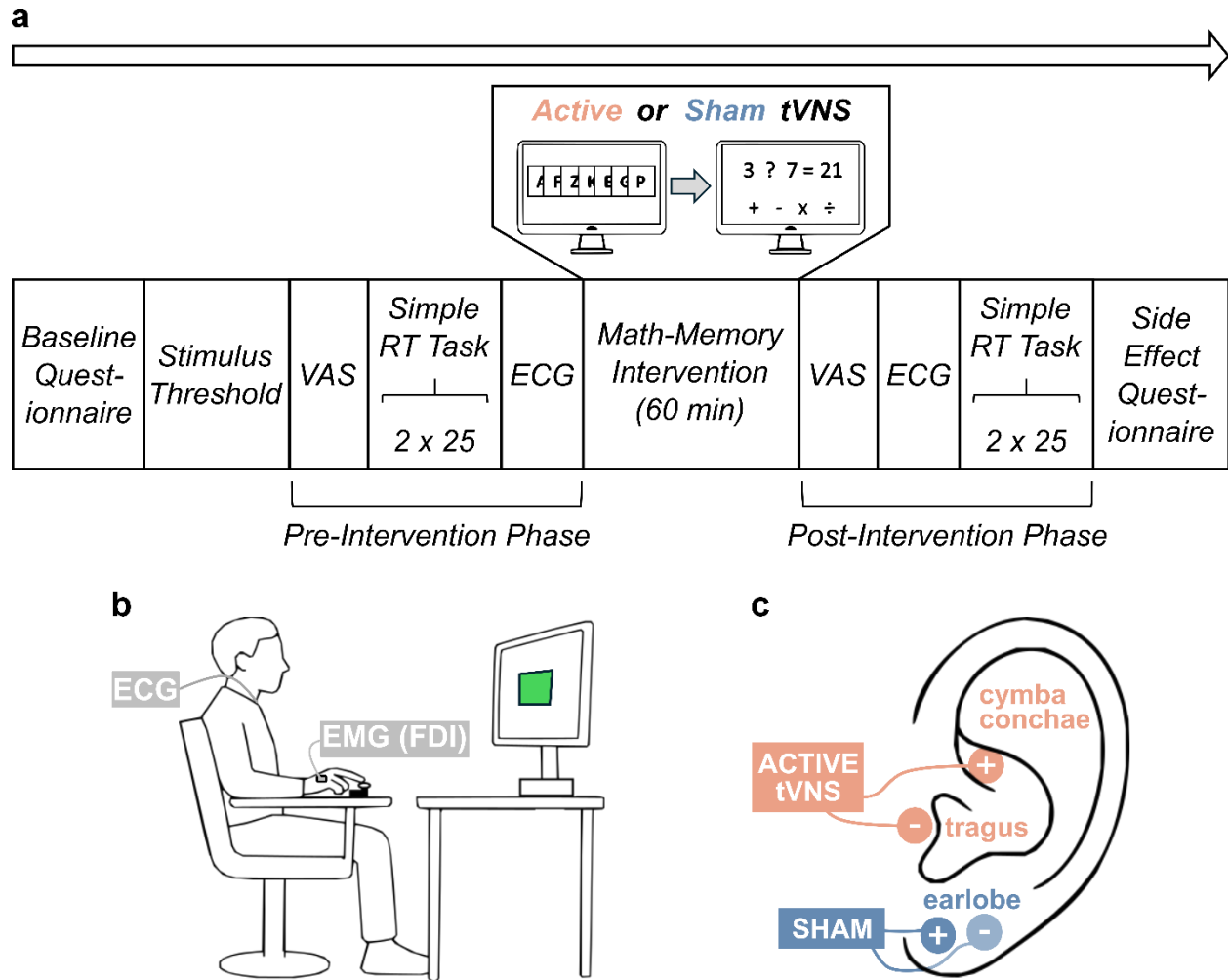


Fig. 6.1 Experimental overview. (a) Experimental timeline, (b) experimental set-up for reaction time tasks, and (c) active and sham tVNS configurations on the left ear are depicted. ECG = electrocardiography; EMG = electromyography; FDI = first dorsal interosseous muscle; RT = reaction time; VAS = visual analog scale.

6.3.3 Subjective Fatigue and Motivation Ratings

Subjective ratings of cognitive fatigue (0 = not at all mentally fatigued, 10 = extremely mentally fatigued), indifference (lack of motivation; 0 = motivated to succeed in the task, 10 = indifferent about the task), and tension (0 = relaxed, 10 = tense) were measured using a 20 cm horizontal

visual analog scale. Participants used a computer mouse to position a marker along each continuous scale according to their current state (Michielsen et al., 2003).

6.3.4 Simple Reaction Time (RT) Task

For the simple RT task, participants placed their right arm on an armrest with the shoulder abducted approximately 30°, elbow flexed near 90°, and forearm pronated position (Fig. 6.1b). The index finger rested lightly on the button of a telegraph key (Ameco AM-K4B) which outputted 0 V when open and 5 V when depressed. Following skin preparation with alcohol, a bipolar pre-amplified surface EMG electrode (Delsys DE-2.1) was placed over the right first dorsal interosseous (FDI) muscle to measure premotor RT. A grounding electrode (carbon-pad, 2-inch square, Easy@home) was positioned over the medial epicondyle of the right elbow. EMG signals were amplified using a Delsys Bagnoli system.

Each RT task trial began with presentation of a fixation cross (1 cm x 1 cm) centered within a 7 cm x 7 cm black square on the monitor. After 1 second, the fixation cross disappeared, serving as the “warning signal”. Following a randomised foreperiod (1.5-2.5 seconds), the square illuminated green to indicate the imperative (go) stimulus. Participants were instructed to respond as quickly as possible by pressing the telegraph key with the index finger. Performance feedback (e.g., RT, anticipation errors) was displayed during a 2-second intertrial interval, before the next trial began. EMG and telegraph key data were recorded continuously for 3 seconds within each trial, beginning 1 second prior to the go-signal and digitally sampled at 4 kHz (National Instruments PCIe-6321).

Participants first completed 20 simple RT task practice trials (pre-intervention only), followed by two blocks of 25 trials before the cognitive fatigue intervention, and two blocks of 25 trials after the intervention.

6.3.5 Electrocardiography (ECG)

ECG was recorded as a non-invasive measure of autonomic regulation. A custom built 3-lead heart rate sensor (AD8232 module) was used to capture heart rate with adhesive electrodes placed below the left and right clavicles and over the left costal margin. Participants were asked to sit quietly without moving during a 40-second recording period, both before and after the cognitive intervention. ECG recordings were sampled at 1000 Hz.

6.3.6 Cognitive Fatigue (CF) Intervention

The cognitive fatigue intervention consisted of a 60-minute Math-Memory dual task (Peters et al., 2022, 2024; Peters & Carlsen, 2025). Participants completed the task using a wireless keyboard placed on a lap-desk. At the start of each trial, seven letters were presented briefly and sequentially at the centre of the computer monitor. Participants were instructed to remember the letters in the order presented while refraining from verbal rehearsal. This was followed by a 45-second math segment in which participants selected the mathematical operator using marked keyboard keys (+, -, /, x) that correctly completed a displayed equation (e.g., $5 ? 3 = 8$, answer = +). Participants were encouraged to correctly solve as many equations as possible during this segment. Accuracy feedback (shown by a green check mark for correct responses or red X for incorrect responses) was provided following each response. After the math segment, participants attempted to recall the last-displayed letter sequence by typing the letters in order into boxes displayed on the computer monitor. Letter recall accuracy feedback (box frames turning red for an incorrect letter/order or green for a correct letter/order) was provided to mark the end of the trial.

In line with evidence suggesting that individualizing cognitive task difficulty can enhance cognitive fatigue induction (O’Keeffe et al., 2020; Staiano et al., 2024), CF task difficulty was

adapted to participant performance to maintain approximately 85% response accuracy. More specifically, after every fourth 45-second trial, stimulus display times and response intervals were adjusted by 10% depending on participant performance, i.e., increased if overall accuracy (averaged across both task segments) dropped below 85% and shortened if accuracy exceeded 85%. Initial display/response interval durations were 3000 ms for math problems and 800 ms for the letter segment.

6.3.7 Transcutaneous Vagus Nerve Stimulation (tVNS)

Active and sham tVNS were applied to different sites on the left ear. Following skin cleansing with alcohol, small (6 mm) Ag/AgCl sintered electrodes (neurospec.com) were secured to the ear using a conductive paste (Ten20). In the active condition, electrodes were positioned with the anode over the cymba conchae and the cathode over the tragus to target the auricular branch of the vagus nerve (Badran et al., 2019; Kreisberg et al., 2021; Fig. 6.1c). In the sham condition, the anode was placed over the posterior aspect of the earlobe, and the cathode over the anterior aspect (Badran et al., 2019; Kreisberg et al., 2021; Fig. 6.1c). The earlobe was chosen for sham stimulation as it is thought to lack vagal innervation (Badran et al., 2018; Frangos et al., 2015).

Electrodes were connected to a wired stimulating device (Grass Technologies S88 stimulator) connected in series with a stimulus isolation unit (Grass Technologies SIU-5) and constant current unit (Grass Technologies CCU1). This setup ensured that the electrical stimulation was isolated from the main voltage, limited to a maximum of 100mA.

Stimulation was delivered continuously throughout the 60-minute cognitive intervention using 200 μ s pulses delivered at 25 Hz in repeating trains (4 second on, 10-11 seconds off; Badran et al., 2019; Su et al., 2025). Stimulation intensity was individualized based on

perceptual threshold testing (1.5 times threshold), never exceeding 5 mA (range = 0.3 – 3.0 mA; Badran et al., 2019; Su et al., 2025).

The tVNS perceptual threshold was defined as the minimum current intensity that would produce a detectable tingling sensation. It was determined at the beginning of each study session using a one-up–one-down staircase procedure (stimulus amplitude was decreased following detection and increased following non-detection), with a starting intensity of approximately 0.5 mA (Badran et al., 2019). Participants completed a brief side-effect questionnaire following each session to quantify any discomfort associated with using the tVNS device (Jacobs et al., 2015; A. Y. Kim et al., 2022; *Appendix C.1.2*).

6.4 Data Reduction

ECG recordings were visually inspected and excessively noisy recording segments (e.g., due to obvious movement) were removed prior to analysis. R-peaks were identified using custom LabVIEW software, and inter-beat intervals (IBIs) were calculated from successive R-peak timings. Mean heart rate (bpm) was calculated from average IBI duration, and heart rate variability (HRV) was quantified using the root mean square of successive differences (RMSSD):

$$RMSSD = \sqrt{\frac{1}{N-1} \sum_{i=1}^{N-1} (IBI_{i+1} - IBI_i)^2}$$

RMSSD values were calculated only when more than 12 IBIs were available to reduce the likelihood of unreliable HRV estimates. Extreme RMSSD values (> 150 ms) were excluded to reduce the influence of artifact contaminated or physiological implausible recordings.

Telegraph key displacement onset was defined as the time at which the key transitioned from the open (0 V) to closed (5 V) position. Premotor RT was defined as EMG burst onset

timing, identified when the rectified, filtered EMG activity exceeded baseline activity by more than 2 *SD*. Researchers visually inspected and adjusted onset markers where necessary (Hodges & Bui, 1996). EMG burst magnitude (Q100; indicative of initial motor drive at the muscle) was calculated as the integrated area of the raw rectified EMG signal recorded within 100 ms following burst onset.

RT task trials were excluded if responses were irregular (e.g., double tap of key press, 12 trials) and were analysed separately if anticipatory (premotor RT < 50 ms: 110 trials; displacement RT < 100 ms: 138 trials). Additional RT outliers exceeding ± 2.5 *SD* from the participant mean were removed from analysis (premotor RT outliers: 85 trials; displacement RT outliers: 85 trials). Practice RT trials were not analysed.

6.5 Statistical Analysis

Statistical analyses were performed using R statistical software version 4.5.3 (R Core Team, 2026). Linear mixed-effect models were fit using the *lmer()* function (package: *lme4*; Bates et al., 2015) to assess the effects of testing time (pre- vs post-intervention) and stimulation condition (active vs sham tVNS) on subjective ratings, mean heart rate, HRV (RMSSD), EMG burst magnitude (Q100), premotor RT, and displacement RT. Premotor RT, displacement RT and burst magnitude were analysed on the log-transformed scale to meet model assumptions. The effect of testing time and stimulation condition on the probability of committing an RT task anticipation error was analysed using a binomial generalized mixed-effect model (logit link; function: *glmer()*, package: *lme4*) given the binary nature of the data (anticipation vs not).

For all analyses, maximal random-effects structures were initially specified. Models with convergence difficulties were refit using the *BOBYQA* optimizer (Powell, 2009). When singular fits or persistent convergence failures occurred, random-effects structures were iteratively

simplified. Random-effects variance-covariance structures were assessed to determine if specified models showed evidence of overparameterization, indicated by highly correlated random effects or principal components explaining negligible variance (Bates et al., 2018; Matuschek et al., 2017). In the case of such overparameterization, models were further simplified until a final parsimonious model was achieved.

The significance of fixed effects was evaluated with Type II Wald χ^2 tests using the *Anova()* function from the car package for generalized mixed models (Brooks et al., 2017; Fox & Weisberg, 2019) and Type III F-tests with Satterthwaite-adjusted degrees of freedom using the *lmerTest* package for linear mixed models (Bates et al., 2015; Kuznetsova et al., 2017). Estimated marginal means (EMMs) were computed using the *emmeans* package (Lenth et al., 2026). For log-transformed variables, EMMs were back-transformed to the response scale. Pairwise comparisons were Holm-Bonferroni corrected. Statistical significance was set at $p \leq .050$, but p -values $< .100$ were considered to be “trending”. As this was a pilot study with a small sample, analyses were treated as exploratory and focused on estimation of effect directions and magnitudes rather than strict inference. As such, all a priori, hypothesis-relevant post hoc comparisons were completed, regardless of fixed effect significance (see Table 6.1).

For analyses using linear mixed models, approximate Cohen’s d (d_a) values were derived from model-based standardized mean differences with total model variance used for standardization (function: *eff_size*, package: *emmeans*; Lenth et al., 2026). For outcomes analysed on the log-transformed scale (premotor RT, displacement RT, and Q100), d_a reflects standardized differences on the log-transformed scale. In the case of the binomial generalized model, odds ratios are instead indicated. Unstandardized effect sizes (mean differences $\pm 95\%$ CI) are also reported (Pek & Flora, 2018). Supplementary analyses (baseline lifestyle/demographic

metrics, tVNS side-effect ratings, and Math-Memory task performance) are described in *Appendix C.2*.

6.6 Results

6.6.1 Baseline Measures

None of the baseline lifestyle metrics assessed (see *Appendix C.3.1*) nor any of the outcome variables (subjective ratings, RT metrics, HR measures) differed significantly between testing sessions at baseline (pre-intervention; Table 6.1).

6.6.2 Subjective Ratings

Subjective cognitive fatigue increased significantly from pre- to post-intervention regardless of stimulation condition ($F(1, 39) = 96.27, p < .001; \Delta = +4.88, 95\% \text{ CI } [3.85, 5.91], d_a = 2.15$). Neither stimulation condition ($F(1, 39) = 0.22, p = .639$) nor the testing time x stimulation condition interaction ($F(1, 39) = 1.47, p = .233$) was significant. Exploratory comparisons suggested a slightly larger increase in subjective cognitive fatigue following the CF task with sham stimulation compared to active, but this difference was not significant (Table 6.1; Fig. 6.2a).

Subjective indifference (lack of motivation) also increased significantly from pre- to post-intervention ($F(1, 39) = 10.52, p = .002; \Delta = +1.18, 95\% \text{ CI } [0.41, 1.94], d_a = 0.58$). No significant effects of stimulation condition ($F(1, 39) = 0.96, p = .334$) or the testing time x stimulation condition interaction ($F(1, 39) = 2.06, p = .159$) were observed. Exploratory analyses suggested a slightly larger increase in task indifference following sham stimulation relative to active (Table 6.1; Fig. 6.2b). Note that significant pre- to post-intervention increases in indifference were observed only in the sham condition (Table 6.1).

Subjective tension increased significantly pre- to post-intervention ($F(1, 39) = 39.54, p < .001; \Delta = +2.27, 95\%CI [1.50, 3.04], d_a = 0.95$). The testing time x stimulation condition interaction was not significant ($F(1, 39) = 0.83, p = .369$) while the main effect of stimulation condition approached significance ($F(1, 39) = 3.00, p = .091$). Exploratory analyses suggested a slightly greater, but non-significant, increase in tension following sham stimulation compared active. Within the post-intervention period, subjective tension was elevated following sham stimulation compared to active at a level that neared significance (Table 6.1; Fig. 6.2c).

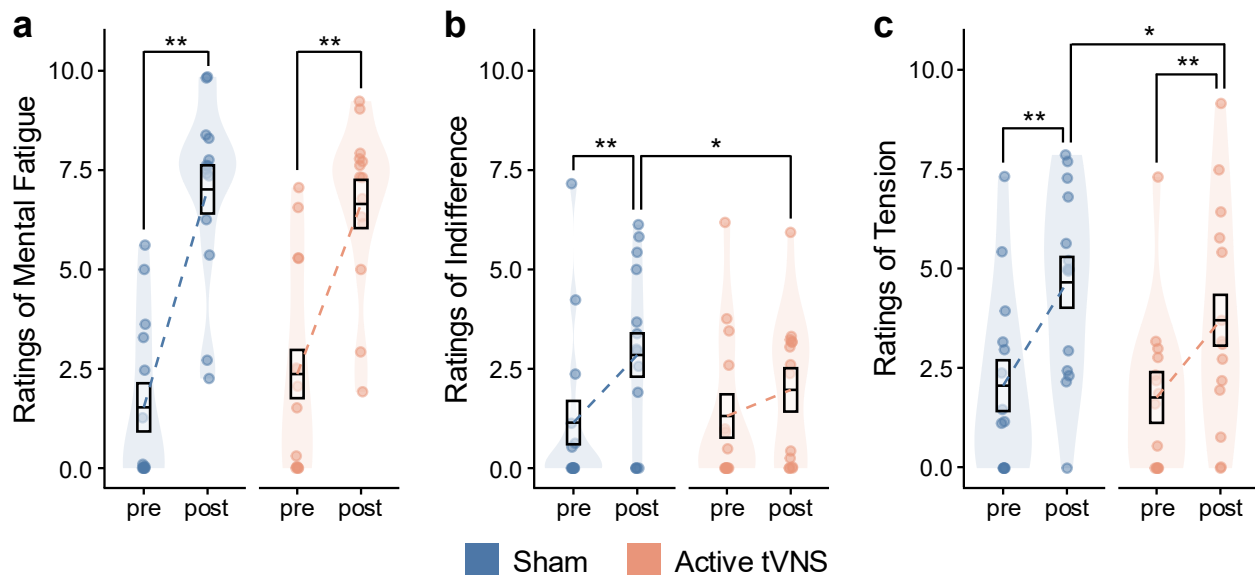


Fig. 6.2 Subjective ratings. Subjective ratings of (a) mental fatigue (0 = not at all mentally fatigued, 10 = extremely mentally fatigued), (b) indifference/ lack of motivation (0 = motivated to succeed in the task, 10 = indifferent about the task), and (c) tension (0 = relaxed, 10 = tense) are shown by testing time (pre-intervention, post-intervention) and stimulation condition (active, sham). Violin plots show the distribution of individual values, with points representing individual participant ratings. Black outlined boxes indicate model-predicted means with the limits showing *SE*. * indicates p -value $< .100$, ** indicates p -value $< .050$.

6.6.3 Reaction Time

Expected pre- to post-intervention slowing of RT (based on previously reported results: Peters et al., 2022, 2024; Peters & Carlsen, 2025) were not initially observed following the Math-Memory intervention in this experiment, contrary to expectations (see *Appendix C.3.2* for this analysis). Thus, to reduce potential influences of practice effects and cognitive fatigue decay, analyses of premotor and displacement RT focused on block 2 vs block 3 (i.e., the 25 trials immediately before (pre) and after (post) the cognitive intervention).

For premotor RT, there was a significant testing block x stimulation condition interaction ($F(1, 1273) = 5.01, p = .025$). The main effect of stimulation condition was not significant ($F(1, 13) = 0.87, p = .367$), while the main effect of testing block approached significance ($F(1, 1273) = 3.25, p = .072$). Post hoc analyses showed significant premotor RT speeding following active stimulation, whereas sham stimulation produced a very small, non-significant slowing. Post-intervention differences between stimulation conditions approached significance, such that slower RT was observed following sham stimulation. The pre- to post-intervention change also differed significantly between stimulus conditions, indicating greater fatigue-related slowing with sham stimulation (Table 6.1; Fig. 6.3a).

For displacement RT, no significant main effects of testing block ($F(1, 1256) = 0.23, p = .635$) or stimulation condition ($F(1, 13) = 0.00, p = .993$) were observed. However, a significant testing block x stimulation condition interaction was present ($F(1, 1257) = 4.31, p = .038$). Post hoc analyses indicated near-significant slowing following sham stimulation, and a small, non-significant speeding effect following active stimulation. The difference in pre- to post-intervention change between conditions approached significance, suggesting greater fatigue-related slowing of displacement RT with sham stimulation (Table 6.1; Fig. 6.3b).

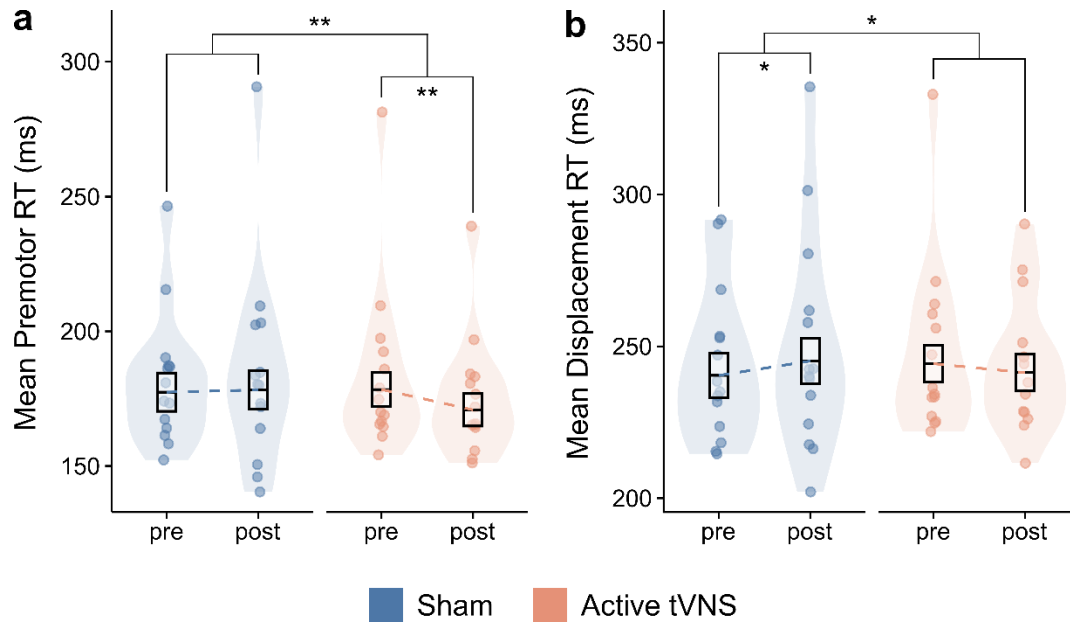


Fig. 6.3 Reaction time. (a) Premotor reaction time (ms) and (b) displacement reaction time (ms) are shown by testing time (pre-intervention, post-intervention) and stimulation condition (active, sham). Only data for block 2 (pre) and block 3 (post) are shown. Violin plots show the distribution of individual values, with points representing individual participant means. Black outlined boxes indicate model-predicted means with the limits showing *SE*. * indicates p -value < .100, ** indicates p -value < .050.

6.6.4 EMG Burst Magnitude (Q100)

Q100 was not significantly affected by testing time ($F(1, 13) = 0.04, p = .852$), or stimulation condition ($F(1, 13) = 0.26, p = .616$). However, a significant testing time x stimulation condition interaction was observed ($F(1, 2550) = 5.40, p = .020$). Post hoc comparisons showed a small, non-significant decline in Q100 following sham stimulation and a non-significant increase following active stimulation. The difference in pre- to post-intervention change between stimulation conditions approached significance, such that a greater increase in Q100 was observed with active stimulation (Table 6.1; Fig. 6.4).

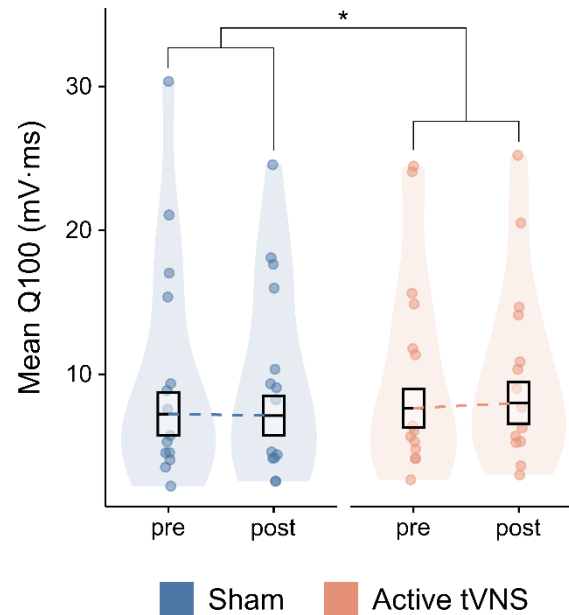


Fig. 6.4 Reaction time task response EMG burst magnitude (Q100). Q100 (mV·ms) is shown by testing time (pre-intervention, post-intervention) and stimulation condition (active, sham). Violin plots show the distribution of individual values, with points representing individual participant means. Black outlined boxes indicate model-predicted means with the limits showing *SE*. * indicates *p*-value < .100.

6.6.5 Anticipatory Reaction Time Errors

Anticipation error rates were not significantly affected by stimulation condition ($\chi^2(1) = 0.12, p = .734$) or testing time ($\chi^2(1) = 0.78, p = .378$). However, the testing time x stimulation condition interaction approached significance ($\chi^2(1) = 3.39, p = .066$). Exploratory post hoc analyses suggested anticipation errors increased significantly following sham stimulation but tended to decrease following active stimulation. The difference in pre- to post-intervention change approached significance, with a greater increase in anticipation observed with sham stimulation (Table 6.1; Fig. 6.5).

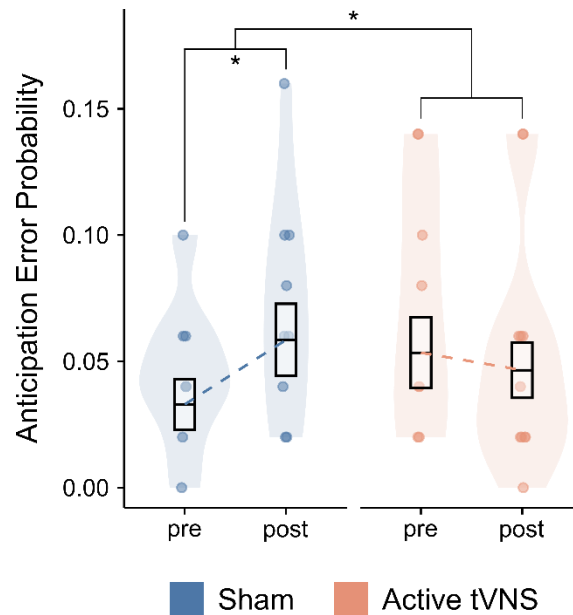


Fig. 6.5 Probability of an anticipatory response error on the RT task. Error probability is shown by testing time (pre-intervention, post-intervention) and stimulation condition (active, sham). Violin plots show the distribution of individual values, with points representing individual participant means. Black outlined boxes indicate model-predicted means with the limits showing *SE*. * indicates p -value < .100.

6.6.6 Heart Rate Measures

Mean heart rate decreased significantly from pre- to post-intervention regardless of stimulation condition ($F(1, 20) = 10.69, p = .004; \Delta = -3.67$ bpm, 95% CI $[-6.05, -1.28], d_a = 0.34$). Neither stimulation condition ($F(1, 13) = 0.38, p = .547$) nor the interaction between testing time x stimulation condition ($F(1, 20) = 0.06, p = .817$) were significant.

HRV (RMSSD) was not significantly affected by testing time ($F(1, 13) = 0.02, p = .880$) or stimulation condition ($F(1, 13) = 2.33, p = .151$). However, the testing time x stimulation condition interaction approached significance ($F(1, 8) = 4.26, p = .072$). Exploratory analyses suggested a trend toward increased HRV following sham stimulation and decreased HRV

following active stimulation, although neither change reached significance (Table 6.1). Within the post-intervention period, HRV was higher following sham stimulation compared to active at a level that closely approached significance (Table 6.1). Further, differences in the pre- to post-intervention change in HRV differed by stimulation condition at a level that approached significance, indicating a greater increase in HRV with sham stimulation (Table 6.1; Fig. 6.6).

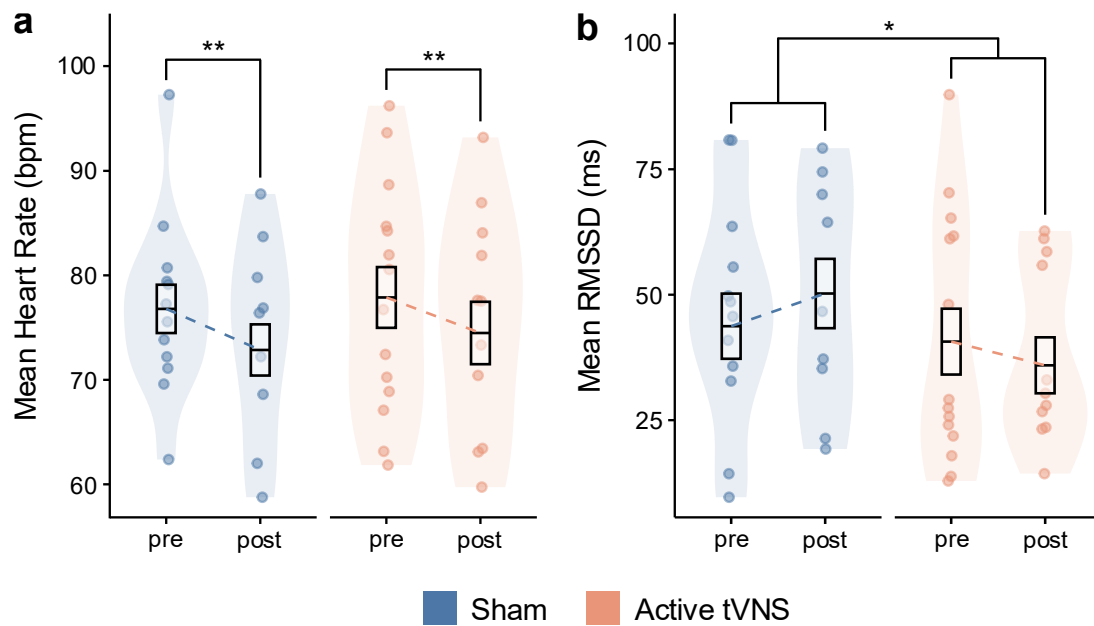


Fig. 6.6 Heart rate measures. (a) Mean heart rate (bpm) and (b) heart rate variability (RMSSD, ms) are shown by testing time (pre-intervention, post-intervention) and stimulation condition (active, sham). Violin plots show the distribution of individual values, with points representing individual participant means. Black outlined boxes indicate model-predicted means with the limits showing *SE*. * indicates p -value $< .100$, ** indicates p -value $< .050$.

Table 6.1 Post hoc comparisons by stimulation condition and testing time. Statistics for premotor and displacement RT reflect comparisons of block 2 (pre-intervention) vs block 3 (post-intervention). S = Sham stimulation, A = Active stimulation; d_a = approximated Cohen's d value; OR = Odd's ratio; * indicates p-value < .100, ** indicates p-value < .050.

	Difference	95% CI	p	Effect size
<i>Subjective Fatigue Ratings</i>				
$\Delta S_{pre} - A_{pre}$	-0.84	[-2.26, 0.59]	.241	0.37 (d_a)
$\Delta S_{post} - A_{post}$	+0.37	[-1.06, 1.79]	.605	0.16 (d_a)
$\Delta S_{post} - S_{pre}$	+5.48	[4.06, 6.91]	< .001**	2.42 (d_a)
$\Delta A_{post} - A_{pre}$	+4.28	[2.86, 5.70]	< .001**	1.88 (d_a)
$\Delta S_{post-pre} - A_{post-pre}$	+1.20	[-0.81, 3.22]	.233	0.53 (d_a)
<i>Subjective Indifference Ratings</i>				
$\Delta S_{pre} - A_{pre}$	-0.17	[-1.22, 0.89]	.749	0.08 (d_a)
$\Delta S_{post} - A_{post}$	+0.88	[-0.18, 1.93]	.099*	0.43 (d_a)
$\Delta S_{post} - S_{pre}$	+1.70	[0.65, 2.78]	.003**	0.83 (d_a)
$\Delta A_{post} - A_{pre}$	+0.66	[-0.40, 1.71]	.210	0.32 (d_a)
$\Delta S_{post-pre} - A_{post-pre}$	+1.04	[-0.45, 2.54]	.163	0.51 (d_a)
<i>Subjective Tension Ratings</i>				
$\Delta S_{pre} - A_{pre}$	+0.30	[-0.76, 1.36]	.566	0.12 (d_a)
$\Delta S_{post} - A_{post}$	+0.95	[-0.11, 2.01]	.075*	0.40 (d_a)
$\Delta S_{post} - S_{pre}$	+2.60	[1.54, 3.66]	< .001**	1.09 (d_a)
$\Delta A_{post} - A_{pre}$	+1.94	[0.88, 3.00]	.001**	0.81 (d_a)
$\Delta S_{post-pre} - A_{post-pre}$	+0.66	[-0.84, 2.16]	.373	0.27 (d_a)
<i>Premotor RT (ms)</i>				
$\Delta S_{pre} - A_{pre}$	-0.97	[-9.53, 7.59]	.811	0.02 (d_a)
$\Delta S_{post} - A_{post}$	+7.42	[1.18, 16.02]	.086*	0.18 (d_a)
$\Delta S_{post} - S_{pre}$	+0.83	[-4.94, 6.61]	.761	0.02 (d_a)
$\Delta A_{post} - A_{pre}$	-7.55	[-13.24, -1.86]	.013**	0.18 (d_a)
$\Delta S_{post-pre} - A_{post-pre}$	+8.39	[0.27, 16.50]	.044**	0.20 (d_a)
<i>Displacement RT (ms)</i>				
$\Delta S_{pre} - A_{pre}$	-3.86	[-10.87, 3.16]	.257	0.09 (d_a)

$\Delta S_{\text{post}} - A_{\text{post}}$	+3.82	[-3.46, 11.11]	.279	0.09 (d_a)
$\Delta S_{\text{post}} - S_{\text{pre}}$	+4.72	[-0.90, 10.34]	.093*	0.11 (d_a)
$\Delta A_{\text{post}} - A_{\text{pre}}$	-2.96	[-8.58, 2.66]	.278	0.07 (d_a)
$\Delta S_{\text{post-pre}} - A_{\text{post-pre}}$	+7.68	[-0.28, 15.60]	.058*	0.19 (d_a)
<i>Q100 ($\mu V \cdot ms$)</i>				
$\Delta S_{\text{pre}} - A_{\text{pre}}$	-0.40	[-3.06, 2.26]	.749	0.06 (d_a)
$\Delta S_{\text{post}} - A_{\text{post}}$	-0.88	[-3.60, 1.84]	.496	0.13 (d_a)
$\Delta S_{\text{post}} - S_{\text{pre}}$	-0.11	[-1.40, 1.17]	.852	0.02 (d_a)
$\Delta A_{\text{post}} - A_{\text{pre}}$	+0.37	[-1.04, 1.77]	.580	0.05 (d_a)
$\Delta S_{\text{post-pre}} - A_{\text{post-pre}}$	-0.48	[-0.96, 0.00]	.051*	0.07 (d_a)
<i>Anticipation Errors (probability)</i>				
$\Delta S_{\text{pre}} - A_{\text{pre}}$	-0.021	[-0.046, 0.005]	.118	0.60 (<i>OR</i>)
$\Delta S_{\text{post}} - A_{\text{post}}$	+0.012	[-0.015, 0.038]	.374	1.27 (<i>OR</i>)
$\Delta S_{\text{post}} - S_{\text{pre}}$	+0.026	[-0.001, 0.052]	.058*	1.82 (<i>OR</i>)
$\Delta A_{\text{post}} - A_{\text{pre}}$	-0.007	[-0.033, 0.020]	.610	0.86 (<i>OR</i>)
$\Delta S_{\text{post-pre}} - A_{\text{post-pre}}$	+0.032	[-0.005, 0.070]	.090*	2.11 (<i>OR</i>)
<i>Mean Heart Rate (bpm)</i>				
$\Delta S_{\text{pre}} - A_{\text{pre}}$	-1.10	[-6.11, 3.91]	.650	0.10 (d_a)
$\Delta S_{\text{post}} - A_{\text{post}}$	-1.62	[-7.03, 3.78]	.539	0.15 (d_a)
$\Delta S_{\text{post}} - S_{\text{pre}}$	-3.93	[-7.53, -0.33]	.034**	0.36 (d_a)
$\Delta A_{\text{post}} - A_{\text{pre}}$	-3.40	[-6.54, -0.26]	.035**	0.31 (d_a)
$\Delta S_{\text{post-pre}} - A_{\text{post-pre}}$	-0.53	[-5.32, 4.26]	.820	0.05 (d_a)
<i>HRV (RMSSD, ms)</i>				
$\Delta S_{\text{pre}} - A_{\text{pre}}$	3.07	[-9.81, 16.00]	.618	0.10 (d_a)
$\Delta S_{\text{post}} - A_{\text{post}}$	14.31	[-0.28, 28.9]	.054*	0.48 (d_a)
$\Delta S_{\text{post}} - S_{\text{pre}}$	6.51	[-7.95, 20.97]	.357	0.22 (d_a)
$\Delta A_{\text{post}} - A_{\text{pre}}$	-4.72	[-18.06, 8.62]	.463	0.16 (d_a)
$\Delta S_{\text{post-pre}} - A_{\text{post-pre}}$	11.20	[-2.06, 24.50]	.087*	0.38 (d_a)

6.7 Discussion

This randomised, single-blind, sham-controlled pilot study explored whether auricular tVNS could mitigate the subjective, psychomotor, and autonomic effects of cognitive fatigue. As expected, the Math-Memory intervention significantly increased subjective ratings of mental fatigue, suggesting a successful cognitive fatigue manipulation. Ratings of indifference (lack of motivation) and tension also increased. Although stimulation condition did not significantly affect these measures, all three subjective outcomes tended to increase more following sham stimulation compared to active stimulation. These findings align with previous work showing reduced subjective fatigue and less impaired focus during sleep deprivation and language learning following tVNS (McIntire et al., 2021; Miyatsu et al., 2024). Other research has reported reduced perceived stress (W.-J. Kim et al., 2025) and elevated motivational drive (Neuser et al., 2020; J. Sun et al., 2026) with active stimulation compared to sham. Considered alongside such findings, the current results (while preliminary) suggest that tVNS may help attenuate fatigue-related sensations, tension, and motivational decline during sustained cognitive effort.

Contrary to expectations, analyses of the full RT data set did not initially show RT slowing similar to that which has been previously observed following the Math-Memory cognitive fatigue intervention (Peters et al., 2022, 2024; Peters & Carlsen, 2025). This likely reflects the limited sample size of the present pilot study. The effects of cognitive fatigue on simple RT in experimental settings can be small (e.g., 7-10 ms; Peters et al., 2022, 2024) and may require substantially larger sample sizes to reliably detect. Additionally, participants may not have been fully acclimated to the RT task despite the practice period (which was quite short), and fatigue effects may have dissipated relatively quickly following completion of the

intervention. To further investigate these RT effects while minimizing the potential influence of practice effects and fatigue decay, exploratory RT analyses focused on the testing blocks immediately before and after the cognitive fatigue intervention. Under these conditions, stimulation-specific effects became apparent. Displacement RT tended to slow and premotor RT remained relatively stable following sham stimulation, whereas active stimulation was associated with relative RT speeding, reaching significance for premotor RT. Similar improvements in RT performance following tVNS have been reported during sleep deprivation (McIntire et al., 2021) and in non-fatigued populations (Gurtubay et al., 2023). Although these findings should be cautiously interpreted, they suggest that tVNS may help counteract cognitive fatigue-related slowing of psychomotor performance.

These RT results were accompanied by stimulation-specific changes in EMG burst magnitude. EMG burst integrated area in the initial 100 ms (Q100) tended to decline following sham stimulation and increase following active stimulation. Although this measure has not been widely explored in the tVNS literature, related work has shown increased corticospinal excitability following cervical tVNS, as reflected by increased motor-evoked potential amplitude (Denyer et al., 2026; Wang et al., 2023). When considered alongside the present observations, these results suggest that tVNS could help maintain both response speed and early motor drive following cognitively fatiguing conditions.

Notably, active stimulation was associated with a trend toward fewer anticipatory response errors on the RT task, whereas the opposite trend was observed with sham stimulation. There is some evidence that inhibitory control may be sensitive to tVNS (Ridgewell et al., 2021). For instance, reduced frontal N2 activity has been observed during NoGo trials (i.e., Go/No-Go RT task where the response should be withheld) following tVNS despite unchanged behavioural

performance (Pihlaja et al., 2020). The authors interpreted this to reflect greater cognitive control efficiency following tVNS, whereby less central effort was required to withhold a prepared response at the same rate (Pihlaja et al., 2020). Other evidence suggests that 60 minutes of tVNS may alter intracortical excitatory and inhibitory balance within M1, increasing short-interval intracortical inhibition and reducing short-interval intracortical facilitation (Gerges et al., 2025). However, behavioural evidence for improved inhibitory control with tVNS remains mixed, with some studies reporting benefits (Beste et al., 2016) and others reporting little to no effect (Borges et al., 2020; Ridgewell et al., 2021). Therefore, while it seems that tVNS may help preserve response inhibition in the present study, it is clear that this is an area requiring further study.

Measures of average heart rate (overall average = 76.3 bpm, $SD = 9.9$ bpm) and heart rate variability (RMSSD, overall average = 43.3 ms, $SD = 22.0$ ms) were within typical ranges for the age group tested (Quer et al., 2020; van den Berg et al., 2018). With sham stimulation, cognitive fatigue was associated with reductions in average HR and trends towards increased HRV, indicative of a shift toward greater parasympathetic dominance. Similar autonomic responses to prolonged cognitive effort have been reported previously, with several studies showing increased cardiac vagal tone in cognitive fatigue (Csathó et al., 2024; Matuz et al., 2021), although such effects may depend on the specific cognitive task used (e.g., Goodman et al., 2025). Conversely, active stimulation appeared to alter this cognitive fatigue-related autonomic response pattern, particularly such that HRV tended to decrease rather than increase following the cognitive fatigue intervention. Previous studies exploring the effects of auricular tVNS on HRV have produced mixed findings, including reports of increased HRV (Geng et al., 2022; Percin et al., 2024), no change (Borges et al., 2019; Šinkovec et al., 2023), and reduced HRV (Altinkaya et al., 2023; Kaduk et al., 2025). Interestingly, Schiweck and colleagues (2025) found that auricular

tVNS reduced HRV in individuals with relatively high baseline RMSSD values while normalizing HRV in those with lower baseline values. If cognitive fatigue increases HRV from baseline, a similar normalizing effect may be occurring here.

Taken together, the present subjective, behavioural, and physiological findings all point in a relatively consistent direction. Specifically, as compared to sham stimulation, active tVNS was associated with trends toward reduced fatigue-related sensations, altered autonomic (HRV) responses, and preserved or improved motor performance in cognitive fatigue. Thus, although this pilot study lacked sufficient power to strongly establish efficacy, the overall pattern suggests that auricular tVNS may help attenuate subjective and psychomotor performance consequences of cognitive fatigue. Cognitive fatigue has been shown to impair reaction time, sustained attention, and motivation across a variety of settings including transportation (M. Guo et al., 2016; Ting et al., 2008), healthcare (Petrut et al., 2020), construction (Li et al., 2019; Yue et al., 2024), military operations (Rabat et al., 2025; Vrijkotte et al., 2016), sport (Habay et al., 2021), and rehabilitation (P.-Y. Chen et al., 2022; Ramage et al., 2019). If future research confirms these effects, auricular tVNS may prove useful as a non-invasive tool to help maintain performance and reduce fatigue-related errors during extended periods of mentally demanding work in such settings. This could be particularly relevant in safety-critical environments where even small motor performance decrements could increase accident risk.

One potential neural mechanism underlying the pattern of results observed here involves activation of the locus coeruleus-norepinephrine (LC-NE) system, which previous work suggests may be modulated by tVNS. In support of this, tVNS has been shown to increase salivary alpha-amylase release (Giraudier et al., 2022), increase pupil diameter (Desbeaumes Jodoin et al., 2015), and augment the amplitude of the P3 event-related potential component (De Taeye et al.,

2014), all of which have been interpreted as indirect markers of LC-NE activity. It has been suggested that LC-NE activation may in turn influence behaviour, perhaps by altering activity in regions such as the basal ganglia (Monti et al., 2025), and/or through norepinephrine-mediated gain control, increasing the signal-to-noise ratio of sensory inputs and potentially improving the efficiency of psychomotor processing (Aston-Jones & Cohen, 2005; Devilbiss, 2019; Pihlaja et al., 2020; Su et al., 2025). More broadly, LC-NE activity is thought to support vigilance, arousal, and wakefulness (Foote & Berridge, 2019; Grant et al., 1988; Samuels & Szabadi, 2008). Thus, while speculative, the current pattern of findings (i.e., reduced fatigue-related sensations, altered HRV responses, and relatively preserved motor performance with active stimulation) may be broadly consistent with LC-NE involvement. Notably, a similar interpretation has been proposed in the context of sleep deprivation, where tVNS was associated with reduced cognitive and subjective effects of fatigue (McIntire et al., 2021).

Importantly, the present findings also support feasibility and tolerability of auricular tVNS over a 60-minute period. Side-effect ratings remained low in both active and sham stimulation conditions, with average ratings not exceeding 2/10 for any reported side-effect. Side-effect profiles were similar between sham and active conditions, no adverse events occurred, and all participants completed the full hour-long stimulation protocol. These observations are consistent with previous reports describing auricular tVNS as a safe, well-tolerated neuromodulation technique (Giraudier et al., 2025; A. Y. Kim et al., 2022; Redgrave et al., 2018).

Several limitations of this work should be acknowledged. First, this was a small pilot study and was likely underpowered to detect subtle effects across outcome measures. As such, several findings are exploratory and should be interpreted cautiously until replicated in larger

samples. Second, the present study examined only one auricular tVNS configuration and set of stimulation parameters. Considerable variability exists across the tVNS literature with respect to stimulation site, parameters, and duration, and different approaches may produce different physiological and behavioural effects. Future work may benefit from direct comparisons of stimulation techniques for cognitive fatigue mitigation, including both auricular and cervical tVNS approaches. Third, the mechanisms underlying tVNS effects were not directly assessed and therefore remain speculative. Future studies may benefit from incorporating more direct neurophysiological measures of LC-NE activity (e.g., ERP or fMRI) alongside subjective, behavioural, and cardiovascular outcomes, to observe the role of this system. Finally, inclusion of more cognitively complex psychomotor tasks, such as choice RT and go/no-go RT paradigms, may help to further clarify the scope of tVNS effects in cognitive fatigue.

6.8 Conclusion

To summarize, the present pilot study provides preliminary evidence that auricular tVNS may help attenuate some of the subjective, psychomotor, and autonomic effects of cognitive fatigue. Although many of the observed effects were modest and require replication with larger samples, active tVNS was associated with a general pattern of preserved or improved psychomotor performance, reduced subjective fatigue-related sensations, and opposing HRV responses relative to sham stimulation following prolonged, fatiguing cognitive effort. As a whole, these findings support continued investigation of tVNS as a potential non-invasive, well-tolerated tool for mitigating cognitive fatigue-related declines in psychomotor performance, while also highlighting the need for future work clarifying the neurophysiological mechanisms underlying these effects.

6.9 References

- Ackerman, P. L. (2011). 100 years without resting. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 11–43). American Psychological Association. <https://doi.org/10.1037/12343-001>
- Adachi, M., Nobukawa, S., & Inagaki, K. (2024). Assessment of driver fatigue-related brain responses and causal factors during driving under different traffic conditions. *Frontiers in Applied Mathematics and Statistics*, 10, 1426253. <https://doi.org/10.3389/fams.2024.1426253>
- Almhdawi, K. A., Jaber, H. B., Khalil, H. W., Kanaan, S. F., Shyyab, A. A., Mansour, Z. M., & Alazrai, A. H. (2021). Post-stroke fatigue level is significantly associated with mental health component of health-related quality of life: A cross-sectional study. *Quality of Life Research*, 30(4), 1165–1172. <https://doi.org/10.1007/s11136-020-02714-z>
- Altinkaya, Z., Öztürk, L., Büyükgüdük, İ., Yanık, H., Yılmaz, D. D., Yar, B., Değirmenci, E., Dal, U., & Veldhuizen, M. G. (2023). Non-invasive vagus nerve stimulation in a hungry state decreases heart rate variability. *Physiology & Behavior*, 258, 114016. <https://doi.org/10.1016/j.physbeh.2022.114016>
- Aranow, C., Atish-Fregoso, Y., Lesser, M., Mackay, M., Anderson, E., Chavan, S., Zanos, T. P., Datta-Chaudhuri, T., Bouton, C., Tracey, K. J., & Diamond, B. (2021). Transcutaneous auricular vagus nerve stimulation reduces pain and fatigue in patients with systemic lupus erythematosus: A randomised, double-blind, sham-controlled pilot trial. *Annals of the Rheumatic Diseases*, 80(2), 203–208. <https://doi.org/10.1136/annrheumdis-2020-217872>
- Aston-Jones, G., & Cohen, J. D. (2005). An Integrative Theory of Locus Coeruleus-Norepinephrine Function: Adaptive Gain and Optimal Performance. *Annual Review of Neuroscience*, 28(1), 403–450. (17712756). <https://doi.org/10.1146/annurev.neuro.28.061604.135709>
- Badran, B. W., Dowdle, L. T., Mithoefer, O. J., LaBate, N. T., Coatsworth, J., Brown, J. C., DeVries, W. H., Austelle, C. W., McTeague, L. M., & George, M. S. (2018). Neurophysiologic effects of transcutaneous auricular vagus nerve stimulation (taVNS) via electrical stimulation of the tragus: A concurrent taVNS/fMRI study and review. *Brain Stimulation*, 11(3), 492–500. <https://doi.org/10.1016/j.brs.2017.12.009>
- Badran, B. W., Huffman, S. M., Dancy, M., Austelle, C. W., Bikson, M., Kautz, S. A., & George, M. S. (2022). A pilot randomized controlled trial of supervised, at-home, self-administered transcutaneous auricular vagus nerve stimulation (taVNS) to manage long COVID symptoms. *Bioelectronic Medicine*, 8(1), 13. <https://doi.org/10.1186/s42234-022-00094-y>
- Badran, B. W., Yu, A. B., Adair, D., Mappin, G., DeVries, W. H., Jenkins, D. D., George, M. S., & Bikson, M. (2019). Laboratory Administration of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS): Technique, Targeting, and Considerations. *Journal of Visualized Experiments*, (143), 10.3791/58984. <https://doi.org/10.3791/58984>

- Balkin, T. J., & Wesensten, N. J. (2011). Differentiation of sleepiness and mental fatigue effects. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 47–66). American Psychological Association. <https://doi.org/10.1037/12343-002>
- Bates, D., Kliegl, R., Vasishth, S., & Baayen, H. (2018). *Parsimonious Mixed Models* (arXiv:1506.04967). arXiv. <https://doi.org/10.48550/arXiv.1506.04967>
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, 67, 1–48. <https://doi.org/10.18637/jss.v067.i01>
- Behrens, M., Gube, M., Chaabene, H., Prieske, O., Zenon, A., Broscheid, K.-C., Schega, L., Husmann, F., & Weippert, M. (2023). Fatigue and Human Performance: An Updated Framework. *Sports Medicine*, 53(1), 7–31. <https://doi.org/10.1007/s40279-022-01748-2>
- Beste, C., Steenbergen, L., Sellaro, R., Grigoriadou, S., Zhang, R., Chmielewski, W., Stock, A.-K., & Colzato, L. (2016). Effects of Concomitant Stimulation of the GABAergic and Norepinephrine System on Inhibitory Control – A Study Using Transcutaneous Vagus Nerve Stimulation. *Brain Stimulation*, 9(6), 811–818. <https://doi.org/10.1016/j.brs.2016.07.004>
- Borges, U., Knops, L., Laborde, S., Klatt, S., & Raab, M. (2020). Transcutaneous Vagus Nerve Stimulation May Enhance Only Specific Aspects of the Core Executive Functions. A Randomized Crossover Trial. *Frontiers in Neuroscience*, 14, 523. <https://doi.org/10.3389/fnins.2020.00523>
- Borges, U., Laborde, S., & Raab, M. (2019). Influence of transcutaneous vagus nerve stimulation on cardiac vagal activity: Not different from sham stimulation and no effect of stimulation intensity. *PLOS ONE*, 14(10), e0223848. <https://doi.org/10.1371/journal.pone.0223848>
- Borges, U., Pfannenstiel, M., Tsukahara, J., Laborde, S., Klatt, S., & Raab, M. (2021). Transcutaneous vagus nerve stimulation via tragus or cymba conchae: Are its psychophysiological effects dependent on the stimulation area? *International Journal of Psychophysiology*, 161, 64–75. <https://doi.org/10.1016/j.ijpsycho.2021.01.003>
- Brazaitis, M., & Satas, A. (2023). Regular short-duration breaks do not prevent mental fatigue and decline in cognitive efficiency in healthy young men during an office-like simulated mental working day: An EEG study. *International Journal of Psychophysiology*, 188, 33–46. <https://doi.org/10.1016/j.ijpsycho.2023.03.007>
- Brooks, M. E., Kristensen, K., Benthem, K. J. van, Magnusson, A., Berg, C. W., Nielsen, A., Skaug, H. J., Mächler, M., & Bolker, B. M. (2017). glmmTMB Balances Speed and Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. *The R Journal*, 9(2), 378–400. <https://doi.org/10.32614/RJ-2017-066>

- Butt, M. F., Albusoda, A., Farmer, A. D., & Aziz, Q. (2020). The anatomical basis for transcutaneous auricular vagus nerve stimulation. *Journal of Anatomy*, 236(4), 588–611. <https://doi.org/10.1111/joa.13122>
- Chan, M. Y., Cohen, H., & Spiegel, B. M. R. (2009). Fewer Polyps Detected by Colonoscopy as the Day Progresses at a Veteran's Administration Teaching Hospital. *Clinical Gastroenterology and Hepatology*, 7(11), 1217–1223. <https://doi.org/10.1016/j.cgh.2009.07.013>
- Chandler, D. J. (2016). Evidence for a specialized role of the locus coeruleus noradrenergic system in cortical circuitries and behavioral operations. *Brain Research*, 1641(Pt B), 197–206. <https://doi.org/10.1016/j.brainres.2015.11.022>
- Chen, P.-Y., Hsieh, S.-H., Lin, C.-K., Wei, L., Su, Y.-K., Tsai, P.-S., & Chiu, H.-Y. (2022). Mental fatigue mediates the relationship between cognitive functions and return to productive activity following traumatic brain injury: A mediation analysis. *Brain Injury*, 36(1), 32–38. <https://doi.org/10.1080/02699052.2022.2034044>
- Chen, Y., Lu, X., & Hu, L. (2023). Transcutaneous Auricular Vagus Nerve Stimulation Facilitates Cortical Arousal and Alertness. *International Journal of Environmental Research and Public Health*, 20(2), Article 2. <https://doi.org/10.3390/ijerph20021402>
- Colzato, L., & Beste, C. (2020). A literature review on the neurophysiological underpinnings and cognitive effects of transcutaneous vagus nerve stimulation: Challenges and future directions. *Journal of Neurophysiology*, 123(5), 1739–1755. <https://doi.org/10.1152/jn.00057.2020>
- Craft, C. L., Islam, T., Berard, J. A., & Walker, L. A. S. (2025). Subjective cognitive fatigability is associated with worse patient-reported physical disability in multiple sclerosis. *Multiple Sclerosis and Related Disorders*, 103, 106720. <https://doi.org/10.1016/j.msard.2025.106720>
- Csathó, Á., Van der Linden, D., & Matuz, A. (2024). Change in heart rate variability with increasing time-on-task as a marker for mental fatigue: A systematic review. *Biological Psychology*, 185, 108727. <https://doi.org/10.1016/j.biopsycho.2023.108727>
- Dallaway, N., Lucas, S. J. E., & Ring, C. (2022). Cognitive tasks elicit mental fatigue and impair subsequent physical task endurance: Effects of task duration and type. *Psychophysiology*, 59(12). <https://doi.org/10.1111/psyp.14126>
- De Taeye, L., Vonck, K., van Bochove, M., Boon, P., Van Roost, D., Mollet, L., Meurs, A., De Herdt, V., Carrette, E., Dauwe, I., Gadeyne, S., van Mierlo, P., Verguts, T., & Raedt, R. (2014). The P3 event-related potential is a biomarker for the efficacy of vagus nerve stimulation in patients with epilepsy. *Neurotherapeutics*, 11(3), 612–622. <https://doi.org/10.1007/s13311-014-0272-3>

- Denyer, R., Su, S., Patnaik, M., & Duque, J. (2026). Four-second trains of transcutaneous vagus nerve stimulation increase online corticospinal excitability and pupil size in humans. *Journal of Neurophysiology*, 135(4), 766–776. <https://doi.org/10.1152/jn.00008.2026>
- Desbeaumes Jodoin, V., Lespérance, P., Nguyen, D. K., Fournier-Gosselin, M.-P., Richer, F., & Centre Hospitalier de l'Université de Montréal, Canada. (2015). Effects of vagus nerve stimulation on pupillary function. *International Journal of Psychophysiology*, 98(3), 455–459. <https://doi.org/10.1016/j.ijpsycho.2015.10.001>
- Dettmers, J., Wendt, C., & Biemelt, J. (2020). Already exhausted when arriving at work? A diary study of morning demands, start-of-work-day fatigue and job performance and the buffering role of temporal flexibility. *European Journal of Work and Organizational Psychology*, 29(6), 809–821. <https://doi.org/10.1080/1359432X.2020.1810666>
- Devilbiss, D. M. (2019). Consequences of tuning network function by tonic and phasic locus coeruleus output and stress: Regulating detection and discrimination of peripheral stimuli. *Brain Research*, 1709, 16–27. <https://doi.org/10.1016/j.brainres.2018.06.015>
- Ezekiel, L., Field, L., Collett, J., Dawes, H., & Boulton, M. (2021). Experiences of fatigue in daily life of people with acquired brain injury: A qualitative study. *Disability and Rehabilitation*, 43(20), 2866–2874. <https://doi.org/10.1080/09638288.2020.1720318>
- Fazackerley, L. A., Hickey, J., Johnston, R. D., Tofari, P. J., Timmins, R. G., Roelands, B., Halson, S. L., Tassignon, B., Verschueren, J., & Russell, S. (2025). Practitioner Perspectives on the Association Between Mental Fatigue and Injury Risk in High-Performance Sport: A Mixed Methods Study. *European Journal of Sport Science*, 25(8), e70028. <https://doi.org/10.1002/ejsc.70028>
- Foote, S. L., & Berridge, C. W. (2019). New Developments and Future Directions in Understanding Locus Coeruleus – Norepinephrine (LC-NE) Function. *Brain Research*, 1709, 81–84. <https://doi.org/10.1016/j.brainres.2018.09.033>
- Fortes, L. S., Gantois, P., de Lima-Júnior, D., Barbosa, B. T., Ferreira, M. E. C., Nakamura, F. Y., Albuquerque, M. R., & Fonseca, F. S. (2023). Playing videogames or using social media applications on smartphones causes mental fatigue and impairs decision-making performance in amateur boxers. *Applied Neuropsychology: Adult*, 30(2), 227–238. <https://doi.org/10.1080/23279095.2021.1927036>
- Fox, J., & Weisberg, S. (2019). *An R companion to applied regression* (Third edition). Sage.
- Frangos, E., Ellrich, J., & Komisaruk, B. R. (2015). Non-invasive Access to the Vagus Nerve Central Projections via Electrical Stimulation of the External Ear: fMRI Evidence in Humans. *Brain Stimulation*, 8(3), 624–636. <https://doi.org/10.1016/j.brs.2014.11.018>
- Geng, D., Liu, X., Wang, Y., & Wang, J. (2022). The effect of transcutaneous auricular vagus nerve stimulation on HRV in healthy young people. *PLOS ONE*, 17(2), e0263833. <https://doi.org/10.1371/journal.pone.0263833>

- Gerges, A. N. H., Graetz, L., Hillier, S., Uy, J., Hamilton, T., Opie, G., Vallence, A.-M., Braithwaite, F. A., Chamberlain, S., & Hordacre, B. (2025). Transcutaneous auricular vagus nerve stimulation modifies cortical excitability in middle-aged and older adults. *Psychophysiology*, 62(1), e14584. <https://doi.org/10.1111/psyp.14584>
- Giraudier, M., Ventura-Bort, C., Burger, A. M., Claes, N., D'Agostini, M., Fischer, R., Franssen, M., Kaess, M., Koenig, J., Liepelt, R., Nieuwenhuis, S., Sommer, A., Usichenko, T., Van Diest, I., von Leupoldt, A., Warren, C. M., & Weymar, M. (2022). Evidence for a modulating effect of transcutaneous auricular vagus nerve stimulation (taVNS) on salivary alpha-amylase as indirect noradrenergic marker: A pooled mega-analysis. *Brain Stimulation*, 15(6), 1378–1388. <https://doi.org/10.1016/j.brs.2022.09.009>
- Giraudier, M., Ventura-Bort, C., Szeska, C., & Weymar, M. (2025). A pooled analysis of the side effects of non-invasive Transcutaneous Auricular Vagus Nerve Stimulation (taVNS). *Frontiers in Human Neuroscience*, 19. <https://doi.org/10.3389/fnhum.2025.1539416>
- Goodman, S. P. J., Collins, B., Shorter, K., Moreland, A. T., Papic, C., Hamlin, A. S., Kassman, B., & Marino, F. E. (2025). Approaches to inducing mental fatigue: A systematic review and meta-analysis of (neuro)physiologic indices. *Behavior Research Methods*, 57(4), 1–29. <https://doi.org/10.3758/s13428-025-02620-7>
- Grant, S. J., Aston-Jones, G., & Redmond, D. E. (1988). Responses of primate locus coeruleus neurons to simple and complex sensory stimuli. *Brain Research Bulletin*, 21(3), 401–410. [https://doi.org/10.1016/0361-9230\(88\)90152-9](https://doi.org/10.1016/0361-9230(88)90152-9)
- Grillon, C., Quispe-Escudero, D., Mathur, A., & Ernst, M. (2015). Mental fatigue impairs emotion regulation. *Emotion*, 15(3), 383–389. <https://doi.org/10.1037/emo0000058>
- Guo, M., Li, S., Wang, L., Chai, M., Chen, F., & Wei, Y. (2016). Research on the Relationship between Reaction Ability and Mental State for Online Assessment of Driving Fatigue. *International Journal of Environmental Research and Public Health*, 13(12), 1174. <https://doi.org/10.3390/ijerph13121174>
- Guo, Z., Chen, R., Zhang, K., Pan, Y., & Wu, J. (2016). The Impairing Effect of Mental Fatigue on Visual Sustained Attention under Monotonous Multi-Object Visual Attention Task in Long Durations: An Event-Related Potential Based Study. *PLOS ONE*, 11(9), e0163360. <https://doi.org/10.1371/journal.pone.0163360>
- Gurtubay, I. G., Perez-Rodriguez, D. R., Fernandez, E., Librero-Lopez, J., Calvo, D., Bermejo, P., Pinin-Osorio, C., & Lopez, M. (2023). Immediate effects and duration of a short and single application of transcutaneous auricular vagus nerve stimulation on P300 event related potential. *Frontiers in Neuroscience*, 17. <https://doi.org/10.3389/fnins.2023.1096865>
- Habay, J., Van Cutsem, J., Verschueren, J., De Bock, S., Proost, M., De Wachter, J., Tassignon, B., Meeusen, R., & Roelands, B. (2021). Mental Fatigue and Sport-Specific Psychomotor Performance: A Systematic Review. *Sports Medicine*, 51(7), 1527–1548. <https://doi.org/10.1007/s40279-021-01429-6>

- Hopstaken, J. F., van der Linden, D., Bakker, A. B., & Kompier, M. A. J. (2015). A multifaceted investigation of the link between mental fatigue and task disengagement. *Psychophysiology*, 52(3), 305–315. <https://doi.org/10.1111/psyp.12339>
- Islam, T., Berard, J. A., & Walker, L. A. S. (2026). Perceived Cognitive Fatigability in Multiple Sclerosis: Input from People with Lived Experience on Unmet Needs. *Canadian Journal of Neurological Sciences*, 1–10. <https://doi.org/10.1017/cjn.2026.10531>
- Jacobs, H. I. L., Riphagen, J. M., Razat, C. M., Wiese, S., & Sack, A. T. (2015). Transcutaneous vagus nerve stimulation boosts associative memory in older individuals. *Neurobiology of Aging*, 36(5), 1860–1867. <https://doi.org/10.1016/j.neurobiolaging.2015.02.023>
- Jacquet, T., Lepers, R., Pageaux, B., & Poulin-Charronnat, B. (2023). Acute smartphone use impairs vigilance and inhibition capacities. *Scientific Reports*, 13(1), 23046. <https://doi.org/10.1038/s41598-023-50354-3>
- Jaydarifard, S., Behara, K., Baker, D., & Paz, A. (2024). Driver fatigue in taxi, ride-hailing, and ridesharing services: A systematic review. *Transport Reviews*, 44(3), 572–590. <https://doi.org/10.1080/01441647.2023.2278446>
- Jia, A., Guo, X., & Tian, S. (2022). Experimental study on the influence of mental fatigue on risk decision-making of miners. *Scientific Reports*, 12(1), 11902. <https://doi.org/10.1038/s41598-022-14045-9>
- Johnson, R. L., & Wilson, C. G. (2018). A review of vagus nerve stimulation as a therapeutic intervention. *Journal of Inflammation Research*, 11, 203–213. <https://doi.org/10.2147/JIR.S163248>
- Jongkees, B. J., Immink, M. A., Finisguerra, A., & Colzato, L. S. (2018). Transcutaneous Vagus Nerve Stimulation (tVNS) Enhances Response Selection During Sequential Action. *Frontiers in Psychology*, 9. <https://doi.org/10.3389/fpsyg.2018.01159>
- Kaduk, K., Petrella, A., Müller, S. J., Koenig, J., & Kroemer, N. B. (2025). Non-Invasive Auricular Vagus Nerve Stimulation Decreases Heart Rate Variability Independent of Caloric Load. *Psychophysiology*, 62(2), e70017. <https://doi.org/10.1111/psyp.70017>
- Kim, A. Y., Marduy, A., de Melo, P. S., Gianlorenco, A. C., Kim, C. K., Choi, H., Song, J.-J., & Fregni, F. (2022). Safety of transcutaneous auricular vagus nerve stimulation (taVNS): A systematic review and meta-analysis. *Scientific Reports*, 12(1), 22055. <https://doi.org/10.1038/s41598-022-25864-1>
- Kim, W.-J., Lee, Y.-S., Hong, K. H., Choi, H., Song, J.-J., & Hwang, H.-J. (2025). Effect of transcutaneous auricular vagus nerve stimulation on stress regulation: An EEG and questionnaire study. *Frontiers in Digital Health*, 7. <https://doi.org/10.3389/fdgth.2025.1593614>
- Kreisberg, E., Esmailpour, Z., Adair, D., Khadka, N., Datta, A., Badran, B. W., Bremner, J. D., & Bikson, M. (2021). High-resolution computational modeling of the current flow in the

- outer ear during transcutaneous auricular Vagus Nerve Stimulation (taVNS). *Brain Stimulation*, 14(6), 1419–1430. <https://doi.org/10.1016/j.brs.2021.09.001>
- Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, 82, 1–26. <https://doi.org/10.18637/jss.v082.i13>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2026). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 2.0.3) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Lerman, I., Klaming, R., Spadoni, A., Baker, D. G., & Simmons, A. N. (2022). Non-invasive cervical vagus nerve stimulation effects on reaction time and valence image anticipation response. *Brain Stimulation*, 15(4), 946–956. <https://doi.org/10.1016/j.brs.2022.06.006>
- Li, J., Li, H., Umer, W., Wang, H., Xing, X., Zhao, S., & Hou, J. (2020). Identification and classification of construction equipment operators' mental fatigue using wearable eye-tracking technology. *Automation in Construction*, 109, 103000. <https://doi.org/10.1016/j.autcon.2019.103000>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835. <https://doi.org/10.1016/j.autcon.2019.102835>
- Linnhoff, S., Koehler, L., Haghikia, A., & Zaehle, T. (2023). The therapeutic potential of non-invasive brain stimulation for the treatment of Long-COVID-related cognitive fatigue. *Frontiers in Immunology*, 13, 935614. <https://doi.org/10.3389/fimmu.2022.935614>
- Marano, M., Anzini, G., Musumeci, G., Magliozzi, A., Pozzilli, V., Capone, F., & Di Lazzaro, V. (2022). Transcutaneous Auricular Vagus Stimulation Improves Gait and Reaction Time in Parkinson's Disease. *Movement Disorders*, 37(10), 2163–2164. <https://doi.org/10.1002/mds.29166>
- Matuschek, H., Kliegl, R., Vasishth, S., Baayen, H., & Bates, D. (2017). Balancing Type I error and power in linear mixed models. *Journal of Memory and Language*, 94, 305–315. <https://doi.org/10.1016/j.jml.2017.01.001>
- Matuz, A., Linden, D. van der, Kisander, Z., Hernádi, I., Kázmér, K., & Csathó, Á. (2021). Enhanced cardiac vagal tone in mental fatigue: Analysis of heart rate variability in Time-on-Task, recovery, and reactivity. *PLOS ONE*, 16(3), e0238670. <https://doi.org/10.1371/journal.pone.0238670>
- McIntire, L. K., McKinley, R. A., Goodyear, C., McIntire, J. P., & Brown, R. D. (2021). Cervical transcutaneous vagal nerve stimulation (ctVNS) improves human cognitive performance under sleep deprivation stress. *Communications Biology*, 4(1), 634. <https://doi.org/10.1038/s42003-021-02145-7>

- Mertens, A., Raedt, R., Gadeyne, S., Carrette, E., Boon, P., & Vonck, K. (2018). Recent advances in devices for vagus nerve stimulation. *Expert Review of Medical Devices*, 15(8), 527–539. <https://doi.org/10.1080/17434440.2018.1507732>
- Michielsen, H. J., De Vries, J., & Van Heck, G. L. (2003). Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *Journal of Psychosomatic Research*, 54(4), 345–352. [https://doi.org/10.1016/S0022-3999\(02\)00392-6](https://doi.org/10.1016/S0022-3999(02)00392-6)
- Miyatsu, T., Oviedo, V., Reynaga, J., Karuzis, V. P., Martinez, D., O'Rourke, P., Key, M., McIntire, L., Aue, W., McKinley, R., Pirolli, P., & Broderick, T. (2024). Transcutaneous cervical vagus nerve stimulation enhances second-language vocabulary acquisition while simultaneously mitigating fatigue and promoting focus. *Scientific Reports*, 14(1), 17177. <https://doi.org/10.1038/s41598-024-68015-4>
- Monti, D. A., Wintering, N., Vedaiei, F., Steinmetz, A., Mohamed, F. B., & Newberg, A. B. (2025). Changes in brain functional connectivity associated with transcutaneous auricular vagus nerve stimulation in healthy controls. *Frontiers in Human Neuroscience*, 19, 1531123. <https://doi.org/10.3389/fnhum.2025.1531123>
- Neuser, M. P., Teckentrup, V., Kühnel, A., Hallschmid, M., Walter, M., & Kroemer, N. B. (2020). Vagus nerve stimulation boosts the drive to work for rewards. *Nature Communications*, 11(1), 3555. <https://doi.org/10.1038/s41467-020-17344-9>
- O'Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics*, 63(1), 1–12. <https://doi.org/10.1080/00140139.2019.1687940>
- Pan, X., Soh, K. G., & Soh, K. L. (2024). Viable strategies for enhancing performance in ball sports by mitigating mental fatigue: A systematic review. *PLOS ONE*, 19(11), e0313105. <https://doi.org/10.1371/journal.pone.0313105>
- Pek, J., & Flora, D. B. (2018). Reporting effect sizes in original psychological research: A discussion and tutorial. *Psychological Methods*, 23(2), 208–225. <https://doi.org/10.1037/met0000126>
- Percin, A., Ozden, A. V., Yenisehir, S., Pehlivanoglu, B. E., & Yılmaz, R. C. (2024). The Effect of In-Ear and Behind-Ear Transcutaneous Auricular Vagus Nerve Stimulation on Autonomic Function: A Randomized, Single-Blind, Sham-Controlled Study. *Journal of Clinical Medicine*, 13(15), 4385. <https://doi.org/10.3390/jcm13154385>
- Peters, K. J., & Carlsen, A. (2025, March). Task-dependent reaction time impairments under cognitive fatigue. *2025 Annual Meeting Abstract Book*. Cognitive Neuroscience Society 32nd Annual Meeting.
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>

- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2024). Visual perceptual processing is unaffected by cognitive fatigue. *Consciousness and Cognition*, 119, 103666. <https://doi.org/10.1016/j.concog.2024.103666>
- Petrut, B., Berindan-Neagoe, I., Feflea, D. I., Hoge, M., Pasca, S., Bujoreanu, C. E., & Bschiepfer, T. (2020). Mental Fatigue Evaluation of Surgical Teams during a Regular Workday in a High-Volume Tertiary Healthcare Center. *Urologia Internationalis*, 104(3–4), 301–308. <https://doi.org/10.1159/000504988>
- Pihlaja, M., Failla, L., Peräkylä, J., & Hartikainen, K. M. (2020). Reduced Frontal Nogo-N2 With Uncompromised Response Inhibition During Transcutaneous Vagus Nerve Stimulation—More Efficient Cognitive Control? *Frontiers in Human Neuroscience*, 14. <https://doi.org/10.3389/fnhum.2020.561780>
- Pitts, J., & Bhatt, T. (2023). Effects of mentally induced fatigue on balance control: A systematic review. *Experimental Brain Research*, 241(1), 13–30. <https://doi.org/10.1007/s00221-022-06464-x>
- Poe, G. R., Foote, S., Eschenko, O., Johansen, J. P., Bouret, S., Aston-Jone, G., Harley, C. W., Manahan-Vaughan, D., Weinshenker, D., Valentino, R., Berridge, C., Chandler, D. J., Waterhouse, B., & Sara, S. J. (2020). Locus coeruleus: A new look at the blue spot. *Nature Reviews. Neuroscience*, 21(11), 644–659. <https://doi.org/10.1038/s41583-020-0360-9>
- Powell, M. J. D. (2009). *The BOBYQA algorithm for bound constrained optimization without derivatives* (Report DAMTP 2009/NA06). University of Cambridge.
- Proost, M., Habay, J., De Wachter, J., De Pauw, K., Rattray, B., Meeusen, R., Roelands, B., & Van Cutsem, J. (2022). How to Tackle Mental Fatigue: A Systematic Review of Potential Countermeasures and Their Underlying Mechanisms. *Sports Medicine*, 52(9), 2129–2158. <https://doi.org/10.1007/s40279-022-01678-z>
- Quer, G., Gouda, P., Galarnyk, M., Topol, E. J., & Steinhubl, S. R. (2020). Inter- and intraindividual variability in daily resting heart rate and its associations with age, sex, sleep, BMI, and time of year: Retrospective, longitudinal cohort study of 92,457 adults. *PLOS ONE*, 15(2), e0227709. <https://doi.org/10.1371/journal.pone.0227709>
- R Core Team. (2026). *R: A language and environment for statistical computing*. [Computer software]. R Foundation for Statistical Computing. <https://www.R-project.org/>
- Rabat, A., Cutsem, J. V., Marcora, S. M., Lambert, A., Markwald, R., Kubala, A. G., & Friedl, K. E. (2025). Fatigue and management of warfighter mental endurance. *BMJ Military Health*. <https://doi.org/10.1136/military-2025-002963>
- Rahmani, V., Marsh, V. L., Aliafsari Mamaghani, E., Soleimani, A., Alizadeh, M., Zadi, O., & Aghazadeh, N. (2025). Mental fatigue of operating room nurses and its relationship with missed perioperative nursing care: A descriptive-analytical study. *BMC Research Notes*, 18(1), 302. <https://doi.org/10.1186/s13104-025-07380-3>

- Ramage, A. E., Tate, D. F., New, A. B., Lewis, J. D., & Robin, D. A. (2019). Effort and Fatigue-Related Functional Connectivity in Mild Traumatic Brain Injury. *Frontiers in Neurology*, 9. <https://doi.org/10.3389/fneur.2018.01165>
- Redgrave, J., Day, D., Leung, H., Laud, P. J., Ali, A., Lindert, R., & Majid, A. (2018). Safety and tolerability of Transcutaneous Vagus Nerve stimulation in humans; a systematic review. *Brain Stimulation*, 11(6), 1225–1238. <https://doi.org/10.1016/j.brs.2018.08.010>
- Ridgewell, C., Heaton, K. J., Hildebrandt, A., Couse, J., Leeder, T., & Neumeier, W. H. (2021). The effects of transcutaneous auricular vagal nerve stimulation on cognition in healthy individuals: A meta-analysis. *Neuropsychology*, 35(4), 352–365. <https://doi.org/10.1037/neu0000735>
- Samuels, E. R., & Szabadi, E. (2008). Functional Neuroanatomy of the Noradrenergic Locus Coeruleus: Its Roles in the Regulation of Arousal and Autonomic Function Part I: Principles of Functional Organisation. *Current Neuropharmacology*, 6(3), 235–253. <https://doi.org/10.2174/157015908785777229>
- Schevernels, H., van Bochove, M. E., De Taeye, L., Bombeke, K., Vonck, K., Van Roost, D., De Herdt, V., Santens, P., Raedt, R., & Boehler, C. N. (2016). The effect of vagus nerve stimulation on response inhibition. *Epilepsy & Behavior*, 64, 171–179. <https://doi.org/10.1016/j.yebeh.2016.09.014>
- Schiweck, C., Aichholzer, M., Brandt, E., Schneider, M., Meyer, K., Hamzehloiya, T., Qubad, M., Uckermark, C., Jacobsen, L., Amaral, K., Auer, J., Bruno, G., Zhao, T., Bouzouina, A., Schillo, S., Hanssen, R., Hahn, T., Repple, J., Matura, S., ... Edwin Thanarajah, S. (2025). The heart knows best: Baseline heart rate variability as guide to transcutaneous auricular vagus nerve stimulation in depression. *Translational Psychiatry*, 15(1), 521. <https://doi.org/10.1038/s41398-025-03780-y>
- Shockley, K. M., Gabriel, A. S., Robertson, D., Rosen, C. C., Chawla, N., Ganster, M. L., & Ezerins, M. E. (2021). The fatiguing effects of camera use in virtual meetings: A within-person field experiment. *Journal of Applied Psychology*, 106(8), 1137–1155. <https://doi.org/10.1037/apl0000948>
- Šinkovec, M., Trobec, R., Kamenski, T., Jerman, N., & Meglič, B. (2023). Hemodynamic responses to low-level transcutaneous auricular nerve stimulation in young volunteers. *IBRO Neuroscience Reports*, 14, 154–159. <https://doi.org/10.1016/j.ibneur.2023.01.010>
- Staiano, W., Romagnoli, M., Salazar Bonet, L. R., & Ferri-Caruana, A. (2024). Adaptive cognitive tasks for mental fatigue: An innovative paradigm for cognitive loading in human performance. *Journal of Science and Medicine in Sport*, 27(12), 883–889. <https://doi.org/10.1016/j.jsams.2024.08.199>
- Su, S., Vanvoorden, T., Le Denmat, P., Zénon, A., Braconnier, C., & Duque, J. (2025). Transcutaneous vagus nerve stimulation boosts accuracy during perceptual decision-making. *Brain Stimulation*, 18(3), 975–986. <https://doi.org/10.1016/j.brs.2025.04.020>

- Sun, H., Soh, K. G., Mohammadi, A., Toumi, Z., Zhang, L., Ding, C., Gao, X., & Tian, J. (2024). Counteracting mental fatigue for athletes: A systematic review of the interventions. *BMC Psychology*, 12(1), 67. <https://doi.org/10.1186/s40359-023-01476-w>
- Sun, J., Gao, D., Zhang, J., Liu, H., Zhou, Y., Ma, C., Zhang, X., Liu, S., Zhao, J., Hao, C., & Xiao, X. (2026). Transcutaneous auricular vagus nerve stimulation for major depressive disorder: Current evidence and future research directions. *Frontiers in Psychiatry*, 17. <https://doi.org/10.3389/fpsy.2026.1788611>
- Sun, L., Peräkylä, J., Holm, K., Haapasalo, J., Lehtimäki, K., Ogawa, K. H., Peltola, J., & Hartikainen, K. M. (2017). Vagus nerve stimulation improves working memory performance. *Journal of Clinical and Experimental Neuropsychology*, 39(10), 954–964. <https://doi.org/10.1080/13803395.2017.1285869>
- Tarn, J., Evans, E., Traianos, E., Collins, A., Stylianou, M., Parikh, J., Bai, Y., Guan, Y., Frith, J., Lendrem, D., Macrae, V., McKinnon, I., Simon, B. S., Blake, J., Baker, M. R., Taylor, J. P., Watson, S., Gallagher, P., Blamire, A., ... Ng, W.-F. (2023). The Effects of Noninvasive Vagus Nerve Stimulation on Fatigue in Participants With Primary Sjögren's Syndrome. *Neuromodulation*, 26(3), 681–689. <https://doi.org/10.1016/j.neurom.2022.08.461>
- Thomas, M., Allen, M. S., Wigle, D. A., Shen, K. R., Cassivi, S. D., Nichols, F. C., & Deschamps, C. (2012). Does Surgeon Workload Per Day Affect Outcomes After Pulmonary Lobectomies? *The Annals of Thoracic Surgery*, 94(3), 966–972. <https://doi.org/10.1016/j.athoracsur.2012.04.099>
- Ting, P.-H., Hwang, J.-R., Doong, J.-L., & Jeng, M.-C. (2008). Driver fatigue and highway driving: A simulator study. *Physiology & Behavior*, 94(3), 448–453. <https://doi.org/10.1016/j.physbeh.2008.02.015>
- Transport Canada. (2023). *Fatigue Management in the Transportation Sector*. Government of Canada. <https://tc.canada.ca/en/binder/58-fatigue-management-transportation-sector>
- Van Cutsem, J., Marcora, S., De Pauw, K., Bailey, S., Meeusen, R., & Roelands, B. (2017). The Effects of Mental Fatigue on Physical Performance: A Systematic Review. *Sports Medicine*, 47(8), 1569–1588. <https://doi.org/10.1007/s40279-016-0672-0>
- van den Berg, M. E., Rijnbeek, P. R., Niemeijer, M. N., Hofman, A., van Herpen, G., Bots, M. L., Hillege, H., Swenne, C. A., Eijgelsheim, M., Stricker, B. H., & Kors, J. A. (2018). Normal Values of Corrected Heart-Rate Variability in 10-Second Electrocardiograms for All Ages. *Frontiers in Physiology*, 9. <https://doi.org/10.3389/fphys.2018.00424>
- Vrijkotte, S., Roelands, B., Meeusen, R., & Pattyn, N. (2016). Sustained Military Operations and Cognitive Performance. *Aerospace Medicine and Human Performance*, 87(8), 718–727. <https://doi.org/10.3357/AMHP.4468.2016>
- Wang, M.-X., Wumiti, A., Zhang, Y.-W., Gao, X.-S., Huang, Z., Zhang, M.-F., Peng, Z.-Y., Oku, Y., & Tang, Z.-M. (2023). Transcutaneous cervical vagus nerve stimulation improved

- motor cortex excitability in healthy adults: A randomized, single-blind, self-crossover design study. *Frontiers in Neuroscience*, 17. <https://doi.org/10.3389/fnins.2023.1234033>
- Wirdnam, M., Ferrar, K., Mayes, S., MacMahon, C., Cook, J., & Rio, E. (2024). “A sprained ankle is the biggest sign of mental fatigue”: A qualitative study of the perceptions and experiences of mental fatigue in professional ballet. *Physical Therapy in Sport*, 65, 154–161. <https://doi.org/10.1016/j.ptsp.2023.12.006>
- Yuan, R., Sun, H., Soh, K. G., Mohammadi, A., Toumi, Z., & Zhang, Z. (2023). The effects of mental fatigue on sport-specific motor performance among team sport athletes: A systematic scoping review. *Frontiers in Psychology*, 14. <https://doi.org/10.3389/fpsyg.2023.1143618>
- Yue, H., Ye, G., Liu, Q., Yang, X., Xiang, Q., & Luo, Y. (2024). Impact of Cognitive Fatigue on Attention and the Implications for Construction Safety: A Neuroscientific Perspective. *Journal of Construction Engineering and Management*, 150(8), 04024102. <https://doi.org/10.1061/JCEMD4.COENG-14711>
- Zeuwts, L. H. R. H., Iliano, E., Smith, M., Deconinck, F., & Lenoir, M. (2021). Mental fatigue delays visual search behaviour in young cyclists when negotiating complex traffic situations: A study in virtual reality. *Accident Analysis & Prevention*, 161, 106387. <https://doi.org/10.1016/j.aap.2021.106387>
- Zhang, H., Guo, Z., Qu, Y., Zhao, Y., Yang, Y., Du, J., & Yang, C. (2022). Cognitive function and brain activation before and after transcutaneous cervical vagus nerve stimulation in healthy adults: A concurrent tcVNS-fMRI study. *Frontiers in Psychology*, 13, 1003411. <https://doi.org/10.3389/fpsyg.2022.1003411>
- Zhang, Z., Xiang, T., Guo, H., Ma, L., Guan, Z., & Fang, Y. (2023). Impact of physical and mental fatigue on construction workers’ unsafe behavior based on physiological measurement. *Journal of Safety Research*, 85, 457–468. <https://doi.org/10.1016/j.jsr.2023.04.014>

Chapter 7. General Discussion

7.1 Summary

Cognitive fatigue (CF), or mental fatigue, is a commonly experienced, transient psychobiological state of perceived exhaustion that occurs with sustained mental effort (Ackerman, 2011; Behrens et al., 2023; Van Cutsem et al., 2017). Although interest in understanding cognitive fatigue dates to the late 1800's (Ackerman, 2011), it is particularly relevant in the modern technological environment. Activities ranging from smartphone use and video games to virtual meetings, VR and extended computer-based work can contribute to CF (Brazaitis & Satas, 2023; Fortes et al., 2023; Jong et al., 2020; Riedl et al., 2023; Souchet et al., 2023; Yasin et al., 2023). Cognitive fatigue is also a common consequence of work in many demanding professions, including healthcare, construction, and transportation (Adachi et al., 2024; Barker & Nussbaum, 2011; Meng et al., 2015; Petrut et al., 2020; Zong et al., 2024).

While CF is common, it is not benign. Its negative impacts on productivity (Biondi et al., 2021; Ricci et al., 2007) and safety (Díaz-García et al., 2026; Pitts & Bhatt, 2023) are well documented. Among other effects, CF has been associated with riskier decision-making and impaired hazard responses in construction (J. Li et al., 2019; Zhang et al., 2023), an increased likelihood of medical errors (Chan et al., 2009; Rahmani et al., 2025; Thomas et al., 2012), elevated injury risk in sport (Fazackerley et al., 2025; Wirdnam et al., 2024), and increased road accident risk (Minusa et al., 2021; Mizuno et al., 2020), with fatigue thought to contribute to 15-20% of serious road crashes annually (van Schagen, 2021).

Despite its prevalence and practical importance, our understanding of how CF affects human performance remains incomplete. To partially address this, this thesis aimed to explore the effects of CF on psychomotor performance – an area particularly relevant to many of the

risks outlined above. Specifically, this thesis used psychomotor reaction time (RT) to index CF-related psychomotor performance deficits. It is well documented that CF impairs RT performance (e.g., Habay et al., 2021; Jaydarifard et al., 2019; Langner et al., 2010; Staiano et al., 2024), and RT tasks such as the psychomotor vigilance task (PVT) are frequently used to assess and monitor CF in both experimental and applied (workplace) settings (Staiano et al., 2024; Talebi et al., 2026; Weetman et al., 2024). However, RT is not necessarily a unitary process. From an information processing perspective, RT reflects the combined contribution of several sub-processes that could be impacted by CF (Donders, 1969; Spijkers & Walter, 1985; Taylor, 1976). This includes detection of the imperative stimulus, selection of an appropriate motor response, preparation of that response, and response initiation (Czyż, 2021; Schmidt et al., 2019). Depending on the task, varying degrees of response inhibition may also be required, e.g., to withhold a prepared response until an imperative stimulus occurs and/or to suppress competing response options (Czyż, 2021; Schmidt et al., 2019).

Although CF has frequently been associated with slower RT, its effect on these individual psychomotor processes has not been well characterized. A clearer understanding of which processes are affected may help explain how CF contributes to real-world performance failures and may be informative for assessing and managing CF-related risk.

On a related note, there is limited evidence about effective methods for counteracting the psychomotor effects of CF. While a variety of interventions have been suggested, many are impractical for use in occupational settings. For instance, truck drivers or air traffic controllers are likely unable to pause their work during a shift in order to meditate or spend time in nature (Sun et al., 2024). Other approaches to mitigating CF rely on ingestion of stimulants or supplements, which may not be a viable or preferred option for many individuals (Proost et al.,

2022). Consequently, practical and accessible approaches to reduce CF-related performance impairments are lacking.

This thesis aimed to address these knowledge gaps. First, we sought to better understand the psychomotor effects of CF by examining its impact on the individual processes that could contribute to slowed RT performance (*Experiments 1-4*). Second, we investigated whether a non-invasive and accessible intervention, transcutaneous vagus nerve stimulation (tVNS), could attenuate the effects of CF on subjective fatigue sensations and psychomotor performance (*Experiment 5*).

The following sections elaborate on the insights gained from this thesis regarding the psychomotor impacts of CF, as well as implications for the assessment and mitigation of fatigue-related performance decrements and the overall limitations of this work. Suggested directions for future research needed to address remaining questions are also integrated throughout this discussion.

7.2 Psychomotor Impacts of Cognitive Fatigue: Current Insights and Future Directions

7.2.1 Response Selection & Inhibition

It has previously been suggested that cognitive fatigue (CF) may have preferential impacts on executive (or “top-down”) forms of central processing (Boksem et al., 2005; Lorist & Faber, 2011; van der Linden, Frese, & Meijman, 2003). Effortful control models of CF propose that prolonged engagement in high-demand cognitive tasks weakens connectivity within control networks or leads to metabolic changes that reduce capacity for top-down regulation of performance (André et al., 2019; Pessiglione et al., 2025; Wiehler et al., 2022). Consistent with this view, several executive processes have been shown to be sensitive to CF, such as cognitive flexibility (Lorist et al., 2000; Plukaard et al., 2015; van der Linden, Frese, & Sonnentag, 2003),

complex planning (van der Linden, Frese, & Meijman, 2003), and value-based decision-making (Blain et al., 2016; Jia et al., 2022; Wiehler et al., 2022). It is logical then, that in the context of psychomotor (RT) performance, more “executively-driven” processes reliant on cognitive control regions such as response inhibition (e.g., as required in go/no-go RT tasks) and response selection (e.g., as required in choice RT tasks) may be particularly vulnerable to CF. This possibility is supported by the fact that both of these psychomotor processes rely on activity in cognitive control regions (Marek & Dosenbach, 2018). For example, the dorsolateral prefrontal and ventrolateral cortices are thought to contribute to response inhibition (Hung et al., 2018; Liddle et al., 2001; Marek & Dosenbach, 2018), while response selection has been linked to the dorsolateral prefrontal cortex (Nathaniel-James & Frith, 2002) and parietal regions (Bunge et al., 2002; Schumacher & D’Esposito, 2002). Further, the anterior cingulate cortex likely contributes to error monitoring in both psychomotor processes (Hung et al., 2018; Liddle et al., 2001; Schumacher & D’Esposito, 2002).

However, despite these neural overlaps and previous reports suggesting that CF negatively impacts inhibitory control (Z. Guo et al., 2018; Kato et al., 2009), the current findings provide little support for any substantial effect of CF on response inhibition. In Experiment 3, go/no-go RT was not significantly slowed relative to the control condition following two of the three cognitively fatiguing interventions, and go/no-go RT task accuracy was broadly unaffected. Similarly, Experiment 4 found no evidence that CF altered pre-movement suppression of corticospinal excitability prior to the go-signal. This transient reduction in corticospinal excitability is generally thought to reflect inhibitory influences within the motor system (Duque et al., 2017). If CF had specific impacts on inhibitory processing, we expected to observe distinct CF-related reductions in premovement suppression (i.e., such that corticospinal excitability

increasingly diverged from the control condition as the go-signal approached). Instead, although corticospinal excitability was elevated overall in CF relative to control, this difference was consistent throughout preparation, providing no evidence for inhibition-specific effects of CF. Somewhat contrarily, we did observe increased anticipatory responding following the CF intervention in Experiment 5, suggesting a reduction in the ability to withhold a prepared response. However, because this pilot study lacked a non-fatigue control condition (and was designed primarily to explore a CF intervention), this provides only limited evidence that CF may influence inhibitory control.

The overall lack of evidence for CF-related inhibitory deficits in this thesis is more consistent with sparse research reporting a null effect of prolonged cognitive work on go/no-go RT or accuracy (Falkenstein et al., 2002; Magnuson et al., 2021) than with more common reports of impaired inhibitory task performance in CF (Z. Guo et al., 2018; Habay et al., 2026; Kato et al., 2009). The reason for this general discrepancy within the literature is unclear; however, an important consideration is that the go/no-go paradigm used in this thesis may not have been adequately sensitive to detect more subtle changes in inhibitory control. Instead, a more direct approach for examining this possibility could employ short-interval intracortical inhibition (SICI). SICI is a TMS-derived measure of inhibitory activity within M1, inferred from the reduction in motor evoked potential amplitude when a suprathreshold test pulse is preceded ~2-5 ms earlier by a subthreshold conditioning pulse (Rothwell et al., 2009). Some previous work has shown increased SICI following no-go stimuli and decreased SICI following go-stimuli in agonist muscles (Sohn et al., 2002). Assessing SICI in a similar fashion following CF and control interventions may therefore provide a different, perhaps more direct, way to examine inhibitory psychomotor control in CF.

In contrast, the findings of this thesis provide somewhat stronger evidence for response selection impairment in CF. In Experiment 3, choice RT exhibited a larger average increase across CF tasks relative to control (+21.59 ms) than simple RT (+9.36 ms) – although notably this difference did not reach statistical significance, and absolute changes (i.e., not relative to control) were very similar (simple RT: +22.3 ms, choice RT = +19.5 ms). Regardless, this pattern could suggest a contribution of response selection demands to CF-related RT slowing. This would align with previous reports demonstrating CF-related impairments in response selection within a 4-choice RT paradigm (Xiao et al., 2015) and sport-based decision-making tasks (Fortes et al., 2025; Smith et al., 2016).

However, it is important to note that the effects of CF on response selection were not uniform. The magnitude of choice RT slowing depended on the nature of the preceding cognitive work, as did response strategy (i.e., the Stroop intervention in particular led to slower choice RT alongside a tendency to prioritize accuracy). This pattern suggests “task-specific” effects of CF on response selection, potentially reflecting overlap in the cognitive demands of the Stroop and choice RT tasks (Behrens et al., 2023; Persson et al., 2007). For example, conflict monitoring demands of the Stroop task may have significantly taxed the anterior cingulate cortex (a cognitive control region implicated in the “facilitation system”; Ishii et al., 2014), reducing its capacity to support conflict monitoring in the subsequent choice RT task. In contrast, the smallest change in choice RT relative to control occurred following the Math-Memory task, which also produced less motivational decline than other CF interventions tested. This raises the possibility that response selection may be more sensitive to demotivation than to CF per se, an idea that has also been suggested in previous work examining prolonged Simon task performance (Möckel et al., 2015). Generally, further research is evidently needed to refine our understanding of the

effects of CF on response selection, perhaps by employing paradigms that systematically manipulate response selection demands. For instance, a Hick's Law paradigm comparing 2-, 4-, and 8-choice RT task performance following CF and control interventions could determine whether CF alters the relationship between the number of stimulus-response alternatives (i.e., response selection demand) and decision time (Hick, 1952).

To summarise, we observed little evidence for CF-related impairments of response inhibition but showed that response selection may be more sensitive to CF, in a relatively complex task-specific manner. Thus, while there may be *some* preferential impact of CF on the more “executive” aspects of psychomotor processing, the continued sensitivity of simple RT (which is thought to demand comparably less response selection and inhibition compared to go/no-go and choice paradigms) indicates that additional psychomotor processes beyond response selection and inhibition must be impacted by cognitive fatigue.

7.2.2 Visual Perceptual Processing

An alternative explanation for psychomotor performance impairments in CF could be related to the time required to detect and process task-relevant stimuli. However, findings from Experiment 2 suggested that the overall speed of perceptual processing was not affected by CF, as indexed by a visual inspection time (IT) task. While simple RT was slowed, no CF-related change in IT task performance (i.e., the minimum exposure duration required for accurate visual discrimination; Vickers & Smith, 1986) was observed. This result appears to be somewhat at odds with electrophysiological recordings showing reduced amplitude of early sensory ERPs in CF (e.g., Boksem et al., 2005; Faber et al., 2012). However as noted previously (*Chapter 3.7*), these ERPs may more closely reflect the requirement of *orienting to*, rather than discriminating, task-relevant stimuli, which was not an explicit requirement of the IT nor the RT tasks used in this Experiment

(as in both cases, stimuli remained stationary within the central visual field; Neuhaus et al., 2010). While an alternative possibility is that CF influences perceptual processing in other sensory modalities (e.g., tactile, auditory), the fact that we repeatedly observed RT slowing in response to visually presented stimuli suggests that this is unlikely to account for CF-related performance decrements.

Notably, the IT task primarily requires recognition of the “pi” figure without a motor response contribution and is therefore considered to rely predominantly on ventral stream processing (object/stimulus identification and recognition), rather than dorsal stream processing (spatial processing and action guidance; Tachibana et al., 2014; Ungerleider & Haxby, 1994). Considering this, a useful extension of the current work would be to examine whether CF differentially affects visuomotor processing systems involved in action guidance. This possibility is consistent with evidence from visuomotor rotation tasks, where increasing CF was associated with reduced explicit, but not implicit, adaptation, indicating that CF may preferentially impair more conscious, strategic aspects of visuomotor control, rather than more automatic sensorimotor recalibration (Apreutesei & Cressman, 2024; David Milner, 2015; Peters & Cressman, 2026). Although the RT tasks used in this thesis may be more strongly ventral in nature due to their limited spatial demands, more real-world RT behaviours, like reaching to intercept a falling object, should place greater demands on dorsal stream processing (Montare, 2016). Accordingly, employing paradigms that more directly isolate visuomotor transformations (e.g., pro-point/anti-point tasks; Cameron et al., 2013; Pisella et al., 2000) may be a particularly informative next step in elucidating how CF impacts perceptual-motor processing, and in turn RT performance.

7.2.3 Response Preparation

Another possibility we addressed is that CF may influence movement preparation, or the process by which the sensorimotor system is configured into an appropriate initial state for voluntary movement, such that rapid and accurate execution can occur when a response is triggered (Carlsen et al., 2012; Wong et al., 2015). This was examined in Experiments 1 and 4, which assessed motor preparation during an RT task using two complementary approaches.

In Experiment 1, a StartReact paradigm was used to probe the level of motor preparation at the time of the go-signal (i.e., while the system is holding a prepared but not yet initiated state; Carlsen et al., 2012). Although CF was successfully induced, indicated by increased subjective fatigue, and RT was slowed, the StartReact effect (both proportion of elicited trials and effect magnitude) was not measurably altered by CF. However, two methodological considerations may have limited sensitivity of the StartReact metric to CF-related changes in preparation. First, the startling stimulus itself may have counteracted CF effects, for example by raising arousal or sympathetic activity, which are typically reduced under CF (Boksem et al., 2005; Csathó et al., 2024). Second, StartReact responses are thought to be mediated primarily by activation of subcortical reticulospinal pathways (Carlsen & Maslovat, 2019, 2026; Tapia et al., 2022). If CF more strongly affects corticospinal mechanisms involved in voluntary motor preparation, this discrepancy could explain the apparent insensitivity of the StartReact effect to CF.

To address this, Experiment 4 examined the effects of CF on movement preparation in a different way, by assessing corticospinal excitability during the preparatory period of a simple RT task using transcranial magnetic stimulation (TMS; Bestmann & Duque, 2016; Hallett, 2007). Contrary to our expectations, results suggested that corticospinal excitability was not reduced in CF and, in some cases, may have been elevated relative to the control condition. This result was

observed throughout the preparatory period and at rest and thus may reflect a general compensatory elevation of neural drive to counteract fatigue-related performance strain. In the context of Ishii's (2014) dual-regulation hypothesis, this could be conceptualized as greater activation of the mental facilitation system to counteract CF-related elevation of inhibition system activity.

Taken together, findings from Experiments 1 and 4 suggest that movement preparation, at least within a simple RT task, is preserved under CF and thus is unlikely to meaningfully contribute to CF-related psychomotor impairments, including slowed RT. Intact or compensatory neural activity in CF has been reported in other contexts, such as preserved contingent negative variation (CNV; an EEG index of preparatory activity; Schouppe et al., 2020), increased functional connectivity between frontal, central, and parietal regions in a dart throwing task (Niu et al., 2024), as well as altered frontal-temporal-occipital connectivity in driving fatigue (Kong et al., 2015). Likewise, an absence of CF-related changes has been noted in other studies assessing corticospinal excitability (Holgado et al., 2023; Kowalski et al., 2022; Rozand et al., 2015), although these effects were not measured during active movement preparation, and no other study to our knowledge has shown *increases* in corticospinal excitability in CF relative to the control condition.

At present, it remains unclear why movement preparation appears resistant to CF. One speculative explanation is that CF may more strongly affect the *updating* of central movement representations rather than the *maintenance* of an already prepared state or may bias control toward more *predictive* rather than *reactive* strategies. Although direct findings in favor of these possibilities are limited, some support does exist. First, this explanation aligns with theoretical views proposing that CF reflects metabolic alterations in cognitive control networks, leading to a

shift toward lower-effort, more automatic actions (Pessiglione et al., 2025). In accordance, CF did not affect automatic responding in a Simon task, but did impair the ability to inhibit or adjust the automatic response set when task demands changed (Salomone et al., 2021). Similarly, in a force-matching motor learning paradigm, cognitively fatigued participants were more likely to rely on previously established response mappings (i.e., forces matching those learned in the acquisition phase) during transfer tests, rather than updating to new force requirements (Khojasteh Moghani et al., 2021).

This idea that CF affects updating more than maintenance could be further tested using task-switching paradigms such as a low-probability switch paradigm (i.e., a choice RT task where participants are typically cued to make one response, and rarely cued to make a different response; Huettel & McCarthy, 2004) or a design with varied pre-cue reliability (i.e., a choice RT task where required responses are mostly reliably pre-cued, but sometimes an unreliable pre-cue is presented; Tzagarakis et al., 2021). In both these paradigms, participants establish a dominant prepared response state that is required on the majority of trials, with occasional low-probability trials requiring a revision of the current motor plan (Tzagarakis et al., 2021). If cognitive fatigue primarily affects updating rather than maintenance of central movement representations, CF-related impairments (e.g., disproportionate RT or accuracy costs) would be expected to emerge primarily on low-probability or invalidly cued trials, while performance on high-probability or validly cued responses would remain preserved in comparison.

Overall while the present thesis does not support a primary role for impaired motor preparation in CF, and in fact suggests potential compensatory preparatory activity, additional experimentation exploring the nuances of response updating versus maintenance may provide further insight into preparatory dynamics under CF.

7.2.4 Attention & Motivation

Although not directly assessed in this thesis (e.g., via eye-tracking or a dedicated attentional control tasks like a Flanker paradigm), changes in attention may certainly contribute to negative psychomotor performance outcomes in CF. Previous work using event-related potential (ERP) and behavioural measures has shown that CF can reduce goal-direction attention and increase susceptibility to distraction by irrelevant stimuli (Boksem et al., 2005; Faber et al., 2012). While we attempted to minimize environmental distractions in laboratory-based experiments (*Experiments 1, 4, and 5*), and participants were instructed to ensure the same in remotely administered experiments (*Experiments 2 and 3*), the potential influence of uncontrolled distractors cannot be excluded, particularly in remote testing.

However, Experiment 2 provides some indirect evidence that points against attention as a central driver of CF effects. In this remote experiment, participants completed both an RT task and an IT task before and after CF manipulation. Reaction time was slowed following CF. If attentional decline or increased distractibility were the primary driver of CF-related psychomotor deficits, a corresponding decline in IT task performance would be expected; however, this was not observed. Similarly, throughout the experiments, performance during the CF-inducing tasks often (although not always) improved over time rather than deteriorating, which is not entirely consistent with attentional breakdown (see *Appendix D, Fig. D.2, Fig. D.4*). In addition, relatively few response omissions (complete lapses) were observed in simple RT performance across experiments (e.g., 1.2% of trials in Experiment 4), further suggesting that attentional changes alone are unlikely to account for CF-related RT slowing in these experiments. Despite this, replication of experiments (such the IT task) alongside a more direct attentional measures

like gaze-tracking may be beneficial in the future to more concretely assess attentional contributions to psychomotor performance deficits in CF.

Motivational decline has also been widely proposed as a key part of the mechanism underlying CF-related performance impairments, including motor outcomes (Boksem & Tops, 2008; Herlambang et al., 2019; Martin et al., 2018). Several studies using commonly employed CF-inducing interventions, such as the Stroop or Time Load Dual-Back tasks, have shown reductions in self-reported motivation following prolonged task performance (Bach et al., 2026; Martin et al., 2018; Read et al., 2026). Consistent with these findings, motivational declines were observed following versions of both of these tasks in Experiment 3 (*Chapter 4, Fig. 4.2b*). In contrast, motivation responded differently to our self-designed Math-Memory intervention. This task was designed to incorporate key features thought to promote CF outlined by Ackerman (2011), including (1) sustained time-on-task; (2) high cognitive load, including dual-tasking (O’Keeffe et al., 2020); (3) a low tolerance for errors; (4) penalties associated with distraction; and (5) substantial time pressure. It was also designed, with the help of pilot feedback, to minimize boredom and preferentially induce “active” (effort-based) rather than “passive” (boredom-based) fatigue, while limiting excessive demotivation as a potential confound. Across experiments, this task reliably induced subjective fatigue while generally producing relatively stable motivation levels compared with control conditions and other CF interventions (e.g., *Appendix A.2; Chapter 4.6.2; Chapter 5.6.1*). Thus, while motivation cannot be excluded as a contributor to CF-related psychomotor deficits, the absence of substantial motivational declines due to the Math-Memory paradigm suggests that it is unlikely to be the main reason for observed RT slowing in this thesis.

7.2.5 Movement Initiation

Cognitive fatigue may influence a remaining stage of psychomotor processing: movement initiation, spanning the transition from a prepared motor state to descending motor output, muscle activation (EMG onset), and the subsequent onset of measurable movement (displacement onset; Czyż, 2021; Kennefick et al., 2014; Rothwell et al., 2021). The findings from this thesis raise the possibility that CF could influence initiation at both the central and peripheral level (Fig. 7.1).

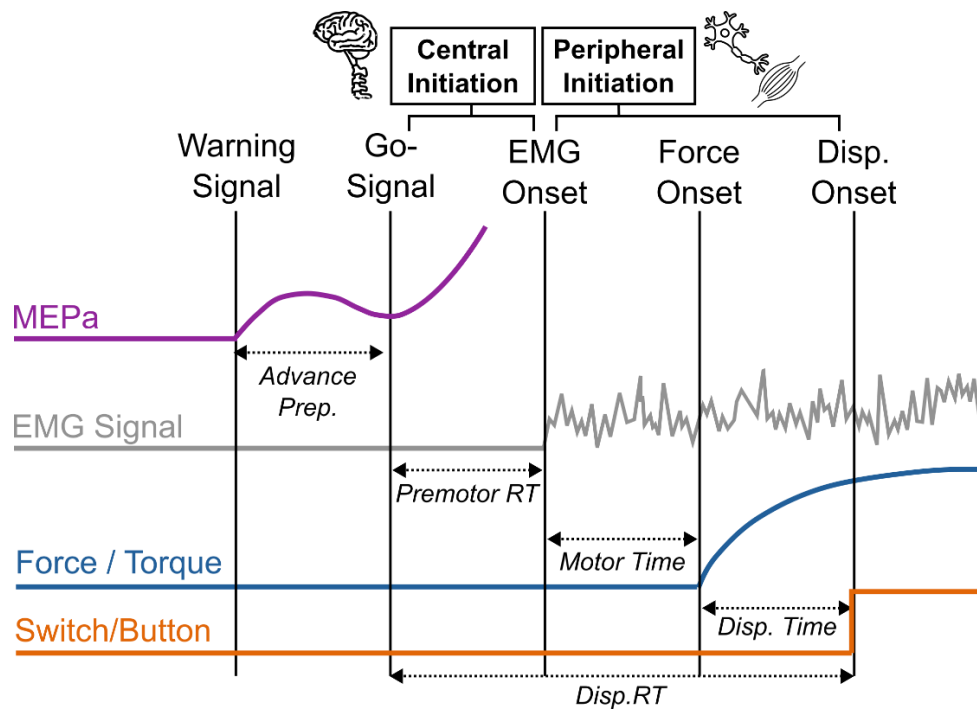


Fig. 7.1 Schematic timeline of events in a simple reaction time task. Cognitive fatigue may influence initiation-related processes at the central level (i.e., the transition from a prepared to initiating state, prolonging premotor RT) and/or peripheral level (i.e., neuromuscular recruitment and subsequent force development, prolonging motor and displacement time). EMG = electromyography, Disp. = displacement, MEPa = motor-evoked potential amplitude, Prep. = preparation, RT = reaction time.

For instance, consistent with a potential influence of CF on central components of movement initiation, a StartReact paradigm (Experiment 1) showed that CF-related slowing of RT was observed for voluntary responses to low-intensity stimuli but was absent for involuntary startle-triggered movements. In other words, when voluntary initiation processes were bypassed, CF-related slowing was no longer evident. This pattern therefore suggests that CF may have particular effects on central release mechanisms.

Mechanistically, this is consistent with the idea that CF could alter cortico–basal ganglia–thalamo–cortical loop dynamics involved in action gating and the release of prepared motor commands (Fig. 7.2). The basal ganglia play a central role in regulating the transition from movement preparation to execution (Hauber, 1998; Purves et al., 2001; Young et al., 2026) and are also considered an important component of facilitation systems involved in sustaining cognitive and physical performance under CF (Ishii et al., 2014; Tanaka et al., 2014). Consistent with this idea, altered basal ganglia function has been associated with CF in several clinical populations, including individuals with chronic fatigue syndrome (Miller et al., 2014), multiple sclerosis (Finke et al., 2015; Langley et al., 2023), and stroke (Boukrina et al., 2026). Collectively, this suggests that CF may slow the release of prepared motor commands via altered basal ganglia-mediated action gating or initiation, potentially contributing to increased RT.

Findings from Experiment 5 exploring tVNS as a CF intervention are also broadly consistent with this interpretation. Transcutaneous VNS has been shown to modulate basal ganglia activity (Badran et al., 2022; Monti et al., 2025; Rajiah et al., 2024), potentially through interactions with the LC-NE system (Benarroch, 2018). In addition, tVNS has been associated with improvements in CF symptoms *and* movement initiation deficits in Parkinson’s disease (Bu et al., 2026; Matsuoka et al., 2025; Sigurdsson et al., 2021), as well as enhanced cognitive and

motor performance in healthy individuals (Matsuoka et al., 2025). While indirect, this evidence suggests that enhanced basal ganglia function may support more efficient central initiation, and in turn underscores the potential for basal-ganglia-related initiation deficits in CF.

Although Experiment 4 did not assess corticospinal excitability after the go-signal (i.e., at movement initiation), it found no evidence of CF-related alterations in the temporal pattern of excitability leading up to the go-signal (only the *overall* level of excitability was elevated; Chapter 5, Fig. 5.5 and Fig. 5.6). These findings of course do not exclude the possibility that CF influences movement initiation – but it could suggest that this may not necessarily occur through reductions in overall levels of initiation-related corticospinal excitability. Instead, it is possible that CF may influence movement initiation by altering the temporal dynamics of motor system activity. Movement initiation is increasingly understood not just as a simple threshold-crossing process, but as dependent on a coordinated spatiotemporal evolution of neural activity within M1 and broader motor-related networks (Balasubramanian et al., 2020; Best et al., 2017; Churchland et al., 2012). From this perspective, CF-related changes in functional connectivity (T. Li et al., 2024; Qi et al., 2019) and oscillatory activity (Hussain et al., 2022; Neige et al., 2023; Tomassini et al., 2026) could alter the timing and synchrony with which central motor neural activity approaches an initiation state, even if the overall *magnitude* of corticospinal excitability remains unchanged. Such alterations could contribute to slowed RT by producing a less efficient or temporally coordinated transition to initiation, delaying the moment at which an initiation threshold is reached, and/or prolonging internal process governing when a movement held in preparation is released, depending on the mechanistic view adopted (Alyahyay et al., 2026; Haith et al., 2016).

Cognitive fatigue may also influence movement initiation at the peripheral level; more specifically, CF-related changes in motor output (e.g., altered motor unit recruitment) could influence the initial conditions of muscle activation following EMG onset. In this scenario, early muscle activity may be translated into force production less efficiently, producing a small additional delay between EMG onset and displacement onset (Eilfort & Filli, 2025). This interpretation is consistent with the modest reductions in EMG amplitude we observed following CF in Experiment 5, which appeared to be somewhat attenuated by tVNS, and may help explain why displacement RT was occasionally and subtly more affected by CF than premotor RT.

Although the mechanisms discussed above are speculative, this thesis provides a strong rationale for future work examining the effects of CF on central and peripheral measures of movement initiation. For example, TMS could be used to assess corticospinal excitability not only during the preparatory foreperiod (as in Experiment 4), but also immediately following the go-signal, allowing characterization of initiation-related corticospinal drive in CF.

Complementary H-reflex measures could be used to quantify changes in descending motor output at the spinal level, while high-density EMG could provide insight into motor unit recruitment dynamics during movement onset. Together, these approaches would provide a more complete characterization of movement initiation in CF and may help identify ways in which CF-related psychomotor performance impairments can be targeted and mitigated.

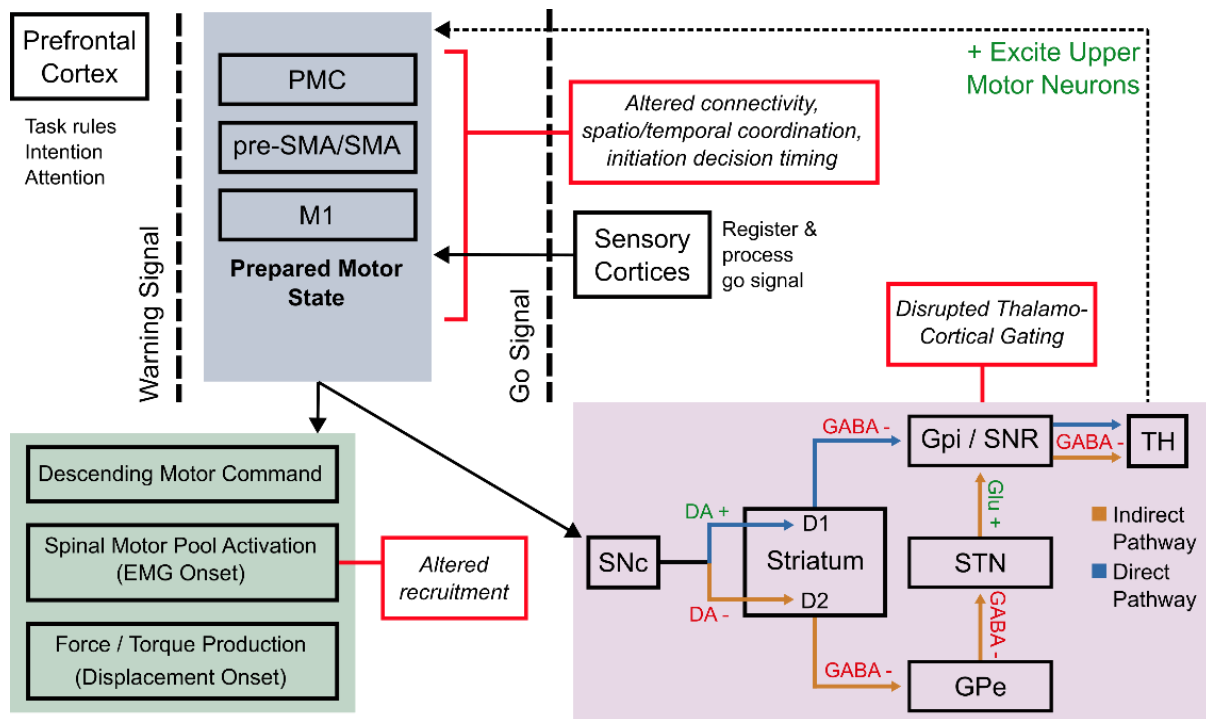


Fig. 7.2 Conceptual model of potential central and peripheral initiation mechanisms underlying cognitive fatigue-related psychomotor performance impairment. Motor preparation involves the premotor cortex (PMC), pre-supplementary/supplementary motor areas (pre-SMA/SMA), and primary motor cortex (M1), which together contribute to establishing a prepared motor state (blue box). Following the go-signal in a simple reaction time task, prepared motor commands are released through central motor pathways involving cortico-basal ganglia-thalamo-cortical circuitry (purple box). They are subsequently transmitted as a descending motor command to the spinal motor neuron pool, resulting in muscle activation (EMG onset) and ultimately displacement (green box). Red boxes indicate potential loci / mechanisms through which cognitive fatigue may influence these processes, including altered motor-related network dynamics in preparation-to-initiation transitions, altered basal ganglia-mediated action gating, and altered translation of muscle activation into force production. D1/D2 = dopamine receptors, DA = dopamine, GABA = gamma-aminobutyric acid, GPe = external globus pallidus, GPi =

internal globus pallidus, SNc = substantia nigra pars compacta, SNr = substantia nigra pars reticulata, STN = subthalamic nucleus, TH = thalamus.

7.3 Applied Insights: Researching, Screening, and Mitigating Cognitive Fatigue

In addition to addressing the primary research question, this thesis has provided several noteworthy contributions to the study, assessment, and mitigation of CF. First, as previously described, we developed a novel Math-Memory intervention for CF induction. Participants often shared anecdotal reports that the task was challenging without being excessively boring or discouraging. Consistent with this, the Math-Memory task produced minimal motivational decline relative to other CF tasks (Stroop, Time Load Dual-Back) and to the control condition, despite being consistently rated as highly mentally fatiguing. At the same time, it typically produced small but reliable RT increases (with the exception of Experiment 4, where TMS may have also acted as a cue affecting RT performance). We also demonstrated that this task, along with the Stroop, Dual-Back, and documentary control tasks, can be successfully deployed remotely for large-scale experimentation when combined with response timestamping and rigorous data screening procedures. Overall, these findings suggest that the Math-Memory task may be an effective tool for experimentally inducing CF in future research, either laboratory-based or remote.

This thesis also contributes to our understanding of RT as a tool for CF monitoring / assessment, particularly through Experiment 3. Reaction time measures are increasingly being explored for fatigue monitoring to promote workplace safety (Brossoit et al., 2023; Evans et al., 2019; Heng et al., 2024), including in construction (Raharjo et al., 2026; Zong et al., 2024), mining (Rogers et al., 2023), trucking (Talebi et al., 2026), healthcare (Byrne et al., 2010; Ferguson et al., 2020; Weetman et al., 2024), and military settings (Main et al., 2023). In fact,

some commercial RT-based tools are already available for workplace use, such the AlertMeter® Fatigue Risk Management System (Predictive Safety, 2026). At the same time, RT-based CF metrics are also being tested for tracking CF in clinical populations (Barrios et al., 2022; Price et al., 2017), and for validating other physiological or neurological CF indicators (M. Guo et al., 2016; F. Li et al., 2022).

The findings of this thesis show that simple RT (and in a different way, choice RT) are sensitive to CF after only one hour of cognitively demanding work. Simple RT exhibited small but consistent increases across experiments, an effect which appeared stable across different types of cognitive work, whereas choice RT was also sensitive to CF but was more dependent on the nature of the preceding mental task. Furthermore, consistent with prior work (e.g., Matsui et al., 2024; Walker et al., 2012), subjective fatigue increased reliably across CF conditions, but did not always correlate directly with RT changes, supporting the value of including both subjective and psychomotor performance-based measures in CF assessment.

Overall, this thesis extends previous evidence demonstrating that remote computer-based RT-based metrics can be used to assess CF (Experiments 2 and 3; Arsintescu et al., 2019; Khitrov et al., 2014). Given that RT tasks are easily comprehended and fast and simple to administer, RT remains a promising tool for CF assessment and monitoring in experimental, clinical, and occupational contexts. Future work may wish to expand on this potential by examining RT sensitivity to more ecologically valid CF scenarios, including longer work durations, repeated cognitive demands across or within workdays, or with combined factors such as stress or sleep deprivation, which may amplify CF effects and associated risks.

Finally, this thesis also provides preliminary evidence that CF effects may be mitigated using non-invasive neurostimulation, specifically tVNS. Although exploratory in nature, our

research suggests that tVNS may help attenuate CF-related changes in psychomotor (RT) performance, subjective fatigue, and autonomic function. From a practical perspective, tVNS is relatively inexpensive, simple to administer, and increasingly accessible through commercially available devices and TENS-based systems (Yap et al., 2020). Advantageously, unlike many CF-mitigation strategies (e.g., meditation, exposure to nature; Sun et al., 2024) tVNS can be applied without interrupting ongoing task performance. It is generally very well tolerated, with infrequent and very mild side-effects (Kim et al., 2022; Redgrave et al., 2018). Nevertheless, substantially larger samples are required to determine whether tVNS reliably mitigates CF effects on psychomotor performance, ideally using an adequately powered, double-blind randomised controlled trial.

7.4 Limitations

There are several limitations that should be considered when interpreting this thesis. First, although the CF-related RT increases observed here are comparable to some previous reports (Langner et al., 2010; Le Mansec et al., 2019), others have reported larger RT effects (~25-40ms; Jaydarifard et al., 2019; Staiano et al., 2024). One likely explanation for this discrepancy is the impact of practice effects. Across experiments, participants completed only a brief RT familiarization period (i.e., 10-20 trials) prior to testing. If performance had not fully stabilized before the pre-test assessment, continued improvement throughout the experimental period could have partially counteracted CF-related slowing. This possibility is supported by several observations, including RT speeding across some control sessions (Experiment 1), RT speeding within pre-test assessments (Experiment 5; *Appendix C.3.2*), and reductions in preparation-related corticospinal excitability over the control intervention in Experiment 4, which may

(speculatively) reflect decreasing effort demands with practice. Future studies should therefore consider longer familiarization periods or separate pre-experiment training sessions.

A second potential reason relates to the Math-Memory intervention. As discussed previously, this task appeared to induce CF while minimizing motivational decline, whereas more commonly used tasks (Stroop, Dual Back) produced clearer reductions in motivation. As a result, larger RT increases reported in some previous studies may reflect the combined influence of *both* motivational decline and CF, rather than CF in (greater) isolation (e.g., Migliaccio et al., 2022; Staiano et al., 2024). This same reasoning may also help explain why the stronger inhibitory control deficits reported elsewhere (Z. Guo et al., 2018; Habay et al., 2026; Kato et al., 2009) were not observed here. Although suppositional, if inhibitory processes are particularly sensitive to motivational changes (Csathó et al., 2026), limited motivational effects of the Math-Memory task could partially account for weaker CF-related inhibitory deficits.

At the same time, it is likely that the Math-Memory intervention did not completely isolate CF effects from other influences. For example, subjective sleepiness or boredom were not directly assessed, somewhat limiting our ability to distinguish active, effort-related CF from more passive forms. In addition, CF is influenced by numerous factors including sleep, caffeine intake, time of day, recent physical activity, and even recent meal consumption (Ackerman, 2011). Where possible, these were addressed via baseline comparisons and between-session contrasts. Baseline differences were generally minimal, and when present (e.g., Experiment 1), they were incorporated into the analysis and interpretation of results. In hindsight, stricter controls of some lifestyle factors may have reduced some variability in our data; however, overly restrictive controls (e.g., fixed sleep requirements or caffeine abstinence) can be difficult to

enforce and may reduce ecological validity by placing participants in conditions that differ from their typical daily routines.

The remote delivery of Experiments 2 and 3 introduces additional limitations. Although participants were instructed via the LabVIEW® application to complete tasks as directed, minimize distractions, and avoid external aids, no technical enforcement measures (e.g., browser locking or visual supervision) were implemented due to platform and privacy constraints. Instead, adherence was carefully evaluated post hoc using strict a priori exclusion criteria. To accommodate greater variability in compliance inherent to remote testing, these studies also used large samples and mixed-effect model analyses with participant-level random intercepts, which are more robust to noisy and unbalanced data than traditional ANOVA approaches (Yu et al., 2022). Nevertheless, some uncontrolled variability related to compliance and testing environment likely remained and should be considered when interpreting these findings.

Additional limitations relate to parameters of the Math-Memory intervention. In Experiments 1 and 2, Math-Memory task difficulty was held constant within and between participants. Given the relatively small RT increases observed (+7.3 and +8.9 ms, respectively), later experiments switched to an adaptive difficulty approach based on evidence that individualized task demands may enhance CF induction (O’Keeffe et al., 2020; Staiano et al., 2024). However, it remains unclear whether this adjustment was beneficial. Increases in subjective fatigue in response to the Math-Memory intervention remained comparable across experiments, suggesting similar levels of CF were induced (e.g., *Appendix A.2; Chapter 4, Table 4.2*). In regards to psychomotor performance, although absolute simple RT increases were larger when the adaptive CF task was implemented in Experiment 3 (+21.2 ms pre- to post-Math-Memory), additional evaluation is complicated by TMS-related effects on RT in Experiment 4

and the small sample size of Experiment 5. Further work is therefore needed to determine whether adaptive, individualized task difficulty meaningfully improves CF induction and/or alters psychomotor performance outcomes using the Math-Memory intervention.

A related issue concerns the initial difficulty calibration of the adaptive Math-Memory task. The intervention was designed to maintain performance at ~85% accuracy, by dynamically adjusting stimulus presentation durations. However, the initial difficulty level may have been too high, resulting in early performance often well below target levels. Consequently, stimulus durations tended to increase over the course of the task, allowing participants to “catch up” to the ~85% threshold (i.e., performance progressively improved over the task; *Appendix D, Fig. D.2c-f, and Fig. D.4c-f*). While stable cognitive performance under increasing CF is not uncommon (e.g., Behrens et al., 2023; Sandry et al., 2014), this pattern made it challenging to clearly track the effects of CF on adaptive cognitive task performance. In hindsight, incorporating an upper limit on stimulus durations have been beneficial, particularly in remote experiments, to reduce the possibility of excessive task disengagement. However, display durations rarely reached extreme values (mean range: 1.24-1.40 s; see *Appendix D, Table D.1, Figs. D.5 – D.7*), and extensive data-screening procedures likely removed most cases of poor engagement.

Several additional limitations warrant consideration. In Experiment 4, we did not anticipate that TMS pulses (i.e., the sound and sensation) might act as a cue influencing RT. As a result, we did not include no-stimulation control trials, limiting our ability to isolate CF-related RT effects independent of TMS influences. Also, small increases in subjective fatigue and RT were sometimes observed following the documentary control condition, despite it being intended as a low-demand baseline. Although this isn’t an uncommon observation (e.g., Daneshgar-Pironneau et al., 2025; Jacquet et al., 2024), it may reflect a “passive” fatigue state: boredom,

reduced arousal, or mild sleepiness due to extended passive viewing. Interestingly, this may have been an inadvertent benefit, as the control condition may have helped account for passive fatigue-related influences. This in turn may have allowed for clearer isolation of “active” CF-specific effects following the CF interventions.

Finally, it is important to note that caution should be taken when extrapolating these findings to real-world contexts. Throughout this thesis, RT was considered from an information processing perspective where performance is conceptualized to arise from a series of partially distinct processing stages (Donders, 1969; Spijkers & Walter, 1985; Taylor, 1976). This framework was advantageous for systematically examining potential sources of CF-related slowing and for generating targeted experimental questions. However, it also represents a simplified view of motor behaviour. In reality, boundaries between processing stages are unlikely to be as distinct as they are often portrayed; rather, perceptual, cognitive, and motor processes likely interact continuously, with substantial overlap in time and in neural substrates (Dmochowski & Norcia, 2015; Haazebroek et al., 2017). Indeed, alternative theoretical perspectives to the information processing model argue that movement may be better understood as a self-organizing phenomenon emerging from interactions between the individual, the task, and the environment (Floegel et al., 2023; Mangalam, 2025; Turvey & Fonseca, 2009). From this viewpoint, CF may not actually influence a single isolated stage of processing but instead alter the dynamics of the perception-action system more broadly. Future work may benefit from exploring the effects of CF on psychomotor performance from this integrated perspective.

Similar considerations apply to the ecological validity of the present findings. While RT paradigms provide a controlled way of isolating specific psychomotor demands, they represent only a “snapshot” of motor performance. In real-world scenarios, motor behaviour is typically

more dynamic, involving both reactionary and internally triggered movements that extend well beyond the requirements of a simple button press or wrist extension, in much more complex environments. Likewise, real-world CF likely also differs from controlled induction. For instance, studying, working, or writing a thesis may induce CF over substantially longer durations of continuous work, and may accumulate over successive bouts or workdays. CF is also likely shaped by a myriad of factors in natural scenarios, such as stress, nutrition, sleep, personality, incentives, and environmental demands. As a result, the effects observed here cannot fully reflect the magnitude or complexity of CF encountered outside the laboratory.

7.5 Concluding Remarks

Psychomotor performance, including RT, is frequently impaired in CF. This thesis aimed to better characterize the psychomotor impacts of CF by assessing its influence on the individual processes contributing to RT performance, and by exploring tVNS as a potential countermeasure. Overall, findings suggest that visual perceptual processing speed, response inhibition, and motor preparation were not significantly impaired by CF, with some evidence of compensatory motor preparation-related neural activity. Motivational and attentional factors also appeared unlikely to account for CF-related changes in RT performance, although notably attention was not directly assessed. While some evidence of a response selection deficit was found, this could not fully explain CF-related increases in simple RT, which places minimal demand on response selection. Taken together, these results instead point toward a response initiation-related mechanism, motivating further research into this possibility. Finally, preliminary evidence suggests that tVNS may attenuate CF-related changes in psychomotor RT, subjective fatigue, and autonomic function, supporting more in-depth investigation of its therapeutic potential and underlying mechanism.

Given the prevalence of cognitive fatigue, its associated productivity costs, and the significant health and safety risks it poses, improving our understanding of how CF influences psychomotor performance and how these effects can be mitigated is an important objective. The present findings contribute to this objective by refining our understanding of how CF influences different psychomotor processing stages and by identifying tVNS as a promising countermeasure worthy of further investigation.

7.6 References

- Ackerman, P. L. (2011). 100 years without resting. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 11–43). American Psychological Association. <https://doi.org/10.1037/12343-001>
- Adachi, M., Nobukawa, S., & Inagaki, K. (2024). Assessment of driver fatigue-related brain responses and causal factors during driving under different traffic conditions. *Frontiers in Applied Mathematics and Statistics*, 10, 1426253. <https://doi.org/10.3389/fams.2024.1426253>
- Alyahyay, M., Ammer, J. J., Kalweit, G., Zhu, H., Adzemovic, A., Kalweit, M., Karvat, G., Schneider, A., Tong, Y., Döbrössy, M. D., Jäckel, Z., Akmesé, C., Vlachos, A., Boedecker, J., & Diester, I. (2026). Mechanisms of premotor-motor cortex interactions during movement initiation. *Cell Reports*, 45(6), 117542. <https://doi.org/10.1016/j.celrep.2026.117542>
- André, N., Audiffren, M., & Baumeister, R. F. (2019). An Integrative Model of Effortful Control. *Frontiers in Systems Neuroscience*, 13, 79. <https://doi.org/10.3389/fnsys.2019.00079>
- Apreutesei, D., & Cressman, E. K. (2024). The effects of mental fatigue on explicit and implicit contributions to visuomotor adaptation. *PLOS ONE*, 19(8), e0307739. <https://doi.org/10.1371/journal.pone.0307739>
- Arsintescu, L., Kato, K. H., Cravalho, P. F., Feick, N. H., Stone, L. S., & Flynn-Evans, E. E. (2019). Validation of a touchscreen psychomotor vigilance task. *Accident Analysis & Prevention*, 126, 173–176. <https://doi.org/10.1016/j.aap.2017.11.041>
- Bach, M. M., Brandstetter, K., Stins, J., & Beek, P. J. (2026). A Comparison of Experimental Methods to Induce Mental Fatigue. *Perceptual and Motor Skills*, 0(0). <https://doi.org/10.1177/00315125261420694>
- Badran, B. W., Dowdle, L. T., Mithoefer, O. J., LaBate, N. T., Coatsworth, J., Brown, J. C., DeVries, W. H., Austelle, C. W., McTeague, L. M., & George, M. S. (2022). Neurophysiologic Effects of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS) via Electrical Stimulation of the Tragus: A Concurrent taVNS/fMRI Study and Review. *Focus*, 20, 80–89. <https://doi.org/10.1176/appi.focus.20110>
- Balasubramanian, K., Papadourakis, V., Liang, W., Takahashi, K., Best, M. D., Suminski, A. J., & Hatsopoulos, N. G. (2020). Propagating Motor Cortical Dynamics Facilitate Movement Initiation. *Neuron*, 106(3), 526–536.e4. <https://doi.org/10.1016/j.neuron.2020.02.011>
- Barker, L. M., & Nussbaum, M. A. (2011). Fatigue, performance and the work environment: A survey of registered nurses. *Journal of Advanced Nursing*, 67(6), 1370–1382. <https://doi.org/10.1111/j.1365-2648.2010.05597.x>

- Barrios, L., Amon, R., Oldrati, P., Hilty, M., Holz, C., & Lutterotti, A. (2022). Cognitive fatigability assessment test (cFAST): Development of a new instrument to assess cognitive fatigability and pilot study on its association to perceived fatigue in multiple sclerosis. *Digital Health*, 8, 20552076221117740. <https://doi.org/10.1177/20552076221117740>
- Behrens, M., Gube, M., Chaabene, H., Prieske, O., Zenon, A., Broscheid, K.-C., Schega, L., Husmann, F., & Weippert, M. (2023). Fatigue and Human Performance: An Updated Framework. *Sports Medicine*, 53(1), 7–31. <https://doi.org/10.1007/s40279-022-01748-2>
- Benarroch, E. E. (2018). Locus coeruleus. *Cell and Tissue Research*, 373(1), 221–232. <https://doi.org/10.1007/s00441-017-2649-1>
- Best, M. D., Suminski, A. J., Takahashi, K., Brown, K. A., & Hatsopoulos, N. G. (2017). Spatio-Temporal Patterning in Primary Motor Cortex at Movement Onset. *Cerebral Cortex*, 27(2), bhv327. <https://doi.org/10.1093/cercor/bhv327>
- Bestmann, S., & Duque, J. (2016). Transcranial Magnetic Stimulation: Decomposing the Processes Underlying Action Preparation. *The Neuroscientist*, 22(4), 392–405. <https://doi.org/10.1177/1073858415592594>
- Biondi, F. N., Cacanindin, A., Douglas, C., & Cort, J. (2021). Overloaded and at Work: Investigating the Effect of Cognitive Workload on Assembly Task Performance. *Human Factors*, 63(5), 813–820. <https://doi.org/10.1177/0018720820929928>
- Blain, B., Hollard, G., & Pessiglione, M. (2016). Neural mechanisms underlying the impact of daylong cognitive work on economic decisions. *Proceedings of the National Academy of Sciences*, 113(25), 6967–6972. <https://doi.org/10.1073/pnas.1520527113>
- Boksem, M. A. S., Meijman, T. F., & Lorist, M. M. (2005). Effects of mental fatigue on attention: An ERP study. *Cognitive Brain Research*, 25(1), 107–116. <https://doi.org/10.1016/j.cogbrainres.2005.04.011>
- Boksem, M. A. S., & Tops, M. (2008). Mental fatigue: Costs and benefits. *Brain Research Reviews*, 59(1), 125–139. <https://doi.org/10.1016/j.brainresrev.2008.07.001>
- Boukrina, O., DeLuca, J., & Wylie, G. R. (2026). The critical role of the basal ganglia in post-stroke fatigue: A pilot study. *NeuroImage: Reports*, 6(1), 100313. <https://doi.org/10.1016/j.ynirp.2025.100313>
- Brazaitis, M., & Satas, A. (2023). Regular short-duration breaks do not prevent mental fatigue and decline in cognitive efficiency in healthy young men during an office-like simulated mental working day: An EEG study. *International Journal of Psychophysiology*, 188, 33–46. <https://doi.org/10.1016/j.ijpsycho.2023.03.007>
- Brossoit, R. M., Crain, T. L., Stevens, S. C., Wong, J. R., & Guasta, L. (2023). Alert at Work? Perceptions of Alertness Testing and Recommendations for Practitioners. *Occupational Health Science*, 7(2), 379–396. <https://doi.org/10.1007/s41542-022-00139-3>

- Bu, Y., Liang, A., Hoffman, B. U., Schiehser, D. M., Case, O., Simmons, A., Klaming, R., Gottfried-Blackmore, A., Mittal, R. K., Puleo, C., Lim, H., & Lerman, I. (2026). A Review of Vagus Nerve Stimulation for Disease: Comprehensive Theory and Evidence for Mechanisms of Action. *Comprehensive Physiology*, 16(2), e70109. <https://doi.org/10.1002/cph4.70109>
- Bunge, S. A., Hazeltine, E., Scanlon, M. D., Rosen, A. C., & Gabrieli, J. D. E. (2002). Dissociable Contributions of Prefrontal and Parietal Cortices to Response Selection. *NeuroImage*, 17(3), 1562–1571. <https://doi.org/10.1006/nimg.2002.1252>
- Byrne, A. J., Oliver, M., Bodger, O., Barnett, W. A., Williams, D., Jones, H., & Murphy, A. (2010). Novel method of measuring the mental workload of anaesthetists during clinical practice. *British Journal of Anaesthesia*, 105(6), 767–771. <https://doi.org/10.1093/bja/aeq240>
- Cameron, B. D., Cheng, D. T., Chua, R., van Donkelaar, P., & Binsted, G. (2013). Explicit knowledge and real-time action control: Anticipating a change does not make us respond more quickly. *Experimental Brain Research*, 229(3), 359–372. <https://doi.org/10.1007/s00221-013-3401-z>
- Carlsen, A. N., & Maslovat, D. (2019). Startle and the StartReact Effect: Physiological Mechanisms. *Journal of Clinical Neurophysiology*, 36(6), 452–459. <https://doi.org/10.1097/WNP.0000000000000582>
- Carlsen, A. N., & Maslovat, D. (2026). What Is the StartReact Effect? *Acta Physiologica*, 242(6), e70235. <https://doi.org/10.1111/apha.70235>
- Carlsen, A. N., Maslovat, D., & Franks, I. M. (2012). Preparation for voluntary movement in healthy and clinical populations: Evidence from startle. *Clinical Neurophysiology*, 123(1), 21–33. <https://doi.org/10.1016/j.clinph.2011.04.028>
- Chan, M. Y., Cohen, H., & Spiegel, B. M. R. (2009). Fewer Polyps Detected by Colonoscopy as the Day Progresses at a Veteran's Administration Teaching Hospital. *Clinical Gastroenterology and Hepatology*, 7(11), 1217–1223. <https://doi.org/10.1016/j.cgh.2009.07.013>
- Churchland, M. M., Cunningham, J. P., Kaufman, M. T., Foster, J. D., Nuyujukian, P., Ryu, S. I., & Shenoy, K. V. (2012). Neural population dynamics during reaching. *Nature*, 487(7405), 51–56. <https://doi.org/10.1038/nature11129>
- Csathó, Á., Van der Linden, D., Jakóczy, G., Gögös, R., & Matuz, A. (2026). Response conflicts in visually guided movements under mental fatigue. *Psychological Research*, 90(3), 79. <https://doi.org/10.1007/s00426-026-02293-7>
- Csathó, Á., Van der Linden, D., & Matuz, A. (2024). Change in heart rate variability with increasing time-on-task as a marker for mental fatigue: A systematic review. *Biological Psychology*, 185, 108727. <https://doi.org/10.1016/j.biopsycho.2023.108727>

- Czyż, S. H. (2021). Variability of Practice, Information Processing, and Decision Making—How Much Do We Know? *Frontiers in Psychology*, 12, 639131. <https://doi.org/10.3389/fpsyg.2021.639131>
- Daneshgar-Pironneau, S., Audiffren, M., Benraïss, A., Métais, A., & André, N. (2025). Mental fatigue impairs endurance performance in a time-to-exhaustion handgrip task: Psychophysiological markers of effort engagement dynamics. *Frontiers in Psychology*, 16, 1611135. <https://doi.org/10.3389/fpsyg.2025.1611135>
- David Milner, A. (2015). Visual Streams: Dorsal and Ventral. In J. D. Wright (Ed.), *International Encyclopedia of the Social & Behavioral Sciences* (2nd ed., pp. 201–206). Elsevier. <https://doi.org/10.1016/B978-0-08-097086-8.55015-6>
- Díaz-García, J., Bray, S. R., García-Calvo, T., Bovolon, L., Berchicci, M., & Ring, C. (2026). Highlighting the Role of Mental Fatigue as a Health Risk Factor: A Narrative Review. *Sports*, 14(3), 106. <https://doi.org/10.3390/sports14030106>
- Dmochowski, J. P., & Norcia, A. M. (2015). Cortical Components of Reaction-Time during Perceptual Decisions in Humans. *PLOS ONE*, 10(11), e0143339. <https://doi.org/10.1371/journal.pone.0143339>
- Donders, F. C. (1969). On the speed of mental processes. *Acta Psychologica*, 30, 412–431. [https://doi.org/10.1016/0001-6918\(69\)90065-1](https://doi.org/10.1016/0001-6918(69)90065-1)
- Duque, J., Greenhouse, I., Labruna, L., & Ivry, R. B. (2017). Physiological Markers of Motor Inhibition during Human Behavior. *Trends in Neurosciences*, 40(4), 219–236. <https://doi.org/10.1016/j.tins.2017.02.006>
- Eilfort, A. M., & Filli, L. (2025). Reticulospinal modulation of muscle activation and electromechanical coupling: Evidence from the StartReact paradigm. *Frontiers in Human Neuroscience*, 19, 1610211. <https://doi.org/10.3389/fnhum.2025.1610211>
- Evans, M. S., Harborne, D., & Smith, A. P. (2019). Developing an Objective Indicator of Fatigue: An Alternative Mobile Version of the Psychomotor Vigilance Task (m-PVT). In L. Longo & M. C. Leva (Eds.), *Human Mental Workload: Models and Applications* (pp. 49–71). Springer International Publishing. https://doi.org/10.1007/978-3-030-14273-5_4
- Faber, L. G., Maurits, N. M., & Lorist, M. M. (2012). Mental Fatigue Affects Visual Selective Attention. *PLOS ONE*, 7(10), e48073. <https://doi.org/10.1371/journal.pone.0048073>
- Falkenstein, M., Hoormann, J., & Hohnsbein, J. (2002). Inhibition-related ERP components: Variation with modality, age, and time-on-task. *Journal of Psychophysiology*, 16(3), 167–175. <https://doi.org/10.1027//0269-8803.16.3.167>
- Fazackerley, L. A., Hickey, J., Johnston, R. D., Tofari, P. J., Timmins, R. G., Roelands, B., Halson, S. L., Tassignon, B., Verschueren, J., & Russell, S. (2025). Practitioner Perspectives on the Association Between Mental Fatigue and Injury Risk in High-

- Performance Sport: A Mixed Methods Study. *European Journal of Sport Science*, 25(8), e70028. <https://doi.org/10.1002/ejsc.70028>
- Ferguson, B. A., Lauriski, D. R., Huecker, M., Wichmann, M., Shreffler, J., & Shoff, H. (2020). Testing Alertness of Emergency Physicians: A Novel Quantitative Measure of Alertness and Implications for Worker and Patient Care. *The Journal of Emergency Medicine*, 58(3), 514–519. <https://doi.org/10.1016/j.jemermed.2019.10.032>
- Finke, C., Schlichting, J., Papazoglou, S., Scheel, M., Freing, A., Soemmer, C., Pech, L., Pajkert, A., Pfüller, C., Wuerfel, J., Ploner, C., Paul, F., & Brandt, A. (2015). Altered basal ganglia functional connectivity in multiple sclerosis patients with fatigue. *Multiple Sclerosis Journal*, 21(7), 925–934. <https://doi.org/10.1177/1352458514555784>
- Floegel, M., Kasper, J., Perrier, P., & Kell, C. A. (2023). How the conception of control influences our understanding of actions. *Nature Reviews Neuroscience*, 24(5), 313–329. <https://doi.org/10.1038/s41583-023-00691-z>
- Fortes, L. S., Gantois, P., de Lima-Júnior, D., Barbosa, B. T., Ferreira, M. E. C., Nakamura, F. Y., Albuquerque, M. R., & Fonseca, F. S. (2023). Playing videogames or using social media applications on smartphones causes mental fatigue and impairs decision-making performance in amateur boxers. *Applied Neuropsychology: Adult*, 30(2), 227–238. <https://doi.org/10.1080/23279095.2021.1927036>
- Fortes, L. S., Lima-Junior, D., Barbosa, B. T., Faro, H. K. C., Ferreira, M. E. C., & Almeida, S. S. (2025). Effect of mental fatigue on decision-making skill and visual search behaviour in basketball players: An experimental and randomised study. *International Journal of Sport and Exercise Psychology*, 23(5). <https://doi.org/10.1080/1612197X.2022.2058055>
- Guo, M., Li, S., Wang, L., Chai, M., Chen, F., & Wei, Y. (2016). Research on the Relationship between Reaction Ability and Mental State for Online Assessment of Driving Fatigue. *International Journal of Environmental Research and Public Health*, 13(12), 1174. <https://doi.org/10.3390/ijerph13121174>
- Guo, Z., Chen, R., Liu, X., Zhao, G., Zheng, Y., Gong, M., & Zhang, J. (2018). The impairing effects of mental fatigue on response inhibition: An ERP study. *PLOS ONE*, 13(6), e0198206. <https://doi.org/10.1371/journal.pone.0198206>
- Haazebroek, P., Raffone, A., & Hommel, B. (2017). HiTEC: A connectionist model of the interaction between perception and action planning. *Psychological Research*, 81(6), 1085–1109. <https://doi.org/10.1007/s00426-016-0803-0>
- Habay, J., Arenales Arauz, Y. L., Proost, M., Schamphoeleer, E., Lathouwers, E., De Pauw, K., Pattyn, N., Van Cutsem, J., & Roelands, B. (2026). Mental Fatigue Negatively Impacts Cognitive and Physical Performance Outcomes: A Large-Scale Randomized Crossover Trial. *Medicine & Science in Sports & Exercise*, 58(2), 225. <https://doi.org/10.1249/MSS.00000000000003852>

- Habay, J., Van Cutsem, J., Verschueren, J., De Bock, S., Proost, M., De Wachter, J., Tassignon, B., Meeusen, R., & Roelands, B. (2021). Mental Fatigue and Sport-Specific Psychomotor Performance: A Systematic Review. *Sports Medicine*, 51(7), 1527–1548. <https://doi.org/10.1007/s40279-021-01429-6>
- Haith, A. M., Pakpoor, J., & Krakauer, J. W. (2016). Independence of Movement Preparation and Movement Initiation. *Journal of Neuroscience*, 36(10), 3007–3015. <https://doi.org/10.1523/JNEUROSCI.3245-15.2016>
- Hallett, M. (2007). Transcranial Magnetic Stimulation: A Primer. *Neuron*, 55(2), 187–199. <https://doi.org/10.1016/j.neuron.2007.06.026>
- Hauber, W. (1998). Involvement of basal ganglia transmitter systems in movement initiation. *Progress in Neurobiology*, 56(5), 507–540. [https://doi.org/10.1016/S0301-0082\(98\)00041-0](https://doi.org/10.1016/S0301-0082(98)00041-0)
- Heng, P. P., Yusoff, H. M., & Hod, R. (2024). Individual evaluation of fatigue at work to enhance the safety performance in the construction industry: A systematic review. *PLOS ONE*, 19(2), e0287892. <https://doi.org/10.1371/journal.pone.0287892>
- Herlambang, M. B., Taatgen, N. A., & Cnossen, F. (2019). The Role of Motivation as a Factor in Mental Fatigue. *Human Factors*, 61(7), 1171–1185. <https://doi.org/10.1177/0018720819828569>
- Hick, W. E. (1952). On the Rate of Gain of Information. *Quarterly Journal of Experimental Psychology*, 4(1), 11–26. <https://doi.org/10.1080/17470215208416600>
- Holgado, D., Jolidon, L., Borragán, G., Sanabria, D., & Place, N. (2023). Individualized Mental Fatigue Does Not Impact Neuromuscular Function and Exercise Performance. *Medicine and Science in Sports and Exercise*, 55(10), 1823–1834. <https://doi.org/10.1249/MSS.00000000000003221>
- Huettel, S. A., & McCarthy, G. (2004). What is odd in the oddball task?: Prefrontal cortex is activated by dynamic changes in response strategy. *Neuropsychologia*, 42(3), 379–386. <https://doi.org/10.1016/j.neuropsychologia.2003.07.009>
- Hung, Y., Gaillard, S. L., Yarmak, P., & Arsalidou, M. (2018). Dissociations of cognitive inhibition, response inhibition, and emotional interference: Voxelwise ALE meta-analyses of fMRI studies. *Human Brain Mapping*, 39(10), 4065–4082. <https://doi.org/10.1002/hbm.24232>
- Hussain, S. J., Vollmer, M. K., Iturrate, I., & Quentin, R. (2022). Voluntary Motor Command Release Coincides with Restricted Sensorimotor Beta Rhythm Phases. *Journal of Neuroscience*, 42(29), 5771–5781. <https://doi.org/10.1523/JNEUROSCI.1495-21.2022>
- Ishii, A., Tanaka, M., & Watanabe, Y. (2014). Neural mechanisms of mental fatigue. *Reviews in the Neurosciences*, 25(4), 469–479. <https://doi.org/10.1515/revneuro-2014-0028>

- Jacquet, T., Poulin-Charronnat, B., Bard, P., & Lepers, R. (2024). Effect of mental fatigue on hand force production capacities. *PLOS ONE*, 19(4), e0298958. <https://doi.org/10.1371/journal.pone.0298958>
- Jaydarifard, S., Tahmasebi Boroujeni, S., & Lavender, A. P. (2019). Mental fatigue impairs simple reaction time in non-athletes more than athletes. *Fatigue: Biomedicine, Health & Behavior*, 7(3), 117–126. <https://doi.org/10.1080/21641846.2019.1632614>
- Jia, H., Lin, C. J., & Wang, E. M. (2022). Effects of mental fatigue on risk preference and feedback processing in risk decision-making. *Scientific Reports*, 12(1), 10695. <https://doi.org/10.1038/s41598-022-14682-0>
- Jong, M. de, Bonvanie, A. M., Jolij, J., & Lorist, M. M. (2020). Dynamics in typewriting performance reflect mental fatigue during real-life office work. *PLOS ONE*, 15(10), e0239984. <https://doi.org/10.1371/journal.pone.0239984>
- Kato, Y., Endo, H., & Kizuka, T. (2009). Mental fatigue and impaired response processes: Event-related brain potentials in a Go/NoGo task. *International Journal of Psychophysiology*, 72(2), 204–211. <https://doi.org/10.1016/j.ijpsycho.2008.12.008>
- Kennefick, M., Maslovat, D., & Carlsen, A. N. (2014). The Time Course of Corticospinal Excitability during a Simple Reaction Time Task. *PLoS ONE*, 9(11), e113563. <https://doi.org/10.1371/journal.pone.0113563>
- Khitrov, M. Y., Laxminarayan, S., Thorsley, D., Ramakrishnan, S., Rajaraman, S., Wesensten, N. J., & Reifman, J. (2014). PC-PVT: A platform for psychomotor vigilance task testing, analysis, and prediction. *Behavior Research Methods*, 46(1), 140–147. <https://doi.org/10.3758/s13428-013-0339-9>
- Khojasteh Moghani, M., Zeidabadi, R., Shahabi Kaseb, M. R., & Bahreini Boroujeni, I. (2021). Mental Fatigue Reduces the Benefits of Self-Controlled Feedback on Learning a Force Production Task. *Perceptual & Motor Skills*, 128(5), 2398–2414. <https://doi.org/10.1177/00315125211037306>
- Kim, A. Y., Marduy, A., de Melo, P. S., Gianlorenco, A. C., Kim, C. K., Choi, H., Song, J.-J., & Fregni, F. (2022). Safety of transcutaneous auricular vagus nerve stimulation (taVNS): A systematic review and meta-analysis. *Scientific Reports*, 12(1), 22055. <https://doi.org/10.1038/s41598-022-25864-1>
- Kong, W., Lin, W., Babiloni, F., Hu, S., & Borghini, G. (2015). Investigating Driver Fatigue versus Alertness Using the Granger Causality Network. *Sensors*, 15(8), 19181–19198. <https://doi.org/10.3390/s150819181>
- Kowalski, K. L., Tierney, B. C., & Christie, A. D. (2022). Mental fatigue does not substantially alter neuromuscular function in young, healthy males and females. *Physiology & Behavior*, 253, 113855. <https://doi.org/10.1016/j.physbeh.2022.113855>

- Langley, C., Masuda, N., Godwin, S., De Marco, G., Smith, A. D., Jones, R., Bruce, J., & Thai, N. J. (2023). Dysfunction of basal ganglia functional connectivity associated with subjective and cognitive fatigue in multiple sclerosis. *Frontiers in Neuroscience*, 17. <https://doi.org/10.3389/fnins.2023.1194859>
- Langner, R., Steinborn, M. B., Chatterjee, A., Sturm, W., & Willmes, K. (2010). Mental fatigue and temporal preparation in simple reaction-time performance. *Acta Psychologica*, 133(1), 64–72. <https://doi.org/10.1016/j.actpsy.2009.10.001>
- Le Mansec, Y., Dorel, S., Nordez, A., & Jubeau, M. (2019). Is reaction time altered by mental or physical exertion? *European Journal of Applied Physiology*, 119(6), 1323–1335. <https://doi.org/10.1007/s00421-019-04124-7>
- Li, F., Chen, C.-H., Lee, C.-H., & Feng, S. (2022). Artificial intelligence-enabled non-intrusive vigilance assessment approach to reducing traffic controller's human errors. *Knowledge-Based Systems*, 239, 108047. <https://doi.org/10.1016/j.knosys.2021.108047>
- Li, J., Li, H., Wang, H., Umer, W., Fu, H., & Xing, X. (2019). Evaluating the impact of mental fatigue on construction equipment operators' ability to detect hazards using wearable eye-tracking technology. *Automation in Construction*, 105, 102835. <https://doi.org/10.1016/j.autcon.2019.102835>
- Li, T., Zhang, D., Wang, Y., Cheng, S., Wang, J., Zhang, Y., Xie, P., & Chen, X. (2024). Research on mental fatigue during long-term motor imagery: A pilot study. *Scientific Reports*, 14(1), 18454. <https://doi.org/10.1038/s41598-024-69013-2>
- Liddle, P. F., Kiehl, K. A., & Smith, A. M. (2001). Event-related fMRI study of response inhibition. *Human Brain Mapping*, 12(2), 100–109. [https://doi.org/10.1002/1097-0193\(200102\)12:2%3C100::AID-HBM1007%3E3.0.CO;2-6](https://doi.org/10.1002/1097-0193(200102)12:2%3C100::AID-HBM1007%3E3.0.CO;2-6)
- Lorist, M. M., & Faber, L. G. (2011). Consideration of the influence of mental fatigue on controlled and automatic cognitive processes and related neuromodulatory effects. In P. L. Ackerman (Ed.), *Cognitive fatigue: Multidisciplinary perspectives on current research and future applications*. (pp. 105–126). American Psychological Association.
- Lorist, M. M., Klein, M., Nieuwenhuis, S., de Jong, R., Mulder, G., & Meijman, T. F. (2000). Mental fatigue and task control: Planning and preparation. *Psychophysiology*, 37(5), 614–625. <https://doi.org/10.1111/1469-8986.3750614>
- Magnuson, J. R., Doesburg, S. M., & McNeil, C. J. (2021). Development and recovery time of mental fatigue and its impact on motor function. *Biological Psychology*, 161, 108076. <https://doi.org/10.1016/j.biopsycho.2021.108076>
- Main, L. C., McLoughlin, L. T., Flanagan, S. D., Canino, M. C., & Banks, S. (2023). Monitoring cognitive function in the fatigued warfighter: A rapid review of cognitive biomarkers. *Journal of Science and Medicine in Sport, Proceedings of the Macquarie University [MQ] Military Biomarker Symposium 2022*, 26, S54–S63. <https://doi.org/10.1016/j.jsams.2023.04.009>

- Mangalam, M. (2025). The illusion of internal models in biological movement. *European Journal of Applied Physiology*, 125(11), 3083–3114. <https://doi.org/10.1007/s00421-025-05963-3>
- Marek, S., & Dosenbach, N. U. F. (2018). The frontoparietal network: Function, electrophysiology, and importance of individual precision mapping. *Dialogues in Clinical Neuroscience*, 20(2), 133–140. <https://doi.org/10.31887/DCNS.2018.20.2/smarek>
- Martin, K., Meeusen, R., Thompson, K. G., Keegan, R., & Rattray, B. (2018). Mental Fatigue Impairs Endurance Performance: A Physiological Explanation. *Sports Medicine*, 48(9), 2041–2051. <https://doi.org/10.1007/s40279-018-0946-9>
- Matsui, T., Takahashi, S., Ochi, G., Yoshitake, S., Funabashi, D., Matsuoka, H., Kagesawa, J., Dobashi, S., Yoshimoto, H., Sakairi, Y., & Takagi, H. (2024). Cognitive decline with pupil constriction independent of subjective fatigue during prolonged esports across player expertise levels. *Computers in Human Behavior*, 156, 108219. <https://doi.org/10.1016/j.chb.2024.108219>
- Matsuoka, M., Yamaguchi, T., & Fujiwara, T. (2025). Transcutaneous auricular vagus nerve stimulation in healthy individuals, stroke, and Parkinson's disease: A narrative review of safety, parameters, and efficacy. *Frontiers in Physiology*, 16, 1693907. <https://doi.org/10.3389/fphys.2025.1693907>
- Meng, F., Li, S., Cao, L., Li, M., Peng, Q., Wang, C., & Zhang, W. (2015). Driving Fatigue in Professional Drivers: A Survey of Truck and Taxi Drivers. *Traffic Injury Prevention*, 16(5), 474–483. <https://doi.org/10.1080/15389588.2014.973945>
- Migliaccio, G. M., Di Filippo, G., Russo, L., Orgiana, T., Ardigò, L. P., Casal, M. Z., Peyré-Tartaruga, L. A., & Padulo, J. (2022). Effects of Mental Fatigue on Reaction Time in Sportsmen. *International Journal of Environmental Research and Public Health*, 19(21), 14360. <https://doi.org/10.3390/ijerph192114360>
- Miller, A. H., Jones, J. F., Drake, D. F., Tian, H., Unger, E. R., & Pagnoni, G. (2014). Decreased Basal Ganglia Activation in Subjects with Chronic Fatigue Syndrome: Association with Symptoms of Fatigue. *PLOS ONE*, 9(5), e98156. <https://doi.org/10.1371/journal.pone.0098156>
- Minusa, S., Mizuno, K., Ojio, D., Tanaka, T., Kuriyama, H., Yamano, E., Kuratsune, H., & Watanabe, Y. (2021). Increase in rear-end collision risk by acute stress-induced fatigue in on-road truck driving. *PLOS ONE*, 16(10), e0258892. <https://doi.org/10.1371/journal.pone.0258892>
- Mizuno, K., Ojio, D., Tanaka, T., Minusa, S., Kuriyama, H., Yamano, E., Kuratsune, H., & Watanabe, Y. (2020). Relationship between truck driver fatigue and rear-end collision risk. *PLOS ONE*, 15(9), e0238738. <https://doi.org/10.1371/journal.pone.0238738>

- Möckel, T., Beste, C., & Wascher, E. (2015). The Effects of Time on Task in Response Selection—An ERP Study of Mental Fatigue. *Scientific Reports*, 5(1), 10113. <https://doi.org/10.1038/srep10113>
- Montare, A. (2016). The Simplest Chronoscope V: A Theory of Dual Primary and Secondary Reaction Time Systems. *Perceptual & Motor Skills*, 123(3), 654–686. <https://doi.org/10.1177/0031512516664893>
- Monti, D. A., Wintering, N., Vedaiei, F., Steinmetz, A., Mohamed, F. B., & Newberg, A. B. (2025). Changes in brain functional connectivity associated with transcutaneous auricular vagus nerve stimulation in healthy controls. *Frontiers in Human Neuroscience*, 19, 1531123. <https://doi.org/10.3389/fnhum.2025.1531123>
- Nathaniel-James, D. A., & Frith, C. D. (2002). The Role of the Dorsolateral Prefrontal Cortex: Evidence from the Effects of Contextual Constraint in a Sentence Completion Task. *NeuroImage*, 16(4), 1094–1102. <https://doi.org/10.1006/nimg.2002.1167>
- Neige, C., Yadav, G., & Derosiere, G. (2023). The Oscillatory Nature of Movement Initiation. *The Journal of Neuroscience*, 43(6), 882–884. <https://doi.org/10.1523/JNEUROSCI.1687-22.2022>
- Neuhaus, A. H., Urbanek, C., Opgen-Rhein, C., Hahn, E., Ta, T. M. T., Koehler, S., Gross, M., & Dettling, M. (2010). Event-related potentials associated with Attention Network Test. *International Journal of Psychophysiology*, 76(2), 72–79. <https://doi.org/10.1016/j.ijpsycho.2010.02.005>
- Niu, S., Guo, J., Hanson, N. J., Wang, K., Chai, J., & Guo, F. (2024). The effects of mental fatigue on fine motor performance in humans and its neural network connectivity mechanism: A dart throwing study. *Cerebral Cortex*, 34(3), bhae085. <https://doi.org/10.1093/cercor/bhae085>
- O’Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics*, 63(1), 1–12. <https://doi.org/10.1080/00140139.2019.1687940>
- Persson, J., Welsh, K. M., Jonides, J., & Reuter-Lorenz, P. A. (2007). Cognitive fatigue of executive processes: Interaction between interference resolution tasks. *Neuropsychologia*, 45(7), 1571–1579. <https://doi.org/10.1016/j.neuropsychologia.2006.12.007>
- Pessiglione, M., Blain, B., Wiehler, A., & Naik, S. (2025). Origins and consequences of cognitive fatigue. *Trends in Cognitive Sciences*, 29(8), 730–749. <https://doi.org/10.1016/j.tics.2025.02.005>
- Peters, E., & Cressman, E. K. (2026). Mental fatigue does not impede visuomotor adaptation driven by implicit processes. *Consciousness and Cognition*, 141, 104041. <https://doi.org/10.1016/j.concog.2026.104041>

- Petrut, B., Berindan-Neagoe, I., Feflea, D. I., Hoge, M., Pasca, S., Bujoreanu, C. E., & Bschleipfer, T. (2020). Mental Fatigue Evaluation of Surgical Teams during a Regular Workday in a High-Volume Tertiary Healthcare Center. *Urologia Internationalis*, 104(3–4), 301–308. <https://doi.org/10.1159/000504988>
- Pisella, L., Gréa, H., Tilikete, C., Vighetto, A., Desmurget, M., Rode, G., Boisson, D., & Rossetti, Y. (2000). An ‘automatic pilot’ for the hand in human posterior parietal cortex: Toward reinterpreting optic ataxia. *Nature Neuroscience*, 3(7), 729–736. <https://doi.org/10.1038/76694>
- Pitts, J., & Bhatt, T. (2023). Effects of mentally induced fatigue on balance control: A systematic review. *Experimental Brain Research*, 241(1), 13–30. <https://doi.org/10.1007/s00221-022-06464-x>
- Plukaard, S., Huizinga, M., Krabbendam, L., & Jolles, J. (2015). Cognitive flexibility in healthy students is affected by fatigue: An experimental study. *Learning and Individual Differences*, 38, 18–25. <https://doi.org/10.1016/j.lindif.2015.01.003>
- Predictive Safety. (2026). *AlertMeter® Fatigue Risk Management System* [Computer software]. <https://predictivesafety.com/alertmeter-fatigue-management-system/>
- Price, E., Moore, G., Galway, L., & Linden, M. (2017). Validation of a Smartphone-Based Approach to In Situ Cognitive Fatigue Assessment. *JMIR mHealth and uHealth*, 5(8), e6333. <https://doi.org/10.2196/mhealth.6333>
- Proost, M., Habay, J., De Wachter, J., De Pauw, K., Rattray, B., Meeusen, R., Roelands, B., & Van Cutsem, J. (2022). How to Tackle Mental Fatigue: A Systematic Review of Potential Countermeasures and Their Underlying Mechanisms. *Sports Medicine*, 52(9), 2129–2158. <https://doi.org/10.1007/s40279-022-01678-z>
- Purves, D., Augustine, G. J., Fitzpatrick, D., Katz, L. C., LaMantia, A.-S., McNamara, J. O., & Williams, S. M. (2001). Modulation of Movement by the Basal Ganglia. In *Neuroscience. 2nd edition*. Sinauer Associates. <https://www.ncbi.nlm.nih.gov/books/NBK10868/>
- Qi, P., Ru, H., Gao, L., Zhang, X., Zhou, T., Tian, Y., Thakor, N., Bezerianos, A., Li, J., & Sun, Y. (2019). Neural Mechanisms of Mental Fatigue Revisited: New Insights from the Brain Connectome. *Engineering*, 5(2), 276–286. <https://doi.org/10.1016/j.eng.2018.11.025>
- Raharjo, N. T., Bratakusumah, S. P., & Mujakar, A. A. (2026). Reaction Time-Based Fatigue Analysis in Construction Workers. *International Journal of Marine Engineering Innovation and Research*, 11(1), 223–232. <https://doi.org/10.12962/j25481479.v11i1>
- Rahmani, V., Marsh, V. L., Aliafsari Mamaghani, E., Soleimani, A., Alizadeh, M., Zadi, O., & Aghazadeh, N. (2025). Mental fatigue of operating room nurses and its relationship with missed perioperative nursing care: A descriptive-analytical study. *BMC Research Notes*, 18(1), 302. <https://doi.org/10.1186/s13104-025-07380-3>

- Rajiah, R., Takahashi, K., Aziz, Q., & Ruffle, J. K. (2024). Brain effect of transcutaneous vagal nerve stimulation: A meta-analysis of neuroimaging evidence. *Neurogastroenterology & Motility*, 36(8), e14484. <https://doi.org/10.1111/nmo.14484>
- Read, J., Guillemin, C., Charonitis, M., Requier, F., Beliy, N., Bahri, M. A., Vandewalle, G., & Collette, F. (2026). Effort and motivation to characterize mental fatigue: Behavior and functional connectivity. *Motivation Science*. <https://doi.org/10.1037/mot0000421>
- Redgrave, J., Day, D., Leung, H., Laud, P. J., Ali, A., Lindert, R., & Majid, A. (2018). Safety and tolerability of Transcutaneous Vagus Nerve stimulation in humans; a systematic review. *Brain Stimulation*, 11(6), 1225–1238. <https://doi.org/10.1016/j.brs.2018.08.010>
- Ricci, J., Chee, E., Lorandean, A., & 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), 1–10. <https://doi.org/10.1097/01.jom.0000249782.60321.2a>
- Riedl, R., Kostoglou, K., Wriessnegger, S. C., & Müller-Putz, G. R. (2023). Videoconference fatigue from a neurophysiological perspective: Experimental evidence based on electroencephalography (EEG) and electrocardiography (ECG). *Scientific Reports*, 13(1), 18371. <https://doi.org/10.1038/s41598-023-45374-y>
- Rogers, W. P., Marques, J., Talebi, E., & Drews, F. A. (2023). IoT-Enabled Wearable Fatigue-Tracking System for Mine Operators. *Minerals*, 13(2), 287. <https://doi.org/10.3390/min13020287>
- Rothwell, J. C., Day, B. L., Thompson, P. D., & Kujirai, T. (2009). Short latency intracortical inhibition: One of the most popular tools in human motor neurophysiology. *The Journal of Physiology*, 587(1), 11–12. <https://doi.org/10.1113/jphysiol.2008.162461>
- Rothwell, J., Antal, A., Burke, D., Carlsen, A., Georgiev, D., Jahanshahi, M., Sternad, D., Valls-Solé, J., & Ziemann, U. (2021). Central nervous system physiology. *Clinical Neurophysiology*, 132(12), 3043–3083. <https://doi.org/10.1016/j.clinph.2021.09.013>
- Rozand, V., Lebon, F., Papaxanthis, C., & Lepers, R. (2015). Effect of mental fatigue on speed–accuracy trade-off. *Neuroscience*, 297, 219–230. <https://doi.org/10.1016/j.neuroscience.2015.03.066>
- Salomone, M., Burle, B., Fabre, L., & Berberian, B. (2021). An Electromyographic Analysis of the Effects of Cognitive Fatigue on Online and Anticipatory Action Control. *Frontiers in Human Neuroscience*, 14, 615046. <https://doi.org/10.3389/fnhum.2020.615046>
- Sandry, J., Genova, H. M., Dobryakova, E., DeLuca, J., & Wylie, G. (2014). Subjective Cognitive Fatigue in Multiple Sclerosis Depends on Task Length. *Frontiers in Neurology*, 5. <https://doi.org/10.3389/fneur.2014.00214>
- Schmidt, R., Lee, T., Winstein, C., Wulf, G., & Zelaznik, H. (2019). *Motor Control and Learning: A Behavioral Emphasis* (6th ed.). Human Kinetics.

- Schouppe, S., Van Oosterwijck, J., Wiersema, J. R., Van Damme, S., Willems, T., & Danneels, L. (2020). Physical or Cognitive Exertion Does Not Influence Cortical Movement Preparation for Rapid Arm Movements. *Motor Control*, 24(4), 473–498. <https://doi.org/10.1123/mc.2019-0115>
- Schumacher, E. H., & D'Esposito, M. (2002). Neural implementation of response selection in humans as revealed by localized effects of stimulus–response compatibility on brain activation. *Human Brain Mapping*, 17(3), 193–201. <https://doi.org/10.1002/hbm.10063>
- Sigurdsson, H. P., Raw, R., Hunter, H., Baker, M. R., Taylor, J.-P., Rochester, L., & Yarnall, A. J. (2021). Noninvasive vagus nerve stimulation in Parkinson's disease: Current status and future prospects. *Expert Review of Medical Devices*, 18(10), 971–984. <https://doi.org/10.1080/17434440.2021.1969913>
- Smith, M. R., Zeuwts, L., Lenoir, M., Hens, N., De Jong, L. M. S., & Coutts, A. J. (2016). Mental fatigue impairs soccer-specific decision-making skill. *Journal of Sports Sciences*, 34(14), 1297–1304. <https://doi.org/10.1080/02640414.2016.1156241>
- Sohn, Y. H., Wiltz, K., & Hallett, M. (2002). Effect of Volitional Inhibition on Cortical Inhibitory Mechanisms. *Journal of Neurophysiology*, 88(1), 333–338. <https://doi.org/10.1152/jn.2002.88.1.333>
- Souchet, A. D., Lourdeaux, D., Pagani, A., & Rebenitsch, L. (2023). A narrative review of immersive virtual reality's ergonomics and risks at the workplace: Cybersickness, visual fatigue, muscular fatigue, acute stress, and mental overload. *Virtual Reality*, 27(1), 19–50. <https://doi.org/10.1007/s10055-022-00672-0>
- Spijkers, W. A. C., & Walter, A. (1985). Response processing stages in choice reactions. *Acta Psychologica*, 58(2), 191–204. [https://doi.org/10.1016/0001-6918\(85\)90007-1](https://doi.org/10.1016/0001-6918(85)90007-1)
- Staiano, W., Romagnoli, M., Salazar Bonet, L. R., & Ferri-Caruana, A. (2024). Adaptive cognitive tasks for mental fatigue: An innovative paradigm for cognitive loading in human performance. *Journal of Science and Medicine in Sport*, 27(12), 883–889. <https://doi.org/10.1016/j.jsams.2024.08.199>
- Sun, H., Soh, K. G., Mohammadi, A., Toumi, Z., Zhang, L., Ding, C., Gao, X., & Tian, J. (2024). Counteracting mental fatigue for athletes: A systematic review of the interventions. *BMC Psychology*, 12(1), 67. <https://doi.org/10.1186/s40359-023-01476-w>
- Tachibana, R., Namba, Y., & Noguchi, Y. (2014). Two Speed Factors of Visual Recognition Independently Correlated with Fluid Intelligence. *PLOS ONE*, 9(5), e97429. <https://doi.org/10.1371/journal.pone.0097429>
- Talebi, E., Rogers, W. P., & Drews, F. A. (2026). Predicting Fatigue of Haul Truck Operators Using Reaction Time. *Mining, Metallurgy & Exploration*, 43(2), 1951–1972. <https://doi.org/10.1007/s42461-025-01415-w>

- Tanaka, M., Ishii, A., & Watanabe, Y. (2014). Neural effect of mental fatigue on physical fatigue: A magnetoencephalography study. *Brain Research*, 1542, 49–55. <https://doi.org/10.1016/j.brainres.2013.10.018>
- Tapia, J. A., Tohyama, T., Poll, A., & Baker, S. N. (2022). The Existence of the StartReact Effect Implies Reticulospinal, Not Corticospinal, Inputs Dominate Drive to Motoneurons during Voluntary Movement. *Journal of Neuroscience*, 42(40), 7634–7647. <https://doi.org/10.1523/JNEUROSCI.2473-21.2022>
- Taylor, D. A. (1976). Stage analysis of reaction time. *Psychological Bulletin*, 83(2), 161–191.
- Thomas, M., Allen, M. S., Wigle, D. A., Shen, K. R., Cassivi, S. D., Nichols, F. C., & Deschamps, C. (2012). Does Surgeon Workload Per Day Affect Outcomes After Pulmonary Lobectomies? *The Annals of Thoracic Surgery*, 94(3), 966–972. <https://doi.org/10.1016/j.athoracsur.2012.04.099>
- Tomassini, A., Torricelli, F., Fadiga, L., & D'Ausilio, A. (2026). Alpha and Beta Corticomotor Phase Dynamics Shape Visuomotor Control on a Single-Trial Basis. *Journal of Neuroscience*, 46(7). <https://doi.org/10.1523/JNEUROSCI.0765-25.2025>
- Turvey, M. T., & Fonseca, S. (2009). Nature of Motor Control: Perspectives and Issues. In D. Sternad (Ed.), *Progress in Motor Control: A Multidisciplinary Perspective* (pp. 93–123). Springer US. https://doi.org/10.1007/978-0-387-77064-2_6
- Tzagarakis, C., West, S., & Pellizzer, G. (2021). Neural Encoding of the Reliability of Directional Information During the Preparation of Targeted Movements. *Frontiers in Neuroscience*, 15. <https://doi.org/10.3389/fnins.2021.679408>
- Ungerleider, L. G., & Haxby, J. V. (1994). ‘What’ and ‘where’ in the human brain. *Current Opinion in Neurobiology*, 4(2), 157–165. [https://doi.org/10.1016/0959-4388\(94\)90066-3](https://doi.org/10.1016/0959-4388(94)90066-3)
- Van Cutsem, J., Marcora, S., De Pauw, K., Bailey, S., Meeusen, R., & Roelands, B. (2017). The Effects of Mental Fatigue on Physical Performance: A Systematic Review. *Sports Medicine*, 47(8), 1569–1588. <https://doi.org/10.1007/s40279-016-0672-0>
- van der Linden, D., Frese, M., & Meijman, T. F. (2003). Mental fatigue and the control of cognitive processes: Effects on perseveration and planning. *Acta Psychologica*, 113(1), 45–65. [https://doi.org/10.1016/S0001-6918\(02\)00150-6](https://doi.org/10.1016/S0001-6918(02)00150-6)
- van der Linden, D., Frese, M., & Sonnentag, S. (2003). The Impact of Mental Fatigue on Exploration in a Complex Computer Task: Rigidity and Loss of Systematic Strategies. *Human Factors*, 45(3), 483–494. <https://doi.org/10.1518/hfes.45.3.483.27256>
- van Schagen. (2021). *Road Safety Thematic Report—Fatigue* (p. 19). European Road Safety Observatory. https://road-safety.transport.ec.europa.eu/european-road-safety-observatory/data-and-analysis/thematic-reports_en

- Vickers, D., & Smith, P. L. (1986). The rationale for the inspection time index. *Personality and Individual Differences*, 7(5), 609–623. [https://doi.org/10.1016/0191-8869\(86\)90030-9](https://doi.org/10.1016/0191-8869(86)90030-9)
- Walker, L. A. S., Berard, J. A., Berrigan, L. I., Rees, L. M., & Freedman, M. S. (2012). Detecting cognitive fatigue in multiple sclerosis: Method matters. *Journal of the Neurological Sciences*, 316(1), 86–92. <https://doi.org/10.1016/j.jns.2012.01.021>
- Weetman, S., Roche, M., Leckie, T., Samuels, T., & Hodgson, L. (2024). Feasibility of application-based psychomotor vigilance testing to assess fatigue in doctors working night shifts and correlation with smartwatch assessed shift intensity. *Occupational and Environmental Medicine*, 81(5), 252–257. <https://doi.org/10.1136/oemed-2023-109311>
- Wiehler, A., Branzoli, F., Adanyeguh, I., Mochel, F., & Pessiglione, M. (2022). A neuro-metabolic account of why daylong cognitive work alters the control of economic decisions. *Current Biology*, 32(16), 3564–3575.e5. <https://doi.org/10.1016/j.cub.2022.07.010>
- Wirdnam, M., Ferrar, K., Mayes, S., MacMahon, C., Cook, J., & Rio, E. (2024). “A sprained ankle is the biggest sign of mental fatigue”: A qualitative study of the perceptions and experiences of mental fatigue in professional ballet. *Physical Therapy in Sport*, 65, 154–161. <https://doi.org/10.1016/j.ptsp.2023.12.006>
- Wong, A. L., Haith, A. M., & Krakauer, J. W. (2015). Motor Planning. *The Neuroscientist*, 21(4), 385–398. <https://doi.org/10.1177/1073858414541484>
- Xiao, Y., Ma, F., Lv, Y., Cai, G., Teng, P., Xu, F., & Chen, S. (2015). Sustained Attention is Associated with Error Processing Impairment: Evidence from Mental Fatigue Study in Four-Choice Reaction Time Task. *PLOS ONE*, 10(3), e0117837. <https://doi.org/10.1371/journal.pone.0117837>
- Yap, J. Y. Y., Keatch, C., Lambert, E., Woods, W., Stoddart, P. R., & Kameneva, T. (2020). Critical Review of Transcutaneous Vagus Nerve Stimulation: Challenges for Translation to Clinical Practice. *Frontiers in Neuroscience*, 14. <https://doi.org/10.3389/fnins.2020.00284>
- Yasin, S., Altunisik, E., & Tak, A. Z. A. (2023). Digital Danger in Our Pockets: Effect of Smartphone Overuse on Mental Fatigue and Cognitive Flexibility. *The Journal of Nervous and Mental Disease*, 211(8), 621. <https://doi.org/10.1097/NMD.0000000000001675>
- Young, C. B., Reddy, V., & Sonne, J. (2026). Neuroanatomy, Basal Ganglia. In *StatPearls*. StatPearls Publishing. <http://www.ncbi.nlm.nih.gov/books/NBK537141/>
- Yu, Z., Guindani, M., Grieco, S. F., Chen, L., Holmes, T. C., & Xu, X. (2022). Beyond t test and ANOVA: Applications of mixed-effects models for more rigorous statistical analysis in neuroscience research. *Neuron*, 110(1), 21–35. <https://doi.org/10.1016/j.neuron.2021.10.030>

- Zhang, Z., Xiang, T., Guo, H., Ma, L., Guan, Z., & Fang, Y. (2023). Impact of physical and mental fatigue on construction workers' unsafe behavior based on physiological measurement. *Journal of Safety Research*, 85, 457–468. <https://doi.org/10.1016/j.jsr.2023.04.014>
- Zong, H., Yi, W., Antwi-Afari, M. F., & Yu, Y. (2024). Fatigue in construction workers: A systematic review of causes, evaluation methods, and interventions. *Safety Science*, 176, 106529. <https://doi.org/10.1016/j.ssci.2024.106529>

Appendix A. Supplementary Material for Chapter 2

A.1 Supplementary Reaction Time Analysis

A.1.1 Analysis

Reaction time (RT) analyses were repeated as outlined in the manuscript (*Chapter 2, Section: 2.6.3*) with an expanded outlier removal cut-off of ± 3 *SD* from the mean RT within each session [cognitive fatigue (CF) and non-fatiguing (NF)] and testing time [pre-test and post-test] and again with no outliers removed.

A.1.2 Results

Expanded Outlier Removal Criterion: RT analysis indicated significant main effects of stimulus ($F(1, 2147) = 263.77, p < .001$) and session type ($F(1,17) = 5.04, p = .038$), which were superseded by a significant stimulus x session type x time interaction ($F(1,2140) = 4.23, p = .040$). As expected, SAS trial RT was significantly shorter than control trial RT in all cases ($p < .001$). Control RT significantly increased from pre- to post-test in the CF session (mean difference = +9.40 ms, $p = .004$) but did not significantly change over the NF session (mean difference = -6.60 ms, $p = .131$). No significant changes in SAS trial RT from pre- to post-test were observed in the CF session (mean difference = +0.40 ms, $p > .999$) nor in the NF session (mean difference = +2.20 ms, $p > .999$). Between-session comparisons demonstrated significantly shorter pre-test control RT in the CF session as compared to the NF session (mean difference = -19.80 ms, $p = .023$). No other significant between-session comparisons were apparent.

Note that the significant differences reported here are the same as those reported in the manuscript (where outlier removal employed a criterion of ± 2 *SD* from the mean RT), with the exception of control trial RT between pre- and post-test in the NF session. While the results in

the main manuscript report this change as significant, the expanded outlier analysis performed here resulted in a non-significant difference ($p = .131$).

Without Outlier Removal: RT analysis of data without outlier removal indicated a significant main effect of stimulus ($F(1, 2173) = 182.63, p < .001$) as well as a marginally significant stimulus x session type x time interaction ($F(1,2173) = 3.91, p = .048$). Again, SAS trial RT was significantly shorter than control trial RT in all cases ($p < .001$). Control RT decreased significantly from pre- to post- test in the NF session (mean difference = -10.0 ms, $p = .037$), and increased, albeit non-significantly from pre- to post-test in the CF session (mean difference = +9.3 ms, $p = .061$). No significant changes in SAS trial RT from pre- to post-test were observed in the CF session (mean difference = +0.1 ms, $p > .999$) nor in the NF session (mean difference = +2.9 ms, $p > .999$). No other significant comparisons were apparent.

Note that the results presented above were similar to those presented in the manuscript but differed in that control RT increases from pre- to post-test in the CF session were not significant in the above analysis. As outliers were not removed in this data set, we note that this could simply be due to the inclusion of potentially non-representative RT values, such as very slow RTs, which may result from failure to perform the task as instructed or from outside distraction.

To verify that a control RT increase in the CF session did exist, despite the inclusion of potentially non-representative RT trials, control and SAS RT data without outliers removed was subsequently re-analysed in isolation, with control RT representing a confirmation of previously documented increases in simple RT in response to CF (a manipulation check), and SAS RT used as an indicator of preparatory changes (the result of interest) [$model = SAS\ RT\ or\ Control\ RT \sim Session*Time + (1 \mid Participant)$]. Analysis of control trial RT demonstrated a significant session

type x time interaction ($F(1,1775) = 13.93, p < .001$). Control RT increased significantly from pre- to post- test in the CF session ($p = .042$) and decreased significantly from pre- to post-test in the NF session ($p = .027$). Between session comparisons indicated significantly faster control RT in the CF session pre-test as compared to the NF session pre-test (mean difference = -20 ms, $p = .038$). Analysis of SAS trial RT indicated only a main effect of session ($F(1, 6.11) = 8.57, p = .026$), with faster SAS RT observed in the CF session (mean difference = -7.4 ms).

Note that the preceding analysis demonstrated very similar results to those presented in the manuscript, differing in that the above analysis demonstrated significantly faster SAS RT overall in the CF session.

A.2 Supplementary Analysis of Individual Subjective Cognitive Fatigue Measures

A.2.1 Methods

Subjective cognitive fatigue levels were assessed using four 10-point measures, each on a separate 200 mm visual analog scale (VAS), delivered before and after the non-fatiguing (NF) and cognitive fatigue (CF) tasks. These measures included energy level (*0-energetic, 10-unenergetic*), stress level (*0-relaxed, 10-tense*), ability to concentrate (*0-able to concentrate, 10-unable to concentrate*), and motivation (*0-motivated to succeed in the task, 10-unmotivated to succeed in the task*).

A.2.2 Analysis

Responses to each metric were assessed with individual linear mixed effects models in R (Bates et al., 2015; R Core Team, 2021). Each model included the fixed effect interaction of testing session (NF, CF) and time (pre-test, post-test), with random intercepts specified for the effect of participant. These models took the following form: *model = Subjective CF Measure ~ Session*Time + (1 | Participant)*.

The significance of fixed effects was explored using analysis of variance (ANOVA) of each model, with F-tests and p-values using Satterthwaite's method for denominator degrees-of-freedom and F-statistic, applied using the *lmerTest* package (Kuznetsova et al., 2017). In all cases, differences with a probability of less than .05 or less were considered significant. Post hoc contrasts with Bonferroni corrections, estimated marginal means, and 95% confidence intervals for each measure were also assessed (Lenth et al., 2021).

A.2.3 Results

Results are summarized in Fig. A.1. For the subjective CF measure of energy level (*0-energetic, 10-unenergetic*), analyses demonstrated a significant main effect of session ($F(1, 57) = 5.21, p = .026$) and testing time ($F(1, 57) = 53.68, p < .001$), but no significant interaction ($F(1, 57) = 2.22, p = .142$). An overall higher score (i.e., less energetic) was observed in the CF session compared to the NF session (mean difference score = 0.81), and in the post-tests compared to the pre-tests (mean difference score = 2.60).

For the subjective CF measure of stress level (*0-relaxed, 10-tense*), analyses demonstrated a significant main effect of session ($F(1, 57) = 16.23, p < .001$), which was superseded by a significant interaction between testing time and session ($F(1, 57) = 6.99, p = .011$). Post hoc contrasts of the interaction effect demonstrated a significantly higher level of stress reported in the CF session post-test as compared to the NF session post-test (mean difference score = 2.35, $p < .001$), with no other significant contrasts.

For the subjective CF measure of ability to concentrate (*0-able to concentrate, 10-unable to concentrate*), analyses demonstrated a significant main effect of session ($F(1, 57) = 17.09, p < .001$) and testing time ($F(1, 57) = 59.19, p < .001$), as well as a significant interaction between time and session ($F(1, 57) = 16.36, p < .001$). Post hoc contrasts of the interaction effect

demonstrated a significantly higher score (i.e., less able to concentrate) in the CF session post-test as compared to the CF session pre-test (mean difference score = 3.46, $p < .001$). A significantly higher score was also observed in the CF session post-test compared to the NF session post-test (mean difference score = 2.41, $p < .001$).

For the subjective CF measure of motivation (*0-motivated to succeed in the task, 10-unmotivated to succeed in the task*), analyses demonstrated a significant main effect of session ($F(1, 57) = 12.71, p < .001$) and testing time ($F(1, 57) = 18.92, p < .001$), but no significant interaction ($F(1, 57) = 0.070, p = .793$). An overall higher score (i.e., less motivated to succeed in the task) was observed in the CF session as compared to the NF session (mean difference = .03), and in the post-tests compared to the pre-tests (mean difference score = 1.25).

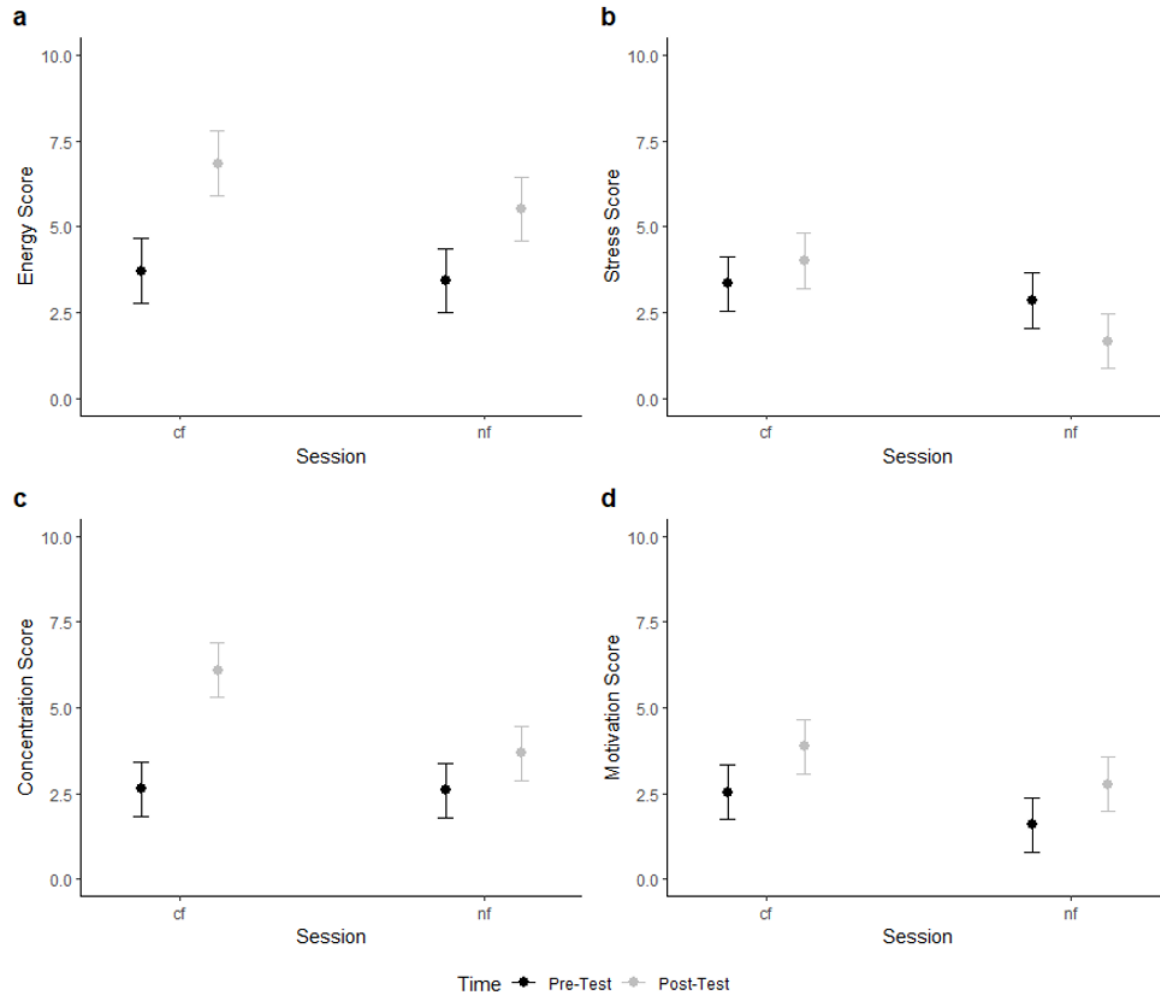


Fig. A.1 Scores for individual subjective cognitive fatigue measures. Mean scores are shown as a function of session (CF = cognitive fatigue, NF = non-fatiguing) and time (pre-test, post-test). (a) Energy level score (0-energetic, 10-unenergetic); (b) stress level score (0-relaxed, 10-tense); (c) ability to concentrate score (0-able to concentrate, 10-unable to concentrate); (d) motivation score (0-motivated to succeed in the task, 10-unmotivated to succeed in the task).

A.3 Supplementary Bayesian Analysis of SAS Trial Reaction Time

A.3.1 Analysis

This analysis determined the statistical Bayes factor (BF_{10}) for the effect of interest; that is, SAS reaction time changes from pre- to post-test in both testing sessions (NF and CF). This analysis was completed using the *BayesFactor* package in R statistical software (Morey & Rouder, 2021). The function *lmBF* was used to compute the Bayes factor (against the intercept only model) for the full model [*full model* = $RT \sim time + subject$, *whichRandom* = 'subject'] and for the null model [*null model* = $RT \sim subject$, *whichRandom* = 'subject']. BF_{10} was then determined by calculating the ratio of the full model (with the effect of time) over the null model (without the effect of time). In this case BF_{10} is the Bayes factor giving the evidence for the alternative hypothesis (SAS RT is different between pre- and post-test) over the null hypothesis (SAS RT is not different between pre- and post-test).

A.3.2 Results

The Bayes factor statistics obtained in analysis of both sessions ($BF_{10} = 0.119 \pm 1.24\%$) indicates that “substantial evidence” exists in favour of the null hypothesis (i.e., SAS RT does not vary from pre- to post-test in either session) (Wetzels et al., 2011).

A.4 Supplementary References

- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, 67, 1–48.
<https://doi.org/10.18637/jss.v067.i01>
- Kuznetsova, A., Brockhoff, P. B., & Christensen, R. H. B. (2017). lmerTest Package: Tests in Linear Mixed Effects Models. *Journal of Statistical Software*, 82, 1–26.
<https://doi.org/10.18637/jss.v082.i13>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Morey, R., & Rouder, J. (2021). *BayesFactor: Computation of Bayes factors for common designs. R package version 0.9.12-4.3*. [Computer software]. <https://CRAN.R-project.org/package=BayesFactor>
- R Core Team. (2021). *R: A language and environment for statistical computing*. [Computer software]. R Foundation for Statistical Computing. <https://www.R-project.org/>
- Wetzels, R., Matzke, D., Lee, M. D., Rouder, J. N., Iverson, G. J., & Wagenmakers, E.-J. (2011). Statistical Evidence in Experimental Psychology: An Empirical Comparison Using 855 t Tests. *Perspectives on Psychological Science*, 6(3), 291–298.
<https://doi.org/10.1177/1745691611406923>

Appendix B. Supplementary Material for Chapter 4

B.1 Supplementary Methods

Data collection was completed from March through October 2024. Among the 402 participants who were included in the final analysis, 270 reported being assigned female at birth (mean age = 21.1 years, ± 5.5 years), and 132 reported being assigned male at birth (mean age = 21.2 years, ± 5.4 years).

Data collection software was compatible with Windows, MacOS, and Linux platforms, and was available in French or English. After the eligibility screen and demographic/lifestyle questionnaire, general task instructions were delivered. These instructions stipulated that the study would require approximately 1.5 hours to complete and emphasized that participants should ensure they have ample uninterrupted time to complete the entire session, without any pauses or breaks. Participants were also instructed to minimize outside distractions (e.g., find a quiet place to complete the study, silence devices/TV/radio), and to avoid using mental aids to help them complete any aspect of the study (e.g., calculator, pen and paper, etc.). Instructions further outlined that participants should not attempt the study at that time (but could return at a later time) if they had consumed alcohol or recreational drugs in the previous six hours. Upon completion of the study, participants were prompted to submit their data by selecting a “send” button before exiting the application, which triggered the data to be automatically and securely emailed to the researchers.

B.1.1 Subjective Ratings

Subjective ratings were made on horizontal linear scales with a length of 528 pixels (actual length would depend on screen size/resolution). In addition to the two rating scales described within the manuscript (cognitive fatigue level, motivation level), two additional scales were

assessed: difficulty concentrating (0 = able to concentrate, 10 = unable to concentrate) and tension level (0 = relaxed, 10 = tense) These scales reflect subcomponents of the Fatigue Assessment Scale (FAS; Michielsen et al., 2003) and those used in our previous research (Peters et al., 2022, 2024).

B.1.2 Reaction Time Tasks

Reaction time stimuli circular diameter was 120 pixels. Reaction time task instructions were delivered visually and in writing. Error feedback was presented indicating missed, incorrect or anticipated response.

B.1.3 Cognitive Interventions

The documentary film intervention was accessed via URL and participants resumed the study when it was complete by selecting a “continue” button. All cognitive interventions were completed using the participants computer mouse and/or keyboard. As described in the manuscript, the cognitive tasks were adaptive, such that difficulty was individually adjusted throughout to maintain a response accuracy of approximately 85%, consistent with evidence that individualizing cognitive task difficulty may enhance mental fatigue induction (O’Keeffe et al., 2020; Staiano et al., 2024). Task difficulty was adapted by adjusting stimulus display times and the time available to respond, based on rolling performance averages computed every ~4 minutes. Details of the exact methods by which performance was assessed and difficulty was adapted within each task are described below.

Math-Memory Dual Task. In this task, participants were instructed to remember the displayed letters in order without verbal rehearsal or note-taking. Responses for the math component (e.g., $6 \times 4 = 10$, answer = +) were made using the computer mouse. Participants were encouraged to correctly complete as many math problems as possible within the trial

interval and were provided ongoing feedback of response accuracy (correct/incorrect indicated by a green check mark or red X). For the letter component, participants inputted the letters into blank boxes using their computer keyboard. Feedback indicating the accuracy of the letter inputs was provided at the end of the trial interval by the box frames turning green if the inputted letter was correct, or red if incorrect. Responses were considered to be errors if they were incorrect or if the response was not made during the response interval (the length of which was adapted throughout). The display/response time for math problems began at 3000 ms and for letter input boxes at 800 ms for the first four trials of the task. Every 4 trials (~4 minutes), accuracy was averaged across both task segments. If performance fell below 85%, task difficulty was decreased by increasing the display/response time within the math and memory segments of the task by 10%. Conversely, if accuracy rose above 85%, task difficulty was increased by reducing the display/response time by 10%.

Modified Incongruent Stroop Task. Within this task, a single word approximately 45 pixels in height was presented at the centre of the study window on each trial. Colour-word combinations were randomly selected with equal probability. Feedback regarding response time and accuracy (correct/incorrect) was presented on each trial. Responses were considered as errors if no response or an incorrect response was made during the response interval (the length of which was adapted throughout). The initial word display/response time was 1500 ms. Every 48 trials (~4 minutes), mean accuracy was used to adjust difficulty for the following 48 trials of the task. If accuracy fell below 85%, task difficulty was decreased by increasing the display/response time by 10%. On the other hand, if accuracy rose above 85%, task difficulty was increased by reducing the display/response time by 10%.

Time Load Dual-Back Task. In this task, numbers and letters were presented in a 12 pixels square black framed box on the screen for a set period of time in alternating order. The frame of the letter/number box turned green for correct responses and turned red for incorrect responses. Responses were considered to be errors if an incorrect response key was pressed or if no response was made during the available response interval. The initial response interval/stimulus display duration was 1500 ms. After 96 trials (~4 minutes), dual-task accuracy was averaged and used to adjust display/response times to maintain 85% accuracy. Specifically, if accuracy fell below 85%, task difficulty was decreased by increasing the display/response time of both letters and numbers by 10%. Conversely, if accuracy rose beyond 85%, task difficulty was increased by reducing the display/response time by 10%.

B.2 Supplementary Data Reduction

Due to the unsupervised nature of remote data collection, significant efforts had to be made to ensure all data included in analyses demonstrated clear adherence to instructions. As such, any data set that did not meet the following criteria was excluded (note that a single data set may fail to meet multiple criteria; see also *Chapter 4, Table 4.1*): time spent on NF task needed to fall between 30-90 minutes (22 data sets flagged); time spent on cognitive fatigue intervention (MM, DB, ST) needed to fall between 50-70 minutes (42 data sets flagged); time spent on simple, go/no-go and choice RT tasks needed to fall within ± 2.5 *SD* from each mean (1 data set flagged); attempted number of MM, ST, or DB task trials needed to be greater than the mean minus 2.5 *SD* (19 data sets flagged); the average number of math problems attempted per trial in the MM task needed to be greater than the mean minus 2.5 *SD* (2 data sets flagged); the average number of letters correctly inputted per trial in the MM task needed to be greater than 1 (6 data sets flagged); the proportion of correct ST and DB task trials needed to be greater than 0.60 (28 data

sets flagged); and the total length of the session needed to be between 70-140 minutes (57 data sets flagged).

Data from 402 data sets were retained for analyses following this reduction (98 data sets removed; 80.4% retained), including 105 data sets with the MM intervention (84% retained), 94 with the ST intervention (75.2% retained), 84 with the DB intervention (80.8% retained), and 119 with the NF intervention (81.5% retained).

Overall performance accuracy within the cognitive interventions was assessed in the retained data sets to ensure it was not unusually high (e.g., > 99% correct) or substantially greater than levels typically reported in comparable tasks, which could indicate poor adherence to instructions (e.g., writing down letters in the MM task). ST intervention accuracy was 82.9% ($SD = 5.3\%$; by-subject maximum = 89.8%), which was comparable to or lower than previous reports (91 - 93% correct; Toth et al., 2019; Wiley et al., 2024). DB task accuracy was also consistent with the literature ($M = 87.4\%$, $SD = 3.8\%$; by-subject maximum = 95.0%; Borragán et al., 2017): ~85 - 90%). Although there are fewer directly comparable values for the MM task, mean letter-response accuracy was 67.0% ($SD = 18.0\%$ correct; by-subject maximum = 96.2%), which did not approximate ceiling-level performance. Overall, this suggests no evidence of systematic non-adherence to instructions in order to improve performance, thus no additional data sets were removed.

Reaction time task responses meeting the following criteria were removed from the main analysis (9.24% of all trials): RT greater than post-test mean RT plus 2 SD (considered to reflect a significant lapse in attention) in the simple RT task (slow = 915.4 ms, 1483 trials), go/no-go RT task (slow = 833.4 ms, 833 trials), and choice RT task (slow = 994.3 ms, 1203 trials); RT less than 100 ms (anticipatory responses) in the simple RT task (386 trials), go/no-go RT task (23

trials), and choice RT task (58 trials); a response on a “no-go” trial (i.e., commission error; 966 trials) in the go/no-go RT task; or an incorrect key response in the choice RT task (2477 trials).

B.3 Supplementary Analyses

Each RT task type was modeled separately to avoid introducing large variance attributable to known baseline differences between tasks (i.e., simple RT < go/no-go RT < choice RT), allowing for a more precise evaluation of effects within each RT task. Note that a Poisson model was chosen to model RT task error counts because count variables typically exhibit non-normal residuals mean-variance relationships that violate assumptions of standard linear models (Aiken et al., 2015). The significance of model fixed-effects was assessed using Type III F-tests for LMMs with Satterthwaite’s approximation and Wald chi-square tests for GLMMs.

Here (in supplementary analyses), subjective ratings of difficulty concentrating and tension level were analysed in the same way as the remaining subjective measures, as described in the manuscript and the preceding paragraph (*Chapter 4.5*).

Supplementary analyses also assessed cognitive task performance across interventions, by modeling the likelihood of a reduction in task difficulty being implemented at any given time – in other words, whether the task was adaptively made easier (e.g., by increasing the time available to respond) on a given trial in response to the performance variable dropping below 85%. The binary outcome variable indicated whether the task difficulty was reduced (1) or left the same/increased (0) and acted as a proxy for performance change. This variable was selected for analyses since it can be easily compared between cognitive interventions, despite differing task demands. To compare changes in the likelihood of a performance decline (difficulty reduction) across cognitive interventions, data from the ST, DB, and MM interventions were combined into a single data set. To normalize trial number across interventions, trial progression

was expressed as a percentage of task completion and binned into 5% intervals. A logistic GLMM was fit to the data using the *glmmTMB* package; this method was chosen for its robustness to sparse binary data, such as when several participants demonstrate only one response type (i.e., only 1's or only 0's; Brooks et al., 2017). Fixed effects included time bin, cognitive intervention type (DB, MM, ST), and their interaction, and participant-level random intercepts were also modelled. The significance of fixed effects was assessed using the *Anova()* function (package: *car*, Fox & Weisberg, 2019). To quantify and compare performance change between cognitive interventions, predicted probabilities of a difficulty reduction at the start ([0%, 5%] bin) and end ([95%, 100%] bin) of each task were extracted using *emmeans* (Lenth et al., 2021). Differences between these estimates were then compared across intervention types using the *contrast()* function along with odds ratios and 95% confidence intervals (Lenth et al., 2021).

B.4 Supplementary Results

B.4.1 Baseline Demographic Information

Comparison of baseline measures obtained on the pre-experimental questionnaire revealed no significant differences between groups (i.e., among participants completing the MM, ST, DB, or NF interventions); sex assigned at birth ($\chi^2(3) = 3.15, p = .369$), age ($H(3) = 1.29, p = .731$), handedness (Fisher's Exact Test: $p = .488$), hours of sleep ($H(3) = 3.02, p = .388$), sleep quality rating ($\chi^2(6) = 3.12, p = .794$), hours since waking ($H(3) = 2.60, p = .458$), whether caffeine had been consumed in the prior 12 hours ($\chi^2(3) = 0.524, p = .914$), the amount of caffeine consumed ($H(3) = 4.78, p = .189$), whether a mental task had been completed since waking ($\chi^2(3) = 4.86, p = .182$), duration of the mental task ($H(3) = 3.47, p = .325$), time since the mental task ($H(3) = 6.25, p = .096$), whether physical activity had been completed since waking ($\chi^2(3) = 0.55, p =$

.909), the duration of physical activity ($H(3) = 0.42, p = .937$), and the time since physical activity ($H(3) = 7.11, p = .069$).

B.4.2 Additional Subjective Ratings: Tension & Concentration

Subjective tension level showed significant main effects of timepoint ($F(1, 398) = 200.98, p < .001$) and intervention ($F(3, 398) = 9.97, p < .001$) with a significant timepoint x intervention interaction ($F(3, 398) = 22.10, p < .001$). Subjective tension level increased more from pre- to post-test over the MM ($\Delta_{vs.NF} = +2.61, 95\% \text{ CI } [1.57, 3.64], p < .001, d_a = 1.09$), ST ($\Delta_{vs.NF} = +2.79, 95\% \text{ CI } [1.72, 3.85], p < .001, d_a = 1.17$), and DB ($\Delta_{vs.NF} = +2.25, 95\% \text{ CI } [1.15, 3.35], p < .001, d_a = 0.94$) interventions compared to NF (Fig. B.1). Similarly, subjective difficulty concentrating also showed significant main effects of timepoint ($F(1, 398) = 239.27, p < .001$) and intervention ($F(3, 398) = 4.39, p = .005$) with a significant timepoint x intervention interaction ($F(3, 398) = 7.89, p < .001$). Difficulty concentrating increased more from pre- to post-test over the MM ($\Delta_{vs.NF} = +1.38, 95\% \text{ CI } [0.27, 2.49], p = .004, d_a = 0.57$), ST ($\Delta_{vs.NF} = +1.55, 95\% \text{ CI } [2.70, 3.60], p = .002, d_a = 0.64$), and DB ($\Delta_{vs.NF} = +1.95, 95\% \text{ CI } [0.77, 3.13], p < .001, d_a = 0.81$) interventions compared to NF (Fig. B.1). No significant differences in subjective tension or difficulty concentrating were observed between interventions (DB, MM, ST) at baseline ($p > .999$ in all cases).

B.4.3 Cognitive Intervention Performance

Task performance during the cognitive interventions as indicated by the probability of a reduction in task difficulty showed significant main effects of time bin ($\chi^2(1) = 58.92, p < .001$) and cognitive intervention ($\chi^2(2) = 249.71, p < .001$). A significant interaction between time bin and cognitive intervention was also observed ($\chi^2(2) = 75.55, p < .001$). Post hoc comparisons demonstrated significant differences between cognitive interventions in the odds of performance

decline (i.e., adaptive reduction in task difficulty) over time. More specifically, the odds of a difficulty reduction occurring increased significantly more across the DB intervention compared to MM (OR = 21.35, 95% CI [9.04, 50.43], $p < .001$) and ST (OR = 3.01, 95% CI [1.47, 6.19], $p < .001$), and across the ST intervention compared to MM (OR = 7.09, 95% CI [3.43, 14.65], $p < .001$). This indicates a steeper performance decline over time in the ST intervention compared to MM, and in the DB intervention compared to both MM and ST. However, it should be noted that the interventions varied significantly in initial performance (Fig. B.2). More specifically, follow-up comparisons between sessions at the first time bin revealed significantly poorer starting performance (higher probability of a difficulty reduction) in the MM intervention compared to DB (OR = 92.01, 95% CI [47.52, 178.13], $p < .001$) and ST (OR = 21.56, 95% CI [12.30, 37.78], $p < .001$), and to a lesser degree, in ST compared to DB (OR = 4.27, 95% CI [2.45, 7.45], $p < .001$).

B.5 Supplementary Figures

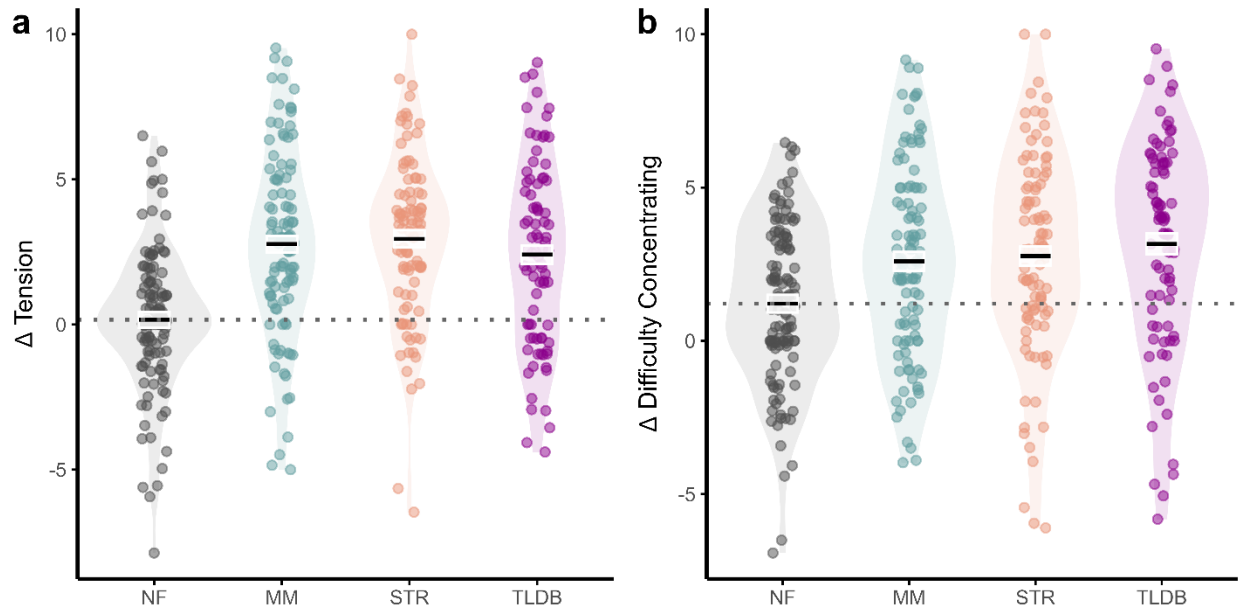


Fig. B.1 Model-estimated mean change in tension and difficulty concentrating. Black solid lines indicate mean pre- to post-intervention change in subjective rating (original scale = 0-10) of (a) tension and (b) difficulty concentrating. White bars show SE, dotted horizontal line indicates Control (NF) mean, and circular points show individual data with violin distributions. NF = Control, MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back.

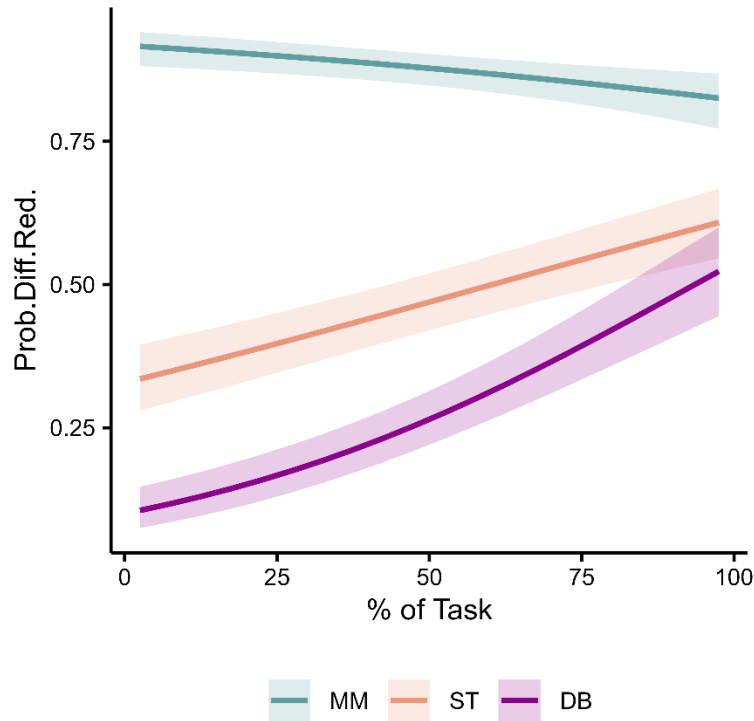


Fig. B.2 Model predicted probability of an adaptive difficulty reduction (proxy for performance decline) in the cognitive interventions. Probability of a difficulty reduction is shown as a function of percentage of task completion (100% = 60 minutes) and intervention type. Difficulty reduction was modelled as a function of task completion bin (5% bins). Error ribbons represent 95% confidence intervals. MM = Math-Memory, ST = Modified Incongruent Stroop, DB = Time Load Dual-Back.

B.6 Supplementary References

- Aiken, L. S., Mistler, S. A., Coxe, S., & West, S. G. (2015). Analyzing count variables in individuals and groups: Single level and multilevel models. *Group Processes & Intergroup Relations*, 18(3), 290–314. <https://doi.org/10.1177/1368430214556702>
- Borragán, G., Slama, H., Bartolomei, M., & Peigneux, P. (2017). Cognitive fatigue: A Time-based Resource-sharing account. *Cortex*, 89, 71–84. <https://doi.org/10.1016/j.cortex.2017.01.023>
- Brooks, M. E., Kristensen, K., Benthem, K. J. van, Magnusson, A., Berg, C. W., Nielsen, A., Skaug, H. J., Mächler, M., & Bolker, B. M. (2017). glmmTMB Balances Speed and Flexibility Among Packages for Zero-inflated Generalized Linear Mixed Modeling. *The R Journal*, 9(2), 378–400. <https://doi.org/10.32614/RJ-2017-066>
- Fox, J., & Weisberg, S. (2019). *An R companion to applied regression* (Third edition). Sage.
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- Michielsen, H. J., De Vries, J., & Van Heck, G. L. (2003). Psychometric qualities of a brief self-rated fatigue measure: The Fatigue Assessment Scale. *Journal of Psychosomatic Research*, 54(4), 345–352. [https://doi.org/10.1016/S0022-3999\(02\)00392-6](https://doi.org/10.1016/S0022-3999(02)00392-6)
- O’Keeffe, K., Hodder, S., & Lloyd, A. (2020). A comparison of methods used for inducing mental fatigue in performance research: Individualised, dual-task and short duration cognitive tests are most effective. *Ergonomics*, 63(1), 1–12. <https://doi.org/10.1080/00140139.2019.1687940>
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2022). Slowed reaction times in cognitive fatigue are not attributable to declines in motor preparation. *Experimental Brain Research*, 240(11), 3033–3047. <https://doi.org/10.1007/s00221-022-06444-1>
- Peters, K. J., Maslovat, D., & Carlsen, A. N. (2024). Visual perceptual processing is unaffected by cognitive fatigue. *Consciousness and Cognition*, 119, 103666. <https://doi.org/10.1016/j.concog.2024.103666>
- Staiano, W., Romagnoli, M., Salazar Bonet, L. R., & Ferri-Caruana, A. (2024). Adaptive cognitive tasks for mental fatigue: An innovative paradigm for cognitive loading in human performance. *Journal of Science and Medicine in Sport*, 27(12), 883–889. <https://doi.org/10.1016/j.jsams.2024.08.199>
- Toth, A. J., Kowal, M., & Campbell, M. J. (2019). The Color-Word Stroop Task Does Not Differentiate Cognitive Inhibition Ability Among Esports Gamers of Varying Expertise. *Frontiers in Psychology*, 10. <https://doi.org/10.3389/fpsyg.2019.02852>

Wiley, K., Berger, P., Friehs, M. A., & Mandryk, R. L. (2024). Measuring the Reliability of a Gamified Stroop Task: Quantitative Experiment. *JMIR Serious Games*, 12(1), e50315. <https://doi.org/10.2196/50315>

Appendix C. Supplementary Material for Chapter 6

C.1 Supplementary Methods

C.1.1 Baseline Lifestyle Questionnaire

Participants completed a brief questionnaire by indicating the number of hours of sleep in the prior 24h, the number of hours since waking, whether there was caffeine intake in the prior 12h, whether any mentally challenging tasks had been completed since waking, and whether any physical activity had been completed since waking.

C.1.2 tVNS Side-Effect Questionnaire

Participants completed a side-effect questionnaire using paper and pen to conclude each testing session. This involved rating the following possible symptoms on a discrete scale of 0-10: headache, dizziness, nausea, ear pain, stinging, burning, itching, pressure under the electrodes, and general discomfort (Badran et al., 2019; Jacobs et al., 2015).

C.2 Supplementary Analyses

Baseline differences in pre-questionnaire variables were assessed across testing sessions.

Continuous baseline variables were analysed using linear mixed-effect models (package: *lme4*) (Bates et al., 2015), and categorical variables were analysed using binomial generalized linear mixed effects models (package: *glmmTMB*; McGillicuddy et al., 2025).

Premotor and displacement RT analyses including all 4 testing blocks (2 blocks pre-intervention, 2 blocks post-intervention) were completed in the same fashion as the 2-testing block analysis outlined in the manuscript (*Chapter 6.5*).

Cognitive task performance was described using the number of correctly recalled letters, the number of correct math responses, the median math RT on each trial, and the stimulus display interval length (which was modified based on performance accuracy throughout the

cognitive task). Beta-binomial generalized linear mixed models (GLMMs; package: *glmmTMB*) were used to analyse the number of correctly inputted letters and correct math responses over time (McGillycuddy et al., 2025). This approach was chosen to account for evidence of greater trial-to-trial variability than would be expected under a standard binomial distribution. Linear mixed-effect models (package: *lme4*) were used to assess changes in median RT of math responses and changes in display interval length over time (Bates et al., 2015). *Emtrends* (package: *emmeans*) was used for post hoc comparisons of cognitive task performance slopes between stimulation conditions (Lenth et al., 2021).

Stimulation side-effects (headache, dizziness, nausea, ear pain, stinging, burning, itching, pressure, general discomfort, and overall/composite severity) were analysed to assess both side-effect prevalence and severity by stimulation condition. Prevalence of each side-effect was first analysed using binomial GLMMs (package: *glmmTMB*) where responses were coded as presence (>0) versus absence ($=0$) of the side-effect (McGillycuddy et al., 2025). Next, side-effect severity was analysed conditional on side-effect presence (i.e., only non-zero ratings were considered) using gaussian GLMMs, to quantify difference in side-effect intensity among those who reported experiencing each side-effect.

C.3 Supplementary Results

C.3.1 Baseline Lifestyle Measures

Most lifestyle/demographic metrics did not significantly vary between testing sessions at baseline, including hours of sleep ($F(1, 15) = 3.40, p = .085$; $M_{\text{Active}} = 7.37\text{h}$, $SD = 1.47\text{h}$; $M_{\text{sham}} = 6.43\text{h}$, $SD = 2.07\text{h}$), hours since waking ($F(1, 14) = 2.57, p = .132$; $M_{\text{Active}} = 3.83\text{h}$, $SD = 2.09\text{h}$; $M_{\text{sham}} = 3.07\text{h}$, $SD = 1.76\text{h}$), and whether there was recent caffeine intake ($\chi^2(1) = 0.00, p > .999$; n active: 14 no, 1 yes; n sham: 1 no, 14 yes), or mental activity ($\chi^2(1) = 1.88, p = .171$; n active:

11 no, 4 yes; n sham: 14 no, 1 yes). The probability of recent physical activity did differ between testing sessions ($\chi^2(1) = 5.38, p = .020$) such that there was a slightly higher probability of recent physical activity prior to the testing session with sham stimulation (n active: 9 no, 6 yes; n sham: 12 no, 3 yes). However, the difference between testing sessions assessed via estimated marginal probabilities was not significant ($p = .807$), suggesting that the overall model effect was likely sensitive to sparse binary data. Thus, it was concluded that the probability of physical activity likely did not differ meaningfully between testing sessions.

C.3.2 Premotor and Displacement RT

Premotor RT was not significantly influenced by the main effect of testing block when all 4 testing blocks considered ($F(3, 2560) = 1.80, p = .145$) or stimulus condition ($F(1, 13) = 0.70, p = .417$). However, there was a significant interaction between testing block and stimulus condition ($F(3, 2560) = 2.88, p = .035$; Fig. C.1a). Post hoc contrasts showed that premotor RT did not differ significantly by block in the session with sham stimulation (all $p > .999$). In the session with active stimulation, the difference between block 2 (pre-intervention) and block 3 (post-intervention) approached significance ($\Delta = -7.51$ ms, 95% CI $[-15.35, 0.34], p = .058$). The difference between block 3 (post-intervention) and block 4 (post-intervention) also approached significance ($\Delta = +7.74$ ms, 95% CI $[-0.20, 15.67], p = .058$).

Displacement RT was not significantly affected by the main effect of testing block when all 4 blocks were considered ($F(3, 2532) = 0.337, p = .798$) or stimulus condition ($F(1, 13) = 0.099, p = .759$), but there was a significant interaction between testing block and stimulus condition ($F(3, 2532) = 2.85, p = .036$; Fig. C.1b). Post hoc contrasts showed no significant differences between testing blocks was observed within the sham or active stimulation condition (all $p > .325$).

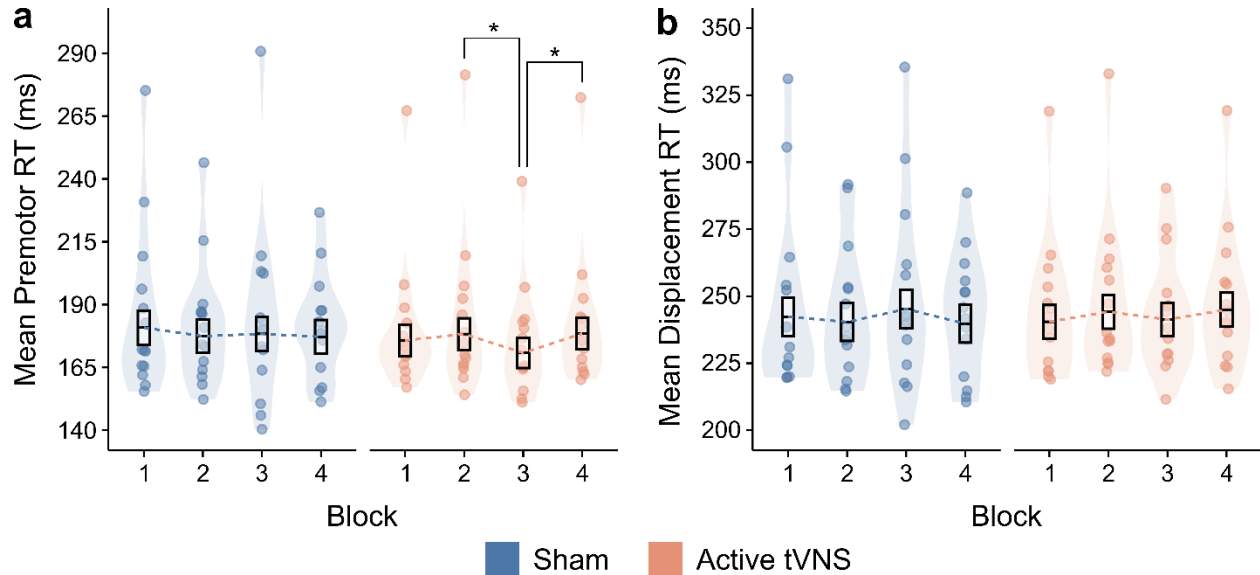


Fig. C.1 Reaction time by testing block. (a) Premotor and (b) displacement reaction time (RT, ms) are shown by testing block (pre-intervention = block 1-2, post-intervention = block 3-4) and stimulation condition (active, sham). Violin plots show the distribution of individual values, with points representing individual participant means. Black outlined boxes indicate model-predicted means with the limits showing *SE*. * indicates p -value < .100.

C.3.3 Cognitive Task Performance

The number of correctly recalled letters did not significantly change over the cognitive task (i.e., by trial number; $\chi^2(1) = 0.86, p = .353$) nor was there a significant stimulation condition x trial number interaction ($\chi^2(1) = 1.07, p = .300$). However, there was significant, overall effect of stimulation condition ($\chi^2(1) = 16.49, p < .001$). More specifically, letter recall accuracy was modestly higher throughout the cognitive intervention with sham stimulation compared to active, with an estimated difference of 6.9 percentage points (95% CI [3.6, 10.2]; Fig. C.2a).

Math problem accuracy was not significantly affected by stimulation condition ($\chi^2(1) = 1.50, p = .221$), or by the stimulation condition x trial number interaction ($\chi^2(1) = 1.92, p = .165$).

The main effect of trial number approached significance ($\chi^2(1) = 3.28, p = .070$) suggesting slight improvement in math performance over time, such that accuracy improved by 0.11 percentage points per trial (95% CI [-0.01, 0.23]; Fig. C.2b).

Median math RT was significantly impacted by trial number ($F(1, 15) = 8.62, p = .010$), becoming faster as the task progressed ($\Delta = -3.62$ ms per trial, 95% CI [-6.24, -0.99]). There was also a significant main effect of stimulation condition ($F(1, 1569) = 3.95, p = .047$), such that responses were overall slower when active stimulation was applied compared to sham ($\Delta = +45.1$ ms, 95% CI [17.7, 72.5]). The interaction between stimulation type and trial number was not significant ($F(1, 1571) = 0.20, p = .656$; Fig. C.2c).

The display interval length was significantly affected by stimulus condition ($F(1, 1569) = 6.11, p = .014$), trial number (i.e., time; $F(1, 15) = 5.78, p = .030$), and by the interaction of stimulus condition and trial number ($F(1, 1570) = 4.05, p = .044$). Post hoc comparisons showed a significantly steeper slope (i.e., a faster increase in display time) with active stimulation (slope = +22 ms per trial) compared to sham stimulation (slope = +16 ms per trial; Δ slope = 6.01 ms per trial, 95% CI [-0.15, 11.9], $p = 0.044$; Fig. C.2d). Note that an increase in display time is indicative of the adaptive cognitive task becoming easier in response to overall performance (letter and math accuracy) below 85%.

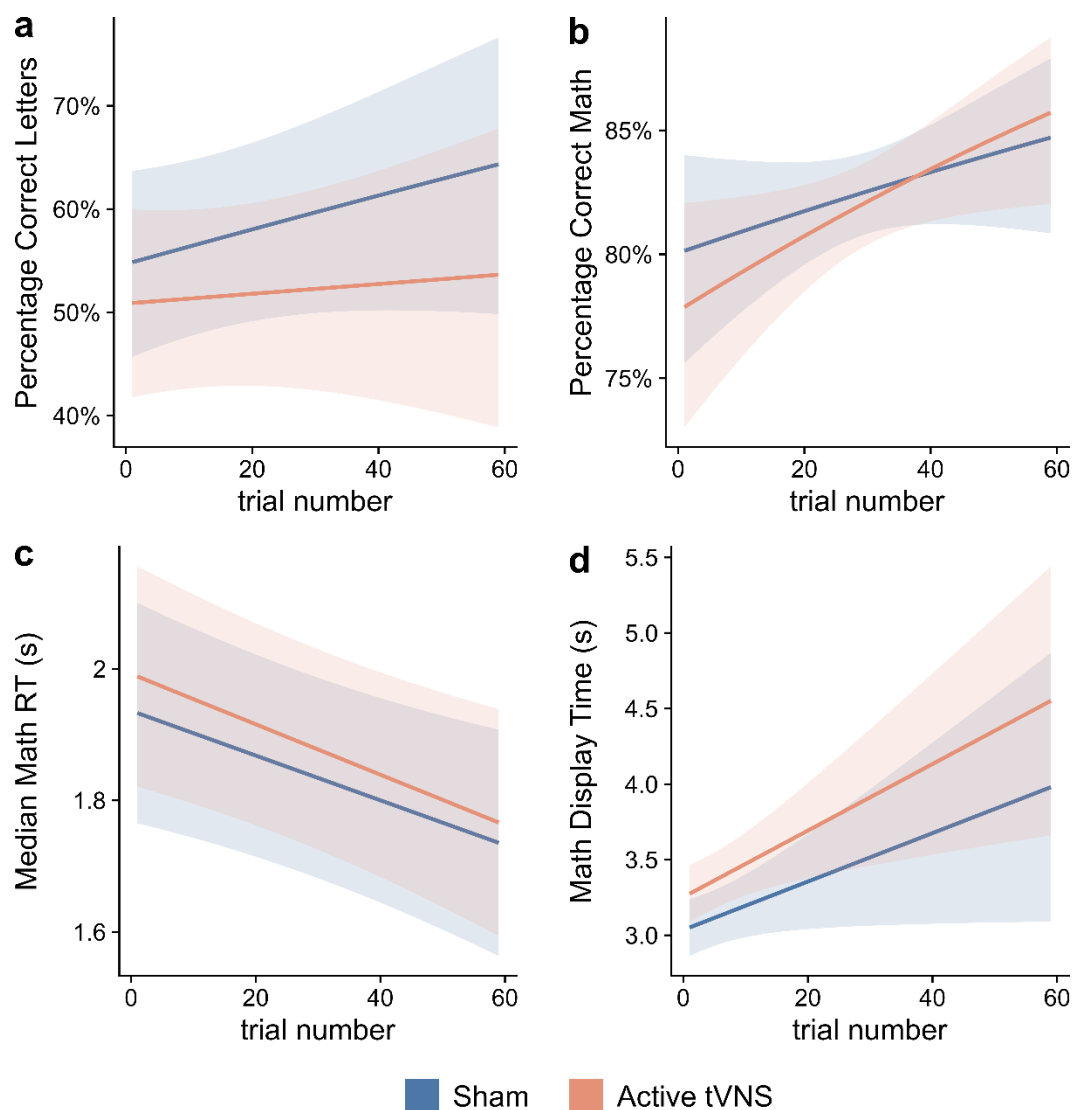


Fig. C.2 Math-Memory cognitive task performance metrics. Performance metrics are shown by trial number (time) and stimulation condition (active, sham). Plots show model predicted mean trajectories in performance over time for (a) Percentage of letters correctly remembered, (b) percentage of math problems correctly completed, (c) median reaction time (RT) of completed math problems, and (d) math problem display time. Shaded regions show 95% confidence intervals.

C.3.4 tVNS Side Effects

Most reported side effects were mild (less than 2 on a 10-point scale) and did not differ between stimulation conditions (see Fig. C.3 and Table C.1). The prevalence of headache as a side-effect was unaffected by stimulus type (n active = 7, n sham = 6). Among those reporting headache as a symptom, the effect of stimulus type on symptom intensity approached significance ($p = .063$), such that it was slightly higher with sham stimulation ($\Delta = 1.11$, 95% CI [1.86, 0.06]). The prevalence of dizziness as a side-effect was unaffected by stimulus type (n active = 3, n sham = 1); there was an inadequate number of dizziness reports to explore symptom intensity. Similarly, only two participants reported nausea as a side-effect (n active = 1, n sham = 1), thus statistics for this variable were incalculable. Reported ear pain was more common (n active = 6, n sham = 5), however its prevalence was not significantly affected by stimulus condition, nor was its reported intensity. Stinging under electrodes was a commonly reported side-effect (n active = 9, n sham = 9), but its prevalence did not vary by stimulus condition, nor did its reported intensity. The prevalence of burning under the electrodes was also equal among stimulus types (n active = 4, n sham = 4) and did not vary in reported intensity between stimulus conditions. Prevalence of pressure under the electrodes was not significantly affected by stimulation condition (n active = 6, n sham = 7), nor was the severity of this side-effect. General discomfort did not differ between stimulation conditions in its prevalence (n active = 8, n sham = 5) or severity.

Only the prevalence of itching near the electrodes was significantly impacted by stimulus condition, such that it was slightly more common with active stimulation (n active = 6, n sham = 4). The reported severity of itching did not differ between stimulation types.

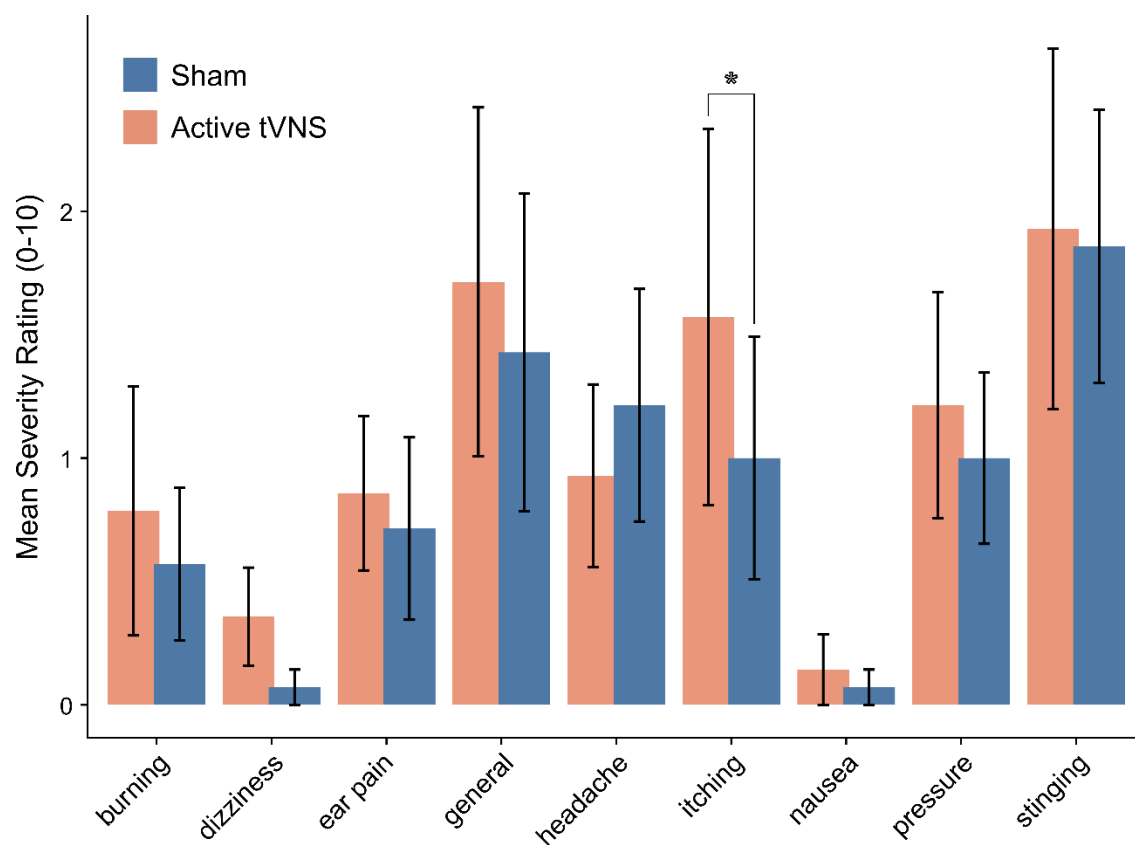


Fig. C.3 Average tVNS side-effect ratings (0-10) by stimulation condition (active, sham). Error bars indicate standard deviation. * indicates p -value $< .050$.

Table C.1 Effect of stimulation condition on reported side-effect prevalence and intensity. NA indicates cases where side-effects were reported too infrequently for stable model estimation. * indicates a p -value approaching significance, ** indicates a significant p -value.

	Prevalence		Intensity	
	χ^2	p	χ^2	p
Headache	0.18	.670	3.46	0.063*
Dizziness	1.07	.302	NA	NA
Nausea	NA	NA	NA	NA
Ear Pain	0.18	.670	0.04	.840
Stinging	0.00	1.00	0.07	.793
Burning	0.00	1.00	0.38	.540
Pressure	0.44	.510	2.53	.112
Itching	5.32	.021**	0.12	.734
General Discomfort	0.61	.437	0.53	.468

C.4 Supplementary References

- Badran, B. W., Yu, A. B., Adair, D., Mappin, G., DeVries, W. H., Jenkins, D. D., George, M. S., & Bikson, M. (2019). Laboratory Administration of Transcutaneous Auricular Vagus Nerve Stimulation (taVNS): Technique, Targeting, and Considerations. *Journal of Visualized Experiments : JoVE*, (143), 10.3791/58984. <https://doi.org/10.3791/58984>
- Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software*, 67, 1–48. <https://doi.org/10.18637/jss.v067.i01>
- Jacobs, H. I. L., Riphagen, J. M., Razat, C. M., Wiese, S., & Sack, A. T. (2015). Transcutaneous vagus nerve stimulation boosts associative memory in older individuals. *Neurobiology of Aging*, 36(5), 1860–1867. <https://doi.org/10.1016/j.neurobiolaging.2015.02.023>
- Lenth, R. V., Buerkner, P., Herve, M., Love, J., Riebl, H., & Singmann, H. (2021). *emmeans: Estimated Marginal Means, aka Least-Squares Means* (Version 1.7.0) [Computer software]. <https://CRAN.R-project.org/package=emmeans>
- McGillycuddy, M., Popovic, G., Bolker, B. M., & Warton, D. I. (2025). Parsimoniously Fitting Large Multivariate Random Effects in glmmTMB. *Journal of Statistical Software*, 112, 1–19. <https://doi.org/10.18637/jss.v112.i01>

Appendix D. Description of Cognitive Intervention Performance

D.1 Summary

This section provides a descriptive overview of participant performance on the cognitively fatiguing interventions. Table D.1 provides descriptive statistics for Math-Memory intervention performance across experiments. Fig. D.1-D.7 visually describe performance on the Math-Memory intervention across experiments. Table D.2 provides descriptive statistics for the Stroop and Time Load Dual-Back interventions in Experiment 3. Fig. D.8 and Fig. D.9 visually describe performance on the Stroop and Time Load Dual-Back interventions in Experiment 3.

D.2 Tables and Figures

Table D.1 Descriptive statistics for Math-Memory intervention performance across experiments;

Letter display duration data were not included for Exp. 1 & 2 as it was not varied.

	Min	Max	Median	Mean	SD
<i>Proportion Letters Correct</i>					
Experiment 1	0.00	1.00	0.71	0.67	0.31
Experiment 2	0.00	1.00	1.00	0.78	0.31
Experiment 3	0.00	1.00	0.57	0.55	0.36
Experiment 4	0.00	1.00	0.71	0.63	0.33
Experiment 5 (active)	0.00	1.00	0.57	0.52	0.36
Experiment 5 (sham)	0.00	1.00	0.57	0.59	0.34
<i>Proportion Math Correct</i>					
Experiment 1	0.58	1.00	0.95	0.94	0.06
Experiment 2	0.23	1.00	0.95	0.93	0.08
Experiment 3	0.00	1.00	0.84	0.77	0.22
Experiment 4	0.00	1.00	0.85	0.83	0.12
Experiment 5 (active)	0.22	1.00	0.84	0.82	0.12
Experiment 5 (sham)	0.20	1.00	0.83	0.82	0.13
<i>Letter Display Duration (seconds)</i>					
Experiment 3	0.22	2.76	1.17	1.28	0.47
Experiment 4	0.30	2.76	1.06	1.24	0.49
Experiment 5 (active)	0.41	1.76	1.29	1.40	0.50
Experiment 5 (sham)	0.20	2.51	1.17	1.25	0.51

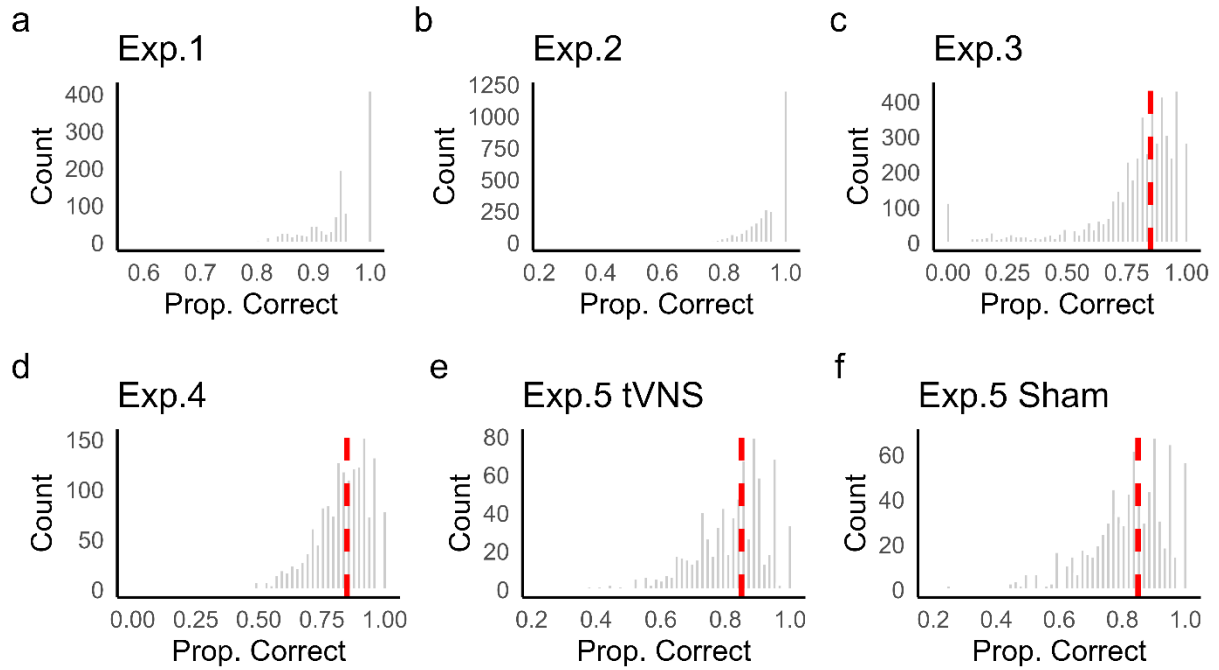


Fig. D.1 Histograms of the proportion of math problems correctly completed in the Math-Memory intervention by experiment. Red dotted lines indicate the target performance level on adaptive versions of the task (proportion correct of 0.85).

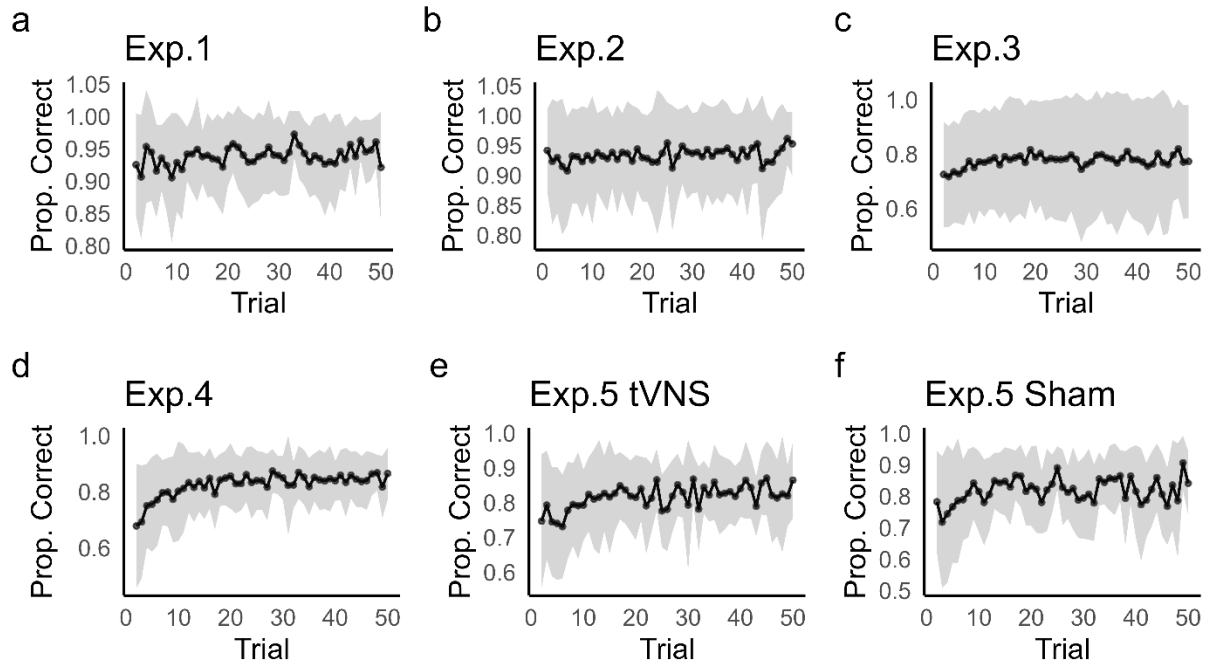


Fig. D.2 Average proportion of math problems correctly completed in the Math-Memory intervention over time (trial number) by experiment. Shaded regions show *SD*. Data are averaged over participants. Note that subjects may have varied in the exact number of trials completed, thus trial number was truncated to 50 to show data representative of the sample.

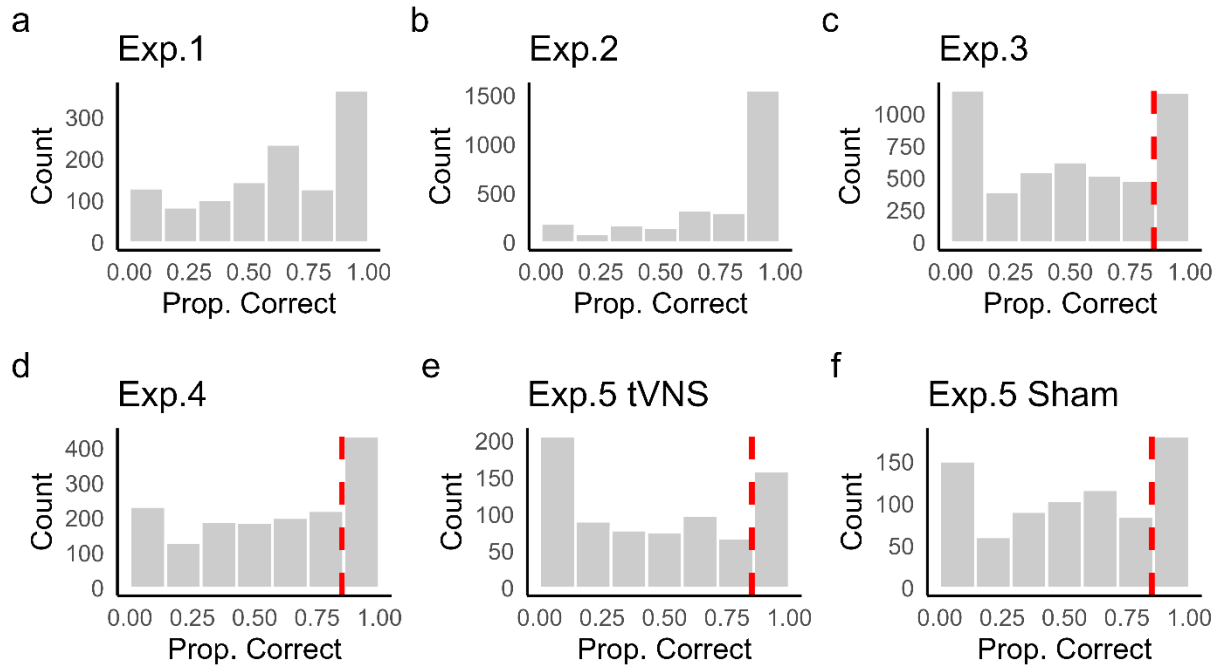


Fig. D.3 Histograms of the proportion of letters correctly remembered in the Math-Memory intervention by experiment. Red dotted lines indicate the target performance level on adaptive versions of the task (proportion correct of 0.85).

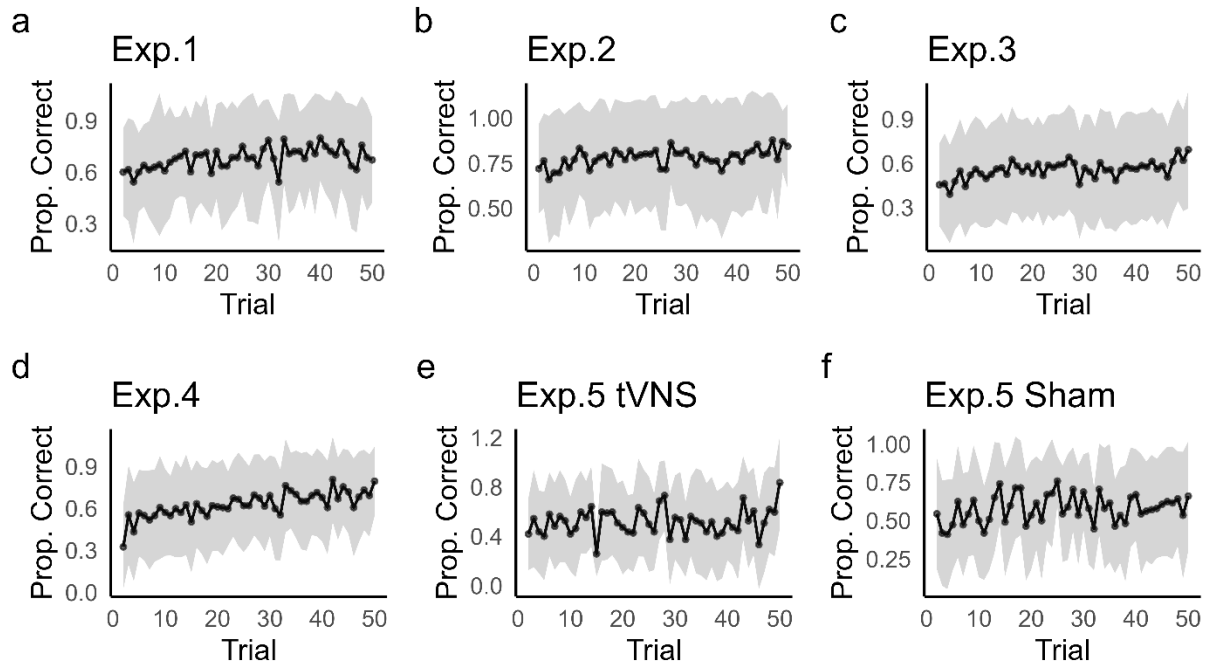


Fig. D.4 Average proportion of letters correctly remembered in the Math-Memory intervention over time (trial number) by experiment. Shaded regions show *SD*. Data are averaged over participants. Note that subjects may have varied in the exact number of trials completed, thus trial number was truncated to 50 to show data representative of the sample.

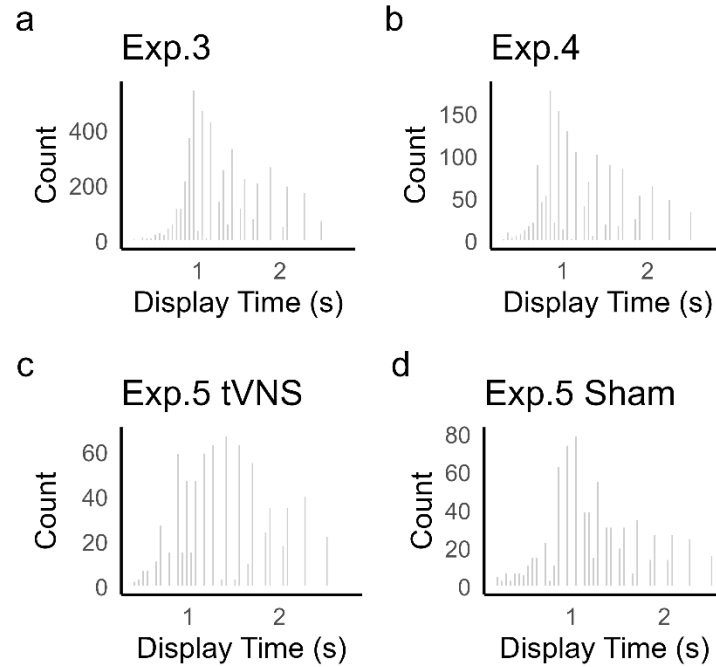


Fig. D.5 Histograms of the letter stimuli display durations in the Math-Memory intervention by experiment. Experiments 1 and 2 were not included as stimulus display time was not varied.

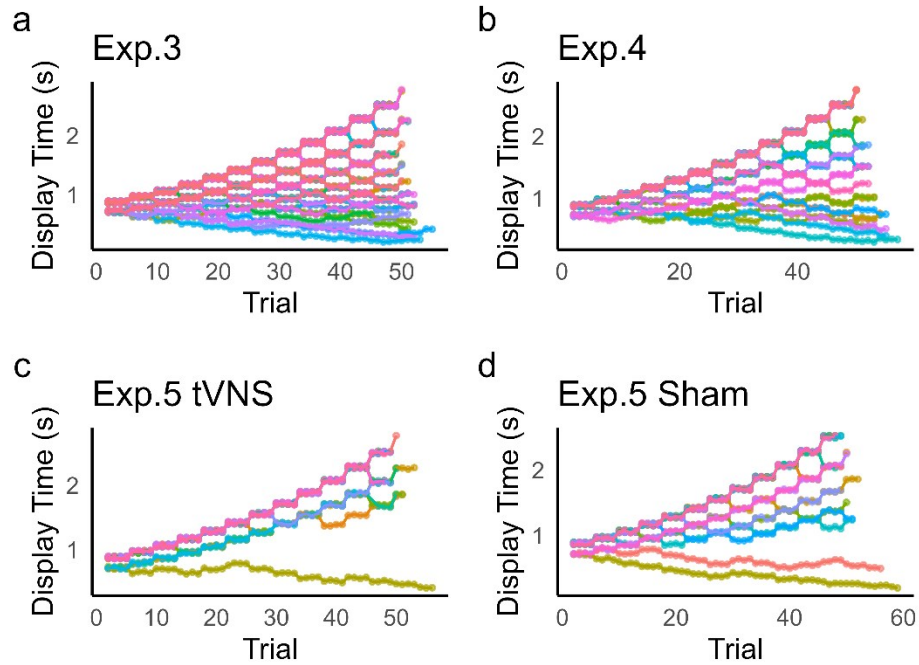


Fig. D.6 Letter stimuli display durations in the Math-Memory intervention over time (trial number) by experiment. Colours show different participants. Experiments 1 and 2 were not included as stimulus display time was not varied.

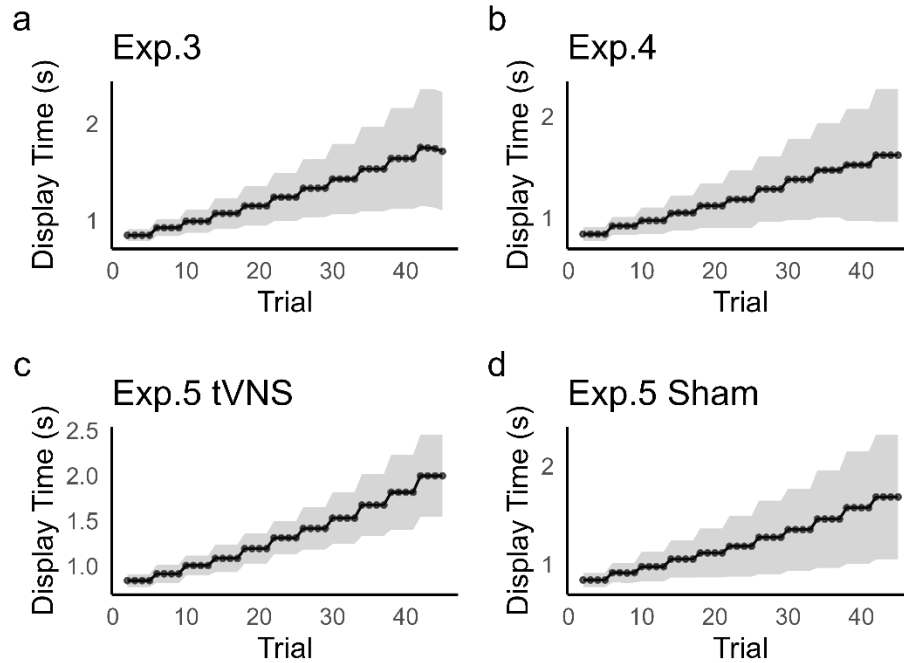


Fig. D.7 Average letter display durations in the Math-Memory intervention over time (trial number) by experiment. Shaded regions show *SD*. Experiments 1 and 2 were not included as stimulus display time was not varied. Data are averaged over participants. Note that subjects may have varied in the exact number of trials completed, thus trial number was truncated to 46 to show data representative of the sample.

Table D.2 Descriptive statistics for Modified Stroop (ST) and Time Load Dual-Back (DB) intervention performance in Experiment 3.

	Min	Max	Median	Mean	SD
<i>Proportion Correct</i>					
DB Intervention	0.00	1.00	1.00	0.88	0.18
ST Intervention	0.00	1.00	1.00	0.83	0.21
<i>Stim. Display Duration (s)</i>					
DB Intervention	0.47	3.54	1.05	1.10	0.39
ST Intervention	0.56	6.82	1.20	1.34	0.70

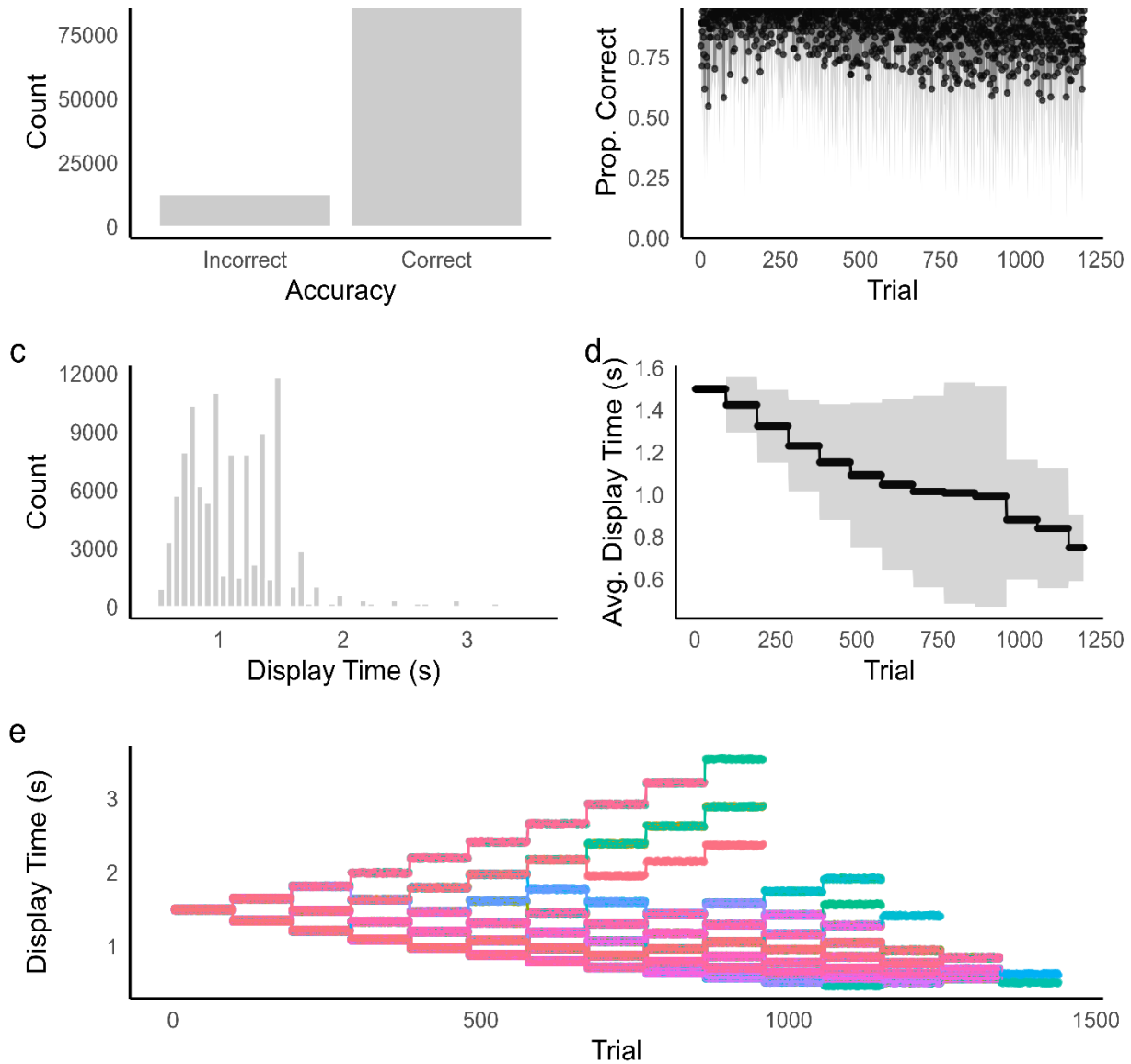


Fig. D.8 Performance on the Time Load Dual-Back (DB) intervention in Experiment 3. (a) Number of correct and incorrect responses made. (b) Proportion of correct responses over time (trial number) with shaded regions showing *SD*. (c) Histogram of letter display durations (s). (d) Average stimulus display duration over time (trial number) with shaded regions showing *SD*. (e) Stimulus display durations over time (trial number), with colours depicting different participants. Note that subjects may have varied in the exact number of trials completed, thus trial number was truncated to 1200 for panels b and d to show data representative of the sample.

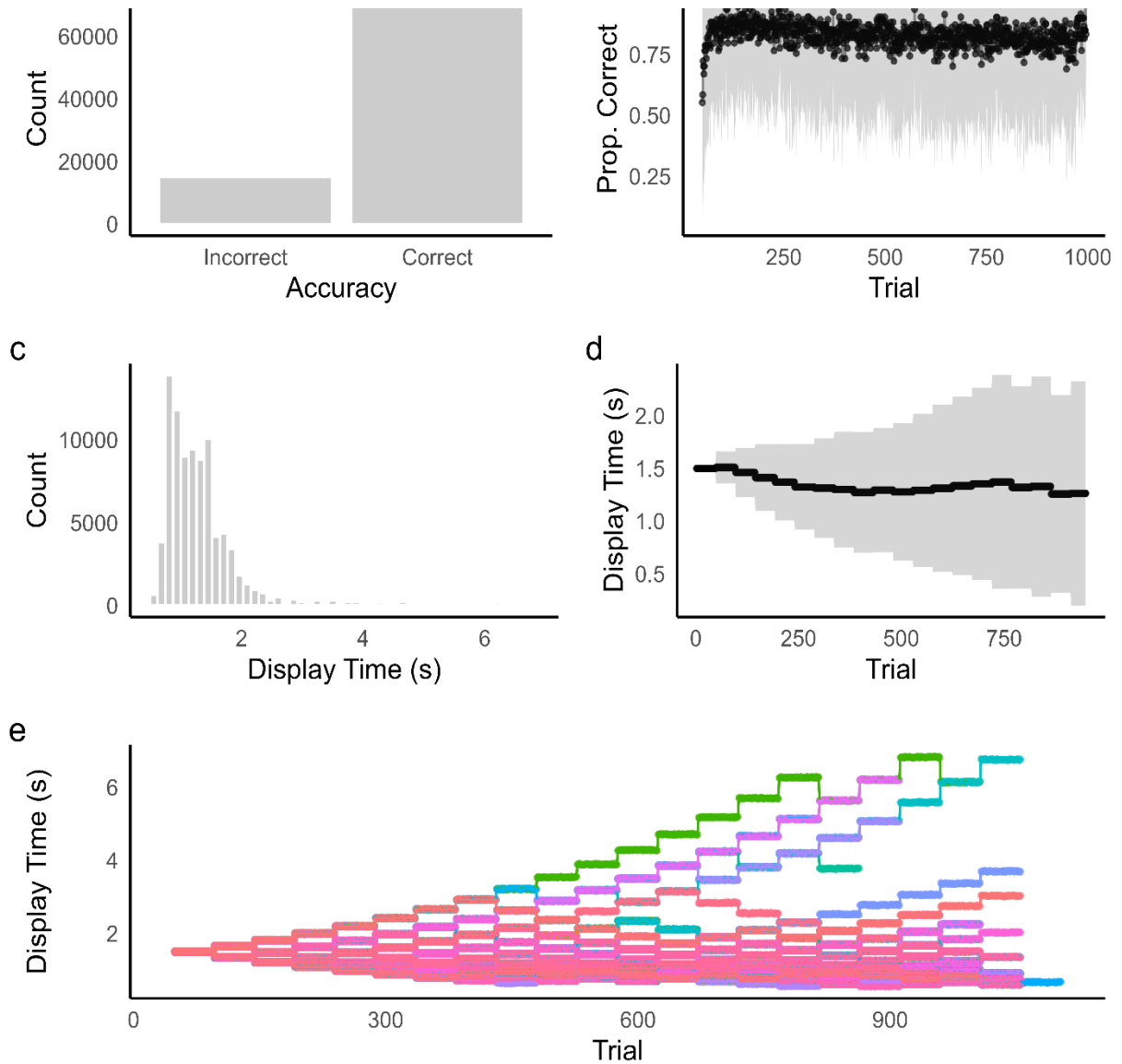


Fig. D.9 Performance on the Modified Stroop (ST) intervention in Experiment 3. (a) Number of correct and incorrect responses made. (b) Proportion of correct responses over time (trial number) with shaded regions showing *SD*. (c) Histogram of letter display durations (s). (d) Average stimulus display duration over time (trial number) with shaded regions showing *SD*. (e) Stimulus display durations over time (trial number), with colours depicting different participants. Note that subjects may have varied in the exact number of trials completed, thus trial number was truncated to 950 for panels b and d to show data representative of the sample.

Appendix E. Materials Used Across Experiments

E.1 Pre-Session Lifestyle Questionnaire

Questionnaire of basic demographic and lifestyle factors. Participants completed this questionnaire prior to each session of all studies with the exception of Experiment 4. Some details of the questionnaire varied by experiment.

Pre-Study Questionnaire

Please respond to the following questions by selecting and/or writing your response. If a question does not apply, leave it blank or write “NA”.

1. What is your sex assigned at birth?	☐ MALE ☐ FEMALE ☐ PREFER NOT TO SAY
2. What is your age (in years)?	_____ YEARS
3. Would you consider yourself to be right-handed, left-handed, or ambidextrous	☐ RIGHT ☐ LEFT ☐ AMBIDEXTROUS
4. How many hours of sleep have you had in the last 24 hours?	_____ HOURS
5. Would you rate last night's quality of sleep as normal, better than normal, or worse than normal?	☐ NORMAL ☐ BETTER ☐ WORSE
6. How many hours has it been since you woke up from sleep?	_____ HOURS
7. Have you consumed food or drink containing caffeine in the last 12 hours?	☐ YES ☐ NO
8. If you replied YES to the previous question, please indicate what caffeinated food or drink was consumed (e.g., coffee)	_____
9. Please also indicate what time you consumed the caffeinated item	_____ AM/PM
10. Please also indicate how much caffeinated food or drink was consumed (e.g., 1 large cup)	_____
11. Have you completed any mentally challenging tasks since waking up (e.g., studying, writing)	☐ YES ☐ NO
12. If you replied YES to the previous question, please indicate how much time you spent on the mental task	_____ HOURS
13. Please also indicate what time you completed the mental task	_____ AM/PM

14. Have you completed any physical activity since waking up (e.g., brisk walk, biking)	☐ YES ☐ NO
15. If you replied YES to the previous question please indicate how much time you spent on the physical activity	_____ MINUTES
16. Please also indicate what time you completed the physical activity	_____ AM/PM

NAME: _____

DATE: _____

TIME: _____

ISPR NUMBER: _____

E.2 Video Descriptions of Cognitive Interventions

Video description of the cognitively fatiguing interventions are available in English and French at [OSF: <https://doi.org/10.17605/OSF.IO/ZRSYU>].

Appendix F. Trial Counts

Tables displaying the mean and range of the number of trials included within experiment, variable, and condition.

Table F.1 By-subject and condition trial count: mean and range of reaction time (SCM+ and Control) in Experiment 1.

Intervention	Pre / Post	Stimulus	Trial Count Average	Trial Count Range
CF	Pre	Control	28.13	24 – 30
CF	Post	Control	26.75	23 – 30
CF	Pre	SCM+	5.81	0 – 10
CF	Post	SCM+	6.06	0 – 10
CTL	Pre	Control	27.31	23 – 30
CTL	Post	Control	26.44	22 – 29
CTL	Pre	SCM+	6.56	0 – 10
CTL	Post	SCM+	5.75	0 – 10

*Note. $n(\text{total}) = 16$ participants; 2 participants contributed 0 trials with SCM+.

Table F.2 By-subject and condition trial count: mean and range of reaction time in Experiment 2.

Intervention	Pre / Post	Trial Count Average	Trial Count Range
CF	Pre	27.97	20 – 30
CF	Post	27.85	13 – 30
CTL	Pre	27.61	19 – 30
CTL	Post	27.66	18 – 30

*Note. $n(\text{total}) = 131$ data sets were retained for RT analyses, comprised of data from 107 unique participants; 24 participants completed both interventions. Trial counts are not presented for IT task responses because all IT task trials were retained in the final sample.

Table F.3 By-subject and condition trial count: mean and range of reaction time in Experiment 3.

Intervention	Pre / Post	RT Task Type	Trial Count Average	Trial Count Range
MM	Pre	Choice	36.95	10 – 40
MM	Post	Choice	36.58	12 – 40
MM	Pre	Go/No-Go	19.62	16 – 20
MM	Post	Go/No-Go	18.82	2 – 20
MM	Pre	Simple	18.45	1 – 20
MM	Post	Simple	17.78	8 – 20
ST	Pre	Choice	37.04	29 – 40
ST	Post	Choice	36.13	1 – 40
ST	Pre	Go/No-Go	19.64	15 – 20
ST	Post	Go/No-Go	19.01	9 – 20
ST	Pre	Simple	18.53	3 – 20
ST	Post	Simple	18.16	5 – 20
DB	Pre	Choice	37.02439	1 – 40
DB	Post	Choice	37.1125	29 – 40
DB	Pre	Go/No-Go	19.41463	11 – 20
DB	Post	Go/No-Go	18.91566	2 – 20
DB	Pre	Simple	18.79012	1 – 20
DB	Post	Simple	18.08537	5 – 20
NF	Pre	Choice	36.68421	7 – 40
NF	Post	Choice	36.08696	3 – 40
NF	Pre	Go/No-Go	19.31624	3 – 20
NF	Post	Go/No-Go	19.38793	10 – 20
NF	Pre	Simple	18.37719	2 – 20
NF	Post	Simple	17.90517	7 – 20

*Note. $n(\text{total}) = 402$ participants. “No-go” trials were not included in counts of Go/No-Go trials.

Table F.4 By-subject and condition trial count: mean and range for cognitive interventions in Experiment 3.

Intervention	Trial Count Average	Trial Count Range
DB	1222.86	864 – 1440
MM	47.57	25 – 55
ST	944.68	672 – 1056

*Note. $n(\text{total}) = 283$ participants.

Table F.5 By-subject and condition trial count: mean and range for response errors in Experiment 3.

Intervention	Pre / Post	RT Task Type	Trial Count Average	Trial Count Range
MM	Pre	Choice	4.03	1 – 40
MM	Post	Choice	5.33	1 – 40
MM	Pre	Go/No-Go	2.46	1 – 20
MM	Post	Go/No-Go	2.97	1 – 20
ST	Pre	Choice	3.21	1 – 40
ST	Post	Choice	3.01	1 – 38
ST	Pre	Go/No-Go	1.83	1 – 9
ST	Post	Go/No-Go	2.42	1 – 15
DB	Pre	Choice	3.68	1 – 40
DB	Post	Choice	4.12	1 – 40
DB	Pre	Go/No-Go	2.68	1 – 20
DB	Post	Go/No-Go	2.70	1 – 20
NF	Pre	Choice	4.35	1 – 40
NF	Post	Choice	4.36	1 – 40
NF	Pre	Go/No-Go	2.67	1 – 20
NF	Post	Go/No-Go	2.60	1 – 20

* $n(\text{total}) = 399$ participants.

Table F.6 By-subject and condition trial count: mean and range of premotor reaction time in Experiment 4.

Intervention	Pre / Post	TMS Timepoint	Trial Count Average	Trial Count Range
CF	Pre	Go-0ms	11.28	8 – 12
CF	Post	Go-0ms	10.84	0 – 12
CF	Pre	Go-150ms	10.66	7 – 12
CF	Post	Go-150ms	10.50	2 – 12
CF	Pre	Go-500ms	10.19	7 – 12
CF	Post	Go-500ms	9.69	2 – 12
CTL	Pre	Go-0ms	11.44	9 – 12
CTL	Post	Go-0ms	11.25	8 – 12
CTL	Pre	Go-150ms	10.31	8 – 12
CTL	Post	Go-150ms	10.44	8 – 12
CTL	Pre	Go-500ms	9.89	4 – 12
CTL	Post	Go-500ms	10.41	5 – 12

**Note.* $n(\text{total}) = 32$ participants. One participant contributed 0 trials to the CF, Post, Go-0ms condition.

Table F.7 By-subject and condition trial count: mean and range of displacement reaction time in Experiment 4.

Intervention	Pre / Post	TMS Timepoint	Trial Count Average	Trial Count Range
CF	Pre	Go-0ms	11.22	9 – 12
CF	Post	Go-0ms	10.91	0 – 12
CF	Pre	Go-150ms	10.72	7 – 12
CF	Post	Go-150ms	10.34	2 – 12
CF	Pre	Go-500ms	10.19	8 – 12
CF	Post	Go-500ms	9.91	2 – 12
CTL	Pre	Go-0ms	11.38	9 – 12
CTL	Post	Go-0ms	11.22	8 – 12
CTL	Pre	Go-150ms	10.38	8 – 12
CTL	Post	Go-150ms	10.47	8 – 12
CTL	Pre	Go-500ms	9.94	4 – 12
CTL	Post	Go-500ms	10.16	5 – 12

**Note.* $n(\text{total}) = 32$ participants. One participant contributed 0 trials to the CF, Post, Go-0ms condition.

Table F.8 By-subject and condition trial count: mean and range of resting motor-evoked potential amplitude in Experiment 4.

Intervention	Pre / Post	Trial Count Average	Trial Count Range
CF	Pre	9.09	0 – 10
CF	Post	9.31	0 – 10
CTL	Pre	9.34	4 – 10
CTL	Post	9.28	6 – 10

**Note.* $n(\text{total}) = 32$ participants. One participant contributed 0 trials in the CF, Pre condition, and one participant contributed 0 trials in the CF, Post condition.

Table F.9 By-subject and condition trial count: mean and range of preparatory motor-evoked potential amplitude in Experiment 4.

Intervention	Pre / Post	TMS Timepoint	Trial Count Average	Trial Count Range
CF	Pre	Go-0ms	10.50	0 – 12
CF	Post	Go-0ms	10.66	0 – 12
CF	Pre	Go-150ms	10.53	0 – 12
CF	Post	Go-150ms	10.66	0 – 12
CF	Pre	Go-500ms	10.69	0 – 12
CF	Post	Go-500ms	10.44	0 – 12
CTL	Pre	Go-0ms	10.44	1 – 12
CTL	Post	Go-0ms	10.66	1 – 12
CTL	Pre	Go-150ms	10.63	0 – 12
CTL	Post	Go-150ms	10.66	0 – 12
CTL	Pre	Go-500ms	10.69	0 – 12
CTL	Post	Go-500ms	10.59	1 – 12

**Note.* $n(\text{total}) = 32$ participants. Four participants contributed 0 trials for at least one condition combination. The number of participants with 0 trials was: CTL, Pre, Go-150ms ($n = 1$); CF, Pre, Go-0ms ($n = 1$); CF, Pre, Go-150ms ($n = 1$); CF, Pre, Go-500ms ($n = 1$); CF, Post, Go-0ms ($n = 2$); CF, Post, Go-150ms ($n = 2$); CF, Post, Go-500ms ($n = 2$); CTL, Pre, Go-150ms ($n = 1$); CTL, Pre, Go-500ms ($n = 1$); CTL, Post, Go-150ms ($n = 1$).

Table F.10 By-subject and condition trial count: mean and range of premotor reaction time in Experiment 5.

Intervention	Block	Trial Count Average	Trial Count Range
Active	1	23.57	20 – 25
Active	2	23.50	20 – 25
Active	3	22.93	19 – 25
Active	4	22.57	18 – 25
Sham	1	23.21	21 – 25
Sham	2	23.43	20 – 25
Sham	3	23.14	18 – 25
Sham	4	22.86	20 – 25

**Note.* $n(\text{total}) = 14$ participants; blocks 1-2 are pre-intervention, blocks 3-4 are post-intervention.

Table F.11 By-subject and condition trial count: mean and range of displacement reaction time in Experiment 5.

Intervention	Block	Trial Count Average	Trial Count Range
Active	1	23.29	18 – 25
Active	2	23.07	20 – 25
Active	3	22.57	19 – 25
Active	4	22.50	18 – 25
Sham	1	23.14	20 – 25
Sham	2	23.36	19 – 25
Sham	3	22.71	17 – 25
Sham	4	22.57	18 – 25

**Note.* $n(\text{total}) = 14$ participants; blocks 1-2 are pre-intervention, blocks 3-4 are post-intervention.

Table F.12 By-subject and condition trial count: mean and range of EMG burst magnitude (Q100) in Experiment 5.

Intervention	Pre / Post	Trial Count Average	Trial Count Range
Active	Pre	47.07	41 – 50
Active	Post	45.50	40 – 49
Sham	Pre	46.64	41 – 50
Sham	Post	46.00	40 – 49

**Note.* $n(\text{total}) = 14$ participants.

Table F.13 By-subject and condition trial count: mean and range of anticipatory responses in Experiment 5.

Intervention	Pre / Post	Trial Count Average	Trial Count Range
Active	Pre	3.63	1 – 7
Active	Post	2.58	0 – 7
Sham	Pre	2.25	0 – 5
Sham	Post	3.56	1 – 8

**Note.* $n(\text{total}) = 13$ participants; One participant contributed no anticipatory responses across any condition and was therefore excluded. Of the remaining participants, one contributed no trials in the Active, Post condition, and one contributed no trials in the Sham, Pre condition.

Appendix G. Certificates of Ethics Approval

Ethics approval certificates from the University of Ottawa Office of Research Ethics and Integrity are presented in order of Experiments 1-5.

Université d'Ottawa
Bureau d'éthique et d'intégrité de la recherche

03/07/2025
University of Ottawa
Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-06-22-7103
Titre du projet / Project Title	Assessing preparation and initiation of voluntary actions using intense stimuli.
Type de projet / Project Type	Recherche de professeur / Professor's research project
Statut du projet / Project Status	Renouvelé / Renewed
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	11/07/2022
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	10/07/2026

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Anthony CARLSEN	École des sciences de l'activité physique / School of Human Kinetics	Chercheur Principal / Principal Investigator
Caroline DUTIL	École des sciences de l'activité physique / School of Human Kinetics	Assistant de recherche / Research Assistant
Christin SADLER	École des sciences de l'activité physique / School of Human Kinetics	Assistant de recherche / Research Assistant
Elias DAHER	École des sciences de l'activité physique / School of Human Kinetics	Assistant de recherche / Research Assistant
Kathleen PETERS	École des sciences de l'activité physique / School of Human Kinetics	Assistant de recherche / Research Assistant

Conditions spéciales ou commentaires / Special conditions or comments

550, rue Cumberland, pièce 154 550 Cumberland Street, Room 154
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada

613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

23/06/2022

Université d'Ottawa

Bureau d'éthique et d'intégrité de la recherche

University of Ottawa

Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-06-22-7909
Titre du projet / Project Title	Investigating the effects of mild cognitive fatigue on sensorimotor processing
Type de projet / Project Type	Projet indépendant d'étudiant / Independent student project
Statut du projet / Project Status	Approuvé / Approved
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	23/06/2022
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	22/06/2023

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Kathleen PETERS	École des sciences de l'activité physique / School of Human Kinetics	Chercheur Principal / Principal Investigator
Anthony CARLSEN	École des sciences de l'activité physique / School of Human Kinetics	Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments

550, rue Cumberland, pièce 154 550 Cumberland Street, Room 154
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada

613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

26/01/2024

Université d'Ottawa

Bureau d'éthique et d'intégrité de la recherche

University of Ottawa

Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL**Numéro du dossier / Ethics File Number**

H-01-24-9961

Titre du projet / Project TitleInvestigating the effects of mild
cognitive fatigue on psychomotor
performance**Type de projet / Project Type**Thèse de doctorat / Doctoral
thesis**Statut du projet / Project Status**

Approuvé / Approved

Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)

26/01/2024

Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)

25/01/2025

Équipe de recherche / Research Team**Chercheur /
Researcher****Affiliation****Role**

Kathleen PETERS

École des sciences de l'activité physique / School of Human
KineticsChercheur Principal / Principal
Investigator

Anthony CARLSEN

École des sciences de l'activité physique / School of Human
Kinetics

Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments550, rue Cumberland, pièce 154 550 Cumberland Street, Room 154
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

02/12/2024

Université d'Ottawa

Bureau d'éthique et d'intégrité de la recherche

University of Ottawa

Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL**Numéro du dossier / Ethics File Number**

H-11-24-10794

Titre du projet / Project Title

Investigating the effects of mild cognitive fatigue on corticospinal excitability in a reaction time paradigm

Type de projet / Project Type

Thèse de doctorat / Doctoral thesis

Statut du projet / Project Status

Approuvé / Approved

Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)

02/12/2024

Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)

01/12/2025

Équipe de recherche / Research Team**Chercheur /
Researcher****Affiliation****Role**

Kathleen PETERS

École des sciences de l'activité physique / School of Human Kinetics

Chercheur Principal / Principal Investigator

Anthony CARLSEN

École des sciences de l'activité physique / School of Human Kinetics

Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments550, rue Cumberland, pièce 154
Ottawa (Ontario) K1N 6N5 Canada550 Cumberland Street, Room 154
Ottawa, Ontario K1N 6N5 Canada613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics

14/07/2025

Université d'Ottawa

Bureau d'éthique et d'intégrité de la recherche

University of Ottawa

Office of Research Ethics and Integrity

CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL**Numéro du dossier / Ethics File Number**

H-07-25-11721

Titre du projet / Project TitleEvaluating the use of
transcutaneous vagus nerve
stimulation to mitigate the
psychomotor impacts of cognitive
fatigue**Type de projet / Project Type**Thèse de doctorat / Doctoral
thesis**Statut du projet / Project Status**

Approuvé / Approved

Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)

14/07/2025

Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)

13/07/2028

Équipe de recherche / Research Team**Chercheur /
Researcher****Affiliation****Role**

Kathleen PETERS

École des sciences de l'activité physique / School of Human
KineticsChercheur Principal / Principal
Investigator

Anthony CARLSEN

École des sciences de l'activité physique / School of Human
Kinetics

Superviseur / Supervisor

Conditions spéciales ou commentaires / Special conditions or comments550, rue Cumberland, pièce 154 550 Cumberland Street, Room 154
Ottawa (Ontario) K1N 6N5 Canada Ottawa, Ontario K1N 6N5 Canada613-562-5387 • 613-562-5338 • ethique@uOttawa.ca / ethics@uOttawa.ca
www.recherche.uottawa.ca/deontologie | www.recherche.uottawa.ca/ethics