Neuroimaging of Endogenous Lapses of Responsiveness

Mohamed Hossameldin Zaky Abdou Mahmoud

A thesis presented for the degree of
Doctor of Philosophy
in
Electrical and Computer Engineering
at the
The University of Canterbury,
Christchurch, New Zealand

March 2022

Abstract

Attention lapses (ALs) and microsleeps (MSs) are complete lapses of responsiveness in which performance is completely disrupted for a short period of time, but consciousness is retained in the case of ALs. ALs are behaviourally different from MSs, as in an AL the eyes remain open whereas in a MS eyes are partially or completely closed. Both ALs and MSs can result in catastrophic consequences, especially in the transportation sector.

Research over the past two decades has investigated the AL and MS phenomena using behavioural and physiological means. However, both ALs and MSs need further investigation to separate the different types of ALs physiologically, and to explore the neural signature of MSs in relation to normal sleep and drowsiness. Hence, the objective of this project was to understand the underlying physiological substrates of endogenous (internal) ALs and MSs which could potentially result in differentiating types of ALs and provide more understanding of MSs.

Data from two previous Christchurch Neurotechnology Research Programme (*NeuroTech*™) studies (C and D) were combined resulting in a total of 40 subjects. During each session, subjects performed a 2-D continuous visuomotor tracking (CVT) task for 50 min (Study C) and 20 min (Study D). For each participant, tracking performance, eye-video, EEG, and fMRI were simultaneously collected. A human expert visually inspected the tracking performance and eye-video recordings to identify and categorize lapses of responsiveness for each participant.

Participants performed the 2-D CVT task without interruptions. The repetitive nature of the task and the lack of a motivational factor made the task monotonous and fatiguing. As a result, it was more likely to introduce boredom leading to task-unrelated thoughts (TUTs), which divides attention between the task and the internal thoughts unrelated to the task, also fatigue which will introduce a trend of vigilance decrement over time.

The project had hypotheses focusing on the changes in the brain’s activity compared to the baseline of good responsiveness tracking. We expected a decrease in dorsal attention network (DAN) activity during ALs due to a decoupling of attention from the external environment. Furthermore, we hypothesized that the ALs were due to involuntary mind-blanks. As such, we expected no change in default mode network (DMN) activity, as would have otherwise been expected if the ALs were due to mind-wandering. Functional connectivity (FC) of the brain was also investigated between the networks of interest which were the DMN, DAN, frontoparietal network (FPN), sensorimotor network (SMN), visual network (VSN), salience network (SN), eye-movement network (EMN), and working memory network (WMN), by analysing data from fMRI. EEG data were also used to perform analysis on ALs and MSs, by analysing changes in power in the delta, theta, alpha, beta, and gamma bands.

Voxel-wise fMRI throughout the whole brain, group-ICA, haemodynamic response (HR) over the regions of interest (ROIs), and FC analyses were performed to reveal the neural signature during ALs. In voxel-wise analysis, a significant increase in activity was found in two regions: the dorsal anterior cingulate cortex (dACC) and the supplementary motor area (SMA). The group-ICA analysis did not show any significant results but did show a trend of increased activity in an independent component (IC) that was spatially correlated with SMN.

Dynamic HR analysis was performed to further investigate findings from the voxel-wise analysis. Our results were not significant but there were strong trends of change. There was a trend of increased HR 7.5 s after the onset of the AL in the left intraparietal sulcus (IPS) of the DAN. There was also a decrease of 2.5 s before the onset of the AL in the right posterior parietal cortex (PPC) of the FPN. There was also an increase in the HR 5 s after the onset of the AL in the dACC of the SN. Finally, an increase in the HR 15 s before the onset of ALs in the left inferior parietal lobule (IPL) of the DMN is a major finding, as it is an indication that a lapse is about to happen. The HR analysis provided consistent findings with the voxel-wise analysis.

FC analysis showed increases in FC within all networks of interest during the ALs. On looking at FC between networks, there was an increase in FC between the DMN and the FPN, no change between the DAN and the FPN, a decrease in FC between the SMN and the FPN, and an increase in FC between the FPN and the VSN. The EMN had an increased FC with the DMN, while it had both increases and decreases in FC with the DAN. There was also an increase in FC between the SN and the DAN, and no change between the SN and the DMN. Finally, a decrease in FC was found between the WMN and the DMN. These findings indicate an overlap between decoupling due to ALs and the process of recovery from ALs.

The EEG analysis showed no significant change in the relative difference between average spectral power during ALs and their average baselines for any band of interest for ALs.

During MSs, there was a significant increase in power relative to responsive baselines in the delta, theta, alpha, beta, and gamma bands. However, we could not be completely sure that all motion-related artefacts had been removed. Hence, we investigated this further by removing the effect of the global signal, which left only an increase in gamma activity, in addition to a trend of decreased activity in the alpha band.

The significant increase in BOLD seen in the voxel-wise analysis is considered to represent the recovery of responsiveness following ALs. This was also seen in trends in group ICA and HR analyses. Overall, findings from the FC analysis show that, in addition to decoupling during ALs, and recovery from ALs, it is highly likely that the ALs during the 2-D CVT task were due to involuntary mind-blanks. This is supported by three major findings: (1) no significant increase in DMN activity in both voxel-wise and HR analyses, (2) the decrease in the HR in the FPN prior to the onset of the AL, and (3) the decrease in FC between the DMN and the WMN. This is further supported behaviourally by the short average duration of ALs (~ 1.7 s), in contrast to what would be likely during mind-wandering.

Finally, the significant results from the EEG analysis of MSs, agreed with the literature in delta, theta, and alpha bands. However, increased power in beta and gamma bands was an important finding. We consider this increased high-frequency activity reflects unconscious ‘cognitive’ activity during a MS aimed at restoring consciousness after having fallen asleep during an active task. This highlights a key behavioural and physiological difference between MSs and sleep. Even after removing the effect of the global signal, we still believe that MSs and sleep are physiologically different in the recovery process.

To summarize our key findings: (1) this is the first study to demonstrate that ALs during a continuous task are likely to be due to involuntary mind-blanks, (2) the increase in the HR in the DMN 15 s before the onset of AL could be a predictive signature of these lapses, and finally (3) MSs are physiologically different from sleep in terms of the recovery process.

This project has improved our understanding of endogenous ALs and MSs and taken us a step closer to accurate detection/prediction systems which can increase prevention of fatal accidents.

Dedication

This project is an essential step towards substantially reducing the adverse consequences of lapses of responsiveness, which will benefit road safety and help save lives.

Preface

This thesis is submitted for the degree of Doctor of Philosophy in Electrical and Electronic Engineering at the University of Canterbury. The research for this thesis was completed between March 2018 and December 2021 while I was enrolled in the Department of Electrical and Computer Engineering at the University of Canterbury. The work was carried out as part of the Christchurch Neurotechnology Research Programme at the New Zealand Brain Research Institute and was supervised by Professor Richard Jones, Dr. Reza Shoorangiz, Dr. Le Yang, and Dr. Govinda Poudel. I was supported by a University of Canterbury Doctoral Scholarship. Prof. Richard Jones kindly supported me to attend an Advanced Academic Writing course at Christchurch College of English Language in addition to the Computational Neuroscience course by Neuromatch Academy in July 2020, also, registration fees of EMBC20 and 21. Dr. Le Yang kindly funded me for an eight-month extension of my PhD. The New Zealand Brain Research Institute kindly funded me to attend the FSL course in Dunedin in February 2019.

CONTRIBUTION

In this project, I analysed data from studies C and D, which were acquired before by other researchers. My focus was on the attention lapses data, which had not been previously analysed. I performed voxel-wise, group ICA, haemodynamic response, and functional connectivity analyses using the fMRI data, in addition to source reconstruction analysis using the EEG data. Also, I performed EEG source reconstruction analysis on the microsleep data, which had not been done previously. However, the microsleep data had been heavily analysed by other researchers.

PUBLICATIONS

Conference papers

- Zaky, M. H., Shoorangiz, R., Poudel, G. R., Yang, L., & Jones, R. D. (2021). Investigating the neural signature of microsleeps using EEG. Proceedings of International Conference of IEEE Engineering in Medicine and Biology Society, 43, 6293-6296.
- Zaky, M. H., Shoorangiz, R., Poudel, G. R., Yang, L., & Jones, R. D. (2020). Neural correlates of attention lapses during continuous tasks. Proceedings of International Conference of IEEE Engineering in Medicine and Biology Society, 42, 3196-3199.

PRESENTATIONS

- July 2020, IEEE Engineering in Medicine and Biology Conference (EMBC), Montreal, Canada. Oral presentation (Virtual, pre-recorded).
- November 2021, IEEE Engineering in Medicine and Biology Conference (EMBC), Guadalajara, Mexico. Oral presentation (Virtual, pre-recorded).
- Visualize your thesis (VYT) 2020, and 2021 (where I won the people’s choice award). Link: https://www.youtube.com/watch?v=RauH-CjjthI
- Three-minute thesis (3MT) 2020, and 2021.
- Health Research Society of Canterbury (HRSC) poster expo 2020, and 2021.

Acknowledgements

I would like to start by thanking Allah for all the chances I got, and the challenges I had in my PhD journey (الحمدلله). I consider myself the luckiest student to be blessed with my supervisory team. They supported me with all the chances I got and helped me to pass all the challenges I went through in my PhD journey.

Prof. Richard gave me the opportunity to be in NZ doing my PhD under his supervision. He helped me in every single step since I first contacted him. His support was even beyond academic work; he helped me overcome the many problems I had on a personal level. He did not save any effort to teach me and guide me in my PhD work especially in writing. He is the best mentor I ever had in my life.

Dr. Reza, since my first day in NZBRI, was supporting me. I was able to fix most of the technical problems in my codes with his guidance, he helped me enhancing the way I think and analyse my data. On a personal level, he always gave me the needed advice at the right time. Thanks to Dr. Le and Dr. Govinda for sharing their insightful comments, technical expertise, and encouragement. My special thanks to Dr. Le for financially supporting me to extend my studies for eight months to be able to work on a very important part of my project and enhance my thesis.

I wish to thank my colleagues at NZBRI, for their friendship, feedback, and advice. I would like to thank Beth Alias, Dr. Michael MacAskill, and Dee Niles for all their help in getting my visas sorted after the many obstacles I had been facing. I would like to thank Dr. Mustafa Almuqbel and Dr. Tracy Melzer for their valuable suggestions and constructive advice during the initial phase of my research. I would like to thank Traci Stanbury for helping me prepare for the "Three Minute Thesis" competition. Finally, I would like to thank Emma Eason, Rebecca Lee, and the rest of my colleagues in NZBRI for being very supportive.

I would like also to thank Deborah Erueti from ECE, who was always there for my support in all UC matters, provide the advice and information, and even acting on my behalf when needed. She helped me sorting all the issues I contacted her for without me worrying about anything.

I would like to extend my thanks to my close friends Honey Htet Htet, Niebert Blair, Ben Wamamili, and Elaine Yeo who made my journey in NZ the best experience. I am very grateful for their friendship and support. Finally, I would like to thank my family for their continuous encouragement, support, and sacrifice throughout my life journey. I am so super grateful to my

parents who did their best so that I can achieve higher education levels. They were always the source of my power. I also wish to thank my sister and my brother-in-law for their constant encouragement.

Table of Contents

List of Abbreviations

ACC	Anterior cingulate cortex
AInsula	Anterior insula
AL	Attention lapse
BEM	Boundary element model
BOLD	Blood-oxygen-level dependent
CONN	Functional connectivity toolbox
CSF	Cerebral spinal fluid
CVT	Continuous visuomotor tracking
DAN	Dorsal attention network
DICS	Dynamic imaging of coherent sources
DIRE	Drowsiness-related impaired-responsiveness event
DMN	Default mode network
DOF	Degree of freedom
EEG	Electroencephalogram
eLORETA	Exact low-resolution electromagnetic tomography
EMN	Eye movement network
EPI	Echo-planar imaging
FC	Functional connectivity
FDR	False discovery rate
FEAT	fMRI expert analysis tool
FEF	Frontal eye field
FEM	Finite element model
FFT	Fast Fourier transform
fMRI	Functional magnetic resonance imaging
FPN	Frontoparietal attention network
FSL	FMRIB’s software library
GA	Gradient artefact
GLM	General linear model
GM	Grey matter
HR	Hemodynamic response

HRF	Hemodynamic response function
ICA	Independent component analysis
IFT	Inverse Fourier transform
IPL	Inferior parietal lobule
IPS	Intra-parietal sulcus
LCMV	Linear constraint minimum variance
LORETA	Low-resolution electromagnetic tomography
LPC	Lateral parietal cortex
LPFC	Lateral prefrontal cortex
MNE	Minimum norm estimates
MNI	Montreal Neurological Institute
MS	Microsleep
PA	Pulse artefact
PCC	Posterior cingulate cortex
PFC	Prefrontal cortex
PPC	Posterior parietal cortex
PVT	Psychomotor vigilance task
RF	Radio frequency
ROI	Region of interest
SART	Sustained attention to response task
SLC	Sensorimotor lateral cortex
sLORETA	Standard low-resolution electromagnetic tomography
SMA	Supplementary motor area
SMG	Sensorimotor gyrus
SMN	Sensorimotor network
SN	Salience network
SNR	Signal-to-noise ratio
SSC	Sensorimotor superior cortex
STM	Short-term memory
TE	Echo time
TFCE	Threshold free cluster enhancement
TR	Repetition time

TUT	Task-unrelated thought
VBIP	Voluntary behaviour impacting performance
VLC	Visual lateral cortex
VMC	Visual medial cortex
VOC	Visual occipital cortex
VSN	Visual network
WM	White matter
WMC	Working memory capacity
WMN	Working memory network
WT	Wavelet transform

Chapter 1: Introduction

1.1 Motivation

When doing a task that requires an intensive focus, especially in applications in which humans cannot be replaced totally by machines given our current technologies (Szikora & Madarász, 2017), having a complete lapse of responsiveness (‘*lapses*’) can lead to a catastrophic event (Cheyne et al., 2006). There are many important but monotonous occupations which are high-risk in terms of potential serious accidents, such as truck drivers, train drivers, pilots, health professionals, and process-control workers (Sagberg, 1999). These kinds of occupations require workers to remain alert for extended periods, despite the challenge of keeping focus especially when the task is boring or exhausting (Thomson et al., 2015a).

Even if we start at a high-performance level in a task, we are unlikely to sustain the same level of performance over an extended period (McKinley et al., 2011). The reason for the drop in performance is that our ability to respond becomes impaired (Peiris et al., 2006; Poudel et al., 2010a). Our performance is likely to drop with time-on-task (Bogler et al., 2017), which can lead to accidents. For example, in the transportation sector many fatal accidents are due to sudden drops in performance. Estimates of accidents on the road in France are 10% due to fatigue (Philip et al., 2001), 21% in USA due to drowsiness (Tefft, 2014), 25% in Australia due to sleep (Naughton & Pierce, 1991), and 2% due to sleepiness in Norway (Philip et al., 2010).

This performance impairment has different grades (Schad et al., 2012), which differs in the decoupling levels (zero to high) from the task, as we might be able to do the task although our performance has decreased. Hence, the impaired response has two main categories: partial and complete (Anderson et al., 2010; Jones et al., 2018). The key point in differentiating between partially and completely impaired responsiveness is performance (Peiris et al., 2004). A simple definition of partial or reduced responsiveness is that the task is being performed but with a poor performance (Jones et al., 2010). Low performance may be due to drowsiness (Huang et al., 2015) or due to attention being divided between the task and other external or internal stimuli (Benedek et al., 2017). Figure 1-1 (Jones et al., 2018) provides an overall taxonomy of impaired responsiveness events.

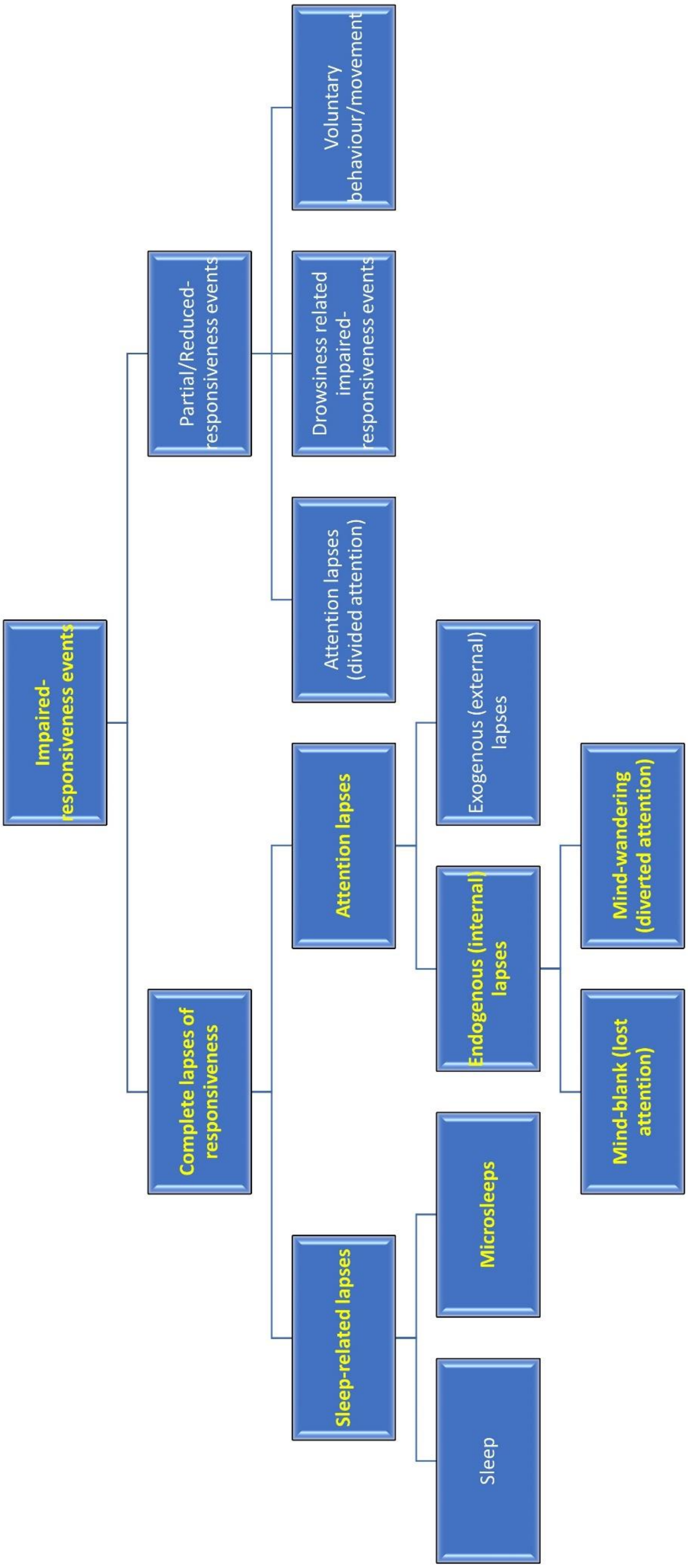


Figure 1-1 The taxonomy of impaired responsiveness events.

1.2 Lapses of responsiveness

Completely-impaired responsiveness, also called lapses of responsiveness (Jones et al., 2010), can happen when we are disconnected from our surroundings, which means zero performance (Peiris et al., 2011). This event might take one of two possible forms: either we are in a microsleep (MS) (Innes et al., 2010) or our attention is not on the task at hand (Unsworth & McMillan, 2014). Compared to partial/reduced responsiveness, complete lapses of responsiveness (‘*lapses*’) can result in fatal accidents, especially in tasks such as driving (Yanko & Spalek, 2013).

Researchers have investigated lapses in performance (Jones et al., 2010; Peiris et al., 2006), analysed behavioural cues and task-related performance (Peiris et al., 2005), and recorded brain activity using different tools (Davidson et al., 2007; Poudel et al., 2010b). Their work has defined lapses as momentary episodes of disturbance in performance in which the subject is unintentionally unable to respond to a task.

The general definition of a lapse has evolved over time, as researchers have started dividing it into different subcategories according to their research findings (Jones, 2011; Jones et al., 2010). Based on behavioural cues and performance on a task, two main subcategories have been identified: MSs and attention lapses (ALs) (Buckley et al., 2016; Peiris et al., 2011).

1.2.1 Microsleeps

Harrison and Horne (1996) defined MSs physiologically as “a short period (between 5 and 14 s) of sleep identified by an electroencephalogram (EEG**)** dominated by theta activity (4—7 Hz), and an absence of alpha activity (8—l2 Hz)”. Poudel et al. (2014) concluded that losing the struggle to stay awake means having shifted from the drowsiness state to the sleep state. The sleep state can be divided into two parts based on duration: sleep event (> 15 s) and MS (<15 s), with the latter falling under the definition of a complete lapse because of its specific albeit arbitrary time limits (Jones, 2011). MSs can be observed through behavioural cues, such as head nodding, eye-closure, and loss of response to external stimuli (Davidson et al., 2005).

MSs are usually associated with increased response time on monotonous tasks (Poudel et al., 2010a) and sleep deprivation (Innes et al., 2013; Poudel et al., 2021; Poudel et al., 2012, 2013, 2018), although they can occur in non-sleep-deprived subjects (Peiris et al., 2006; Poudel et al., 2014). They are directly involved in many fatal accidents in driving (Akerstedt, 2008; Vanlaar et al., 2008).

1.2.2 Attention lapses

MSs and ALs are similar in that they cause a complete failure to respond on tasks for short periods of time (Jones, 2011). Moreover, their occurrences are positively correlated with time-on-task (Buckley et al., 2016; Derosière et al., 2015). However, MSs and ALs differ in oculometric features (Anderson et al., 2010; Benedek et al., 2017). In a MS, eyes are partially or completely closed (Jones et al., 2010), whereas an AL usually occurs with eyes open (Anderson et al., 2010; Buckley et al., 2016; Jones, 2011).

The causes and consequences of falling asleep during driving have been substantially discussed in the literature due to their massive effect on human safety (Dawson & Reid, 1997; Harrison & Horne, 1996; Horne & Reyner, 1995; Naughton & Pierce, 1991; Sagberg, 1999). In contrast, there has been much less research on ALs, despite their fatal consequences in the transportation sector (Yanko & Spalek, 2013).

Looking more specifically at ALs, we can perceive that if participants are not focusing on the task while they are awake then their attention might have shifted to something else (Unsworth & McMillan, 2014). It might be external, like looking from the car's window or being busy with other stuff inside the car (Anderson et al., 2010; Unsworth & McMillan, 2014), or something internal where our attention has been prisoned in our thoughts chamber (D'Mello et al., 2016). The task’s nature (boring, fatiguing, etc.) (Larue et al., 2015), time-on-task (Poudel et al., 2013), and individual differences (Unsworth & McMillan, 2014) are important factors that should also be taken into account in studying any type of lapse.

The literature currently discusses two opposing theories of vigilance decrement: boredom or mindlessness and resource depletion or mental exhaustion (Helton & Warm, 2008). According to the boredom or mindlessness explanation, the vigilance deficit occurs as a result of a lack of exogenously supported attention during vigilance tasks (Manly et al., 1999; Robertson et al., 1997). As a result, the subject must maintain endogenously motivated attention to the key stimuli. In vigilance tasks, rare crucial signals are separated by extended periods; subjects may lose their focus of attention during these intervals. Subjects then develop a mindless, automatic attitude towards their vigilant job. Later, subjects become overtaken by task-unrelated thoughts (TUTs), as awareness drifts away from the task (Giambra, 1995; Smallwood et al., 2004). Thus, from this perspective, the fundamental mechanism for detecting faults in vigilance settings is the subject’s disengagement from the task due to preoccupation with TUTs and the subject’s subsequent automated approach to the job. This idea is borne out by phenomenological observations indicating that many subjects find vigilance tasks tedious (Scerbo, 1998).

The alternative resource depletion or mental exhaustion theory of vigilance attributes detection failures in vigilance mostly to a loss in available attention resources. According to research, there are only a finite number of cognitive resources accessible for information processing (Kahneman, 1973; Matthews et al., 2000). This limited resource concept has been extensively used to explain vigilance task findings (Davies & Parasuraman, 1982; Hancock, 1989; Helton & Warm, 2008; Temple et al., 2000; Warm et al., 2008). During vigilance tasks, subjects must make active, continuous distinctions between signal and noise stimuli (target vs. non-signal stimuli) in the face of considerable ambiguity. There are few opportunities for rest. The continual nature of mental labour required for alertness precludes resource replenishing. As a result, the resources deplete with time, resulting in a decrease in performance efficiency. Recent research has supported the resource theory of vigilance by demonstrating that the vigilance decline is followed by a decrease in cerebral blood flow velocity, a possible physiological resource indicator (Hitchcock et al., 2003; Schnittger et al., 1997; Shaw et al., 2009).

In addition, another theoretical model for explaining the link between subjective effort and performance outcomes has been developed by Kurzban et al. (2013). A major assumption of this paradigm is that using an executive control system on a long-term basis incurs a "cost" in the form of effort. As a result, the degree to which a subject retains executive control is defined by a function representing this mental cost, which is compared against the subject's prospective rewards. Executive control processes may deteriorate with time in the context of vigilance-like activities, as the ‘gains’ associated with maintaining regulated processing over time may be subjectively modest (because this effort yields no benefits on the vast majority of trials). Indeed, it may make perfect sense to refer to declining executive control over time in such tasks as ‘adaptive’ (for a similar argument see (Hancock, 2013), and to see mind-wandering as a behavioural by-product of this adaptive process. In other words, motivation wanes with time as a result of the monotonous and unrewarding character of vigilance activities. As a result, the mind-wanders more frequently. It is even possible that mind-wandering occurs early in the activity regardless of the goal to focus on the task (i.e., it is spontaneous in nature), but that later in the task, when motivation wanes, mind-wandering occurs as a result of a lack of effort to focus on the task (i.e., it is intentional or deliberate in nature).

Helton and Russell (2011) explored the two explanations for ALs through a feature present/absent sustained attention to response task (SART): (1) task monotony that leads to expanding distraction because of TUTs (i.e., mind-wandering), (2) task demands that lead to exhausting the resources of information-processing required for performing the task. They found that ALs are more likely to be caused by resource depletion and cognitive overloading, although they did not totally reject the possibility of mindlessness and boredom.

Recently, Thomson et al. (2015a) investigated two possible explanations for sustained ALs. According to one theory, monotony in the task results in a growing engagement with internal thought (i.e., mind-wandering). By another theory, task demands result in the exhaustion of information-processing resources required to complete the task. To reconcile seemingly contradictory findings regarding whether vigilance declines are caused by mind-wandering or resource depletion, they combined elements of attentional-resource (Smallwood, 2010; Smallwood & Schooler, 2006) and control-failure (McVay & Kane, 2010) theories of mind-wandering. They contended that neither a mind-wandering form of the underload theory (based on attentional resources) nor a resource-depletion variant of the overload hypothesis can adequately account for the process. They provided a novel paradigm for explaining ALs as a function of time-on-task by merging elements of two distinct theories of mind-wandering: attentional-resource theory (Smallwood & Schooler, 2006) and control-failure theory (McVay & Kane, 2010). They then used their ‘resource-control’ theory to account for declines in performance on sustained-attention tasks. They argued that their resource-control theory accounts not only for recent findings in the literature on sustained attention, vigilance, and mind-wandering, but also for classic empirical findings.

Propensity for ALs varies substantially between subjects, based on cognitive abilities and other individual differences (Unsworth et al., 2010) and environment factors (Burdett et al., 2016). ALs can occur during simple every-day activities, such as reading a book and watching television, without any consequences or can occur during an active task such as driving and lead to catastrophic accidents (Weissman et al., 2006).

1.2.2.1 Diverted-attention lapses

The dangerous consequences of MSs and ALs are quite clear, especially when it comes to health and safety (Galéra et al., 2012; Terry & Terry, 2015). Diverting our attention from task-related thoughts to task-unrelated thoughts (TUTs) is linked to some factors: (1) finite attention resources which decrease with time-on-task (Derosière et al., 2015), (2) the effect of highly automated systems on human operators, known as human-machine miscommunication (Gouraud et al., 2017). The issue emerges when operators are experiencing the effects of carelessness and alertness decrement; subsequently, when computerization does not carry on as required, understanding the framework or reclaiming manual control might be challenging (Gouraud et al., 2017), (3) the task nature if not cognitively stimulating (Larue et al., 2015), and (4) competing internally and externally directed cognition because of limitations of processing capacity (Benedek et al., 2017).

Exogenous

External distraction is simply a stimulus not related to the task that usually affects visual attention as it attracts eye movements (Domkin et al., 2013), it can also be auditory and affect the overall performance (Wood et al., 2006; Ziegler et al., 2018).

Endogenous

Endogenous distraction refers to mind-wandering and mind-blanking. Mind-wandering, where attention shifts from task at hand to self-generated thoughts (Huijser et al., 2018), may be voluntary, in which a participant chooses to divide his/her attention between task-related thoughts and TUTs (D’Mello, 2016; Ottaviani et al., 2015) and usually does not completely decouple attention from the external world, such as driving back from work while thinking about what to have for dinner. This event is characterized by maintaining responsiveness while doing the task, although the performance may or may not be affected, as other factors like driving experience will play an important role in the scene (Zhang & Chan, 2014). This should not be considered as a complete impaired-responsiveness event but partial.

Mind-wandering can also be involuntary, where our thoughts conquer our mind and decouple us from the external world while shifting our attention in a time-oriented manner (Smallwood & Schooler, 2015), or a personal trait (Burdett et al., 2016; Gil-Jardiné et al., 2017). These events are commonly called *mind-wandering* (Chaudhary et al., 2017; Daniel et al., 2010; Ward & Wegner, 2013; Weinstein et al., 2017), *daydreaming* (Wang et al., 2009), and *TUTs* (Unsworth & McMillan, 2014). These type of lapses have a long history with the occurrence of accidents (Yanko & Spalek, 2013).

Mind-blanking, in which the mind ‘goes away’ (Ward & Wegner, 2013), is a lapse in which there is a complete loss of attentional focus while being awake, where we do not remember when and why it started, when it ended, and what happened in between, or what brought us out of it. Mind-blanking has been considered to be an extreme case of decoupling of perception and attention (Ward & Wegner, 2013), which is different than moments of meta-cognitive failures where the mind fails momentary to monitor the surroundings. This phenomenon has been called *mind-blanking* (Ward & Wegner, 2013), *ALs* (Buckley et al., 2016), *sustained-attention lapses* (Head & Helton, 2012; Jones et al., 2010), *blank-in-mind* (Moraitou & Efklides, 2009), *attentional blink* (Gillard-Crewther et al., 2007), and *lost attention lapses* (Jones et al., 2018).

Whether we are engaged in a task-related thought or TUT, our memory will be a key factor, as we either use our experience to call information needed for the task, or we find ourselves thinking about other thoughts from past or future (Hutchinson & Turk-Browne, 2012) such as in mind-wandering. However, mind-blanking is more likely to be associated with failure in memory processes (Efklides & Touroutoglou, 2010; Moraitou & Efklides, 2009).

Investigation of ALs has challenges, as it is very difficult to distinguish between the two types of endogenous ALs, i.e., mind-wandering and mind-blanks, and accurately classify them using behavioural cues only, such as performance on a task or any extracted oculometric features (Ward & Wegner, 2013).

1.3 Objectives

This chapter has provided a general overview of the types of lapses of responsiveness. These lapses have a significant effect on safety when they occur during tasks like driving. Two main categories of complete lapses of responsiveness were introduced: MSs and ALs. Details were also given on diverted ALs, externally and especially internally, including mind-wandering and mind-blanking.

Although the literature has investigated ALs and MSs during various tasks, there remains a lack of understanding of these two phenomena. Given their association with a high risk of fatal accidents, and as driving is a continuous task, we should investigate these lapses within a continuous task. ALs can be broken into mind-wandering and mind-blanking, but mind-blanking has been far less investigated than mind-wandering. Also, are MSs simply brief instances of sleep or are they physiologically different? To achieve this, both the strengths of fMRI, with its high spatial resolution, and EEG with its high temporal resolution, were considered.

An important contribution is to reveal the neural signature of lapses of responsiveness when performing the 2-D continuous visuomotor tracking (CVT) task, which is demanding as it requires maintaining attention to the task at all times, and also monotonous as it keeps repeating its pattern. In addition to not interfering with the task by using thought probes, and depend only on the behavioural features and tracking performance to rate the lapses.

This project aimed to provide more understanding of the two phenomena of ALs and MSs. The main interest was to reveal what happens inside the brain during these two lapses. Voxel-wise, group independent component analysis (ICA), haemodynamic response (HR) of regions of interest (ROIs), functional connectivity (FC), and reconstructed brain sources were analysed to assist answering the “what” question. This helped us to draw conclusion about these lapses within a continuous task without interrupting the participants while performing the task.

Chapter 2: Lapses of Responsiveness: A Behavioural Review

2.1 Significance of research on lapses of responsiveness

Although it might appear trivial, as lapses are something that occurs daily and in different situations where they cause no harm. Conversely, ALs can result in severe injuries and deaths. In a study by Galéra et al. (2012), 955 drivers injured in a vehicle crash were interviewed between 2010-2011, in which 52% reported mind-wandering just before the crash, and its content was highly distracting (defined as intense mind-wandering) in 13%. Another study by Gil-Jardiné et al. (2017), interviewed 954 drivers injured in a vehicle crash over 2013–2015, where 39% of respondents were classified with a mind-wandering trait and 13.5% reported a disturbing thought just before the crash.

Falling asleep while driving has a dramatic effect on safety. Royal (2003) reported the results of a national survey on drowsy driving, with an estimate of 0.8 to 1.88 million sleep-related accidents between 1997 and 2002. In England, a police report on vehicle accidents showed that 679 were sleep-related between 1987 to 1994 (Horne & Reyner, 1995). A report from Norway estimated that 146 accidents were sleep-related (Philip et al., 2010). Finally in Thailand, approximately 1212 accidents over a six-month period were sleep-related (Leechawengwongs et al., 2006).

2.2 Behavioural characteristics of attention lapses

2.2.1 Mind-wandering

Our consciousness rarely keeps one topic in mind for a long period without change, as its dynamic nature causes our minds to unintentionally decouple from perceptual information (Schad et al., 2012; Smallwood & Schooler, 2015) and external stimuli completely (Huijser et al., 2018). Then shifts to inner thoughts (Berthié et al., 2015) that can be emotional or distractive (Lemercier et al., 2014), based on the content of the thoughts (Critcher & Gilovich, 2010). This is the mind-wandering phenomenon, which is characterized by a brief failure of attention to the task at hand, and results in impaired performance and increased reaction time (He et al., 2011).

Many studies on mind-wandering have been based on correlations with oculometric features to investigate behavioural cues. In reading comprehension tasks, which are widely used in mind-wandering studies, Schad et al. (2012) investigated episodes of mind-wandering by detecting longer eye-gaze duration while reading and found that attention decouples in a graded rather than dichotomous fashion. The same conclusion of longer fixation duration in reading while mind-wandering was also reached by Foulsham et al. (2013b), Bixler and D’Mello (2016), and Reichle et al. (2010). A high eye-blink rate has also been shown to be associated with mind-wandering (Daniel et al., 2010). In addition, Pepin et al. (2018) concluded that gaze fixation is higher during mind-wandering episodes while performing a problem-solving task and also in a driving simulator; while driving in a straight line through an urban residential area, participants were interrupted by right and left bends. Anagram and sentence generation tasks have also been used to show that mind-wandering is associated with increased duration of fixations and saccades (Benedek et al., 2017).

Unsworth and Robison (2016b) examined pupil metrics during the psychomotor vigilance task (PVT) and concluded that participants had smaller pupil diameters when off-task compared to on-task. These results are inconsistent with previous research by Franklin et al. (2013), who noted that when off-task, participants had large-pupil diameters compared to on-task. The reason behind these contradictory results might be in the tasks used, as in Franklin et al. (2013), participants were performing a reading task. Therefore, differences may appear because of how challenging the tasks are, as in PVT, the participants are required to keep attention on-task while in the reading task there are opportunities to intentionally divert attention from the task.

In a recent study, using four experiments based on PVT with each experiment customized to result in a different arousal level, Unsworth and Robison (2018a) investigated the relation between arousal and different stages of mind-wandering using pupillometry. They showed that mind-wandering has a heterogeneous nature and suggested that each form of mind-wandering is related to a different arousal state (low, intermediate, or high) and different pupil metrics and that behavioural and pupillary measures can be consumed to trace mind-wandering states. They also found that mind-wandering and mind-blanking have similar tonic pupil diameters while increasing external attention to the task. However, while increasing internal attention (more active mind-wandering), tonic pupil diameter was larger in mind-wandering than in mind blanking.

In addition to objective (indirect) techniques of measuring mind-wandering such as oculometric features and reaction times, subjective (direct) techniques have also been used. Subjective techniques are based on the subject's engagement in evaluating the current state of mind. These techniques require the subject to report the mind's state and have two models of reporting: (1) self-caught where the subject indicates any shift in attention and reports freely within the task, (2) probe-caught, which is more popular, once the task is stopped after observing a lack of performance, the subject is asked to choose the most applicable option from a list (Weinstein, 2018). These choices can be classified into four categories: (i) binary, giving the participants only one choice (e.g., mind-wandering) and participants decide whether it applies to them by answering yes or no; (ii) dichotomous, giving participants two contrasting choices (on-task vs. mind-wandering); (iii) categorical, giving participants multiple choices of what they are focusing on (e.g., the lecture, the time, the computer, or something else); and (iv) scale, where participants express their thought on a scale such as a 6-point Likert scale from on-task to off-task (Weinstein et al., 2017).

Although the probe-caught technique appears rational, for more than a decade researchers have not agreed on a single method of using it (Weinstein et al., 2017). The findings of previous works are not comparable due to variations in the probe-caught-techniques used. Another major shortcoming is that it depends on the subject's report (Weinstein, 2018). Hence, any misunderstanding from the subject regarding the current mind state can lead to inaccurate results (Gouraud et al., 2017; Unsworth & McMillan, 2014; Ward & Wegner, 2013). Additionally, studies in the literature have used slightly different definitions for mind-wandering, which is likely to lead to conflicting findings (Seli et al., 2018a). Another problem is that this technique has not been tested in continuous tasks but given that it depends on stopping the subject while doing the task to ask about his/her thoughts, it will interfere with a continuous task, such as continuous visuomotor or driving, and turn it into a discrete task.

2.2.2 Mind-blanking

Mind-wandering is characterized by more importance being given to TUTs at the expense of reduced attention on the task. Essentially, our attention simply drifts from the task at hand to the endogenous train of thoughts. In contrast, instead of our thoughts wandering, in mind-blanks, our thinking stops, and we enter a blank state.

Moraitou and Efklides (2009) used different questionnaire strategies to compare the experience of blank-in-mind with the experience of lack of knowledge when a failure to produce a proper response occurs. They found that the blank-in-mind experience comes with failure in cognition and memory compared to the lack of knowledge experience. In the case of the blank-in-mind, no attempt is made to retrieve information due to potential disruption of brain networks, whereas no related information is available to retrieve with the lack of knowledge.

Other researchers have called the blank-in-mind phenomenon mind-blanking. Using seven experiments, Ward and Wegner (2013) provided evidence that mind-blanking exists and is distinct a mental state from mind-wandering. Mind-blanking has also been investigated in neurological disorders. Van den Driessche et al. (2017) found that children (ages 6–12) with attention-deficit/hyperactivity disorder reported higher mind-blanks compared to mind-wandering during a go/no-go task.

Unsworth and Robison (2018a) using four different PVTs to examine mind-wandering and mind-blanking in terms of their similarities and differences. Their results show that, compared to mind-wandering, mind-blanking is less likely to happen, and slower reactions are also related to mind-blanking. Regarding pupil diameter, in events where attention is directed externally, both mind-wandering and mind-blanking show the same tonic pupil diameters, but when attention is directed endogenously (internally), tonic pupil diameter is greater in mind-wandering than mind-blanking.

2.3 Behavioural characteristics of microsleeps

The detection of MSs through behavioural measures is relatively easier than ALs, due to a major feature of MSs being eye closure with a duration long enough not to be considered a long blink (Anderson et al., 2010). Head movements with MSs can also be helpful, although this needs high-computational hardware (Al-Rahayfeh & Faezipour, 2013). Some studies (Ghosh et al., 2015; Malla et al., 2010) have used video-based measures to detect eye closure. This method depends on the identification of the top and bottom eyelids, after identification of the eye from the face, followed by classification of the image into three states: eyes opened, eyes closed, and eyes partially closed. Or, if the algorithm is more advanced, it can estimate the percentage of eyes closure. However, this method can face issues like the correct detection of one of the lids and lighting conditions. Also, it should be noted that eye-video will perform better on individuals compared to a system that can be generalized to many.

Poudel et al. (2021) recorded the right-eye movement of participants who were performing a 2-D CVT task, they found that the pupil size reduces by 20% in association with MSs.

Other studies (McIntire et al., 2013; Wilkinson et al., 2013) considered using an eye-tracer device, which is a camera attached to an eyeglass frame which can provide measures like blink frequency, and blink duration, and percentage of eye closure. The behavioural system of sleep/MSs detection is important not only to reduce critical accidents, but also for the fitness to drive assessment (Skorucak et al., 2020).

2.4 Individual differences

As all humans have unique biometrics that differentiate them from everyone else, even an identical twin, and cognitive abilities also differ between humans, it is naïve to expect subjects to perform exactly the same in any task. The relationship between ability at sustained attention/cognition and cortical structure on individual differences was studied by Mitko et al. (2019). They found an association between enhanced sustained attention and increased cortical thickness over the visual, somatomotor, frontal, and parietal regions in the right hemisphere. The regions involved were identified to be parts of dorsal attention, ventral attention, somatomotor, and visual networks. Also, Clemente et al. (2021) investigated the relationship between the white matter (WM) pathways and the susceptibility to ALs. Their findings indicated that there is an association between ALs and the variation of microstructure of frontoparietal WM tract.

McAvinue et al. (2012) examined age-related changes in the central aspects of visual attention: namely, sustained attention, attentional selectivity, and attentional capacity. SART was employed to measure sustained attention, and theory of visual attention-based assessment to measure attentional selectivity and capacity. They found evidence of age-related decline in each of the measured variables. The same association was concluded by Morris and Dawson (2008).

Rosenberg et al. (2016) used FC as a neuromarker of sustained attention. They identified functional brain networks whose strength during a sustained attention task predicted individual differences in performance. Finally, Roebuck et al. (2016), through a continuous performance task, showed that error propensity and reaction time variations on continuous performance tasks cannot solely be interpreted as evidence of inattention. They reflect individual differences due to stimulus-specific influences that must be considered when studying deficits in sustained attention. Here, the main factors that create the individual differences are listed.

2.4.1 Vigilance

Vigilance is the term used by psychologists and cognitive neuroscientists to refer to the sustained attention ability in a task even an extended period of time (Davies & Parasuraman, 1982; Parasuraman et al., 1998) , where vigilance decrement has been defined as "the decline in attention requiring performance over an extended period of time" (Mackworth, 1964). Robison and Brewer (2019) did a meta-analysis study by analysing six different datasets and comparing the results, in which they found that vigilance can be seen as a trait-level cognitive ability.

2.4.2 Working memory capacity

Engle (2002) hypothesized that working memory capacity (WMC) “is about using attention to maintain or suppress information”. Engle et al. (1999) also argued that WMC “is not really about storage or memory per se, but about the capacity for controlled, sustained attention in the face of interference or distraction”. Theories of WMC, which are the attention-based, suggest that executive-control capabilities play an important role in performing tasks that require WMC and higher-order cognition (Braver et al., 2007; Hasher et al., 2007; Hasher & Zacks, 1988; Kane et al., 2007; Unsworth & Engle, 2007; Unsworth & Spillers, 2010). The impact of ALs on WMC measures was examined by Unsworth and Robison (2016a). Their results supported the idea that ability to pay attention to a task and resisting ALs is essential to performance, as found by the WMC measures.

2.4.3 Fluid intelligence

General fluid ability/intelligence has been described as being able to solve unfamiliar problems using conventional thinking methods” (Carroll, 1993; Cattell, 1963). It usually conflicts with general crystallized ability, defined as “the ability to answer questions or solve problems in familiar domains using knowledge and strategies acquired through education, training, or acculturation” (Kyllonen & Kell, 2017). Crawford (1991) performed a memory task and an attention test to explore the relation between sustained attention and fluid intelligence, and found that fluid intelligence is not automatic mental processing but is based on mental capabilities. Holm et al. (2011) used a simple rhythmic motor task to investigate the relation between intelligence and reaction time, and found that temporal variability in reaction time is related to cognitive performance.

2.4.4 Tendency to mind-wander

Albert et al. (2018) used SART to predict risky driving among young drivers. They found an association between tendency to mind-wander and individual differences between drivers. A similar conclusion on the association between mind-wandering and individual differences was found by Neigel et al. (2019a), although they linked propensity to mind-wander to reduced performance.

Thomson et al. (2015b) used SART to show that individuals who have a high tendency to mind-wander, and who under-invest attention in the external environment, will have less attentional blinks, which were shown to be a momentary loss of control rather than a lapse due to limited attentional resources (Di Lollo et al., 2005; Gillard-Crewther et al., 2007).

2.5 Influence of motivation

Motivation can boost sustained attention through increased effort (Massar et al., 2018). Esterman et al. (2016) used two tasks with two different motivational scales: one with small monetary loss and one with large loss. They showed that the possibility of large loss can attenuate the vigilance decrement. The same conclusion was reached by Massar et al. (2016) and Neigel et al. (2019b). According to Esterman et al. (2017), by comparing motivated (rewarded) and unmotivated blocks on a sustained attention task, the motivated blocks induced more activation in task-positive regions of the brain.

Based on a prolonged SART study by Reteig et al. (2019), increased motivation cannot fully restore attentional performance caused by vigilance decrement. Also, using a sustained attention task, Seli et al. (2017) showed that motivation to do the task can reduce mind-wandering, whether intentional or unintentional.

2.6 Summary

This chapter focused on behavioural understanding of lapses of responsiveness —ALs and MSs— plus the significance of lapse research. There was also a general overview of the individual differences based on cognitive abilities such as vigilance, WMC, fluid intelligence, and tendency to mind-wander. Also mentioned was the relationship between motivation and sustained attention.

Chapter 3: Understanding fMRI

3.1 Introduction to fMRI

fMRI is a non-invasive technique used in neuroimaging for studying functioning and structure of the human brain. Ogawa et al. (1990) showed that fMRI can visualize brain function by measuring the blood-oxygen-level dependent (BOLD) signal. This chapter lists the methods used to carry out the analysis of fMRI data. We used FMRIB's software library (FSL) (Jenkinson et al., 2012) available at (www.fmrib.ox.ac.uk/fsl).

3.1.1 Magnetic resonance signal

An MRI scanner is a cylindrical tube surrounded by an extremely strong electromagnet. For example, the magnetic field strength used in the clinical studies is mostly 3T, almost 50,000 times stronger than that of the earth's magnetic field. The scanner's magnetic field affects atomic nuclei.

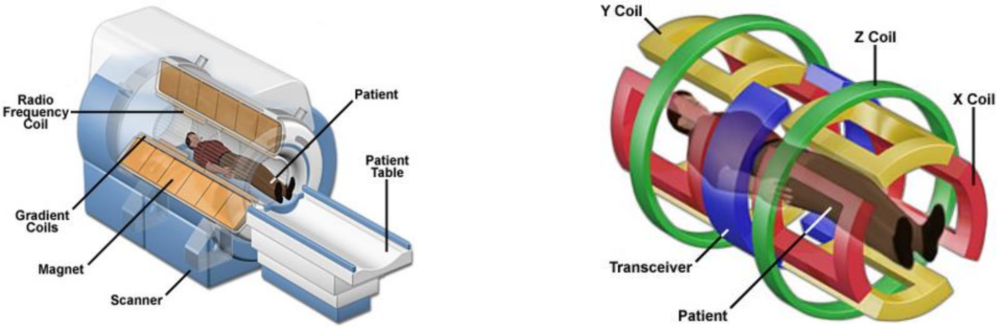


Figure 3-1 (a) Magnetic resonance imaging (MRI) Scanner, (b) MRI scanner gradient magnets. The internal structure of the MRI scanner (from Coyne, 2018).

From Figure 3-1, the parts of the scanner are: (1) radio frequency (RF) coil: a transceiver that transmits and receives RF signals, (2) main magnet coil: generates a homogeneous time-invariant magnetic field, and (3) gradient coils (magnets): (i) X magnet coil: generates a fluctuating magnetic field from left to right, (ii) Y magnet coil: generates a fluctuating magnetic field from top to bottom, and (iii) Z magnet coil: generates a fluctuating magnetic field from head to toe (Buxton, 2013; Woolrich et al., 2016). With the strong external magnetic field from the scanner, the nuclear magnetic moments are changed from being randomly oriented to being aligned with the field. This results in the creation of a net longitudinal magnetization following the same direction of the field, and this net magnetization is large enough to be measured (Buxton, 2013; Woolrich et al., 2016), see Figure 3-2.

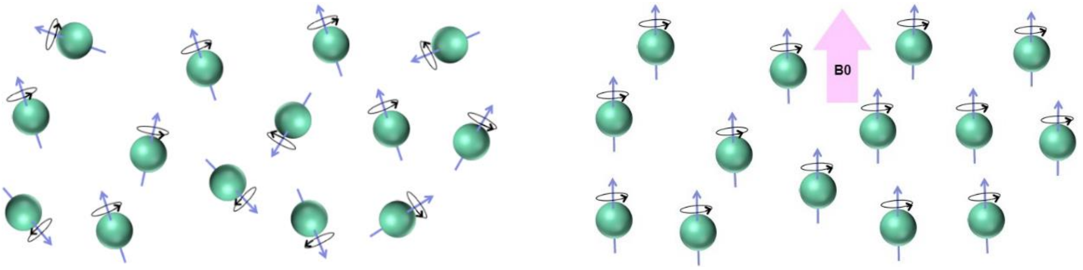


Figure 3-2 Nuclear magnet: (a) without external magnetic field, (b) with external magnetic field. The effect of the external magnetic field on the nuclei (from Lindquist & Wager, 2013).

3.1.1.1 What MRI measures?

MRI detects the magnetic signal from each hydrogen nucleus in water (H_2O) as the nuclei consists of only one proton. The idea is that the signal strength of the hydrogen nuclei changes with the surroundings, and that smooths the discrimination between WM, grey matter (GM), and cerebral spinal fluid (CSF) in structural brain images. The protons are shown as positively charged spheres that keep spinning. As a result, a net magnetic moment rises along the spins' axis (Buxton, 2013; Woolrich et al., 2016), see Figure 3-3.

Figure 3-3 Protons magnetic properties. Behaviour of a proton (from Lindquist & Wager, 2013).

A single proton magnetization cannot be measured using MRI, but the net magnetization M inside a volume can be. It can be shown as a vector represented by two components (Buxton, 2013; Woolrich et al., 2016), see Figure 3-4.

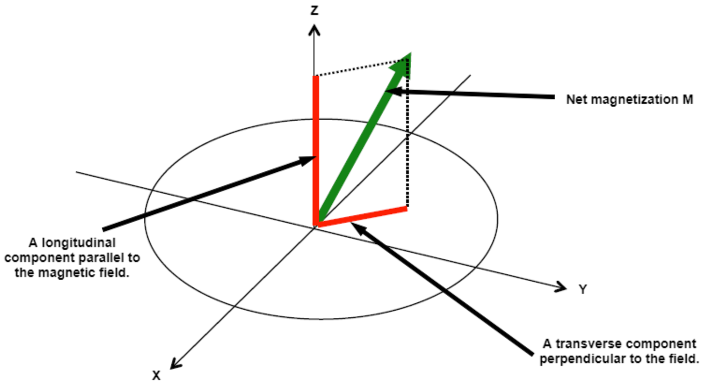


Figure 3-4 The net magnetization and its components. Adapted (from Lindquist & Wager, 2013).

The hydrogen nuclei precess with a random phase about the field and with an angular frequency specified by Larmor frequency (Horowitz, 2012), see Figure 3-5. The phases of all nuclei are aligned and then the nuclei are 'tipped over' using an RF pulse. As a result, the longitudinal magnetization is decreased, and a new transverse magnetization is established (Buxton, 2013; Woolrich et al., 2016).

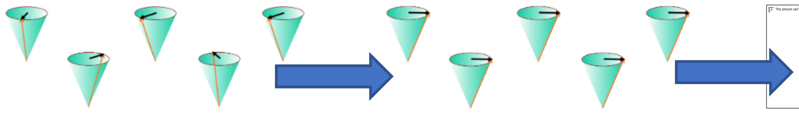


Figure 3-5 From longitudinal magnetization to transversal magnetization. The radio frequency effect on the nuclei (from Lindquist & Wager, 2013).

Following the RF pulse, the system returns to equilibrium, during which the transverse magnetization disappears gradually (transversal relaxation), and the longitudinal magnetization rises gradually back to its original magnitude (longitudinal relaxation). Within this process, a signal is created, and the RF receiver coil measures it (Buxton, 2013; Woolrich et al., 2016).

- Longitudinal relaxation: happens when the spins get back to their parallel state and as a result, the net magnetization is restored along the longitudinal direction, represented by a time constant T1 (Buxton, 2013; Woolrich et al., 2016), see Figure 3-6.
- Transverse relaxation: is the absence of net magnetization in the transverse plane because of the lack of phase coherence, represented by a time constant T2 (Buxton, 2013; Woolrich et al., 2016), see Figure 3-7.

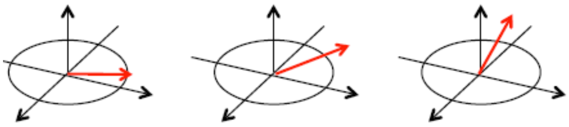


Figure 3-6 Longitudinal relaxation following the radio frequency (RF) pulse (from Lindquist & Wager, 2013).

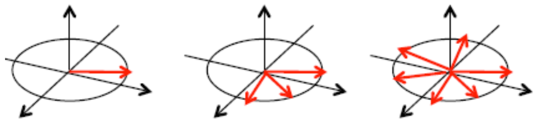


Figure 3-7 Transverse relaxation after removing the RF (from Lindquist & Wager, 2013).

3.1.2 MRI image formation

The objective of MRI is to build a picture or a grid of numbers that relate to spatial areas.

3.1.2.1 K-space

In k-space, the spatial frequencies of the MR image are represented by an array of numbers. The spatial resolution of the image is impacted by the number of k-space measurements. An MR image is the inverse Fourier transform (IFT) of k-space (Jenkinson & Smith, 2006; Lindquist, 2008), see Figure 3-8.

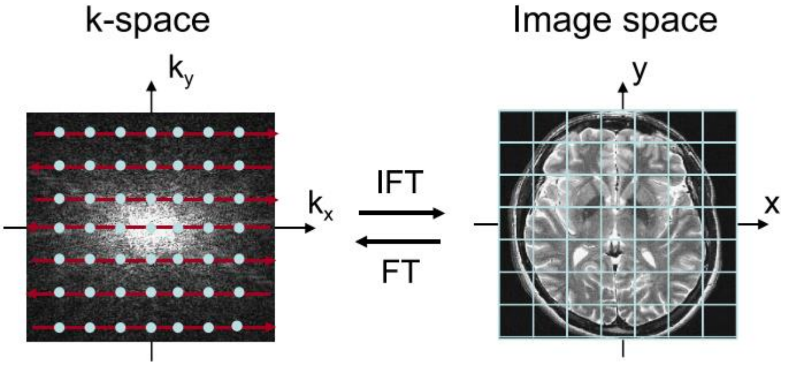


Figure 3-8 MRI image construction. Inverse Fourier transform (IFT) should be applied to transform the numbers into an image of the brain (from Lindquist, 2008).

T1-weighted and T2-weighted images are different for different tissues. The difference lies in echo time (TE) and repetition time (TR) used to produce each image as they are longer in T2 than T1, they can clarify boundaries between CSF, which appears to be dark in T1 and bright in T2, GM and WM. Likewise, because T2*, which is the impact of the interaction between T2 and local inhomogeneities in the magnetic field, is sensitive to flow and oxygenation, it is used in functional brain imaging.

3.1.3 BOLD signal

The BOLD signal is not a direct measure of neural activity. Instead, it allows us to measure the ratio of oxygenated to deoxygenated haemoglobin in the blood by measuring the metabolic demands (oxygen consumption) coming from active neurons. Neurons receive oxygen through haemoglobin in capillary red blood cells. An increased demand of oxygen in blood flow going to regions that are active occurs when the neural activity increases. The haemoglobin changes its magnetic state based on the oxygenation process, this change in magnetic property results in a change in the MR signal of blood based on the degree of oxygenation (Pauling & Coryell, 1936), and this can be used for brain activity detection. This form of MRI is known as BOLD fMRI imaging (Bijsterbosch et al., 2017; Buxton, 2013; Glover, 2011; Lindquist, 2008; Wager & Lindquist, 2015; Woolrich et al., 2016), see Figure 3-9.

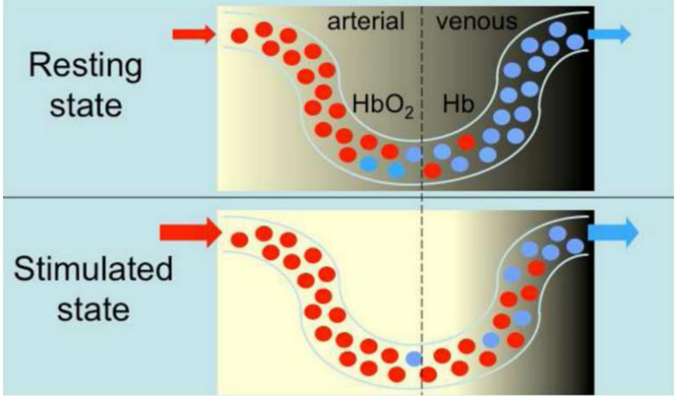


Figure 3-9 The blood oxygenated level dependent (BOLD) signal. HbO_2 represents red blood cells that are fully oxygenated (red circles) and Hb represents red blood cells that are fully deoxygenated (blue circles). HbO_2 will replace Hb when there is a neural activity as it consumes more oxygen (from Glover, 2011).

3.1.3.1 Hemodynamic response function (HRF)

It is important to highlight the changing direction of oxygenation with increased activity. It is expected that blood oxygenation will increase because of activation, but the reality is not that simple. A transient decrease in blood oxygenation, known as the "initial dip", occurs first following an increase in the neural activity. The "initial dip" is then followed by a dramatic increase in the blood flow that overcompensates the oxygen demand, such that the blood oxygenation substantially increases after neural activation, reaching a peak at about 6 s before falling slightly below the baseline, known as "post-stimulus undershoot" (Buxton, 2001; Lindquist, 2008; Rosa et al., 2015; Wager & Lindquist, 2015; Woolrich et al., 2016; Woolrich et al., 2004b), see Figure 3-10.

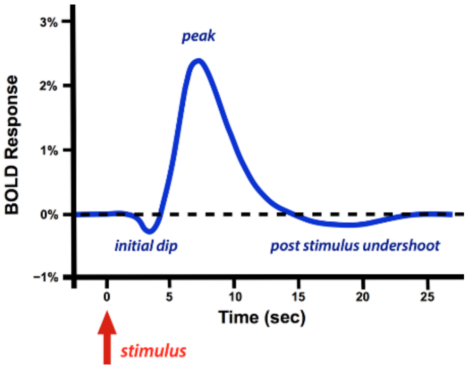


Figure 3-10 HRF is a delayed response after a stimulus occur (from Elster, 2016).

3.1.4 fMRI artefacts and noise

The BOLD fMRI signal contains multiple sources of noise related to the hardware and participants themselves. Sources of noise are: (1) thermal noise caused by the motion of free electrons in the system, (2) spikes caused by instability of the gradient and magnetic fields, (3) interaction between head movement and the magnetic field, (4) physiological effects, like heartbeat and respiration. All fMRI data contain artefacts, and it is very difficult to deal with major artefacts during analysis, so one aims to avoid or minimize them during data acquisition (Huettel et al., 2004; Wager & Lindquist, 2015; Woolrich et al., 2016).

3.1.5 Spatial and temporal characteristics of fMRI

fMRI, like other brain imaging techniques, is characterized by temporal resolution and spatial resolution (Huettel et al., 2004; Wager & Lindquist, 2015), see Figure 3-11.

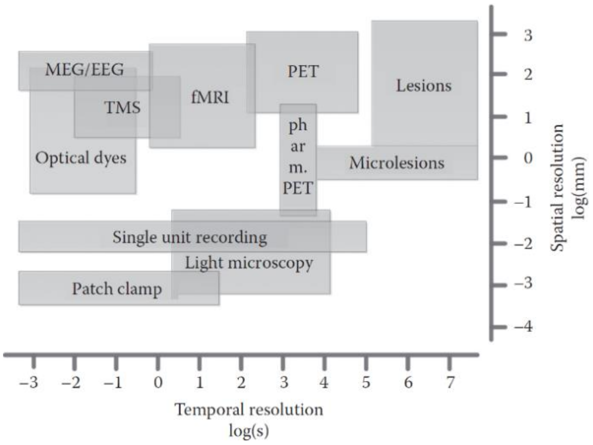


Figure 3-11 Comparison of spatial and temporal resolutions. The fMRI has a relatively good spatial resolution and acceptable temporal resolution (from Liu et al., 2016).

Spatial resolution defines the ability to localize BOLD activity to a particular area of the brain. Voxel size is the primary measure of spatial resolution in fMRI. Each voxel is a 3-D cube or rectangular prism. Each brain volume consists of thousands of voxels. The MRI brain volume is a function of field of view, matrix size, and slice thickness used to acquire the fMRI data. The field of view defines the coverage of the imaging volume within a slice. The number of voxels in a 2-D plane is determined by the matrix size, which is normally in powers of 2 to facilitate the use of the fast Fourier transform (FFT) in the image reconstruction. Slice thickness is the third parameter, which determines the depth of each voxel, see Figure 3-12.

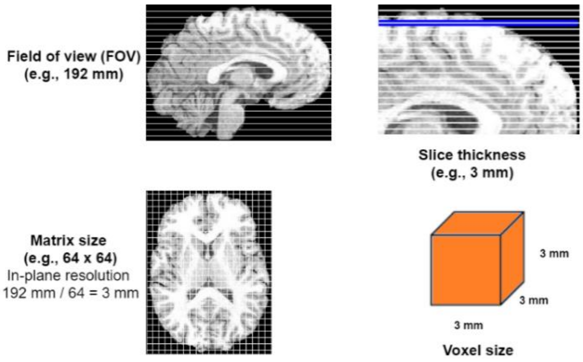


Figure 3-12 Spatial resolution terminologies (from Wager & Lindquist, 2015).

Temporal resolution is the shortest duration of neural activity separated out by fMRI. For a typical pulse sequence in fMRI, one brain volume is acquired per TR. TR typically takes 1–3 s.

3.1.6 fMRI study design

The goal is to induce the human subject to carry out tasks or experience psychological states that will be studied and effectively detect related brain signals related to those psychological states (Lindquist, 2008; Wager & Lindquist, 2015; Woolrich et al., 2016).

3.1.6.1 Controlled experiments

Controlled experiments are conducted by presenting carefully-timed experimental conditions of pre-defined duration during fMRI scanning. The type of experimental conditions depends on the research questions being asked; at least two types of condition: task and baseline are required, see Figure 3-13.

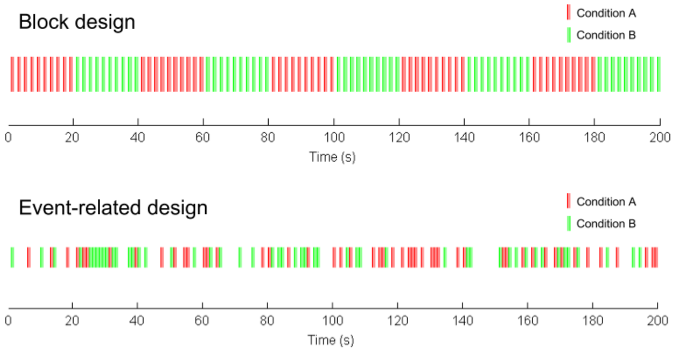


Figure 3-13 fMRI study design (from Lindquist, 2008).

Block design

Multiple repetitions of a given experimental condition are strung together in a block, alternating between one or more condition blocks and one or more control/resting blocks.

Event-related design

In an event-related design, the experimental conditions are presented in a randomized order, rather than being blocked. As a result, responses to individual events are separable because of the temporal sequencing.

3.1.6.2 Behaviourally-driven experiments

In behaviourally-driven experiments, behaviours of interest, such as sleep, eye-blinks, drowsiness, MSs, and ALs, are uncontrolled and spontaneous while doing a task such as the 2-D CVT task (Poudel, 2010).

3.1.7 Data acquisition protocol

The most commonly used fMRI data acquisition pulse sequence technique is the echo-planar imaging (EPI). In the EPI sequence, rapid gradient switching allows fast acquisition of the brain data, which increases temporal resolution, making it the pulse-sequence of choice in most fMRI studies (Amaro & Barker, 2006).

3.2 Pre-processing pipeline for fMRI

Pre-processing uses many image/signal processing techniques to minimize the noise and artefacts in the raw MR data. These steps are critical to achieve a valid statistical analyses and to greatly boost the power of the following analyses (Bijsterbosch et al., 2017; Jenkinson & Smith, 2006; Lindquist, 2008; Smith et al., 2004; Wager & Lindquist, 2015; Woolrich et al., 2016), see Figure 3-14.

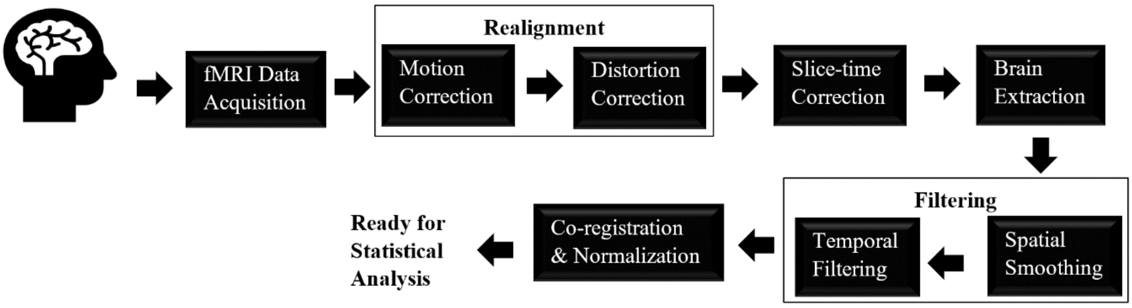


Figure 3-14 Preprocessing pipeline. Adapted (from Lindquist, 2008).

3.2.1 fMRI data acquisition

After acquiring the MR scans, there are three types of images for each subject: structural, functional, and field maps (Wager & Lindquist, 2015).

3.2.1.1 Structural

An anatomical image, also called a T1-weighted image, is a single image captured for each subject. It has a very high spatial resolution and clearly shows the contrast between the WM and the GM of the brain. The acquisition takes ~5 min, see Figure 3-15.

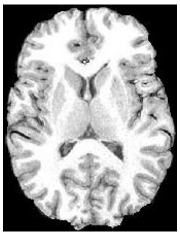


Figure 3-15 Structural image of brain.

3.2.1.2 Functional

In BOLD images, also called T2*-weighted images, are captured from each subject in a time series. They have a lower spatial resolution than T1 images, but still acceptable, and have a much shorter acquisition time of ~2.5 s., see Figure 3-16.

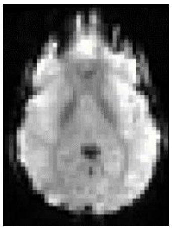


Figure 3-16 Functional image of brain.

3.2.1.3 Field maps

Field maps are maps of magnetic field inhomogeneities in the scanner. They are images captured at two different echo times (TE1 and TE2), which show how the magnetic field varies within the scanner. If needed, they are used only in pre-processing, see Figure 3-17.

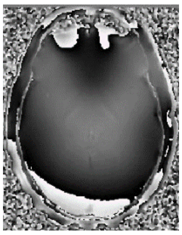


Figure 3-17 Field map image of brain.

3.2.1.4 Basic terminology of fMRI

Before presenting the data analysis, the following terms need to be understood (Wager & Lindquist, 2015), see Figure 3-18, Figure 3-19, and Figure 3-20.

fMRI experiment hierarchy

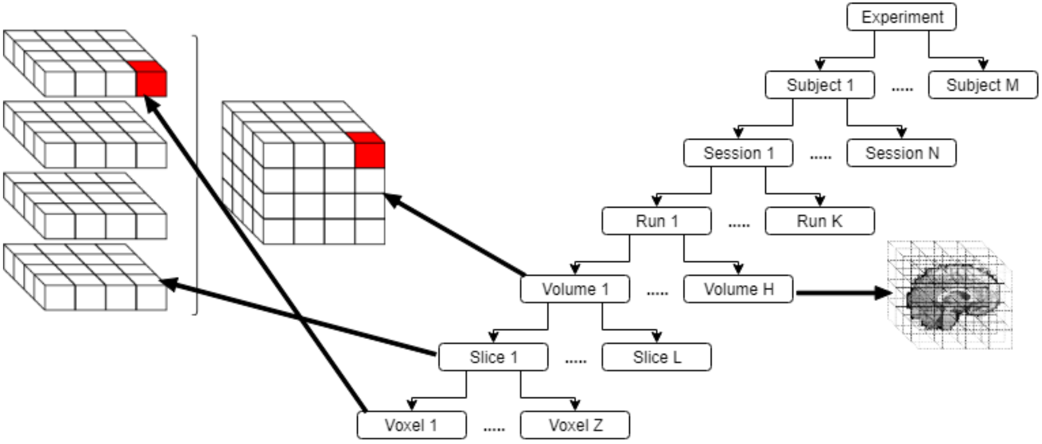


Figure 3-18 fMRI experiment hierarchy. A number of voxels creates a slice, then slices create a volume, then volumes create a run, and runs create a session. There can be multiple sessions for the same subject. Finally a single experiment will include many subjects, adapted (from Wager & Lindquist, 2015).

Brain organization

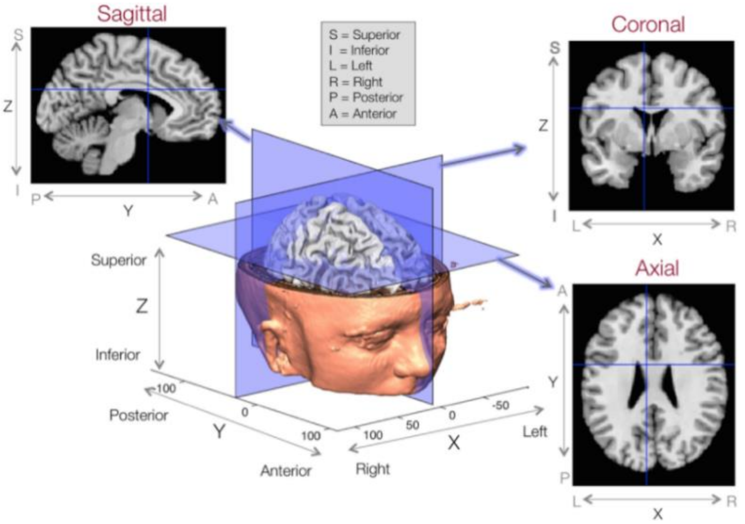


Figure 3-19 Brain organization. A 3-D view of a volume, it is a complete scan of the brain in three different coordinates (from Wager & Lindquist, 2015).

BOLD image

Each BOLD image consists of ~100,000 voxels, the image is represented by 4 dimensions (3-D space and 1-D time). A short time duration TR (2-3s) separates each full scans of the brain. The intensity of each voxel might change with each scan and these changes are combined to produce a time-series (Lindquist, 2008).

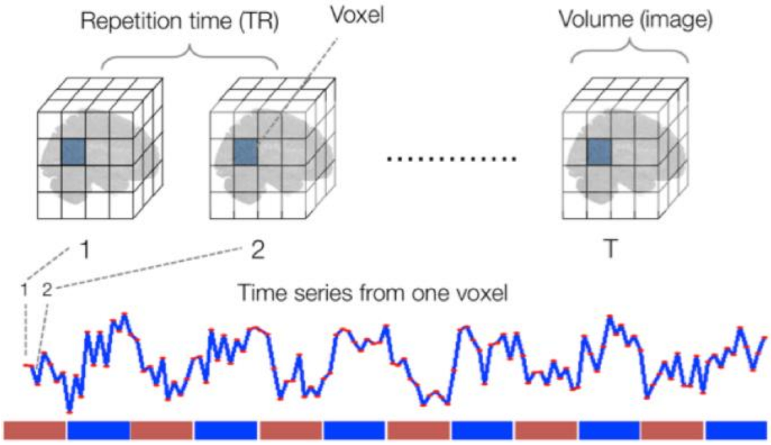


Figure 3-20 BOLD voxel time series. The signal captured from a single voxel is presented in the form of time series with numbers changing for each volume (from Wager & Lindquist, 2015).

3.2.2 Realignment

Because people often move their head during the scanning session, a realignment of each of the images in a functional time series is needed so that they are all in the same orientation (Jenkinson & Smith, 2006; Lindquist, 2008).

3.2.2.1 Motion correction

When a participant's head moves during the fMRI scanning session, the brain's position will change over time. This means that any voxel's time series does not always correspond to the same point in the brain. Within a session, motion correction works on finding an orientation to apply for all images and resampling the original data to the new orientation. This is done by applying a separate 3-D image registration to each image, separately but in order, with a previously determined reference image (usually image 1 but not always recommended) (Jenkinson et al., 2002; Kim et al., 1999), see Figure 3-21.

As all images in an fMRI experiment are from the same object, taken with the same MR sequence, rigid body transformation is recommended. This transformation is based on 6 parameters which varies with time. They include 3 sets of translations and 3 sets of rotations, in total 6 degrees of freedom (DOF), along with intra-modal voxel-similarity functions (like normalized correlation) which are typically used to model the change between one image and the next. The aim is to align the input image with the target image, see Figure 3-22.

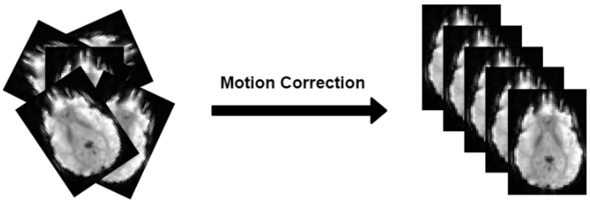


Figure 3-21 Motion correction role. Adapted (from Jenkinson et al., 2002).

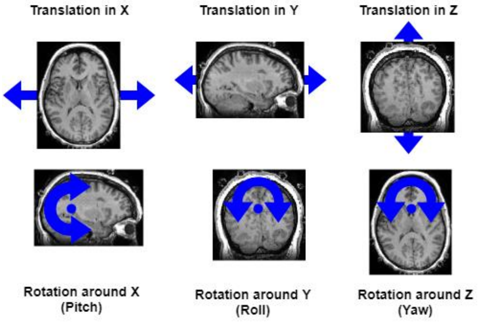


Figure 3-22 Rigid body transformation - 6 degrees of freedom (DOF). Adapted (from Jenkinson et al., 2002).

3.2.2.2 Brain extraction

In this step, non-brain parts are eliminated (e.g., skull, CSF, etc.), by element-wise multiplying the original image with a brain mask (Smith, 2002), see Figure 3-23.

Figure 3-23 Brain extraction procedures.

3.2.2.3 Distortion correction

Motion correction solves the voxel correspondence problem – the same voxel now contains the same bit of the brain over the entire time series. However, it doesn't solve all movement-related problems. Interactions between movement and field inhomogeneity remains. Inhomogeneities in the magnetic field affect both signal strength and spatial encoding of signals, causing dropouts and distortions (Hong et al., 2015; Jenkinson, 2003).

To correct for distortion, an unwarping step is needed. Unwarping aims to estimate the effects of interactions between field inhomogeneity and movement, and compensate for them. The field map images are used in this step (Jenkinson, 2003; Jezzard, 2012), see Figure 3-24.

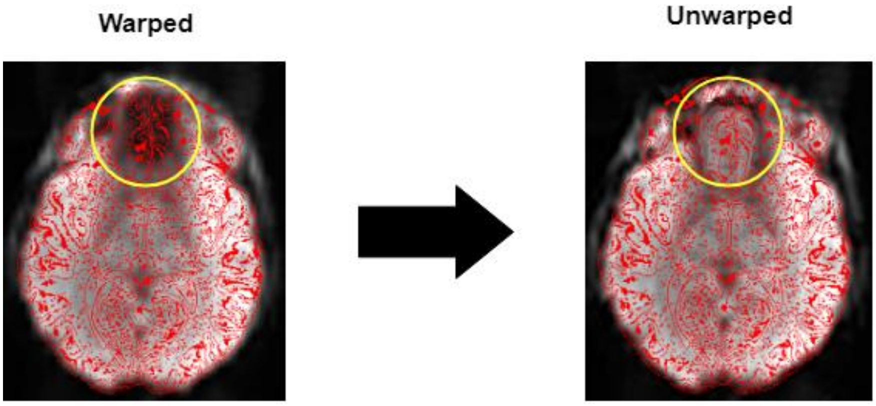


Figure 3-24 The unwarping process: A field map, obtained by comparing the phase differences of two gradient echo images taken with different TEs, depicts the spatial fluctuation of the magnetic field and can be used to compute a voxel displacement map and unwrap the distorted EPI images.

3.2.3 ICA data exploration

ICA can be applied to decompose the 4-D fMRI images into independent components, then these components are manually labelled as signal or noise components (Griffanti et al., 2017), and the noise components are removed. This technique of noise removal was followed based on Caballero-Gaudes and Reynolds (2017) recommendation, as the other alternative of accounting for regressors that represents motion parameters has the problem of ignoring the motion that happened between volumes, which is the case in the fMRI expert analysis tool (FEAT).

3.2.4 Slice-time correction

Most functional sequences collect data in discrete slices. This means that each slice is captured in a time allocated for that slice only. Slice timing correction aims to align all voxels to a common timing by adjusting each of the voxel time-series (Jenkinson et al., 2002). The first slice timing is usually chosen to be the reference timing. The temporal adjustment is usually done by moving the values of the time series in the time domain slightly forward or backward (as all corrections are less than one TR), using some form of interpolation (Jenkinson & Smith, 2006; Lindquist, 2008; Parker et al., 2017; Sladky et al., 2011), see Figure 3-25.

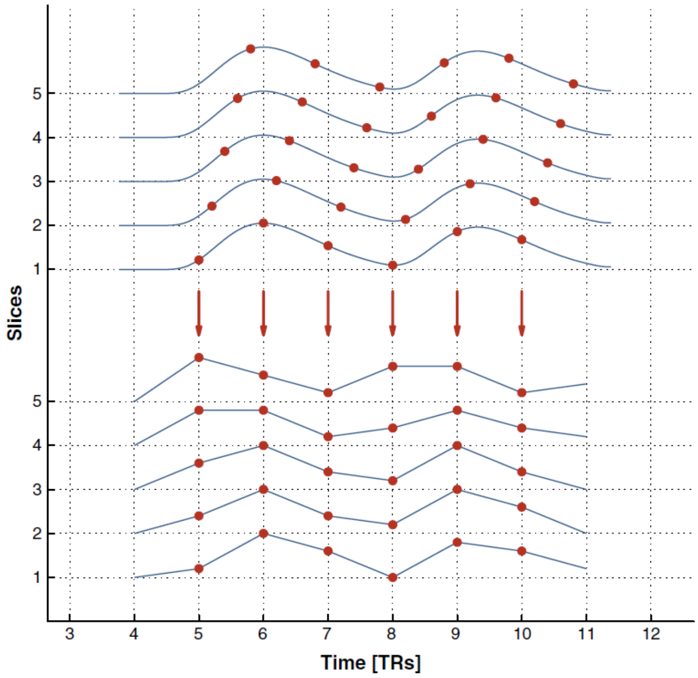


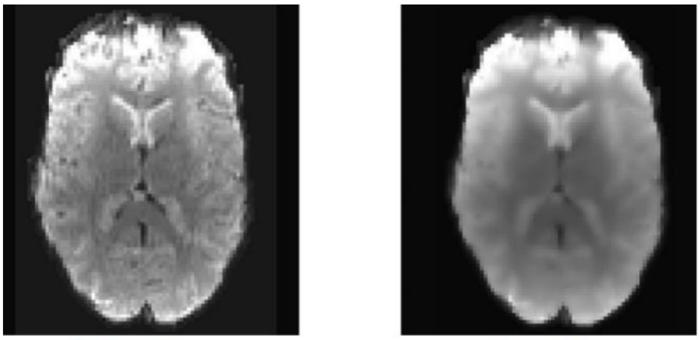
Figure 3-25 Slice-time correction: Individual slices of hemodynamic responses are obtained at different moments in time (top), resulting in an aberration in the scanned data (bottom). In slices obtained later, the observed time courses of a hemodynamic response reach their maximum amplitude earlier. Without sufficient correction, this results in biased estimators in fMRI analyses. (from Sladky et al., 2011).

3.2.5 Filtering

Filtering removes unwanted frequency components from the fMRI data (Jenkinson & Smith, 2006; Lindquist, 2008). Through FEAT, high-pass filtering and spatial smoothing can be done.

3.2.5.1 Spatial filtering (smoothing)

This step is applied to each of the functional brain volumes. Smoothing (averaging) replaces the value at each voxel with a weighted average of the values surrounding that voxel. This increases the signal-to-noise ratio (SNR) by reducing the random noise which gives more validity to statistical results. The only problem is that the spatial resolution is reduced. The most commonly used technique is Gaussian filtering (Mikl et al., 2008), see Figure 3-26. For spatial smoothing, the value of the spatial filter’s width is in mm; based on Jenkinson and Smith (2006), a width between 3—10 mm is recommended to increase SNR.



No Smoothing

Smoothing

Figure 3-26 Smoothed version of brain image.

3.2.5.2 Temporal filtering

This step is applied to each voxel's BOLD time series, see Figure 3-27 for illustration on a sine wave.

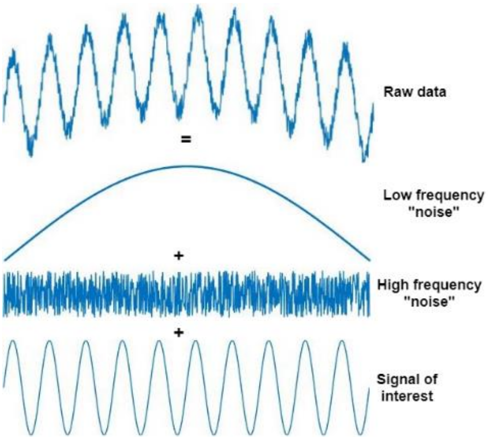


Figure 3-27 Raw data decomposed into different components.

High-pass filtering

High-pass filtering aims to remove all slowly-varying unwanted signals in each voxel's time series. These unwanted signals can be due to physiological effects, such as heartbeat and breathing, or drifts coming from the scanner that can be attributed to hardware instability.

Low-pass filtering

Low-pass filtering aims to reduce high-frequency noise in each voxel's time series, without affecting the desired signal. When using high- and low-pass filtering together, it is necessary to design the filter carefully, so that it removes the noise only and keeps the desired signal. Low-pass filtering, however, is not always recommended, as when used with event-related experiments, it can cause problems as these desired signals are changing rapidly. The smoothness of the time-series is another issue, as low-pass filtering increases smoothness ("smoothness" makes the intensity of each time point closer to the values of its neighbours more than the values of any point elsewhere) after smoothing and leads to loss of valuable information. More analysis is needed to correct for the low-pass filtering effect, as the significances are more likely to be overestimated, which can lead to false positives (Caparelli & Tomasi, 2008).

3.3 Co-registration and normalization

This step is needed to compare individuals by mapping all the separate scans of each subject to a single template, which is essential for group analysis (Jenkinson et al., 2002; Jenkinson & Smith, 2006; Lindquist, 2008).

3.3.1 Co-registration

This process registers low-contrast functional T2* images with high-contrast structural T1 images. This allows one to visualize single-subject task activations overlaid on the individual's anatomical information. It also facilitates transforming fMRI images to a standard brain atlas more straightforward (Jenkinson & Smith, 2001), see Figure 3-28.

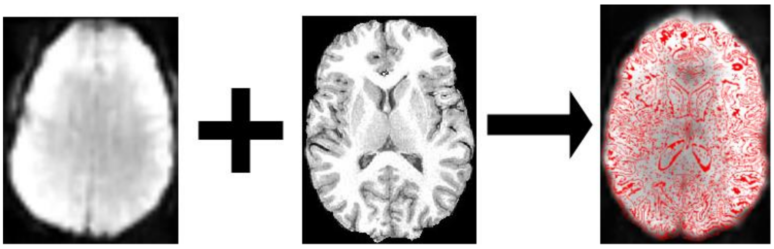


Figure 3-28 Registering a functional image to structural image for each subject.

3.3.1.1 Functional to structural

In this step, the functional 4D images are registered to their structural (anatomical) image as a first step towards transferring them to standard space.

3.3.1.2 Structural to standard

In this step, the structural image is registered to standard space.

3.3.2 Normalization

3.3.2.1 Functional to standard

This process registers between subject's functional/structural data to a standard space data set. All brains are different, so, basically, normalization tries to fit the images to the standard brain by stretching, squeezing and warping each brain. The most commonly used template (atlas) is the Montreal Neurological Institute 152 (MNI152; averaged from T1 MRI images of 152 subjects). This process can reduce the spatial resolution, see Figure 3-29.

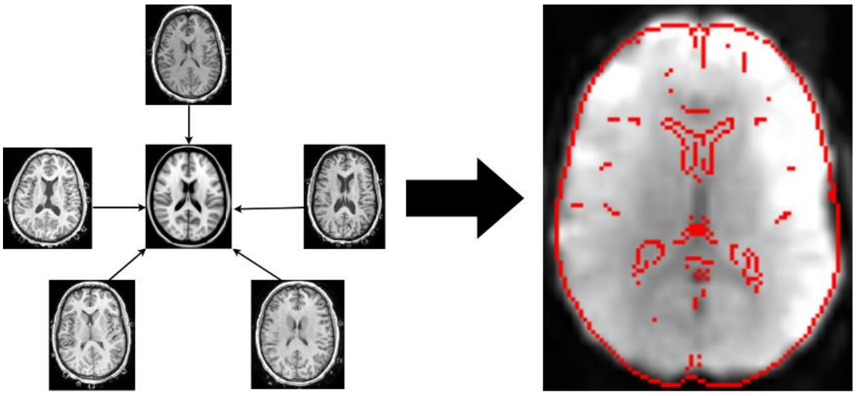


Figure 3-29 Registering functional/structural images of each subject to MNI152 template.

3.4 Statistical analysis for fMRI

Statistical analysis is applied to fMRI data to achieve multiple goals: (1) localize task-activated brain areas, (2) determine networks related to certain brain function, and (3) predict the psychological states or predict disease progression. Statistical maps are generated by converting the statistics to a probability value based on the DOF or the number of unconstrained data points and appropriate thresholding (Smith, 2004; Wager & Lindquist, 2015; Woolrich et al., 2016), see Figure 3-30.

This step is involved in both subject level and group level statistical analysis. Through this step, the BOLD signal can be represented as accurately as possible with multiple explanatory variables and confounds plus an error term. A good representation will help the algorithm to find the significant regions of the brain (if any) that follow a certain contrast.

Figure 3-30 fMRI statistical analysis illustrated. Adapted (from Woolrich et al., 2016).

3.4.1 General linear models

The basic idea behind general linear models (GLM)-based analysis of a subject’s fMRI data is that the observed data is equal to a weighted combination of several predictor variables plus an additive error term. The model functions are assumed to have known shapes (i.e., straight line, or known curve), but their amplitudes (i.e., slopes) are unknown and need to be estimated (Pernet, 2014; Poline & Brett, 2012; Wager & Lindquist, 2015; Woolrich et al., 2016; Woolrich et al., 2001), see Figure 3-31.

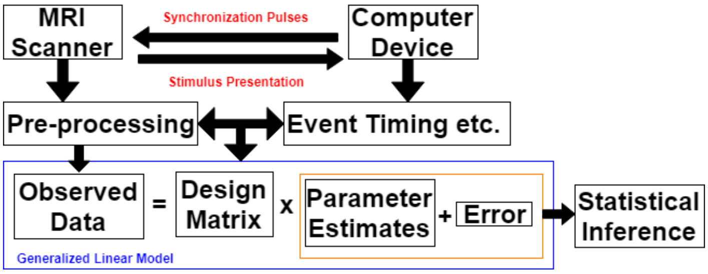


Figure 3-31 General linear model (GLM) illustrated. (Adapted (from Woolrich et al., 2016).

GLM is a univariate method, which builds models for independent voxels' time series (Smith, 2004). On the other hand, multivariate methods use all the data at once to build the model (Friston et al., 1994). GLM, although being a simple and strong method for modelling data, it is highly affected by mismodelling (Lindquist, 2008), which could lead to power loss and increase in the false positive rates, it also depends on assumptions that might not be valid always (Monti, 2011; Poline & Brett, 2012). However, multivariate methods are highly affected by subject-related artefacts, such as motion-related artefacts, compared to GLM (Zhang et al., 2009; Zhang et al., 2008). We cannot assume that the GLM used has covered all the regressors needed to minimize the residual errors. But since the distortion correction step, which is one of the motion-related artefacts, has not been done due to lack of data, using the GLM approach is more valid. Also, since a motion censoring instead of a motion regression approach was used to correct for motion artefacts, the quality of denoising is highly improved (Siegel et al., 2014).

In analysis, regressors are normally generated by convolving the time-course of the experimental paradigm, known as explanatory variables, with the HRF, see Figure 3-32.

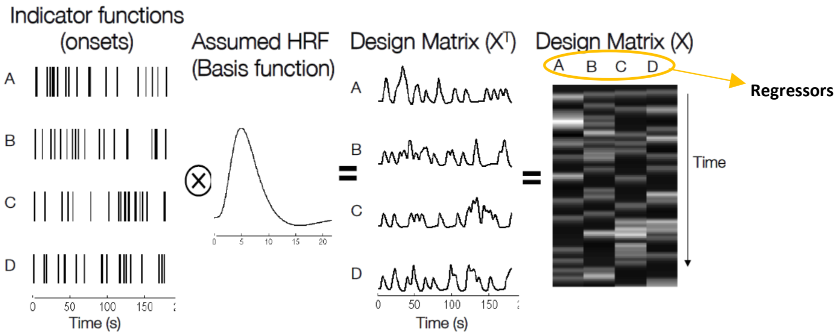


Figure 3-32 The design matrix is the result of convolution of the HRF basis function and the onsets of each event during the experiment (from Wager & Lindquist, 2015). This generates regressors that best account for the changes in the actual BOLD signal. The differences between the actual and estimated BOLD signals are the residuals.

There are two types of regressors: (1) experimental regressors, that represent those variables which you control based on your experiment, the type of variable used affects how it will be represented in the design matrix, (2) regressors of no interest or nuisance regressors, which represent those variables you did not manipulate but you know or suspect may have an effect, such as the 6 movement regressors (3 rotations & 3 translations), motion outliers matrix, or physiological factors (e.g., heart rate and breathing). By including nuisance regressors in the design matrix, the amount of error will be decreased.

3.4.2 Within-subject analysis

The aim of the first-level statistical analysis is to calculate how much each regressor factor X affects the observed (BOLD signal) value of Y by determining β which represents the regressor factor's weight.

3.4.2.1 Building the GLM

A good design matrix will best represent the BOLD fMRI signal (Monti, 2011), see Figure 3-34. Hence, regressors explaining much of the BOLD signal will have high magnitude parameter weights (larger β values), whereas regressors explaining little of the BOLD signal will have parameter weights close to zero. The residual (ε) is the residual error term. It is the difference between the actual data and the value predicted for it with the model, where the intercept is the mean level of fMRI signal over time, and across all conditions, for a particular voxel. The GLM can be simply represented via matrix notation (Monti, 2011), as Figure 3-33:

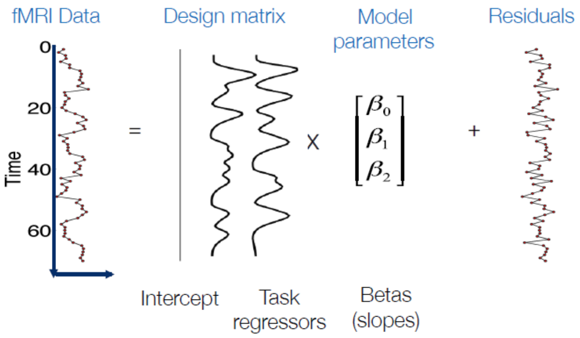


Figure 3-33 GLM for 1st-level analysis. Adapted (from Monti, 2011).

After fitting the GLM as in Figure 3-34, the estimated parameters (β) are used to create the contrast image, so significant activations present in the voxel can be determined.

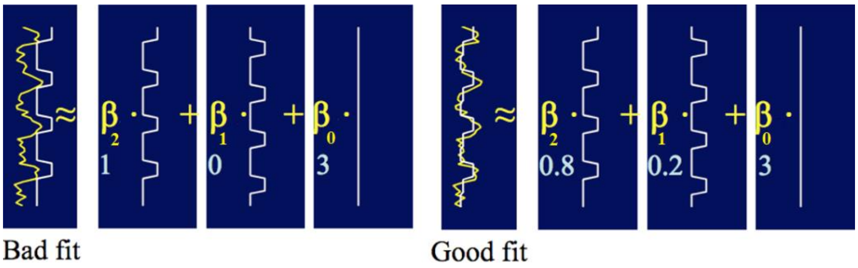


Figure 3-34 The effect of beta value. Changing the beta parameters to get the best fit, adapted (from Woolrich et al., 2016).

Using FEAT, a GLM model can be built by accounting for events-of-interest regressors, task-related regressors, and their temporal derivatives. The model can then be temporally filtered based on FEAT recommendations. In the model setup, the shape of the events-of-interest regressors file has a three-column format (onset, duration, last column is by default 1), and one-column format for task-related regressors, then the regressors are convolved with an HRF function. A double-Gamma HRF can then be used as is commonly the case (Wager & Lindquist, 2015; Woolrich et al., 2016).

3.4.2.2 Contrasts

In this step, the scientific question (hypothesis) is addressed by setting the contrasts to certain condition/s, for example event A relative to baseline or event A relative to event B. After having the GLM model ready, FEAT can estimate the signal magnitude in response to a certain condition.

3.4.3 Group analysis

Group analysis can follow two strategies: one is only limited to the sample (i.e., subjects) of a certain study whereas and the other allows one to make valid inferences based on the population that the sample was taken from (Monti, 2011; Wager & Lindquist, 2015; Woolrich et al., 2016). The aim of this analysis is to generalize the results to a population of unobserved data by performing analysis on a group of subjects from the same experiment.

Group analysis of fMRI data can be performed using fixed-effect or mixed-effect analysis, see Figure 3-35. Fixed-effect analysis assumes that the experimental effect is the same for all subjects. It ignores any inter-subject variance in the BOLD data, taking only within-subject variance into account. All subjects are modelled using a single linear model assuming only one variability source. Fixed-effects analysis restricts statistical inference to the particular sample of subjects. The results are highly sensitive to outliers. Thus, the use of fixed-effect group analysis is thus generally discouraged in multi-subject fMRI studies.

In contrast, the mixed-model approach, which is a parametric approach, takes both the within-subject and inter-subject variances into account. It is based on the two-stage summary statistics approach which has two stages (Friston et al., 1998). In stage one, the data from each subject is analyzed separately, resulting in individual means and within-subject variances that will be fed into the group model. Stage two uses all the individual means and within-subject variances to estimate the between-subject variance, and then supplies group inferences (Beckmann et al., 2003; Monti, 2011; Woolrich et al., 2004a).

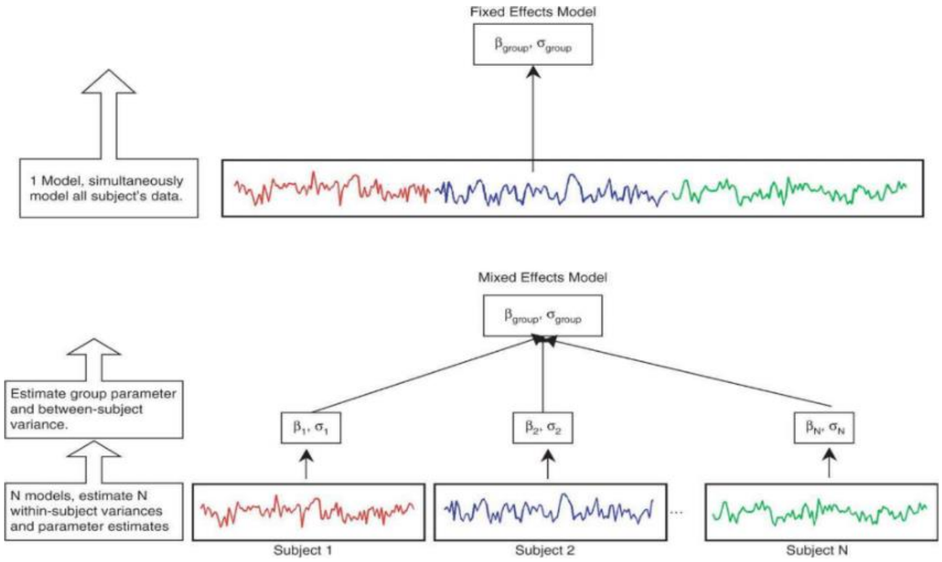


Figure 3-35 Schematic illustration of fixed-effect and mixed model analysis (from Mumford & Poldrack, 2007).

3.4.3.1 Corrections for multiple comparisons

In fMRI data, each brain volume contains thousands of voxels. Since a statistical test is conducted on each individual voxel, the possibility of false-positive results is high. To reduce the chances of false positives, multiple comparison correction must be applied (Monti, 2011; Wager & Lindquist, 2015; Woolrich et al., 2016).

Choosing a suitable threshold value is important to decide whether voxels are ‘active’ or not. The standard method to perform multiple comparisons is by controlling the probability of achieving a false positive for each statistical test through tuning the threshold for every voxel in the brain simultaneously. In neuroimaging, many approaches have been suggested by researchers to control the false positive rate. The major difference between methods is whether they are based on family-wise error rate, which is the chance of obtaining one or more false positive voxels (or clusters) anywhere in the brain, or for the false discovery rate (FDR), which is the proportion of false positives among all rejected tests (Wager & Lindquist, 2015; Woolrich et al., 2016).

Threshold-free cluster enhancement (TFCE) (Smith & Nichols, 2009) is also used to correct for multiple comparisons as it addresses the problems of threshold dependence and localisation in cluster inference compared to cluster-extent based thresholding (Woo et al., 2014). Also, the widely used cluster-extent based thresholding method, as reported in (Yeung, 2018), has been shown to produce corrected results that are erroneous (Eklund et al., 2016), which calls into question the validity of these published results.

3.5 Group-ICA analysis

Hypothesis-driven analysis methods like voxel-wise analysis in fMRI have a limitation: given that the BOLD signal is a complex mixture of signal sources, some might be of interest and the majority might be noise due to different reasons. The main idea is to best represent the BOLD signal through the model, which is usually a GLM (Worsley & Friston, 1995), and for that to happen, the most accurate information, in the form of regressors (conditions which are tested against the null hypothesis) and confounds needs to be available. However, this is not always the case. The main problem comes from the model assuming it has all (or at least the majority) of information needed which represents the spatiotemporal characteristics of the BOLD signal. But since many parts of the signal are not even modelled, they will bias the parameter estimation and cause an inflation to the residual error, which might largely remove any chance of finding a significant result.

ICA (Comon, 1994) is an exploratory technique which can be applied to fMRI as an alternative method to the hypothesis-driven method. ICA can find maximally statistically-independent spatial sources which reconstructs the data (Beckmann et al., 2000; McKeown et al., 1998). It has been shown to outperform hypothesis-driven methods in challenging data (Calhoun et al., 2006; McKeown et al., 2003).

3.6 Functional connectivity

The human brain is an efficient and complex network, formed by from multiple brain regions each performing a unique function, in addition to the continuous process of sharing information between these brain regions. In the past, a major interest in brain research was to investigate the functionality of the brain regions. However, as the development of research tools has progressed, a new interest on functionally exploring interactions between brain regions has emerged. FC has been defined as “temporal dependence of neuronal activity patterns of anatomically separated brain regions” (Aertsen et al., 1989; Friston et al., 1993). In other words, to measure the similarity between two brain regions through the signals generated in each of them by using a correlation method, for example, so that if the signals from two regions are correlated, this can indicate two regions being connected (Shirer et al., 2012).

FC can reveal a deep understanding of the brain and how different brain networks communicate and collaborate in the form of networks, where we can explore the underlying mechanisms of the brain during a human behaviour or when facing a neurodegenerative diseases (Bullmore & Sporns, 2009; Greicius, 2008). FC has been shown to be practical during resting-state studies by investigating the co-activation level through a functional time-series of different brain regions (Biswal et al., 1995; Damoiseaux et al., 2006; Greicius et al., 2003; Lowe et al., 2000; Salvador et al., 2005). There are two main types of FC analysis: (1) voxel-based methods, and (2) node-based methods (Bijsterbosch et al., 2017), each of which can answer specific research questions. The key rule is whether the analysis is primarily interested in certain brain regions, which might form a well-known network, or not, because if the ROIs are known, then the node-based methods will be more appropriate. But if there are no specified ROIs, voxel-based methods can be used.

3.7 Summary

In this chapter, the physical and neurophysiological bases of fMRI, its spatiotemporal characteristics, and its application to investigating brain function have been reviewed. The MR signal is generated by application of an external magnetic field and electromagnetic energy to the subjects. The BOLD signal is observed due to changes in the oxyhemoglobin-deoxyhemoglobin ratio during neuronal activity.

The BOLD fMRI data need to be pre-processed to reduce the variability in the BOLD signal and prepare the data for statistical analysis. Statistical analysis of fMRI involves identification of the brain regions that show a significant change in BOLD activity during the time periods of interest within each subject and determining the significance of the effect within and across subjects. The BOLD fMRI technique can provide an unparalleled insight into brain function, by using voxel-wise, group ICA, and FC analyses. The brain mechanisms underlying spontaneous behaviours such as MSs and ALs can be investigated by recording multiple behaviours and physiological characteristics simultaneously with fMRI data.

Chapter 4: Understanding EEG

4.1 Introduction to the Electroencephalogram (EEG)

The optimum brain imaging technique will have both high spatial and temporal resolutions, be portable, inexpensive, and non-invasive; however, this does not exist (yet). fMRI is well known for its high spatial resolution, but lacks high temporal resolution. EEG can add the missing part by its high temporal resolution (Tatum IV, 2014).

4.1.1 What is EEG?

EEG is a non-invasive imaging technique that measures the electrical activity of the brain from multiple locations on the scalp based on a standard spatial system. These measures primarily reflect neuroelectric activity generated in the cortex (Tong & Thakor, 2009).

4.1.2 What does the EEG device measure?

EEG measures a synchronized electrical activity of a populations of neurons, where the neuron is the building block of the central nervous system (Bear et al., 2007).

4.1.2.1 The neuron

A neuron consists of three main parts: (1) the cell body (soma) which contains the nucleus, receives the stimuli from other neurons, processes them, and, after reaching a certain threshold, the cell fires a pulse through the axon to transmit the information to other neurons, (2) the axon, a medium that the pulse of the cell passes through to the axon terminals, and (3) the dendrites, which connect with the axon terminals of other neurons (Bear et al., 2007), see Figure 4-1.

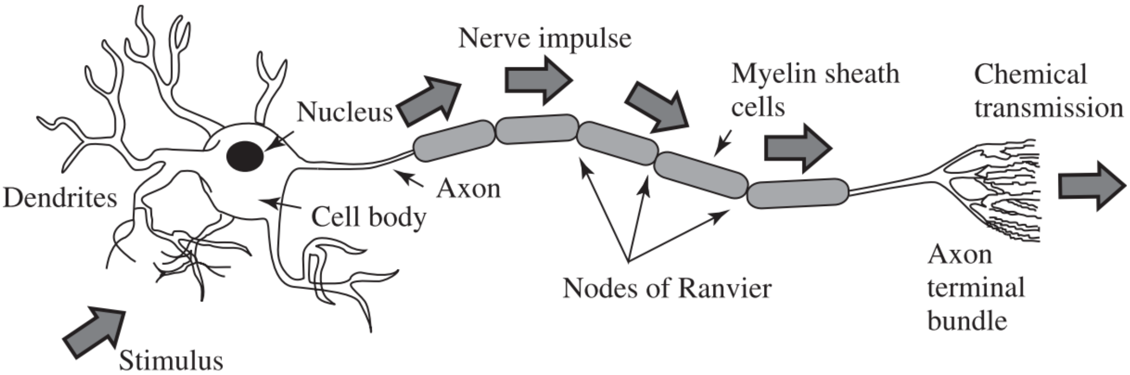


Figure 4-1 Structure of a typical neuron (from Atwood & MacKay, 1989).

Dendrites are not physically connected to the axon terminals of other neurons, but instead, the connection occurs through a small cleft called the synaptic gap. The dendrites of one neuron can be connected to millions of axons from other neurons (Martini & Bartholomew, 1998).

EEG cannot measure the signal coming from one neuron, the cerebral cortex neuron named pyramidal cell to be exact (Bear et al., 2007), as it is too small. The brain has plentiful number of neurons that are constantly active. To achieve a certain goal in the brain, a large group of neurons work together, and this produces a sudden large electrical current that can be measured by the EEG. However, some conditions need to be fulfilled for this to happen (Wessel, 2006), as illustrated schematically in Figure 4-2.

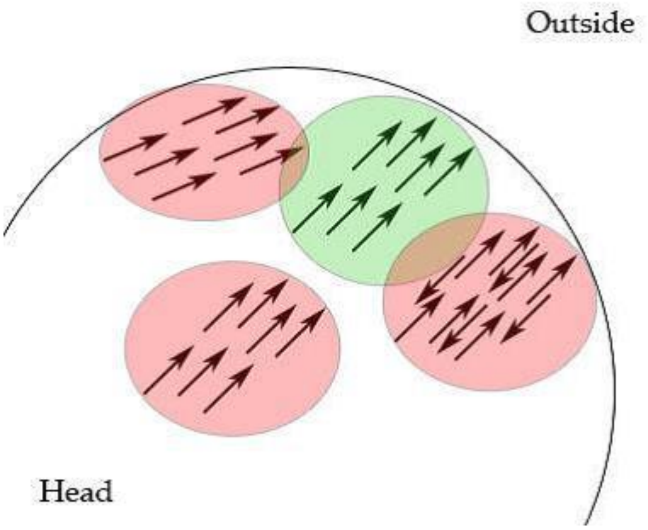


Figure 4-2 Cross section of the head: The activity from the neurons in the green circle only can be measured (from Wessel, 2006).

- To achieve the best measurement of signal by the EEG, the group of neurons must produce an electric current perpendicular to the scalp.
- The group of neurons must fire in parallel.
- The group of neurons must fire with the same polarity, otherwise they cancel each other out.

Because of these constrains, the majority of neuronal activities cannot be measured by the EEG.

4.1.3 Brain rhythms

Based on frequency ranges, there are five major spectral bands: delta (δ), theta (θ), alpha (α), beta (β), gamma (γ) (Hammond, 2007; Kirmizi-Alsan et al., 2006; Niedermeyer & da Silva, 2005; Tatum IV, 2014; Teplan, 2002), see Table 4-1.

Table 4-1 Brain waves.

Wave	Frequency (Hz)	Mental State	Location
Delta	2–4 Hz	Deep sleep	Center cerebrum and parietal lobes
Theta	4–8 Hz	Consciousness but drowsy	Positions not related to activity
Alpha	8–14 Hz	Relaxation without paying attention	Occipital and parietal lobes
Beta	14–30 Hz	External active attention	Parietal and frontal lobes
Gamma	≥ 30 Hz	Associated with cognitive and memory	Somatosensory cortex

4.1.4 EEG recording

EEG uses electrodes with high conductivity (low impedance, preferred to be less than 5 kΩ) for scalp recordings. These electrodes are set according to a spatial standard known as 10-20 system, where electrodes are separated by 10-20 % of the total head's circumference distance. The number of electrodes is usually 16-20, although other systems exist with 32, 64, 128, and even 256 electrodes (Klem et al., 1999). Previously, the electrodes were placed manually which was time-consuming and not practical, but currently, readymade caps with the electrodes attached to their proper positions are used; these caps are easily fit for different subjects (Fisch & Spehlmann, 1999), see Figure 4-3.

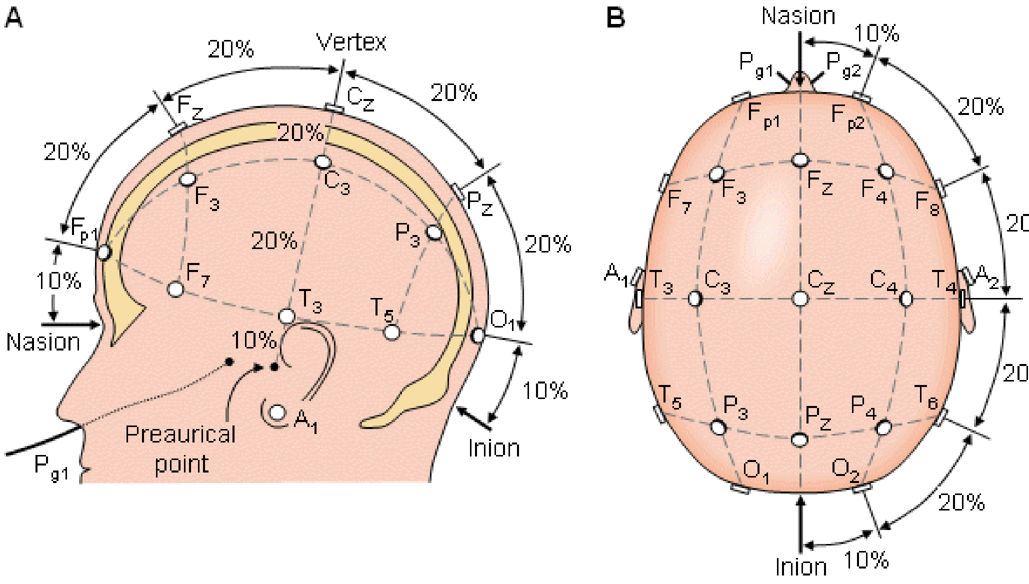


Figure 4-3 The electrodes in the 10-20 international electroencephalogram (EEG) replacement system (from Niedermeyer & da Silva, 2005).

4.1.4.1 Montages

The recorded EEG signal is the difference between an electrode and a reference. This set up can be in two montages: (1) monopolar, which is the difference between the electrode of interest and a reference of a passive electrode such as (A_1 or A_2) or a reference that represents the average of all electrodes, (2) bipolar, which is the difference between two adjacent electrodes. The standard notation for electrodes uses capital letter and numbers, with odd numbers representing the left side, the letter F represents electrodes above the frontal lobe, P for parietal lobe, T for temporal lobe, O for occipital lobe, C for the central part of the brain, and Z for the midline (Teplan, 2002), see Figure 4-4.

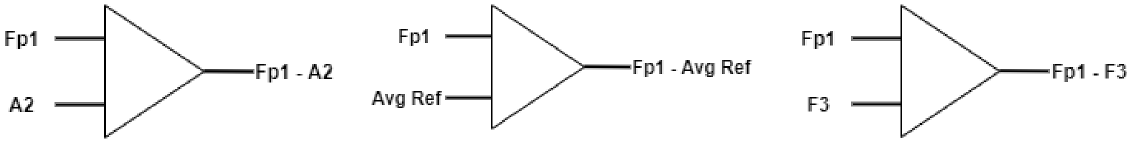


Figure 4-4 EEG recording montages. The image at the left is monopolar with earlobe A_2 electrode as a reference. The image in the middle is monopolar with an average of all electrodes as a reference. The image on the right is bipolar between two electrodes.

4.1.4.2 Electrodes

Electrodes are simply a mean to sense electric potential on the scalp to the input of amplification and filtration circuits of the EEG machine. To provide the best EEG recordings, a good contact should exist between the electrode and head. Electrodes are generally made from different types of metal. However, the conductivity is affected by the electrode-scalp impedance, so a conducting solution such as gel or paste is placed between the electrode and the head, although some electrodes are gel-free (dry) (Fisch & Spehlmann, 1999). Some of the popular electrodes types are: (i) the electrode caps with disposable electrodes (no gel or pre-gelled) usually used in medical applications for hygienic precautions, (ii) electrode caps with reusable disc electrodes (gold, silver, stainless steel, or tin), which are used in research mostly, (iii) headbands/headsets which are commercial and used by public, and (iv) needle electrodes which are used in invasive recordings (Sanei & Chambers, 2007).

4.2 Pre-processing pipeline of EEG

After the acquisition of the raw EEG data, the data should be pre-processed for enhancement. Noise sources, which commonly contaminate the EEG signal can be physiological such as sweating, movement, cardiac pulse, and muscle activity, or non-physiological such as power-line noise and bad/broken electrode contact (Michel & Brunet, 2019). In order to achieve a high SNR, these noise sources and artefacts should be identified carefully then removed. Doing this manually by visually inspecting the data is the most guaranteed way, although it can require considerable time and hard work. However, with the increasing need to analyse larger datasets, automatic noise removal techniques are highly used but should still be followed by visual inspection for validation (Pernet et al., 2018). The following describes the main pre-processing pipeline steps, see Figure 4-5.

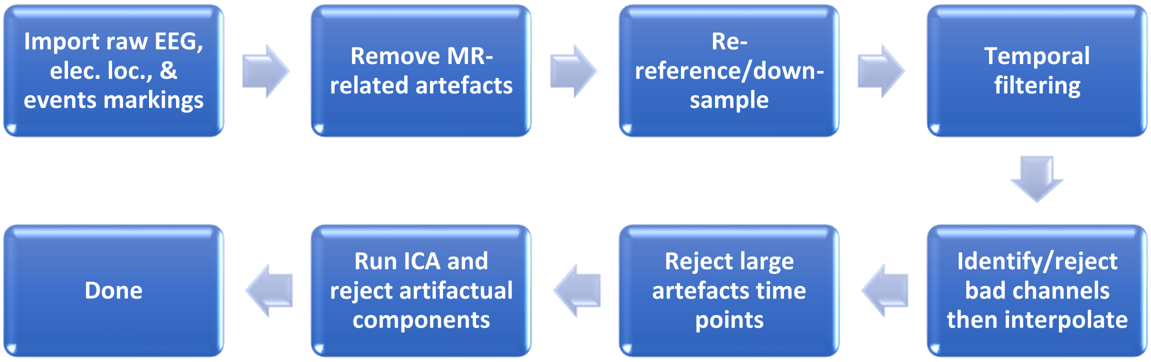


Figure 4-5 EEG Pre-processing pipeline.

4.2.1 MR-induced EEG artefacts

The simultaneous EEG-fMRI data recordings introduce artefacts into the EEG. Here the magnetic resonance artefacts affecting the EEG are discussed. There are two main types of this noise: gradient artefacts (GAs) and pulse artefacts (PAs) (Abreu et al., 2018).

4.2.1.1 Gradient artefacts

During fMRI scanning, the time-varying magnetic field gradients in the scanner (Allen et al., 2000; Niazy et al., 2005) induce an electromotive force into the conducting loop between the EEG and the subject's head. Hence, an artificial voltage, called GA, is created on the EEG electrodes (Grouiller et al., 2007). This artefact has a voltage amplitude which is higher than the average EEG amplitude, and has a similar frequency spectrum to that of the EEG signal. So, removing this GA is not a straightforward process.

4.2.1.2 Pulse artefacts

The PAs, also known as ballistocardiogram artefact, are one of the major artefacts in simultaneous EEG-fMRI recordings. Inside the scanner's static magnetic field, blood pulsation in the arteries of the scalp causes electrode movement which creates the artefact. PA is hard to remove due to being: (1) highly non-stationary, (2) shares the same frequency range as EEG signal, (3) dependant on the spatial configuration of the electrodes in the magnetic field, and (4) dependant on changes with the strength of the scanner's static magnetic field (Debener et al., 2008; Iannotti et al., 2015).

The concept behind the methods used to remove these two major artefacts is based on the temporal variations of these artefacts. Using temporal principal component analysis, a set of basis functions can be identified. These basis functions can describe the temporal variations of these artefacts, which will then be fitted to and subtracted from the raw EEG signals, which will result in artefacts-free results (Niazy et al., 2005).

4.2.2 Temporal filtration

A temporal filter will remove all frequencies not related to the signal of interest; this can be done by a band-pass filter. In addition, notch filters can be used to remove specific frequencies (power-line noise ~ 50 Hz) if they fall within the range of interest (Michel & Brunet, 2019; Tong & Thakor, 2009). The range of filtering is range based on the question of the study; the focus of the research guides the scope of the filter's band, and also the technique (Jiang et al., 2019; Urigüen & Garcia-Zapirain, 2015).

4.2.3 Down sampling

After temporal filtering, as most of the frequencies not related to the study are removed, the EEG can be down-sampled. This can help dramatically in reducing the size of the data and save on storage space. Based on the Nyquist theorem, the down-sampling frequency should be at least double the highest remaining frequency in the data. Practically, as filters are not perfectly sharp, the recommended value for the down-sampling frequency is four times the highest remaining frequency in the data (Michel & Brunet, 2019).

4.2.4 Referencing

Based on the EEG acquisition device, this step can be avoided. For example, the Neuroscan headset does its own referencing directly. To attain optimal signals, referencing is needed to reject the common mode signal in post processing. Choices for referencing includes: (1) using the signal from a certain channel as a reference (e.g. mastoid electrode), or averaging the two mastoids electrodes, (2) choose the reference to be the overall average signal (Bigdely-Shamlo et al., 2015; Gabard-Durnam et al., 2018).

4.2.5 Bad electrodes removal

Due to displacement while recording or high impedances, some electrodes are best removed from further analysis because of data corruption. However, these electrodes can be interpolated in later processing using nearby electrodes (Bigdely-Shamlo et al., 2015; Gabard-Durnam et al., 2018).

4.2.6 EEG-specific artefacts

Regardless of having fMRI recordings alongside the EEG, other artefacts can still contaminate the EEG data (Tong & Thakor, 2009; Urigüen & Garcia-Zapirain, 2015). A broad knowledge of the types of these artefacts is necessary to exclude them efficiently.

4.2.6.1 Large artefacts rejection

Another step, which is validated by the visual inspection of continuous data, is reject obvious large artefacts from the EEG data, usually large electrode movement or muscle artefacts which have a transient high frequency, discontinuity in the data, or other events such as linear drifts.

4.2.6.2 Ocular artefacts

Ocular artefacts have a significant impact on EEG data. They originate from eye movement and blinking, and share similar amplitude and frequency ranges, as EEG (Schlögl et al., 2007; Tong & Thakor, 2009; Wallstrom et al., 2004).

4.2.6.3 Muscle artefacts

Muscle artefacts are well known to be a tough problem because different muscles are involved (Urigüen & Garcia-Zapirain, 2015). Activities like talking, sniffing, and swallowing produce muscle activities which are close to the EEG recording sites on the scalp (Goncharova et al., 2003; Tong & Thakor, 2009).

4.2.6.4 Cardiac artefacts

Cardiac artefacts are generated when an electrode is placed on top of or close to a blood vessel which expands or shrinks due to the heart working cycle (Hamal & bin Abdul Rehman, 2013; Tong & Thakor, 2009).

4.2.6.5 Extrinsic artefacts

Besides the artefacts listed above, external artefacts can also introduce interference into the EEG signal:

- Instrument artefacts: Caused by misplacement of electrodes and movement of cables.
- Electromagnetic interference: Caused by surroundings devices and power lines.

- Volume conduction artefacts: As multiple EEG electrodes are used for acquisition; an artefact will be introduced because of the coherence between the EEG electrodes (Nolte et al., 2004).

4.2.7 Blind source separation

EEG signals acquired from all electrodes can be decomposed into components that represent these signals (Ohara et al., 2004; Zhukov et al., 2000). One of the methods widely used is ICA (Winkler et al., 2014b), which decomposes the signals from multi-electrodes components so that they become as statistically independent as possible (Vigário, 1997). This helps identify irrelevant and noisy components so that they can be subsequently removed (Qin et al., 2004). After removing the unwanted components, the data can be reconstructed (Coyle et al., 2004).

As best practice in denoising EEG data with ICA (Grin-Yatsenko et al., 2010; Piazza et al., 2016), the non-stereotyped artefact (e.g., signal discontinuity) should be rejected before applying ICA, as this improves the performance of ICA at distinguishing common artefacts from neural signals. This denoising process, as suggested by Rong-Yi and Zhong (2005), can be enhanced when ICA is followed by a subsequent wavelet transform (WT) (Bentley & McDonnell, 1994), a process called wavelet-enhanced ICA (W-ICA), which is ideal for biomedical applications.

The pipeline of W-ICA is based on three stages: (1) decomposing the EEG data using ICA, (2) applying the WT to remove low-amplitude artefacts based on a threshold from each component without removing the component, then the components will be translated back into EEG signal format (Castellanos & Makarov, 2006), finally (3) another run of ICA to separate the neural components from the artefact components, and removal of the artefact components will be carried out after the contrast between the neural and artefacts components is increased due to wavelet thresholding (Castellanos & Makarov, 2006).

4.3 EEG source reconstruction and localization

The drawback of EEG is its relatively low spatial resolution. In order to study the physiological activity of the brain using EEG alone, it is necessary to overcome, as good as possible, the low spatial resolution. Hence, precise localization of the activity source is a major task (Michel & Brunet, 2019). However, this is an ill-posed problem, as there is no unique solution, due to the number of sources being many times greater than the number of electrodes.

To localize the activity, the analysis needs to solve two models: (1) the forward model from the cortical source to the signal at each electrode, (i.e.) the signal measured at the scalp is a linear combination of multiple sources in the brain (Brookings et al., 2009), see Figure 4-6, and (2) the inverse model which represents the opposite direction.

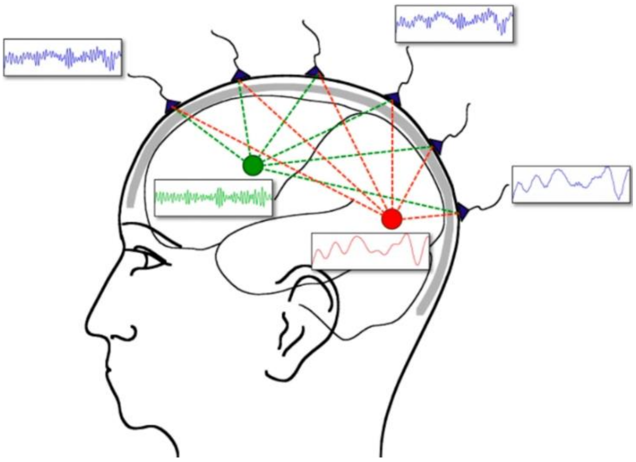


Figure 4-6 EEG sources linear combination (from Singh, 2018).

4.3.1 The forward problem

In order to explain how the activities from neural sources combine to create electrical potentials measured by external EEG electrodes, given the different conductivities of essential head tissues (WM, GM, CSF, skull, and scalp), we need to solve the forward problem. This is achieved by creating a volume conduction model, which is used to estimate the field distribution based on channel positions, a source model, and a head model. The more accurate these are, the higher quality the forward model will be, see Figure 4-7. For a review on the mathematical models, see Hallez et al. (2007).

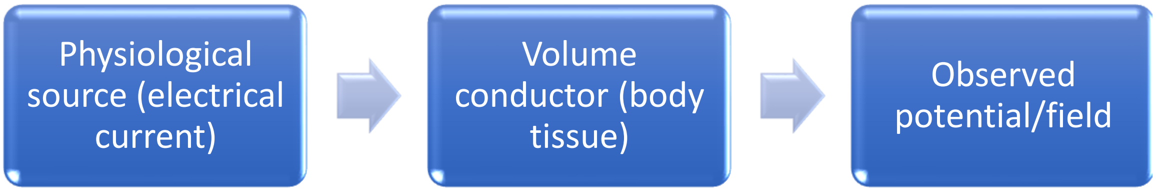


Figure 4-7 Forward model of EEG.

4.3.1.1 The geometrical description

Given that the highest accuracy is desired, it is desirable to use the subject’s anatomical MRI if available. This allows extraction of realistic information on the skin, skull, CSF, GM, and WM, when the T1 image is segmented into different tissues. If not available, a standard atlas can be used. The segmented head can be used to create a mesh for each tissue, with the mesh being triangulation or hexahedron.

4.3.1.2 The head model

Forming the volume conduction model is a critical process which is not straightforward, and which can require assumptions regarding the conductivity of each tissue. The main physiological challenge is that the electrical potentials are not evenly distributed on the scalp, due to differences in the skull’s thickness across the head.

The head model can also be represented as a sphere with uniform conducting material or a three-shell model consisting of three spheres representing the brain, skull, and scalp, or even more accurate with multiple spherical layers. However, commonly used models, which are more realistic, are boundary element model (BEM) (Akalin-Acar & Gençer, 2004), and finite element model (FEM) (Wolters et al., 2006).

Both of these latter methods can be used with a subject’s MRI, although, in terms of computational complexity, BEM with its three layers is much faster compared to FEM. However, as FEM takes the different tissues of the brain (WM, GM, CSF) into consideration, it produces to more accurate results (Miinalainen et al., 2019; Vorwerk et al., 2014; Vorwerk et al., 2012).

The EEG electrodes also need to be aligned with the same coordinates as the volume conduction model. This process might require a manual alignment according to the anatomical landmarks if the volume conduction model is based on the subject’s MRI. If not, an EEG electrode template can be used. Finally, the head model can be calculated based on the volume conduction model and the aligned electrodes.

4.3.1.3 The source model

The source model, also called the grid, determines the 3-D coordinates (XYZ) of dipoles on the 3-D cortical surface (source space). It basically assumes that the signals measured by the EEG electrodes are approximately generated by dipoles, or layers of dipoles to cover a larger cortical area, that represent sources. The source model is commonly be limited to GM sources. In addition, different distributions for the number of sources can be used.

4.3.1.4 Lead field

The previous acquired properties (head model, source model, and the aligned electrodes) allow the creation of what is called “lead field”. The lead field relates the activity measured on a specific electrode to different brain sources. All of this leads to more precise localization (Michel & He, 2012).

4.3.2 The inverse problem

The goal here is to estimate strength and location of signal sources (dipoles) that generate the EEG signals measured at the electrodes, see Figure 4-8. As there are extremely large number of signal sources, these sources can be merged in a similarly large number of ways to generate the same activity patterns measured by the electrodes. This is what makes the inverse problem ill-posed. This means that it is not possible to invert the forward model without applying prior assumptions to the model. For a more review of the mathematical model, see Grech et al. (2008).

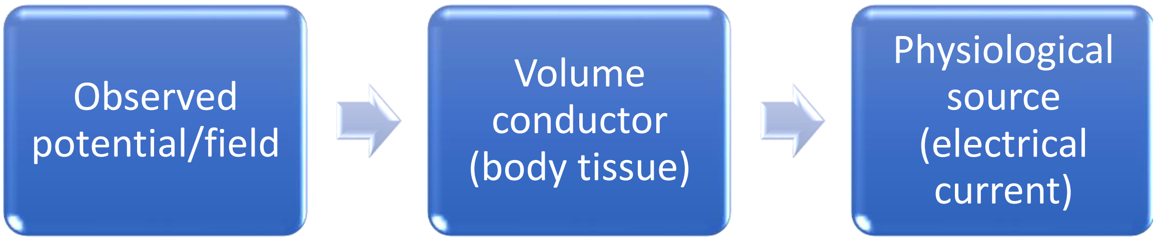


Figure 4-8 Inverse model of EEG.

4.3.2.1 Solving the inverse problem

Two categories of methods are used to solve the inverse problems (Baillet et al., 2001; Grech et al., 2008; Yao & Dewald, 2005): (a) parametric and (b) non-parametric. Parametric methods (also called spatial filtering methods) priory assume a fixed number of dipoles, then extract all the model’s information in some parameters. After that there is no need for the data. In non-parametric methods (also called distributed source models), both the parameters and the data’s current state are used to locate the sources.

4.3.2.2 Non-parametric methods

The solution space for the distributed source model is based on points distribution in 3-D space. A uniform grid is constructed throughout the brain, and the points which fall on the cortical surface are retained. Next, a current density vector, whose moment components are unknown, is placed at each point on the remaining grid. In each grid point, the total electric neuronal activity filling the volume that surrounds the grid point, also known as voxel, is represented by the current density vector. (Tong & Thakor, 2009).

Commonly used non-parametric methods are minimum norm estimates (MNE) and their generalizations (Dale & Sereno, 1993), low-resolution electromagnetic tomography (LORETA) (Marqui et al., 1994), standardized low-resolution brain electromagnetic tomography (sLORETA) (Pascual-Marqui, 2002), exact low-resolution brain electromagnetic tomography (eLORETA) (Pascual-Marqui, 2007, 2009), and local autoregressive average (LAURA) (Michel et al., 2004).

LORETA is a linear method that allows the 3-D reconstruction of sources in the brain to solve the inverse problem, which was shown to be a valid method from a neurophysiological perspective (Marqui et al., 1994). It uses a spherical head model that constitutes of three shells (skin, skull, and cortex) and is registered to a Talairach human brain atlas (Talairach, 1988). A 3-D grid will represent the brain volume, where each grid point (voxel) holds a source with a fixed position, however, the solution is limited to GM and hippocampus only. The electromagnetic field measured on the scalp determines the intensity and direction of the electrical activity at each source. One of the assumptions of this method is giving a higher probability for neighbouring neurons to be simultaneously active. LORETA method results in low spatial resolution images, which means the location with maximum activity will be affected by dispersion, this is because LORETA applies a spatial smoothing using a discrete spatial Laplacian operator. Although LORETA has a low spatial resolution, it was shown to have a high localizing accuracy, especially with deep sources (Pascual-Marqui, 1999), also it outperforms MNE by reconstructing deep sources as important as surface ones (Grech et al., 2008), in addition, the referencing method used while recording the EEG does not affect the reconstruction process (Pascual-Marqui, 1999). The mathematical background is provided here (Tong & Thakor, 2009).

Pascual-Marqui made the first modification on LORETA and proposed a new method called sLORETA (Pascual-Marqui, 2002), it standardizes the current density used to estimate the source localization and does not use the Laplacian operator, which is similar to what was suggested by Dale (Dale et al., 2000). In sLORETA, the MNE approach is used to estimate the current density, which will then be standardized using its expected standard deviation, as standard deviation is originated by measurements noise and also biological noises from actual sources. The technique proposed by Dale results in a systematic nonzero localization error even when the noise levels are small Although, sLORETA is similar to Dale’s method, as MNE is used to estimate the current density and the standardized values of the current density estimates determine the localization inference. There is a difference in how sLORETA adopts the standardization for current density, which will result in a lower localization error when compared to Dale’s technique. However, sLORETA is still affected by the low resolution, because of regularization in solution for stability purpose. Also, when the sources to be estimated have their spreads overlapped, sLORETA will fail to localize them (Jatoi & Kamel, 2018).

Another enhancement was made to minimize the localization error, especially with deeper sources by introducing a weight matrix; eLORETA method was introduced to achieve a zero-mean localization error (Pascual-Marqui, 2007), while keeping the standardized nature of sLORETA. The eLORETA method is not affected by the existence of noises such as measurement and biological related, in addition it was shown to be an adaptive technique which depends on data (Jatoi & Kamel, 2018).

4.3.2.3 Parametric methods

Beamforming is an adaptive spatial filtering technique for source localization. Its estimate of activity is calculated based on the weighted sum of the potentials of the scalp from different locations. The goal is to maintain the desired signal's components from a certain location, while preventing interference from other locations (Van Hoey et al., 1999). This method seems to be linear in the first sense, but as the weights used in the calculation are based on time-varying EEG measures, this method cannot be linear. The beamformer is efficient when a low number of dipoles are involved in the generation of the EEG activity, on the condition that the time series of these dipoles have low correlations. However, it will fail if the sources are correlated. It is important to highlight that this imaging method cannot estimate current density, so one cannot control to what extent the image will comply with real EEG measures (Tong & Thakor, 2009). Beamformers are highly sensitive to electrode misplacement (Dalal et al., 2014), unrealistic model of head volume (Neugebauer et al., 2017), and errors of forward models in general, in addition, estimating a covariance matrix from noisy data is challenging (Hosseini et al., 2018). Beamformer was shown to have a high performance when applied to ROI, which is hypothesis driven, this is very important when the prior knowledge of the research question is available (Oswal et al., 2014).

Commonly used parametric methods are beamforming techniques such as linear constraint minimum variance (LCMV) (Van Veen et al., 1997), dynamic imaging of coherent sources (DICS) (Gross et al., 2001), brain electric source analysis (BESA) (Hoechstetter et al., 2004), and subspace techniques such as multiple-signal classification algorithm (MUSIC) (Mosher & Leahy, 1998, 1999).

LCMV (Van Veen et al., 1997) strictly applies the idea of enhancing the desired sources while supressing the rest. It uses the adaptive spatial filters, after calculating their weights by means of a covariance matrix of the EEG's time series (Barnes & Hillebrand, 2003), regardless of the noise covariance (Vrba & Robinson, 2001). Isolating the calculation of the signals generated at different brain areas leads to independent solution at each point. LCMV can be however, highly affected by any small mismatches between true and estimated models (Hossein Hosseini et al., 2018; Vorobyov et al., 2003). DICS (Gross et al., 2001) enhances over LCMV; it used cross-spectral density instead of covariance matrix to compute the spatial filter in frequency domain based on realistic head models, where it will be applied at the sensor level. However, DICS has two major drawbacks: (1) the assumptions of unconstrained single dipole model that does not correlate linearly with other dipoles, which will only be valid in the case of intermediate coherence and sufficient SNR (Gross et al., 2001), (2) the self-coherence is one in all defined regions.

4.3.2.4 Comparisons of inverse techniques

Halder et al. (2019) compared parametric and non-parametric source localization technique. This comparison led to no clear winner, although, some techniques were superior in certain situations. DICS and eLORETA were used to compute the sources underlying 40-Hz activity. For the distributed dipole scenario, the focal width of eLORETA was better than DICS with higher SNR. Also, eLORETA had greater control of the false positive ratio, but the localization error of DICS was less than eLORETA. Jatoi et al. (2014) compared eLORETA and sLORETA, and showed that eLORETA is superior for localizing sources with sharper images compared to sLORETA. Also, the ability to suppress less significant sources is higher for eLORETA compared to sLORETA (Jatoi et al., 2014).

4.4 Spectral and statistical analysis of EEG

4.4.1 Data epoching

Focusing on events of interest, a time-window is applied to the continuous EEG data in order to extract these epochs (Möcks & Gasser, 1984), so the result will be a matrix of [electrodes x time x epochs], where *time* is the duration of the epoch, and *epochs* is the number of events extracted from the continuous EEG data.

4.4.2 Frequency representation of EEG

The spectral content of EEG is of central interest. Spectral analysis methods commonly used in EEG for this purpose include FFT, Hilbert transform, and WT. The study objective determines whether frequency analysis, time-frequency analysis, or wavelet is most appropriate. Details on the three methods applied to EEG are provided by Freeman and

Quiroga (2012). Since the interest is to see the change of power in defined EEG bands, a basic FFT will be enough, as Bruns (2004) has shown that FFT, Hilbert transform, and WT give similar spectral amplitude in practical application to neural signals.

After extracting epochs related to the event of interest, and transforming them into the frequency domain, the EEG band of interest will be extracted through a band pass filter with limits defined based on the band. The mean power of the band of interest related to the chosen event can then be calculated for each source of the inverse model of each subject separately.

4.4.3 Statistical test and correction

The final part of the analysis is to compare the average of events to the average of their baselines statistically. After calculating an average event and an average baseline for each subject, each having the same number of sources with one value for each source. The relative difference between the average event and average baseline can then be calculated for each subject to be used in the group stats. Source statistics should be applied to compare the percentage change to the null hypothesis of zero. Statistical analyses can be performed using permutation tests (Maris & Oostenveld, 2007; Maris et al., 2007), and the results corrected for multiple comparisons over sources and bands of interest, using a method such as family-wise cluster correction (Maris & Oostenveld, 2007) or TFCE (Mensen & Khatami, 2013).

4.5 Summary

In this chapter, the physical and neurophysiological basis of EEG, its spatiotemporal characteristics, and its application to investigating brain function were reviewed. Following a standard setup, EEG measures electrical activity on the scalp generated by multiple sources in the brain. The measured EEG signal must be cleaned and denoised from MR-related noise and EEG-specific artefacts. Because of the low spatial resolution of the EEG, a brain-model needs to be created to find the sources of the signals by means of source localizations and reconstruction methods. EEG signals can be split into defined frequency bands. Statistical analysis can be performed on the band of interest after epoching the time slots of the event of interest. The strength of EEG is in its high temporal resolution. Hence, in the case of short-duration type of events, where fMRI cannot catch the changes in neural signature, EEG is up to the challenge. Brain mechanisms underlying spontaneous behaviours such as MSs and ALs can be investigated by recording multiple behaviours and physiological measures, such as EEG simultaneously.

Chapter 5: Lapses of Responsiveness: A Physiological Review

5.1 Neural signatures of attention lapses

5.1.1 Mind-wandering

For increased understanding of the mind-wandering phenomenon, several studies have looked at neural activities related to this mind state.

5.1.1.1 fMRI Analysis

Brain imaging techniques such as fMRI have been used widely in studies on mind-wandering. Mind-wandering has been found to be positively associated with activity in default mode network (DMN), which has been shown to have increased activity during the resting wakefulness when not engaging in any external task (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007; Zhou & Lei, 2018).

Smallwood et al. (2012) hypothesized that perceptual information from dorsal attention network (DAN), along with autobiographical information from the DMN, steers the frontoparietal network (FPN) to either maintain attention to endogenous (internal) trains of thought and lose focus on external stimuli creating the mind-wandering process or vice-versa. FPN is associated with the regulation process of changing from external to internal attention and vice versa by changing its FC between DMN and DAN (Chica et al., 2013; Cole et al., 2013; Dixon et al., 2018; Macaluso & Doricchi, 2013; Spreng et al., 2010; Zanto & Gazzaley, 2013).

Also, Esposito et al. (2018) and Chai et al. (2012) concluded that the DMN and DAN typically show negatively correlated activity during both spontaneous oscillations and task execution. Fox et al. (2005) and Fox et al. (2006) showed that the DAN sustains external attention, as there is an association between DAN activity and processing information from the external world. On the other hand, the DMN is activated when we are decoupled from the external world, and our attention has shifted to process TUTs (mind-wandering) (Mason et al., 2007). Also, research by Kawagoe et al. (2019) showed that in mind-wandering, in thoughts related to both past and future, a bilateral increase in activity was found partially found in DMN regions in medial superior frontal gyrus and anterior cingulate cortex (ACC)/medial prefrontal cortex.

Through a resting-state study, Godwin et al. (2017) found an association between the trait of mind-wandering and increased FC within the DMN, as well as increased FC between DMN and FPN. He et al. (2021), through a longitudinal resting-state study, explored FC during mind-wandering. They found a stable association between mind-wandering and the FC between FPN and DMN, also a positive correlation between the frequency of mind-wandering and the FC within DMN. Increased FC within the DMN and between the DMN and the salience network (SN) have also been shown to be associated with mind-wandering in an fMRI study by Kucyi et al. (2017) using a tapping task. The SN aids in the detection of significant environmental cues and prioritises the most important among internal and extra-personal stimuli in order to guide behaviour. Thus, the SN facilitates the creation of appropriate behavioural responses to salient stimuli by target brain regions. When a salient event is noticed, the SN plays a vital and causal role in switching between task-related networks and the DMN to allow access to attention and working memory resources. What distinguishes the SN is that it initiates a cascade of cognitive control signals that have a significant impact on how such a stimulus is processed later (Menon & Uddin, 2010). Finally, Zhou and Lei (2018) used SART and found an association between mind-wandering and increased FC between DMN and visual network (VSN), while FC between FPN and VSN decreased.

The working memory network (WMN) plays an important role in mind-wandering. Mind-wandering is defined as a state in which attention is diverted to internal thoughts unrelated to the task (Ward & Wegner, 2013). These thoughts might be related to the past or future (Hartmann et al., 2014), which means the brain's memory is involved.

Wang et al. (2009) used fMRI in a task-free state followed by a memory task to hypothesize that offline memory reprocessing, in which the mind is disconnected from external input and starts looking at older memories, overlaps with the process of mind-wandering and is associated with high activity in the DMN. The DMN appeared to contain spontaneous thought-process networks consisting of the left precuneus, the left angular gyrus/superior occipital gyrus, the left inferior parietal lobule (IPL), the medial prefrontal gyrus, and the left hippocampus/para-hippocampus region. These networks appeared to be correlated with the frequency of occurrences of mind-wandering during natural resting and offline memory reprocessing states.

In summary, the DMN plays a substantial role in the mind-wandering process, whether through its increased activation or increased FC within its core regions and with other networks such as the FPN, VSN, and SN. On the other hand, the DAN, which is anticorrelated with the DMN, takes a major part in the external attention process, through its increased activation, and FC with other networks such as the FPN. A summary of fMRI literature on mind-wandering is in Table 5-1.

5.1.1.2 EEG Analysis

Increased EEG alpha activity over task-related brain regions is correlated with low levels of attention and poor performance (Macdonald et al., 2011). Also, when attention is externally directed in demanding tasks, the alpha EEG activity is reduced over the task-related brain areas (Rajagovindan & Ding, 2011; Sauseng et al., 2005). Molina et al. (2019) used a PVT and found that an increase in power in the alpha, theta, and beta bands in central-medial, parieto-occipital, and frontal regions of the brain was correlated with slow reaction time. Alpha band activity, which is inversely correlated with the activity in task-related regions (Liu et al., 2014), plays an important role in mind-wandering. Alpha activity increase has also been found to be associated with mind-wandering during demanding cognitive tasks, such as the speeded performance task (Compton et al., 2019) and the switching task (Arnau et al., 2020).

Research on mind-wandering by Baldwin et al. (2017) used a 20-min monotonous freeway-driving scenario. Mind-wandering events were characterized by reduced speed and increased lane-variability. They found that mind-wandering was associated with increased power in the alpha band. In a resting state study, Mo et al. (2013) used EEG-fMRI simultaneously, found an association between increased alpha power and increased DMN activity with opened eyes, which could be associated with mind-wandering process. This increased power was associated with an increase in DMN activity related to ALs/mind-wandering (slow reaction time) (Mason et al., 2007; Weissman et al., 2006).

The low-frequency EEG bands (delta and theta) were also hypothesized to be associated with mind-wandering. Andrillon et al. (2019) proposed that ALs could be explained by local-sleep phenomena, which is different from MS according to the authors. Local sleep was introduced by Huber et al. (2004) in sleep-related research and Vyazovskiy et al. (2011) in wakefulness-related research. What makes local sleep a unique state is that it carries combined transient and neurophysiological features from wakefulness and the different stages and depths of sleep as it is local in both space and time (Andrillon et al., 2019). Andrillon et al. (2019) hypothesised that if local sleep, defined by increases in delta and/or theta activities (slow-wave power), occurs within attentional networks, it could triggers the deactivation of attentional networks, and hence the activation of DMN (Chai et al., 2012; Esposito et al., 2018), which is associated with mind-wandering (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007). So, it can cause mind-wandering.

Andrillon et al. (2021) used EEG to study ALs while performing GO/NoGo tasks. Thought probes were used as an indicator for the mental state. Mind-wandering was defined as a shift of attention from task-related to task-unrelated thoughts. They found that slow waves, which are known to be associated with transitioning to sleep (Siclari et al., 2014) or local sleep (Andrillon et al., 2019; Bernardi et al., 2015; D'Ambrosio et al., 2019; Hung et al., 2013; Vyazovskiy et al., 2011), preceded reports of mind-wandering over the frontal EEG electrodes.

Braboszcz and Delorme (2011) investigated mind-wandering, and suggested it is associated with low alertness and decreased sensory processing. In a breath-counting task, they found increased theta and delta activity during mind-wandering, while alpha and beta activities decreased. An increase in delta activity was also found by Harmony et al. (1996) when shifting attention to internal processing of mental tasks.

van Son et al. (2019a) looked at the association between mind-wandering and the ratio between theta and beta activities, they used a breath-counting task, and found that the frontal theta/beta ratio is correlated with mind-wandering. The same task was used by van Son et al. (2019b), where fMRI data were collected, they found that FC during mind-wandering is associated with the theta/beta ratio, in which there was an increase in FC within the DMN and a decrease within central executive network.

Gamma band activity has also been found to be positively associated with mind-wandering. Qin et al. (2011) investigated, using EEG, the difference between subjectively-reported mind-wandering, which is based on thought probes, and behaviourally-indexed mind-wandering, which is based on performance errors. They used time-frequency analysis and found higher gamma activity in bilateral frontal-central areas in subjectively-reported relative to behaviourally-indexed mind-wandering. To investigate further, they used beamformer source imaging, and found that the gamma band had higher activity in the bilateral frontal cortices, supplemental motor area, paracentral cortex, and right inferior temporal cortex in subjectively-reported compared to behaviourally-indexed mind-wandering. In addition, beta activity was higher over bilateral frontal and central-parietal areas, and alpha activity was lower over medial central-parietal areas during subjectively-reported mind-wandering, whereas during behaviourally-indexed mind-wandering, alpha band activity was higher over medial frontal areas and theta activity was also high over left frontal-temporal areas. Their findings indicate that subjectively-reported mind-wandering is associated with processes of executive control.

Simultaneous recording of EEG-fMRI was used to investigate mind-wandering while performing a fast-paced SART (Groot et al., 2021). Participants were told to self-report mind-wandering. Groot et al. (2021) found that the neural signature of mind-wandering, when compared to responsive external attention, to be a deactivation in DMN, and an activation in the task-related network. Their result in the task-related network was not surprising, as task-related network has been shown to be involved in spontaneous thought processes (Christoff et al., 2009; Dixon et al., 2018; Fox et al., 2015). In contrast, DMN which is known to be activated during mind-wandering, was found to be inversely associated with the “in-the-zone” or good performance, while DAN was found to be associated with “out-of-zone” or weak performance (Esterman et al., 2014; Kucyi et al., 2017; Yamashita et al., 2020). Also, they found decreased FC within both DMN and the task-related network, and an increased FC between these two networks. In addition, delta, theta, and alpha bands had widespread increases, in contrast, beta was reduced.

To summarize, increased alpha activity is associated with lower attention levels in general, plus mind-wandering, which is correlated with the increased activity in DMN. Low-frequency EEG bands (delta and theta) were also associated with mind-wandering if they increased over the attention-related regions. In addition, increased beta and gamma activities were correlated with subjectively-reported mind-wandering. A summary of EEG literature on mind-wandering is given in Table 5-2.

Table 5-1 Summary of fMRI physiological findings on mind-wandering.

Research	fMRI Findings
(Andrews-Hanna, 2012)	- Increased DMN activity.
(Andrews-Hanna et al., 2010)	
(Mason et al., 2007)	
(Zhou & Lei, 2018)	
(Kawagoe et al., 2019)	
(Wang et al., 2009)	
(Fox et al., 2005)	

(Fox et al., 2006)	• Increased DAN activity.
(Spreng et al., 2010)	• FPN acts as a hub that manages the change from external to internal.
(Dixon et al., 2018)	
(Esposito et al., 2018)	• DMN and DAN are anticorrelated.
(Chai et al., 2012)	
(Godwin et al., 2017)	• Increased FC between FPN and DMN.
(He et al., 2021)	
(Godwin et al., 2017)	• Increased FC within DMN.
(He et al., 2021)	
(Kucyi et al., 2017)	
(Kucyi et al., 2017)	• Increased FC between DMN and SN.
(Zhou & Lei, 2018)	• Increased FC between DMN and VSN. • Decreased FC between FPN and VSN.

Table 5-2 Summary of EEG physiological findings on mind-wandering.

Research	EEG Findings
(Compton et al., 2019)	• Increased alpha EEG activity.
(Arnau et al., 2020)	
(Baldwin et al., 2017)	
(Mo et al., 2013)	• Increased alpha EEG activity. • Increased DMN activity.
(Andrillon et al., 2021)	• Slow waves preceded reports of mind-wandering over the frontal EEG electrodes.
(Andrillon et al., 2019)	• Hypothesised increases in delta and/or theta EEG activities, occurs in the task-related networks is associated with mind-wandering.
(Braboszcz & Delorme, 2011)	• Increased theta and delta EEG activities.
(van Son et al., 2019a)	• Frontal theta/beta ratio is correlated with mind-wandering.

(van Son et al., 2019b)	• Frontal theta/beta ratio is correlated increased FC within DMN, and decreased FC within central executive network.
(Qin et al., 2011)	• Association between subjectively-reported mind-wandering and increased gamma and beta EEG activities. • Association between behaviourally-indexed mind-wandering and increased alpha and theta EEG activities.
(Groot et al., 2021)	• Decreased DMN activity. • Increased task-related network activity. • Increased delta, theta, and alpha EEG activities. • Decreased beta EEG activity.

5.1.2 Mind-blanking

For increased understanding of the mind-blanking phenomenon, several studies have investigated neural activities related to this mind state. Based on subjective reports of ALs from subjects, Ward and Wegner (2013) concluded that mind-wandering and mind-blanking are two distinct mental states. Unsworth and Robison (2016b, 2018a) considered that mind-wandering has multiple levels and is different from the mind-blanking (inattentive) state behaviourally. In addition, mind-wandering is operationally different from mind-blanking, although both of them are common when it comes to decoupling attention from external tasks. Mind-blanking is defined as an empty mind state which more likely does not involve memory recall (Ward & Wegner, 2013).

5.1.2.1 fMRI Analysis

Research by Kawagoe et al. (2019) showed through a resting-state study that the mind-blanking state can be intentionally achieved by simply trying to think of nothing. The neural signature of mind-blanking was represented by changes in activity of DMN: activation in the bilateral ventral ACC and medial prefrontal cortex, and deactivation in the left Broca's area, left hippocampus, and bilateral superior frontal gyrus/supplementary motor area (SMA). A summary of fMRI literature on mind-blanking is in Table 5-3.

5.1.2.2 EEG Analysis

Andrillon et al. (2019) hypothesised that if local sleep, defined by increases in delta and/or theta activities, occurs in the DMN, it can cause mind-blanking. Their hypothesis was based on previous findings that associated the reduction of endogenous thoughts with the increase of slow-wave power over DMN regions. Also, when local sleep occurs within regions such as precuneus or posterior cingulate cortex (PCC) defined as “hot zone” (Siclari et al., 2017), could lead to a minimal experience of thoughts (blank), which is the case in white dreams within sleep (Fazekas et al., 2019; Windt et al., 2016).

Andrillon et al. (2021) used EEG to study ALs while performing GO/NoGo tasks. Thought probes were used as an indicator for the mental state. Mind-blanking was defined as an empty mind (absence of thoughts). They found that slow waves, which are known to be associated with transitioning to sleep (Siclari et al., 2014) or local sleep (Andrillon et al., 2019; Bernardi et al., 2015; D’Ambrosio et al., 2019; Hung et al., 2013; Vyazovskiy et al., 2011), preceded reports of ALs (mind-blanking) over frontal and posterior EEG electrodes. Castiglione et al. (2019) have explored beta activity when intentionally clearing the mind from any thoughts. They used a think/no-think task while recording EEG and found an increase in activity in right frontal beta in the successful versus the unsuccessful trials. A summary of EEG literature on mind-blanking is in Table 5-4.

Table 5-3 Summary of fMRI physiological findings on mind-blanking.

Research	fMRI Findings
(Kawagoe et al., 2019)	• Changes in activity of DMN. • Activation in the bilateral ventral ACC and medial prefrontal cortex. • Deactivation in the left Broca’s area, left hippocampus, and bilateral superior frontal gyrus/SMA.

Table 5-4 Summary of EEG physiological findings on mind-blanking.

Research	EEG Findings
(Andrillon et al., 2021)	• Slow waves preceded reports of mind-blanking (no thoughts in mind) over the frontal and posterior EEG electrodes.

(Andrillon et al., 2019)	• Hypothesised increases in delta and/or theta EEG activities, occurs in the DMN is associated with mind-blanking (no thoughts in mind).
(Castiglione et al., 2019)	• Increased beta EEG activity is associated with the state of (no thoughts in mind).

5.2 Neural signature of microsleeps

For a more in depth understanding of the microsleep phenomenon, a few studies have investigated the neural signature of microsleeps.

5.2.1 fMRI Analysis

Using a 2-D CVT task while recording fMRI, MSs was found to be associated with a decrease in BOLD activity in the bilateral thalamus, posterior cingulate gyrus, and medial frontal cortex, and an increase in BOLD activity in the inferior frontal cortex, posterior parietal cortex, and parahippocampal regions (Jones et al., 2010; Poudel et al., 2014; Poudel et al., 2009). Poudel et al. (2014) also investigated the correlation between the activity of BOLD signal and MSs while accounting for EEG theta and alpha activities as regressors. They found a positive correlation between post-central theta activity and MSs, in addition to a negative correlation between the occipital alpha activity and MSs. A summary of fMRI literature on microsleeps is in Table 5-5.

5.2.2 EEG Analysis

Peiris et al. (2006) used a 1-D CVT task with non sleep-deprived participants while recording EEG, and found that an increase in spectral power for delta, theta, and alpha bands, while beta and gamma bands had reduced spectral power. Poudel et al. (2010a) studied the relationship between MSs detected while performing a 2-D CVT task and the EEG theta band. They found a correlation between tracking error and theta activity at the Pz EEG electrode, but after removing the MSs from the data, that the correlation dropped substantially, showing that MSs heavily contribute to the performance fluctuations during the task.

Jonmohamadi et al. (2016) also used a 2-D CVT task while recording EEG. They found that MSs are more likely to be associated with spindles of alpha activity, generated in the bilateral anterior temporal gyri and hippocampi. These spindles were very similar to spindles in stage II sleep. Also, theta activity was generated from the bilateral frontal-orbital cortex.

Wang et al. (2020) used a flight simulator, as a practical real-time application, with participants who were pilots. The task had a monotonous nature which facilitated the occurrence of MSs. There was no change in activity in either the beta or theta bands, while there was a reduction in activity in delta and increased activity in alpha. A summary of EEG literature on microsleeps is in Table 5-6.

Table 5-5 Summary of fMRI physiological findings on microsleeps.

Research	fMRI Findings
(Poudel et al., 2009)	• Decrease in activity in the bilateral thalamus, posterior cingulate gyrus, and medial frontal cortex. • Increase in activity in the inferior frontal cortex, posterior parietal cortex, and parahippocampal regions.
(Jones et al., 2010)	
(Poudel et al., 2014)	

Table 5-6 Summary of EEG physiological findings on microsleeps.

Research	EEG Findings
(Peiris et al., 2006)	• Increased delta, theta, and alpha EEG activities. • Decreased beta and gamma EEG activities.
(Poudel et al., 2010a)	• Association between theta EEG activity and MSs.
(Jonmohamadi et al., 2016)	• Association between MSs and spindles of alpha activity. • Association between MSs and theta activity.
(Wang et al., 2020)	• Increased alpha EEG activity. • Decreased delta EEG activity. • No evidence of change was found in beta and theta EEG activities.

5.3 Summary

This chapter focused on the physiological side of MSs and on endogenous ALs, and its two types: mind-wandering and mind-blanking. It showed how these lapses have been measured physiologically to reveal neural signatures using by looking at changes in activation (fMRI) or power (EEG) in the brain networks of interest. Plus, changes in FC within and between various brain networks.

One of the key findings of mind-wandering literature is the activity increase of DMN, which is anticorrelated with DAN, in addition to the increased FC between DMN and FPN. In addition to the power increase of the EEG alpha band. Mind-blanking was correlated with a partial activity increase of DMN. Finally, MSs were correlated with activity increase in frontal and posterior parietal areas, in addition to decrease activity in the thalamus. Also, MSs were correlated with the power increase of delta, theta, and alpha EEG bands.

Chapter 6: Aims and Hypotheses

6.1 Gaps in knowledge

6.1.1 Attention lapses

Research on ALs needs further investigations into their underpinning physiological mechanisms. Investigations of endogenous ALs in a more definitive, instead of generalized, approach will lead to better understanding of different types of ALs. Compared to mind-wandering, little research has investigated mind-blanking. In particular, to the best of our knowledge, mind-blanking has been poorly understood from a physiological perspective. Therefore, more research employing brain imaging techniques such as fMRI and EEG are needed to better understand ALs which could be due to mind-blanking and/or mind-wandering. Previous studies have used the subjective 'think-of-nothing' state (Kawagoe et al., 2019), a reading comprehension task (Ward & Wegner, 2013), and discrete tasks like the go/no-go task (Van den Driessche et al., 2017) to investigate mind-blanking, but no study has used a continuous task (e.g. like visuomotor tracking), which can best detect the presence, onsets, and offsets of ALs (mind-blanking and/or mind-wandering).

6.1.2 Microsleeps

The phenomenon of MSs is still far from being fully understood. Behaviourally, they are similar to sleep, although the difference in duration makes them distinct. However, there is much more to discover on the physiological side. MSs were found to be associated with stage II sleep (Jonmohamadi et al., 2016), however, given the behavioural differences in terms of duration to come out of sleep, MSs might represent a stage of relief from sleep pressure (Poudel et al., 2018), and not a deactivation process similar to normal sleep (Poudel et al., 2014). Hence, the relation between MSs and sleep should be further investigated on a wider scale.

6.2 Key questions

From gaps in the literature, there are several important questions we aim to explore in this project:

- What are the neural signatures of endogenous ALs during a continuous visuomotor tracking?
- Are endogenous ALs during a continuous visuomotor tracking mind-blanks or mind-wanderings?

- Are MSs physiologically different from sleep?

6.3 Aim

The objective of this project was to increase our understanding of the behavioural characteristics and physiology underlying lapses of responsiveness —MSs and endogenous ALs— during a 2-D CVT task.

6.4 Hypotheses

6.4.1 Neural signatures of endogenous attention lapses.

Q1: Are ALs associated with decreased DAN activity during a 2-D CVT.

- **Hypothesis 1:** In a 2-D CVT task, there is lower neural activity in DAN during endogenous ALs.
- **Rationale:** Fox et al. (2005) showed that the DAN has higher neural activity during focused external attention, whereas endogenous ALs are considered to occur when attention is decoupled from external stimuli (Buckley et al., 2016). This implies that when the tracking performance drops to zero without the loss of consciousness during an AL, a complete decoupling from external environment is expected, which correlates with reduced activity in DAN.
- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a voxel-wise analysis to analyse ALs and check the activity in the DAN compared to baseline of good responsive tracking. FEAT (GUI and scripting) from FSL (Jenkinson et al., 2012) will be used to do the analysis. In addition, ROI analysis will be performed on the DAN specifically by analysing the average time series in each region of the DAN.

Q2: During a 2-D CVT, will endogenous ALs be associated with decreased FC between FPN and DAN?

- **Hypothesis 2:** In a 2-D CVT, FC between FPN and DAN decreases during ALs.
- **Rationale:** In endogenous ALs there is a complete decoupling from the external environment, in which DMN is highly associated with internal processes (Eichele et al., 2008; Kawagoe et al., 2019; Weissman et al., 2006). On the other hand, the

relation between increased activity of DAN and external attention is well stablished (Chai et al., 2012; Fox et al., 2006; Fox et al., 2005; Vossel et al., 2014). Since FPN is involved in the process of changing from attention externally to internally directed and vice versa by changing its FC between DMN and DAN (Dixon et al., 2018; Spreng et al., 2010), it is expected that FC between FPN and DAN will decrease during ALs.

- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a FC analysis to analyse ALs and examine the FC between the FPN and DAN when comparing ALs to the baseline of good responsiveness tracking. The FC toolbox (CONN) (Whitfield-Gabrieli & Nieto-Castanon, 2012) will be used to do the analysis.

Q3: During a 2-D CVT, will endogenous ALs be associated with decreased FC between FPN and sensorimotor network (SMN)?

- **Hypothesis 3:** In a 2-D CVT, FC between FPN and SMN decreases during ALs.
- **Rationale:** During ALs, there is complete decoupling from the external world and the subject is unable to perform the task. The 2-D CVT requires visuospatial coordination in order to keep tracking, which involves SMN (Cavina-Pratesi et al., 2006; Shibasaki et al., 1993; Wildgruber et al., 1997). The FPN is associated with the coordination of visuospatial attention (Lückmann et al., 2014; Marek & Dosenbach, 2018; Scolari et al., 2015), in addition, during an AL there is decoupling from external attention, which will stop performing the visuomotor task. This suggests that FC between FPN and SMN will decrease.
- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a FC analysis to analyse ALs and examine the FC between the FPN and SMN when comparing ALs to the baseline of good responsiveness tracking. CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) will be used to do the FC analysis.

Q4: During a 2-D CVT, will endogenous ALs be associated with decreased FC between FPN and VSN?

- **Hypothesis 4:** In a 2-D CVT, FC between FPN and VSN decreases during ALs.
- **Rationale:** During ALs, there is complete decoupling from the external world and the subject will be unable to perform the task. The 2-D CVT requires visuospatial coordination in order to keep tracking, which will involve VSN (Desimone & Duncan, 1995; Helfrich et al., 2013) while performing the task. The FPN is associated with the coordination of visuospatial attention (Lückmann et al., 2014; Marek & Dosenbach, 2018; Scolari et al., 2015), in addition, during an AL there will be a decoupling from external attention, which will stop performing the visuomotor task. This suggests that FC between FPN and VSN will decrease.
- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a FC analysis to analyse ALs and examine the FC between the FPN and VSN when comparing ALs to the baseline of good responsiveness tracking. CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) will be used to do the FC analysis.

Q5: During a 2-D CVT, will endogenous ALs be associated with decreased FC between DAN and EMN?

- **Hypothesis 5:** In a 2-D CVT, FC between DAN and EMN decreases during ALs.
- **Rationale:** Coiner et al. (2019) introduced a network called the eye movement network (EMN) which includes cortical regions such as ventral precuneus and PCC of DMN, frontal eye field (FEF) of DAN, lateral prefrontal cortex (LPFC) of FPN, and medial and occipital of VSN. During ALs, there is complete decoupling from the external world and the subject will be unable to perform the task. The 2-D CVT requires visual fixation on a disc on a screen, which will force the eye to move. Given the decoupling, it is expected that the FC between DAN and EMN will decrease.
- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.

- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a FC analysis to analyse ALs and examine FC between the DAN and EMN when comparing ALs to the baseline of good responsiveness tracking. CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) will be used to do the FC analysis.

Q6: During a 2-D CVT, will endogenous ALs be associated with decreased FC between DMN and WMN?

- **Hypothesis 6:** In a 2-D CVT, FC between DMN and WMN decreases during ALs.
  Rationale: A recent finding showed that memory and attention actually lapse together (deBettencourt et al., 2019). The relation between working memory and attention is important, as working memory serves as a space where attention can maintain relevant information to be used in a task (Chun, 2011). Zokaei et al. (2014) added that the resources needed to perform a demanding task and also maintain information in the visual working memory are common.
  Mind-wandering is operationally different from mind-blanking, although both are common when it comes to decoupling attention from external tasks. Mind-wandering is defined as a state in which attention is diverted to internal thoughts unrelated to the task (Burdett et al., 2016; Huijser et al., 2018; Ottaviani et al., 2015; Weinstein et al., 2017). These thoughts might be related to the past or future, which means that attention is focused on memories (Hutchinson & Turk-Browne, 2012; Wang et al., 2009). On the other hand, memory processes are more likely not to be associated with mind-blanking, which is s state of an empty mind while being behaviourally awake (Kawagoe et al., 2019; Ward & Wegner, 2013).
  WMN defined by Piccoli et al. (2015), has four regions right and left LPFC of FPN, and right and left IPS of DAN. Using a visuo-spatial working memory paradigm, Piccoli et al. (2015) focused on the dynamic FC between DMN and WMN, they found that the FC between DMN and WMN changes with task phases (encoding, maintenance, and retrieval). Although they were not studying any ALs, but during the maintenance phase, which has a similar behaviour to mind-wandering, DMN and WMN were found to be anti-correlated. So, it is expected that the FC between WMN and DMN will decrease due to ALs during 2-D CVT task.

- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a FC analysis to analyse ALs and examine FC between the DMN and WMN when comparing ALs to the baseline of good responsiveness tracking. CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) will be used to do the FC analysis.

Q7: During a 2-D CVT, will endogenous ALs be associated with increased EEG alpha activity?

- **Hypothesis 7:** In a 2-D CVT, EEG alpha power increases in the posterior brain area during endogenous ALs.
- **Rationale:** There is an association between increased visual alpha power and increased DMN activity (Mo et al., 2013) when eyes are opened in a resting state, while the increased activity of DMN is associated with decoupling from external environment (Eichele et al., 2008; Weissman et al., 2006). In addition, increased EEG alpha power over task-related brain regions is correlated with low levels of attention and poor performance (Macdonald et al., 2011). Also, when attention is externally directed to demanding tasks, alpha EEG activity is reduced in task-related brain areas (Rajagovindan & Ding, 2011; Sauseng et al., 2005).

  A study on ALs using PVT showed a positive correlation between increased (slow) reaction time and increase in activity of alpha EEG band over parieto-occipital, central-medial, and frontal regions (Molina et al., 2019). Using a Simon task, there was a power increase in the alpha band in parieto-occipital regions during ALs (van Driel et al., 2012). This indicates that the alpha power is related to the process of ALs through various tasks, which might be the case for the continuous task too.
- **Significance:** Improving our understanding of the physiological aspects of endogenous ALs during a 2-D CVT.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use EEG data to perform a source-reconstruction analysis to analyse ALs and statistically to the baseline of good responsiveness tracking. EEGLAB toolbox (Delorme & Makeig, 2004) will be used to do the pre-processing and

Fieldtrip (Oostenveld et al., 2011) will be used to do the source-reconstruction and statistical analysis.

6.4.2 Mind-blanks versus mind-wandering

Q8: Are the ALs during a 2-D CVT task due to involuntary mind-blanking?

- **Hypothesis 8:** ALs during a 2-D CVT are due to involuntary mind-blanking.
- **Rationale:** An AL is considered a state of complete loss of performance which is associated with decoupling (Schad et al., 2012; Smallwood & Schooler, 2015). This decoupling results in disconnecting attention from the external environment (performing the task), and complete loss of attention, in the case of mind-blanking (Ward & Wegner, 2013), that could also be voluntary where the mind is intentionally cleared from thoughts (Kawagoe et al., 2019). Kawagoe et al. (2019) found an increase in DMN activity due to voluntary mind-blanking (clearing the mind of any thought). The fact that "Kawagoe et al. (2019) found an increase in DMN activity due to voluntary mind-blanking" is because (i) it was voluntary and (ii) the likely impossibility of being able to think of 'nothing', and hence their so-called voluntary mind-blanks were actually a form of mind-wandering. So, we expect no increase in DMN activity during involuntary mind-blanks during a CVT task.

  In the case of mind-wandering, FC between FPN and DMN increases (Godwin et al., 2017; He et al., 2021), which supports the generation of internal thoughts, which is the opposite of what happens during mind-blanking, in which there is nothing in mind while remaining awake (Ward & Wegner, 2013). The FPN is associated with two important memory functions: declarative memory retrievals and updating of working memory (Borst & Anderson, 2013). These functions seem to be involved in the mind-wandering phenomenon, which is voluntary by nature. So, it is expected that FC between FPN and DMN will decrease due to involuntary mind-blanking during 2-D CVT task.

  Coiner et al. (2019) introduced a network called EMN which includes cortical regions such as ventral precuneus and PCC of DMN, FEF of DAN, LPFC of FPN, and medial and occipital of VSN. Mind-wandering is associated with eye movements (Hartmann et al., 2014), and in addition shows different oculometric features than mind-blanking, except in low arousal (Unsworth & Robison, 2018a). So, it is expected that FC between EMN and DMN will decrease due to involuntary mind-blanking during a 2-D CVT.

While awake, the brain through local sleep performs sleep-related cognitive functions, such as cellular maintenance, by giving neurons a break for maintenance after being activated for long (Vyazovskiy & Harris, 2013). Research by Andrillon et al. (2019) on ALs and their relation to the local sleep phenomenon which is different than MS according to the authors, they hypothesised that local sleep could be used as a model to explain ALs; if local sleep, defined by an increase in delta and/or theta (slow-wave) activities, happened within DMN will lead to the reduction of endogenous thoughts, which will cause mind-blanking. So, it is expected that involuntary mind-blanking will be correlated with the increase of delta/theta EEG activity within DMN due to local-sleep during 2-D CVT task.

- **Significance:** Improving our understanding of the behavioural and physiological aspects of mind-blanking and getting us a step closer to having accurate detection/prediction systems.
- **Study Outline:** We will use Study C and Study D (Rested), in which momentary drops in tracking performance with opened eyes (i.e., ALs) were identified by an expert. We will use fMRI data to perform a voxel-wise analysis to analyse ALs compared to baseline of good responsive tracking. FEAT (GUI and scripting) from FSL (Jenkinson et al., 2012) will be used to do the analysis. In addition, ROI analysis will be performed by analysing the average time series at each region. We will use fMRI data to perform a FC analysis to analyse ALs and examine the FC when comparing ALs to the baseline of good responsiveness tracking. CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012) will be used to do the FC analysis. We will use EEG data to perform a source-reconstruction analysis to analyse ALs statistically to the baseline of good responsiveness tracking. EEGLAB (Delorme & Makeig, 2004) will be used to do the pre-processing and Fieldtrip (Oostenveld et al., 2011) will be used to do the source-reconstruction and statistical analysis.

6.4.3 Microsleeps and sleep

Q9: Are microsleeps physiologically different from normal sleep?

- **Hypothesis 9:** Microsleeps during a 2-D CVT task are brief instances of sleep but are physiologically different from normal sleep.
- **Rationale:** At a certain level of drowsiness, the state of the brain shifts from wakefulness to sleep (Poudel et al., 2014), if the sleep state was (<15 s), it is

considered a MS (Jones, 2011). MS is behaviourally different from normal sleep in terms of duration. There is a correlation between increased activities in low-frequency (delta, theta, and alpha) EEG bands and MSs (Peiris et al., 2006), also sleep (De Gennaro et al., 2001). So, the difference is not so much in the process of going from wake/drowsiness to sleep (i.e., they have in common the brain’s need for, and drive to, sleep. Rather, the difference is the reverse process of going from sleep to wake i.e., a ‘consequence’ centre in the unconscious brain recognizes that the brain has gone to sleep during an active task and ‘tells’ the brain that it needs to wake up to continue the task. Hence, the brain initiates a wake-up process to recover consciousness and, hence responsiveness. Physiological support for this recovery process was found by Poudel et al. (2014), where there is increased BOLD activity in several areas of cortex during MSs. Also, while shifting from wakefulness to deep sleep and slow-wave sleep, a reduction was found in different cortical and subcortical areas (Kaufmann et al., 2006).

Olcese et al. (2018) found that the brain could perform cognitive functions that are more related to the awake state of the brain by responding, up to a certain level, to the sensory stimulations. As beta (Cannon et al., 2014; Schmidt et al., 2019) and gamma (Carr et al., 2012; Fries, 2009; Melloni et al., 2007; Rouhinen et al., 2013; Tallon-Baudry, 2009; Windt et al., 2016) are associated with higher cognitive functions during wakefulness. This indicates that a positive correlation might exist between MSs and high-frequency (beta and gamma) EEG bands as part of the recovery process.

- **Significance:** Improving our understanding of the physiological aspects of MSs and getting us a step closer to having accurate detection/prediction systems.
- **Study Outline:** We will use Study C and Study D (Rested), in which MSs were identified by an expert. We will use EEG data to perform a source-reconstruction analysis to analyse MSs and statistically analyse these sources when comparing MSs to the baseline of good responsiveness tracking. EEGLAB (Delorme & Makeig, 2004) will be used to do the pre-processing and Fieldtrip (Oostenveld et al., 2011) will be used to do the source-reconstruction and statistical analysis.

Chapter 7: Project Datasets

This research does not require new data collection as we have the data we need:

- Two previous studies in the Christchurch Neurotechnology Research Programme (NeuroTech™) on MSs and ALs which include fMRI plus EEG recordings i.e., Study C (Poudel, 2010; Poudel et al., 2010a; Poudel et al., 2014; Poudel et al., 2010b) and Study D (Innes et al., 2013; Poudel et al., 2012, 2013, 2018), which are immensely valuable for our research.

However, as a result of using data from our previous studies:

- Our behavioural gold standard of identifying the lapses events is limited to MSs and to non-specific ALs — i.e., we are unclear as to whether the ALs are a result of mind-blanking or mind-wandering or even MS without eye closure.
- We have difficulty extracting useful oculometric features due to low-quality eye-video recordings from camera in MRI scanner.

7.1 Study C

The description of the experiment is in Table 7-1,

Table 7-1 Study C summarized.

Participants	- Twenty healthy participants (10M, 10F). - Ages between 21 and 45 years (average 29.3 years). - No history of neurological, psychiatric, or sleep disorders.
Experiment	<u>Before the experiment:</u> - Participants were required to wear an Actiwatch (Mini Inc. Bend OR, USA) for the 6 days and 5 nights before the experiment to record their sleep/wake habits. - Participants were required to go to bed between 10 PM and 12 AM daily and sleep for 7.0-8.5 hours. - In the 4 hours before the session, stimulants, and depressants (alcohol, coffee, and nicotine) were not allowed. - Participants were served instant noodles for lunch before the session.

	- Participants were given earplugs to reduce the high acoustic noise coming from the scanner, in addition to pads on both sides to minimize head motion.
	Task Description and Signal Acquisition: - Sessions were held within the timeframe of 1 PM — 4 PM. - Participants performed 2-D CVT task in which they tracked a disk on a computer screen using a finger-based joystick for 50 min. - The whole brains of the participants were imaged simultaneously using a Signa HDx 3.0 T MRI Scanner (GE Medical Systems, TR 2.5 s) with an eight-channel head coil and 64-ch. EEG (MagLink). In addition, a video of the right eye was continuously recorded using a Visible EyeTM system (Avotec Inc.).
Ethical Approval	New Zealand South B Regional Ethics Committee

Data from this study were used in previous analyses and publications on MSs: behavioural (Innes et al., 2010), using fMRI (Poudel et al., 2014; Poudel et al., 2010b), and EEG (Poudel et al., 2010a; Toppi et al., 2016).

7.2 Study D

The description of the experiment is in Table 7-2,

Table 7-2 Study D summarized.

Participants	- Twenty right-handed healthy participants (10M, 10F). - Ages between 20 and 37 years (average 24.9 years). - No history of neurological, psychiatric, or sleep disorders.
Experiment	Before the experiment: - Participants were required to wear an Actiwatch for the 6 days and 5 nights before the experiment to record their sleep/wake habits. - Participants were required to go to bed between 10 PM and 12 AM daily and sleep for 7.0-8.5 hours. - Participants went to the laboratory three times (one week separates between each visit). In the first visit, they became familiar with the experiment protocol, were informed to wear an Actiwatch (Respironics Inc., PA, USA), and were asked to keep records of their

	sleep habits for the 6 days and 5 nights before each session. They were asked to record the time of intake of caffeine, alcohol, and food daily. - Rested and sleep-restricted imaging sessions occurred in the second and third visits, their order was counterbalanced between participants. - In the week prior to the rested session as well as the week prior to the sleep-restricted session, participants were required to sleep normal hours. In the sleep-restricted session, participants were asked to reduce their time in bed to 4 hours (3:00 - 7:00 AM) in the night before the scanning. - After sleep-restriction, participants were asked not to perform any activity that might affect their safety such as driving. Furthermore, participants were asked not to consume alcohol, caffeine, and nicotine in any of the imaging sessions' days. - On each scanning day, the participants were at the laboratory an hour prior to the scanning session. - The records of the Actiwatch and the sleep diary were checked before each scanning session to confirm that the participants followed the sleep schedule instructions required for the study. - A lunch of hot noodles was served to the participants before each session. - Participants were given earplugs to reduce the high acoustic noise coming from the scanner, in addition to pads on both sides to minimize head motion.
	<u>Task Description and Signal Acquisition:</u> - The sessions started at 1 PM and lasted for one hour and a half. - In each session (rested and sleep restricted), participants performed 2-D CVT task in which they tracked random continuously moving disk on a computer screen using a finger-based joystick for 20 min. - The whole brains of the participants were imaged simultaneously using a Signa HDx 3.0 T MRI Scanner (GE Medical Systems, TR 2.5 s) with an eight-channel head coil and 64-ch. EEG (MagLink).

	In addition, a video of the right eye was continuously recorded using a Visible EyeTM system (Avotec Inc.).
Ethical Approval	New Zealand South B Regional Ethics Committee

Data from this study were used in previous analyses and publications on MSs: behavioural (Innes et al., 2013), and fMRI (Poudel et al., 2012, 2013, 2018).

7.3 fMRI recording

A Signa HDx 3.0T MRI Scanner (GE Medical Systems, Waukesha, WI) was used for structural and fMRI scanning, see Table 7-3.

Table 7-3 Details of data collected from the MRI scanner.

Image type	Details
T1-weighted	• It is the structural image of the brain with high resolution. • TR: 6.5 ms. • TE: 2.8 ms. • Inversion time (TI): 400 ms • FOV: 225x250 mm. • Matrix: 512x512. • Slice thickness: 1 mm. • Number of slices: 158. • Scan time: 4.5 min.
T2*-weighted	• EPI was used to acquire these functional images. • To allow for T1 equilibration, The first five images of each session were discarded. • TR: 2.5 s. • TE: 35 ms. • FOV: 220x220 mm. • Slice thickness: 4.5 mm. • Number of slices: 33. • Number of volumes: 240. • Scan time: 10 min.

Field map	• To correct for the EPI distortion, which is caused by the magnetic field inhomogeneity, this image was acquired per subject. • Echo spacing: 700 µs. • TR: 580 ms. • TE: 6.0 ms and 8.2 ms.

7.4 EEG recording

Continuous EEG was acquired using a Neuroscan Maglink cap (64 Channel), SynAmps2 amplifiers, and Scan 4.4 software (Compumedics Neuroscan, Charlotte, NC, USA), in addition the following were recorded:

- Vertical EOG using Ag-AgCl bipolar electrodes that were placed above and below the left eye.
- Bipolar chest ECG and pulse oximetry.

7.5 Eye-video recording

Eye-video was captured using a Visible Eye™ system incorporating a fibre-optic camera (Avotec Inc., Stuart FL, and USA). The video was recorded on a PC at 25 fps using custom software.

7.6 Task

To sample visuomotor response with high temporal resolution (60 Hz), a 2-D CVT task was used, see Figure 7-1.

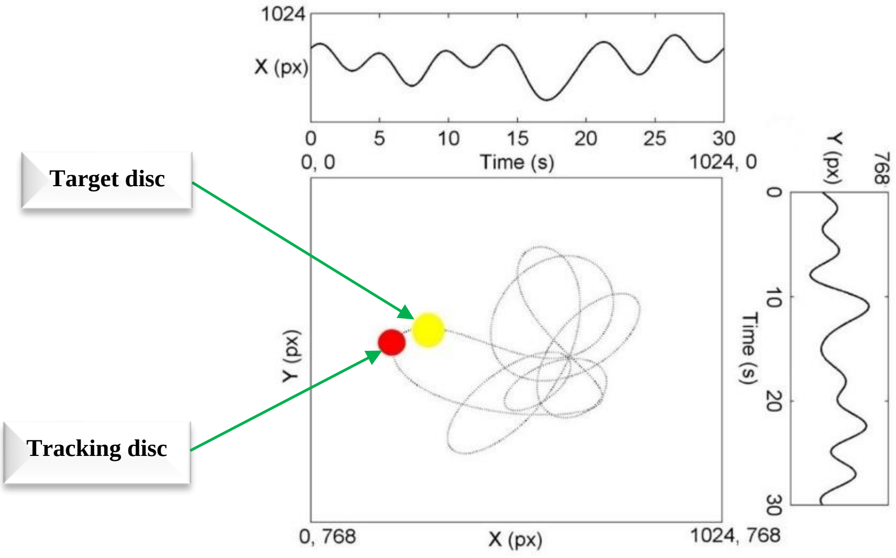


Figure 7-1 2-D Continuous visuomotor tracking (CVT) task (from Poudel et al., 2008).

The subjects were asked to keep track of a target continuously moving on a computer screen, based on a pseudo-random 2-D pattern, and with no flat spots. Seven sinusoids, whom frequencies were evenly spaced from 0.033 to 0.231 Hz, were added to generate the horizontal and vertical components of the target. Then to fit the 1024 x 760 pixels resolution screen, the target amplitude was scaled. This produced a 2-D periodic target trajectory (T = 30 s) with a velocity range of 63–285 pixels/s (Poudel et al., 2008). The tracking task was presented via SV-7021 fibre-optic glasses (Avotec, Stuart, FL, USA) at a resolution of 1024 x 768 pixels and an 18 x 13° field of view. The target disc was 0.7°, and response disc was 0.6° of visual angle in diameter.

7.7 Events rating

By means of video recording of the right eye of each subject, the behavioural data from each study were rated to as follows (Poudel, 2010):

7.7.1 Microsleeps

1- Definition: A MS is a brief ($\lesssim$ 15 s) involuntary lapse in consciousness in which a person has a suspension of performance and falls asleep momentarily.

2- Operational: (1) flat/incoherent tracking > 500 ms [nearly all flat during at least part of event], full or partial phasic eye closure, except for blinks, and clear behavioural indications of drowsiness/sleepiness. If this event's duration exceeds 15 s, it is considered a sleep episode.

7.7.2 Attention lapses

An AL is a lapse in responsiveness in which performance is completely disrupted but consciousness is retained. There are two primary types of AL:

Lost-attention lapse (Mind-blank)

1- Definition: A lost-AL is a lapse in which there is a loss of conscious attentional focus but with no loss of consciousness. They include 'mind-blanks' and 'auto-pilots' but don't necessarily correspond to complete losses of attention – i.e., a level of subconscious attention is retained (e.g., driving on autopilot). They appear as complete brief cessations of performance on tasks with continuous stimuli or as substantially delayed responses on tasks with intermittent stimuli.

2- Operational: (1) flat/incoherent tracking > 500 ms, (2) no phasic eye closure other than normal blinks, (3) not directly related to level of arousal and, hence, can occur when being alert, fatigued, or drowsy.

Diverted-attention lapses

1- Definition: A diverted AL is a lapse in which attentional focus is retained but which has been diverted onto something other than the primary task. There are two sub-types of diverted-ALs: (1) internal/endogenous distraction (mind-wandering) – e.g., thinking about something else, and (2) external/exogenous distraction – e.g., looking at the radio while driving.

2- Operational: (1) flat/incoherent tracking > 500 ms, (2) no phasic eye closure other than normal blinks, and (3) not directly related to the level of arousal and, hence, can occur when being alert, fatigued, or drowsy. Either (A) extended gaze away from the task (exogenous distraction), or (B) minimal eye movement (endogenous distraction) (difficult to differentiate from a lost-AL).

7.7.3 Drowsiness-related impaired-responsiveness events (DIREs)

1- Definition: A distinct drowsiness-related transient reduction – but not complete loss – of performance.

2- Operational: (1) epoch of very poor, but not incoherent, tracking relative to baseline tracking for > 500 ms, and (2) full or partial phasic eye closure, except for blinks.

7.7.4 Voluntary behaviour impacting performance (VBIP)

1. Definition: A voluntary behaviour which adversely impacts performance.
2. Operational: (1) can be fatigue-related (e.g., voluntary eye closure [excluding blinks], rubbing eyes, squeezing eyes shut), (2) can be non-fatigue-related (e.g., sneezing, cramp in hand), (3) usually flat/incoherent tracking > 500 ms but can be partially compensated for via predictive motor planning, (4) clearly voluntary (e.g., temporary relief from fatigue).

7.8 Events of interest in studies

7.8.1 Attention lapses

7.8.1.1 Study C

- Duration (mean, range): (2.14, 0.52 – 8.13) s.
- Total number of events: 68

- Total number of subjects with ALs: 16 out of 20.

7.8.1.2 Study D (Rested)

- Duration (mean, range): (1.52, 0.53 – 3.2) s.
- Total number of events: 29
- Total number of subjects with ALs: 11 out of 20.

7.8.2 Microsleeps

7.8.2.1 Study C

- Duration (mean, range): (3.6, 0.52 – 14.4) s.
- Total number of events: 1314
- Total number of subjects with MSs: 14 out of 20.

7.8.2.2 Study D (Rested)

- Duration (mean, range): (2.5, 0.72 – 9.72) s.
- Total number of events: 319
- Total number of subjects with MSs: 11 out of 20.

Chapter 8: fMRI Voxel-Wise Analysis of Attention Lapses

8.1 Introduction

In this chapter, fMRI data were used to answer hypotheses 1 and part of 8. The aim was to reveal the changes in activity in regions from the whole brain. Voxel-wise and group ICA were performed. The chapter is structured as follows: the analysis pipelines were first introduced, then the results of each analysis, and finally, the findings were discussed, and hypotheses were answered.

8.2 Method

8.2.1 Data

To increase the statistical power, the combination of the two studies was necessary. Study C fMRI tracking data were split into two runs (25 min each) because of the machine limitations, both runs represent the same session. Only subjects who had at least 2 ALs per run were considered for analysis from each study. Study C only had 11 subjects who experienced at least two ALs (62 ALs) with an average duration of 1.82 (0.52—8.13 s.). Study D had rested and sleep-deprivation sessions, but we only focused on the rested session. The same selection criteria to was applied to Study D rested session, where the subjects who had corrupted data were rejected, there were 6 subjects (23 ALs) with an average duration of 1.6 (0.53—2.72 s.). Combining two studies resulted in a total number of 17 subjects and a total number of 85 ALs with a mean duration of 1.74 s (0.52-8.13 s).

8.2.2 Voxel-wise analysis

Voxel-wise analysis was done using FEAT v6.00 from FMRIB’s software library (FSL*)* (Jenkinson et al., 2012) available at (www.fmrib.ox.ac.uk/fsl).

8.2.2.1 Pre-processing and denoising

Motion correction in our analysis was done using the toolbox MCFLIRT (Jenkinson et al., 2002), which linearly registers all functional volumes in a run to the middle one. Brain-extraction step was performed using BET (Jenkinson et al., 2005; Smith, 2002). We could not perform distortion correction as most of the field map images were not available.

A 5-mm spatial smoothing, was chosen according to Jenkinson and Chappell (2018), as approximately 1.5-2 times the voxel size, which is the length of any side of the isotropic voxel, is preferred to balance between SNR and being able to find significant activity in small regions. The 100-s was chosen for the temporal filtering. Based on Zarahn et al. (1997)

and Mitra and Pesaran (1999); 100 s is sufficient to remove low frequency noise, but not remove frequency components related to the task, in which the target pattern repeats every 30 s.

Through FEAT, MELODIC ICA (Smith et al., 2004) was used to perform the denoising of fMRI BOLD signals. The noise components were identified through visual inspection (Griffanti et al., 2017; Kelly et al., 2010; Salimi-Khorshidi et al., 2014). ICA-AROMA (Pruim et al., 2015), which is a toolbox capable of automatically identifying noise components caused by head movements, was used to visually inspect and validate the components labelled for rejection. The noisy components removal was repeated twice, as recommended by Caballero-Gaudes and Reynolds (2017), which is more efficient in revealing all noise components. Slice time correction was done after the denoising step to detect any motion occurred between slices and remove it (Caballero-Gaudes & Reynolds, 2017).

8.2.2.2 Registration

Registration between functional and structural images was done using FMRIB’s linear image registration tool (FLIRT) (Jenkinson et al., 2002; Jenkinson & Smith, 2001) using a rigid-body transformation — 6 DOF, which includes 3 rotations, and 3 translations. The FEAT default MNI152-2 mm was used as a standard space. The linear registration between structural images and MNI was carried out using FLIRT with 12 (affine) DOF. The normalization step between functional images and MNI was done through FEAT by transferring the 4-D images to standard space.

8.2.2.3 Statistical analysis

To test the hypotheses, statistical analyses were performed. Data from studies C and D were combined, as they were collected from the same MRI machine with exactly the same setup, and the subjects were doing the same task under the same conditions.

First-level analysis

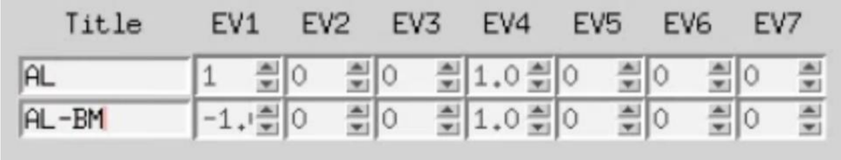
The GLM model was built in this stage for each run per subject. The comparison conditions were set up to compare ALs versus the baseline of good tracking, also verses MSs, see Figure 8-1. Also, this model accounted for all the explanatory variables and other parameters determined by the experimenter. In the analysis of ALs, MSs, DIREs, Sleep, ALs, and VBIP, and their temporal derivatives were accounted for (Woolrich et al., 2001).

In addition, task-related parameters such as: target speed-variability (63–285 pixels/s), poor-responsive tracking, as defined below, and their temporal derivatives were accounted for, see Figure 8-2.

- The target speed-variability regressor is the tracking-target related speed-variability, the regressor was calculated as follows: the average target speed-variability during each TR (2.5 s) was calculated using a moving-window of 2.5 s without overlap, then the average target speed-variability time-series was scaled to a unit height. This regressor was accounted for to remove the effect of changing the target speed from the baseline.
- The poor-responsive tracking regressor is based on the error of tracking response relative to the target, the tracking error was calculated based on the following formula at each time point.

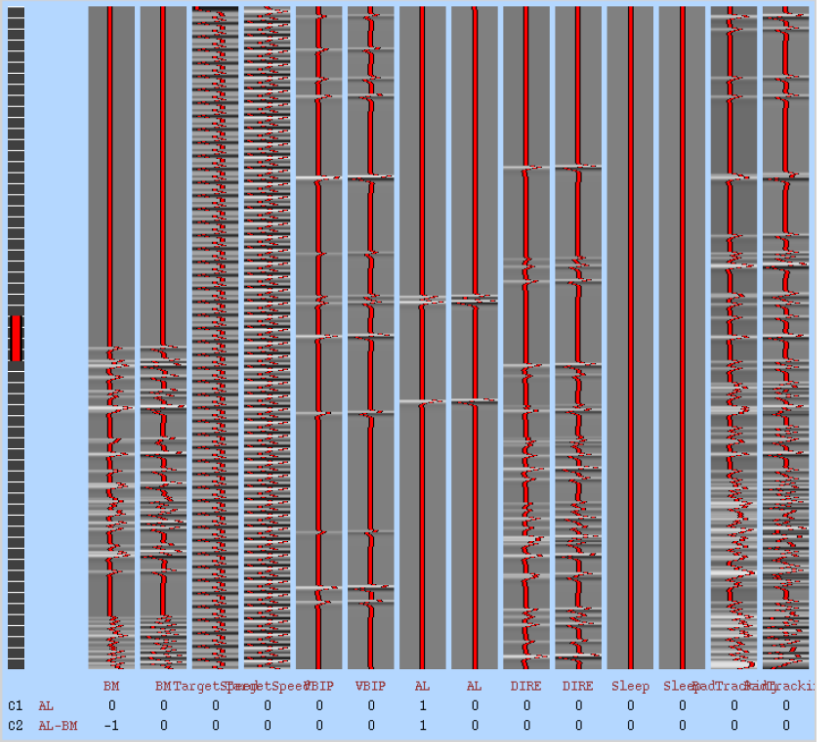
  $$\text{Tracking error} = \sqrt{(Y_{\mathrm{Tar}} - Y_{\mathrm{Res}})^2 + (X_{\mathrm{Tar}} - X_{\mathrm{Res}})^2}$$

  The regressor was calculated as follows: (1) the average tracking-error during each TR (2.5 s) was calculated using a moving-window of 2.5 s without overlap, (2) the average tracking-error time series was scaled to a unit height, (3) the regressor, which is a binary array having a value of one during poor tracking, was defined using a threshold calculated based on tracking error in the first 2 min of the session. This threshold is the mean tracking error of the first 2 min plus two standard deviations of the tracking error in the first 2 min. This aids in comparing the event of interest against the durations of only good responsive tracking.



Title	EV1	EV2	EV3	EV4	EV5	EV6	EV7
AL	1	0	0	1.0	0	0	0
AL-BM	-1.	0	0	1.0	0	0	0

Figure 8-1 Contrasts setup, which determines the comparisons made.



		BM	BM	TargetSpeed	TargetSpeed	VBIP	VBIP	AL	AL	DIRE	DIRE	Sleep	Sleep	BadTracking	BadTracki
C1	AL	0	0	0	0	0	0	1	0	0	0	0	0	0	0
C2	AL-BM	-1	0	0	0	0	0	1	0	0	0	0	0	0	0

Figure 8-2 Design matrix of the first-level stats analysis. The regressors in the model are: behavioural microsleeps (BM), Target-speed-variability, voluntary behaviour impacting performance (VBIP), attention lapses (AL), drowsiness-related responsiveness events (DIRE), Sleep, and Bad tracking.

Second-level analysis

This step was an intermediate stage to average the runs per subject where there was more than one run (Woolrich et al., 2001). This was applied to subjects from Study C who had ALs in two runs.

Group-level analysis

The last step was to average over all subjects (Woolrich et al., 2004a). As we were interested only in the GM of the brain, a segmentation step was applied to the BOLD images from the second-level stage using FAST (Zhang et al., 2001). The test for significance was done using permutation test via Randomise (Winkler et al., 2014a), which is nonparametric (Nichols & Holmes, 2002). Nonparametric methods have been shown to outperform parametric ones under varying smoothness, thresholds, and degrees of freedom (Hayasaka & Nichols, 2003; Holmes et al., 1996; Thirion et al., 2007). After performing the permutation test, correction for multiple comparisons was applied using TFCE at $p < 0.05$ (two-tailed) to determine the activation and deactivations regions (Friston et al., 1995; Worsley, 2001). This step was done using scripting of FSL's Randomise function. Based on online documentation of the

Randomise function, with less than 20 subjects in the group analysis, like our case of 17 subjects, then variance smoothing of 5 should be applied.

8.2.3 Group-level ICA analysis

In addition to voxel-wise analysis, which when corrected for multiple comparisons reduces the chances of getting significant results, we analysed the group ICA for the subjects of interest. Then we used spatial correlation to match the resulting components to the networks of interest (if any). Then we checked the significance of each component. To do that we used MELODIC toolbox v3.15 (Beckmann et al., 2005; Beckmann & Smith, 2004, 2005) from FSL. The analysis was done for the 17 subjects of interest in the combined studies.

8.2.3.1 Pre-processing and registration

Pre-processing was done based on section 8.2.2.1 and registration based on section 8.2.2.2 for the combined studies through FSL.

8.2.3.2 Group independent components

We visualized different numbers of ICs (10, 15, 20, 25, and 30), and after visual inspection of each level, and the spatial correlation of the ICs with different resting-state networks of CONN (Whitfield-Gabrieli & Nieto-Castanon, 2012), 25 ICs were chosen as the best representation of networks.

8.2.3.3 Dual-regression

To estimate each subject's spatial maps out of the group-level ICs, dual regression was applied to the group average ICs (Beckmann et al., 2009; Nickerson et al., 2017).

8.2.3.4 Statistical analysis

A GLM was created for each subject to see which components were significant under the contrasts made. Then, for the group-analysis, permutation testing was done using Randomise to test for significance, this step gave us a t-value for each IC which was then converted to p-value for the next step. The p-values from all ICs were corrected for multiple comparisons using FDR (Benjamini & Hochberg, 1995; Benjamini & Yekutieli, 2001).

8.3 Results

8.3.1 Voxel-wise group-level analysis

This analysis was done to discover the neural signature of ALs relative to the baseline of good tracking. In addition, ALs were compared to MSs.

8.3.1.1 Attention lapses versus baseline of good tracking

The group analysis of ALs versus baseline of good tracking revealed only activations, see Table 8-1 and Figure 8-3.

Table 8-1 Significant clusters of increased BOLD activity during attention lapses.

Cluster	Voxels	Z-MAX	MAX X (mm)	MAX Y (mm)	MAX Z (mm)
1	199	3.49	8	8	38

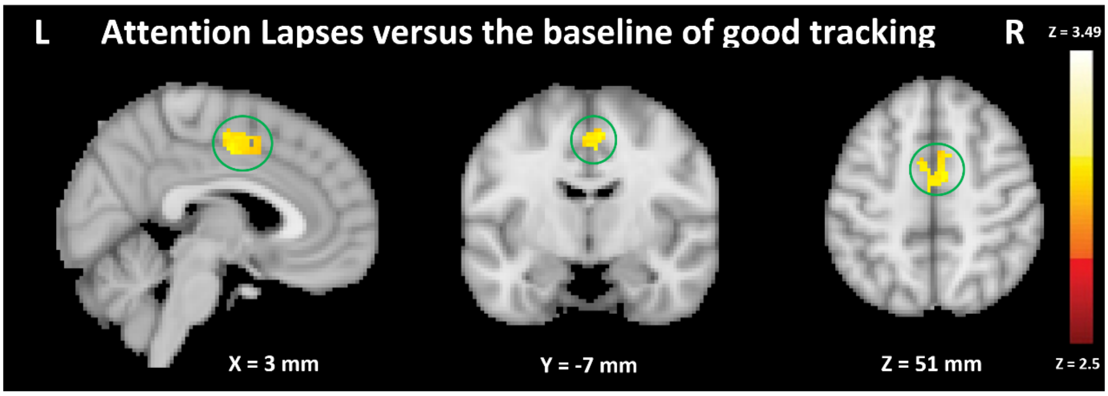


Figure 8-3 Group-level significance result of the increased BOLD activity for attention lapses versus the baseline of good responsive tracking. The cluster is labelled in MNI coordinates. The activities in the cluster are circled in green for axial, sagittal, and coronal slices.

The Atlasquery toolbox was used to report brain regions related to the cluster following Randomise. The Harvard-Oxford cortical atlas was the reference, and only major regions that contributed to more than 50% of the cluster were reported in Table 8-2.

Table 8-2 Regions forming clusters of increased BOLD activity during attention lapses.

Clusters	Regions	Lobe	Side
1	Juxtapositional Lobule Cortex (formerly Supplementary Motor Area)	Frontal	L,R
	Cingulate Cortex, anterior division	Frontal	L,R

8.3.1.2 Attention lapses versus microsleeps

The one-sample t-test group analysis for ALs versus MSs did not reveal any significant results.

8.3.2 Group ICA analysis

Group-level ICA analysis was done to discover the neural signature of ALs relative to baseline of good tracking. In addition, ALs were compared to MSs.

8.3.2.1 Attention lapses versus baseline of good tracking

The group analysis for ALs versus the baseline of good tracking was done using Randomise, it did not reveal any significant results after correction for multiple comparisons using FDR correction over the ICs. However, it revealed a trend of activation in one IC with a t-value of 2.477.

After spatially correlating the IC with resting state networks (DMN, DAN, FPN, SN, VSN, and SMN) from CONN, we found a correlation of 0.25 between the IC and SMN, see Table 8-3 and Figure 8-4,

Table 8-3 Clusters representing a trend of increased BOLD activity during attention lapses from group ICA.

Cluster	Voxels	Z-MAX	MAX X (mm)	MAX Y (mm)	MAX Z (mm)
1	9597	7.64	54	6	24
2	3570	7.28	-44	4	26

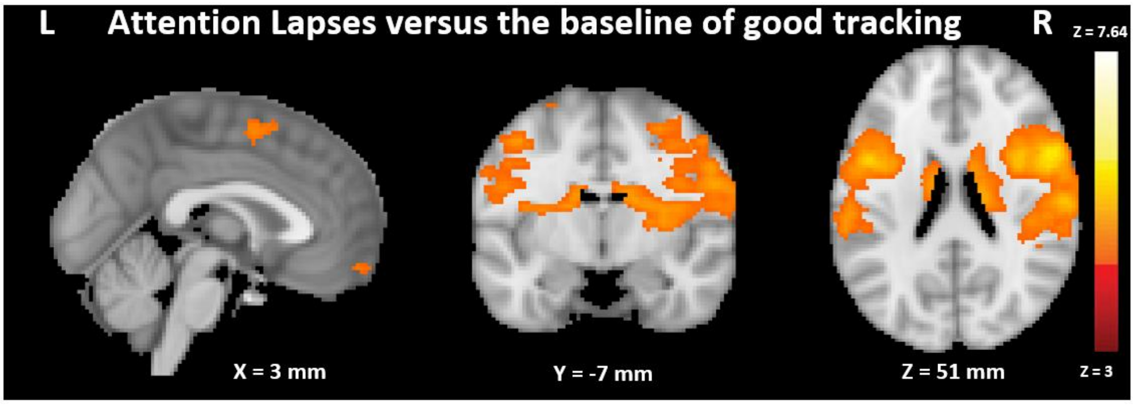


Figure 8-4 Group-level trend of activity change of increased BOLD activity for attention lapses versus baseline of good responsive tracking within two clusters representing one independent component. The clusters are labelled in MNI coordinates.

The Atlasquery toolbox was used to report brain regions related to each cluster following Randomise. The Harvard-Oxford cortical and subcortical atlases were the reference, and only major regions that contributed to more than 50% of each cluster are reported in Table 8-4.

Table 8-4 Regions forming clusters representing a non-significant trend of increased BOLD activity within an IC during attention lapses.

Clusters	Regions	Lobe	Side
1	Precentral Gyrus	Frontal	L
	Postcentral Gyrus	Parietal	L

	Supramarginal Gyrus, anterior division	Parietal	L
	Inferior Frontal Gyrus, pars opercularis	Frontal	L
	Central Opercular Cortex	Parietal	L
	Parietal Operculum Cortex	Parietal	L
	Caudate	Subcortical	L
2	Precentral Gyrus	Frontal	R
	Postcentral Gyrus	Parietal	R
	Supramarginal Gyrus, anterior division	Parietal	R
	Inferior Frontal Gyrus, pars opercularis	Frontal	R
	Central Opercular Cortex	Parietal	R
	Parietal Operculum Cortex	Parietal	R
	Putamen	Subcortical	R

8.3.2.2 Results of attention lapses versus microsleeps

The group analysis, done using randomise, for ALs versus MSs did not reveal any significant results after correction for multiple comparisons over the ICs using FDR correction.

8.4 Discussion

The neural signature of ALs during 2-D CVT task has been investigated in the combined studies. Our results revealed activation in one cluster (Figure 8-3 and Table 8-1). The regions dorsal ACC and SMA, found by voxel-wise analysis, fell partially within 2 brain networks: SN and SMN. We also found the insignificant IC from the group ICA analysis to be spatially correlated with SMN (Table 8-3, Table 8-4, and Figure 8-4). No deactivations were found.

In terms of duration of the ALs, 27 subjects had an average duration of 1.98 s, with a minimum duration of 0.51 s and a maximum of 8.13 s. Hence, the majority (78%) of ALs, were shorter than the TR (2.5 s) of the fMRI. In our fMRI analysis, a total of 17 subject were included, each with at least 2 ALs. The total number of ALs was 85 with an average duration of 1.74 s.

An AL is considered a state of complete loss of performance associated with the process of decoupling (Schad et al., 2012; Smallwood & Schooler, 2015). This decoupling process will result in disconnecting attention from the external environment (performing the task), and either divert the attention internally, in the case of mind-wandering (Berthié et al., 2015), or lose the attention completely, in the case of mind-blanking (Ward & Wegner, 2013). This behavioural change is reflected in physiological changes in several brain networks.

Performing the task requires external attention which is associated with activation in DAN (Fox et al., 2006; Fox et al., 2005; Vossel et al., 2014). Also, shifting attention internally to focus on spontaneous thoughts (mind-wandering) (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007) is correlated with the increased activity in DMN, and DMN activity was shown to be associated with spontaneous thoughts (Wang et al., 2009), which indicates the involvement of memory. In addition, voluntary mind-blanking (intentionally freeing the mind from thoughts) is associated with activation of ventral ACC and medial prefrontal cortex (mPFC) of DMN (Kawagoe et al., 2019). However, the memory processes are more likely not to be involved in involuntary mind-blanking (Efklides & Touroutoglou, 2010; Moraitou & Efklides, 2009). So, we expected to see a decreased activity in DAN due to ALs, and no change in activity in DMN due to involuntary mind-blanks.

Limitations of our analysis, (1) low statistical power, (2) we did not know whether ALs were mind-wandering or mind-blanking or a mixture of both, and (3) the average duration of ALs was less than the TR of fMRI. The task we used in both studies was a 2-D CVT task, in which the subjects were asked to track with a finger joystick, which implies that participants used their fingers, while inside an MRI (Poudel et al., 2008) for 50 min in Study C and 20 min in Study D. This task is both monotonous, as the pattern of the task is repeatable, and fatiguing, as it requires continuous performance at a high level. We did not use a thought probe technique to estimate the type of AL, but used observations of simultaneous tracking performance and eye-video recording for each subject. A human expert labelled these lapses into multiple categories including MSs and ALs.

Our analysis did not reveal any significant changes in either DMN or DAN. However, a significant activity increase was found in two regions: dorsal ACC which is part of SN, and SMA which is part of SMN. Increased activation in SMA is associated with the finger movement (Shibasaki et al., 1993; Wildgruber et al., 1997) and both preparation and execution of eye movement (Coiner et al., 2019), which is the case in our task as the subjects use their fingers for tracking. Bogler et al. (2017) supported this by concluding that activation in the SMA is unlikely to reflect task-unspecific vigilance. In addition, Kawagoe et al. (2019) found a decrease in activity in SMA due to voluntary mind-blanks which is the opposite of what we found, this supports that our ALs are more likely to be involuntary mind-blanks.

Activation in the dorsal ACC is associated with brief ALs (Weissman et al., 2006), as it is responsible for bringing attention back to the normal state (Banich et al., 2000; MacDonald et al., 2000; Paus, 2001; Weissman et al., 2005), which is performing the task in our case which involve oculomotor control (Coiner et al., 2019), after the drop in attention that happened because of the AL. Altogether, our results were not, possibly because of the temporal limitation, related to the duration of the ALs, but more likely to be after ALs, which would explain finger planning to continue performing the task by finding an increased activity in SMA. Increased activation in SN is also associated with low performance (Esterman et al., 2013; Esterman et al., 2014).

Given that the average duration of ALs was less than the TR of the fMRI, some of the changes due to ALs are more likely not to be revealed. Also, the low statistical power might have affected finding significant changes in DAN and DMN. However, our significant finding is still associated with ALs, decoupling from external task, and the cessation of performance in general. In addition, no significant deactivation was found in any brain region. This might be due to the low statistical power, and the short average duration of ALs compared to the TR of MRI which might cause the fMRI not to be able picking any signature of ALs in the deactivation side.

Group ICA did not reveal any significance, however, after correction for multiple comparisons, there were a trend of increased activity in one IC, which was spatially correlated with SMN. Which supports the idea that what we found is more likely to be related to what happen after the AL.

We hypothesized in this chapter: during endogenous ALs in a 2-D CVT task there will be lower neural activity in DAN. Also given the literature of mind-wandering and voluntary mind-blanks, there will no change in activity in DMN if ALs were due to involuntary mind-blanks. Based on our lack of voxel-wise and group ICA findings, we found no evidence to accept Hypothesis 1, however, we partially accept Hypothesis 8. We also did not find any physiological evidence that ALs are different from MSs.

8.5 Summary

This chapter started by describing the data used to analyse ALs, then introducing the analysis pipeline in detail for both voxel-wise and group ICA starting by pre-processing, co-registration and normalization, and finally first-level and group-level statistical analyses. Two Hypotheses (H1 and part of H8) was explored in this chapter, H1 could not be accepted based on findings, but H8 was partially accepted. In addition, no evidence was found through testing the DMN activity to associate the ALs in our task with mind-wandering or voluntary mind-blanks. However, our significant findings were discussed in the light of literature and how they relate to ALs.

Chapter 9: Haemodynamic Response ROI Analysis for Attention Lapses

9.1 Introduction

In the previous chapter, voxel-wise analysis was performed on the whole brain to reveal the brain regions associated with ALs. According to the hypotheses, we expected to see decrease in activity in DAN, in addition, an increase in activity in DMN if ALs were due to mind-wandering or voluntary mind-blanks. However, there was no significant change in either of these networks. In this chapter, ALs were further analysed and the focus is on the dynamics of the HR in spherical ROIs, rather than the whole brain.

9.2 Method

9.2.1 Analysis data

Same as section 8.2.1.

9.2.2 Pre-processing and registration

The pre-processing was done as in section 8.2.2.1 and registration as in section 8.2.2.2 for the combined studies through FSL.

9.2.3 Haemodynamic response analysis

The pre-processed, denoised, and registered-to-MNI BOLD images from each subject were used. Binary spherical masks of 10-mm radius (515 voxels) were created around coordinates that represented each region. These coordinates were based on the literature of ALs (Fox et al., 2015; Kawagoe et al., 2019; Mittner et al., 2014; Rosenberg et al., 2015) following a recommendation from Poldrack (2007) and Mumford (2012) on how to choose the ROIs – see Table 9-1. The processed functional images and spherical masks were used to generate average time series of all of the voxels within each mask, per ROI for each subject. The average of the time series was converted to percentage (Liu et al., 2017). The regressors (MSs, DIRE, VBIP, and Sleep) and the confounds (Target Speed and Bad Tracking) were first convolved with a canonical HRF from SPM toolbox, then regressed out of the average time series. The onsets of ALs were synchronized at t = 0 s, and windows of -20 s to 20 s were clipped around the onsets. These windowed ALs were then averaged per subject for each ROI. Finally at each time point (2.5 s spacing), the median of the average ALs time series (-20 s to 20 s) over all subjects was calculated, in addition to the first and third quartiles.

To explore the change of the median HR of ALs at each ROI, a permutation test was performed, in which the median HR of ALs at each ROI was compared to random events. The same process used to generate the percentage time series of ALs was followed, but with random events (i.e., not synchronized with AL onsets). For each subject, 2000 (number of permutations) random time series were generated. Then 2000 medians were calculated over subjects to be statistically compared to the median of ALs for each time point (-20 s to 20 s with a step of TR) (Winkler et al., 2014a), and a p-value was calculated at each time point. These p-values were not corrected for multiple comparisons; hence, we used a threshold of $p < 0.01$ as a measure of trend of change. For visualization, the median of ALs (plotted in red) was overlaid on the 2000 medians of random events (plotted in grey). This process was done for each ROI separately.

We focused primarily on the 5-s after the onset of the AL, as, according to Lindquist and Wager (2007), the peak of the HRF occurs approximately 5-s after the onset of the event (impulse or step).

Table 9-1 MNI coordinates of the region of interest used based on attention lapses literature.

Network	Region	Max-X (mm)	Max-Y (mm)	Max-Z (mm)
DMN	PCC	-1	-55	26
	Medial PFC	0	60	-5
	Precuneus	-8	-56	39
	Left IPL	-46	-72	25
	Right IPL	56	-51	33
DAN	Left IPS	-60	-36	40
	Right IPS	59	-35	41
	Left FEF	-32	1	49
	Right FEF	32	0	50
FPN	Left PPC	-46	-58	49
	Right PPC	52	-52	45
	Left DLPFC	-37	38	23
	Right DLPFC	38	42	15
SN	Dorsal ACC	8	8	38
	Ventral ACC	-2	42	0

9.3 Results

9.3.1 Haemodynamic response analysis of the significant voxel-wise cluster

To visualize the time series of ALs found in the significant cluster (199 voxels) resulted from the voxel-wise analysis, we used the binary mask of the cluster. The time series of the significant cluster is shown in Figure 9-1. As expected, the maximum peak was at the 5-s time point, and had a p-value at the threshold 0.01.

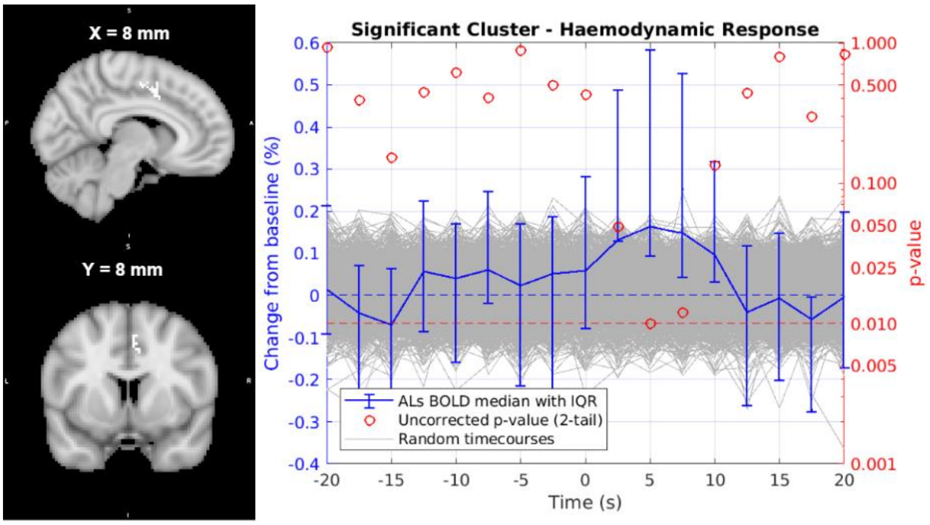
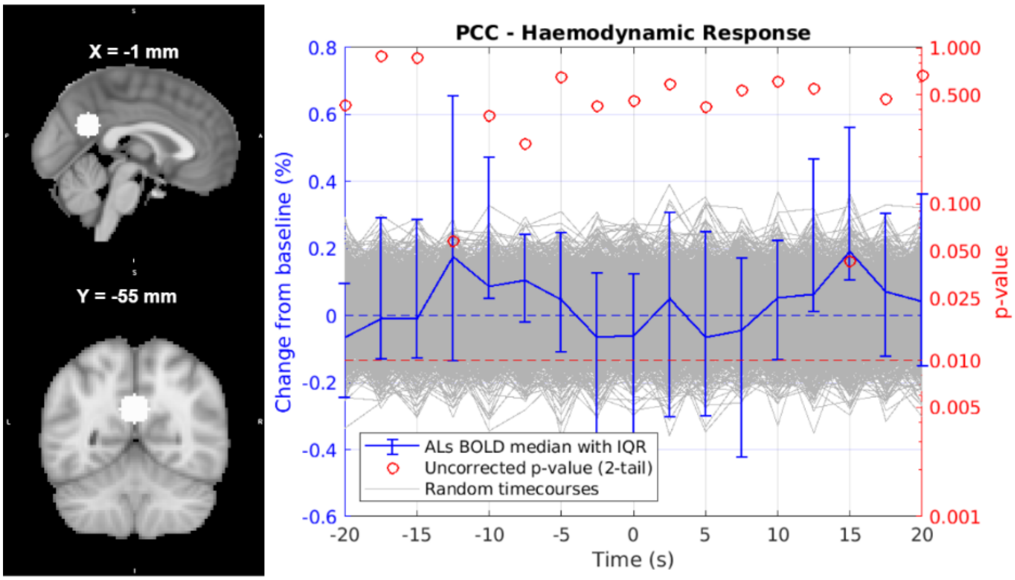


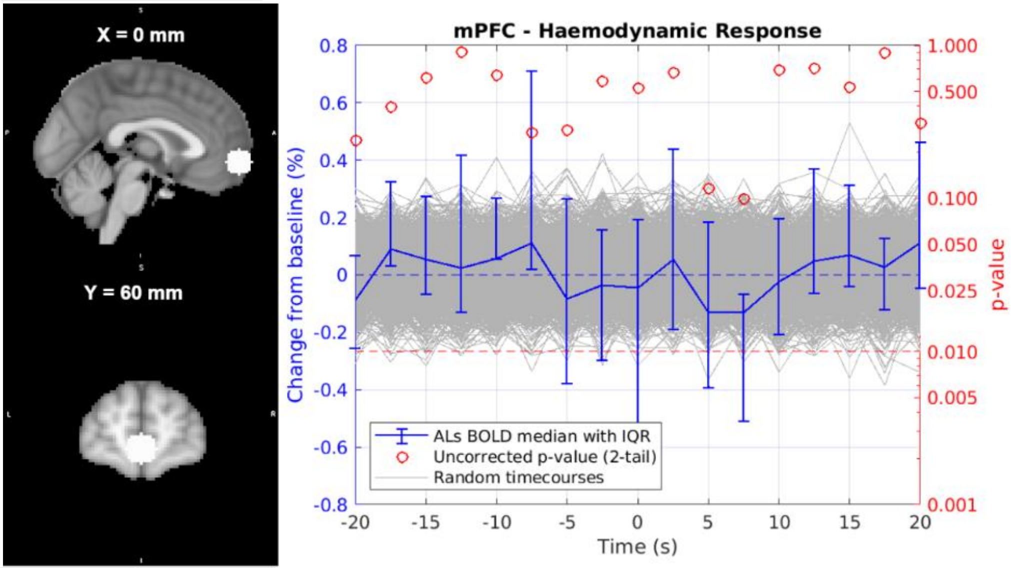
Figure 9-1 Average of haemodynamic response in significant regions during attention lapses.

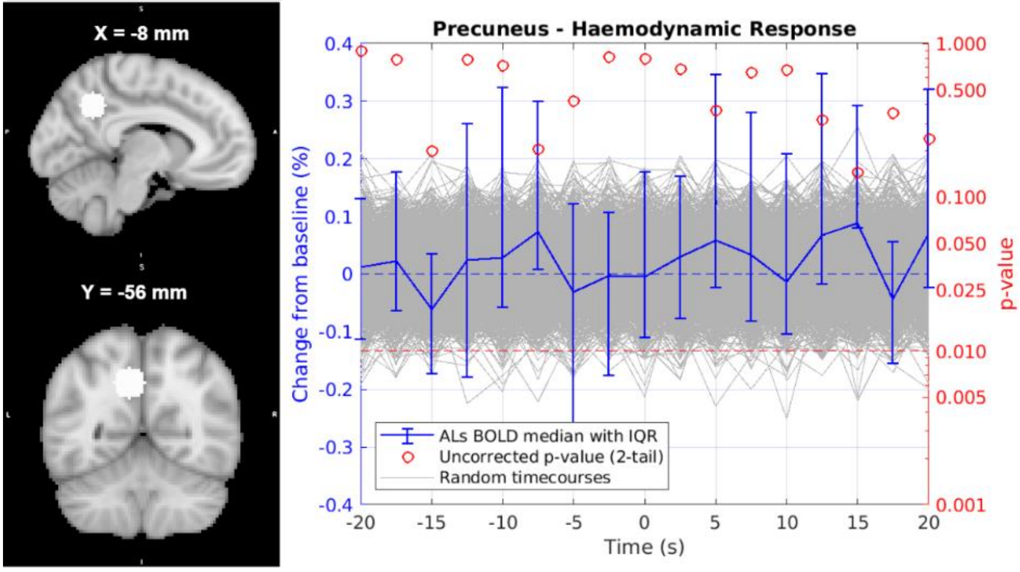
9.3.2 Haemodynamic response analysis of the regions of interest

To investigate hypotheses 1 and 8 further, we looked at the trend of change of the HR time-series in the brain ROI of DMN in Figure 9-2, DAN in Figure 9-3, FPN in Figure 9-4, and SN in Figure 9-5. DMN was represented by medial PFC (MPFC), PCC, Precuneous, and right and left IPL. DAN was represented by right and left FEF and right and left IPS. While FPN was represented by right and left posterior parietal cortex (PPC), and right and left dorsolateral-prefrontal cortex (DLPFC). Finally, SN was represented by dorsal and ventral ACC.

For DMN, only left IPL had p-values less than the p = 0.01 threshold at -15 s (p = 0.008) and -12.5 s (p = 0.005), where the HR had a trend of increase. DAN showed a trend of increase in HR around 7.5 s in left IPS (p = 0.004). FPN showed a trend of decrease at -2.5 s (p = 0.009) in the right PPC. Finally, the dorsal ACC of SN, which has the same peak coordinates as the significant cluster, showed a trend of increased HR at 5 s (p = 0.002) and 7.5 s (p = 0.001).


X = -1 mm
Y = -55 mm
PCC - Haemodynamic Response
Change from baseline (%)
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
p-value
1.000
0.500
0.100
0.050
0.025
0.010
0.005
0.001
-20
-15
-10
-5
0
5
10
15
20
Time (s)
ALs BOLD median with IQR
Uncorrected p-value (2-tail)
Random timecourses


X = 0 mm
Y = 60 mm
mPFC - Haemodynamic Response
Change from baseline (%)
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
p-value
1.000
0.500
0.100
0.050
0.025
0.010
0.005
0.001
-20
-15
-10
-5
0
5
10
15
20
Time (s)
ALs BOLD median with IQR
Uncorrected p-value (2-tail)
Random timecourses


X = -8 mm
Y = -56 mm
Precuneus - Haemodynamic Response
Change from baseline (%)
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
p-value
1.000
0.500
0.100
0.050
0.025
0.010
0.005
0.001
-20
-15
-10
-5
0
5
10
15
20
Time (s)
ALs BOLD median with IQR
Uncorrected p-value (2-tail)
Random timecourses

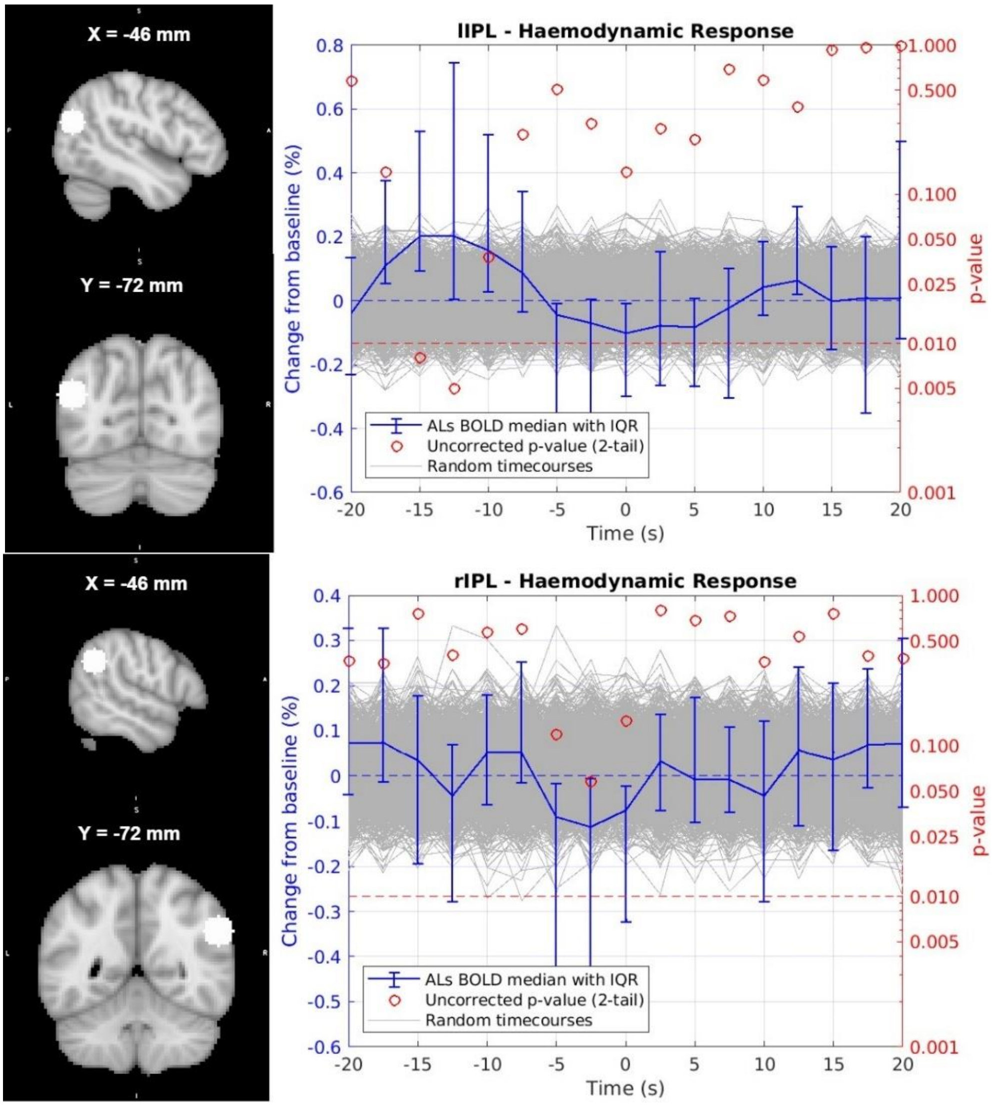
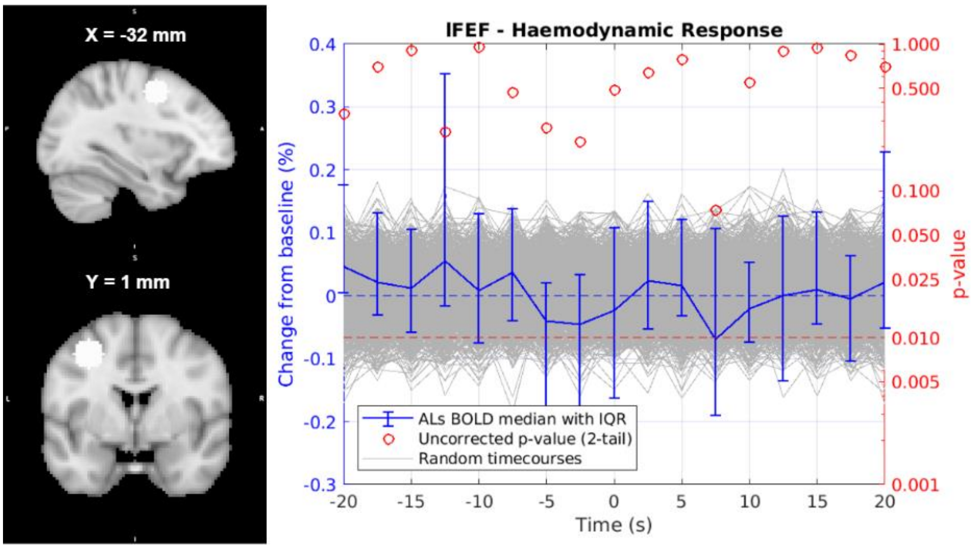


Figure 9-2 Average of haemodynamic response in regions of default mode network during attention lapses.



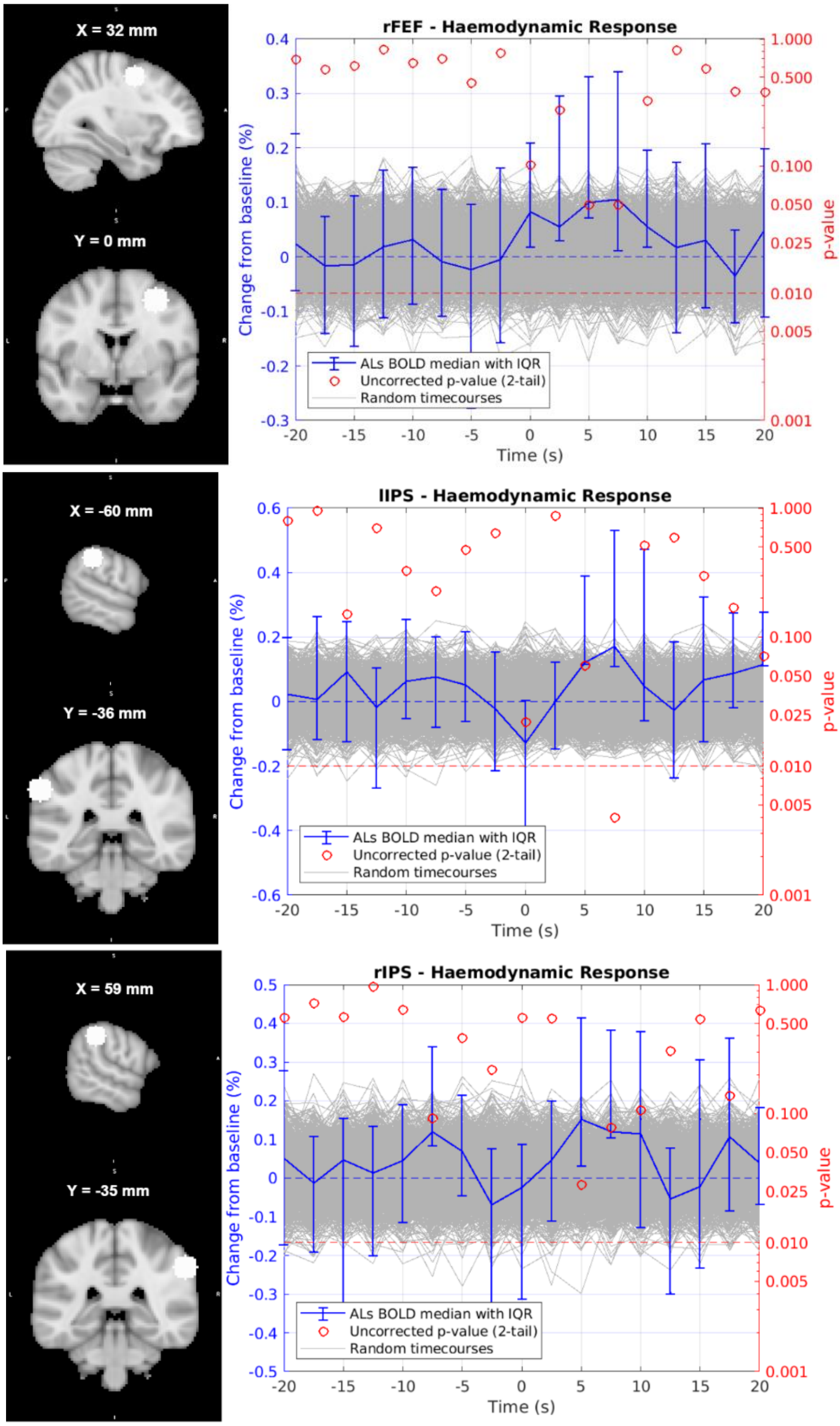
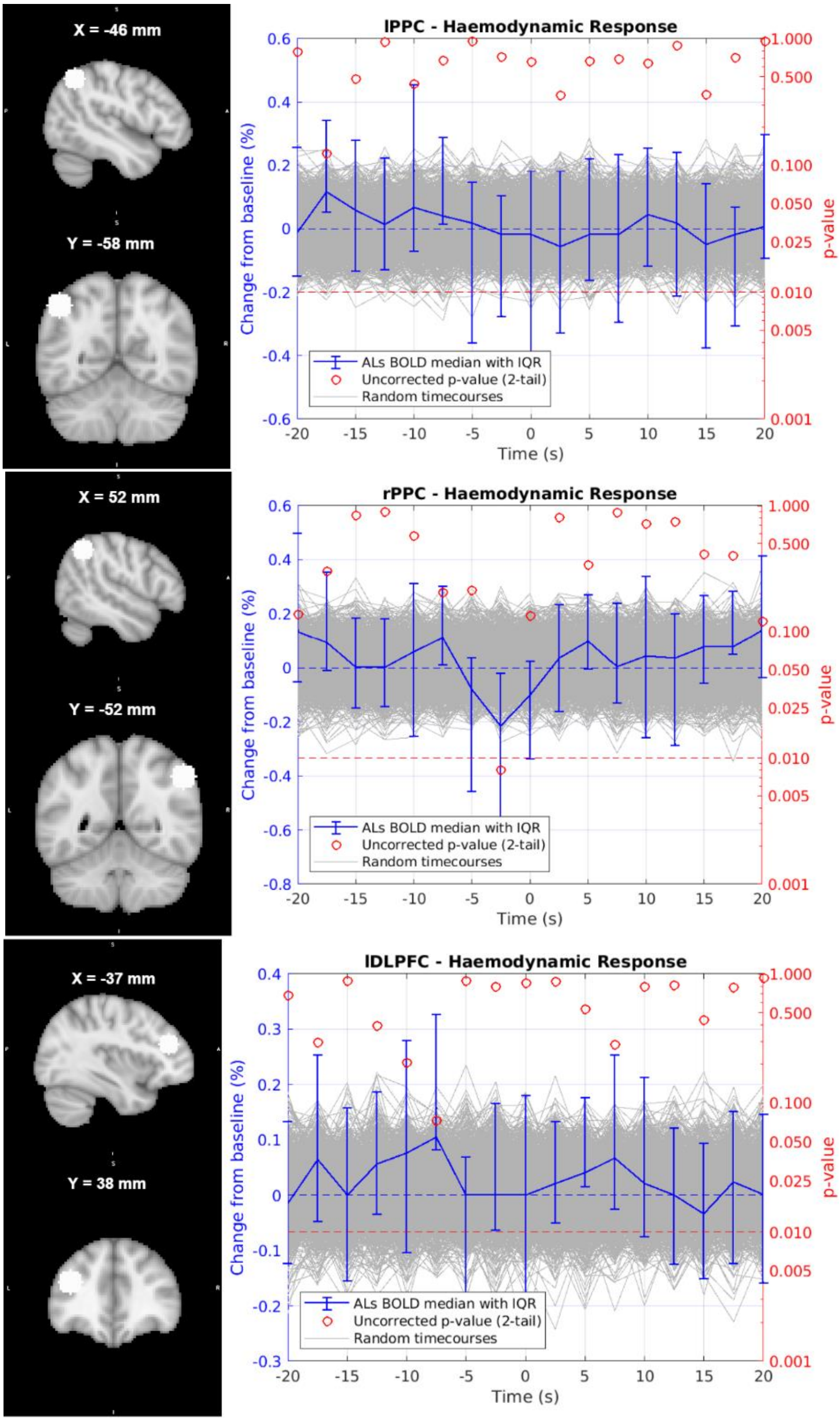


Figure 9-3 Average of haemodynamic response in regions of dorsal attention network during attention lapses.


X = -46 mm
Y = -58 mm
lPPC - Haemodynamic Response
Change from baseline (%)
p-value
Time (s)
ALs BOLD median with IQR
Uncorrected p-value (2-tail)
Random timecourses
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
1.000
0.500
0.100
0.050
0.025
0.010
0.005
0.001
-20
-15
-10
-5
0
5
10
15
20
X = 52 mm
Y = -52 mm
rPPC - Haemodynamic Response
Change from baseline (%)
p-value
Time (s)
ALs BOLD median with IQR
Uncorrected p-value (2-tail)
Random timecourses
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
1.000
0.500
0.100
0.050
0.025
0.010
0.005
0.001
X = -37 mm
Y = 38 mm
lDLPFC - Haemodynamic Response
Change from baseline (%)
p-value
Time (s)
ALs BOLD median with IQR
Uncorrected p-value (2-tail)
Random timecourses
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
1.000
0.500
0.100
0.050
0.025
0.010
0.005
0.001

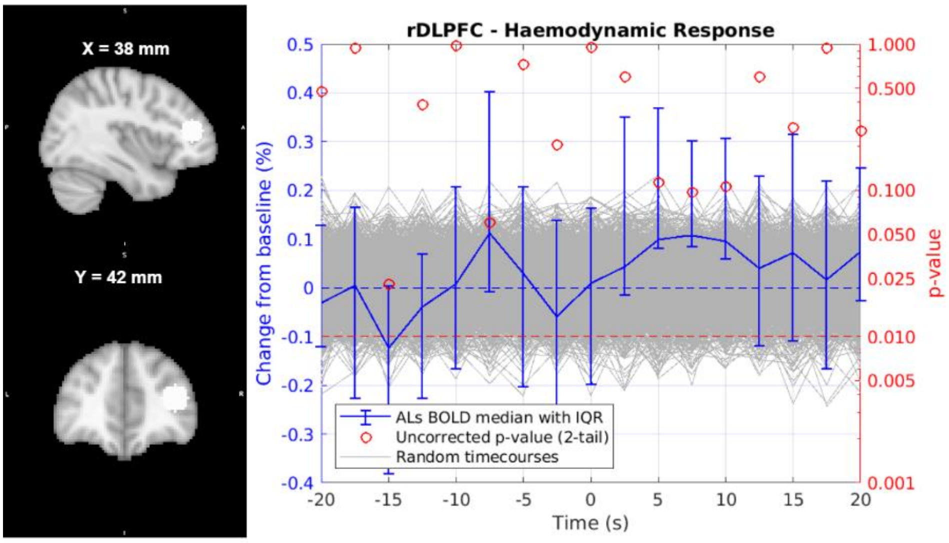


Figure 9-4 Average of haemodynamic response in regions of frontoparietal network during attention lapses.

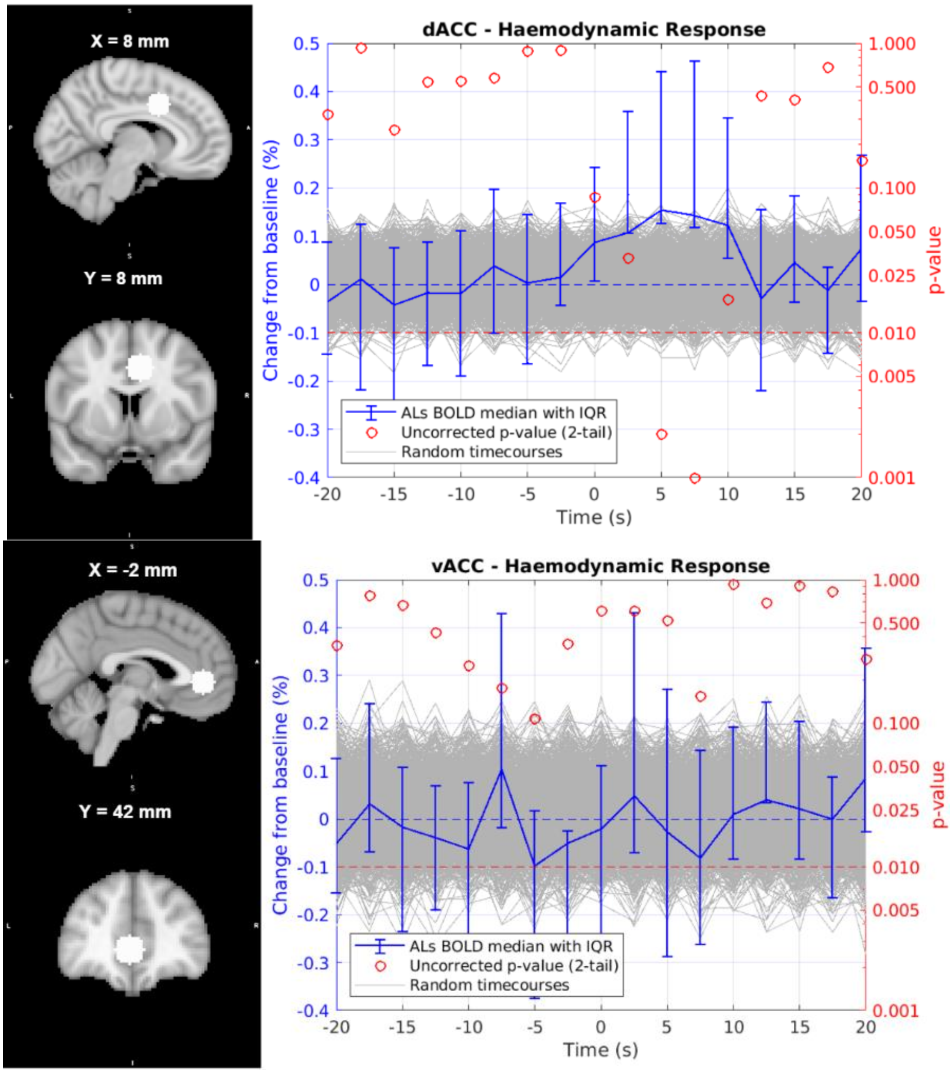


Figure 9-5 Average of haemodynamic response in regions of salience network during attention lapses.

9.4 Discussion

In the previous chapter, voxel-wise analysis did not reveal any significant changes in HR in either DMN or DAN. However, a significant increase in activity was found in a small cluster which partially included two regions: posterior/dorsal ACC and interior SMA based on the Harvard-Oxford atlas. To explore further, we looked at trends of dynamic changes in the BOLD time-series in the spherical ROI in both DMN, DAN and SN, in addition to FPN. We also further explored our findings by looking at the significant voxel-wise cluster in SN.

Based on Lindquist and Wager (2007), BOLD changes due to HRF should be seen from 5 to 10 s after the onset, where the onset of ALs is at 0. As expected, there was an increased HR around the 5-s timepoint in the significant cluster. The time series of the left IPL of DMN showed a trend of change at around 15-s before the onset of ALs. In contrast, a substantial increase in activity would have been expected if the AL was due to mind-wandering (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007). Increased activity in DMN has been associated with a voluntary “think-of-nothing” mind-blanking state (Kawagoe et al., 2019). On the other hand, mind-blanks are more likely to be represented by *involuntary* “nothing-in-mind” state in which it is considered there is no memory recall (Ward & Wegner, 2013). This indicates that all, or at least the majority, of the ALs seen in our 2-D CVT task were more likely to be due to involuntary mind-blanks. The lack of any substantial increase in activity during ALs also indicates that DMN is most likely not involved in involuntary mind-blanking.

An increased HR 15 s prior to the onset in the left IPL, where left IPL is associated with sensorimotor processing and spatial cognition (Wang et al., 2017), is an important finding. Increased activation in DMN at a substantial number of seconds prior to loss of responsiveness indicates that ALs may result from a process that begins prior to the AL (Smallwood, 2011).

The left IPS in the DAN had a trend of increased HR 7.5 s. The relation between the increased activity of DAN and external attention is well established (Fox et al., 2006; Fox et al., 2005; Vossel et al., 2014). This indicates that activity in part of the DAN increases after the onset to assist or reflect the process of coming out of the AL. DMN activity, which is positively associated with mind-wandering (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007) and voluntary mind-blanking (Kawagoe et al., 2019), has been shown to be anticorrelated with the activity of DAN, at least in some circumstances (Chai et al., 2012; Esposito et al., 2018). However, the literature has contradictory findings regarding DAN during mind-wandering: DAN can show increased activity (Christoff et al., 2009; Groot et al., 2021; Mittner et al., 2014), but also decreased activity (Mittner et al., 2016). Also, the literature shows that DAN can have increased activity in cases when task performance is low (Esterman et al., 2013; Esterman et al., 2014; Kucyi et al., 2017). Our physiological findings in DMN and DAN, together with behavioural characteristics, indicates that it is highly unlikely that the ALs seen in our 2-D CVT task were due to mind-wandering.

The dorsal ACC (part of SN) showed a trend of increased HR activity at 5 s and 7.5 s. Increased activation in dorsal ACC is associated with brief ALs (Weissman et al., 2006), as the dorsal ACC is responsible for helping regain focused attention (Banich et al., 2000; MacDonald et al., 2000; Paus, 2001; Weissman et al., 2005), which, in our case, is performing the 2-D CVT task, after losing attention due to the AL. In contrast, the ventral ACC, which is associated with “think-of-nothing” voluntary mind-blanking state (Kawagoe et al., 2019), did not show any trend of HR activity change around the 5-s timepoint, which appears to reflect the key difference between our involuntary ALs and the volitional ALs investigated by Kawagoe et al. (2019).

The FPN is core to the decoupling process (Dixon et al., 2018; Macaluso & Doricchi, 2013; Spreng et al., 2010), as it sustains attention internally by connecting to DMN in the case of mind-wandering (Godwin et al., 2017; He et al., 2021), or externally by connecting to DAN. There was a trend of decrease in HR activity around the -2.5-s timepoint. Given that FPN is associated with the regulation of the change from external to internal and vice versa, finding a trend of drop in HR may before the onset of ALs indicate that FPN is not associated with these ALs in case they are due to mind-wandering. Also, may indicate that FPN is contributing to decoupling process due to ALs, as FPN is associated with the coordination of visuospatial attention (Lückmann et al., 2014; Marek & Dosenbach, 2018; Scolari et al., 2015).

In terms of limitations, we could not directly compare results from mind-wandering and mind-blanking as we do not have distinct behavioural gold standards of these. Also, given that the average duration of ALs (1.74 s) was less than the TR (2.5 s) of the fMRI, some changes due to ALs were less likely to have been revealed. Also, low statistical power due to relatively low numbers of subjects and ALs, and relatively small effect sizes of changes in BOLD activity could well have adversely affected finding significant changes in all of the ROIs investigated via dynamic HR analysis.

9.5 Summary

This chapter introduced further analysis of ALs to investigate ROIs in networks of particular interest. It started by describing the analysis pipeline in detail for HR analysis after following the same procedure for pre-processing, co-registration and normalization used in the voxel-wise analysis. This chapter has revealed 2 important trends of activity changes that indicates: (1) ALs are more likely being involuntary mind-blanks rather than mind-wandering or voluntary mind-blanks (first to be shown in a continuous task) and (2) increased activity in DMN (left IPS) is more likely to provide a biomarker predictive of, and substantially preceding, an impending AL.

Chapter 10: fMRI Functional Connectivity Analysis of Attention Lapses

10.1 Introduction

In this chapter, fMRI data were used to answer hypotheses 2 to 6, and parts of 8. The aims were to (i) investigate changes in functional connectivity of endogenous ALs versus the baseline of good responsive tracking within and between the networks of interest, pre-defined in CONN: DMN, DAN, FPN, VSN, SMN, and SN, and (ii) reveal evidence in support of whether the ALs were mind-wandering or mind-blanking. In addition, the pre-defined networks: WMN (Piccoli et al., 2015) and EMN (Coiner et al., 2019) were also examined, see Table 10-1. A total of 17 subjects and 85 ALs with an average duration of 1.74 s from Studies C and D were used in this analysis.

Table 10-1 Regions within network of interest.

Network	State
DMN	Medial PFC (1, 55, -3)
	Left lateral parietal cortex (LPC) (-39, -77, 33)
	Right LPC (47, -67, 29)
	PCC (1, -61, 38)
DAN	Left FEF (-27, -9, 64)
	Right FEF (30, -6, 64)
	Left IPS (-39, -43, 52)
	Right IPS (39, -42, 54)
FPN	Left LPFC (-43,33,28)
	Left PPC (-46, -58, 49)
	Right LPFC (41, 38, 30)
	Right PPC (52, -52, 45)
VSN	Visual medial cortex (VMC) (2, -79, 12)
	Visual occipital cortex (VOC) (0, -93, -4)
	Left visual lateral cortex (VLC) (-37, -79, 10)
	Right VLC (38, -72, 13)
SMN	Left sensorimotor lateral cortex (SLC) (-55, -12, 29)
	Right SLC (56, -10, 29)
	Sensorimotor superior cortex (SSC) (0, -31, 67)

SN	ACC (0, 22, 35)
	Left anterior insula (AInsula) (-44, 13, 1)
	Right AInsula (47, 14, 0)
	Left rostral PFC (RPFC) (-32, 45, 27)
	Right RPFC (32, 46, 27)
	Left sensorimotor gyrus (SMG) (-60, -39, 31)
	Right SMG (62, -35, 32)
WMN	Left LPFC (-43,33,28)
	Right LPFC (41, 38, 30)
	Left IPS (-39, -43, 52)
	Right IPS (39, -42, 54)
EMN	PCC (1, -61, 38)
	Left LPFC (-43,33,28)
	Right LPFC (41, 38, 30)
	Left FEF (-27, -9, 64)
	Right FEF (30, -6, 64)
	VMC (2, -79, 12)
	VOC (0, -93, -4)

10.2 Method

10.2.1 Analysis tool

CONN-fMRI v20b (http://www.nitrc.org/projects/conn) software (Whitfield-Gabrieli & Nieto-Castanon, 2012) was used.

10.2.2 Pre-processing and registration

CONN, which is a SPM (Ashburner, 2012) based software, uses SPM to do the pre-processing. So for consistency, the same pre-processing and registration parameters were used as in 8.2.2.1 and 8.2.2.2. The following pre-processing pipeline was used, which included: motion correction, spatial smoothing using a Gaussian kernel with a full-width-at-half maximum of 5 mm, temporal filtering at 100 s (0.01 Hz), slice-time correction, functional to structural registration at 6 DOF, and using MNI as the atlas.

10.2.3 Subject (1st-level) analysis

10.2.3.1 Denoising

To reduce noise, CONN uses the anatomical CompCor approach (Behzadi et al., 2007). Segmentation to identify the WM and CSF from the structure images of the subjects, then CompCor via principal components analysis extracts 5 components each from WM and CSF. These components, in addition to the six motion parameters and their temporal derivatives, scrubbing of high-motion data points based on the artefact removal tool (ART) (Mazaika et al., 2005), and our defined covariates BadTracking, TargetSpeed, MS, DIRE, Sleep, and VBIP events were all used as confounds in the denoising step to remove their effect from the data, see Figure 10-1. This is a carpet plot which unravels each volume from a 3-D cube of voxels into a 2-D plot of squares, each column represents an individual volume, and each row is an individual voxel in that volume. Denoising smooths out the rougher transitions between voxels that are probably caused by motion scanner drift and physiological noise, and the time-series plot of the global signal reflects this smoothing out as well.

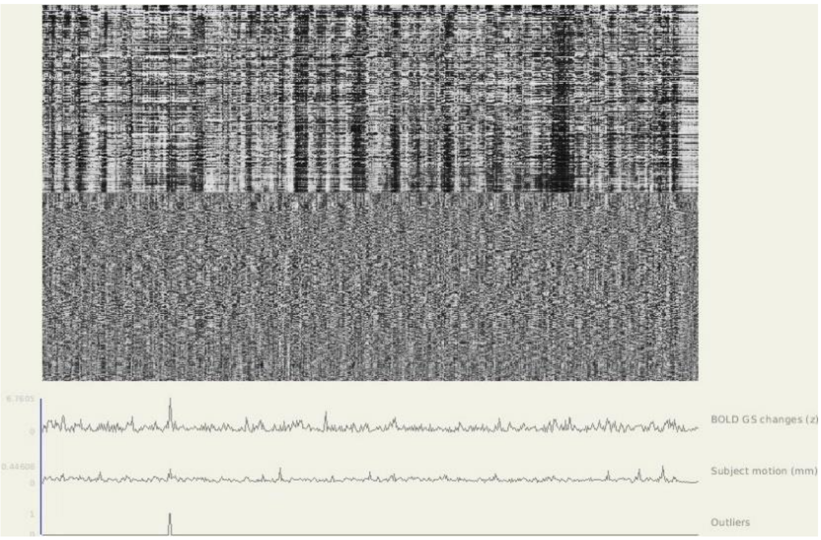


Figure 10-1 Result of the denoising step to the BOLD signal in CONN. The top carpet plot represents the signal before denoising, while the bottom carpet plot represents the signal after denoising. Here only one volume was identified as an outlier.

10.2.3.2 Modelling

Weighted GLM FC analysis was used to do the ROI-to-ROI analysis for each subject, HRF weighting was used to weight the scans within each condition when computing condition-specific connectivity measures. Bivariate correlation was used as an outcome measure for the second-level analysis.

10.2.4 Group (2nd-level) analysis

The subjects' ROI-to-ROI maps were used for the group analysis. A one-sample t-test was applied using parametric multivariate statistics (Jafri et al., 2008). A two-sided FDR correction for network-based statistics (Zalesky et al., 2010) was used to correct for multiple comparisons at $p < 0.05$ to reveal significant connections. The analysis was done to check the FC of ALs versus baseline of good responsiveness tracking.

10.3 Results

10.3.1 FC analysis for attention lapses versus baseline of good tracking

FC was checked within DMN, FPN, DAN, SMN, SN, VSN, WMN, and EMN are listed in Table 10-2, and between DMN-FPN, DAN-FPN, SMN-FPN, VSN-FPN, DAN-EMN, DMN-EMN, WMN-DMN, in addition to SN-DMN, and SN-DAN are listed in Table 10-3. All results are corrected for multiple comparisons using FDR $p < 0.05$.

Table 10-2 Significant changes in functional connectivity within networks for attention lapses versus baseline.

FC	State	T(16)	P_FDR
Within DMN	Increase in FC between left LPC & right LPC	5.25	0.001
	Increase in FC between PCC & right LPC	3.56	0.008
Within DAN	Increase in FC between right FEF & left FEF	4.78	0.001
	Increase in FC between right IPS & left IPS	4.12	0.002
	Increase in FC between right FEF & right IPS	3.42	0.007
	Increase in FC between left FEF & left IPS	2.38	0.045
Within FPN	Increase in FC between left PPC & right PPC	6.44	<0.001
	Increase in FC between left LPFC & right LPFC	5.30	<0.001
	Increase in FC between left LPFC & left PPC	5.26	<0.001
	Increase in FC between right LPFC & left PPC	4.31	0.001
	Increase in FC between right LPFC & right PPC	4.02	0.001
	Increase in FC between left LPFC & right PPC	3.89	0.001
Within VSN	Increase in FC between left VLC & right VLC	4.04	0.006
	Increase in FC between VMC & right VLC	2.69	0.049
Within SMN	Increase in FC between right SLC & left SLC	4.84	0.001
	Increase in FC between right SLC & SSC	2.96	0.012
	Increase in FC between left SLC & SSC	2.84	0.012

Within SN	Increase in FC between right SMG & left SMG	7.87	<0.001
	Increase in FC between right AInsula & left AInsula	5.31	0.001
	Increase in FC between right AInsula & left SMG	5.07	0.001
	Increase in FC between right RPFC & left RPFC	5.00	0.001
	Increase in FC between left AInsula & left SMG	4.93	0.001
	Increase in FC between ACC & left RPFC	4.90	0.001
	Increase in FC between right AInsula & ACC	3.48	0.009
	Increase in FC between left AInsula & right SMG	3.31	0.012
	Increase in FC between right AInsula & right SMG	3.12	0.015
	Increase in FC between ACC & right RPFC	2.82	0.026
Within WMN	Increase in FC between left LPFC & right LPFC	5.30	<0.001
	Increase in FC between left IPS & right IPS	4.12	0.002
Within EMN	Increase in FC between left LPFC & right LPFC	5.30	0.002
	Increase in FC between left LPFC & VOC	3.24	0.036
	Decrease in FC between PCC & VOC	-2.98	0.046
	Increase in FC between left FEF & right FEF	4.78	0.002

FC analysis within DMN, DAN, FPN, VSN, SMN, SN, EMN, and WMN showed an increased FC in all networks, and no significantly decreased FC except in EMN between PCC and VOC. The DMN has increased FC between the PCC and right and left LPC. DAN showed an increased FC within right and left FEF, and within right and left IPS. FPN had an increase in FC within right and left LPFC, and within right and left PPC. There was an increase in FC of VSN between VMC and right and left VLC. In addition, SMN increased in FC between right and left SLC and SSC. Also, increased FC within SN in regions: right and left SMG, right and left AInsula, ACC, and right and left RPFC. An increased FC was also found in WMN within right and left LPFC, and within right and left IPS.

Table 10-3 Significant changes in functional connectivity between networks for attention lapses versus baseline.

FC	State	T(16)	P_FDR
DMN-FPN	Increase in FC between right LPC & right PPC	3.70	0.007
	Increase in FC between right LPC & left PPC	2.88	0.030
	Increase in FC between left LPC & left PPC	2.60	0.049
DAN-FPN	No change in FC	N/A	N/A

DMN-EMN	Increase in FC between PCC & right LPC	3.56	0.030
	Increase in FC between left LPFC & right LPFC	5.30	0.002
	Increase in FC between left LPFC & VOC	3.24	0.046
	Increase in FC between left FEF & right FEF	4.78	0.003
DAN-EMN	Increase in FC between left LPFC & right LPFC	5.30	0.003
	Increase in FC between left FEF & right FEF	4.78	0.004
	Increase in FC between right IPS & right FEF	3.42	0.026
	Decrease in FC between right IPS & VOC	-3.41	0.026
	Decrease in FC between VOC & left LPFC	3.24	0.030
	Decrease in FC between right IPS & VMC	-3.04	0.039
	Decrease in FC between PCC & VOC	-2.98	0.039
VSN-FPN	Increase in FC between right VLC & left LPFC	4.80	0.001
	Increase in FC between right VLC & right PPC	3.75	0.005
	Increase in FC between left VLC & left LPFC	4.25	0.003
	Increase in FC between left VLC & left PPC	3.35	0.010
	Increase in FC between left VLC & right LPFC	3.25	0.011
	Increase in FC between VOC & left LPFC	3.24	0.011
	Increase in FC between VMC & left LPFC	2.62	0.034
SMN-FPN	Decrease in FC between SSC & right PPC	-4.09	0.003
	Decrease in FC between SSC & right LPFC	-3.44	0.008
	Decrease in FC between SSC & left PPC	-3.16	0.013
	Decrease in FC between SSC & left LPFC	-2.40	0.046
DMN-WMN	Decrease in FC between right LPC & right IPS	-4.06	0.006
SN-DMN	No change in FC	N/A	N/A
SN-DAN	Increase in FC between left SMG & right IPS	4.37	0.003
	Increase in FC between left SMG & left IPS	3.95	0.006
	Increase in FC between right SMG & right IPS	3.40	0.016

FC analysis between networks showed both increased and decreased FC. When testing FC between FPN and DMN, there were increases in FC between right and left LPC and right and left PPC, but no change in FC was found between FPN and DAN. FC between EMN and DMN showed increases within right and left LPFC, and within right and left FEF, also between PPC and right LPC, and between left LPFC and VOC. However, FC between EMN and DAN showed both increases and decreases; increases in FC within right and left LPFC, and within right and left FEF, also between right IPS and right FEF. While FC between right IPS and VOC, between VOC and left LPFC, between right IPS and VMC, and between PCC & VOC have decreased.

FC between FPN and SMN has decreased; there were decreases in FC between SSC and right and left PPC, and right and left LPFC. There were increases in FC between VSN and FPN among all the regions right and left VLC, VOC, and VMC of VSN, and right and left LPFC and right and left PPC of FPN. When testing FC between DAN and SN, we found increases in FC between right and left SMG and right and left IPS. No change in FC was found between SN and DMN. Finally, a decrease in FC was found between right LPC of DMN and right IPS of WMN (defined nodes).

Significant between-network FC changes are also shown in ring display for DAN and DMN in Figure 10-2, and DMN-FPN, DAN-FPN, and FPN in Figure 10-3, and for DMN-EMN, DAN-EMN, and EMN in Figure 10-4, also for SMN-FPN and VSN-FPN in Figure 10-5, and for SN-DMN, SN-DAN, and SN in Figure 10-6. Finally, for WMN and DMN-WMN in Figure 10-7.

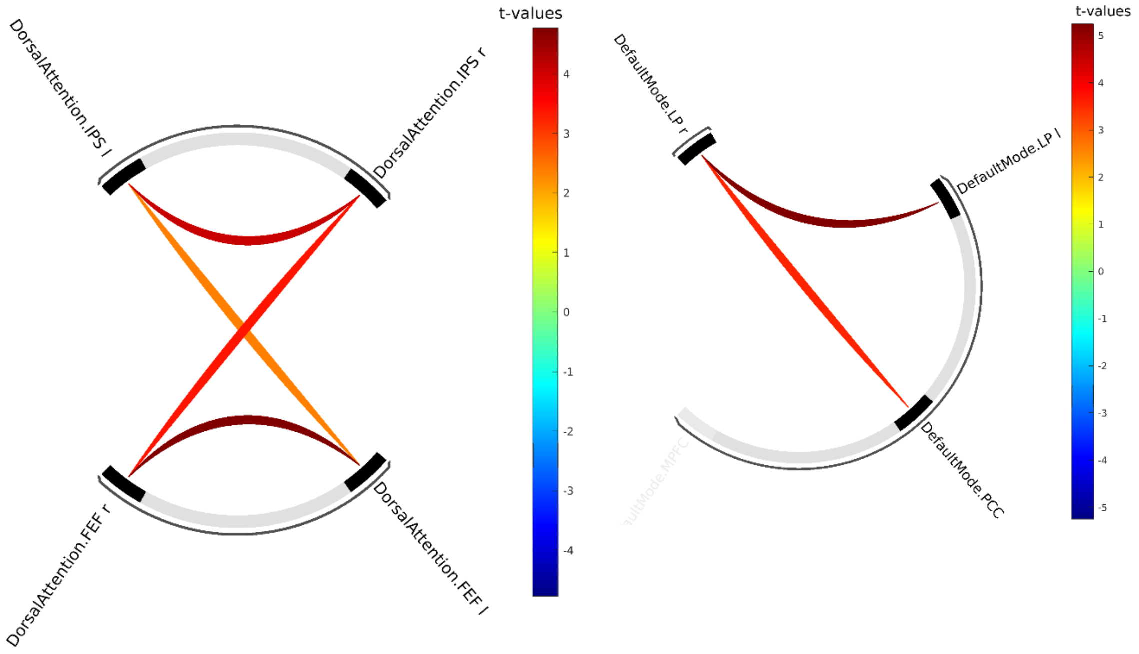


Figure 10-2 Significant within-network functional connectivity (FC) changes shown in a ring display of three FC measures: within dorsal attention network (left), and within default mode network (right).

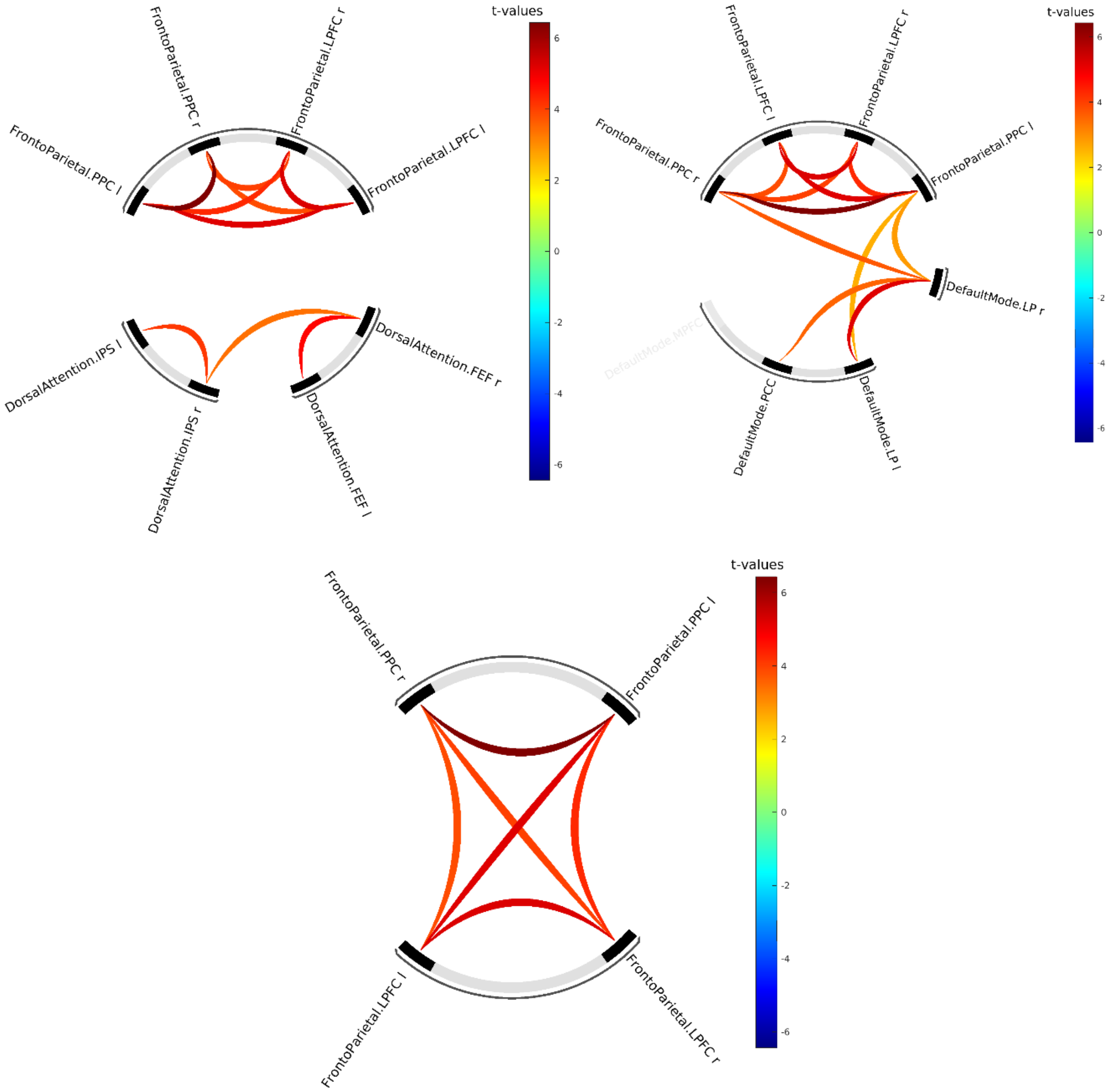


Figure 10-3 Significant functional connectivity (FC) changes shown in a ring display of three FC measures: between frontoparietal network-dorsal attention network (top left), between frontoparietal network-default mode network (top right), and within frontoparietal network (bottom).

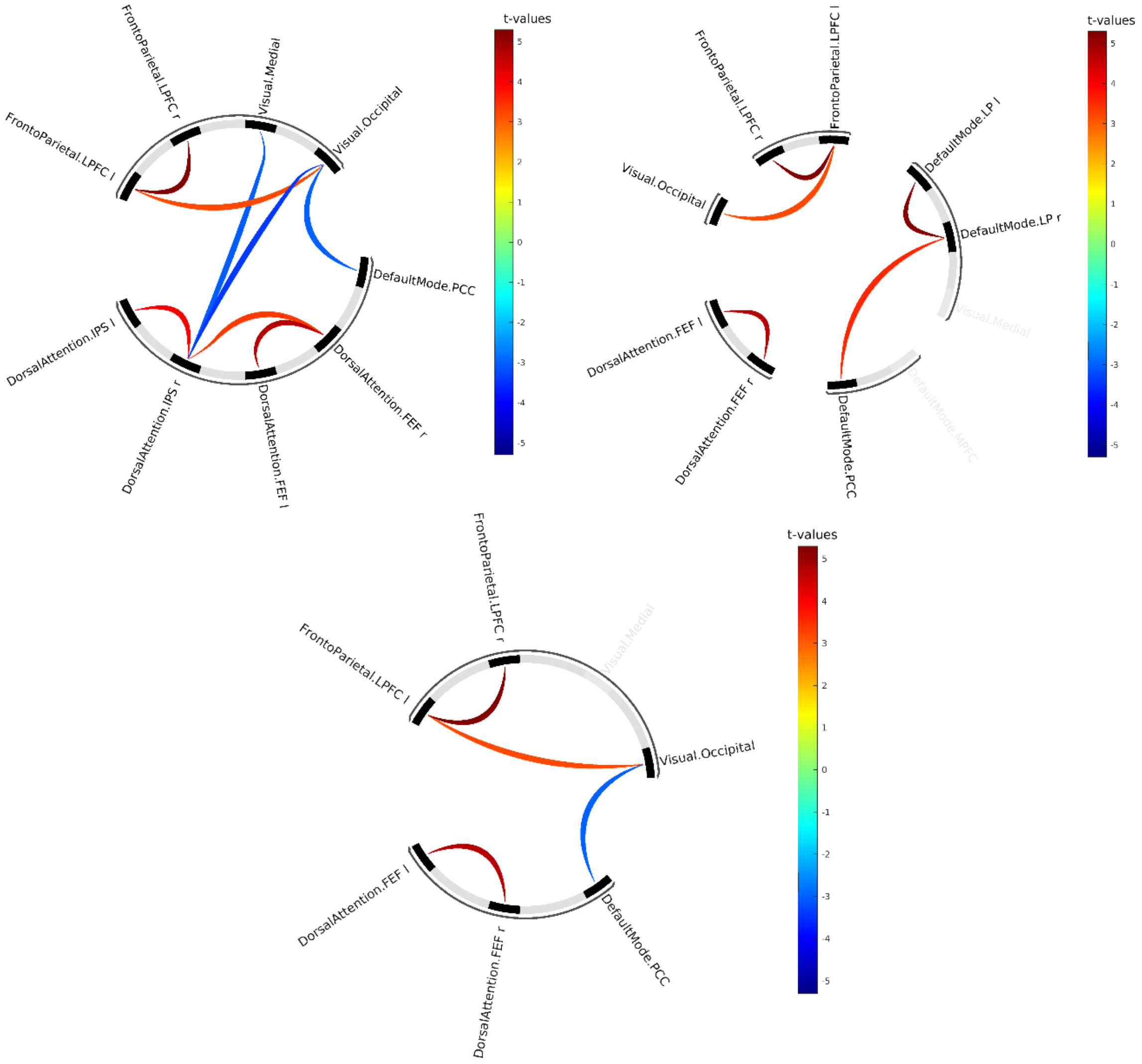


Figure 10-4 Significant functional connectivity (FC) shown in a ring display of three FC measures: between dorsal attention network-eye movement network (top left), between default mode network-eye movement network (top right), within eye movement network (bottom).

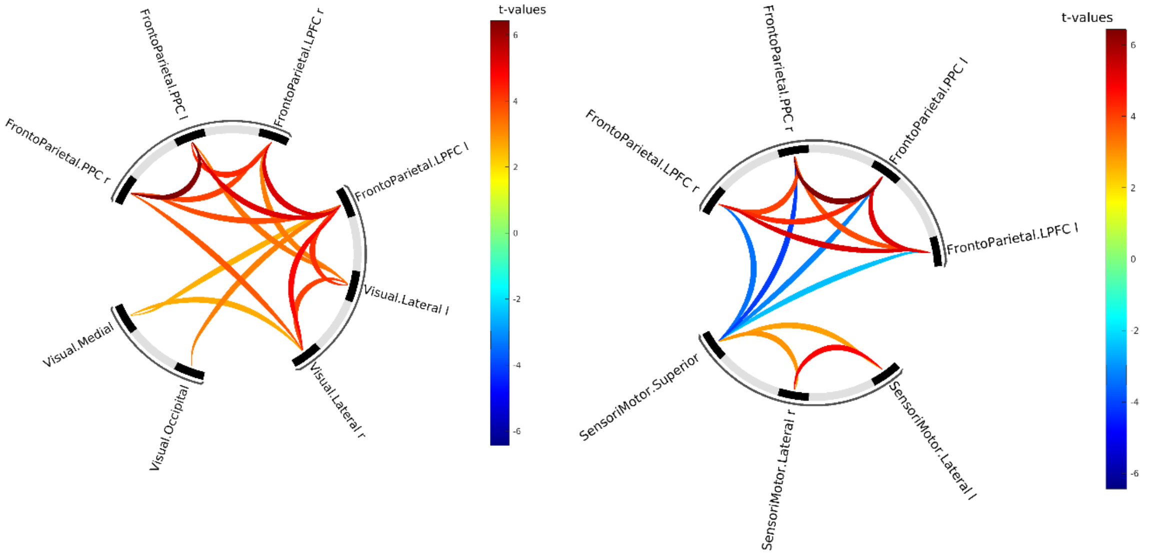


Figure 10-5 Significant functional connectivity (FC) shown in a ring display of three FC measures: between visual network-frontoparietal network (top left), between sensorimotor network-frontoparietal network (top right).

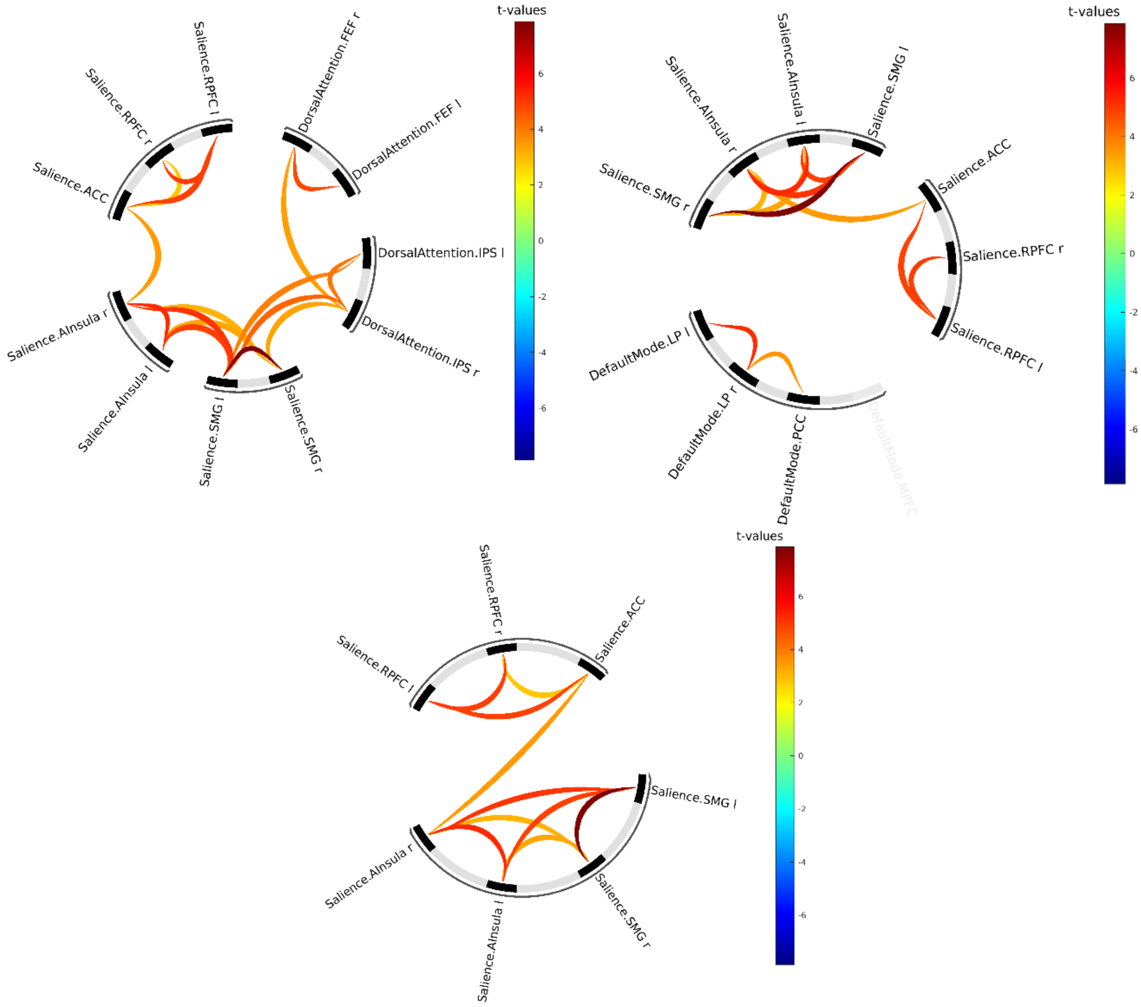


Figure 10-6 Significant functional connectivity (FC) shown in a ring display of three FC measures: between salience network-dorsal attention network (top left), between salience network -default mode network (top right), within salience network (bottom).

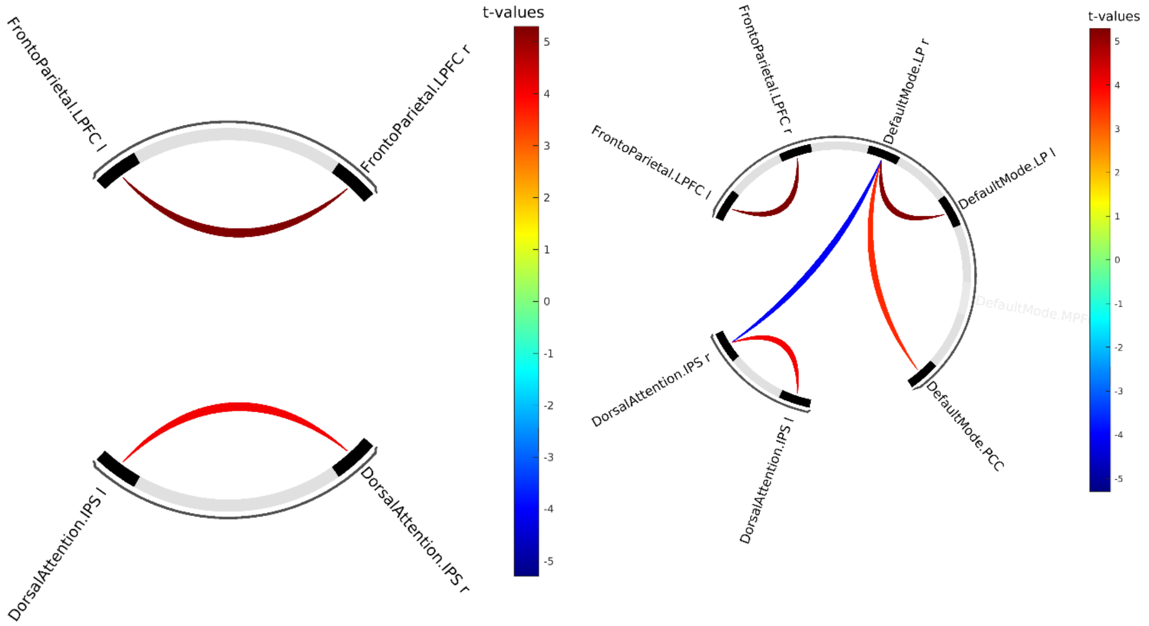


Figure 10-7 Significant functional connectivity (FC) shown in a ring display of three FC measures: within working memory network (left), between working memory network-default mode network (right).

10.3.2 Changes in functional connectivity between attention lapses and microsleeps

We examined FC within and between networks of interest: DMN, DAN, FPN, VSN, and SMN to reveal changes in FC between ALs and MSs. The analyses did not reveal any significant changes in FC between ALs and MSs.

10.4 Discussion

ROI-to-ROI FC analysis for ALs versus the baseline of good responsive tracking was performed on the combined studies (Table 10-2 and Table 10-3). The analysis targeted FC within and between the networks of interest: DMN, DAN, FPN, VSN, SMN, SN, EMN and WMN. The total number of ALs was 85 with an average duration of 1.74 s, which is less than the TR (2.5 s) of fMRI.

We found an increased FC between DMN and FPN, while no change in FC between FPN and DAN. Also, increased FC between DMN and EMN, while FC between DAN and EMN showed both increases and decreases. In addition, FC between FPN and VSN increased, while FC between FPN and SMN decreased. Finally, FC between DMN and WMN has decreased.

During an AL, there is a complete decoupling from external environment (Ward & Wegner, 2013). Given the association between FPN and directing attention from external to internal and vice versa (Dixon et al., 2018; Spreng et al., 2010), and the association between DAN and external attention (Fox et al., 2006; Fox et al., 2005; Vossel et al., 2014), a decrease in FC between DAN and FPN was expected during ALs. As the 2-D CVT requires visual fixation on target and response stimuli on a screen, this requires the eyes to move, and this does not happen during ALs due to complete decoupling. Thus, a decrease in FC between DAN and EMN was expected.

Finally, given the association between FPN and the visuospatial attention coordination (Lückmann et al., 2014; Marek & Dosenbach, 2018; Scolari et al., 2015), decreased FC between FPN and SMN was expected during ALs relative to FC when performing the 2-D CVT (Cavina-Pratesi et al., 2006; Shibasaki et al., 1993; Wildgruber et al., 1997) and likewise between FPN and VSN (Desimone & Duncan, 1995; Helfrich et al., 2013).

The decoupling process during an AL results in disconnecting attention from the external environment (performing the task), with attention being either diverted internally, as in mind-wandering (Berthié et al., 2015), or completely lost as in mind-blanking (Ward &

Wegner, 2013). This behavioural change is reflected in physiological changes in several brain networks. Since shifting attention internally to focus on spontaneous thoughts (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007) or freeing the mind from thoughts in voluntary mind-blanks is associated with activation of DMN based on (Kawagoe et al., 2019). DMN was found to be a core network in the process of decoupling (Eichele et al., 2008; Weissman et al., 2006).

Mind-wandering is quite different from mind-blanking, although both involve at least partial decoupling of attention from an external task (Ward & Wegner, 2013). Mind-wandering is defined as a state in which attention is diverted to internal TUTs. These thoughts might be related to the past or future, which means the brain's memory is involved (Hutchinson & Turk-Browne, 2012; Wang et al., 2009) and given the anticorrelation between WMN and DMN when focusing on a memorized stimulus (Piccoli et al., 2015), a decrease in FC between DMN and WMN might be expected if mind-wandering was present. Because of the association between DMN and FPN in the generation of TUTs (Smallwood et al., 2012), an increased FC between these two networks would be expected during mind-wandering. Likewise, an increase in FC between DMN and EMN would be expected given the association between mind-wandering and eye movements (Hartmann et al., 2014).

In contrast, mind-blanking is defined as an empty mind state which more likely does not involve memory recall (Kawagoe et al., 2019; Ward & Wegner, 2013). Failure in short-term memory (STM) processing, according to Moraitou and Efklides (2009) and Efklides and Touroutoglou (2010), is associated with a blank-in-mind or mind-blanking, in which there is nothing in mind while being behaviourally awake (Ward & Wegner, 2013), which is different than failing to interact and/or process information from the environment. In addition, attention and memory are highly associated when functioning (Chun, 2011), sharing resources (Zokaei et al., 2014), and lapsing (deBettencourt et al., 2019). So, decreases in FC between DMN and WMN, and between DMN and EMN were expected if mind-blanking was present. However, blank-in-mind might simply be a temporary loss of control as opposed to loss of attention (Di Lollo et al., 2005). Finally, given the association between FPN and memory functions (Borst & Anderson, 2013), a decrease in FC between FPN and DMN would be expected for mind-blanking.

To reveal what happens during ALs in our 2-D CVT task, we investigated FC between DAN and FPN, where we found no significant change. A decrease in FC between FPN and DAN was expected for ALs due to decoupling. However, if attention was being directed externally before the AL (i.e., when tracking), then no change in FC could mean that attention was still being directed externally during the AL (e.g., an externally-diverted lapse). On the other hand, finding increased FC between both right and left LPC of DMN and right and left PPC of FPN supports the idea that these ALs are associated with internal thoughts that could be task-related given the very short average duration of our ALs. However, another view might be that these ALs are due to mind-wandering because of the increased FC between FPN and DMN (Godwin et al., 2017; He et al., 2021; Smallwood et al., 2012). Also, the increased FC within DMN agrees with the same view (Godwin et al., 2017; He et al., 2021; Kucyi et al., 2017).

FC between DAN and EMN was investigated, where we found both increases and decreases: increases in FC within right and left LPFC, and within right and left FEF, also between right IPS and right FEF. While FC between right IPS and VOC, between VOC and left LPFC, between right IPS and VMC, and between PCC and VOC have decreased. However, FC between DMN and EMN showed only increases within right and left LPFC, and within right and left FEF, also between PPC and right LPC, and between left LPFC and VOC. Both FC between DAN and EMN, and between DMN and EMN agrees on finding increased FC within right and left LPFC, and within right and left FEF. If the ALs were due to mind-wandering, then this is expected, as FEF in addition to IPS are associated with oculomotor control (all eye movements) (Tomassini et al., 2007; Umarova et al., 2010). Also, LPFC contributes to the processing of eye movements (Pierrot-Deseilligny et al., 2004; Pierrot-Deseilligny et al., 2003). This falls in line with the relation between mind-wandering and eye movements (Hartmann et al., 2014).

Increased FC between VOC of VSN, which is associated with processing the visual stimuli (Coiner et al., 2019), and DMN supports that ALs again are due to mind-wandering as the increased FC between DMN and VSN was shown to be associated with mind-wandering (Zhou & Lei, 2018), while the decreased FC between VSN and DAN is associated with decoupling.

However, given the short average duration of our ALs, it is highly unlikely that subjects had time to think about memories within the AL duration. The initiative of moving eyes, which was shown in the increased FC between the regions responsible for eye movements of EMN and DMN, also DAN, could indicate a process of regaining attention before being fully attending to the task as the regions of EMN responsible for processing visual input had decreased FC with DAN.

The decreases in FC between SSC of SMN and right and left PPC, and right and left LPFC of FPN again supports the idea of decoupling as during ALs, there will be no interaction with the task as expected. But, finding increased FC between right and left VLC, VOC, and VMC of VSN, and right and left LPFC and right and left PPC of FPN was not expected based on the idea of decoupling. Also, according to Zhou and Lei (2018), decreased FC between FPN and VSN was found when comparing mind-wandering to being on-task. However, this increase in FC might be associated with getting out of the AL, as VLC and VMC were shown to be associated with the control of pursuit eye movements, in addition to maintaining the visual stability (Kan et al., 2008).

Finally, we found a decrease in FC between right LPC of DMN and right IPS of WMN (defined by Piccoli et al. (2015)). This serves in ALs favour in general as it was not expected to see an increased FC between WMN and DMN in either mind-wandering (Piccoli et al., 2015), or mind-blanking given that it is a state of an empty mind (Kawagoe et al., 2019; Ward & Wegner, 2013).

Based on the findings, we have evidence to accept Hypotheses 3, 5 and 6, but no evidence to support acceptance of Hypotheses 2 and 4. Given the short average duration of ALs, we found support that the ALs during 2-D CVT task are more likely to be due to mind-blanking and not mind-wandering.

Another interesting finding is the relationship between SN, DMN, and DAN. Based on Maillet et al. (2019), FC between SN and DMN increases when performing a task that requires internal attention, while connectivity between SN and DAN increases when performing a task that requires external attention. We found no change in FC between SN and DMN, while there was an increase in FC between right and left IPS of DAN and an increase in FC between right and left SMG of SN. Given that SN is responsible for switching between DMN and task-related networks (Goulden et al., 2014; Menon & Uddin, 2010), and the short average duration of ALs, we conclude that an increase in FC between SN and DAN could be associated with the process of recovery from an AL.

10.5 Summary

This chapter started by introducing the analysis pipeline in detail starting by pre-processing, co-registration and normalization, denoising, and finally first-level and group-level statistical analyses. Hypotheses (2 to 6, and parts of 8) were explored. We found support for decoupling during ALs, and that ALs during 2-D CVT task are more likely to be involuntary mind-blanks and not mind-wandering. Our significant findings were discussed in the light of literature and how they relate to ALs.

Chapter 11: EEG Analysis of Attention Lapses

11.1 Introduction

In this chapter, EEG data were used to investigate hypothesis 7 and part of hypothesis 8. The aim was to reveal the neural signature of endogenous ALs compared with good responsive tracking (baseline) within the delta, theta, alpha, beta, and gamma EEG bands by statistically analysing reconstructed cortical sources.

11.2 Method

11.2.1 Data

The analysis was based on Studies C and D, as both had exactly the same EEG setup and task. The only difference was that the subjects had task duration of 50 min in Study C, but only 20 min was in Study D. The total number of subjects who had ALs EEG data from the two studies was 27, with 97 events. This number dropped to 16 subjects and 60 events because of missed or corrupted EEG data.

11.2.2 Data acquisition

EEG data were recorded from 64-channel scalp locations using the QuickCap (Compumedics, Neuroscan, Charlotte, NC, USA). The reference electrode was placed between Cz and Pz and the ground electrode was placed close to Fz. Electrodes on the cap were placed according to the 10-20 international standard. Electrode organization for VEOG/EEG recording and electrode placement on the cap is illustrated in Figure 11-1 and Table 11-1. VEOG was recorded by placing bipolar Ag-AgCl sintered electrodes above and below the centre of the left eye, amplifying the signal using Synamps2 amplifiers, and recording the signal using Scan 4.4 software.

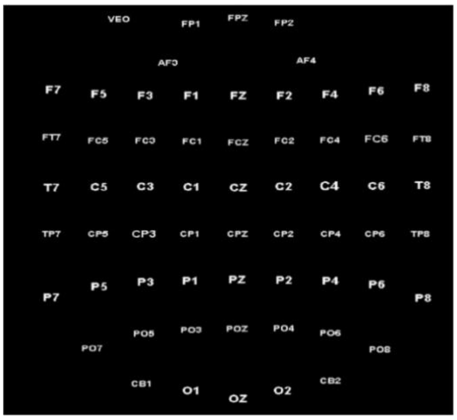


Figure 11-1 Organization of electrodes in the QuickCap used for VEOG/EEG recording with the front at the top of the diagram (from Poudel, 2010).

Table 11-1 Acquisition parameters used for VEOG/EEG recording.

Characteristics	**Quality**
Sampling frequency	10 kHz
Low-pass filter	200 Hz
Notch filter	50 Hz
Impedance	< 20 kΩ

11.2.3 Pre-processing and denoising

This part of the analysis was done using MATLAB v20b in conjunction with the EEGLAB toolbox v2020_0 (Delorme & Makeig, 2004) and multiple plug-ins called through EEGLAB.

As our EEG data were recorded inside an MR scanner, MR-related artefacts were introduced. There were two sources of artefacts specifically associated with simultaneous acquisition with MR: gradient and cardio-ballistic. The fmrib plug-in (Iannetti et al., 2005; Niazy et al., 2005) was used to minimize MR-related artefacts, as illustrated in Figure 11-2.

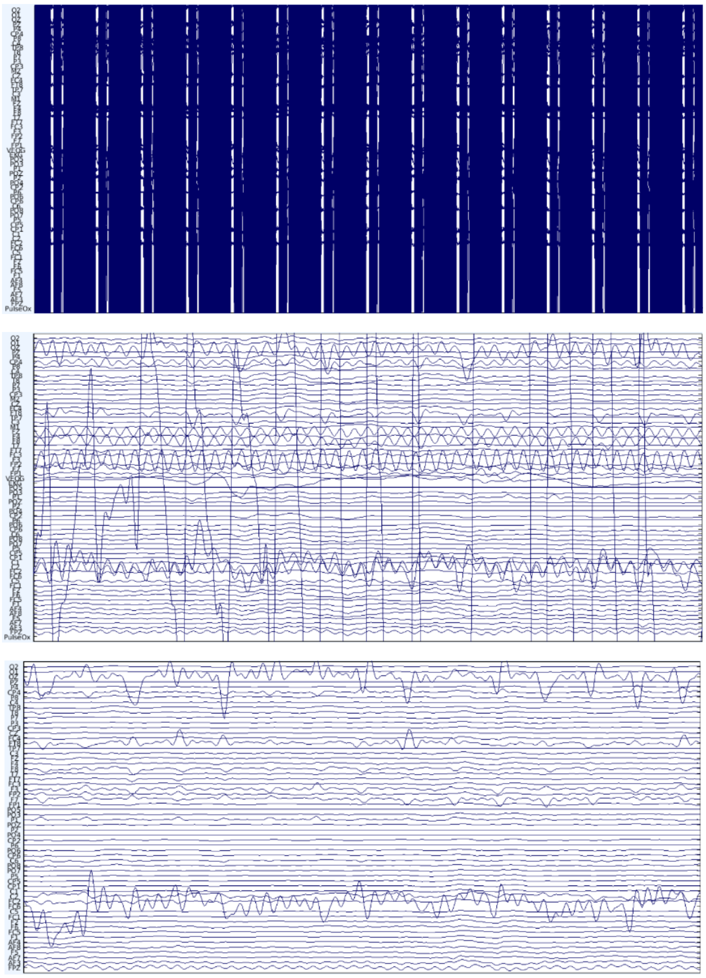


Figure 11-2 Illustration of the process of MR-related artefacts removal: On the top is the raw data with both gradient and cardio-ballistic artefacts. The middle image is the stage after gradient artefacts removal. The bottom image is after pulse artefacts removal.

The data were down-sampled from 10 kHz to 500 Hz to reduce storage space and processing time. The data were re-referenced to the common average. The data were high-pass filtered at 1 Hz to remove the slow drift.

PrepPipeline plug-in (Bigdely-Shamlo et al., 2015) was used to identify bad electrodes and remove line noise. The channels were re-referenced to the average of all electrodes. Through visualizing the spectral maps or by checking the properties of each electrode, we were able to identify which electrodes to remove. Bad electrodes had out-of-EEG voltage range and/or smooth spectra, as shown in Figure 11-3.

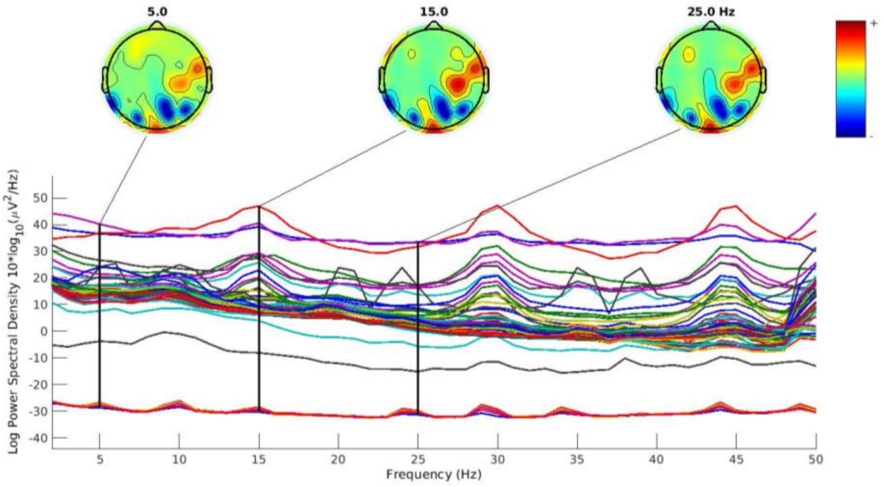


Figure 11-3 Example of frequency spectra of EEG electrodes showing some smooth curves around -27 dB representing bad electrodes.

Due to the number of electrodes interpolated and the location of these electrodes, all subjects from Study D were excluded in the end. The number of electrodes interpolated was ≥ 25% (i.e. ≥ 15 out of 60) or interpolated electrodes were adjacent to each other, as illustrated in Figure 11-4 and Table 11-2. The labelled electrodes were interpolated and, as shown in subject 212, only 13 electrodes, which were spread on the scalp, were interpolated, subject 308 had 18 interpolated electrodes, which were near to each other. After the pre-processing and removal of Study D subjects due to the bad quality, only 10 subjects remained with 38 ALs and an average duration of 1.82 s.

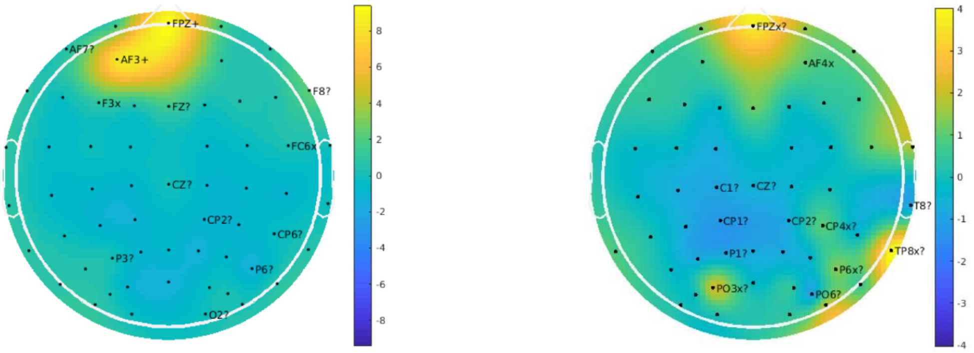


Figure 11-4 Examples of subjects with the same number of interpolated electrodes: subject 212 on the left was accepted, while subject 308 on the right was rejected.

Table 11-2 Electrodes-interpolation report for Studies C and D.

Study	Subject	Number of interpolated electrodes
C	203	10
C	206	5
C	207	8
C	208	6
C	210	3
C	211	4
C	212	13
C	213	3
C	214	2
C	215	4
C	216	6
C	217	2
C	218	8
C	220	5
D	306	13
D	308	18
D	310	19
D	311	14
D	312	13
D	315	10
D	316	16
D	321	17
D	322	16
D	324	18

Through the artefacts subspace reconstruction (ASR) plug-in (Chang et al., 2020) large artefacts were corrected. The ASR cut-off parameter chosen was 25, as suggested in (Chang et al., 2020), the result is illustrated in Figure 11-5.

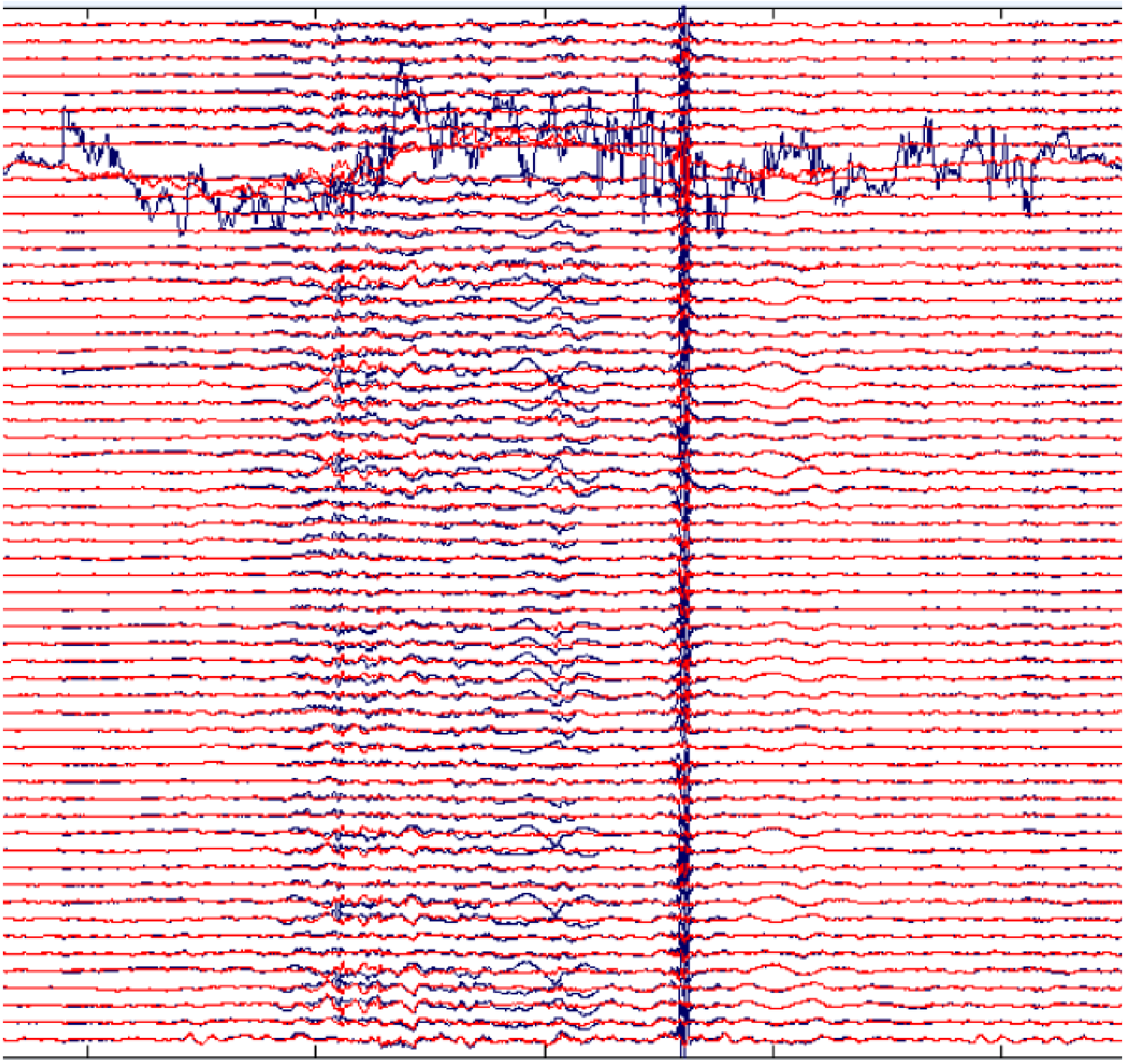


Figure 11-5 Illustration of the performance of artefacts subspace reconstruction (ASR) algorithm. EEG data before ASR correction are in blue and after correction in red.

ICA (Makeig et al., 1996) was applied to decompose the EEG signals into temporally independent time courses corresponding to brain and nonbrain sources using EEGLAB. This step was done to remove noisy components including ocular artefacts (eye blinks), muscle artefacts, cardiac artefacts, in addition to extrinsic artefacts. Wavelet-enhanced ICA (wICA) was used to decompose the EEG signal and remove large artefacts using a threshold (Delorme et al., 2007). Another run of ICA with the ICLABEL plug-in was performed to identify and reject non-EEG components (Pion-Tonachini et al., 2019).

11.2.4 Source reconstruction

The FieldTrip toolbox (v20210418) for EEG/MEG-analysis (FC Donders Centre for Cognitive Neuroimaging, Nijmegen, The Netherlands; see http://fieldtrip.fcdonders.nl/) (Oostenveld et al., 2011) was used for source reconstruction and statistical analysis.

Following pre-processing, subject-based brain modelling was performed by solving the forward model followed by the inverse model.

The structural (T1) image of each subject was used to create an accurate forward model. Each image was initially resliced and segmented into GM, WM, CSF, skull, and scalp. The Simbio plug-in (Vorwerk et al., 2018) was used to create a hexahedral head model using the finite element method (FEM) technique, which is recommended when using the T1 of each subject (Vorwerk et al., 2014; Vorwerk et al., 2012). Electrode positions were manually realigned to the head model based on electrode marks located on the T1 image of each subject, as generated by the MR machine, as illustrated in Figure 11-6.

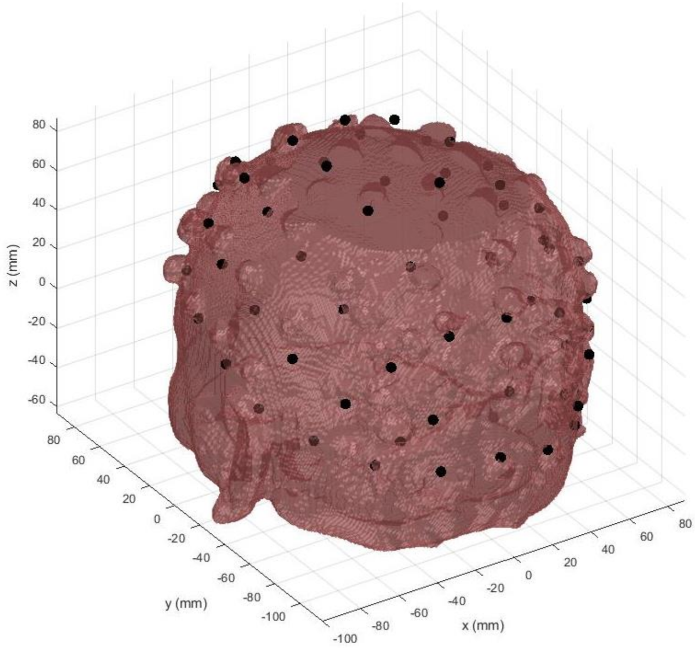


Figure 11-6 Illustration of electrodes alignment to the head volume. The black dots should fit as closely as possible in the marks.

The head model and T1 of each subject were used to create the source model, which was then normalised to a source model template of 5 mm resolution. Only sources within the GM were analysed, as suggested by Pascual-Marqui (2007). The last step was to create the lead field from the head volume, source model, and the aligned electrodes of each subject.

Inverse modelling was done using eLORETA (Pascual-Marqui, 2007, 2009) to estimate the magnitudes of the sources at different frequencies. Finally, averaging was done over trials and over the frequencies of each band for each subject to obtain the value per source representing the average of the frequencies in a specific band for the ALs of each subject. These values were then used for the group statistics.

Two confounding variables were accounted for by removing their effects from the EEG data: (1) tracking-target-speed-related variability, and (2) poor responsive tracking, defined using a threshold calculated based on the tracking error of the first 2 min of the session. The two confounds were resampled to match the number of EEG data points. The events of interest (MSs or ALs) were segmented out of the EEG data. These segments were then combined as trials for each subject and used in the inverse modelling. As the primary interest was in the change of activity for different EEG bands, each trial was divided into event data, MSs with a time window of 2 s starting from the onset, and baseline data, with a window of 2 s before the onset, and ALs, which have a shorter average duration, with a time window of 1 s starting from the onset, and baseline data, with a window of 1 s before the onset. The FFT was used to calculate the activity for each band of interest: delta (2–4 Hz), theta (4–8 Hz), alpha (8–14 Hz), beta (14–30 Hz), and gamma (30–45 Hz).

11.2.5 Statistical analysis

An average event AL and an average baseline for each subject were used, each having the same number of sources with one value for each source. The relative difference between the average events and the average baselines was calculated for each subject to be used in the group stats. Source statistics were applied to compare the percentage relative difference to the null hypothesis of zero. Statistical analyses were performed using permutation tests (Maris & Oostenveld, 2007; Maris et al., 2007), and the results were corrected for multiple comparisons over the 8551 sources using TFCE (Mensen & Khatami, 2013) of p-value < 0.05 (two-tailed). We did not correct for multiple comparisons over the five bands because of the limited statistical power.

11.3 Results

The whole analysis pipeline was successfully validated using artificial data, see Appendix A. After performing the statistical analysis using permutation testing followed by correction for multiple comparisons using TFCE with p-value < 0.05 (two-tailed), no significant change in activity was found, in any band of interest. Our next step was to further explore if there were any changes in activity with a p-value < 0.2 (two-tailed). Trends of increases in the beta and gamma bands only were found. No trends of changes were found in delta, theta, and alpha at p-value < 0.2 (two-tailed).

11.3.1 Marginal changes in beta band during attention lapses

Nonsignificant changes in beta band in ALs are shown in Figure 11-7. The smallest p-value approaching significance was 0.065 (one-tail). The median of the percentage relative change refers to the effect sizes.

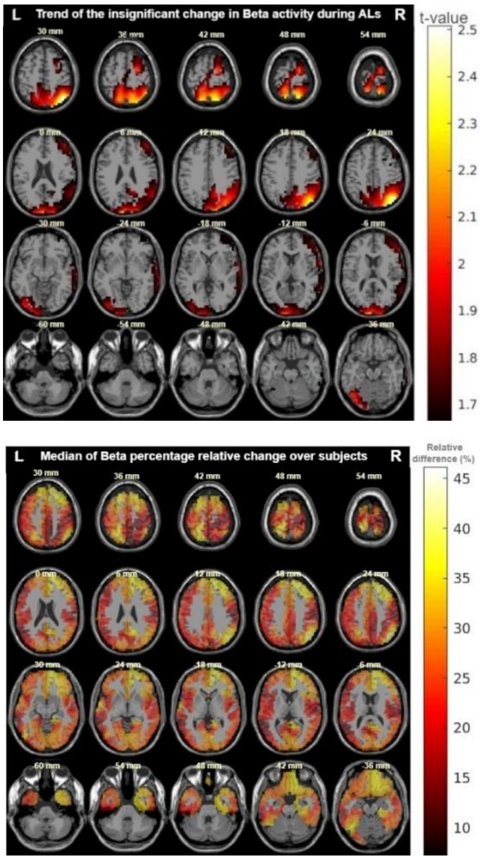


Figure 11-7 Top: group-level trend of change in activity of the relative difference between attention lapses and baseline for the beta band. Bottom: median of the relative change over subjects.

The Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the trends of increased activity. The Harvard-Oxford cortical atlas was used as a reference, see Table 11-3.

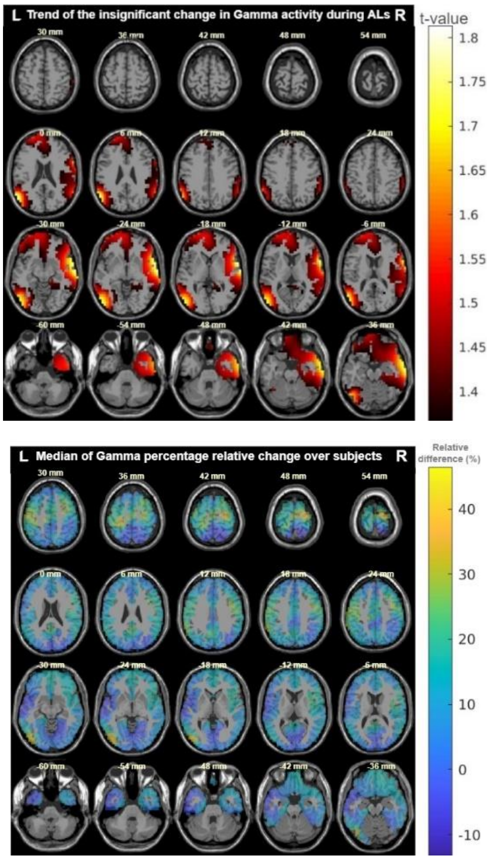
Table 11-3 Major regions of the cluster representing changes in beta in attention lapses.

Cluster	Region	Lobe	Side
1	Lateral Occipital Cortex, superior division	Occipital	LR
	Frontal Pole	Frontal	R
	Precentral Gyrus	Frontal	LR
	Precuneous Cortex	Parietal	LR
	Occipital Pole	Occipital	LR
	Middle Frontal Gyrus	Frontal	LR
	Postcentral Gyrus	Parietal	LR

	Lateral Occipital Cortex, inferior division	Occipital	L
	Superior Frontal Gyrus	Frontal	L
	Superior Parietal Lobule	Parietal	L
	Cingulate Gyrus, posterior division	Parietal	L
	Lingual Gyrus	Occipital	L
	Frontal Medial Cortex	Frontal	L
	Subcallosal Cortex	Frontal	L
	Temporal Pole	Temporal	R

11.3.2 Marginal changes in gamma band during attention lapses

The nonsignificant changes in the gamma band in ALs are shown in Figure 11-8. The smallest p-value approaching significance was 0.085 (one-tail). The median of the percentage relative change refers to the effect sizes.


L Trend of the insignificant change in Gamma activity during ALs R

L Median of Gamma percentage relative change over subjects R

Figure 11-8 Top: a group-level trend of change in activity of the relative difference between attention lapses and baseline for the gamma band. Bottom: the median of the relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the trends of increased activity. The Harvard-Oxford cortical atlas was used as a reference, Table 11-4.

Table 11-4 Major regions of the clusters representing changes in gamma in attention lapses.

Clusters	Region	Lobe	Side
1	Precuneous Cortex	Parietal	R
	Supracalcarine Cortex	Occipital	R
	Cingulate Gyrus, posterior division	Parietal	L
2	Superior Frontal Gyrus	Frontal	R
	Middle Frontal Gyrus	Frontal	R
	Precentral Gyrus	Frontal	R
	Postcentral Gyrus	Parietal	R
3	Middle Temporal Gyrus, temporooccipital part	Temporal	LR
	Inferior Temporal Gyrus, temporooccipital part	Temporal	L
	Supramarginal Gyrus, posterior division	Parietal	L
	Angular Gyrus	Parietal	LR
	Lateral Occipital Cortex, superior division	Occipital	L
	Lateral Occipital Cortex, inferior division	Occipital	L
	Temporal Occipital Fusiform Cortex	Temporal	L
	Occipital Fusiform Gyrus	Occipital	L
4	Frontal Pole	Frontal	LR
	Insular Cortex	Insular	R
	Temporal Pole	Temporal	R
	Middle Temporal Gyrus, posterior division	Temporal	R
	Frontal Medial Cortex	Frontal	L
	Paracingulate Gyrus	Frontal	LR
	Frontal Orbital Cortex	Frontal	LR
	Subcallosal Cortex	Frontal	L
	Cingulate Gyrus, anterior division	Frontal	L
	Superior Temporal Gyrus, posterior division	Temporal	R
	Inferior Temporal Gyrus, posterior division	Temporal	R
	Central Opercular Cortex	Parietal	R

11.4 Discussion

EEG source analysis for ALs versus the baseline of good tracking was performed on the combined studies C and D. The analysis targeted the changes in five EEG bands of interest: delta, theta, alpha, beta, and gamma. Ten subjects had a total of 38 ALs with an average duration of 1.82 s. No significant change was found in any band, however, a nonsignificant increased activity was found in beta and gamma bands.

During ALs correlated with prolonged reaction times, there is a decoupling from external environment which is associated with increased DMN activity (Eichele et al., 2008; Weissman et al., 2006). Increased alpha activity was associated with long reaction times

(Molina et al., 2019). Also, an association has been found between increased DMN activity and increased alpha activity when eyes are opened in a resting state (Mo et al., 2013). In addition, increased alpha activity over task-related brain regions was found to be correlated with weak attention and poor performance (Liu et al., 2014; Macdonald et al., 2011), while reduced alpha activity over task-related brain regions was found to be correlated with more attention directed externally to a demanding task (Rajagovindan & Ding, 2011; Sauseng et al., 2005). So, it was expected to see an increase in alpha activity during ALs in 2-D CVT task.

Research by Andrillon et al. (2019) on ALs and their relation to the local sleep phenomenon, which is different from MS, hypothesised that local sleep could be used as a model to explain ALs through the activity of delta and theta. Andrillon et al. (2021) supported that by finding an association between slow waves, which is associated with local sleep (Andrillon et al., 2019; Bernardi et al., 2015; D'Ambrosio et al., 2019; Hung et al., 2013; Vyazovskiy et al., 2011), and the reports of both mind-wandering and involuntary mind-blanking. So according to Andrillon et al. (2019), if local sleep, defined by an increase in delta and/or theta (slow-wave) activities, occurs within the attentional networks it will cause mind-wandering due to activating DMN instead of the attentional networks, but if it occurs within DMN, it will cause involuntary mind-blanking due to the reduction of endogenous thoughts.

Analysis of changes in EEG activity of ALs did not reach statistical significance in any band to accept our hypotheses. Notwithstanding, in order to explore the null hypotheses for Hypothesis 7 and part of Hypothesis 8, the research done on ALs using EEG will be discussed, then our view given the trends of changes in activity found in gamma and beta EEG bands will be added.

If we consider the trends of increased activity in both beta and gamma to be real, then we should re-hypothesize our previous views. Since we did not have a means to distinguish between mind-wandering and mind-blanking, we built our hypotheses based on the literature which is near entirely mind-wandering.

Beta and gamma activities were found increased during subjectively-reported mind-wandering (Qin et al., 2011), which means that the subjects were aware of their mind-wandering. Increased gamma activity was found to be associated with voluntary allocation of attention (shifting attention) (Landau et al., 2007), and memory processes (recall memories) (Herrmann et al., 2010). However, increased beta activity has been found correlated with intentional clearing of the mind from any thoughts (Castiglione et al., 2019), and has also been found to be inversely correlated with mind-wandering (Groot et al., 2021; van Son et al., 2019a; van Son et al., 2019b), but increased beta could be associated with the attempts to keep performing the task despite the fatigue (Craig et al., 2012; Huang et al., 2007). Given the short duration of ALs, it is more likely that the increase of the high-frequency EEG beta and gamma activities is related to the recovery from ALs, also there is a possibility that these ALs are white dreams, given the association between white dreams and the increased activity over the posterior area of the brain (Fazekas et al., 2019). We could not compare ALs to MSs due to the insufficient number of subjects available that have both ALs and MSs.

11.5 Summary

This chapter started by describing the data used to analyse ALs, then introducing the analysis pipeline in detail starting by pre-processing, source reconstruction, and finally statistical analysis. Two hypotheses (7 and related part of 8) were explored, but there is no strong evidence to support these hypotheses. The non-significant changes found in beta and gamma EEG bands are more likely to be associated with the recovery from ALs, but also could be associated with white dreams.

Chapter 12: EEG Analysis of Microsleeps

12.1 Introduction

In this chapter, EEG data were used to explore Hypothesis 9. The aim was to reveal the neural signature of MSs versus the baseline of good responsive tracking within the delta, theta, alpha, beta, and gamma EEG bands by statistically analysing reconstructed sources.

12.2 Method

The same analysis procedure of ALs was applied to MSs (Section 11.2) was applied to MSs. The only difference was in the duration of the MS event (2 s) and the baseline (2 s) when segmented from the EEG data. The analysis was based on Studies C and D, as both had the same EEG setup and task. The only difference was in the duration of task: 50 min in Study C and 20 min in Study D. The MSs started with 25 subjects from the two studies with 1633 events. This number dropped to 21 with 1392 events before the analysis because of missed or corrupted data. After performing the statistical analysis using permutation testing followed by correction for multiple comparisons using TFCE with p-value < 0.05 (two-tailed).

12.3 Results

After pre-processing and total removal of Study D subjects due to the poor-quality EEG, the number of subjects reduced to 11 with 984 events, and an average duration of 3.53 s. Significant increases in activities in the five bands of interest: delta, theta, alpha, beta, and gamma were found. However, no significant decrease in activity was found in any of the five bands.

12.3.1 Changes in activity in delta band during microsleeps

The significant results in delta band for MSs is shown tomographically in Figure 12-1. The median of the percentage relative change refers to the effect sizes.

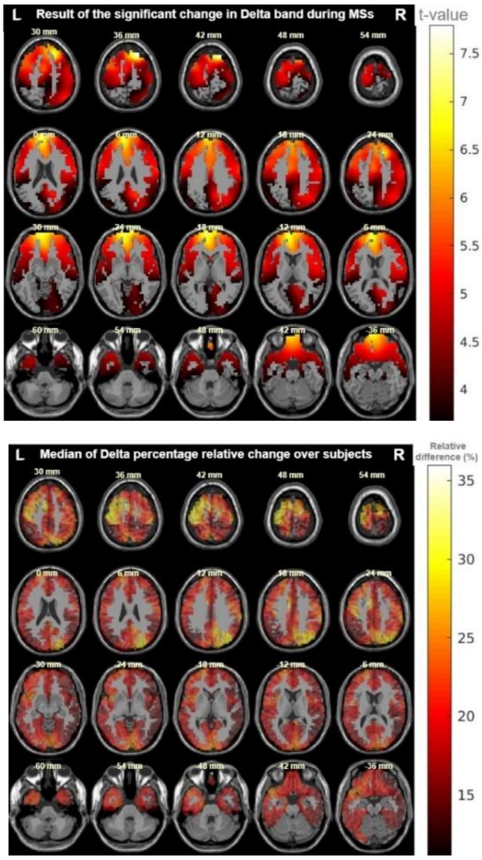


Figure 12-1 Group-level result of the significant activity change of the relative difference between the microsleeps and baseline for the delta band (shown in axial view at the top). On the bottom is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the increased activity. The Harvard-Oxford cortical atlas was used as a reference, see Table 12-1.

Table 12-1 Major regions of the cluster representing the change of delta in microsleeps.

Cluster	Region	Lobe	Side
1	Frontal Pole	Frontal	LR
	Middle Frontal Gyrus	Frontal	LR
	Precentral Gyrus	Frontal	LR
	Postcentral Gyrus	Parietal	LR
	Lateral Occipital Cortex, superior division	Occipital	LR
	Precuneous Cortex	Parietal	LR
	Occipital Pole	Occipital	LR

12.3.2 Changes in activity in theta band during microsleeps

The significant results in theta band for MSs are shown tomographically in Figure 12-2. The median of the percentage relative change refers to the effect sizes.

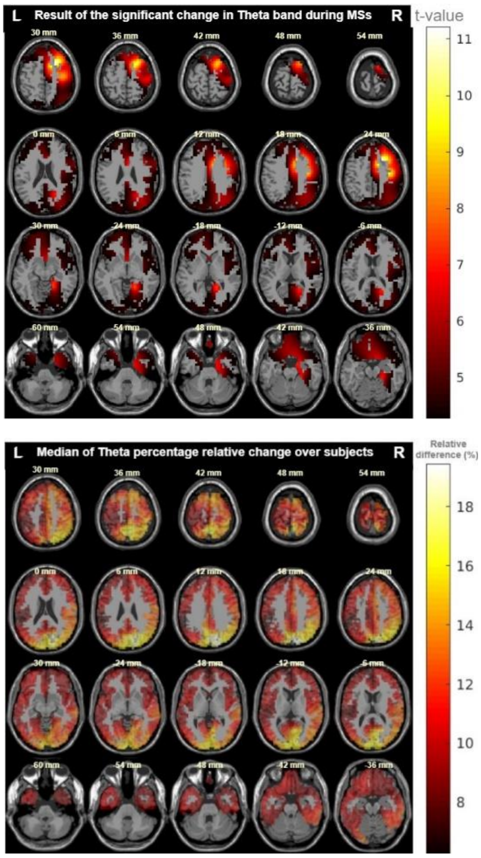


Figure 12-2 Group-level result of the significant activity change of the relative difference between the microsleeps and baseline for the theta band (shown in axial view at the top). On the bottom is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the increased activity. The Harvard-Oxford cortical atlas was used as a reference, see Table 12-2.

Table 12-2 Major regions of the cluster representing the change of theta in microsleeps.

Cluster	Region	Lobe	Side
1	Frontal Pole	Frontal	LR
	Middle Frontal Gyrus	Frontal	LR
	Precentral Gyrus	Frontal	LR
	Temporal Pole	Temporal	L
	Postcentral Gyrus	Parietal	R
	Lateral Occipital Cortex, superior division	Occipital	LR
	Precuneous Cortex	Parietal	LR
	Occipital Pole	Occipital	LR
	Lateral Occipital Cortex, inferior division	Occipital	L

12.3.3 Changes in activity in alpha band during microsleeps

The significant results in alpha band for MSs are shown tomographically in Figure 12-3. The median of the percentage relative change refers to the effect sizes.

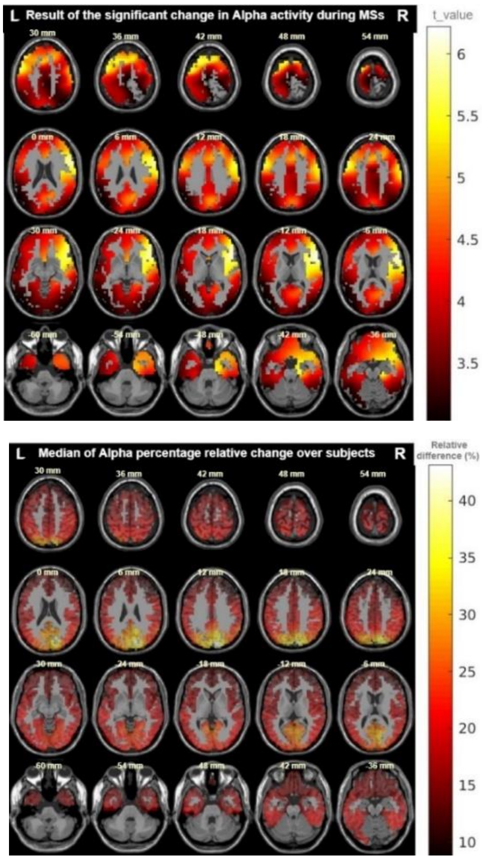


Figure 12-3 Group-level result of the significant activity change of the relative difference between the microsleeps and baseline for the alpha band (shown in axial view at the top). On the right is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the increased activity. The Harvard-Oxford cortical atlas was used as a reference, see Table 12-3.

Table 12-3 Major regions of the cluster representing the change of alpha in microsleeps.

Cluster	Region	Lobe	Side
1	Frontal Pole	Frontal	LR
	Superior Frontal Gyrus	Frontal	LR
	Middle Frontal Gyrus	Frontal	LR
	Precentral Gyrus	Frontal	LR
	Temporal Pole	Temporal	LR
	Postcentral Gyrus	Parietal	LR
	Lateral Occipital Cortex, superior division	Occipital	R
	Precuneous Cortex	Parietal	LR

	Occipital Pole	Occipital	LR

12.3.4 Changes in activity in beta band during microsleeps

The significant results in beta band for MSs are shown tomographically in Figure 12-4. The median of the percentage relative change refers to the effect sizes.

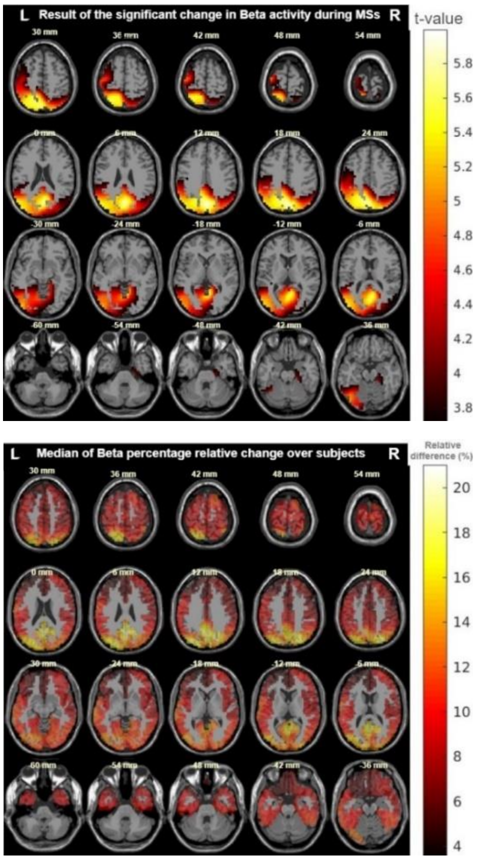


Figure 12-4 Group-level result of the significant activity change of the relative difference between the microsleeps and baseline for the beta band (shown in axial view at the top). On the bottom is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the increased activity. The Harvard-Oxford cortical atlas was used as a reference, see Table 12-4.

Table 12-4 Major regions of the cluster/s representing the change of beta in microsleeps.

Cluster	Region	Lobe	Side
1	Superior Temporal Gyrus, anterior division	Temporal	R
	Superior Temporal Gyrus, posterior division	Temporal	R
	Middle Temporal Gyrus, anterior division	Temporal	R
	Middle Temporal Gyrus, posterior division	Temporal	R
	Planum Temporale	Temporal	R
2	Frontal Pole	Frontal	R

	Juxtapositional Lobule Cortex (formerly Supplementary Motor Cortex)	Frontal	R
3	Superior Frontal Gyrus	Frontal	R
	Middle Frontal Gyrus	Frontal	LR
	Precentral Gyrus	Frontal	LR
	Postcentral Gyrus	Parietal	L
	Superior Parietal Lobule	Parietal	LR
	Angular Gyrus	Parietal	R
	Lateral Occipital Cortex, superior division	Occipital	LR
	Lateral Occipital Cortex, inferior division	Occipital	LR
	Precuneous Cortex	Parietal	LR
	Lingual Gyrus	Occipital	LR
	Occipital Pole	Occipital	LR
	Cingulate Gyrus, posterior division	Parietal	R
	Occipital Fusiform Gyrus	Occipital	R

12.3.5 Changes in activity in gamma band during microsleep

The results for gamma band of MSs are shown tomographically in Figure 12-5. The median of the percentage relative change refers to the effect sizes.

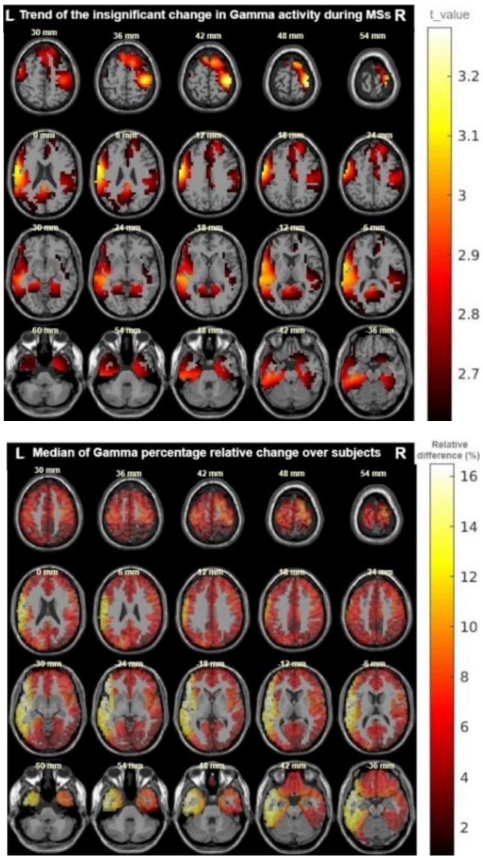


Figure 12-5 Group-level result of the significant activity change of the relative difference between the microsleeps and baseline for the gamma band (shown in axial view at the top). On the bottom is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the increased activity. The Harvard-Oxford cortical atlas was used as a reference, see Table 12-5.

Table 12-5 Major regions of the cluster representing the change of gamma in microsleeps.

Cluster	Region	Lobe	Side
1	Frontal Pole	Frontal	LR
	Middle Frontal Gyrus	Frontal	LR
	Precentral Gyrus	Frontal	LR
	Temporal Pole	Temporal	LR
	Postcentral Gyrus	Parietal	LR
	Lateral Occipital Cortex, superior division	Occipital	LR
	Lateral Occipital Cortex, inferior division	Occipital	L
	Precuneous Cortex	Parietal	LR
	Occipital Pole	Occipital	L

12.4 Global signal removal

Following the source-reconstruction, EEG analysis on the five bands of interest (delta, theta, alpha, beta, and gamma) compared MSs relative to their baselines. We found a significant increase in all bands (i.e., a global increase). To further investigate this, we estimated the magnitude of sources in all of the bands of interest after regressing out the global signal, which was the estimated magnitude of sources after averaging all frequencies of interest (2–45 Hz). This step was done to explore the possibility that the global increase in power might have arisen due to increases in non-EEG biosignals and/or artefacts and not actually due to increased EEG activity during MSs.

Another group-level analysis was performed using permutation testing and TFCE to correct for multiple comparisons at a p-value < 0.05 (two-tailed). We found a significant increase in gamma activity, similar to before removing the global signal. Conversely, there was a trend of decreased activity in alpha band ($p = 0.0328$), which is the opposite to the significant increase in alpha band before removing the global signal. In addition, no change in delta, theta, and beta bands was found after removing the global signal, although the three bands had significant increase in activities before removing the global signal.

12.4.1 Trend of activity changes in alpha band during microsleeps after global signal regression

The trend of change in alpha band activity for MSs after global signal regression are shown tomographically in Figure 12-6. The median of the percentage relative change refers to the effect sizes.

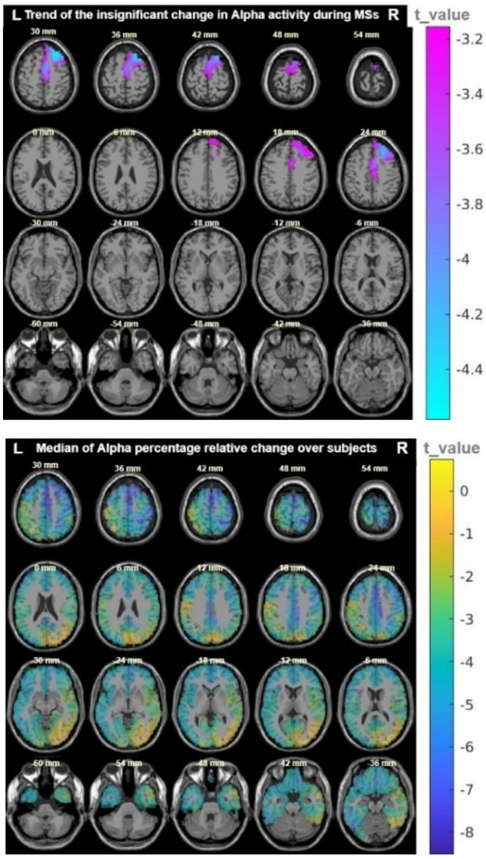


Figure 12-6 Group-level result of the trend of activity change in the relative difference between the microsleeps and baseline for the alpha band (shown in axial view at the top) after global signal regression. On the bottom is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the decreased activity after global signal regression. The Harvard-Oxford cortical atlas was used as a reference – see Table 12-6.

Table 12-6 Major regions of the cluster/s representing the change of alpha in microsleeps after global signal regression.

Cluster	Region	Lobe	Side
1	Frontal Pole	Frontal	LR
	Superior Frontal Gyrus	Frontal	LR
	Middle Frontal Gyrus	Frontal	R
	Precentral Gyrus	Frontal	LR

	Juxtapositional Lobule Cortex (formerly Supplementary Motor Cortex)	Frontal	LR
	Paracingulate Gyrus	Frontal	LR
	Cingulate Gyrus, anterior division	Frontal	LR

12.4.2 Changes in activity in gamma band during microsleep after global signal regression

The results for gamma band of MSs after global signal regression are shown tomographically in Figure 12-7. The median of the percentage relative change refers to the effect sizes.

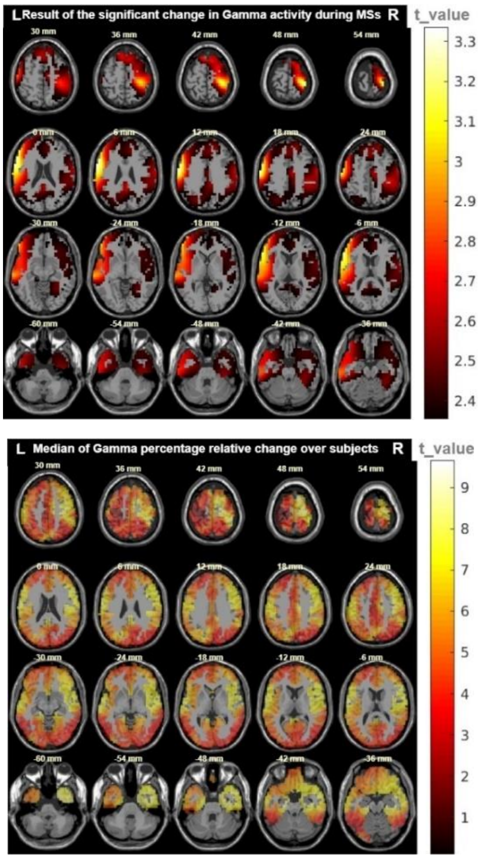


Figure 12-7 Group-level result of the significant activity change of the relative difference between the microsleeps and baseline for the gamma band (shown in axial view at the top) after global signal regression. On the bottom is the median of the percentage relative change over subjects.

Atlasquery toolbox, from FSL (FMRIB's Software Library; www.fmrib.ox.ac.uk/fsl), was used to find the brain regions forming the clusters representing the increased activity after global signal regression. The Harvard-Oxford cortical atlas was used as a reference, see Table 12-7.

Table 12-7 Major regions of the cluster representing the change of gamma in microsleeps after global signal regression.

Cluster	Region	Lobe	Side
1	Frontal Pole	Frontal	LR
	Superior Frontal Gyrus	Frontal	R
	Precentral Gyrus	Frontal	LR
	Frontal Orbital Cortex	Frontal	LR
	Paracingulate Gyrus	Frontal	L
	Middle Frontal Gyrus	Frontal	L
	Middle Temporal Gyrus, posterior division	Temporal	L
	Temporal Pole	Temporal	LR
	Postcentral Gyrus	Parietal	LR
	Precuneous Cortex	Parietal	L
	Angular Gyrus	Parietal	R
	Lateral Occipital Cortex, superior division	Occipital	LR

12.5 Discussion

The EEG source analysis for MSs versus the baseline of good tracking was performed on Study C. The analysis targeted the changes in five EEG bands of interest: delta, theta, alpha, beta, and gamma. Eleven subjects had a total of 984 MSs with an average duration of 3.53 s. In our analysis, significant increases in delta, theta, alpha, beta, gamma bands activities were found. Also, there was no significant decrease in activity in any band.

Given the behavioural difference between MSs and sleep in terms of duration. We expected them to be physiologically different, not in the process of shifting from wakefulness to sleep, but in shifting from sleep to wakefulness. It is expected that, as part of the recovery process from MSs, there will be a positive correlation between MSs and the high-frequency EEG bands (beta and gamma).

Our findings match findings from a 1-D CVT study in which, increased EEG spectral power was seen in delta, theta, and alpha bands during MSs (Peiris et al., 2006). However, they also found no increases in beta and decreased gamma. Given that a 1-D CVT task was used, overlapping flat spots and eye closure then label them as MSs, especially if detecting the onsets and durations of MSs were affected by low resolution, might cause inaccuracy in their findings. By using a 2-D CVT task and a high resolution, we did overcome that.

In another study, in which a 2-D CVT was used, a small correlation between visuomotor performance and theta activity in the posterior region was found with MSs included (Poudel et al., 2010a). However, that correlation dropped when the MSs were removed, indicating that MSs contributed substantially to performance fluctuations and EEG theta activity during an extended task. Our results confirmed this association between MSs and the increase in theta activity.

Finding a correlation between MSs compared to baseline and increase of theta activity confirms finding by Jonmohamadi et al. (2016), who used a 2-D CVT task to explore the EEG containing MSs to detect activity and find the locations of the sources of such activity. They discovered that MSs are often associated with theta activity, which is most likely generated bilaterally from the frontal orbital cortex area. We found a similar pattern, as an increase in theta activity in the frontal lobe. Our alpha-band results match their results of an association between MSs and increase in alpha-band activity in the anterior temporal lobes and hippocampi, which correspond to the spindles of Stage-2 sleep (Jonmohamadi et al., 2016), and has also been found to be associated with sleep-maintaining processes (Pivik & Harman, 1995).

In a flight simulator study for participants (pilots), which was designed to maintain a constant/monotonous work environment, EEG spectral activity represented in delta, theta, alpha, and beta bands were analysed during MS. Delta activity decreased, and alpha activity increased across the scalp, and no change was found in beta or theta (Wang et al., 2020). When compared to our MS results from a 2-D CVT task, which is demanding and fatiguing, our results agreed in alpha but were different in the other bands, as we found an increase in delta, theta, and beta. In a resting state study, a reduction in activity across the scalp for delta, theta, alpha, and beta bands from voluntary eyes-closure to eyes-opening conditions was found, reflecting the cortical processing of visual input (Barry et al., 2007). This agrees with our findings in MSs, even when eyes were involuntarily closed, as we change from eyes-opening to eyes-closure.

Previous analysis of the BOLD fMRI part of our study for MSs (Poudel et al., 2014) showed activation in the frontoparietal and temporo-occipital areas, which overlapped with regions from source-reconstructed increased activities for delta, theta, alpha, and gamma bands for MSs. In the same paper, other tests were undertaken to investigate the correlation between BOLD activity when accounting for theta and alpha activities as regressors using a moving window of 2.5 s. A positive correlation was shown between the post-central theta fluctuations and MSs, while the occipital alpha fluctuations negatively correlated with MSs. Given the superiority of EEG in terms of temporal resolution, we expected EEG to provide a more accurate representation of changes in activity. We compared each band versus the baseline of 2 s before the onset of the event in a time-locked manner, and showed a similar positive correlation between theta activity and MSs at the post-central area, even when theta was represented by a low temporal resolution (2.5 s) regressor, but with the high temporal resolution, we also found a positive association between alpha-band activity and MSs in the occipital region.

Our results, which shows an increase in activity in all bands during MS, have a similar neural pattern to REM. In a study by Simor et al. (2019), EEG was used to investigate REM sleep and its two microstates: tonic and phasic. The tonic period showed an increase in activity in alpha and beta bands over the frontocentral region which represent resting-wakefulness, while the phasic period showed an increase in the low frequency (delta and theta) co-existing with an increase in gamma band activity, which is a combination between deep-sleep (represented in delta and theta) and wake-like activity (represented in gamma).

Earlier research by De Gennaro et al. (2001) investigated the wakefulness-sleep transition and found that alpha-band spreads anteriorly when shifting from wakefulness to sleep. Also, an increase in EEG activity in the range of slow frequencies (< 7 Hz), in the range of delta and theta, after the sleep onset at the centro-frontal scalp locations. These results match our findings as we compared MSs starting from onset to 2 s later versus the 2 s just before the onset as a baseline.

There is an association between alertness (performing higher cognitive functions) and high-frequency (beta and gamma) EEG bands. Beta activity has been associated with the facilitation of cognitive operations (Cannon et al., 2014), and with the process of filtering distraction (Schmidt et al., 2019). Gamma activity has been associated with attention (Rouhinen et al., 2013), memory (Pauling & Coryell, 1936), perception (Melloni et al., 2007), and cortical processing (Fries, 2009; Tallon-Baudry, 2009).

These associations are very important. As to end a MS state, reconnecting with the external environment will be a priority to the brain, which will require gaining perception to the surroundings, in addition to the attention-memory synchronization. This will need the brain to facilitate these cognitive operations, in order to process any upcoming external input through the cortical regions while filtering any distraction out. Hence, finding an increase in the high-frequency (beta and gamma) EEG bands during MSs might indicate a recovery process from MS, which is supported by finding increased BOLD activity by Poudel et al. (2014) after analysing the simultaneous fMRI using the same data.

This interpretation of results is based on the assumption that the significant increased activities in all bands found were due to MSs. However, that does not completely exclude the possibility that some residual artefacts, due to electromyographic contamination for example (Bullock et al., 2021; Daniel et al., 2018; Jansen et al., 2012; Jorge et al., 2015; Muthukumaraswamy, 2013; Spencer et al., 2018), might have prevented an accurate detection of the underlying neuronal signal. As the result found was a global increase in activity, we further investigated this by removing the global signal effect. We found a significant increase in only gamma band but no changes in delta, theta, and beta bands, plus a trend of reduced alpha activity.

There was a limitation for us to account for potential motion-related artefacts (abrupt head movements) due to not collecting the measures needed to account for motion-related noise, which is a necessary step for the optimal design of the analysis pipeline, as not all motion-related artefacts are automatically removed with standard steps (Bullock et al., 2021; Daniel et al., 2018; Jorge et al., 2015; Muthukumaraswamy, 2013; Spencer et al., 2018).

That leads us to one of two possibilities: (1) Subjects were already in a sleeping position in the MRI scanner, and were struggling to stay awake prior to a MS (Poudel et al., 2014), making it likely that the transition to a MS was smooth with a no/minimal movement of the head, and the global increase in EEG over the cortical areas was real and matches the global increase in the cortical areas using fMRI (Poudel et al., 2014); (2) There were unaccounted-for motion-related artefacts, which caused increased global increased power in the EEG signals, and by removing that effect we ended with the true underlying EEG signals.

If the first possibility was true, then MSs in a 2-D CVT task are more likely to be highly associated with increased activity in low-frequency bands (Jonmohamadi et al., 2016; Peiris et al., 2006; Poudel et al., 2010a; Poudel et al., 2014; Wang et al., 2020). Also, MSs and Stage-2 sleep are more likely to be similar in alpha EEG activity. In addition, MSs are different from normal sleep behaviourally in terms of duration, and physiologically in terms with the correlation with high-frequency (beta and gamma) EEG bands. This gives evidence to support acceptance of Hypothesis 9 that MSs are different from sleep physiologically.

On the other hand, if the second possibility is true, then MSs in a 2-D CVT task are more likely to be highly associated with decreased activity in alpha band and increased gamma activity. The increased gamma activity has been associated with multiple higher cognitive function which will aid the process of breaking a MS state such as: attention (Rouhinen et al., 2013), memory (Pauling & Coryell, 1936), perception (Melloni et al., 2007), and cortical processing (Fries, 2009; Tallon-Baudry, 2009). Similarly, decreased alpha activity in the fronto-central regions has been associated with the awakening process from a recovery sleep, which is associated with high cognitive impairment (Balkin & Badia, 1988; Ferrara et al., 1999; Ferrara et al., 2000; Tassi et al., 2006), following extended sleep-deprivation when compared to normal sleep (Gorgoni et al., 2015). If we consider that a MS is a sort of a ‘recovery’ sleep, then the increased gamma and decreased alpha indicates a trial from the brain to break the MS state and recover from it.

12.6 Summary

This chapter started by describing the data used to analyse MSs, the same analysis procedures used with ALs was used with MSs. One hypothesis (H9) was explored in this chapter. Based on the findings, we cannot fully accept it due to being unable to unequivocally eliminate the possibility of the increased global power being due to motion-related noise, although the need to account for this noise is still questionable (Bullock et al., 2021). In the Discussion (Sec. 12.5), we compared our findings, before removing the global-signal effect, with the literature which agreed in the correlation between MSs and the increase in delta, theta, and alpha EEG activities, which are associated with sleep/MS. However, finding an increase in beta and gamma bands activity during MSs is a major finding. This could indicate that MSs is different from sleep both behaviourally and physiologically, but does not confirm the physiological part.

Chapter 13: General Discussion

13.1 Summary of analyses

In this project, we analyzed ALs and MSs physiologically using EEG and fMRI data from two studies (C and D). Participants performed the same task 2-D CVT but with different durations (50 min and 20 min, respectively). Voxel-wise analysis, group ICA analysis, HR analysis, and FC analysis for ALs using fMRI were performed. In addition, we used EEG to perform source reconstruction analysis for both ALs and MSs and explored their neural signatures over five EEG bands (delta, theta, alpha, beta, and gamma). After statistical analysis using permutations testing, we corrected for multiple comparisons at a p-value < 0.05 for fMRI (except for HR analysis a threshold of p-value < 0.01 was used without correction for multiple comparisons) and EEG, and reported the significant results. For analyses that were not significant, we reported trends of changes in activity at higher p-values.

13.2 Summary of all results

13.2.1 Attention lapses

For the voxel-wise analysis, we compared BOLD activities during ALs to a baseline of good responsiveness tracking (where subjects were performing the task at a high level based on a threshold). Increased activity was seen in the SMA and dorsal ACC bilaterally. This was matched by seeing increased BOLD activity in the HR analysis of the cluster that came out significant from the voxel-wise analysis.

In addition, HR analysis showed trends of dynamic changes in BOLD time-series at ROIs from DMN, DAN, SN, and FPN. There was an increase of HR 15 s prior to the onset in the left IPL of DMN. The left IPS in the DAN had an increased HR 7.5 s. The dorsal ACC (part of SN) showed increased HR activity at 5 s and 7.5 s. There was a trend of decrease in HR activity around the -2.5-s timepoint in the right PPC of FPN. Group ICA analysis failed to find any significant results. However, a trend of increased activity was found in an IC that is spatially correlated with SMN from CONN.

ROI-to-ROI FC analysis was performed in brain networks of interest, that are associated with ALs and sustained attention (DMN, DAN, FPN, VSN, SMN, EMN, WMN, and SN) to explore the changes in FC during ALs. We checked FC within and between networks. Significant results were shown in ring displays. We found an increased FC between DMN and FPN, while no change in FC between FPN and DAN. Also, increased FC between DMN and EMN, while FC between DAN and EMN showed both increases and decreases. In addition, FC between FPN and VSN increased, while FC between FPN and SMN decreased. Finally, FC between DMN and WMN has decreased.

We also compared ALs to MSs using voxel-wise, group ICA, and FC analyses but found no trend of differences in changes in activity. We could not do that using EEG because of the insufficient number of subjects who have both ALs and MSs. This should be investigated further as it raises the possibility that the ALs might be MSs with eyes open.

EEG analysis was performed for subjects from Study C only, as the subjects from Study D did not pass the pre-processing stage. We analyzed the reconstructed sources during ALs for the five EEG bands of interest (delta, theta, alpha, beta, and gamma), but found no significant results in the relative difference between the ALs and the baseline at any band. But there were non-significant changes of increased activity in the beta band over regions in the frontal, parietal, and occipital lobes. Other non-significant changes of increased activity were found in the gamma band in regions in the frontal, parietal, temporal, insular, and occipital lobes.

13.2.2 Microsleeps

In the analysis of MSs using EEG, significant results were found of increased activity in the relative difference between the MSs and baselines of good responsive tracking in five EEG bands (delta, theta, alpha, beta, gamma). Delta band during MSs showed increased activity over bilateral regions in frontal, parietal, and occipital lobes. For theta band, we found an increased activity over bilateral regions in frontal and occipital lobes. Alpha band increased activity was located over bilateral regions that are part of frontal and parietal lobes. Finally, for the beta band, regions of increased activity were located in the occipital lobe. For the increased activity of gamma, the regions were located at the frontal, parietal, and occipital lobes bilaterally.

Following this global increase in power in all EEG bands, further analysis was performed to examine the removal of the global signal effect. We found the same significant increase in gamma band, a trend of decrease in alpha band ($p = ??$, two-tailed), and no change in delta, theta, and beta bands.

13.3 Physiological analysis – Best practice

In our analysis, we gave a reason for each analysis step in order to commit to the best practice guidelines made by the Committee on Best Practices in Data Analysis and Sharing

(COBIDAS) for the open science in neuroimaging (Pernet et al., 2018; Pernet & Poline, 2015). These guidelines were made to achieve transparency and credibility between researchers by publicly sharing the research methodology with full details, the raw data that was used in the research, and a full explanation of how the results were interpreted (Gilmore et al., 2017; Nichols et al., 2017).

This is important, as in Poldrack et al. (2008), the analysis packages that are widely used by researchers produce results that can be misinterpreted and have advanced features that can be misused. It is also important to mention that some researchers, because of freedom of analysis, tend to play with the analysis parameters until they get results that meet their hypotheses (Gorgolewski & Poldrack, 2016). According to Carp (2012), who tested enormous multiple analysis pipelines on the same data to test the flexibility of the analysis parameters on the final result, some of the pipelines led to substantially different results from other pipelines, which again proves the point.

13.4 Visuomotor task

The task used in this project was a 2-D CVT task, in which the subjects went for 50 min of tracking in Study C and 20 min in Study D. Participants were asked to use a finger-based joystick to continuously follow a disk moving on a computer screen, so it is a relatively demanding task because the subjects have to continuously pay attention and react to the task, and the fact that they did not know when the task would be over. A similar approach was used in a continuous performance study by Petilli et al. (2018). They asked their participants to finger tap with a sustained pace, which was proven to be effective in measuring the sustained attention. However, according to Roebuck et al. (2016), errors in continuous-performance tasks cannot necessarily be interpreted in terms of reduced vigilance or fluctuations of attention (Mackworth, 1948; Montes et al., 2016), as the errors can also be related to changes in characteristics (e.g., speed) of the target.

AL events were defined as complete stops in performing a task with eyes open. So, ALs were complete losses of attention for an average of ~ 2 s. It was not possible to definitively label the behavioural gold-standard ALs as mind-wandering or mind-blanking, as there is currently no means of determining this objectively or subjectively (e.g., some form of subjective reporting technique) without interrupting the task. On the other hand, with no interference of the continuity of the task (e.g., by subjective reporting which was not used), it was possible to identify the onset and duration of the ALs. Identifying MSs behaviourally is relatively easier than ALs, as MSs include eye closure.

13.5 Views on lapses of responsiveness

13.5.1 Attention lapses

ALs are a mysterious phenomenon and are difficult to describe. There are multiple theories aimed at understanding the reality behind them and, they are highly dependent on several factors related to the task being performed. These include type of task such as discrete or continuous, time-on-task (Derosière et al., 2015), task complexity (Larue et al., 2015; Seli et al., 2018b), age (López-Ramón et al., 2011), and environmental factors (Burdett et al., 2016).

The two major theories of ALs both refer to task monotony and task demands (Head & Helton, 2014; Helton & Russell, 2011, 2012; Thomson et al., 2015a). If the task is not challenging, the subject will tend to divert their attention completely to TUTs or at least divide attention between the task and TUTs. This means the mind will more likely start to wander (Burdett et al., 2019; Schad et al., 2012; Unsworth & Robison, 2016b), which might happen “involuntary” too (Seli et al., 2016b; Smallwood & Schooler, 2006). This should be taken into consideration when studying mind-wandering (Seli et al., 2016a). However, dividing attention might be exhaustive as it calls different brain networks to be activated at the same time such as FPN, DAN, and SN (Santangelo, 2018), also the interaction between DMN, FPN, DAN, and SN is associated with being able to perform a dual-task including both internal and external attention (Maillet et al., 2019). In addition, the interaction between DMN, FPN, and VSN is associated with mind-wandering (Godwin et al., 2017; He et al., 2021; Zhou & Lei, 2018).

The other explanation is that the task is demanding. This can drain one’s ability to focus and exhaust cognitive processing resources (Head & Helton, 2014; Helton & Russell, 2011, 2012), although this changes from subject to subject (Unsworth et al., 2010). The demanding task increases the chance of ALs (Buckley et al., 2016). The DMN, which is known to be associated with mind-wandering (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007), has been found to be active in both scenarios, i.e., when the task is monotonous (Danckert & Merrifield, 2018), and when the task is demanding (Fortenbaugh et al., 2018).

In support of the resource theory, which represents the demanding task, Helton and Russell (2012) used a visual vigilance task to examine the effect of mental breaks if added to recharge the cognitive energy dropped according to the resource theory. They made a change to the vigilance task by adding a brief task switch (content-free cues) to reduce the drops in alertness by changing the task goal momentary through deactivation and reactivation of the task and compared between two groups, one with the changed task and the other without. However, there was no difference between the two groups, which they considered indicates that the drop in performance in a demanding task is associated with resource depletion and not conscious disengagement due to boredom.

Also, if the performing well in the task does not offer a "reward", it more likely that the subject's desire to invest effort in the task will drop, could be from the start, but definitely closer to the end. This means the task loses attentional resources "effort" for TUTs (mind-wandering), which will increase if the task was monotonous (Kurzban et al., 2013).

Although our 2-D CVT task is demanding, as it requires continuous performance without any break, it is also monotonous as (1) the pattern repeats every 30 s, the subject gets used to it, and (2) no reward was offered for good performance. Most importantly, the average duration of the ALs in the task is relatively small to contain mind-wandering, however, it does not exclude the effect of mind-wandering that might lead to a complete drop in performance later. Since we do not know the type of AL, our theory to explain the ALs we have will be a combination of the two main theories following (Thomson et al., 2015a).

Thirteen of 15 subjects in Study C and 8 of 11 subjects in Study D had their first AL ~5 min after starting the task. Five minutes are long enough for most people to get used to the task. So, based on that we could combine the two theories under the following scenario: the subject got used to the demanding task so started to divert their attention to TUTs (Krimsky et al., 2017). According to Jonides et al. (2007), exceeding the processing capacity of the brain's STM results in failure to process, especially if the task is not a priority given the limits of WMC (Myers et al., 2017) as no motivational factor was introduced. This results an AL due to a combination of resource depletion (Helton & Warm, 2008) and memory failure (Adam & Vogel, 2017; deBettencourt et al., 2019).

WMC has been shown to be an important factor when it comes to mind-wandering. Those who have a high WMC have more ability to accommodate other thoughts, so they will not report them as ALs like those who have a low WMC (Unsworth & Robison, 2016a), as they are able to limit both “voluntary” and “involuntary” mind-wandering events (Soemer & Schiefele, 2020). In a study by Domkin et al. (2013), participants performed a tracking task with a hand-held task screen pen. They found that eye-hand coordination fails in subjects with low WMC compared to those with a high WMC when distractors are shown. WMC was also considered when studying how working memory supports “situation awareness” in drivers on the road (Johannsdottir & Herdman, 2010), as the task of driving can be disturbed by other vehicles.

A link can be drawn between attention and memory, as, based on LaBar et al. (1999), both spatial attention and working memory intersect in the neural networks sub-serving each other, mainly in the frontoparietal regions. Also, they might share the same attentional resources. Recent research has even shown that memory and attention actually lapse together (deBettencourt et al., 2019). The relationship between working memory and attention is important, as working memory processes (such as maintenance) reflect sustained attention, in which working memory serves as a space where attention can keep relevant information to be used in a task (Chun, 2011). Zokaei et al. (2014) considered that the resources needed to perform a demanding task and also maintain information in visual working memory are common.

Failure in STM processing, according to Moraitou and Efklides (2009) and Efklides and Touroutoglou (2010), is associated with mind-blanking, in which there is nothing in mind while being behaviorally awake (Ward & Wegner, 2013). However, that mind-blanking might simply be a temporary loss of control (Di Lollo et al., 2005), so cautions should be there when describing that mental state. Thomson et al. (2015b) studied the relation between mind-wandering and mind-blanking through a rapid serial visual presentation task. They found that the higher the tendency to mind-wander, the smaller the duration of ‘attentional blink’.

In the process of coming out of a lapse certain brain regions are activated, and certain brain networks connected. Being in a lapse with no interaction with the external world is more likely to make the brain at rest. Based on Treserras et al. (2009), there is no FC between DMN and SMN during rest. The SN is the network responsible for switching between DMN and task-related networks (Goulden et al., 2014; Menon & Uddin, 2010). The increased activity of dorsal ACC, which is part of SN, was found to be associated with momentary ALs (Weissman et al., 2006). Also, Weissman et al. (2005) found an association between dorsal ACC and the process of focusing attention on relevant stimuli as opposed to distractions. During the transition to attention, Li et al. (2021) found a “transient” increase in activity in SN regions including ACC and SMA. Wen et al. (2018) linked the ACC to working memory, by showing that ACC is constantly active during all the phases of working memory. Activation in ventral ACC has also been associated with voluntarily mind-blanking events (Kawagoe et al., 2019). This shows that ACC is a key player in ALs (mind-blanks) and the process of transitioning back to sustained attention.

We were unable to definitively classify the type of ALs occurring in our 2-D CVT task by thought probe or any other behavioural means. However, given our results, we can strongly speculate on the type of ALs we observed. During the ALs, subjects completely lost visuomotor responsiveness. This was seen physiologically via disengagement from the external task, as evident by our findings of a decrease in FC between FPN and SMN, a decrease in FC between DAN and EMN, and a decrease in FC between DMN and WMN. However, no decrease in DAN activity was found through the voxel-wise analysis. Also, no decrease in FC between FPN and DAN was found, this is against what we expected to happen due to decoupling.

Because of the short average duration of ALs in our task. We think that the subjects were mind-wandering while performing the task due to the task being repetitive, and we expect mind-wandering to happen before the ALs, although we have no evidence of such. If true, mind-wandering will consume the attentional resources and conquer part of WMC. Although increased FC within DMN, between FPN and DMN, and between DMN and EMN during ALs were found during ALs. It is not confirming evidence of mind-wandering regardless of their association with mind-wandering (Godwin et al., 2017; He et al., 2021; Kucyi et al., 2017; Smallwood et al., 2012). The main reason of that speculation is the short average duration of ALs in our task.

Instead, this is an indication of internal thoughts that could be task-related as a preparation for getting-out-of-lapses processes. In addition, the non-significant increase in beta and gamma EEG activities can be hypothesized to be associated with getting-out-of-lapses processes, although being associated with mind-wandering (Qin et al., 2011). This is because beta is associated with attempts to keep performing the task (Craig et al., 2012; Huang et al., 2007), and gamma is associated with allocation of attention and memory processes (Herrmann et al., 2010; Landau et al., 2007). Also, these ALs could be associated with “white dreams" given the association between white dreams and high-frequency EEG activities at the posterior part of the brain (Fazekas et al., 2019), which is what was found, although not significant.

There was no significant increase in DMN activity during the ALs, which provides the most critical support to speculate that the ALs not being due to either mind-wandering (Andrews-Hanna, 2012; Andrews-Hanna et al., 2010; Mason et al., 2007) or voluntary mind-blanks (Kawagoe et al., 2019). However, through HR analysis, we found a brief but significant increase in DMN activity ~12–15 s prior to the onset of AL, but we cannot confirm that this increase is related to mind-wandering prior to ALs. Also, opposite to the neural signature of voluntary mind-blanks (Kawagoe et al., 2019), we found increased activity in SMA bilaterally due to ALs (involuntary mind-blanks).

Given the short average duration of ALs (mean 1.7 s) compared to the TR (2.5 s) of the fMRI, we speculate that our findings on within-the-lapse processes are overlapped with getting-out-of-the-lapse processes. Our findings from voxel-wise analysis of increased activity in dorsal ACC and SMA are associated with breaking the lapse state and reconnecting to the task. This is supported by the increased FC between FPN and VSN, and between SN and DAN, while no change in FC was found between SN and DMN. It is also supported by increases in HR in DAN.

Further support to speculate that the ALs in our 2-D CVT task being involuntary mind-blanks is a drop in HR just prior to AL in FPN which was shown to be associated with visuospatial attention (Lückmann et al., 2014; Marek & Dosenbach, 2018; Scolari et al., 2015), and working memory (Borst & Anderson, 2013). We consider that coordination between attention and memory was affected by resource depletion due to the attempt to perform the task while engaging in extended TUTs, which led to involuntary mind-blanks. The speculation that mind-blanks were indeed involuntary is supported by HR analysis in which there was no significant change in the ventral ACC, as opposed to that reported for voluntary 'blank in mind' (Kawagoe et al., 2019).

However, we cannot completely exclude ALs being due to mind-wandering, as maybe the complete drop in performance in ALs is a last phase of a deep mind-wandering state. It could also be an internal thought without having any experience of the content upon awakening "white dream" while having eyes open. This could make sense if we considered the increase in FC between FPN and DMN, and the increase in FC within DMN were working on generating thoughts, but due to the decrease in FC between WMN and DMN, in addition to the lack of increased DMN activity, these thoughts could not be handled.

Finally, it is very important to realize that mind-blanking is a complex phenomenon. Still far from being fully understood, and the research is trying to explain it through various experiments. In probe-based studies, mind-blanks are reported based on how the subject has experienced them, so they could be due to meta-cognitive failure (Ward & Wegner, 2013), or something else, and mistakenly reported as mind-blanks. Since there is no universally-accepted means of identifying mind-blanks, we cannot assume that a certain definition is more accurate than the others. Hence, we cannot exclude other definitions without specifically testing them, and even then, it would not be scientific to confirm one finding over another, because the analysis is based on statistics and mind-blanks are very subjective. In our studies, our gold standard for ALs was behavioural, by observing visuomotor performance and eye-video recordings, rather than by simply asking subjects whether *thought* they had a mind-blank, or mind-wandering, or something else.

13.5.2 Microsleeps

Behaviourally, identification of MSs is relatively straightforward (at least compared with ALs), as they can be characterized by loss of responsiveness to external stimuli, prolonged eye-closure (relative to blinks), and, albeit not necessarily, head nodding (Davidson et al., 2005). The important feature of our 2-D CVT task (Poudel et al., 2008) is that the target is always moving, has a defined minimum speed, and has no flat spots. Through this, it is possible to precisely determine the onset and duration of MSs, within the arbitrary duration of a MS of ≲15 s (Jones et al., 2010).

Many factors should be considered when looking at MSs. Fatigue is one of these important factors. In our task that requires continuous visual sustained attention, and goes for a relatively long period (50 min or 20 min), it is more likely to be affected by mental fatigue as the performance will be impaired over time due to the drop in the attentional resources available which in turn will reduce the processing of information and decision making (Guo et al., 2016). Although it is highly dependent on individual differences (Tran et al., 2020), theta activity has also been shown to be an important sign of the effect of mental fatigue on the cognitive processing and control capacities (Wascher et al., 2014), as the rate of mental fatigue is highly affected by task characteristics (Gartenberg et al., 2018).

Drowsiness (sleepiness) is another important factor. Drowsiness on its own has been shown to enhance distraction while performing a monotonous task (Anderson & Horne, 2006). According to Slater (2008), drowsiness can be defined as "a progressive loss of cortical network processing efficiency, requiring the recruitment of greater amounts of cortical tissue to perform the same task". This means that being drowsy requires more attentional resources to perform a task. This is supported by Canales-Johnson et al. (2020), who suggested that when drowsy, the cognitive system will apply a neural compensatory mechanism. Alpha activity decreases with sleepiness when eyes are closed (Putilov & Donskaya, 2014). This relationship was previously found by Strijkstra et al. (2003) in addition to a correlation between sleepiness and increase in theta activity. According to Anderson et al. (2010), MSs were highly affected by sleepiness in a 30-min PVT session.

There are two primary alternating states of the human brain: wakefulness and sleep. However, these two states are not mutually exclusive. This means there is no state of full wakefulness when awake, or complete deep sleep during the sleep period, as each state comprises different stages/grades (Guo et al., 2016; Kleitman, 1963; Lindsley, 1952; Saper et al., 2005). There are also momentary events which can change the nature of the brain state for a relatively short time (Albert et al., 2018; Buckley et al., 2016; Guo et al., 2016; Neigel et al., 2019a; Roebuck et al., 2016; Seli et al., 2017; Thomson et al., 2015b; Unsworth & Robison, 2016a). The occurrence of these sudden breakdowns in responsiveness, called 'lapses', is correlated with many factors, including human abilities and traits, and type and duration of task.

Changes in state from wake to sleep or vice versa do not happen instantaneously, but with a transition (Fuller et al., 2006; Gallopin et al., 2005; Hara & Sakurai, 2011; Saper et al., 2010; Song & Tagliazucchi, 2020). Within this transition the brain is either gaining vigilance when trying to be fully awake after sleep but struggling, or when you are affected by drowsiness after your brain is exhausted as it needs some rest while being awake for a long time or while doing an activity that is mentally fatigues (Canales-Johnson et al., 2020; D'Ambrosio et al., 2019; Tsai et al., 2014). MSs ($\lesssim$15 s) can be an unstable stage before falling into a light sleep (Andrillon et al., 2019; Hertig-Godeschalk et al., 2020) or as a brief sleep for the brain to refresh and re-organize, similar to that of the normal sleep process (Tsai et al., 2014). Although MSs are not always followed by sleep, they can be interpreted as an indicator of sleep (Harrison & Horne, 1996).

As the 2-D CVT task is prolonged, continuous, has a repetitive target, and requires a subject to keep following the target, and there is no motivational factor (reward/punishment) for doing the task, and as they are lied in a sleeping position, it is expected that at least many subjects would become drowsy and their ability to stay awake would become impaired with time. It is also likely that will cause drops in performance a few seconds before MSs. As a result of the state of drowsiness – i.e., stage I of NREM sleep (Niedermeyer, 1999b) – it will often progress into a state of deep drowsiness (Niedermeyer, 1999a) on its way to the transition to light sleep (stage II). MSs will often occur in this transition stage.

MSs in demanding tasks like the 2-D CVT task are correlated with increase in activity of delta, theta, and alpha EEG bands (Jonmohamadi et al., 2016; Peiris et al., 2006; Poudel et al., 2010a). According to De Gennaro et al. (2001), who looked at the neural signature of the transition regions between wakefulness and sleep using EEG, he found that at the start of the transition there is an increase of activity in delta and theta bands, and as the transition progresses, alpha band activity increases as well. Niedermeyer (1999b) referred to stage I of sleep by dominance of theta band activity once falling asleep, which could be easily alerted. Picchioni et al. (2008) compared the early part of stage I sleep to wakefulness and found increased activity in medial frontal gyrus and precuneus of DMN. Similarly, Poudel et al. (2014) found that in the non-sleep-deprived wake state there is a correlation between MSs and increased activity in medial frontal gyrus and precuneus of DMN. This agrees with our finding of increased delta, theta, and alpha EEG activity in medial frontal gyrus and precuneus of DMN during MSs in our 2-D CVT task.

However, we found an increased activity in the high-frequency EEG bands (beta and gamma). Beta and gamma are known to be associated with higher cognitive functions such as attention (Rouhinen et al., 2013), perception (Melloni et al., 2007), filtering distraction (Schmidt et al., 2019), memory processes (Pauling & Coryell, 1936), and cortical processing (Cannon et al., 2014; Fries, 2009; Tallon-Baudry, 2009). This highlights the possibility that increased beta and gamma activities are assisting the brain to recover from MSs, which agrees with the finding of increased BOLD activity by Poudel et al. (2014) using the same data.

There was, however, a limitation when analysing the MSs data. Although the standard pre-processing pipeline was applied to remove the noise caused by simultaneous recording of EEG-fMRI, we cannot assume that there were no motion-related artefacts or, if there were, that they were completely removed. Since we did not collect measures of the head motion inside the scanner to make sure that the subjects did not move when transitioning from wakefulness to sleep and vice-versa, we cannot simply assume that there was no movement.

However, by looking at the setup, the subjects were already in a comfortable sleeping position with their heads maintained within foam padding. Unremoved motion artefacts can be noticed in EEG data acquired inside an MRI scanner as a result of the induced current at electrodes when they are moving within a magnetic field, as explained by Faraday's law (Yan et al., 2009). We found an increase in power in all five bands, which leaves largely unresolved the important question: Were these findings caused by unremoved motion-artefacts?

To investigate this question, we re-performed the analysis of MS after regressing out the global signal effect. We found a difference in the previous results, as all the significant changes in delta, theta, and beta bands disappeared. Also, we found a trend of decreased activity in alpha band. However, the significant increase in gamma activity remained. Given our results, and findings from the literature, we consider it likely that, during the MSs, the brain initiates activities to recover from the MS state and reconnect with the active task.

Given the differences in durations between MSs and sleep, we expected them to be physiologically different. By comparing our findings after regressing out the global effect to the literature on the awakening-from-sleep process, we found differences. There are increases in alpha and theta activities in the first 10 min following awakening from normal sleep (Tassi et al., 2006), while Ferrara et al. (2006) and Marzano et al. (2011) found that in non-sleep-deprived subjects there were a global-scalp reduction in beta in addition to a posterior increase in delta activities when comparing post-sleep awakening to pre-sleep wakefulness. Finally, Gorgoni et al. (2015) found decreased alpha and beta activities in the fronto-central part of the brain after sleep-deprived subjects were awakened from recovery sleep. This indicates that it is highly likely that MSs and sleep are physiologically different in the process of ending the sleep state.

Chapter 14: Conclusion and Future Research

14.1 Summary and key findings

Studying lapses of responsiveness is important in many sectors but especially the transport sector (driving, pilots, etc.). These lapses are considered to be associated with complete decoupling from the external environment, where performance of a task requiring continuous attention drops to zero momentary. The main challenge facing researchers is finding a unified way to define complete lapses of responsiveness, partial lapses of responsiveness, and their different types in terms of behavioural characteristics (especially frequency and durations). This challenge on its own makes the interpretation of any new results from studies of ALs, when compared to the literature, a riddle.

In our analysis we were interested in complete lapses of responsiveness (ALs and MSs). Given their major effect on road safety, we aimed to increase our understanding of the behavioural characteristics and physiology underlying lapses of responsiveness. We used a 2-D CVT task by combining two studies (C and D), which is demanding given their session durations (50 min and 20 min). The task is monotonous, as it repeats itself in a periodic pattern (every 30 s) and without any dual-task distractions, such as was done by Buckley et al. (2016). There was also no motivational influence (e.g., financial reward). This task is similar to that on the road, in which a driver spends a long time on the same lane, and possibly the same speed, which correlates with a high propensity for complete lapses of responsiveness.

We used simultaneous EEG, fMRI, visuomotor tracking, and eye-video recording to observe the performance of participants, and events of complete lapses of responsiveness were rated by a human expert. We classified events of no response as ALs (eyes opened) or MSs (eyes closed). In addition, we labelled events of partial drop in performance (partial eye closure) as DIREs. Drops in performance that did not fit any specific lapse category were labelled as VBIP. We also kept record of the variability of tracking target speed, and durations of poor performance.

The ALs were analyzed using fMRI data from the combined studies via voxel-wise, group ICA, HR, and FC analyses. We used EEG to analyze both ALs and MSs by reconstructing cortical sources and explored the relative difference between the average of events and their baselines in five bands of interest: delta, theta, alpha, beta, and gamma.

Because of the short duration of most ALs compared to the TR (2.5 s) in our fMRI, we consider our findings on the neural signature of an AL are likely to contain an overlap of physiological processes (i) causal of the behavioural lost-attention state itself, (ii) processes during the AL aimed at bringing the brain out of its lost-attention state, and (iii) processes immediately following the recovery of attention and responsiveness. Although, as we were unable to behaviourally determine the *type* of AL, we expected ALs to be due to mind-blanking (involuntary) given the average short duration, as it is unlikely to think about memories (mind-wandering) in ~ 1.7 s, or to be able to "fully" clear the mind from thoughts.

On comparing ALs to the baseline of responsive tracking via voxel-wise analysis in the GM of the brain, we found increased activity in the SN – specifically dorsal ACC and ventral SMA. We consider this is related to the process of ending the AL.

In the HR analysis, we focused on ROIs. We first confirmed our findings from the voxel-wise analysis. We also found a trend of increase in the HR at 7.5 s after the onset of AL in left IPS of DAN, which we also consider is related to the process of ending the AL. In the right PPC of FPN, we found a trend of decrease at -2.5 s in the rPPC represent a drop in FPN activity which could have led to a loss of visuospatial attention and visuomotor response preceding the onset of AL as part of the decoupling process. In addition, an increase in the left IPL of DMN at around 12–15 s prior to the onset of the AL, which was not expected, may reflect mind-wandering as a precursor to an AL, but we cannot confirm that.

Finally, no change was found in the ventral ACC which support excluding the possibility that ALs are due to voluntary mind-blanking. In addition to the lack of increased DMN activity that is associated with voluntary mind-blanks, and highly associated with mind-wandering. Also, the significant increase in activity in SMA that was found in our ALs (involuntary mind-blanks) compared to the decrease in activity in SMA due to the voluntary mind-blanks. This supports excluding both, but does not confirm.

Group ICA analysis did not show any significant results but there was a trend of increased activity in an IC which was spatially correlated with SMN. This may also be related to the process of recovery from the AL.

FC analysis provided major findings through the different connections that were tested. The connections between FPN and both DMN and DAN were tested, and a significant increase in FC was found between FPN and DMN, which, in addition to the significant increase in FC within DMN, is associated with mind-wandering according to literature. However, the short average duration of ALs, supports excluding the possibility that the ALs being due to mind-wandering, as instead it could be due to task-related thoughts as part of the breaking the state of AL, or involuntary mind-blanking.

We also tested the FC between EMN and both DMN and DAN. We found an increase in FC between the regions responsible for eye movement from EMN and both DMN and DAN. This, together with a decrease in FC between the regions responsible for visual processing and DAN, supports the decoupling process during ALs. To further test for decoupling, FC between FPN and both VSN and SMN were tested. A decrease in FC between FPN and SMN was found, which supports decoupling during ALs, as there is no performance of the task. But the finding of increased FC between FPN and VSN, is more likely to represent the process of reconnecting with the task. A decrease in FC between the WMN and DMN supports the presence of involuntary mind-blanking. Finally, increased FC between SN and DAN is considered to be consistent with the process of getting out of the AL.

Finally, on the EEG side of ALs, we found non-significant increased activity in beta and gamma bands, which could be considered associated with the process of recovery from ALs, or possibly white dreams given their association with high-frequency EEG activities. However, more statistical power is needed to claim that association.

To conclude on the AL side, because of the extended and repetitive nature of the task, we consider that subjects would likely have been mind-wandered for a considerable proportion of time on the task. But given that the task is also demanding, as it requires continuous performance, the subjects were keen to have both task-related thoughts and TUTs, which eventually, with the aid of mental fatigue and possibly drowsiness, led to draining limited working memory and central executive functions and subsequent attentional shutdowns – i.e., involuntary mind-blanks. The brain then recovers and restarts carrying out the task.

In the MS analysis, we focused only on EEG, as the parallel fMRI data had been previously analysed and reported (Poudel et al., 2014). We found increased activity in the delta, theta, alpha, beta, and gamma EEG bands. Based on our findings and the behavioural difference, we believe that MS is physiologically different from sleep in the recovery process. However, due to a limitation in the data collected, we did not have any measure of continuous head motion, so cannot completely exclude the possibility that the global increase in EEG power may have been partially or wholly caused by unremoved motion. So, the global signal effect was removed in a further analysis, which resulted in removing the increase in delta, theta, and beta bands. However, the increase in gamma activity remained. In addition, a trend of decreased alpha activity was found, which is the opposite of what was found before removing the global signal effect. Overall, we believe that MSs are physiologically different from sleep in the recovery process even after removing the global signal effect.

14.2 Review of hypotheses

In this project we had nine hypotheses divided into three groups of three main key questions: (1) what are the neural signatures of endogenous ALs during a continuous visuomotor tracking? (2) are endogenous ALs during a continuous visuomotor tracking mind-blanks or mind-wandering? and (3) are MSs physiologically different from sleep?

To answer the first question, we had seven hypotheses. Given what we found, we believe that there was a decoupling state during the AL.

Hypothesis 1: In a 2-D CVT task, there is lower neural activity in DAN during endogenous ALs. ➔ We found no evidence to accept this hypothesis.

Based on the voxel-wise analysis, there were no significant change in any of DAN regions. We further analysis that in the HR analysis, and we found a trend of increased activity 5 s after the onset, which is associated with the recovery process.

Hypothesis 2: In a 2-D CVT, FC between FPN and DAN decreases during ALs. ➔ We found no evidence to accept this hypothesis.

We could not find evidence using the FC analysis within ALs, but we should consider doing a dynamic FC to see what happened before and after.

Hypothesis 3: In a 2-D CVT, FC between FPN and SMN decreases during ALs. ➔ Our evidence supports this hypothesis.

This falls with our expectations about the decoupling process, as ALs will lead into a complete drop in performing the task which is based on visuomotor response.

Hypothesis 4: In a 2-D CVT, FC between FPN and VSN decreases during ALs. ➔ Our evidence rejects this hypothesis.

We found evidence for the opposite change using the FC analysis within ALs, and this is expected to be associated with the recovery process. But we should consider doing a dynamic FC to see what happened before and after.

Hypothesis 5: In a 2-D CVT, FC between DAN and EMN decreases during ALs. ➔ Our evidence supports this hypothesis.

We found a decrease in FC between DAN and the regions associated with processing visual input from EMN. This was expected as part of the decoupling process.

Hypothesis 6: In a 2-D CVT, FC between DMN and WMN decreases during ALs. ➔ Our evidence supports this hypothesis.

This finding is very important to support that ALs are due to mind-blanking more than mind-wandering given their short average duration.

Hypothesis 7: In a 2-D CVT, EEG alpha power increases in the posterior brain area during endogenous ALs. ➔ We found no evidence to accept this hypothesis.

We could not find any evidence of change, not even a trend of change of EEG alpha activity to be associated with ALs. We are still expecting to see changes, maybe with more statistical power.

To answer the second question, we had one hypothesis, where each carried multiple expectations trying to speculate the type of AL.

Hypothesis 8: ALs during a 2-D CVT are due to involuntary mind-blanking. ➔ We found limited evidence to accept this hypothesis.

Finding no significant increase in DMN activity whether by voxel-wise or HR analyses is very important to exclude the possibility of ALs being due to mind-wandering. Also, the increased FC between FPN and DMN, and between EMN and DMN, given the short average duration of ALs, could be associated with task-related thoughts, which again exclude the possibility of ALs being due to mind-wandering. Finally, our EEG findings cannot exclude the association of local-sleep to explain ALs, but given our low statistical power, it is worth re-investigating this with higher statistical power.

To answer the third question, we had one hypothesis.

Hypothesis 9: Microsleeps during a 2-D CVT task are brief instances of sleep but are physiologically different from normal sleep. ➔ We found limited evidence to accept this hypothesis.

Given the behavioural difference between MSs and sleep in terms of duration, we consider that they are different from a physiological perspective, particularly in terms of the process of regaining wakefulness. We are aware of a limitation in being unable to exclude the possibility of MS-synchronous artefacts due to EMG or head motion. However, we consider motion artefacts to be very unlikely due to movement-constrained setup inside the MRI scanner.

14.3 Limitations

Although the task we used is novel, and carries a great potential in adding more to the understanding of lapses in general, there were several problems and limitations in our data.

Statistical power: Combining our two studies resulted in 40 subjects, but a lower number of subjects (17) in fMRI and (10) in EEG reached the statistical analysis step in ALs, while MSs had (11) in EEG analysis. This is because of the low number of ALs found in subjects from studies C and D which were used in fMRI analysis. For EEG analysis, Study D was excluded because it did not pass the pre-processing stage. Finally, some subjects had corrupted/incomplete data so were excluded from the beginning.

Field maps: Field map images were not collected for all subjects in both studies. As a result, we were unable to perform magnetic field distortion correction for any subject in order to have a consistent pipeline of analysis. This step is believed to increase SNR in the fMRI analysis if performed, and may have helped revealing results in areas highly affected by magnetic field distortion.

Individual differences: Differences between individuals in WMC (Adam et al., 2015), fluid intelligence (Unsworth et al., 2010), vigilance (Robison & Brewer, 2019), oculometrics (Unsworth et al., 2020), and human brain structure (Clemente et al., 2021; Mitko et al., 2019), are likely to have influenced our results and studying these would likely have given us additional important insights into lapses. However, such measures were not collected.

Behavioural gold standards: We studied ALs to determine their neural signature. However, we were limited by being unsure whether these were instances of mind-wandering or mind-blanking or a combination of both. The addition of a thought probe technique may have helped in identification of type of AL, but such techniques have their own serious limitations. There is no standard approach, and most are based on the subjective reports that might not be accurate (Robison et al., 2019; Weinstein, 2018; Weinstein et al., 2017; Wiemers & Redick, 2019). Also, thought probes would seriously interfere with the continuous nature of our task. Notwithstanding, to our knowledge, thought probes are the only means by which it is possible to gain an albeit-questionable behavioral gold standard to differentiate the two types of ALs (Zanesco et al., 2020).

However, another approach could be to differentiate the types of ALs via their neural signature based on literature.

Eye-video and Oculometrics: We wished to increase our understanding of the behavioural characteristics of ALs, as this would help in associating the physiological findings to behavioural ones, which later could be used in the detection/prediction systems. We had eye-video recordings of only the right eye from a digital camera (Malla et al., 2010), which was low resolution and could not be used for quantitative oculometrics; to collect accurate and precise features of the eyes movements and pupil measures. However, the eye-video recordings we had were enough to determining eye-closure and hence MSs.

Camera-based studies are common in the literature for eye movements and gaze (Borza et al., 2016; Cheung & Peng, 2015; Kristjansson et al., 2009; Meng & Zhao, 2017; Yu et al., 2015; Zhao et al., 2019), and there is a huge interest into using eye trackers (Benedek et al., 2017; Franklin et al., 2013; Jubera-García et al., 2019; Kang et al., 2014; Konishi et al., 2017; Massar et al., 2018; Steindorf & Rummel, 2020; Unsworth & Robison, 2016b, 2018a; Unsworth et al., 2018; Van Den Brink et al., 2016). The question of which to choose lies in the processing efficiency according to Al-Rahayfeh and Faezipour (2013). In the case of real-time applications, both the processing time and hardware should be considered, in addition, when using a camera-based system, the background noise, lighting conditions, and distance to camera should be considered.

Based on the literature, many studies have looked at the behavioural characteristics of mind-wandering events from on-task events (Benedek et al., 2017; Bixler & D’Mello, 2016; Daniel et al., 2010; Foulsham et al., 2013a; Pepin et al., 2018; Reichle et al., 2010; Schad et al., 2012; Unsworth & Robison, 2016b, 2018b). None of these studies looked at the characteristics of mind-wandering and mind-blanking events in a continuously demanding task which requires sustained attention all the time. According to Unsworth and Robison (2018b), no single measure is fully predictive of whether a person is experiencing a lapse or not, so using a combination is more likely to achieve a better performance. That is why having precise measures is essential for an informative behavioural study of ALs.

Fusion of EEG and fMRI: Because of limitations in the EEG data available from Studies C and D, we were limited in what we could obtain EEG-wise, as opposed to fMRI-wise, on ALs. Consequently, we were unable to fuse the two modalities, and, hence, unable to gain the benefits of maximal temporal and spatial resolution.

Motion-related artefacts: It is very important to account for motion-related artefacts, because of the substantial effect they can have on the SNR of the data (Yan et al., 2009), which can, otherwise, result in findings being questionable (Jansen et al., 2012). Due to our limited collected measures of motion, we were unable to account for head movement. The literature suggests multiple solutions during the setup phase to minimize the adverse effect of motion artefacts in the processing phase (Bullock et al., 2021). The most accurate is to attach motion tracking sensors to the EEG cap (Bullock et al., 2021; Daniel et al., 2018; Jorge et al., 2015; Spencer et al., 2018).

14.4 Future research

Given our current data from both studies C and D, in order to proceed with further investigation of ALs, a new study could be conducted which could remove, as much as possible, the limitations mentioned above. However, the current data could still be used to further investigate the following:

- Doing fMRI HRs of MSs and comparing these with our ALs – Could our ALs actually be MSs with eyes open? Although they are behaviourally different, in terms of whether the eyes are open or closed, the fact that ALs (involuntary mind-blanks) are associated with a complete drop in performance, highlights an important question about whether some of our brain regions are sleeping (local-sleep) as has been suggested (Andrillon et al., 2021; Andrillon et al., 2019). Hence, testing this is highly desirable.
- Cluster analysis of ALs to see if they are actually a mix of mind-blanks, mind-wandering, MSs with eyes open, or other. Using an unsupervised clustering technique modified for fMRI data (Aljobouri et al., 2018; Qin & Suganthan, 2004), testing the possibility that the ALs we have are all related to one cluster (one type of AL, such as mind-blanks), or two clusters (mind-blanks and mind-wandering), or even more, and compare the neural signature to those in the literature would be of value.

For the MSs, since we have collected simultaneous EEG and fMRI data, we could investigate MSs using the fusion of EEG and fMRI (Ritter & Villringer, 2006) from the current data. This would allow us to benefit from both the high temporal resolution of EEG and the simultaneously recorded high spatial resolution of fMRI. However, caution is needed due to the noise added from each technique to the other technique's data (Bullock et al., 2021). A quantitative evaluation would be helpful to make sure that the regions or frequencies of interest are not corrupted before starting the analysis (Schrooten et al., 2019). The most common method used in the fusion of EEG and fMRI is 'EEG-informed fMRI', which is basically a prediction of the BOLD signal in each voxel dependent on the EEG signals (Abreu et al., 2018; Murta et al., 2015).

Initiating a new study would be of particular value in further investigation of ALs. In terms of the limitations mentioned in Section 14.3, having a sufficient number of subjects in the analysis stage (20 – 30 or more) would be highly desirable (Pajula & Tohka, 2016; Thirion et al., 2007; Turner et al., 2018). All of the measures not collected in Studies C and D, such as field maps, ECG, and respiratory activity, plus individual differences in measures of vigilance, working memory capacity, and fluid intelligence, should be considered. The most accurate means to collect oculometric features would be very desirable, including eye-position trackers. This, in addition to the tracking performance measure, would help build a more accurate gold standard. Also, different cameras could be used to capture not only the face but also the head, body, and hands (tracking fingers), in order to accurately label determine voluntary movements. For the task design, since it's essential to know the type of ALs, a standard definition of what is an AL, mind-wandering, and mind-blanking is needed. The tracking device should be redesigned to use both hands, one for continuous tracking and one for reporting the mental state based on the self-caught method without necessitating stopping the continuous task. A preceding pilot study would be desirable to ensure that the new experimental paradigm is optimized.

Finally, if possible, it would be of considerable value to collect fMRI with the lowest TR possible and to collect simultaneous multi-channel EEG, so as to be able to perform fusion analyses of the two modalities and gain the benefits of both high temporal and spatial resolution. This would assist in separating the decoupling and recovery phases of ALs. The average duration of the ALs in the 2-D CVT task was 1.74 s, and the TR of the fMRI was 2.5 s. So, it is not possible to distinguish between these two separate phases from fMRI alone. The continuous task provided a good estimate of the actual duration of these ALs. To be able to perform dynamic FC on different phases of ALs, an MRI with a much shorter TR (< 1 s) is needed. A similar procedure to that of Poudel et al. (2018), where the focus was on the transient changes of MSs, which are generally much longer than ALs, could be followed.

The challenge then would be the HR, as only MSs (> 5 s) were used by Poudel et al. (2018) to ensure that activity at the onset of MSs was separated from that at the end of MSs; hence, dividing the MS event into stages was possible. Notwithstanding, it may still not be possible to satisfactorily separate the two phases of ALs.

The fMRI-based DFC of mind-wandering has been investigated (Denkova et al., 2019; Kucyi, 2018; Kucyi & Davis, 2014), with the primary aim being to determine the onset and duration of mind-wandering. Toolboxes such as CONN and GIFT were used, with a sliding window (~ 40–60 s) and step size of 1 TR, as mind-wanderings are events which likely often extend over many fMRI temporal samples. The sliding window analysis focused on uninterrupted continuous temporal dynamics.

Another approach to DFC of ALs would be to use reconstructed EEG sources, with their high temporal resolution. Dynamic/time-varying FC was used by Toppi et al. (2012) and time-varying effective connectivity by Toppi et al. (2016) to investigate changes immediately-before, during, and immediately-after MSs, with a temporal resolution of 200 ms. Hence, in the 2-D CVT task, where ALs have an average duration of 1.74 s (max < 5 s), and are highly unlikely to be mind-wandering, EEG is much more appropriate to separate the decoupling and recovery phases.

References

Abreu, R., Leal, A., & Figueiredo, P. (2018). EEG-informed fMRI: a review of data analysis methods. *Frontiers in Human Neuroscience, 12*, 29.

Adam, K. C., Mance, I., Fukuda, K., & Vogel, E. K. (2015). The contribution of attentional lapses to individual differences in visual working memory capacity. *Journal of Cognitive Neuroscience, 27*(8), 1601-1616.

Adam, K. C. S., & Vogel, E. K. (2017). Confident failures: Lapses of working memory reveal a metacognitive blind spot. *Attention, Perception, & Psychophysics, 79*(5), 1506-1523.

Aertsen, A. M., Gerstein, G. L., Habib, M. K., & Palm, G. (1989). Dynamics of neuronal firing correlation: modulation of "effective connectivity". *Journal of Neurophysiology, 61*(5), 900-917.

Akalin-Acar, Z., & Gençer, N. G. (2004). An advanced boundary element method (BEM) implementation for the forward problem of electromagnetic source imaging. *Physics in Medicine & Biology, 49*(21), 5011.

Akerstedt, T. (2008). Consensus Statement: Fatigue and accidents in transport operations. *Journal of Sleep Research, 9*(4), 395-395.

Al-Rahayfeh, A., & Faezipour, M. (2013). Eye Tracking and Head Movement Detection: A State-of-Art Survey. *IEEE Journal of Translational Engineering in Health and Medicine, 1*, 2100212-2100212.

Albert, D. A., Ouimet, M. C., Jarret, J., Cloutier, M.-S., Paquette, M., Badeau, N., & Brown, T. G. (2018). Linking mind wandering tendency to risky driving in young male drivers. *Accident Analysis & Prevention, 111*, 125-132.

Aljobouri, H. K., Jaber, H. A., Koçak, O. M., Algin, O., & Çankaya, I. (2018). Clustering fMRI data with a robust unsupervised learning algorithm for neuroscience data mining. *Journal of Neuroscience Methods, 299*, 45-54.

Allen, P. J., Josephs, O., & Turner, R. (2000). A Method for Removing Imaging Artifact from Continuous EEG Recorded during Functional MRI. *NeuroImage, 12*(2), 230-239.

Amaro, E., & Barker, G. J. (2006). Study design in fMRI: Basic principles. *Brain and Cognition, 60*(3), 220-232.

Anderson, C., & Horne, J. A. (2006). Sleepiness Enhances Distraction During a Monotonous Task. *Sleep, 29*(4), 573-576.

Anderson, C., Wales, A. W. J., & Horne, J. A. (2010). PVT lapses differ according to eyes open, closed, or looking away. *Sleep, 33*(2), 197-204.

Andrews-Hanna, J. R. (2012). The brain’s default network and its adaptive role in internal mentation. *The Neuroscientist, 18*(3), 251-270.

Andrews-Hanna, J. R., Reidler, J. S., Huang, C., & Buckner, R. L. (2010). Evidence for the default network's role in spontaneous cognition. *Journal of Neurophysiology, 104*(1), 322-335.

Andrillon, T., Burns, A., Mackay, T., Windt, J., & Tsuchiya, N. (2021). Predicting lapses of attention with sleep-like slow waves. *Nature Communications, 12*(1), 3657-3657.

Andrillon, T., Windt, J., Silk, T., Drummond, S. P. A., Bellgrove, M. A., & Tsuchiya, N. (2019). Does the mind wander when the brain takes a break? Local sleep in wakefulness, attentional lapses and mind-wandering. *Frontiers in Neuroscience, 13*, 949.

Arnau, S., Löffler, C., Rummel, J., Hagemann, D., Wascher, E., & Schubert, A.-L. (2020). Inter-trial alpha power indicates mind wandering. *Psychophysiology, 57*(6), e13581.

Ashburner, J. (2012). SPM: a history. *NeuroImage, 62*(2), 791-800.

Atwood, H. L., & MacKay, W. A. (1989). *Essentials in Neurophysiology*: BC Decker.

Baillet, S., Mosher, J. C., & Leahy, R. M. (2001). Electromagnetic brain mapping. *IEEE Signal Processing Magazine, 18*(6), 14-30.

Baldwin, C. L., Roberts, D. M., Barragan, D., Lee, J. D., Lerner, N., & Higgins, J. S. (2017). Detecting and quantifying mind wandering during simulated driving. *Frontiers in Human Neuroscience, 11*, 406-406.

Balkin, T. J., & Badia, P. (1988). Relationship between sleep inertia and sleepiness: Cumulative effects of four nights of sleep disruption/restriction on performance following abrupt nocturnal awakening. *Biological Psychology, 27*(3), 245-258.

Banich, M. T., Milham, M. P., Atchley, R., Cohen, N. J., Webb, A., Wszalek, T., . . . Shenker, J. (2000). fMRI studies of Stroop tasks reveal unique roles of anterior and posterior brain systems in attentional selection. *Journal of Cognitive Neuroscience, 12*(6), 988-1000.

Barnes, G. R., & Hillebrand, A. (2003). Statistical flattening of MEG beamformer images. *Human Brain Mapping, 18*(1), 1-12.

Barry, R. J., Clarke, A. R., Johnstone, S. J., Magee, C. A., & Rushby, J. A. (2007). EEG differences between eyes-closed and eyes-open resting conditions. *Clinical Neurophysiology, 118*(12), 2765-2773.

Bear, M. F., Connors, B. W., & Paradiso, M. A. (2007). *Neuroscience* (Vol. 2): Lippincott Williams & Wilkins.

Beckmann, C., Tracey, I., Noble, J., & Smith, S. (2000). Combining ICA and GLM: A hybrid approach to fMRI analysis. *NeuroImage, 11*(5), S643.

Beckmann, C. F., DeLuca, M., Devlin, J. T., & Smith, S. M. (2005). Investigations into resting-state connectivity using independent component analysis. *Philosophical Transactions of the Royal Society B: Biological Sciences, 360*(1457), 1001-1013.

Beckmann, C. F., Jenkinson, M., & Smith, S. M. (2003). General multilevel linear modeling for group analysis in FMRI. *NeuroImage, 20*(2), 1052-1063.

Beckmann, C. F., Mackay, C. E., Filippini, N., & Smith, S. M. (2009). Group comparison of resting-state FMRI data using multi-subject ICA and dual regression. *NeuroImage, 47*(Suppl 1), S148.

Beckmann, C. F., & Smith, S. M. (2004). Probabilistic independent component analysis for functional magnetic resonance imaging. *IEEE Transactions on Medical Imaging, 23*(2), 137-152.

Beckmann, C. F., & Smith, S. M. (2005). Tensorial extensions of independent component analysis for multisubject FMRI analysis. *NeuroImage, 25*(1), 294-311.

Behzadi, Y., Restom, K., Liau, J., & Liu, T. T. (2007). A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. *NeuroImage, 37*(1), 90-101.

Benedek, M., Stoiser, R., Walcher, S., & Körner, C. (2017). Eye behavior associated with internally versus externally directed cognition. *Frontiers in Psychology, 8*(1092).

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal statistical society: series B (Methodological), 57*(1), 289-300.

Benjamini, Y., & Yekutieli, D. (2001). The control of the false discovery rate in multiple testing under dependency. *Annals of Statistics*, 1165-1188.

Bentley, P. M., & McDonnell, J. T. E. (1994). Wavelet transforms: an introduction. *Electronics & Communication Engineering Journal, 6*(4), 175-186. Retrieved from https://digital-library.theiet.org/content/journals/10.1049/ecej_19940401

Bernardi, G., Siclari, F., Yu, X., Zennig, C., Bellesi, M., Ricciardi, E., . . . Tononi, G. (2015). Neural and Behavioral Correlates of Extended Training during Sleep Deprivation in Humans: Evidence for Local, Task-Specific Effects. *The Journal of Neuroscience, 35*(11), 4487.

Berthié, G., Lemercier, C., Paubel, P.-V., Cour, M., Fort, A., Galéra, C., . . . Maury, B. (2015). The restless mind while driving: drivers' thoughts behind the wheel. *Accident Analysis & Prevention, 76*, 159-165.

Bigdely-Shamlo, N., Mullen, T., Kothe, C., Su, K.-M., & Robbins, K. A. (2015). The PREP pipeline: standardized preprocessing for large-scale EEG analysis. *Frontiers in Neuroinformatics, 9*(16).

Bijsterbosch, J., Smith, S. M., & Beckmann, C. F. (2017). *Introduction to Resting State FMRI Functional Connectivity*: Oxford University Press.

Biswal, B., Zerrin Yetkin, F., Haughton, V. M., & Hyde, J. S. (1995). Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. *Magnetic Resonance in Medicine, 34*(4), 537-541.

Bixler, R., & D'Mello, S. (2016). Automatic gaze-based user-independent detection of mind wandering during computerized reading. *User Modeling and User-Adapted Interaction, 26*(1), 33-68.

Bogler, C., Vowinkel, A., Zhutovsky, P., & Haynes, J.-D. (2017). Default network activity is associated with better performance in a vigilance task. *Frontiers in Human Neuroscience, 11*, 623.

Borst, J. P., & Anderson, J. R. (2013). Using model-based functional MRI to locate working memory updates and declarative memory retrievals in the fronto-parietal network. *Proceedings of the National Academy of Sciences of the United States of America, 110*(5), 1628-1633.

Borza, D., Darabant, A. S., & Danescu, R. (2016). Real-time detection and measurement of eye features from color images. *Sensors, 16*(7), 1105.

Braboszcz, C., & Delorme, A. (2011). Lost in thoughts: Neural markers of low alertness during mind wandering. *NeuroImage, 54*, 3040-3047.

Braver, T. S., Gray, J. R., & Burgess, G. C. (2007). Explaining the many varieties of working memory variation: Dual mechanisms of cognitive control. In A. Miyake, A. Conway, & C. Jarrold (Eds.), *Variation in working memory* (Vol. 75, pp. 106): Oxford University Press.

Brookings, T., Ortigue, S., Grafton, S., & Carlson, J. (2009). Using ICA and realistic BOLD models to obtain joint EEG/fMRI solutions to the problem of source localization. *NeuroImage, 44*(2), 411-420.

Bruns, A. (2004). Fourier-, Hilbert- and wavelet-based signal analysis: are they really different approaches? *Journal of Neuroscience Methods, 137*(2), 321-332.

Buckley, R. J., Helton, W. S., Innes, C. R. H., Dalrymple-Alford, J. C., & Jones, R. D. (2016). Attention lapses and behavioural microsleeps during tracking, psychomotor vigilance, and dual tasks. *Consciousness and Cognition, 45*, 174-183.

Bullmore, E., & Sporns, O. (2009). Complex brain networks: graph theoretical analysis of structural and functional systems. *Nature Reviews Neuroscience, 10*(3), 186-198.

Bullock, M., Jackson, G. D., & Abbott, D. F. (2021). Artifact Reduction in Simultaneous EEG-fMRI: A Systematic Review of Methods and Contemporary Usage. *Frontiers in Neurology, 12*.

Burdett, B. R. D., Charlton, S. G., & Starkey, N. J. (2016). Not all minds wander equally: The influence of traits, states and road environment factors on self-reported mind wandering during everyday driving. *Accident Analysis & Prevention, 95*, 1-7.

Burdett, B. R. D., Charlton, S. G., & Starkey, N. J. (2019). Mind wandering during everyday driving: An on-road study. *Accident Analysis & Prevention, 122*, 76-84.

Buxton, R. B. (2001). The Elusive Initial Dip. *NeuroImage, 13*(6), 953-958.

Buxton, R. B. (2013). The physics of functional magnetic resonance imaging (fMRI). *Reports on Progress in Physics., 76*(9), 096601-096601.

Caballero-Gaudes, C., & Reynolds, R. C. (2017). Methods for cleaning the BOLD fMRI signal. *NeuroImage, 154*, 128-149.

Calhoun, V. D., Adali, T., Giuliani, N., Pekar, J., Kiehl, K., & Pearlson, G. (2006). Method for multimodal analysis of independent source differences in schizophrenia: combining gray matter structural and auditory oddball functional data. *Human Brain Mapping, 27*(1), 47-62.

Canales-Johnson, A., Beerendonk, L., Blain, S., Kitaoka, S., Ezquerro-Nassar, A., Nuiten, S., . . . Bekinschtein, T. A. (2020). Decreased Alertness Reconfigures Cognitive Control Networks. *The Journal of Neuroscience, 40*(37), 7142.

Cannon, J., McCarthy, M. M., Lee, S., Lee, J., Börgers, C., Whittington, M. A., & Kopell, N. (2014). Neurosystems: brain rhythms and cognitive processing. *The European Journal of Neuroscience, 39*(5), 705-719.

Caparelli, E. C., & Tomasi, D. (2008). K-space spatial low-pass filters can increase signal loss artifacts in Echo-Planar Imaging. *Biomedical Signal Processing and Control, 3*(1), 107-114.

Carp, J. (2012). On the Plurality of (Methodological) Worlds: Estimating the Analytic Flexibility of fMRI Experiments. *Frontiers in Neuroscience, 6*(149).

Carr, M. F., Karlsson, M. P., & Frank, L. M. (2012). Transient slow gamma synchrony underlies hippocampal memory replay. *Neuron, 75*(4), 700-713.

Carroll, J. B. (1993). *Human cognitive abilities: A survey of factor-analytic studies*: Cambridge University Press.

Castellanos, N. P., & Makarov, V. A. (2006). Recovering EEG brain signals: Artifact suppression with wavelet enhanced independent component analysis. *Journal of Neuroscience Methods, 158*(2), 300-312.

Castiglione, A., Wagner, J., Anderson, M., & Aron, A. (2019). Preventing a Thought from Coming to Mind Elicits Increased Right Frontal Beta Just as Stopping Action Does. *Cerebral Cortex, 29*, 2160 - 2172.

Cattell, R. B. (1963). Theory of fluid and crystallized intelligence: A critical experiment. *Journal of Educational Psychology, 54*(1), 1-22.

Cavina-Pratesi, C., Valyear, K. F., Culham, J. C., Köhler, S., Obhi, S. S., Marzi, C. A., & Goodale, M. A. (2006). Dissociating Arbitrary Stimulus-Response Mapping from Movement Planning during Preparatory Period: Evidence from Event-Related Functional Magnetic Resonance Imaging. *The Journal of Neuroscience, 26*(10), 2704-2713.

Chai, X. J., Castañón, A. N., Öngür, D., & Whitfield-Gabrieli, S. (2012). Anticorrelations in resting state networks without global signal regression. *NeuroImage, 59*(2), 1420-1428.

Chang, C. Y., Hsu, S. H., Pion-Tonachini, L., & Jung, T. P. (2020). Evaluation of Artifact Subspace Reconstruction for Automatic Artifact Components Removal in Multi-Channel EEG Recordings. *IEEE Transactions on Biomedical Engineering, 67*(4), 1114-1121.

Chaudhary, P., Chaudhary, L., Tripathi, P., & Varshney, T. (2017). *Revealing the scope of mind wandering software effects, techniques and applications.* Proceedings of 7th International Conference on Cloud Computing, Data Science & Engineering - Confluence 671-673.

Cheung, Y.-m., & Peng, Q. (2015). Eye gaze tracking with a web camera in a desktop environment. *IEEE Transactions on Human-Machine Systems, 45*(4), 419-430.

Cheyne, J. A., Carriere, J. S. A., & Smilek, D. (2006). Absent-mindedness: Lapses of conscious awareness and everyday cognitive failures. *Consciousness and Cognition, 15*(3), 578-592.

Chica, A. B., Bartolomeo, P., & Lupiáñez, J. (2013). Two cognitive and neural systems for endogenous and exogenous spatial attention. *Behavioural Brain Research, 237*, 107-123.

Christoff, K., Gordon, A. M., Smallwood, J., Smith, R., & Schooler, J. W. (2009). Experience sampling during fMRI reveals default network and executive system contributions to mind wandering. *Proceedings of the National Academy of Sciences, 106*(21), 8719.

Chun, M. M. (2011). Visual working memory as visual attention sustained internally over time. *Neuropsychologia, 49*(6), 1407-1409.

Clemente, A., Domínguez D, J. F., Imms, P., Burmester, A., Dhollander, T., Wilson, P. H., . . . Caeyenberghs, K. (2021). Individual differences in attentional lapses are associated with fiber-specific white matter microstructure in healthy adults. *Psychophysiology*, e13871.

Coiner, B., Pan, H., Bennett, M. L., Bodien, Y. G., Iyer, S., O'Neil-Pirozzi, T. M., . . . Stern, E. (2019). Functional neuroanatomy of the human eye movement network: a review and atlas. *Brain Structure and Function, 224*(8), 2603-2617.

Cole, M. W., Reynolds, J. R., Power, J. D., Repovs, G., Anticevic, A., & Braver, T. S. (2013). Multi-task connectivity reveals flexible hubs for adaptive task control. *Nature Neuroscience, 16*(9), 1348–1355.

Comon, P. (1994). Independent component analysis, a new concept? *Signal Processing, 36*(3), 287-314.

Compton, R. J., Gearinger, D., & Wild, H. (2019). The wandering mind oscillates: EEG alpha power is enhanced during moments of mind-wandering. *Cognitive, Affective, & Behavioral Neuroscience, 19*(5), 1184-1191.

Coyle, S., Ward, T., Markham, C., & McDarby, G. (2004). On the suitability of near-infrared (NIR) systems for next-generation brain–computer interfaces. *Physiological Measurement, 25*(4), 815.

Coyne, K. (2018). MRI: A Guided Tour. Retrieved from https://nationalmaglab.org/education/magnet-academy/learn-the-basics/stories/mri-a-guided-tour

Craig, A., Tran, Y., Wijesuriya, N., & Nguyen, H. (2012). Regional brain wave activity changes associated with fatigue. *Psychophysiology, 49*(4), 574-582.

Crawford, J. (1991). The relationship between tests of sustained attention and fluid intelligence. *Personality and Individual Differences, 12*(6), 599-611.

Critcher, C. R., & Gilovich, T. (2010). Inferring attitudes from mind wandering. *Personality and Social Psychology Bulletin, 36*(9), 1255-1266.

D'Mello, S., Kopp, K., Bixler, R. E., & Bosch, N. (2016). *Attending to attention: Detecting and combating mind wandering during computerized reading*. Paper presented at the CHI Conference Extended Abstracts on Human Factors in Computing Systems, San Jose, California, USA.

D'Ambrosio, S., Castelnovo, A., Guglielmi, O., Nobili, L., Sarasso, S., & Garbarino, S. (2019). Sleepiness as a Local Phenomenon. *Frontiers in Neuroscience, 13*(1086).

D'Mello, S. K. (2016). Giving eyesight to the blind: Towards attention-aware AIED. *International Journal of Artificial Intelligence in Education, 26*(2), 645-659.

Dalal, S., Rampp, S., Willomitzer, F., & Ettl, S. (2014). Consequences of EEG electrode position error on ultimate beamformer source reconstruction performance. *Frontiers in Neuroscience, 8*(42).

Dale, A. M., Liu, A. K., Fischl, B. R., Buckner, R. L., Belliveau, J. W., Lewine, J. D., & Halgren, E. (2000). Dynamic statistical parametric mapping: combining fMRI and MEG for high-resolution imaging of cortical activity. *Neuron, 26*(1), 55-67.

Dale, A. M., & Sereno, M. I. (1993). Improved localizadon of cortical activity by combining EEG and MEG with MRI cortical surface reconstruction: a linear approach. *Journal of Cognitive Neuroscience, 5*(2), 162-176.

Damoiseaux, J. S., Rombouts, S. A. R. B., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., & Beckmann, C. F. (2006). Consistent resting-state networks across healthy subjects. *Proceedings of the National Academy of Sciences of the United States of America, 103*(37), 13848-13853.

Danckert, J., & Merrifield, C. (2018). Boredom, sustained attention and the default mode network. *Experimental Brain Research, 236*(9), 2507-2518.

Daniel, A. J., Smith, J. A., Spencer, G. S., Jorge, J., Bowtell, R., & Mullinger, K. J. (2018). Exploring the relative efficacy of motion artefact correction techniques for EEG data acquired during simultaneous fMRI. *Human Brain Mapping, 40*(2), 578-596.

Daniel, S., Jonathan, S. A. C., & Cheyne, J. A. (2010). Out of mind, out of sight: Eye blinking as indicator and embodiment of mind wandering. *Psychological Science, 21*(6), 786-789.

Davidson, P. R., Jones, R. D., & Peiris, M. T. R. (2005). *Detecting behavioral microsleeps using EEG and LSTM recurrent neural networks.* Proceedings of IEEE Engineering in Medicine and Biology 27th Annual Conference 5754-5757.

Davidson, P. R., Jones, R. D., & Peiris, M. T. R. (2007). EEG-based lapse detection with high temporal resolution. *IEEE Transactions on Biomedical Engineering, 54*(5), 832-839.

Davies, D. R., & Parasuraman, R. (1982). *The psychology of vigilance*: Academic Press.

Dawson, D., & Reid, K. (1997). Fatigue, alcohol and performance impairment. *Nature, 388*, 235.

De Gennaro, L., Ferrara, M., Curcio, G., & Cristiani, R. (2001). Antero-posterior EEG changes during the wakefulness–sleep transition. *Clinical Neurophysiology, 112*(10), 1901-1911.

Debener, S., Mullinger, K. J., Niazy, R. K., & Bowtell, R. W. (2008). Properties of the ballistocardiogram artefact as revealed by EEG recordings at 1.5, 3 and 7 T static magnetic field strength. *International Journal of Psychophysiology, 67*(3), 189-199.

deBettencourt, M. T., Keene, P. A., Awh, E., & Vogel, E. K. (2019). Real-time triggering reveals concurrent lapses of attention and working memory. *Nature Human Behaviour, 3*, 808–816.

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods, 134*(1), 9-21.

Delorme, A., Sejnowski, T., & Makeig, S. (2007). Enhanced detection of artifacts in EEG data using higher-order statistics and independent component analysis. *NeuroImage, 34*(4), 1443-1449.

Denkova, E., Nomi, J. S., Uddin, L. Q., & Jha, A. P. (2019). Dynamic brain network configurations during rest and an attention task with frequent occurrence of mind wandering. *Human Brain Mapping, 40*(15), 4564-4576.

Derosière, 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.

Desimone, R., & Duncan, J. (1995). Neural Mechanisms of Selective Visual Attention. *Annual Review of Neuroscience, 18*(1), 193-222.

Di Lollo, V., Kawahara, J.-i., Shahab Ghorashi, S. M., & Enns, J. T. (2005). The attentional blink: Resource depletion or temporary loss of control? *Psychological Research, 69*(3), 191-200.

Dixon, M. L., De La Vega, A., Mills, C., Andrews-Hanna, J., Spreng, R. N., Cole, M. W., & Christoff, K. (2018). Heterogeneity within the frontoparietal control network and its relationship to the default and dorsal attention networks. *Proceedings of the National Academy of Sciences, 115*(7), E1598.

Domkin, D., Sörqvist, P., & Richter, H. O. (2013). Distraction of eye-hand coordination varies with working memory capacity. *Journal of Motor Behavior, 45*(1), 79-83.

Efklides, A., & Touroutoglou, A. (2010). Prospective memory failure and the metacognitive experience of "Blank in the Mind". In A. Efklides & P. Misailidi (Eds.), *Trends and Prospects in Metacognition Research* (pp. 105-126). Boston, MA: Springer US.

Eichele, T., Debener, S., Calhoun, V. D., Specht, K., Engel, A. K., Hugdahl, K., . . . Ullsperger, M. (2008). Prediction of human errors by maladaptive changes in event-related brain networks. *Proceedings of the National Academy of Sciences, 105*(16), 6173-6178.

Eklund, A., Nichols, T. E., & Knutsson, H. (2016). Cluster failure: Why fMRI inferences for spatial extent have inflated false-positive rates. *Proceedings of the National Academy of Sciences, 113*(28), 7900.

Elster, A. D. (2016). BOLD and Brain Activity. Retrieved from http://mriquestions.com/does-boldbrain-activity.html

Engle, R. W. (2002). Working Memory Capacity as Executive Attention. *Current Directions in Psychological Science, 11*(1), 19-23.

Engle, R. W., Kane, M. J., & Tuholski, S. W. (1999). Individual differences in working memory capacity and what they tell us about controlled attention, general fluid intelligence, and functions of the prefrontal cortex. In A. Miyake & P. Shah (Eds.), *Models of working memory: Mechanisms of active maintenance and executive control.* (pp. 102-134). New York, NY, US: Cambridge University Press.

Esposito, R., Cieri, F., Chiacchiaretta, P., Cera, N., Lauriola, M., Di Giannantonio, M., . . . Ferretti, A. (2018). Modifications in resting state functional anticorrelation between default mode network and dorsal attention network: comparison among young adults, healthy elders and mild cognitive impairment patients. *Brain Imaging and Behavior, 12*(1), 127-141.

Esterman, M., Grosso, M., Liu, G., Mitko, A., Morris, R., & DeGutis, J. (2016). Anticipation of monetary reward can attenuate the vigilance decrement. *PLoS ONE, 11*(7).

Esterman, M., Noonan, S. K., Rosenberg, M., & DeGutis, J. (2013). In the zone or zoning out? Tracking behavioral and neural fluctuations during sustained attention. *Cerebral Cortex, 23*(11), 2712-2723.

Esterman, M., Poole, V., Liu, G., & DeGutis, J. (2017). Modulating reward induces differential neurocognitive approaches to sustained attention. *Cerebral Cortex, 27*(8), 4022-4032.

Esterman, M., Rosenberg, M. D., & Noonan, S. K. (2014). Intrinsic fluctuations in sustained attention and distractor processing. *Journal of Neuroscience, 34*(5), 1724-1730.

Fazekas, P., Nemeth, G., & Overgaard, M. (2019). White dreams are made of colours: What studying contentless dreams can teach about the neural basis of dreaming and conscious experiences. *Sleep Medicine Reviews, 43*, 84-91.

Ferrara, M., Curcio, G., Fratello, F., Moroni, F., Marzano, C., Pellicciari, M. C., & De Gennaro, L. (2006). The electroencephalographic substratum of the awakening. *Behavioural Brain Research, 167*(2), 237-244.

Ferrara, M., De Gennaro, L., & Bertini, M. (1999). The effects of slow-wave sleep (SWS) deprivation and time of night on behavioral performance upon awakening. *Physiology & Behavior, 68*(1), 55-61.

Ferrara, M., de Gennaro, L., Casagrande, M., & Bertini, M. (2000). Selective slow-wave sleep deprivation and time-of-night effects on cognitive performance upon awakening. *Psychophysiology, 37*(4), 440-446.

Fisch, B. J., & Spehlmann, R. (1999). *Fisch and Spehlmann's EEG primer: basic principles of digital and analog EEG*: Elsevier Health Sciences.

Fortenbaugh, F. C., Rothlein, D., McGlinchey, R., DeGutis, J., & Esterman, M. (2018). Tracking behavioral and neural fluctuations during sustained attention: A robust replication and extension. *NeuroImage, 171*, 148-164.

Foulsham, T., Farley, J., & Kingstone, A. (2013a). Mind wandering in sentence reading: Decoupling the link between mind and eye. *Canadian Journal of Experimental Psychology/Revue canadienne de psychologie expérimentale, 67*(1), 51-59.

Foulsham, T., Farley, J., & Kingstone, A. (2013b). Mind wandering in sentence reading: Decoupling the link between mind and eye. *Canadian Journal of Experimental Psychology, 67*(1), 51-59.

Fox, K. C. R., Spreng, R. N., Ellamil, M., Andrews-Hanna, J. R., & Christoff, K. (2015). The wandering brain: Meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes. *NeuroImage, 111*, 611-621.

Fox, M. D., Corbetta, M., Snyder, A. Z., Vincent, J. L., & Raichle, M. E. (2006). Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proceedings of the National Academy of Sciences, 103*(26), 10046-10051.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences of the United States of America, 102*(27), 9673-9678.

Franklin, M. S., Broadway, J. M., Mrazek, M. D., Smallwood, J., & Schooler, J. W. (2013). Window to the wandering mind: Pupillometry of spontaneous thought while reading. *Quarterly Journal of Experimental Psychology, 66*(12), 2289-2294.

Freeman, W., & Quiroga, R. Q. (2012). *Imaging brain function with EEG: advanced temporal and spatial analysis of electroencephalographic signals*: Springer Science & Business Media.

Fries, P. (2009). Neuronal Gamma-Band Synchronization as a Fundamental Process in Cortical Computation. *Annual Review of Neuroscience, 32*(1), 209-224.

Friston, K., Frith, C., Liddle, P., & Frackowiak, R. (1993). Functional connectivity: the principal-component analysis of large (PET) data sets. *Journal of Cerebral Blood Flow & Metabolism, 13*(1), 5-14.

Friston, K. J., Ashburner, J., Frith, C. D., Poline, J. B., Heather, J. D., & Frackowiak, R. S. (1995). Spatial registration and normalization of images. *Human Brain Mapping, 3*(3), 165-189.

Friston, K. J., Fletcher, P., Josephs, O., Holmes, A., Rugg, M. D., & Turner, R. (1998). Event-related fMRI: characterizing differential responses. *NeuroImage, 7*(1), 30-40.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. P., Frith, C. D., & Frackowiak, R. S. J. (1994). Statistical parametric maps in functional imaging: A general linear approach. *Human Brain Mapping, 2*(4), 189-210.

Fuller, P. M., Gooley, J. J., & Saper, C. B. (2006). Neurobiology of the Sleep-Wake Cycle: Sleep Architecture, Circadian Regulation, and Regulatory Feedback. *Journal of Biological Rhythms, 21*(6), 482-493.

Gabard-Durnam, L. J., Mendez Leal, A. S., Wilkinson, C. L., & Levin, A. R. (2018). The Harvard Automated Processing Pipeline for Electroencephalography (HAPPE): Standardized Processing Software for Developmental and High-Artifact Data. *Frontiers in Neuroscience, 12*(97).

Galéra, C., Orriols, L., M'Bailara, K., Laborey, M., Contrand, B., Ribéreau-Gayon, R., . . . Lagarde, E. (2012). Mind wandering and driving: responsibility case-control study. *British Medical Journal, 345*, e8105.

Gallopin, T., Luppi, P. H., Cauli, B., Urade, Y., Rossier, J., Hayaishi, O., . . . Fort, P. (2005). The endogenous somnogen adenosine excites a subset of sleep-promoting neurons via A2A receptors in the ventrolateral preoptic nucleus. *Neuroscience, 134*(4), 1377-1390.

Gartenberg, D., Gunzelmann, G., Hassanzadeh-Behbaha, S., & Trafton, J. G. (2018). Examining the role of task requirements in the magnitude of the vigilance decrement. *Frontiers in Psychology, 9*, 1504.

Ghosh, S., Nandy, T., & Manna, N. (2015, 2015//). *Real Time Eye Detection and Tracking Method for Driver Assistance System.* Proceedings of Advancements of Medical Electronics, New Delhi 13-25.

Giambra, L. M. (1995). A laboratory method for investigating influences on switching attention to task-unrelated imagery and thought. *Consciousness and Cognition: An International Journal, 4*(1), 1-21.

Gil-Jardiné, C., Née, M., Lagarde, E., Schooler, J., Contrand, B., Orriols, L., & Galera, C. (2017). The distracted mind on the wheel: Overall propensity to mind wandering is associated with road crash responsibility. *PLoS ONE, 12*(8), e0181327.

Gillard-Crewther, S., Lawson, M. L., Bello, K., & Crewther, D. P. (2007). The visual attentional blink reflects constraints on temporal visual processing, not just a lapse of visual memory. *Clinical and Experimental Optometry, 90*(4), 282-289.

Gilmore, R. O., Diaz, M. T., Wyble, B. A., & Yarkoni, T. (2017). Progress toward openness, transparency, and reproducibility in cognitive neuroscience. *Annals of the New York Academy of Sciences, 1396*(1), 5.

Glover, G. H. (2011). Overview of functional magnetic resonance imaging. *Neurosurgery Clinics of North America, 22*(2), 133-139.

Godwin, C. A., Hunter, M. A., Bezdek, M. A., Lieberman, G., Elkin-Frankston, S., Romero, V. L., . . . Schumacher, E. H. (2017). Functional connectivity within and between intrinsic brain networks correlates with trait mind wandering. *Neuropsychologia, 103*, 140-153.

Goncharova, I. I., McFarland, D. J., Vaughan, T. M., & Wolpaw, J. R. (2003). EMG contamination of EEG: spectral and topographical characteristics. *Clinical Neurophysiology, 114*(9), 1580-1593.

Gorgolewski, K. J., & Poldrack, R. A. (2016). A practical guide for improving transparency and reproducibility in neuroimaging research. *PLoS Biology, 14*(7), e1002506.

Gorgoni, M., Ferrara, M., D'Atri, A., Lauri, G., Scarpelli, S., Truglia, I., & De Gennaro, L. (2015). EEG topography during sleep inertia upon awakening after a period of increased homeostatic sleep pressure. *Sleep Medicine, 16*(7), 883-890.

Goulden, N., Khusnulina, A., Davis, N. J., Bracewell, R. M., Bokde, A. L., McNulty, J. P., & Mullins, P. G. (2014). The salience network is responsible for switching between the default mode network and the central executive network: Replication from DCM. *NeuroImage, 99*, 180-190.

Gouraud, J., Delorme, A., & Berberian, B. (2017). Autopilot, mind wandering, and the out of the loop performance problem. *Frontiers in Neuroscience, 11*, 541.

Grech, R., Cassar, T., Muscat, J., Camilleri, K. P., Fabri, S. G., Zervakis, M., . . . Vanrumste, B. (2008). Review on solving the inverse problem in EEG source analysis. *Journal of Neuroengineering and Rehabilitation, 5*(1), 25.

Greicius, M. (2008). Resting-state functional connectivity in neuropsychiatric disorders. *Current Opinion in Neurology, 21*(4), 424-430.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: A network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences, 100*(1), 253.

Griffanti, L., Douaud, G., Bijsterbosch, J., Evangelisti, S., Alfaro-Almagro, F., Glasser, M. F., . . . Smith, S. M. (2017). Hand classification of fMRI ICA noise components. *NeuroImage, 154*, 188-205.

Grin-Yatsenko, V. A., Baas, I., Ponomarev, V. A., & Kropotov, J. D. (2010). Independent component approach to the analysis of EEG recordings at early stages of depressive disorders. *Clinical Neurophysiology, 121*(3), 281-289.

Groot, J. M., Boayue, N. M., Csifcsák, G., Boekel, W., Huster, R., Forstmann, B. U., & Mittner, M. (2021). Probing the neural signature of mind wandering with simultaneous fMRI-EEG and pupillometry. *NeuroImage, 224*, 117412.

Gross, J., Kujala, J., Hämäläinen, M., Timmermann, L., Schnitzler, A., & Salmelin, R. (2001). Dynamic imaging of coherent sources: Studying neural interactions in the human brain. *Proceedings of the National Academy of Sciences, 98*(2), 694.

Grouiller, F., Vercueil, L., Krainik, A., Segebarth, C., Kahane, P., & David, O. (2007). A comparative study of different artefact removal algorithms for EEG signals acquired during functional MRI. *NeuroImage, 38*(1), 124-137.

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).

Halder, T., Talwar, S., Jaiswal, A. K., & Banerjee, A. (2019). Quantitative Evaluation in Estimating Sources Underlying Brain Oscillations Using Current Source Density Methods and Beamformer Approaches. *eNeuro, 6*(4), ENEURO.0170-0119.2019.

Hallez, H., Vanrumste, B., Grech, R., Muscat, J., De Clercq, W., Vergult, A., . . . Van Huffel, S. (2007). Review on solving the forward problem in EEG source analysis. *Journal of Neuroengineering and Rehabilitation, 4*(1), 46.

Hamal, A. Q., & bin Abdul Rehman, A. W. (2013). *Artifact Processing of Epileptic EEG Signals: An Overview of Different Types of Artifacts.* Proceedings of 2013 International Conference on Advanced Computer Science Applications and Technologies 358-361.

Hammond, D. C. (2007). What Is Neurofeedback? *Journal of Neurotherapy, 10*(4), 25-36.

Hancock, P. A. (1989). A Dynamic Model of Stress and Sustained Attention. *Human Factors, 31*(5), 519-537.

Hancock, P. A. (2013). In search of vigilance: The problem of iatrogenically created psychological phenomena. *American Psychologist, 68*(2), 97-109.

Hara, J., & Sakurai, T. (2011). Interaction between sleep mechanisms and orexin neurons. *Sleep and Biological Rhythms, 9*(1), 38-43.

Harmony, T., Fernández, T., Silva, J., Bernal, J., Díaz-Comas, L., Reyes, A., . . . Rodríguez, M. (1996). EEG delta activity: an indicator of attention to internal processing during performance of mental tasks. *International Journal of Psychophysiology, 24*(1), 161-171.

Harrison, Y., & Horne, J. A. (1996). Occurrence of 'microsleeps' during daytime sleep onset in normal subjects. *Electroencephalography and Clinical Neurophysiology, 98*(5), 411-416.

Hartmann, M., Martarelli, C. S., Mast, F. W., & Stocker, K. (2014). Eye movements during mental time travel follow a diagonal line. *Consciousness and Cognition, 30*, 201-209.

Hasher, L., Lustig, C., & Zacks, R. (2007). Inhibitory mechanisms and the control of attention.

Hasher, L., & Zacks, R. T. (1988). Working memory, comprehension, and aging: A review and a new view. *Psychology of Learning and Motivation, 22*, 193-225.

Hayasaka, S., & Nichols, T. E. (2003). Validating cluster size inference: random field and permutation methods. *NeuroImage, 20*(4), 2343-2356.

He, H., Li, Y., Chen, Q., Wei, D., Shi, L., Wu, X., & Qiu, J. (2021). Tracking resting-state functional connectivity changes and mind wandering: A longitudinal neuroimaging study. *Neuropsychologia, 150*, 107674.

He, J., Becic, E., Lee, Y.-C., & McCarley, J. S. (2011). Mind wandering behind the wheel: Performance and oculomotor correlates. *Human Factors, 53*(1), 13-21.

Head, J., & Helton, W. S. (2012). Natural scene stimuli and lapses of sustained attention. *Consciousness and Cognition, 21*(4), 1617-1625.

Head, J., & Helton, W. S. (2014). Sustained attention failures are primarily due to sustained cognitive load not task monotony. *Acta Psychologica, 153*, 87-94.

Helfrich, R. F., Becker, H. G. T., & Haarmeier, T. (2013). Processing of Coherent Visual Motion in Topographically Organized Visual Areas in Human Cerebral Cortex. *Brain Topography, 26*(2), 247-263.

Helton, W. S., & Russell, P. N. (2011). Feature absence–presence and two theories of lapses of sustained attention. *Psychological Research, 75*(5), 384-392.

Helton, W. S., & Russell, P. N. (2012). Brief mental breaks and content-free cues may not keep you focused. *Experimental Brain Research, 219*(1), 37-46.

Helton, W. S., & Warm, J. S. (2008). Signal salience and the mindlessness theory of vigilance. *Acta Psychologica, 129*(1), 18-25.

Herrmann, C. S., Fründ, I., & Lenz, D. (2010). Human gamma-band activity: A review on cognitive and behavioral correlates and network models. *Neuroscience & Biobehavioral Reviews, 34*(7), 981-992.

Hertig-Godeschalk, A., Skorucak, J., Malafeev, A., Achermann, P., Mathis, J., & Schreier, D. R. (2020). Microsleep episodes in the borderland between wakefulness and sleep. *Sleep, 43*(1).

Hitchcock, E. M., Warm, J. S., Matthews, G., Dember, W. N., Shear, P. K., Tripp, L. D., . . . Parasuraman, R. (2003). Automation cueing modulates cerebral blood flow and vigilance in a simulated air traffic control task. *Theoretical Issues in Ergonomics Science, 4*(1-2), 89-112.

Hoechstetter, K., Bornfleth, H., Weckesser, D., Ille, N., Berg, P., & Scherg, M. (2004). BESA source coherence: a new method to study cortical oscillatory coupling. *Brain Topography, 16*(4), 233-238.

Holm, L., Ullén, F., & Madison, G. (2011). Intelligence and temporal accuracy of behaviour: unique and shared associations with reaction time and motor timing. *Experimental Brain Research, 214*(2), 175.

Holmes, A. P., Blair, R. C., Watson, J. D. G., & Ford, I. (1996). Nonparametric Analysis of Statistic Images from Functional Mapping Experiments. *Journal of Cerebral Blood Flow & Metabolism, 16*(1), 7-22.

Hong, X., To, X. V., Teh, I., Soh, J. R., & Chuang, K.-H. (2015). Evaluation of EPI distortion correction methods for quantitative MRI of the brain at high magnetic field. *Magnetic Resonance Imaging, 33*(9), 1098-1105.

Horne, J. A., & Reyner, L. A. (1995). Sleep related vehicle accidents. *British Medical Journal, 310*(6979), 565-567.

Horowitz, A. L. (2012). *MRI physics for physicians*: Springer Science & Business Media.

Hossein Hosseini, S. A., Sohrabpour, A., Akcakaya, M., & He, B. (2018). Electromagnetic Brain Source Imaging by Means of a Robust Minimum Variance Beamformer. *IEEE Transactions on Biomedical Engineering, 65*(10), 2365-2374.

Hosseini, S. A. H., Sohrabpour, A., Akçakaya, M., & He, B. (2018). Electromagnetic Brain Source Imaging by Means of a Robust Minimum Variance Beamformer. *IEEE Transactions on Biomedical Engineering, 65*(10), 2365-2374.

Huang, C.-S., Pal, N. R., Chuang, C.-H., & Lin, C.-T. (2015). Identifying changes in EEG information transfer during drowsy driving by transfer entropy. *Frontiers in Human Neuroscience, 9*(570).

Huang, R.-S., Jung, T.-P., & Makeig, S. (2007). *Event-related brain dynamics in continuous sustained-attention tasks.* Proceedings of International Conference on Foundations of Augmented Cognition 65-74.

Huber, R., Felice Ghilardi, M., Massimini, M., & Tononi, G. (2004). Local sleep and learning. *Nature, 430*(6995), 78-81.

Huettel, S. A., Song, A. W., & McCarthy, G. (2004). *Functional magnetic resonance imaging* (Vol. 1): Sinauer Associates Sunderland, MA.

Huijser, S., van Vugt, M. K., & Taatgen, N. A. (2018). The wandering self: Tracking distracting self-generated thought in a cognitively demanding context. *Consciousness and Cognition, 58*, 170-185.

Hung, C.-S., Sarasso, S., Ferrarelli, F., Riedner, B., Ghilardi, M. F., Cirelli, C., & Tononi, G. (2013). Local experience-dependent changes in the wake EEG after prolonged wakefulness. *Sleep, 36*(1), 59-72.

Hutchinson, J. B., & Turk-Browne, N. B. (2012). Memory-guided attention: Control from multiple memory systems. *Trends in Cognitive Sciences, 16*(12), 576-579.

Iannetti, G. D., Niazy, R. K., Wise, R. G., Jezzard, P., Brooks, J. C. W., Zambreanu, L., . . . Tracey, I. (2005). Simultaneous recording of laser-evoked brain potentials and continuous, high-field functional magnetic resonance imaging in humans. *NeuroImage, 28*(3), 708-719.

Iannotti, G. R., Pittau, F., Michel, C. M., Vulliemoz, S., & Grouiller, F. (2015). Pulse artifact detection in simultaneous EEG–fMRI recording based on EEG map topography. *Brain Topography, 28*(1), 21-32.

Innes, C. R. H., Poudel, G. R., & Jones, R. D. (2013). Efficient and regular patterns of nighttime sleep are related to increased vulnerability to microsleeps following a single night of sleep restriction. *Chronobiology International, 30*(9), 1187-1196.

Innes, C. R. H., Poudel, G. R., Signal, T. L., & Jones, R. D. (2010). *Behavioural microsleeps in normally-rested people.* Proceedings of Annual International Conference IEEE Engineering Medicine Biology Society 4448-4451.

Jafri, M. J., Pearlson, G. D., Stevens, M., & Calhoun, V. D. (2008). A method for functional network connectivity among spatially independent resting-state components in schizophrenia. *NeuroImage, 39*(4), 1666-1681.

Jansen, M., White, T. P., Mullinger, K. J., Liddle, E. B., Gowland, P. A., Francis, S. T., . . . Liddle, P. F. (2012). Motion-related artefacts in EEG predict neuronally plausible patterns of activation in fMRI data. *NeuroImage, 59*(1), 261-270.

Jatoi, M. A., & Kamel, N. (2018). EEG inverse problem I: Classical techniques. In *Brain Source Localization Using EEG Signal Analysis* (pp. 63-75): CRC Press.

Jatoi, M. A., Kamel, N., Malik, A. S., & Faye, I. (2014). EEG based brain source localization comparison of sLORETA and eLORETA. *Australasian Physical & Engineering Sciences in Medicine, 37*(4), 713-721.

Jenkinson, M. (2003). Fast, automated, N-dimensional phase-unwrapping algorithm. *Magnetic Resonance in Medicine, 49*(1), 193-197.

Jenkinson, M., Bannister, P., Brady, M., & Smith, S. (2002). Improved Optimization for the Robust and Accurate Linear Registration and Motion Correction of Brain Images. *NeuroImage, 17*(2), 825-841.

Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W., & Smith, S. M. (2012). FSL. *NeuroImage, 62*(2), 782-790.

Jenkinson, M., & Chappell, M. (2018). *Introduction to neuroimaging analysis*: Oxford University Press.

Jenkinson, M., Pechaud, M., & Smith, S. (2005). *BET2: MR-based estimation of brain, skull and scalp surfaces.* Proceedings of 11th Ann. Meet. Org. Hum. Brain Map. 167.

Jenkinson, M., & Smith, S. (2001). A global optimisation method for robust affine registration of brain images. *Medical Image Analysis, 5*(2), 143-156.

Jenkinson, M., & Smith, S. M. (2006). Pre-processing of BOLD fMRI data. In (pp. 1): Oxford University Centre for Functional MRI of the Brain (FMRIB).

Jezzard, P. (2012). Correction of geometric distortion in fMRI data. *NeuroImage, 62*(2), 648-651.

Jiang, X., Bian, G.-B., & Tian, Z. (2019). Removal of Artifacts from EEG Signals: A Review. *Sensors (Basel, Switzerland), 19*(5), 987.

Johannsdottir, K. R., & Herdman, C. M. (2010). The role of working memory in supporting drivers' situation awareness for surrounding traffic. *Human Factors, 52*(6), 663-673.

Jones, R. (2011). Arousal-related lapses of responsiveness: Characteristics, detection, and underlying mechanisms. *Sleep & Biological Rhythms, 9*(4), 222.

Jones, R. D., Innes, C. R. H., & Shoorangiz, R. (2018). *Reduced-responsiveness events: Taxonomy and definitions*. Retrieved from Internal report of NeuroTech

Jones, R. D., Poudel, G. R., Innes, C. R. H., Davidson, P. R., Peiris, M. T. R., Malla, A. M., . . . Bones, P. J. (2010). *Lapses of responsiveness: Characteristics, detection, and underlying mechanisms.* Proceedings of Annual International Conference of the IEEE Engineering in Medicine and Biology 1788-1791.

Jonides, J., Lewis, R. L., Nee, D. E., Lustig, C. A., Berman, M. G., & Moore, K. S. (2007). The mind and brain of short-term memory. *Annual Review of Psychology, 59*(1), 193-224.

Jonmohamadi, Y., Poudel, G. R., Innes, C. R. H., & Jones, R. D. (2016). Microsleeps are associated with stage-2 sleep spindles from hippocampal-temporal network. *International Journal of Neural Systems, 26*(04), 12pp.

Jorge, J., Grouiller, F., Gruetter, R., Van Der Zwaag, W., & Figueiredo, P. (2015). Towards high-quality simultaneous EEG-fMRI at 7 T: detection and reduction of EEG artifacts due to head motion. *NeuroImage, 120*, 143-153.

Jubera-García, E., Gevers, W., & Van Opstal, F. (2019). Influence of content and intensity of thought on behavioral and pupil changes during active mind-wandering, off-focus, and on-task states. *Attention, Perception, & Psychophysics, 82*(3), 1125-1135.

Kahneman, D. (1973). *Attention and effort* (Vol. 1063): Citeseer.

Kan, S., Misaki, M., Koike, T., & Miyauchi, S. (2008). Different modulation of medial superior temporal activity across saccades: a functional magnetic resonance imaging study. *NeuroReport, 19*, 133-137.

Kane, M. J., Conway, A. R., Hambrick, D. Z., & Engle, R. W. (2007). Variation in working memory capacity as variation in executive attention and control. In A. Miyake, A. Conway, & C. Jarrold (Eds.), *Variation in working memory* (Vol. 1, pp. 21-48): OUP USA.

Kang, O. E., Huffer, K. E., & Wheatley, T. P. (2014). Pupil dilation dynamics track attention to high-level information. *PLoS ONE, 9*(8), e102463.

Kaufmann, C., Wehrle, R., Wetter, T. C., Holsboer, F., Auer, D. P., Pollmächer, T., & Czisch, M. (2006). Brain activation and hypothalamic functional connectivity during human non-rapid eye movement sleep: an EEG/fMRI study. *Brain, 129*(3), 655-667.

Kawagoe, T., Onoda, K., & Yamaguchi, S. (2019). The neural correlates of "mind blanking": When the mind goes away. *Human Brain Mapping, 0*(0).

Kelly, R. E., Alexopoulos, G. S., Wang, Z., Gunning, F. M., Murphy, C. F., Morimoto, S. S., . . . Hoptman, M. J. (2010). Visual inspection of independent components: Defining a procedure for artifact removal from fMRI data. *Journal of Neuroscience Methods, 189*(2), 233-245.

Kim, B., Boes, J. L., Bland, P. H., Chenevert, T. L., & Meyer, C. R. (1999). Motion correction in fMRI via registration of individual slices into an anatomical volume. *Magnetic Resonance in Medicine, 41*(5), 964-972.

Kirmizi-Alsan, E., Bayraktaroglu, Z., Gurvit, H., Keskin, Y. H., Emre, M., & Demiralp, T. (2006). Comparative analysis of event-related potentials during Go/NoGo and CPT: decomposition of electrophysiological markers of response inhibition and sustained attention. *Brain Research, 1104*(1), 114-128.

Kleitman, N. (1963). *Sleep and wakefulness*: University of Chicago Press.

Klem, G. H., Lüders, H. O., Jasper, H., & Elger, C. (1999). The ten-twenty electrode system of the International Federation. *Electroencephalography and Clinical Neurophysiology, 52*(3), 3-6.

Konishi, M., Brown, K., Battaglini, L., & Smallwood, J. (2017). When attention wanders: Pupillometric signatures of fluctuations in external attention. *Cognition, 168*, 16-26.

Krimsky, M., Forster, D. E., Llabre, M. M., & Jha, A. P. (2017). The influence of time on task on mind wandering and visual working memory. *Cognition, 169*, 84-90.

Kristjansson, S. D., Stern, J. A., Brown, T. B., & Rohrbaugh, J. W. (2009). Detecting phasic lapses in alertness using pupillometric measures. *Applied Ergonomics, 40*(6), 978-986.

Kucyi, A. (2018). Just a thought: How mind-wandering is represented in dynamic brain connectivity. *NeuroImage, 180*, 505-514.

Kucyi, A., & Davis, K. D. (2014). Dynamic functional connectivity of the default mode network tracks daydreaming. *NeuroImage, 100*, 471-480.

Kucyi, A., Hove, M. J., Esterman, M., Hutchison, R. M., & Valera, E. M. (2017). Dynamic brain network correlates of spontaneous fluctuations in attention. *Cerebral Cortex, 27*(3), 1831-1840.

Kurzban, R., Duckworth, A., Kable, J. W., & Myers, J. (2013). An opportunity cost model of subjective effort and task performance. *Behavioral and Brain Sciences, 36*(6), 661-679.

Kyllonen, P., & Kell, H. (2017). What Is Fluid Intelligence? Can It Be

Improved? In M. Rosén, K. Yang Hansen, & U. Wolff (Eds.), *Cognitive Abilities and Educational Outcomes* (pp. 15-37): Springer International Publishing.

LaBar, K. S., Gitelman, D. R., Parrish, T. B., & Mesulam, M.-M. (1999). Neuroanatomic overlap of working memory and spatial attention networks: a functional MRI comparison within subjects. *NeuroImage, 10*(6), 695-704.

Landau, A., Esterman, M., Robertson, L., Bentin, S., & Prinzmetal, W. (2007). Different Effects of Voluntary and Involuntary Attention on EEG Activity in the Gamma Band. *The Journal of Neuroscience, 27*, 11986 - 11990.

Larue, G. S., Rakotonirainy, A., & Pettitt, A. N. (2015). Predicting reduced driver alertness on monotonous highways. *IEEE Pervasive Computing, 14*(2), 78-85.

Leechawengwongs, M., Leechawengwongs, E., Sukying, C., & Udomsubpayakul, U. (2006). Role of drowsy driving in traffic accidents: a questionnaire survey of Thai commercial bus/truck drivers. *Journal-Medical Association of Thailand, 89*(11), 1845.

Lemercier, C., Pêcher, C., Berthié, G., Valéry, B., Vidal, V., Paubel, P.-V., . . . Maury, B. (2014). Inattention behind the wheel: How factual internal thoughts impact attentional control while driving. *Safety Science, 62*, 279-285.

Li, R., Ryu, J. H., Vincent, P., Springer, M., Kluger, D., Levinsohn, E. A., . . . Blumenfeld, H. (2021). The pulse: Transient fMRI signal increases in subcortical arousal systems during transitions in attention. *NeuroImage, 232*, 117873.

Lindquist, M., & Wager, T. (2013). Principles of fMRI 1. Retrieved from https://www.coursera.org/learn/functional-mri#

Lindquist, M. A. (2008). The statistical analysis of fMRI data. *Statistical Science, 23*(4), 439-464.

Lindquist, M. A., & Wager, T. D. (2007). Validity and power in hemodynamic response modeling: A comparison study and a new approach. *Human Brain Mapping, 28*(8), 764-784.

Lindsley, D. B. (1952). Psychological phenomena and the electroencephalogram. *Electroencephalography and Clinical Neurophysiology, 4*(4), 443-456.

Liu, A., Li, J., McKeown, M. J., & Wang, Z. J. (2016). Brain Connectivity Assessed with Functional MRI. In K. Iniewski (Ed.), *MRI: Physics, image reconstruction, and analysis*: CRC Press.

Liu, T. T., Nalci, A., & Falahpour, M. (2017). The global signal in fMRI: Nuisance or Information? *NeuroImage, 150*, 213-229.

Liu, Y., Bengson, J., Huang, H., Mangun, G. R., & Ding, M. (2014). Top-down Modulation of Neural Activity in Anticipatory Visual Attention: Control Mechanisms Revealed by Simultaneous EEG-fMRI. *Cerebral Cortex, 26*(2), 517-529.

López-Ramón, M. F., Castro, C., Roca, J., Ledesma, R., & Lupiañez, J. (2011). Attentional networks functioning, age, and attentional lapses while driving. *Traffic Injury Prevention, 12*(5), 518-528.

Lowe, M. J., Dzemidzic, M., Lurito, J. T., Mathews, V. P., & Phillips, M. D. (2000). Correlations in Low-Frequency BOLD Fluctuations Reflect Cortico-Cortical Connections. *NeuroImage, 12*(5), 582-587.

Lückmann, H. C., Jacobs, H. I. L., & Sack, A. T. (2014). The cross-functional role of frontoparietal regions in cognition: internal attention as the overarching mechanism. *Progress in Neurobiology, 116*, 66-86.

Macaluso, E., & Doricchi, F. (2013). Attention and predictions: control of spatial attention beyond the endogenous-exogenous dichotomy. *Frontiers in Human Neuroscience, 7*, 685.

MacDonald, A. W., Cohen, J. D., Stenger, V. A., & Carter, C. S. (2000). Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. *Science, 288*(5472), 1835-1838.

Macdonald, J., Mathan, S., & Yeung, N. (2011). Trial-by-Trial Variations in Subjective Attentional State are Reflected in Ongoing Prestimulus EEG Alpha Oscillations. *Frontiers in Psychology, 2*(82).

Mackworth, J. F. (1964). Performance decrement in vigilance, threshold, and high-speed perceptual motor tasks. *Canadian Journal of Psychology, 18*(3), 209.

Mackworth, N. H. (1948). The breakdown of vigilance during prolonged visual search. *Quarterly Journal of Experimental Psychology, 1*(1), 6-21.

Maillet, D., Beaty, R. E., Kucyi, A., & Schacter, D. L. (2019). Large-scale network interactions involved in dividing attention between the external environment and internal thoughts to pursue two distinct goals. *NeuroImage, 197*, 49-59.

Makeig, S., Bell, A. J., Jung, T.-P., & Sejnowski, T. J. (1996). *Independent component analysis of electroencephalographic data.* Proceedings of Advances in Neural Information Processing Systems 145-151.

Malla, A. M., Davidson, P. R., Bones, P. J., Green, R., & Jones, R. D. (2010). *Automated video-based measurement of eye closure for detecting behavioral microsleep.* Proceedings of 2010 Annual International Conference of the IEEE Engineering in Medicine and Biology 6741-6744.

Manly, T., Robertson, I. H., Galloway, M., & Hawkins, K. (1999). The absent mind:: further investigations of sustained attention to response. *Neuropsychologia, 37*(6), 661-670.

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.

Maris, E., & Oostenveld, R. (2007). Nonparametric statistical testing of EEG- and MEG-data. *Journal of Neuroscience Methods, 164*(1), 177-190.

Maris, E., Schoffelen, J.-M., & Fries, P. (2007). Nonparametric statistical testing of coherence differences. *Journal of Neuroscience Methods, 163*(1), 161-175.

Marqui, R. P., Michel, C. M., & Lehmann, D. (1994). Low-resolution electromagnetic tomography–a new method for localizing electrical activity in the brain. *International Journal of Psychophysiology, 18*(1), 49-65.

Martini, F., & Bartholomew, E. (1998). The integumentary system. In *Fundamentals of anatomy and physiology (Prentice Hall, New Jersey)* (pp. 148-161).

Marzano, C., Ferrara, M., Moroni, F., & De Gennaro, L. (2011). Electroencephalographic sleep inertia of the awakening brain. *Neuroscience, 176*, 308-317.

Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: The default network and stimulus-independent thought. *Science, 315*(5810), 393-395.

Massar, S. A., Lim, J., Sasmita, K., & Chee, M. W. (2016). Rewards boost sustained attention through higher effort: A value-based decision making approach. *Biological Psychology, 120*, 21-27.

Massar, S. A., Sasmita, K., Lim, J., & Chee, M. W. (2018). Motivation alters implicit temporal attention through sustained and transient mechanisms: A behavioral and pupillometric study. *Psychophysiology, 55*(12), e13275.

Matthews, G., Davies, D. R., Stammers, R. B., & Westerman, S. J. (2000). *Human performance: Cognition, stress, and individual differences*: Psychology Press.

Mazaika, P. K., Whitfield, S., & Cooper, J. C. (2005). Detection and repair of transient artifacts in fMRI data. *NeuroImage, 26*(Suppl 1), S36.

McAvinue, L. P., Habekost, T., Johnson, K. A., Kyllingsbæk, S., Vangkilde, S., Bundesen, C., & Robertson, I. H. (2012). Sustained attention, attentional selectivity, and attentional capacity across the lifespan. *Attention, Perception, & Psychophysics, 74*(8), 1570-1582.

McIntire, L., McKinley, R. A., McIntire, J., Goodyear, C., & Nelson, J. (2013). Eye metrics: An alternative vigilance detector for military operators. *Military Psychology, 25*(5), 502-513.

McKeown, M. J., Hansen, L. K., & Sejnowsk, T. J. (2003). Independent component analysis of functional MRI: what is signal and what is noise? *Current Opinion in Neurobiology, 13*(5), 620-629.

McKeown, M. J., Makeig, S., Brown, G. G., Jung, T. P., Kindermann, S. S., Bell, A. J., & Sejnowski, T. J. (1998). Analysis of fMRI data by blind separation into independent spatial components. *Human Brain Mapping, 6*(3), 160-188.

McKinley, R. A., McIntire, L. K., Schmidt, R., Repperger, D. W., & Caldwell, J. A. (2011). Eye metrics: An alternative vigilance detector for military operators. *Human Factors, 53*(4), 403-414.

McVay, J. C., & Kane, M. J. (2010). Does mind wandering reflect executive function or executive failure? Comment on Smallwood and Schooler (2006) and Watkins (2008). *Psychological Bulletin, 136*(2), 188-197.

Melloni, L., Molina, C., Pena, M., Torres, D., Singer, W., & Rodriguez, E. (2007). Synchronization of neural activity across cortical areas correlates with conscious perception. *The Journal of neuroscience : the official journal of the Society for Neuroscience, 27*(11), 2858-2865.

Meng, C., & Zhao, X. (2017). Webcam-based eye movement analysis using CNN. *IEEE Access, 5*, 19581-19587.

Menon, V., & Uddin, L. Q. (2010). Saliency, switching, attention and control: a network model of insula function. *Brain Structure & Function, 214*(5-6), 655-667.

Mensen, A., & Khatami, R. (2013). Advanced EEG analysis using threshold-free cluster-enhancement and non-parametric statistics. *NeuroImage, 67*, 111-118.

Michel, C. M., & Brunet, D. (2019). EEG Source Imaging: A Practical Review of the Analysis Steps. *Frontiers in Neurology, 10*.

Michel, C. M., & He, B. (2012). EEG mapping and source imaging. In *Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields: Sixth Edition* (pp. 1179-1202): Wolters Kluwer Health Adis (ESP).

Michel, C. M., Murray, M. M., Lantz, G., Gonzalez, S., Spinelli, L., & Grave de Peralta, R. (2004). EEG source imaging. *Clinical Neurophysiology, 115*(10), 2195-2222.

Miinalainen, T., Rezaei, A., Us, D., Nüßing, A., Engwer, C., Wolters, C. H., & Pursiainen, S. (2019). A realistic, accurate and fast source modeling approach for the EEG forward problem. *NeuroImage, 184*, 56-67.

Mikl, M., Mareček, R., Hluštík, P., Pavlicová, M., Drastich, A., Chlebus, P., . . . Krupa, P. (2008). Effects of spatial smoothing on fMRI group inferences. *Magnetic Resonance Imaging, 26*(4), 490-503.

Mitko, A., Rothlein, D., Poole, V., Robinson, M., McGlinchey, R., DeGutis, J., . . . Esterman, M. (2019). Individual differences in sustained attention are associated with cortical thickness. *Human Brain Mapping, 40*(11), 3243-3253.

Mitra, P. P., & Pesaran, B. (1999). Analysis of Dynamic Brain Imaging Data. *Biophysical Journal, 76*(2), 691-708.

Mittner, M., Boekel, W., Tucker, A. M., Turner, B. M., Heathcote, A., & Forstmann, B. U. (2014). When the Brain Takes a Break: A Model-Based Analysis of Mind Wandering. *The Journal of Neuroscience, 34*(49), 16286-16295.

Mittner, M., Hawkins, G. E., Boekel, W., & Forstmann, B. U. (2016). A neural model of mind wandering. *Trends in Cognitive Sciences, 20*(8), 570-578.

Mo, J., Liu, Y., Huang, H., & Ding, M. (2013). Coupling between visual alpha oscillations and default mode activity. *NeuroImage, 68*, 112-118.

Möcks, J., & Gasser, T. (1984). How to select epochs of the EEG at rest for quantitative analysis. *Electroencephalography and Clinical Neurophysiology, 58*(1), 89-92.

Molina, E., Sanabria, D., Jung, T.-P., & Correa, Á. (2019). Electroencephalographic and peripheral temperature dynamics during a prolonged psychomotor vigilance task. *Accident Analysis & Prevention, 126*, 198-208.

Montes, S. A., Introzzi, I. M., Ledesma, R. D., & López, S. S. (2016). Selective attention and error proneness while driving: research using a conjunctive visual search task. *Avances en Psicología Latinoamericana, 34*(2), 195-203.

Monti, M. (2011). Statistical analysis of fMRI time-series: A critical review of the GLM approach. *Frontiers in Human Neuroscience, 5*(28).

Moraitou, D., & Efklides, A. (2009). The blank in the mind questionnaire (BIMQ). *European Journal of Psychological Assessment, 25*(2), 115-122.

Morris, L., & Dawson, S. (2008). *Relationships between age, executive function and driving behaviour.* Proceedings of Proceedings of the Australasian road safety research, policing and education conference 96-103.

Mosher, J. C., & Leahy, R. M. (1998). Recursive MUSIC: a framework for EEG and MEG source localization. *IEEE Transactions on Biomedical Engineering, 45*(11), 1342-1354.

Mosher, J. C., & Leahy, R. M. (1999). Source localization using recursively applied and projected (RAP) MUSIC. *IEEE Transactions on Signal Processing, 47*(2), 332-340.

Mumford, J. A. (2012). A power calculation guide for fMRI studies. *Social Cognitive and Affective Neuroscience, 7*(6), 738-742.

Mumford, J. A., & Poldrack, R. A. (2007). Modeling group fMRI data. *Social Cognitive and Affective Neuroscience, 2*(3), 251-257.

Murta, T., Leite, M., Carmichael, D. W., Figueiredo, P., & Lemieux, L. (2015). Electrophysiological correlates of the BOLD signal for EEG-informed fMRI. *Human Brain Mapping, 36*(1), 391-414.

Muthukumaraswamy, S. (2013). High-frequency brain activity and muscle artifacts in MEG/EEG: A review and recommendations. *Frontiers in Human Neuroscience, 7*.

Myers, N. E., Stokes, M. G., & Nobre, A. C. (2017). Prioritizing information during working memory: beyond sustained internal attention. *Trends in Cognitive Sciences, 21*(6), 449-461.

Naughton, M., & Pierce, R. (1991). Sleep apnoea's contribution to the road toll. *Australian and New Zealand Journal of Medicine, 21*(6), 833-834.

Neigel, A. R., Claypoole, V. L., Fraulini, N. W., Waldfogle, G. E., & Szalma, J. L. (2019a). Where is my mind? Examining mind-wandering and vigilance performance. *Experimental Brain Research, 237*(2), 557-571.

Neigel, A. R., Claypoole, V. L., & Szalma, J. L. (2019b). Effects of state motivation in overload and underload vigilance task scenarios. *Acta Psychologica, 197*, 106-114.

Neugebauer, F., Möddel, G., Rampp, S., Burger, M., & Wolters, C. H. (2017). The Effect of Head Model Simplification on Beamformer Source Localization. *Frontiers in Neuroscience, 11*(625).

Niazy, R. K., Beckmann, C. F., Iannetti, G. D., Brady, J. M., & Smith, S. M. (2005). Removal of FMRI environment artifacts from EEG data using optimal basis sets. *NeuroImage, 28*(3), 720-737.

Nichols, T. E., Das, S., Eickhoff, S. B., Evans, A. C., Glatard, T., Hanke, M., . . . Poline, J.-B. (2017). Best practices in data analysis and sharing in neuroimaging using MRI. *Nature Neuroscience, 20*(3), 299-303.

Nichols, T. E., & Holmes, A. P. (2002). Nonparametric permutation tests for functional neuroimaging: A primer with examples. *Human Brain Mapping, 15*(1), 1-25.

Nickerson, L. D., Smith, S. M., Öngür, D., & Beckmann, C. F. (2017). Using dual regression to investigate network shape and amplitude in functional connectivity analyses. *Frontiers in Neuroscience, 11*, 115.

Niedermeyer, E. (1999a). Maturation of EEG: development of walking and sleep patterns. In E. Niedermeyer & F. Lopes da Silva (Eds.), *Electroencephalography Basic Principles, Clinical Applications, and Related Fields*. Lippincott, Williams and Wilkins, Philadelphia, Pennsylvania: Lippincott Williams & Wilkins.

Niedermeyer, E. (1999b). Sleep and EEG. In E. Niedermeyer & F. Lopes da Silva (Eds.), *Electroencephalography Basic Principles, Clinical Applications, and Related Fields*. Lippincott, Williams and Wilkins, Philadelphia, Pennsylvania: Lippincott Williams & Wilkins.

Niedermeyer, E., & da Silva, F. L. (2005). *Electroencephalography: basic principles, clinical applications, and related fields*: Lippincott Williams & Wilkins.

Nolte, G., Bai, O., Wheaton, L., Mari, Z., Vorbach, S., & Hallett, M. (2004). Identifying true brain interaction from EEG data using the imaginary part of coherency. *Clinical Neurophysiology, 115*(10), 2292-2307.

Ogawa, S., Lee, T. M., Kay, A. R., & Tank, D. W. (1990). Brain magnetic resonance imaging with contrast dependent on blood oxygenation. *Proceedings of the National Academy of Sciences of the United States of America, 87*(24), 9868-9872.

Ohara, S., Crone, N. E., Weiss, N., Treede, R.-D., & Lenz, F. A. (2004). Cutaneous painful laser stimuli evoke responses recorded directly from primary somatosensory cortex in awake humans. *Journal of Neurophysiology, 91*(6), 2734-2746.

Olcese, U., Oude Lohuis, M. N., & Pennartz, C. M. A. (2018). Sensory Processing Across Conscious and Nonconscious Brain States: From Single Neurons to Distributed Networks for Inferential Representation. *Frontiers in Systems Neuroscience, 12*(49).

Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J.-M. (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience, 2011*, 156869-156869.

Oswal, A., Litvak, V., Brown, P., Woolrich, M., & Barnes, G. (2014). Optimising beamformer regions of interest analysis. *NeuroImage, 102 Pt 2*, 945-954.

Ottaviani, C., Shahabi, L., Tarvainen, M., Cook, I., Abrams, M., & Shapiro, D. (2015). Cognitive, behavioral, and autonomic correlates of mind wandering and perseverative cognition in major depression. *Frontiers in Neuroscience, 8*(433), 1-9.

Pajula, J., & Tohka, J. (2016). How Many Is Enough? Effect of Sample Size in Inter-Subject Correlation Analysis of fMRI. *Computational Intelligence and Neuroscience, 2016*, 2094601-2094601.

Parasuraman, R., Warm, J., & See, J. (1998). Brain systems of vigilance. In R. Parasuraman (Ed.), *The attentive brain* (pp. 221–256): Cambridge, MA: The MIT Press.

Parker, D., Liu, X., & Razlighi, Q. R. (2017). Optimal slice timing correction and its interaction with fMRI parameters and artifacts. *Medical Image Analysis, 35*, 434-445.

Pascual-Marqui, R. D. (1999). Review of methods for solving the EEG inverse problem. *International Journal of Bioelectromagnetism, 1*(1), 75-86.

Pascual-Marqui, R. D. (2002). Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. *Methods and Findings in Experimental & Clinical Pharmacology, 24*(Suppl D), 5-12.

Pascual-Marqui, R. D. (2007). Discrete, 3D distributed, linear imaging methods of electric neuronal activity. Part 1: exact, zero error localization. *arXiv*.

Pascual-Marqui, R. D. (2009). Theory of the EEG inverse problem. In N. Thakor & S. Tong (Eds.), *Quantitative EEG analysis: methods and clinical applications* (pp. 121-140): Artech House.

Pauling, L., & Coryell, C. D. (1936). The magnetic properties and structure of hemoglobin, oxyhemoglobin and carbonmonoxyhemoglobin. *Proceedings of the National Academy of Sciences, 22*(4), 210.

Paus, T. (2001). Primate anterior cingulate cortex: where motor control, drive and cognition interface. *Nature Reviews Neuroscience, 2*(6), 417-424.

Peiris, M. T. R., Jones, R. D., Carroll, G. J., & Bones, P. J. (2004). *Investigation of lapses of consciousness using a tracking task: preliminary results.* Proceedings of 26th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 4721-4724.

Peiris, M. T. R., Jones, R. D., Davidson, P. R., Carroll, G. J., & Bones, P. J. (2006). Frequent lapses of responsiveness during an extended visuomotor tracking task in non-sleep-deprived subjects. *Journal of Sleep Research, 15*(3), 291-300.

Peiris, M. T. R., Jones, R. D., Davidson, P. R., Carroll, G. J., Parkin, P. J., Signal, T. L., . . . Bones, P. J. (2005). *Identification of vigilance lapses using EEG/EOG by expert human raters.* Proceedings of Annual International Conference of the IEEE Engineering in Medicine and Biology Society 5735-5738.

Peiris, T. R. M., Paul, R. D., Philip, J. B., & Richard, D. J. (2011). Detection of lapses in responsiveness from the EEG. *Journal of Neural Engineering, 8*(1), 15pp.

Pepin, G., Malin, S., Jallais, C., Moreau, F., Fort, A., Navarro, J., . . . Gabaude, C. (2018). Do distinct mind wandering differently disrupt drivers? Interpretation of physiological and behavioral pattern with a data triangulation method. *Consciousness and Cognition, 62*, 69-81.

Pernet, C., Garrido, M., Gramfort, A., Maurits, N., Michel, C., Pang, E., . . . Puce, A. (2018). Best practices in data analysis and sharing in neuroimaging using MEEG. *Nature Neuroscience, 20*, 299–303.

Pernet, C., & Poline, J.-B. (2015). Improving functional magnetic resonance imaging reproducibility. *Gigascience, 4*(1), 15.

Pernet, C. R. (2014). Misconceptions in the use of the general linear model applied to functional MRI: a tutorial for junior neuro-imagers. *Frontiers in Neuroscience, 8*, 1.

Petilli, M. A., Trisolini, D. C., & Daini, R. (2018). Sustained-Paced Finger Tapping: A Novel Approach to Measure Internal Sustained Attention. *Frontiers in Psychology, 9*(881).

Philip, P., Sagaspe, P., Lagarde, E., Leger, D., Ohayon, M. M., Bioulac, B., . . . Taillard, J. (2010). Sleep disorders and accidental risk in a large group of regular registered highway drivers. *Sleep Medicine, 11*(10), 973-979.

Philip, P., Vervialle, F., Le Breton, P., Taillard, J., & Horne, J. A. (2001). Fatigue, alcohol, and serious road crashes in France: factorial study of national data. *British Medical Journal, 322*(7290), 829-830.

Piazza, C., Cantiani, C., Akalin-Acar, Z., Miyakoshi, M., Benasich, A. A., Reni, G., . . . Makeig, S. (2016). ICA-derived cortical responses indexing rapid multi-feature auditory processing in six-month-old infants. *NeuroImage, 133*, 75-87.

Picchioni, D., Fukunaga, M., Carr, W. S., Braun, A. R., Balkin, T. J., Duyn, J. H., & Horovitz, S. G. (2008). fMRI differences between early and late stage-1 sleep. *Neuroscience Letters, 441*(1), 81-85.

Piccoli, T., Valente, G., Linden, D. E. J., Re, M., Esposito, F., Sack, A. T., & Salle, F. D. (2015). The default mode network and the working memory network are not anti-correlated during all phases of a working memory task. *PLoS ONE, 10*(4), e0123354.

Pierrot-Deseilligny, C., Milea, D., & Müri, R. M. (2004). Eye movement control by the cerebral cortex. *Current Opinion in Neurology, 17*(1).

Pierrot-Deseilligny, C., Müri, R. M., Ploner, C. J., Gaymard, B., Demeret, S., & Rivaud-Pechoux, S. (2003). Decisional role of the dorsolateral prefrontal cortex in ocular motor behaviour. *Brain, 126*(6), 1460-1473.

Pion-Tonachini, L., Kreutz-Delgado, K., & Makeig, S. (2019). ICLabel: An automated electroencephalographic independent component classifier, dataset, and website. *NeuroImage, 198*, 181-197.

Pivik, R., & Harman, K. (1995). A reconceptualization of EEG alpha activity as an index of arousal during sleep: all alpha activity is not equal. *Journal of Sleep Research, 4*(3), 131-137.

Poldrack, R. A. (2007). Region of interest analysis for fMRI. *Social Cognitive and Affective Neuroscience, 2*(1), 67-70.

Poldrack, R. A., Fletcher, P. C., Henson, R. N., Worsley, K. J., Brett, M., & Nichols, T. E. (2008). Guidelines for reporting an fMRI study. *NeuroImage, 40*(2), 409-414.

Poline, J.-B., & Brett, M. (2012). The general linear model and fMRI: Does love last forever? *NeuroImage, 62*(2), 871-880.

Poudel, G. R. (2010). *Functional Magnetic Resonance Imaging of Lapses of Responsiveness During Visuomotor Tracking: A Thesis Submitted for the Degree of Doctor of Philosophy at the University of Otago, New Zealand*: University of Otago.

Poudel, G. R., Hawes, S., Innes, C. R. H., Parsons, N., Drummond, S. P. A., Caeyensberghs, K., & Jones, R. D. (2021). RoWDI: rolling window detection of sleep intrusions in the awake brain using fMRI. *Journal of Neural Engineering, 18*(5), 056063.

Poudel, G. R., Innes, C. R. H., Bones, P. J., & Jones, R. D. (2010a, Aug. 31 2010-Sept. 4 2010). *The relationship between behavioural microsleeps, visuomotor performance and EEG theta.* Proceedings of Annual International Conference of the IEEE Engineering in Medicine and Biology Society 4452-4455.

Poudel, G. R., Innes, C. R. H., Bones, P. J., Watts, R., & Jones, R. D. (2014). Losing the struggle to stay awake: Divergent thalamic and cortical activity during microsleeps. *Human Brain Mapping, 35*(1), 257-269.

Poudel, G. R., Innes, C. R. H., & Jones, R. D. (2012). Cerebral perfusion differences between drowsy and nondrowsy individuals after acute sleep restriction. *Sleep, 35*(8), 1085-1096.

Poudel, G. R., Innes, C. R. H., & Jones, R. D. (2013). Distinct neural correlates of time-on-task and transient errors during a visuomotor tracking task after sleep restriction. *NeuroImage, 77*, 105-113.

Poudel, G. R., Innes, C. R. H., & Jones, R. D. (2018). Temporal evolution of neural activity and connectivity during microsleeps when rested and following sleep restriction. *NeuroImage, 174*, 263-273.

Poudel, G. R., Jones, R. D., & Innes, C. R. (2008). A 2-D pursuit tracking task for behavioural detection of lapses. *Australasian Physical & Engineering Sciences in Medicine, 31*(4), 528.

Poudel, G. R., Jones, R. D., Innes, C. R., Watts, R., Signal, T. L., & Bones, P. J. (2009). *fMRI correlates of behavioural microsleeps during a continuous visuomotor task.* Proceedings of 2009 Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2919-2922.

Poudel, G. R., Jones, R. D., Innes, C. R. H., Watts, R., Davidson, P. R., & Bones, P. J. (2010b). Measurement of BOLD changes due to cued eye-closure and stopping during a continuous visuomotor task via model-based and model-free approaches. *IEEE Transactions on Neural Systems and Rehabilitation Engineering, 18*(5), 479-488.

Pruim, R. H. R., Mennes, M., van Rooij, D., Llera, A., Buitelaar, J. K., & Beckmann, C. F. (2015). ICA-AROMA: A robust ICA-based strategy for removing motion artifacts from fMRI data. *NeuroImage, 112*, 267-277.

Putilov, A. A., & Donskaya, O. G. (2014). Alpha attenuation soon after closing the eyes as an objective indicator of sleepiness. *Clinical and Experimental Pharmacology and Physiology, 41*(12), 956-964.

Qin, A. K., & Suganthan, P. N. (2004). Robust growing neural gas algorithm with application in cluster analysis. *Neural Networks, 17*(8), 1135-1148.

Qin, J., Perdoni, C., & He, B. (2011). Dissociation of subjectively reported and behaviorally indexed mind wandering by EEG rhythmic activity. *PLoS ONE, 6*(9), e23124(23127pp).

Qin, L., Ding, L., & He, B. (2004). Motor imagery classification by means of source analysis for brain–computer interface applications. *Journal of Neural Engineering, 1*(3), 135.

Rajagovindan, R., & Ding, M. (2011). From Prestimulus Alpha Oscillation to Visual-evoked Response: An Inverted-U Function and Its Attentional Modulation. *Journal of Cognitive Neuroscience, 23*(6), 1379-1394.

Reichle, E. D., Reineberg, A. E., & Schooler, J. W. (2010). Eye movements during mindless reading. *Psychological Science, 21*(9), 1300-1310.

Reteig, L. C., Van Den Brink, R. L., Prinssen, S., Cohen, M. X., & Slagter, H. A. (2019). Sustaining attention for a prolonged period of time increases temporal variability in cortical responses. *Cortex, 117*, 16-32.

Ritter, P., & Villringer, A. (2006). Simultaneous EEG–fMRI. *Neuroscience & Biobehavioral Reviews, 30*(6), 823-838.

Robertson, I. H., Manly, T., Andrade, J., Baddeley, B. T., & Yiend, J. (1997). Oops!': performance correlates of everyday attentional failures in traumatic brain injured and normal subjects. *Neuropsychologia, 35*(6), 747-758.

Robison, M., & Brewer, G. (2019). Individual differences in vigilance: Implications for measuring sustained attention and its association with other cognitive abilities and psychological constructs. *PsyArXiv*.

Robison, M. K., Miller, A. L., & Unsworth, N. (2019). Examining the effects of probe frequency, response options, and framing within the thought-probe method. *Behavior Research Methods, 51*(1), 398-408.

Roebuck, H., Freigang, C., & Barry, J. G. (2016). Continuous performance tasks: Not just about sustaining attention. *Journal of Speech, Language, and Hearing Research, 59*(3), 501-510.

Rong-Yi, Y., & Zhong, C. (2005). Blind source separation of multichannel electroencephalogram based on wavelet transform and ICA. *Chinese Physics, 14*(11), 2176-2180.

Rosa, P. N., Figueiredo, P., & Silvestre, C. J. (2015). On the distinguishability of HRF models in fMRI. *Frontiers in Computational Neuroscience, 9*, 54.

Rosenberg, M. D., Finn, E. S., Constable, R. T., & Chun, M. M. (2015). Predicting moment-to-moment attentional state. *NeuroImage, 114*, 249-256.

Rosenberg, M. D., Finn, E. S., Scheinost, D., Papademetris, X., Shen, X., Constable, R. T., & Chun, M. M. (2016). A neuromarker of sustained attention from whole-brain functional connectivity. *Nature Neuroscience, 19*(1), 165.

Rouhinen, S., Panula, J., Palva, J. M., & Palva, S. (2013). Load dependence of β and γ oscillations predicts individual capacity of visual attention. *The Journal of neuroscience : the official journal of the Society for Neuroscience, 33*(48), 19023-19033.

Royal, D. (2003). *National survey of distracted and drowsy driving attitudes and behavior: 2002*. Retrieved from https://one.nhtsa.gov/people/injury/drowsy_driving1/survey-distractive03/index.htm

Sagberg, F. (1999). Road accidents caused by drivers falling asleep. *Accident Analysis & Prevention, 31*(6), 639-649.

Salimi-Khorshidi, G., Douaud, G., Beckmann, C. F., Glasser, M. F., Griffanti, L., & Smith, S. M. (2014). Automatic denoising of functional MRI data: Combining independent component analysis and hierarchical fusion of classifiers. *NeuroImage, 90*, 449-468.

Salvador, R., Suckling, J., Coleman, M. R., Pickard, J. D., Menon, D., & Bullmore, E. (2005). Neurophysiological Architecture of Functional Magnetic Resonance Images of Human Brain. *Cerebral Cortex, 15*(9), 1332-1342.

Sanei, S., & Chambers, J. A. (2007). *EEG signal processing*: John Wiley & Sons.

Santangelo, V. (2018). Large-scale brain networks supporting divided attention across spatial locations and sensory modalities. *Frontiers in Integrative Neuroscience, 12*, 8.

Saper, C. B., Fuller, P. M., Pedersen, N. P., Lu, J., & Scammell, T. E. (2010). Sleep state switching. *Neuron, 68*(6), 1023-1042.

Saper, C. B., Scammell, T. E., & Lu, J. (2005). Hypothalamic regulation of sleep and circadian rhythms. *Nature, 437*(7063), 1257-1263.

Sauseng, P., Klimesch, W., Stadler, W., Schabus, M., Doppelmayr, M., Hanslmayr, S., . . . Birbaumer, N. (2005). A shift of visual spatial attention is selectively associated with human EEG alpha activity. *European Journal of Neuroscience, 22*(11), 2917-2926.

Scerbo, M. W. (1998). What's so boring about vigilance? In *Viewing psychology as a whole: The integrative science of William N. Dember.* (pp. 145-166). Washington, DC, US: American Psychological Association

Schad, D. J., Nuthmann, A., & Engbert, R. (2012). Your mind wanders weakly, your mind wanders deeply: Objective measures reveal mindless reading at different levels. *Cognition, 125*(2), 179-194.

Schlögl, A., Keinrath, C., Zimmermann, D., Scherer, R., Leeb, R., & Pfurtscheller, G. (2007). A fully automated correction method of EOG artifacts in EEG recordings. *Clinical Neurophysiology, 118*(1), 98-104.

Schmidt, R., Herrojo Ruiz, M., Kilavik, B. E., Lundqvist, M., Starr, P. A., & Aron, A. R. (2019). Beta Oscillations in Working Memory, Executive Control of Movement and Thought, and Sensorimotor Function. *The Journal of Neuroscience, 39*(42), 8231-8238.

Schnittger, C., Johannes, S., Arnavaz, A., & Münte, T. F. (1997). Relation of cerebral blood flow velocity and level of vigilance in humans. *NeuroReport, 8*(7), 1637-1639.

Schrooten, M., Vandenberghe, R., Peeters, R., & Dupont, P. (2019). Quantitative Analyses Help in Choosing Between Simultaneous vs. Separate EEG and fMRI. *Frontiers in Neuroscience, 12*, 1009-1009.

Scolari, M., Seidl-Rathkopf, K. N., & Kastner, S. (2015). Functions of the human frontoparietal attention network: Evidence from neuroimaging. *Current Opinion in Behavioral Sciences, 1*, 32-39.

Seli, P., Kane, M. J., Smallwood, J., Schacter, D. L., Maillet, D., Schooler, J. W., & Smilek, D. (2018a). Mind-wandering as a natural kind: A family-resemblances view. *Trends in Cognitive Sciences, 22*(6), 479-490.

Seli, P., Konishi, M., Risko, E. F., & Smilek, D. (2018b). The role of task difficulty in theoretical accounts of mind wandering. *Consciousness and Cognition, 65*, 255-262.

Seli, P., Risko, E. F., & Smilek, D. (2016a). On the necessity of distinguishing between unintentional and intentional mind wandering. *Psychological Science, 27*(5), 685-691.

Seli, P., Risko, E. F., Smilek, D., & Schacter, D. L. (2016b). Mind-wandering with and without intention. *Trends in Cognitive Sciences, 20*(8), 605-617.

Seli, P., Schacter, D. L., Risko, E. F., & Smilek, D. (2017). Increasing participant motivation reduces rates of intentional and unintentional mind wandering. *Psychological Research, 83*, 1057–1069.

Shaw, T. H., Warm, J. S., Finomore, V., Tripp, L., Matthews, G., Weiler, E., & Parasuraman, R. (2009). Effects of sensory modality on cerebral blood flow velocity during vigilance. *Neuroscience Letters, 461*(3), 207-211.

Shibasaki, H., Sadato, N., Lyshkow, H., Yonekura, Y., Honda, M., Nagamine, T., . . . Konishi, J. (1993). Both primary motor cortex and supplementary motor area play an important role in complex finger movement. *Brain, 116*(6), 1387-1398.

Shirer, W. R., Ryali, S., Rykhlevskaia, E., Menon, V., & Greicius, M. D. (2012). Decoding subject-driven cognitive states with whole-brain connectivity patterns. *Cerebral Cortex, 22*(1), 158-165.

Siclari, F., Baird, B., Perogamvros, L., Bernardi, G., LaRocque, J. J., Riedner, B., . . . Tononi, G. (2017). The neural correlates of dreaming. *Nature Neuroscience, 20*(6), 872-878.

Siclari, F., Bernardi, G., Riedner, B. A., LaRocque, J. J., Benca, R. M., & Tononi, G. (2014). Two Distinct Synchronization Processes in the Transition to Sleep: A High-Density Electroencephalographic Study. *Sleep, 37*(10), 1621-1637.

Siegel, J. S., Power, J. D., Dubis, J. W., Vogel, A. C., Church, J. A., Schlaggar, B. L., & Petersen, S. E. (2014). Statistical improvements in functional magnetic resonance imaging analyses produced by censoring high-motion data points. *Human Brain Mapping, 35*(5), 1981-1996.

Simor, P., van Der Wijk, G., Gombos, F., & Kovács, I. (2019). The paradox of rapid eye movement sleep in the light of oscillatory activity and cortical synchronization during phasic and tonic microstates. *NeuroImage, 202*, 116066.

Singh, G. (2018). *EEG Source Localization: A Machine Learning Approach.* (Master’s Thesis). University of Tartu,

Skorucak, J., Hertig-Godeschalk, A., Achermann, P., Mathis, J., & Schreier, D. R. (2020). Automatically Detected Microsleep Episodes in the Fitness-to-Drive Assessment. *Frontiers in Neuroscience, 14*, 8-8.

Sladky, R., Friston, K. J., Tröstl, J., Cunnington, R., Moser, E., & Windischberger, C. (2011). Slice-timing effects and their correction in functional MRI. *NeuroImage, 58*(2), 588-594.

Slater, J. D. (2008). A definition of drowsiness: One purpose for sleep? *Medical Hypotheses, 71*(5), 641-644.

Smallwood, J. (2010). Why the Global Availability of Mind Wandering Necessitates Resource Competition: Reply to McVay and Kane (2010). *Psychological Bulletin, 136*, 202-207.

Smallwood, J. (2011). The footprints of a wandering mind: further examination of the time course of an attentional lapse. *Cognitive Neuroscience, 2*(2), 91-97.

Smallwood, J., Brown, K., Baird, B., & Schooler, J. W. (2012). Cooperation between the default mode network and the frontal–parietal network in the production of an internal train of thought. *Brain Research, 1428*, 60-70.

Smallwood, J., Davies, J. B., Heim, D., Finnigan, F., Sudberry, M., O'Connor, R., & Obonsawin, M. (2004). Subjective experience and the attentional lapse: Task engagement and disengagement during sustained attention. *Consciousness and Cognition, 13*(4), 657-690.

Smallwood, J., & Schooler, J. W. (2006). The restless mind. *Psychological Bulletin, 132*(6), 946.

Smallwood, J., & Schooler, J. W. (2015). The science of mind wandering: Empirically navigating the stream of consciousness. *Annual Review of Psychology, 66*(1), 487-518.

Smith, S. M. (2002). Fast robust automated brain extraction. *Human Brain Mapping, 17*(3), 143-155.

Smith, S. M. (2004). Overview of fMRI analysis. *The British Journal of Radiology, 77*(suppl_2), S167-S175.

Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., . . . Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage, 23*, S208-S219.

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *NeuroImage, 44*(1), 83-98.

Soemer, A., & Schiefele, U. (2020). Working memory capacity and (in) voluntary mind wandering. *Psychonomic Bulletin & Review, 27*(4), 758-767.

Song, C., & Tagliazucchi, E. (2020). Linking the nature and functions of sleep: insights from multimodal imaging of the sleeping brain. *Current Opinion in Physiology, 15*, 29-36.

Spencer, G. S., Smith, J. A., Chowdhury, M. E. H., Bowtell, R., & Mullinger, K. J. (2018). Exploring the origins of EEG motion artefacts during simultaneous fMRI acquisition: Implications for motion artefact correction. *NeuroImage, 173*, 188-198.

Spreng, R. N., Stevens, W. D., Chamberlain, J. P., Gilmore, A. W., & Schacter, D. L. (2010). Default network activity, coupled with the frontoparietal control network, supports goal-directed cognition. *NeuroImage, 53*(1), 303-317.

Steindorf, L., & Rummel, J. (2020). Do your eyes give you away? A validation study of eye-movement measures used as indicators for mindless reading. *Behavior Research Methods, 52*(1), 162-176.

Strijkstra, A. M., Beersma, D. G. M., Drayer, B., Halbesma, N., & Daan, S. (2003). Subjective sleepiness correlates negatively with global alpha (8–12 Hz) and positively with central frontal theta (4–8 Hz) frequencies in the human resting awake electroencephalogram. *Neuroscience Letters, 340*(1), 17-20.

Szikora, P., & Madarász, N. (2017, 14-16 Nov. 2017). *Self-driving cars - The human side.* Proceedings of IEEE 14th International Scientific Conference on Informatics 383-387.

Talairach, J. (1988). Co-planar stereotaxic atlas of the human brain-3-dimensional proportional system. *An Approach to Cerebral Imaging*.

Tallon-Baudry, C. (2009). The roles of gamma-band oscillatory synchrony in human visual cognition. *Frontiers in Bioscience-Landmark, 14*(1), 321-332.

Tassi, P., Bonnefond, A., Engasser, O., Hoeft, A., Eschenlauer, R., & Muzet, A. (2006). EEG spectral power and cognitive performance during sleep inertia: The effect of normal sleep duration and partial sleep deprivation. *Physiology & Behavior, 87*(1), 177-184.

Tatum IV, W. O. (2014). *Handbook of EEG interpretation*: Demos Medical Publishing.

Tefft, B. C. (2014). *Prevalence of motor vehicle crashes involving drowsy drivers, United States, 2009-2013*. Retrieved from https://newsroom.aaa.com/wp-content/uploads/2014/11/AAAFoundation-DrowsyDriving-Nov2014.pdf

Temple, J. G., Warm, J. S., Dember, W. N., Jones, K. S., LaGrange, C. M., & Matthews, G. (2000). The Effects of Signal Salience and Caffeine on Performance, Workload, and Stress in an Abbreviated Vigilance Task. *Human Factors, 42*(2), 183-194.

Teplan, M. (2002). Fundamentals of EEG measurement. *Measurement Science Review, 2*(2), 1-11.

Terry, C. P., & Terry, D. L. (2015). Cell phone-related near accidents among young drivers: Associations with mindfulness. *Journal of Psychology, 149*(7), 665-683.

Thirion, B., Pinel, P., Mériaux, S., Roche, A., Dehaene, S., & Poline, J.-B. (2007). Analysis of a large fMRI cohort: Statistical and methodological issues for group analyses. *NeuroImage, 35*(1), 105-120.

Thomson, D. R., Besner, D., & Smilek, D. (2015a). A resource-control account of sustained attention: Evidence from mind-wandering and vigilance paradigms. *Perspectives on Psychological Science, 10*(1), 82-96.

Thomson, D. R., Ralph, B. C., Besner, D., & Smilek, D. (2015b). The more your mind wanders, the smaller your attentional blink: An individual differences study. *Quarterly Journal of Experimental Psychology, 68*(1), 181-191.

Tomassini, V., Jbabdi, S., Klein, J. C., Behrens, T. E. J., Pozzilli, C., Matthews, P. M., . . . Johansen-Berg, H. (2007). Diffusion-Weighted Imaging Tractography-Based Parcellation of the Human Lateral Premotor Cortex Identifies Dorsal and Ventral Subregions with Anatomical and Functional Specializations. *The Journal of Neuroscience, 27*(38), 10259.

Tong, S., & Thakor, N. V. (2009). Theory of the EEG Inverse Problem. In M. L. Yarmush & C. J. James (Eds.), *Quantitative EEG analysis methods and clinical applications* (pp. 121-137): Artech House.

Toppi, J., Astolfi, L., Poudel, G. R., Babiloni, F., Macchiusi, L., Mattia, D., . . . Jones, R. D. (2012). *Time-Varying Functional Connectivity for Understanding the Neural Basis of Behavioral Microsleeps*. Paper presented at the 34th Annual International Conference of the IEEE EMBS.

Toppi, J., Astolfi, L., Poudel, G. R., Innes, C. R. H., Babiloni, F., & Jones, R. D. (2016). Time-varying effective connectivity of the cortical neuroelectric activity associated with behavioural microsleeps. *NeuroImage, 124*(Pt A), 421-432.

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.

Treserras, S., Boulanouar, K., Conchou, F., Simonetta-Moreau, M., Berry, I., Celsis, P., . . . Loubinoux, I. (2009). Transition from rest to movement: brain correlates revealed by functional connectivity. *NeuroImage, 48*(1), 207-216.

Tsai, P.-J., Chen, S. C.-J., Hsu, C.-Y., Wu, C. W., Wu, Y.-C., Hung, C.-S., . . . Lin, C.-P. (2014). Local awakening: Regional reorganizations of brain oscillations after sleep. *NeuroImage, 102*, 894-903.

Turner, B. O., Paul, E. J., Miller, M. B., & Barbey, A. K. (2018). Small sample sizes reduce the replicability of task-based fMRI studies. *Communications Biology, 1*(1), 62.

Umarova, R. M., Saur, D., Schnell, S., Kaller, C. P., Vry, M.-S., Glauche, V., . . . Weiller, C. (2010). Structural Connectivity for Visuospatial Attention: Significance of Ventral Pathways. *Cerebral Cortex, 20*(1), 121-129.

Unsworth, N., & Engle, R. W. (2007). The nature of individual differences in working memory capacity: active maintenance in primary memory and controlled search from secondary memory. *Psychological Review, 114*(1), 104.

Unsworth, N., & McMillan, B. D. (2014). Similarities and differences between mind-wandering and external distraction: A latent variable analysis of lapses of attention and their relation to cognitive abilities. *Acta Psychologica, 150*, 14-25.

Unsworth, N., Miller, A. L., & Robison, M. K. (2020). Individual differences in lapses of sustained attention: Oculometric indicators of intrinsic alertness. *Journal of Experimental Psychology: Human Perception and Performance, 46*(6), 569.

Unsworth, N., Redick, T. S., Lakey, C. E., & Young, D. L. (2010). Lapses in sustained attention and their relation to executive control and fluid abilities: An individual differences investigation. *Intelligence, 38*(1), 111-122.

Unsworth, N., & Robison, M. K. (2016a). The influence of lapses of attention on working memory capacity. *Memory & Cognition, 44*(2), 188-196.

Unsworth, N., & Robison, M. K. (2016b). Pupillary correlates of lapses of sustained attention. *Cognitive, Affective, & Behavioral Neuroscience, 16*(4), 601-615.

Unsworth, N., & Robison, M. K. (2018a). Tracking arousal state and mind wandering with pupillometry. *Cognitive, Affective, & Behavioral Neuroscience, 18*, 638–664.

Unsworth, N., & Robison, M. K. (2018b). Tracking arousal state and mind wandering with pupillometry. *Cognitive, Affective, & Behavioral Neuroscience*.

Unsworth, N., Robison, M. K., & Miller, A. L. (2018). Pupillary Correlates of Fluctuations in Sustained Attention. *Journal of Cognitive Neuroscience, 30*(9), 1241-1253.

Unsworth, N., & Spillers, G. J. (2010). Working memory capacity: Attention control, secondary memory, or both? A direct test of the dual-component model. *Journal of Memory and Language, 62*(4), 392-406.

Urigüen, J. A., & Garcia-Zapirain, B. (2015). EEG artifact removal—state-of-the-art and guidelines. *Journal of Neural Engineering, 12*(3), 031001.

Van Den Brink, R. L., Murphy, P. R., & Nieuwenhuis, S. (2016). Pupil diameter tracks lapses of attention. *PLoS ONE, 11*(10), e0165274.

Van den Driessche, C., Bastian, M., Peyre, H., Stordeur, C., Acquaviva, É., Bahadori, S., . . . Sackur, J. (2017). Attentional lapses in Attention-Deficit/Hyperactivity Disorder: Blank rather than wandering thoughts. *Psychological Science, 28*(10), 1375-1386.

van Driel, J., Ridderinkhof, K. R., & Cohen, M. X. (2012). Not All Errors Are Alike: Theta and Alpha EEG Dynamics Relate to Differences in Error-Processing Dynamics. *The Journal of Neuroscience, 32*(47), 16795.

Van Hoey, G., Van de Walle, R., Vanrumste, B., D'Havse, M., Lemahieu, I., & Boon, P. (1999). *Beamforming techniques applied in EEG source analysis.* Proceedings of ProRISC 545-549.

van Son, D., De Blasio, F. M., Fogarty, J. S., Angelidis, A., Barry, R. J., & Putman, P. (2019a). Frontal EEG theta/beta ratio during mind wandering episodes. *Biological Psychology, 140*, 19-27.

van Son, D., de Rover, M., De Blasio, F. M., van der Does, W., Barry, R. J., & Putman, P. (2019b). Electroencephalography theta/beta ratio covaries with mind wandering and functional connectivity in the executive control network. *Annals of the New York Academy of Sciences, 1452*(1), 52.

Van Veen, B. D., Van Drongelen, W., Yuchtman, M., & Suzuki, A. (1997). Localization of brain electrical activity via linearly constrained minimum variance spatial filtering. *IEEE Transactions on Biomedical Engineering, 44*(9), 867-880.

Vanlaar, W., Simpson, H., Mayhew, D., & Robertson, R. (2008). Fatigued and drowsy driving: A survey of attitudes, opinions and behaviors. *Journal of Safety Research, 39*(3), 303-309.

Vigário, R. N. (1997). Extraction of ocular artefacts from EEG using independent component analysis. *Electroencephalography and Clinical Neurophysiology, 103*(3), 395-404.

Vorobyov, S. A., Gershman, A. B., & Zhi-Quan, L. (2003). Robust adaptive beamforming using worst-case performance optimization: a solution to the signal mismatch problem. *IEEE Transactions on Signal Processing, 51*(2), 313-324.

Vorwerk, J., Cho, J.-H., Rampp, S., Hamer, H., Knösche, T. R., & Wolters, C. H. (2014). A guideline for head volume conductor modeling in EEG and MEG. *NeuroImage, 100*, 590-607.

Vorwerk, J., Clerc, M., Burger, M., & Wolters, C. H. (2012). Comparison of Boundary Element and Finite Element Approaches to the EEG Forward Problem. *Biomedical Engineering, 57*(SI-1-Track-O), 795-798.

Vorwerk, J., Oostenveld, R., Piastra, M. C., Magyari, L., & Wolters, C. H. (2018). The FieldTrip-SimBio pipeline for EEG forward solutions. *BioMedical Engineering OnLine, 17*(1), 37.

Vossel, S., Geng, J. J., & Fink, G. R. (2014). Dorsal and ventral attention systems: Distinct neural circuits but collaborative roles. *The Neuroscientist, 20*(2), 150-159.

Vrba, J., & Robinson, S. E. (2001). Signal Processing in Magnetoencephalography. *Methods, 25*(2), 249-271.

Vyazovskiy, V. V., & Harris, K. D. (2013). Sleep and the single neuron: the role of global slow oscillations in individual cell rest. *Nature Reviews Neuroscience, 14*(6), 443-451.

Vyazovskiy, V. V., Olcese, U., Hanlon, E. C., Nir, Y., Cirelli, C., & Tononi, G. (2011). Local sleep in awake rats. *Nature, 472*(7344), 443-447.

Wager, T. D., & Lindquist, M. A. (2015). *Principles of fMRI*: Lean Publishing.

Wallstrom, G. L., Kass, R. E., Miller, A., Cohn, J. F., & Fox, N. A. (2004). Automatic correction of ocular artifacts in the EEG: a comparison of regression-based and component-based methods. *International Journal of Psychophysiology, 53*(2), 105-119.

Wang, C., Guragain, B., Verma, A. K., Archer, L., Majumder, S., Mohamud, A., . . . Tavakolian, K. (2020). Spectral Analysis of EEG During Microsleep Events Annotated via Driver Monitoring System to Characterize Drowsiness. *IEEE Transactions on Aerospace and Electronic Systems, 56*(2), 1346-1356.

Wang, J., Xie, S., Guo, X., Becker, B., Fox, P. T., Eickhoff, S. B., & Jiang, T. (2017). Correspondent Functional Topography of the Human Left Inferior Parietal Lobule at Rest and Under Task

Revealed Using Resting-State fMRI and Coactivation Based Parcellation. *Human Brain Mapping, 38*(3), 1659-1675.

Wang, K., Yu, C., Xu, L., Qin, W., Li, K., Xu, L., & Jiang, T. (2009). Offline memory reprocessing: Involvement of the brain's default network in spontaneous thought processes. *PLoS ONE, 4*(3), e4867.

Ward, A. F., & Wegner, D. M. (2013). Mind-blanking: When the mind goes away. *Frontiers in Psychology, 4*, 650.

Warm, J. S., Parasuraman, R., & Matthews, G. (2008). Vigilance Requires Hard Mental Work and Is Stressful. *Human Factors, 50*(3), 433-441.

Wascher, E., Rasch, B., Sänger, J., Hoffmann, S., Schneider, D., Rinkenauer, G., . . . Gutberlet, I. (2014). Frontal theta activity reflects distinct aspects of mental fatigue. *Biological Psychology, 96*, 57-65.

Weinstein, Y. (2018). Mind-wandering, how do I measure thee with probes? Let me count the ways. *Behavior Research Methods, 50*(2), 642-661.

Weinstein, Y., De Lima, H. J., & van der Zee, T. (2017). Are you mind-wandering, or is your mind on task? The effect of probe framing on mind-wandering reports. *Psychonomic Bulletin & Review, 25*(2), 754-760.

Weissman, D. H., Gopalakrishnan, A., Hazlett, C., & Woldorff, M. (2005). Dorsal anterior cingulate cortex resolves conflict from distracting stimuli by boosting attention toward relevant events. *Cerebral Cortex, 15*(2), 229-237.

Weissman, D. H., Roberts, K. C., Visscher, K. M., & Woldorff, M. G. (2006). The neural bases of momentary lapses in attention. *Nature Neuroscience, 9*, 971-978.

Wen, X., Wang, H., Liu, Z., Liu, C., Li, K., Ding, M., & Wu, X. (2018). Dynamic top-down configuration by the core control system during working memory. *Neuroscience, 391*, 13-24.

Wessel, M. (2006). *Pioneering research into brain computer interfaces.* (Master's Thesis). Delft University of Technology

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: A functional connectivity toolbox for correlated and anticorrelated brain networks. *Brain Connectivity, 2*(3), 125-141.

Wiemers, E. A., & Redick, T. S. (2019). The influence of thought probes on performance: Does the mind wander more if you ask it? *Psychonomic Bulletin & Review, 26*(1), 367-373.

Wildgruber, D., Erb, M., Klose, U., & Grodd, W. (1997). Sequential activation of supplementary motor area and primary motor cortex during self-paced finger movement in human evaluated by functional MRI. *Neuroscience Letters, 227*(3), 161-164.

Wilkinson, V. E., Jackson, M. L., Westlake, J., Stevens, B., Barnes, M., Swann, P., . . . Howard, M. E. (2013). The accuracy of eyelid movement parameters for drowsiness detection. *Journal of Clinical Sleep Medicine, 9*(12), 1315-1324.

Windt, J. M., Nielsen, T., & Thompson, E. (2016). Does Consciousness Disappear in Dreamless Sleep? *Trends in Cognitive Sciences, 20*(12), 871-882.

Winkler, A., Ridgway, G., Webster, M., Smith, S., & Nichols, T. (2014a). Permutation inference for the general linear model. *NeuroImage, 92*, 381-397.

Winkler, I., Brandl, S., Horn, F., Waldburger, E., Allefeld, C., & Tangermann, M. (2014b). Robust artifactual independent component classification for BCI practitioners. *Journal of Neural Engineering, 11*(3), 035013.

Wolters, C. H., Anwander, A., Tricoche, X., Weinstein, D., Koch, M. A., & Macleod, R. S. (2006). Influence of tissue conductivity anisotropy on EEG/MEG field and return current computation in a realistic head model: a simulation and visualization study using high-resolution finite element modeling. *NeuroImage, 30*(3), 813-826.

Woo, C.-W., Krishnan, A., & Wager, T. D. (2014). Cluster-extent based thresholding in fMRI analyses: Pitfalls and recommendations. *NeuroImage, 91*, 412-419.

Wood, J., Chaparro, A., Hickson, L., Thyer, N., Carter, P., Hancock, J., . . . Ybarzabal, F. (2006). The effect of auditory and visual distracters on the useful field of view: Implications for the driving task. *Investigative Ophthalmology & Visual Science, 47*(10), 4646-4650.

Woolrich, M. W., Beckmann, C. F., Nichols, T. E., & Smith, S. M. (2016). Statistical Analysis of fMRI Data. In M. Filippi (Ed.), *fMRI techniques and protocols*

(Vol. 41, pp. 183-239): Humana Press.

Woolrich, M. W., Behrens, T. E. J., Beckmann, C. F., Jenkinson, M., & Smith, S. M. (2004a). Multilevel linear modelling for FMRI group analysis using Bayesian inference. *NeuroImage, 21*(4), 1732-1747.

Woolrich, M. W., Behrens, T. E. J., & Smith, S. M. (2004b). Constrained linear basis sets for HRF modelling using Variational Bayes. *NeuroImage, 21*(4), 1748-1761.

Woolrich, M. W., Ripley, B. D., Brady, M., & Smith, S. M. (2001). Temporal autocorrelation in univariate linear modeling of FMRI data. *NeuroImage, 14*(6), 1370-1386.

Worsley, K. J. (2001). Statistical analysis of activation images. In *Functional Magnetic Resonance Imaging: An Introduction to Methods*: Oxford Scholarship Online.

Worsley, K. J., & Friston, K. J. (1995). Analysis of fMRI time-series revisited—again. *NeuroImage, 2*(3), 173-181.

Yamashita, A., Rothlein, D., Kucyi, A., Valera, E. M., & Esterman, M. (2020). Two dominant brain states reflect optimal and suboptimal attention. *bioRxiv*, 2020.2001.2031.928523.

Yan, W. X., Mullinger, K. J., Brookes, M. J., & Bowtell, R. (2009). Understanding gradient artefacts in simultaneous EEG/fMRI. *NeuroImage, 46*(2), 459-471.

Yanko, M. R., & Spalek, T. M. (2013). Route familiarity breeds inattention: A driving simulator study. *Accident Analysis & Prevention, 57*, 80-86.

Yao, J., & Dewald, J. P. A. (2005). Evaluation of different cortical source localization methods using simulated and experimental EEG data. *NeuroImage, 25*(2), 369-382.

Yeung, A. W. K. (2018). An updated survey on statistical thresholding and sample size of fMRI studies. *Frontiers in Human Neuroscience, 12*, 16-16.

Yu, S., Ou, W., You, X., Jiang, X., Zhu, Y., Mou, Y., . . . Chen, C. P. (2015). *Webcam-Based Visual Gaze Estimation Under Desktop Environment.* Proceedings of International Conference on Neural Information Processing 457-466.

Zalesky, A., Fornito, A., & Bullmore, E. T. (2010). Network-based statistic: Identifying differences in brain networks. *NeuroImage, 53*(4), 1197-1207.

Zanesco, A. P., Denkova, E., Witkin, J. E., & Jha, A. P. (2020). Experience sampling of the degree of mind wandering distinguishes hidden attentional states. *Cognition, 205*, 104380.

Zanto, T. P., & Gazzaley, A. (2013). Fronto-parietal network: flexible hub of cognitive control. *Trends in Cognitive Sciences, 17*(12), 602-603.

Zarahn, E., Aguirre, G. K., & D'Esposito, M. (1997). Empirical analyses of BOLD fMRI statistics. I. Spatially unsmoothed data collected under null-hypothesis conditions. *NeuroImage, 5*(3), 179-197.

Zhang, J., Anderson, J. R., Liang, L., Pulapura, S. K., Gatewood, L., Rottenberg, D. A., & Strother, S. C. (2009). Evaluation and optimization of fMRI single-subject processing pipelines with NPAIRS and second-level CVA. *Magnetic Resonance Imaging, 27*(2), 264-278.

Zhang, J., Liang, L., Anderson, J. R., Gatewood, L., Rottenberg, D. A., & Strother, S. C. (2008). A Java-based fMRI Processing Pipeline Evaluation System for Assessment of Univariate General Linear Model and Multivariate Canonical Variate Analysis-based Pipelines. *Neuroinformatics, 6*(2), 123-134.

Zhang, T., & Chan, A. H. S. (2014). Sleepiness and the risk of road accidents for professional drivers: A systematic review and meta-analysis of retrospective studies. *Safety Science, 70*, 180-188.

Zhang, Y., Brady, M., & Smith, S. (2001). Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm. *IEEE Transactions on Medical Imaging, 20*(1), 45-57.

Zhao, S., Bury, G., Milne, A., & Chait, M. (2019). Pupillometry as an objective measure of sustained attention in young and older listeners. *Trends in Hearing, 23*, 2331216519887815.

Zhou, X., & Lei, X. (2018). Wandering minds with wandering brain networks. *Neuroscience Bulletin, 34*(6), 1017-1028.

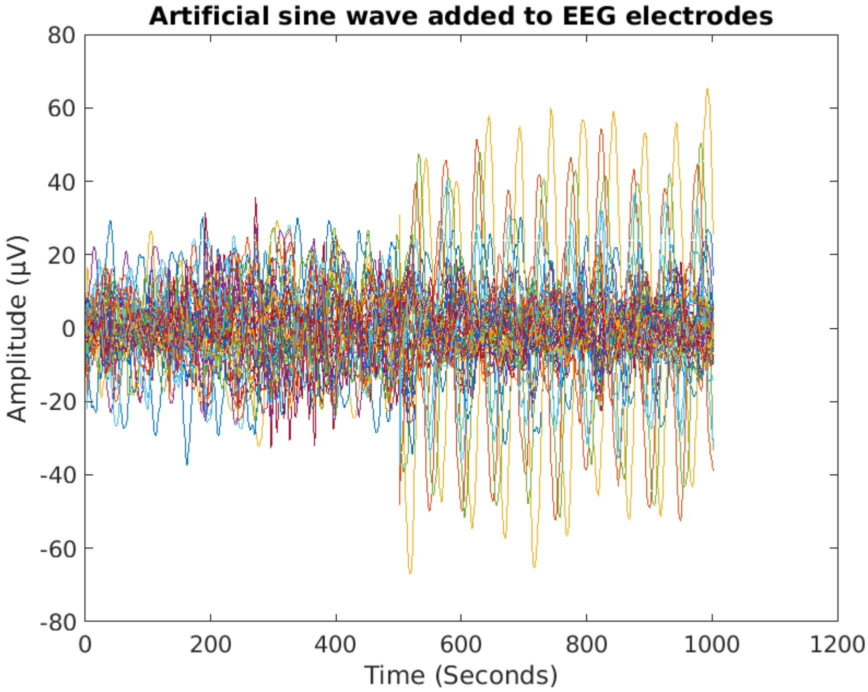
Zhukov, L., Weinstein, D., & Johnson, C. (2000). Independent component analysis for EEG source localization. *IEEE Engineering in Medicine and Biology Magazine, 19*(3), 87-96.

Ziegler, D. A., Janowich, J. R., & Gazzaley, A. (2018). Differential impact of interference on internally- and externally-directed attention. *Scientific Reports, 8*, 2498.

Zokaei, N., Heider, M., & Husain, M. (2014). Attention is required for maintenance of feature binding in visual working memory. *Quarterly Journal of Experimental Psychology, 67*(6), 1191-1213.

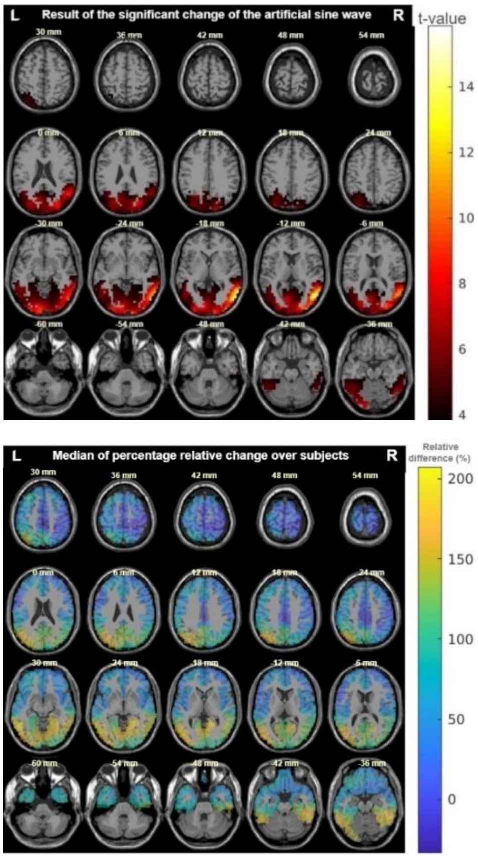
Appendix A: EEG Pipeline Validation using an Artificial Signal

To validate that the integrity of the pipeline, we added an artificial signal with a certain frequency to the events of interest at certain EEG electrodes (O2, O1, Oz, PO5, PO3, POz, PO4, PO6, PO8, PO7). Subsequently, we ran the source reconstruction technique and expected to see a change in activity in the underlying sources at the scalp location of the EEG electrodes after statistical analysis and correction for multiple comparisons. We added a 10-Hz sine wave with an amplitude equal to two times the norm of EEG signal for each electrode and subject to the 10 electrodes around the occipital lobe. The sine wave had a random phase for each electrode. This wave was added to the event duration, while another wave with equal amplitude (i.e., norm of EEG signal) was added to the baseline in order to make it the dominant signal, as shown below.



A plot for the EEG electrodes after adding the sine wave added to both average event and average baseline with two different amplitudes.

The validation process was done by adding the artificial wave to the AL events (38 events), in order to test the statistical power of our data given the current SNR = 2. The same analysis procedure was followed by using FFT for the frequency analysis and eLORETA for the source reconstruction. Permutation testing was applied to examine the relative difference between the average events to the average baseline of each subject. In total, there were 10 subjects and results were corrected for multiple comparisons with TFCE and a p-value < 0.01 (two-sided). The median of the percentage relative change refers to the effect sizes.



Group-level result of the significant change activity of the relative difference between the event of artificial sine wave added to the ALs and baseline at SNR = 2 (shown in axial view at the top). On the bottom is the median of the percentage relative change over subjects.