Spatial Attention and Alertness in Healthy Adults

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Glossary of Abbreviations

AUD	Australian Dollar
CI	Confidence Interval
cm	Centimetres
CMA	Comprehensive Meta-Analysis
D2	Day 2
D4	Day 4
D5	Day 5
D7	Day 7
DAN	Dorsal Attention Network
EEG	Electroencephalography
FFT	Fast Fourier Transform
FLANDERS	Flinders Handedness Survey
fMRI	Functional Magnetic Resonance Imaging
h	Hours
Hz	Hertz
ICA	Independent Component Analysis
Km	Kilometre
KSS	Karolinska Sleepiness Scale
M	Mean
m	Metre
Mean RRT	Reciprocal of the Mean Reaction Time
mm	Millimetre
ms	Milliseconds
PIST	Parietal Inferior-to-Superior Tract
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PVT	Psychomotor Vigilance Task
RT	Reaction Time
rTMS	Repetitive Transcranial Magnetic Stimulation
SD	Standard Deviation
SLF	Superior Longitudinal Fasciculus
SNS	Sympathetic Nervous System
SSS	Stanford Sleepiness Scale
VAN	Ventral Attention Network

Contextual Statement

This thesis is submitted as a 'Thesis Containing Published Research' in accordance with the University of South Australia's Academic Regulations for Higher Degrees by Research Clause 16.1.1.b. This model permits the inclusion of one or more published works as well as conventional chapters. It is required that publications be produced, published or accepted for publication in peer-reviewed journals or conference proceedings during the student's candidature. The requirements of a 'Thesis Containing Published Research' are as follows:

- Each publication must be peer-reviewed and recognised for the University's publication collection.
- Each publication must be published or accepted for publication pending revisions for publication in significant journals, books and/or conference proceedings relevant to the discipline.
- Conference papers published in conference proceedings and book chapters can only be included where there is evidence of peer-review of the full work.
- For publications that have been accepted for publication pending revisions, the principal supervisor must provide written confirmation that revisions required by referees and/or the editor have been made. This confirmation must be incorporated in an appendix to the thesis.
- Each co-authored publication included in the thesis must be accompanied by a statement by the candidate describing the contribution of each author to each publication. The statements must be signed by each author and incorporated in an appendix to the thesis.
- The candidate must be the greatest or equal greatest contributor to any co-authored publications included in the thesis.
- The subject matter of the publications must be closely related and form a cohesive narrative.
- The publications must be compliant with Copyright law and intellectual property requirements.
- Where copyright has been assigned to the publisher, permission will need to be sought to reproduce the work in the print and digital versions of the thesis. It is the candidate's responsibility to obtain permission to reproduce the work in the

thesis. Permission statements from publishers must be included as an appendix to the thesis.

- Publications published, accepted, or submitted for publication prior to commencing the degree, either at University of South Australia or at another university, must not be included in the thesis.

Publication Context

The current thesis contains two papers published in peer-reviewed international journals in the field of Psychology. The thesis also contains one paper which is currently under peer-review at an international journal. An overview of authorship contribution and written permissions from co-authors are included for each chapter and can be found in Appendix A and Appendix B respectively. Licence and journal publication policy to permit use of the publications in the thesis can be found in Appendix C. The following section will describe how each published work within the thesis is critically placed within the research field and its context in the current thesis, as required according to the "guidelines for presentation of the thesis, or exegesis" approved by the Research Degrees Committee – October 2015.

Chapter Two

Chandrakumar, D., Keage, H. A., Gutteridge, D., Dorrian, J., Banks, S., & Loetscher, T. (2019). Interactions between Spatial Attention and Alertness in Healthy Adults: A Meta-Analysis. *Cortex*, 119, 61-73. Doi: 10.1016/j.cortex.2019.03.016

The manuscript contained in chapter 2 was the first meta-analysis to quantitatively synthesise research in the area of spatial attention and alertness in healthy adults. The manuscript was submitted for publication in October 2018 and was accepted for publication in *Cortex* in March 2019 following peer review and manuscript revisions. This chapter investigated the first and second aims of the thesis and is a direct research output from my candidature.

Chapter Three

Chandrakumar, D., Dorrian, J., Banks, S., Keage, H. A., Coussens, S., Gupta, C., Centofanti, S. A., Stepien, J. M., & Loetscher, T. (2020). The Relationship between Alertness and Spatial Attention under Simulated Shiftwork. *Scientific reports,* 10. Doi:10.1038/s41598-020-71800-6

Chapter 3 contains an experimental study investigating the relationship between alertness and spatial attention under a 7-day simulated shiftwork protocol. This study was the first to utilise a simulated shiftwork protocol to examine changes in spatial attention relative to alertness. The manuscript was submitted in March 2020 and was accepted for publication in *Scientific Reports* in July 2020. This chapter investigated the second aim of the thesis and is a direct research output from my candidature.

Chapter Four

Chandrakumar, D., Coussens, S., Keage, H.A.D., Banks, S., Dorrian, J., & Loetscher, T. (Under review). Monotonous driving induces shifts in spatial attention as a function of handedness.

Chapter 4 examined the spatial attention alertness relationship under a time-on-task manipulation involving a driving simulator. In this chapter, we investigated an underexplored population, left-handers, and explored the transfer effects of simpler computerised laboratory-based findings in a more everyday applicable task using a simulated driving task. This chapter investigated the second aim of the thesis. The manuscript was submitted for peer review in October 2020. This chapter investigated the second aim of the thesis and is a direct research output from my candidature.

Funding and Scholarship Statement

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Thesis Summary

Impairments in allocating attention to relevant locations in the environment can have implications for health and safety. An emerging line of research suggests that the ability to attend quickly to left- and right-sided stimuli varies as a function of a person's level of alertness. That is, under lowered alertness, it is proposed that attention shifts towards the right. The understanding of the mechanisms and factors influencing this relationship between alertness and spatial attention is currently limited, but a better understanding may contribute critical information in assisting the management of human error to minimise injuries and accidents.

The overarching aim of the thesis was to investigate the relationship between alertness and spatial attention in healthy adults. The specific aims were to (1) synthesise the current state of research and its gaps on the relationship between spatial attention and alertness in healthy adults, and (2) identify modulators that affect spatial attention and alertness relationships. To address these aims, a meta-analysis on the spatial attention and alertness relationship was conducted as a first step (Chapter Two). The meta-analysis provided evidence for a small effect (Cohen's d =.302) of alertness on spatial attention with a rightward and leftward shift in attention being associated with decreased and increased alertness, respectively. Further, we identified handedness as a potential modulator of the spatial attention and alertness relationship and revealed a lack of investigations in real-world conditions. In Chapter Three, the spatial attention and alertness relationship was investigated relative to fluctuations in alertness across seven days of simulated shiftwork. We found some evidence for a slight neglect of the left side and a narrowing of attention with lowered alertness. The findings were not definitive and depended on the measures used to assess spatial attention and alertness. In Chapter Four, we examined the spatial attention and alertness relationship in a time-on-task condition using simulated driving in both left-handers and right-handers. We found that monotonous driving induces shifts in attention as a function of handedness. Right-handers reacted slower to the leftmost stimuli, while left-handers showed the opposite pattern (although not statistically significant) with time-on-task.

The thesis corroborates evidence that alertness levels influence the allocation of attention in space. Handedness was recognised as a critical modulator in determining the direction of attentional shifts with fluctuations in alertness. Moreover, the spatial

attention and alertness relationship was also observed in experimental manipulations that attempted to simulate more real-world applicable conditions such as shiftwork (Chapter Three) and driving (Chapter Four). However, the extent to which such findings apply to real-world consequences is currently unclear. An important next step will be to establish the real-world safety implications of the interactions between alertness and spatial attention. This may consequently inform avenues to minimise accidents and injuries.

Declaration

This thesis presents work carried out by myself and does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university

To the best of my knowledge it does not contain any materials previously published or written by another person except where due reference is made in the text; and all substantive contributions by others to the work presented, including jointly authored publications, are clearly acknowledged.



Dilushi Chandrakumar

14.01.2021

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Chapter One: Introduction

Responding and reacting appropriately to the environment is of utmost importance for survival. There is growing evidence that the deployment of spatial attention can be compromised under conditions of lowered alertness such that attention shifts towards the right side of the environment. This has potential health and safety implications for everyday activities such as driving and performing tasks that involve task engagement for prolonged periods of time. Driving under lowered alertness conditions could lead to delayed responses to information on one side. This could have devasting consequences if, for example, a pedestrian unexpectedly crosses and a drowsy driver is delayed in processing and reacting to stimuli from that side. In occupational settings, security screening personal might miss crucial information on one side more often than on the other side of the monitor if their level of alertness is low. Given the potential implications for safety and welfare, a better understanding of the spatial attention and alertness relationship may contribute critical information in assisting the management of human error to minimise injuries and accidents.

1.1 Spatial attention

Spatial attention can be defined as the ability to process and direct attention to stimuli in the environment (Posner & Petersen, 1990). The perpetual system is consistently presented with a larger amount of sensory information than it can process and consequently filters incoming stimuli to determine which stimuli need to be attended to (Driver, 2001). Spatial attention is crucial for sufficiently responding to and navigating the environment as the inability to respond appropriately could have safety implications. Striking examples of the consequences of compromised spatial attention arise from neglect patients, who have experienced lesions to one side of their brain following a stroke. Spatial neglect patients can experience a range of difficulties associated with compromised spatial attention towards the side opposite to their brain lesion (Heilman & Van Den Abell, 1980; Robertson, Mattingley, Rorden, & Driver, 1998). Patients with a right brain lesion may fail to observe and interact with information on the left side of their environment. They may walk into objects on their left, fail to dress or shave the left side and ignore individuals standing to their left, particularly when there are simultaneously competing information on their right side (Mesulam, 1999). Findings from neglect

patients have contributed to the understanding of how spatial attention is regulated in the brain.

Both the left and right hemispheres are implicated in directing attention to the environment, and the location where attention is directed towards can be explained by current theoretical frameworks. Kinsbourne's interhemispheric theory suggests that each hemisphere directs attention contralaterally, such that the left hemisphere directs attention to the right hemifield and the right hemisphere directs attention to the left hemifield (Kinsbourne, 1977). This theory postulates that the two hemispheres rival each other through reciprocal inhibitory mechanisms and the deployment of spatial attention is the outcome of this interhemispheric competition. The higher the asymmetry in hemispheric activation, the higher the degree of spatial bias in the contralateral hemifield of the hemisphere with hyperactivation. According to the hemispatial theory, however, the right hemisphere is implicated in attending to both the left and right hemifields, whereas the left hemisphere attends only to the right hemifield (Heilman & Van Den Abell, 1980). This theory supports the right hemisphere as having a stronger influence on spatial attentional allocation. Findings from neuroimaging studies show a more prominent activation in the fronto-parietal cortical regions of the right hemisphere whilst engaging in spatial tasks. These studies support the dominant influence of the right hemisphere in spatial attentional allocation (Çiçek, Deouell, & Knight, 2009; Le, Stojanoski, Khan, Keough, & Niemeier, 2015; Mesulam, 1981; Shulman et al., 2010). Pseudoneglect, the tendency to bias attention towards the left in the healthy brain, is reported in the literature and is believed to result from the right hemisphere's dominance in allocating visuospatial attention (Bowers & Heilman, 1980).

1.2 Measuring spatial attention

Measures of spatial attention can be broadly categorised into judgement and detection tasks. Judgement tasks require participants to judge the spatial qualities of stimuli. The most used measures of spatial attention in both healthy and clinical populations are line bisection tasks. These tasks require participants to bisect a horizontal line, such that the segments on the left and right sides are equal (Jewell & McCourt, 2000). The Landmark Task is a variant of the line bisection task, and this task contains pre-bisected lines, where participants are required to judge which side of the pre-bisected

line is longer or shorter (Milner, Brechmann, & Pagliarini, 1992). Another example of judgement tasks includes the Greyscales, which involves making judgements on stimuli luminance (Mattingley, Bradshaw, Nettleton, & Bradshaw, 1994). Detection tasks measure detection and response times to stimuli presented on the left and right sides. A greater proportion of stimulus detection and faster response times to one side over the other suggests an attentional bias towards that side. Examples of some response time tasks used in the literature are the Partial Report Task (Matthias et al., 2009; Wiegand et al., 2017), Rapid Serial Visual Presentation Task (Newman, O'Connell, & Bellgrove, 2013), Random Dot Motion Task (Newman et al., 2014), and Visual Letter Task (Dodds et al., 2008).

A Landmark task (Milner et al., 1992) and a detection task were used in Chapter Three of the thesis, to investigate both judgement and detection approaches to measuring spatial attention. These tasks have been used in the literature to assess spatial biases following alterations to alertness levels in healthy adults (Bellgrove, Dockree, Aimola, & Robertson, 2004; Dodds, Muller, & Manly, 2009; Dodds et al., 2008; Newman et al., 2014; Newman et al., 2013; Wiegand et al., 2017). Of importance to note is the finding that these tasks can reliably measure spatial attention, however, there are no inter-task correlations between them (Learmonth, Gallagher, Gibson, Thut, & Harvey, 2015). Hence, this might suggest that different measures capture different underlying mechanisms.

1.3 Alertness

Alertness can be defined as general wakefulness and readiness to respond to stimuli (Posner & Rafal, 1987; Strum & Willmes, 2001) and this definition of alertness will be used throughout the thesis. Increases and decreases in alertness can correspond with an amplified or a diminished ability to perform cognitively, respectively. Decreased alertness is associated with increased response times, lapses in judgement, and error rates (Fimm & Blankenheim, 2016). This suggests sufficient alertness levels are necessary for optimal functioning.

Alertness can be distinguished into tonic and phasic components. Tonic alertness refers to general alertness, lasting minutes to hours, and is believed to be reliant on the

fronto-parietal networks in the right hemisphere (Bartolomeo, Thiebaut De Schotten, & Chica, 2012). This component of alertness is intrinsically regulated and is necessary for complex processes such as cognitive control and working memory. Tonic alertness fluctuates throughout a day, rising and falling at different times (Petersen & Posner, 2012). Phasic alertness, on the other hand, can be defined as momentary alertness, lasting for short durations such as within seconds. This component of alertness is influenced externally and is involved in orientating and selective attention processes. For example, phasic alertness can be altered by presenting a warning signal (Sturm & Willmes, 2001). Some studies have identified slight differences in lateralisation of phasic and tonic alertness. Two neuroimaging studies identified the left hemisphere as more strongly implicated in detecting warning signals (Coull, Frith, Büchel, & Nobre, 2000; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005). Similarly, Ivry, Robertson, and Robertson (1998) suggested the left and right hemispheres are involved in the regulation of phasic alertness and tonic alertness, respectively.

Whilst alertness can be separated into tonic and phasic components, there is currently a discrepancy in the literature regarding the terms and underlying constructs used to describe alertness. For example, the terms sleepiness, drowsiness, fatigue, arousal, activation, alertness, vigilance, and sustained attention are used in the literature, with some of these terms used interchangeably. Furthermore, differing fields use different terms. For example, in sleep research, the terms sleepiness and drowsiness are more commonly used. Whereas, arousal and sustained attention are terms more commonly used in cognitive psychology, and vigilance is commonly used by psychologists and cognitive neuroscientists (Oken, Salinsky, & Elsas, 2006). Hence the differences in definitions and understanding of the constructs across disciplines, and the terms being used interchangeably, make it difficult to assertion the exact construct each study addresses.

1.4 Measuring alertness

Measures of alertness can be broadly categorised into self-reports, behavioural assays (e.g., reaction time measures), and physiological measures of alertness such as skin conductance and neural activity. Galvanic skin response (GSR) can be used to measure the activation of endocrine sweat glands, which is linked to the sympathetic nervous system activity. The more activated the sweat glands, the more conducive the

skin becomes, and increases in skin conductance can suggest increased alertness (Figner & Murphy, 2011). Electroencephalography (EEG) alpha relative power is a commonly used marker for alertness (Klimesch, 1999). Changes in alpha over time can indicate activation and inhibition of certain cortical regions (Sauseng et al., 2005). High alpha power is associated with lowered levels of alertness (Benwell et al., 2019; Kecklund & Åkerstedt, 1993).

In the thesis, the Stanford sleepiness scale (SSS; Hoddes, Dement, & Zarcone, 1972) the Karolinska sleepiness scale (KSS; Åkerstedt & Gillberg, 1990), and the Psychomotor vigilance task (PVT; Dinges & Powell, 1985) provided self-report and behavioural measures of alertness. The PVT is sensitive to detecting changes in alertness as the task requires subjects to respond to stimuli as quickly as possible (Dinges & Powell, 1985). Changes in sympathetic nervous system activation over time through skin conductance and alpha power derived from EEG were used as physiological measures of alertness in Chapter Four of the thesis. Relative power was investigated in the thesis as relative power is found to be more reliable than absolute power when analysing EEG from cognitive tasks (Fernández et al., 1993). Relative power (compared to absolute power) also allows for a larger estimation of the dominant frequency and a lower estimation of frequencies outside the range of the specified frequency band (Klimesch, 1999).

1.5 Manipulating alertness relative to spatial attention

Experimental manipulations commonly employed to decrease alertness in healthy subjects comprise of sleep deprivation (Fimm & Blankenheim, 2016; Heber, Valvoda, Kuhlen, & Fimm, 2008), sleep restriction (Barclay & Myachykov, 2017), circadian rhythmicity (i.e., desynchronisation between time of day and chronotype; Cazzoli et al., 2014; Dorrian, McLean, Banks, & Loetscher, 2017), and prolonged task exposure (i.e., time-on-task; Benwell, Thut, Learmonth, & Harvey, 2013; Newman et al., 2013). Whereas manipulations used to increase alertness have used designs involving phasic alerting tones or cues (Bareham, Bekinschtein, Scott, & Manly, 2015; Bareham, Manly, Pustovaya, Scott, & Bekinschtein, 2014), and the use of psychostimulants (Dodds et al., 2009).

1.6 Interactions between spatial attention and alertness in healthy populations

Previous research indicates that under lowered alertness, attention shifts towards the right, such that the left-sided environmental space is neglected to some extent (Bellgrove et al., 2004; Corbetta & Shulman, 2011; Manly, Dobler, Dodds, & George, 2005). Manly et al. (2005) investigated changes between two alertness conditions (one high and the other low in shiftworkers) and reported a rightward shift in attention under low alertness conditions. Similarly, studies which reduced alertness via sleep deprivation have demonstrated a rightward shift in attention (Fimm, Willmes, & Spijkers, 2006; Heber et al., 2008). Fimm, Willmes, and Spijkers (2015) found mixed results, such that their covert attention paradigm showed a slowed response to left-sided stimuli under sleep deprivation, whereas there was no difference in performance to the left and right side in the overt attention paradigm. Other studies reported no differences in spatial bias following changes to alertness (Matthias et al., 2009; Schmitz, Deliens, Mary, Urbain, & Peigneux, 2011). Additionally, the majority of studies in healthy participants have utilised experimental paradigms which decrease alertness. Therefore, studies investigating the increase in alertness and its influence on spatial attention are currently limited with no clear-cut findings (e.g., Dodds et al., 2009). Similarly, Wiegand et al. (2017) found no differences in spatial bias when employing alerting cues within a task, but Thomas et al. (2017) demonstrated a leftward shift in attention with increased alertness respectively, when employing alerting cues.

To uncover the discrepancy and establish a consensus in the current literature, the thesis sought out to further investigate the relationship between alertness and spatial attention in healthy adults. The thesis also sought out to investigate the specific conditions which lead to shifts in attention following changes to alertness levels, as this can assist with identifying conditions which are most susceptible to spatial attentional shifts. Gaining a deeper understanding for the spatial attention and alertness relationship in healthy adults can potentially lead to assisting with accident and injury minimisation.

1.7 A framework of the relationship between spatial attention and alertness

The current dominating model accounting for the relationship between spatial attention and alertness proposed that the relationship is mediated by two neural attentional networks. These networks are the bilateral dorsal attentional network (DAN)

and the right-lateralised ventral attentional network (VAN), and they determine where attention is allocated in the environment (Corbetta & Shulman, 2011). The DAN within each hemisphere is believed to be responsible for directing attention contralaterally and consists of the intra-parietal sulcus, superior parietal lobule, the frontal eye field, and the dorsolateral prefrontal cortex within both hemispheres (Bartolomeo et al., 2012; Vossel, Geng, & Fink, 2014). The framework proposed by Corbetta and Shulman (2011) incorporates the interhemispheric theory (Kinsbourne, 1977), indicating that there is asymmetry in activation across the two hemispheres and continuous competition for hemispheric activation. The hemisphere which gains an activation advantage directs attention contralaterally. The VAN is believed to have stronger connections in the right hemisphere and is implicated in non-spatial aspects of attention, such as reorientation towards stimuli, the detection of salient and unexpected stimuli, alertness, and the maintenance of alertness over time (Corbetta, Patel, & Shulman, 2008; Corbetta & Shulman, 2002, 2011). The VAN comprises the temporo-parietal junction and the ventral frontal cortex (inferior and middle gyri) in the right hemisphere (Bartolomeo et al., 2012). White matter tracts connect the DAN and VAN, allowing the two networks to interact. More specifically, the superior longitudinal fasciculus (SLF) II and the parietal inferior-to-superior tract (PIST) are identified as connecting the DAN and VAN (Bartolomeo et al., 2012; Catani et al., 2017; Thiebaut De Schotten et al., 2011). The right anterior insular and inferior frontal gyrus are also regions identified as connecting the two networks (Asplund, Todd, Snyder, & Marois, 2010; Cazzoli et al., 2020; He et al., 2007). Changes in alertness within the VAN are thought to impact the interhemispheric competition in the DAN. For example, a decrease in alertness can lead to the left hemisphere gaining an activation advantage due to hypoactivation of the right-sided DAN. This consequently leads to a rightward bias in attention and left-sided neglect. Hence, according to this model decreased alertness should associate with a rightward bias in attention and increased alertness should associate with a leftward bias in attention. Whilst the proposed model is compelling, Corbetta and Shulman (2011) have indicated that, in its current form, it is provisional and exploratory. A review by Mengotti, Käsbauer, Fink, and Vossel (2020) identified studies in the literature supporting the bilateral nature of the DAN. However, the acceptance for the VAN being right-hemisphere lateralised was questioned. For example, there is evidence for the left temporoparietal junction also playing a role in attending to unexpected events (Geng & Mangun, 2011; Weidner, Krummenacher,

Reimann, Müller, & Fink, 2009), instead of this function being confined to the right temporoparietal junction (Corbetta et al., 2008; Corbetta & Shulman, 2002, 2011; Vossel et al., 2014). Hence, the conflicting findings highlight some uncertainty around the organisation and function of the VAN.

Currently, the neural basis of the spatial attention and alertness relationship in healthy adults is underexplored (see Thiebaut De Schotten et al., 2011; Newman et al., 2013; Paladini et al., 2017 for some exceptions). Paladini et al. (2017) investigated cortical excitability through employing transcranial magnetic stimulation to both the left and right posterior parietal cortices. The authors concluded that the left posterior parietal cortex was more excitable than the right PPC during lowered alertness conditions, and the right compared to the left posterior parietal cortex was more excitable under high alertness conditions. Activation in the left posterior parietal cortex under lowered alertness conditions corresponded with eye fixations towards the right. Newman et al. (2013) investigated alpha power over the two hemispheres under conditions of low and high alertness and reported increased alpha absolute power in the right compared to the left parieto-occipital regions during low alertness suggesting cortical deactivation in the right hemisphere with lowered alertness. This decreased alertness was linked with faster reaction times to right-sided stimuli. Thiebaut De Schotten et al. (2011) used diffusion imaging and reported finding strong right lateralisation in the regions connecting the dorsal and ventral networks, which was linked to the degree of pseudoneglect (i.e., the extent of the leftward attentional bias) displayed by participants on both judgement and detection tasks.

1.8 The current thesis

The overarching aim of the thesis was to investigate the relationship between alertness and spatial attention in healthy adults, in the context of implications for accident and injury prevention. More specifically, the aims were to: 1) synthesise the current state of research and its gaps on the relationship between spatial attention and alertness in healthy adults; and 2) identify modulators that affect spatial attention and alertness relationships.

There are three empirical chapters within the thesis investigating these aims and a concluding chapter summarising the findings. The second chapter of the thesis

quantitatively collates the findings from the current literature on spatial attention and alertness in healthy adults, to determine whether the Corbetta and Shulman (2011) framework is supported overall. This chapter involves conducting a meta-analysis to compute effect sizes to quantify the evidence in support of the framework. This chapter also aims to identify the modulators of this spatial attention and alertness relationship. An understanding for the current state of research on the relationship between alertness and spatial attention from this chapter also helps uncover the specific areas of research that are underexplored to guide future research.

The third chapter of the thesis examines whether simulated shiftwork results in corresponding shifts in attention depending on whether alertness in high or low during specific testing sessions throughout seven days of a simulation protocol. In this chapter, the sleep/wake cycle of the participants is manipulated to observe its corresponding changes in the alertness and spatial attention relationship. The findings from this chapter may have implications for occupations that result in a disruption to the sleep/wake cycle, such as in the case of shiftwork.

The fourth chapter investigates the effect of decreased alertness, resulting from prolonged task exposure, and its association with driving performance. This chapter tests the Corbetta and Shulman (2011) framework through investigating changes in electroencephalography, skin conductance, and behaviour with time-on-task. This chapter aims to employ a task with real-world application to assess how everyday activities, such as driving, can be implicated by the alertness and spatial attention relationship: a gap in the current literature that was identified in Chapter Two. In Chapter Four, both left-handed and right-handed participants were recruited to assess recent evidence suggesting that left-handers show the opposite relationship between alertness and spatial attention (i.e., a leftward bias with decreasing alertness and a rightward bias with increasing alertness, see Bareham et al., 2015). The results from this study may have implications for understanding the behavioural and neural changes associated with lowered alertness under everyday conditions, such as driving. This study may also assist in uncovering the alertness and spatial attention relationship in an underexplored research population: left-handers.

The concluding chapter of the thesis is the general discussion, and the aim of this section is to integrate the findings from the three empirical chapters and to relate the

findings to the broader literature. This chapter also outlines the key contributions of the thesis to the field of spatial attention and alertness. Limitation of the thesis and suggestions for future research are also discussed within this chapter.

Chapter Two: Interactions between spatial attention and alertness in healthy adults: A meta-analysis

2.1 Abstract

Attending to the visuospatial field is paramount for safety. The inability to sufficiently allocate attention in the environment could lead to unfavourable consequences. One's ability to attend quickly to left- and right-sided stimuli can vary depending on the person's level of alertness. A dominant model of this relationship proposes that low alertness is associated with a rightward bias in attention, with increases in alertness shifting attention leftward. The current study sought to synthesise the literature on spatial attention and alertness and identify modulators of this relationship in healthy adults. Nineteen articles meeting inclusion criteria were identified for meta-analysis. A small effect of alertness on spatial bias (d = .302) with no evidence for a systematic publication bias was found. Of the five investigated modulators, namely, the experimental design relative to alertness, direction of alertness manipulation, measurement of alertness, the nature of the spatial task, and handedness, only the latter was identified as a significant modulator of the relationship between alertness and spatial attention. The review's findings tie in with the influential framework by Corbetta and Shulman (2011) and support the idea to increase alertness as a rehabilitation approach to reduce inattention to the left side in neglect patients. Findings also suggest a need for future research to investigate neurological processes that underlie the alertness and spatial attention relationship, and a need to examine the transfer effects of laboratory-based experiments for real-world implications.

2.2 Introduction

The ability to attend to one's surroundings is paramount for safety in an environment with competing stimuli; failure to attend to relevant stimuli can result in accident and injury. An emerging line of research suggests the ability to attend quickly to left- and right-sided stimuli varies as a function of a person's level of alertness. That is, under lowered alertness, we seem to attend more to the right than the left side of space, and it has been proposed that a decrease in alertness is associated with attentional shifts towards the right (Bellgrove et al., 2004; Matthias et al., 2009; Paladini et al., 2016). Such a rightward attentional shift can be characterised by slowed reaction time to stimuli presented on the left (Fimm et al., 2006; Heber et al., 2008) misidentification of stimuli presented on the left as being on the right (Bareham et al., 2014), and relative inattention to left-sided information (Manly et al., 2005). If these laboratory-based findings transfer to the real world, these attentional shifts towards the right might have significant implications for everyday activities such as driving (e.g., diminished efficiency in reacting to hazards on the left). Given that spatial attentional changes are under-explored in the pathway from reduced alertness to error (Dorrian, McLean, Banks, & Loetscher, 2017), the goal of this review is to summarise the current literature examining the interactions between spatial attention and alertness. Understanding the mechanisms modulating spatial attention can have implications for accident prevention as this could give rise to information which can assist with management of human error, leading to injury and accident minimisation.

The rightward bias with low alertness in healthy populations has a striking resemblance to the characteristic bias seen in spatial neglect patients following stroke. However, the bias is more pronounced in neglect patients (Corbetta & Shulman, 2011). Neglect patients have difficulty attending to the side of the world opposite to their lesion (Heilman, Watson, & Valenstein, 2003; Vallar, 2001). Although many patients recover, some right-hemisphere patients with left-neglect often have persisting symptoms (Husain & Rorden, 2003). Intriguingly, these neglect patients have concurrent difficulty in maintaining alertness, suggesting that alertness and spatial attention are closely intertwined, and that deficient alertness may be a key mechanism underlying spatial biases in neglect. Therefore, a better understanding of factors influencing the deployment

of spatial attention in healthy populations might inform the rehabilitation of patients suffering from spatial neglect.

A difficulty in synthesising the relevant literature is the lack of consensus regarding the definition of alertness. Alertness, vigilance, sleepiness, activation, arousal, fatigue and sustained attention are overlapping constructs and the definition and understanding of these constructs may differ between disciplines such as human factors, neurology, cognitive neuroscience, and psychology. Furthermore, alertness can be categorised into tonic (or intrinsic) alertness, which refers to internal control of arousal without external cues and has a timescale of minutes or hours (Sturm et al., 1999; Sturm & Willmes, 2001); or phasic alertness, which refers to response readiness following external cues and has a timescale of milliseconds (Posner & Rafal, 1987; Sturm et al., 1999). Irrespective of the alertness term employed, all terms referring to either internal or external control of arousal were included in the review. For the purpose of this review, alertness is defined as general wakefulness and readiness to respond to stimuli (Posner & Rafal, 1987; Sturm & Willmes, 2001), and herein, this definition of alertness will be used throughout the review.

2.2.1 The current model of interactions between spatial attention and alertness.

The control of spatial attention has been captured by theories such as Kinsbourne's interhemispheric competition theory (Kinsbourne, 1977) and Heilman's hemispatial theory (Heilman & Van Den Abell, 1980; Szczepanski & Kastner, 2013). According to the interhemispheric competition theory, each of the two hemispheres allocates attention towards the opposite side of space. The hemispheres rival each other by means of reciprocal inhibitory mechanisms and the deployment of spatial attention is the outcome of this inter-hemispheric competition. Damage to the right hemisphere interrupts the inhibitory projections to the left hemisphere, and a reduction in inhibition results in hyper-activation of the left hemisphere, which leads to an exaggerated attentional bias towards the right side of space, and consequently to left-sided neglect (Kinsbourne, 1977). According to the hemispatial theory, the right hemisphere is dominant in spatial attention, allocating attention to both hemifields, whereas the left

hemisphere is constrained to allocating attention towards the contralateral hemifield (Heilman & Van Den Abell, 1980). These theories provide an understanding of the neural mechanisms of spatial attention; however, they do not explain the influence of alertness on spatial attention.

The current understanding of the interactions between spatial functions and alertness is greatly shaped by research in patients with right hemisphere lesions and left-sided neglect. Several studies demonstrated that increasing patients' level of alertness, for example, by using phasic alerting tones (Robertson et al., 1998), placing a patient's feet into cold water (Woods et al., 2012), and using self-instructions (e.g., "be alert"; Robertson, Tegnér, Tham, Lo, & Nimmo-Smith, 1995), enhance the ability to respond to left-sided stimuli and alleviate neglect symptoms. Additionally, improvements in performance on tasks assessing neglect symptoms have been associated with increased activity in the right hemisphere following alertness training in neglect patients (Thimm, Fink, Küst, Karbe, & Sturm, 2006).

The findings of interactions between alertness and left-sided neglect were incorporated into an influential framework that distinguishes between the bilateral dorsal attentional network (DAN) and the right-lateralised ventral attentional network (VAN; Corbetta et al., 2008; Corbetta & Shulman, 2011; He et al., 2007). The DAN consists of the fronto-parietal regions of both hemispheres and directs attention to the contralateral hemispace (Newman et al., 2013). The VAN is lateralised in the right hemisphere and is associated with non-spatial aspects of attention, such as reorienting attention, detecting behaviourally relevant stimuli, alertness and maintenance of alertness over time (Corbetta et al., 2008; Langner & Eickhoff, 2013; Newman et al., 2013). The VAN and DAN directly interact with each other. It is postulated that the DAN's left and right fronto-parietal regions are in constant competition for hemispheric activation (Kingstone, 2016; Manly et al., 2005). The hemisphere which succeeds in gaining greater activation, allocates attention to its contralateral side (Corbetta & Shulman, 2011; Kinsbourne, 1970).

Neglect patients following right-hemisphere lesions commonly experience lowered levels of alertness, compared to patients with similar lesions in the left hemisphere (Corbetta & Shulman, 2011). According to the DAN/VAN model, this reduced alertness may lead to a rightward attentional bias. This is due to reduced activity

in the right-lateralised VAN interacting with a finely balanced bilateral DAN. With low alertness, activity in the right DAN is believed to decrease, which alleviates inhibitory control over the left DAN regions, biasing attention rightward (Corbetta et al., 2008; Corbetta & Shulman, 2011; He et al., 2007; Newman et al., 2013).

2.2.2 The current literature.

Healthy alert participants generally show a bias towards the left side, known as pseudoneglect (Corbetta & Shulman, 2011; Jewell & McCourt, 2000). As a result, increasing alertness should enhance this leftward bias, whilst decreasing alertness reduces the leftward bias. Currently, it is unclear whether, overall, the literature quantitatively supports the proposed rightward shift in attention with declining alertness in healthy participants. Some studies have reported findings supporting this relationship (Bareham et al., 2014; Bellgrove et al., 2004), whilst others do not support these findings (Fimm & Blankenheim, 2016; Schmitz et al., 2011). Therefore, the primary aim of the review is to quantify the relationship between alertness and spatial attention in a meta-analysis. A secondary aim of the review is to identify modulators of this relationship. A confirmation of the effect and the identification of its modulators may assist in strengthening and refining current theoretical models of attention. Furthermore, understanding the influence of lowered alertness on spatial attention may enable translation to the accident and injury prevention field. A better understanding of the relationship between alertness and spatial attention in healthy populations might also assist with identifying potential therapeutic targets and inform rehabilitation approaches for patients suffering from spatial neglect.

The novelty of the meta-analysis is to provide a consolidated and quantitative review of the literature on spatial attention and alertness in healthy adults. Meta-analyses rank on the top of the evidence hierarchy and outcomes from meta-analyses provide a more precise estimate of the effect than any individual study. Individual studies can have inflated effect sizes due to being underpowered, being a false positive, and might be more likely to be published if a significant result was obtained than null-results. The current meta-analysis procedure will control for these potential confounding factors by pooling the effects of multiple studies using a random effects models and by conducting four publication bias assessments.

2.3 Methods

2.3.1 Literature search and inclusions.

A systematic search of the literature on alertness and spatial attention was conducted on March 22, 2018. The databases PsychINFO and Embase were searched using the following search terms: (left* or right* or spatial) adj2 (bias or shift or deviation or asymmetr* or preference) OR Pseudoneglect AND (Sustained Attenti* OR Concentrat* OR Vigilan* OR Sleep* OR Fatigue OR Alert* OR Arousal OR Awake). No terms were mapped to subject headings. Inclusion criteria were: human adult participants, original peer-reviewed research articles, published in English, and reporting lateralisation or left/right spatial biases relative to alertness. Only studies with a sample of healthy populations were included in the review. Studies were included in the meta-analysis if they reported a statistical association or the appropriate descriptive statistics to infer the relationship between alertness and spatial bias. Studies with multiple experiments were included if at least one of the experiments met criteria to be included in the review.

The review was conducted adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009). A total of 3349 records were identified following the initial search. Another 10 records were identified through snowballing. Abstracts and titles were screened by two authors (DC and DG), identifying 93 full text articles to be assessed for eligibility. Twenty-two articles remained following the application of exclusion criteria. Three of these studies (Paladini et al., 2016; Paladini et al., 2017; Spagna, Martella, Fuentes, Marotta, & Casagrande, 2016) and one experiment from two studies (Manly et al., 2005; Schmitz et al., 2011) were excluded because effect size data or descriptive statistics which could infer effect sizes to be used for quantitative synthesis were not reported. This left 19 studies in the quantitative synthesis. Refer to Figure 2.1 for the review process.

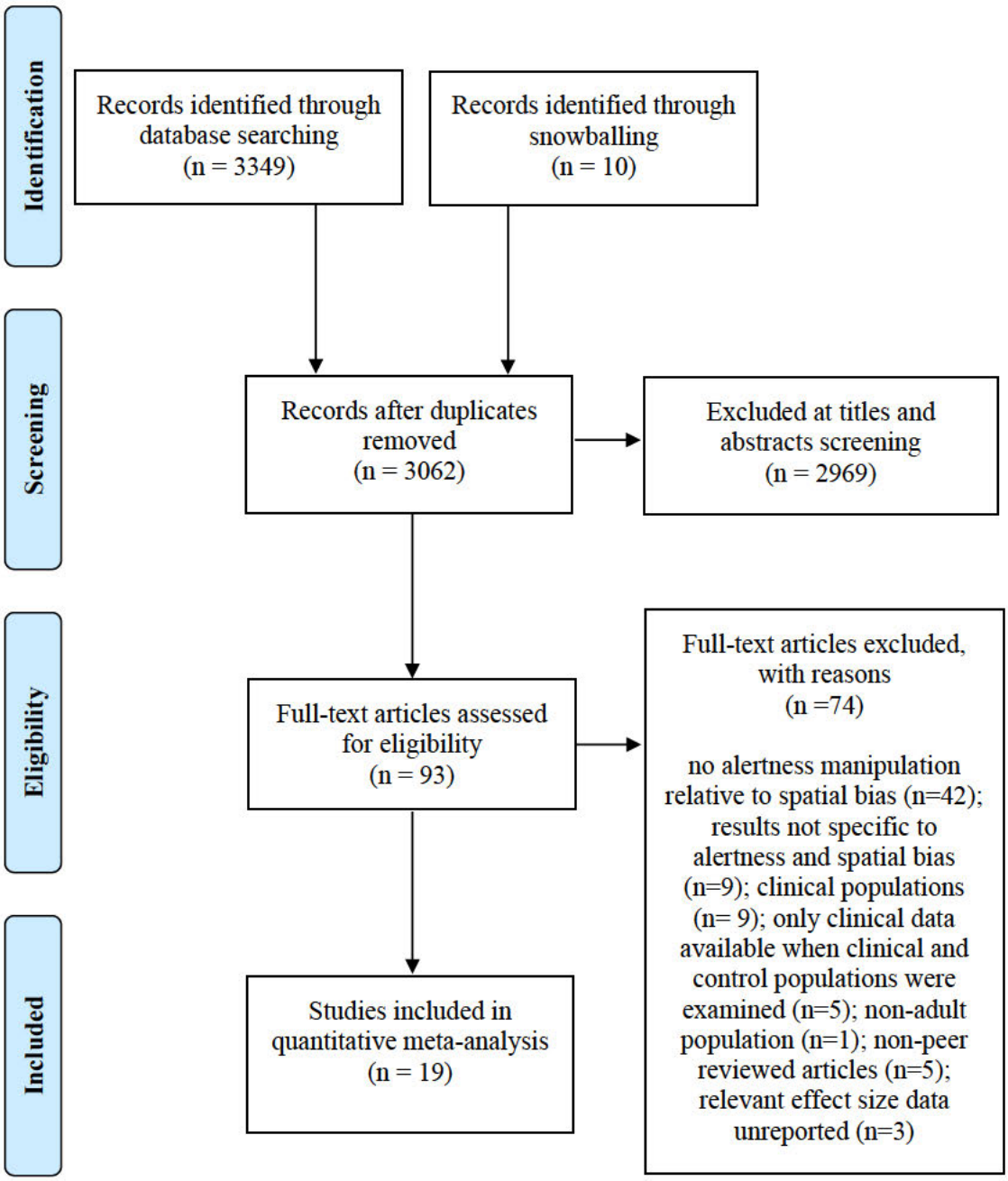


Figure 2.1. Flow chart of the search process and article selection for the review (n=number).

The following data were extracted from each included study: the spatial measures used, the alertness measures used, the statistical association between the spatial and alertness measures, and experimental design, along with participant demographics (age, gender distributions, and handedness), and sample size.

2.3.2 Meta-analysis procedure and effect size calculation.

Comprehensive Meta-Analysis Software (CMA, Version 3.3.070, Biostat, Englewood, NJ) was used to conduct meta-analyses. Effect sizes (standardized mean difference (Cohen's *d*), its 95% confidence interval and *p* values) were computed by entering reported study statistics, such as means and standard deviations, *F, t, p,* and *r,* into CMA.

For each study reporting multiple measures or multiple experiments, the effect sizes of these measures were aggregated using the arithmetic mean, so that there was one effect size per study for the overall effect size calculation. For example, the overall effect size for the study by Fimm and Blankenheim (2016) was calculated by first computing the Cohen's *d* value for each of their four measures (i.e., prosaccades, antisaccades, gap/overlap, and covert orienting) and then the mean Cohen's *d* of the four measures was calculated. In instances where different participants were used across experiments, the effect size for each participant group was collated for the overall effect size calculation.

The overall effect size was calculated by pooling all 19 effects of the selected studies in a random effects model, with effect sizes (i.e., *d*) of .2, .5, and .8 being considered a small, medium, and large effect, respectively (Cohen, 1988). A positive effect size is in line with the current dominating model of the relationship between alertness and spatial attention, indicating either a rightward bias with low alertness or a leftward bias with high alertness. A negative effect indicates the opposite (i.e., a leftward bias with low alertness and a rightward bias with high alertness).

When screening the literature, several methodological differences between the included studies were observed. Since these differences may reveal important insights on modulating factors of the interaction between alertness and spatial attention, subgroup analyses were run on five identified factors. The first factor was based on the experimental design used to contrast effects of low and high alertness on spatial attention,

distinguishing between approaches which deprived participants of sleep, exposed participants to a long task (time-on-task), alerted participants momentary with auditory tones (phasic alertness) and other approaches (between-subjects design which had participants with high and low levels of alertness). The second factor investigated the direction of alertness (i.e., increased or decreased) in moderating spatial bias. The third factor assessed whether the alertness and spatial attention relationship differed depending on whether a participant's level of alertness was measured objectively or subjectively. The fourth investigated factor was the task used to measure spatial attention, with these tasks being broadly categorised into detection and judgements tasks in the review. The final factor assessed handedness, comparing right-handed and non-right-handed samples. Differences between subgroups were assessed using Q statistic. For these analyses, the Q value, which represents total variance, was calculated.

2.3.3 Publication bias.

Rosenthal's fail-safe *N* method was used to calculate the number of studies which would be required before a significant *p* value became non-significant when combined with the selected studies (Borenstein, Hedges, Higgins, & Rothstein, 2009; Rosenthal, 1979). For this approach, it is assumed that the effect size of the missing studies is zero and the rule of thumb is that the fail-safe *N* value should be more than five times the number of included studies in the analysis plus 10 (Rosenthal, 1979).

To investigate publication bias in relation to the reported effect sizes, a funnel plot was statistically tested for asymmetries using Egger's regression intercept test (Egger, Smith, Schneider, & Minder, 1997). A *p* value smaller than .1 was considered as indicating a significant asymmetry and publication bias.

Lastly, Duval and Tweedie's Trim and Fill method (Duval & Tweedie, 2000) was employed. This method estimates an unbiased estimate of the effect by imputing missing studies based on the funnel plot's asymmetry.

2.4 Results

2.4.1 Overall effect.

The overall effect size from the 19 included studies was d =.302 (95% CI .125 – .480, p=.001). The small overall effect size provides some evidence that lowered and increased level of alertness are associated with rightward and leftward attentional shifts, respectively. Moderate heterogeneity across the studies was evident as indicated by an I^2 of 62.6%. See Figure 2.2 for a forest plot of the overall effect size and distribution.

2.4.2 Subgroup analyses.

2.4.2.1 Alertness experimental design.

Different experimental designs were used to contrast the effects of lower and higher alertness levels on spatial attention. These different experimental designs were classified into four categories: time-on-task (12 studies), sleep (3 studies), phasic alerting (2 studies), and other approaches (2 studies). Refer to Table 1 for a detailed account of individual studies.

Time-on-task designs involve changes to task performance over time, resulting from lowered alertness with time expended on the task (Paladini et al., 2016; van der Hulst, Meijman, & Rothengatter, 2001). Time-on-task approaches in the reviewed studies ranged from 40 to 120 minutes, and sleep deprivation approaches ranged from 11 to 28 hours. Task performance prior to sleep deprivation is considered a high alertness condition, whereas task performance following sleep deprivation is considered a low alertness condition. Another approach, phasic alerting, comprised of studies that involved using auditory tones (as cues prior to stimulus presentation) to increase momentary alertness during task performance. Designs classified as 'other' comprised of studies which did not involve an explicit manipulation of alertness (i.e., these studies compared subjects with varying levels of alertness, using a between-subjects design).

There was no evidence overall that any one of these four designs leads to stronger attentional effects (Q(3)=4.925, p=.177, n=19). It cannot be ruled out that this lack of evidence is due to a small number of studies in some categories and their relative poor precision in estimating effect sizes, as indicated by the large confidence intervals. Furthermore, examining the individual effect size calculations for each category reveals that there is evidence that sleep and time-on-task designs lead to the predicted rightward bias with low alertness and leftward bias with high alertness pattern, but there is

insufficient evidence for phasic alerting and other approaches as the confidence interval of the estimated effect size is crossing zero (Table 2.2).

2.4.2.2 Alertness direction.

Increasing and decreasing levels of alertness are thought to shift attention to the left and right side of space, respectively. Some studies in this review decreased alertness using paradigms such as time-on-task exposure or sleep deprivation, whereas others increased alertness using cues, alerting tones, or psychostimulants. A subgroup analysis found that the effect size for increasing (3 studies) and decreasing (14 studies) alertness did not significantly differ in magnitude ($Q(1)=1.410$, $p=.235$, $n=17$). Furthermore, studies decreasing, but not increasing alertness were found to show a significant spatial shift (Table 2.2).

2.4.2.3 Alertness measurement.

Studies were divided into two categories based on whether the alertness measure used by the study was objective (e.g., the measure of alertness level was based on electrophysiological characteristics) or subjective (i.e., the measure of alertness was based on participants' self-reports). A sub-analysis between these two categories revealed that the measurement of alertness did not influence the effect size ($Q(1)=.269$, $p=.604$, $n=17$). The 95% confidence interval for both category effect sizes did not cross zero (see Figure 2.2). Thus, both objective and subjective alertness measurements show the rightward bias with low alertness and leftward bias with high alertness pattern (Table 2.2).

2.4.2.4 Spatial task demands.

The spatial tasks were categorised into tasks that required the detection of stimuli (i.e., tasks that required speeded responses, with reaction time as the primary outcome) which were grouped into detection tasks (n=8), and tasks that required participants to decide on the spatial properties of stimuli (e.g., longer line segments of a bisected line), which were categorised as judgement tasks (n=11). The subgroup analysis revealed no

difference between judgement and detection tasks (Q(1)=.017, *p*=.897, n=19). Moreover, the confidence interval is not crossing zero for either category (Table 2.2), suggesting that the link between alertness and spatial attention is found with both detection and judgement tasks.

2.4.2.5 Handedness.

Studies were categorised based on participant handedness and the subgroup analysis for this categorisation revealed that the effect size differs depending on handedness (Q(2)=14.174, *p*=.001, *n*=17). Pooling the effect sizes of studies which only included right-handed participants reveals the expected positive effect size, but studies with both left- and right-handers, and studies with only non-right-handed participants (i.e., self-identified left-handers) do not show a significant effect of alertness on spatial attention (Figure 2.2; Table 2.2). The estimated effect size for non-right-handed participants was negative and significantly different from right-handed participants (Q(1)=13.895, *p*<.001, n=14).

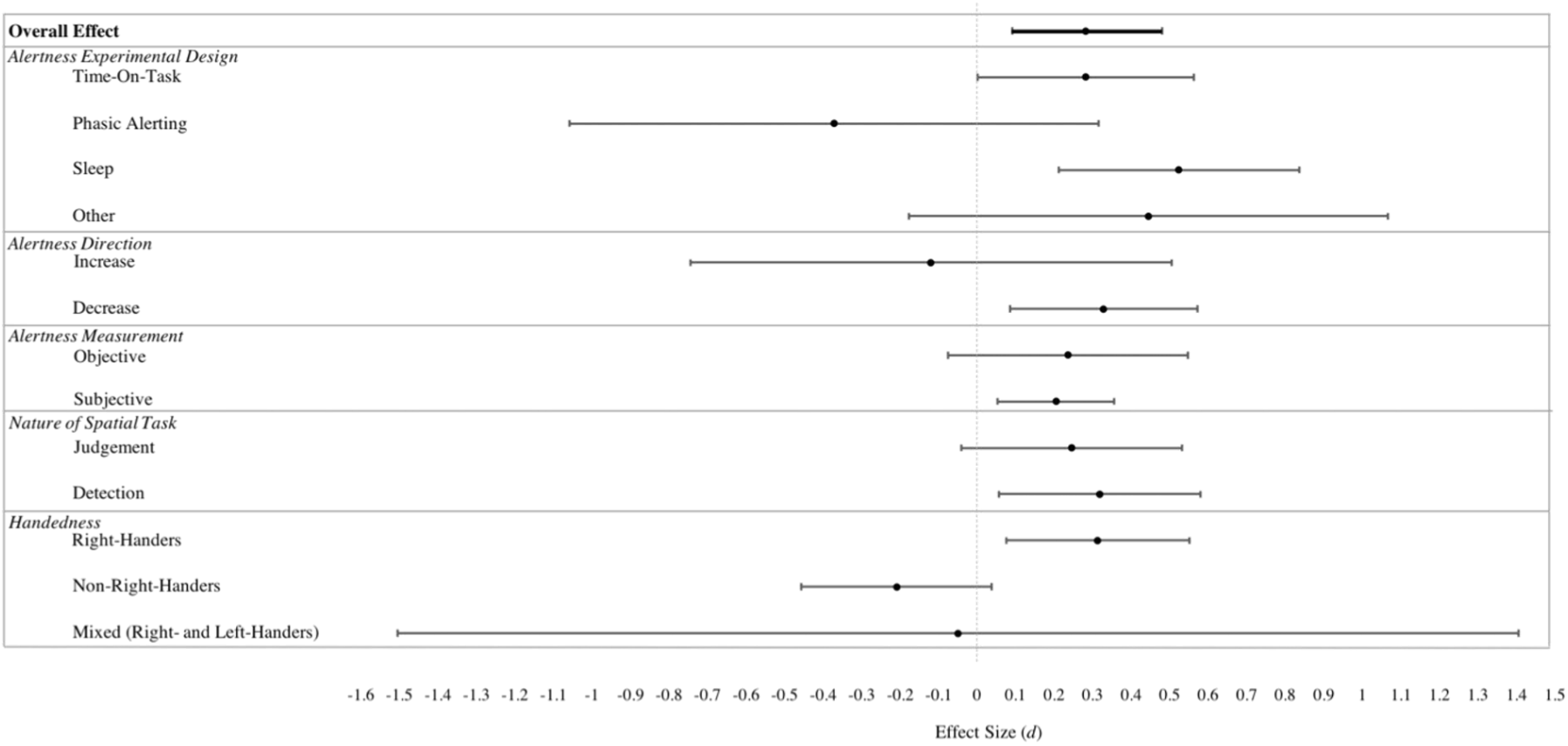


Figure 2.2. Overall and subgroup effect sizes with their corresponding 95% confidence interval. A positive effect size indicates a leftward and rightward shift with increased and lowered levels of alertness, respectively.

Table 2.1

Studies selected for meta-analysis and their calculated effect sizes.

Study	Participant characteristics (age and gender distributions)	Alertness approach (time-on-task, sleep, phasic alerting, or other[#])[%]	Alertness direction	Alertness measure*	Spatial measure (Sub-analysis task categorization)	Handedness	Computed effect size (standard difference in means)	95% confidence interval	P-value
Bareham et al., 2015	*N*=26 (14M, 12F), *M*=24.4, *SD*=4.5, range=18-35years	Time-on-task (40-50 minutes)	Decrease	Objective: EEG (theta, alpha); RT; error rate	Lateralised auditory stimulus detection task (detection)	Non-right-handers	-.209	-.456 – .038	.097
Bareham et al., 2014	*N*=26 (9M, 17F), *M*=24.2, *SD*=5 years	Time-on-task (40-50 minutes)	Decrease	Objective: EEG (theta, alpha); RT; error rate	Lateralised auditory stimulus detection task (detection)	Right-handers	.714	.445 – .983	<.001
Bellgrove et al., 2004	*N*=48 (18M, 30F), range=21-45 years	Other (alert and drowsy categories based on task performance)		Objective: Behaviour (errors on Sustained Attention to Response Task)	Greyscales task (judgement)	Right-handers	.832	.242 – 1.421	.006
Benwell, Harvey et al., 2013	*N*=32 (18M, 14F), *M*=22.3, *SD*=2.6 years	Time-on-task (70-80 minutes)	Decrease	Subjective: SSS	Landmark Task (judgement)	Right-handers	1.396	-.776 – 3.568	.208
Benwell, Thut, et al., 2013	*N*=28 (13M, 15F), *M*=22.9, *SD*=3.6, range= 19-37 years	Time-on-task (70-80 minutes)	Decrease	Subjective: SSS	Landmark Task (judgement)	Right-handers	-.023	-.811 – .765	.954

Dodds et al., 2009	*N*=18 (9M, 9F), range=20-35 years	Time-on-task (60 minutes)	Increase	Subjective: VAS	Landmark Task (judgement)	-	.479	-.291 – 1.249	.223
Dodds et al., 2008	*N*=42 (17M, 25F), *M*=39.8, *SD*=20.7 years	Time-on-task (60 minutes)	Decrease	Objective: accuracy on secondary tasks	Visual Letter Task (detection)	[+]Mixed (81% right-handed)	.506	.185 – 0.827	.002
Dorrian et al., 2017	*N*=530 (318M, 212F), *M*=34.7, *SD*=10.5 years	Other (time of day)		Subjective: KSS, Samn-Perelli Scale, Horne and Ostberg Morningness-eveningness scale	Landmark Task (judgement)	Right-handers	.185	.014 – .356	.034
Dufour et al., 2007	*N*=30 (15M, 15F), *M*=22.8 years for males & *M*=23.8 years for females	Time-on-task (60 minutes)	Decrease	Subjective: KSS	Landmark Task (judgement)	Right-handers	.516	-1.015 – 2.047	.509
Fimm et al., 2006	*N*=13 (8M, 3F), range=26-34 years	Sleep (28 hour sleep deprivation)	Decrease	Time[^]	Computerised RT task (detection)	[+]Mixed (91% right-handed)	.748	.080 – 1.416	.028
Fimm et al., 2016	*N*=13 (13M), *M*=25.6, *SD*=4.2, range=20-39 years	Time-on-task (45 minutes)	Decrease	Objective: RT	Covert Orienting Task (detection)	Right-handers	-.142	-.853 – .569	.696
Heber et al., 2008	*N*=20 (20M), *M*=26.2, range=21-31 year	Sleep (24 hour sleep deprivation)	Decrease	Time[^]	Covert Attention Task (detection)	Right-handers	.481	.018 – 0.944	.042

Manly et al., 2005	*N*=10 (6M, 4F), *M*=38.4, *SD*=10.1 years	Time-on-task (40 minutes)	Decrease	Subjective: SSS	Landmark Task (judgement)	-	-.105	-.842 – .632	.780
Matthias et al. 2009	*N*=16 (8M, 8F), *M*=24.2, *SD*=2.6, range=21-30 years	Time-on-task (session 1: 60 minutes, session 2: 120 minutes)	Decrease	Objective: RT	Partial Report Task (detection)	Right-handers	-.041	-.372 – .290	.808
Newman et al., 2014	*N*=82 (33M, 49F), *M*=23, range=18-47 years	Time-on-task (48 minutes)	Decrease	Objective: EEG (alpha)	Random Dot Motion Task (detection)	Right-handers	.953	-.025 – 1.931	.056
Newman et al., 2013	*N*=66 (26M, 40F), *M*=24, range=18-47 years	Time-on-task (48 minutes)	Decrease	Objective: RT	Rapid Serial Visual Presentation (detection)	Right-handers	.575	.061 – 1.089	.028
Schmitz et al., 2011	*N*=14 (6M, 8F), *M*=24.8, *SD*=1.6 years	Sleep (11 hour sleep deprivation)	Decrease	Subjective: KSS	Landmark Task (judgement)	Right-handers	.432	-.115 – .979	.122
Thomas et al., 2017									
Experiment 1	*N*=36 (8M, 28F), *M*=21.1, *SD*=3.8 years	Phasic alerting (auditory tones)	Increase	Objective: RT	Landmark Task (judgement)	Right-handers	.369	.016 – .722	.040
Experiment 2	*N*=48 (12M, 36F), *M*=24.5, *SD*=8.5 years	Phasic alerting (auditory tones)	Increase	Objective: RT	Landmark Task (judgement)	[+]Mixed (50% right-handed)	-.129	-.693 – .435	.654
Wiegard et al., 2017	*N*=18 (6M, 12F), *M*=25, *SD*=3, range=20-30 years	Phasic alerting (auditory tones)	Increase	Objective: EEG (Event-Related Lateralisation)	Partial Report Task (detection)	-	-.125	-.590 – .340	.598

Note. [#]Other refers to studies that did not involve a sleep, time-on-task, or phasic alerting manipulation of alertness. [%]Time intervals are approximate. Only available information reported. *N*= sample size; M= males; F= females; *M*= mean; *SD*= standard deviation; EEG= Electroencephalography; RT= reaction time; SSS=Stanford Sleepiness Scale;

KSS=Karolinska Sleepiness Scale; VAS=Visual Analogue Scale; LANT=Lateralized Attention Network Task. *In cases where more than one alertness measure was used, only those used in the analysis comparing spatial bias and alertness are reported in the table. ^Both objective and subjective alertness measures were used in these experiments, however, these measures of alertness were not used in the analysis comparing spatial bias and alertness. +Mixed refers to samples with left-handed and right-handed participants.

Table 2.2

Individual effect size calculations.

Sub-category grouping	n	Effect size (standard difference in means; *d*)	Standard Error	95% CI	*p* value
Alertness experimental design					
Time-on-task	12	.281	.143	.00 – .562	.050*
Sleep	3	.523	.159	.211 – .836	.001**
Phasic alerting	2	-.372	.350	-1.059 – .315	.288
Other	2	.444	.317	-.177 – 1.065	.161
Alertness direction					
Increase	3	-.120	.319	-.745 – .505	.707
Decrease	14	.328	.124	.085 – .572	.008*
Alertness measurement					
Objective	10	.236	.159	-.076 – .547	.138
Subjective	7	.204	.077	.053 – .356	.008*
Spatial task demands					
Judgement	11	.245	.147	-.042 – .532	.094
Detection	8	.318	.133	.056 – .579	.017*
Handedness					
Right-handers	13	.313	.121	.076 – .550	.010*
Non-right-handers	1	-.209	.126	-.456 – .038	.097
Mixed (right- and left-handers)	3	-.050	.742	-1.504 – 1.405	.947
Overall effect	19	.281	.098	.090 – .472	.004*

Note. One study (Thomas, Barone, Flew, & Nicholls, 2017) included two experiments: one with only right-handers and one with both left- and right-handers, hence these experiments were separated in the analysis and were considered as individual studies. *Analysis significant at p ≤.05 level. **Analysis significant at the p ≤.001 level.

2.4.2.6 Publication bias.

Four different methods were applied to assess publication bias in the meta-analysis. The fail-safe *N* rule of thumb was met: the calculated fail-safe *N* was 128. That is, 128 studies with a mean effect size of zero would need to be added to the meta-analysis before the results would become non-significant. This number is larger than 105 (i.e., 5 times the number of included studies plus 10) and is thus not raising concerns.

While the funnel plot may seem slightly asymmetric (Figure 2.3), there was statistically no significant plot asymmetry according to the results of the Egger's regression intercept test (intercept = 0.800, standard error = 0.724, $t(17) = 1.106$, $p = .284$). This assessment method does not indicate a significant bias in the published literature.

The Duval and Tweedie's trim and fill method produced an adjusted overall effect size of 0.279 (95% CI 0.104 to 0.454) in the 19 included studies after two studies were imputed. While this best estimate of the unbiased effects size is slightly smaller than the calculated overall effect size (d =0.302), this small difference is not indicative of a systematic publication bias.

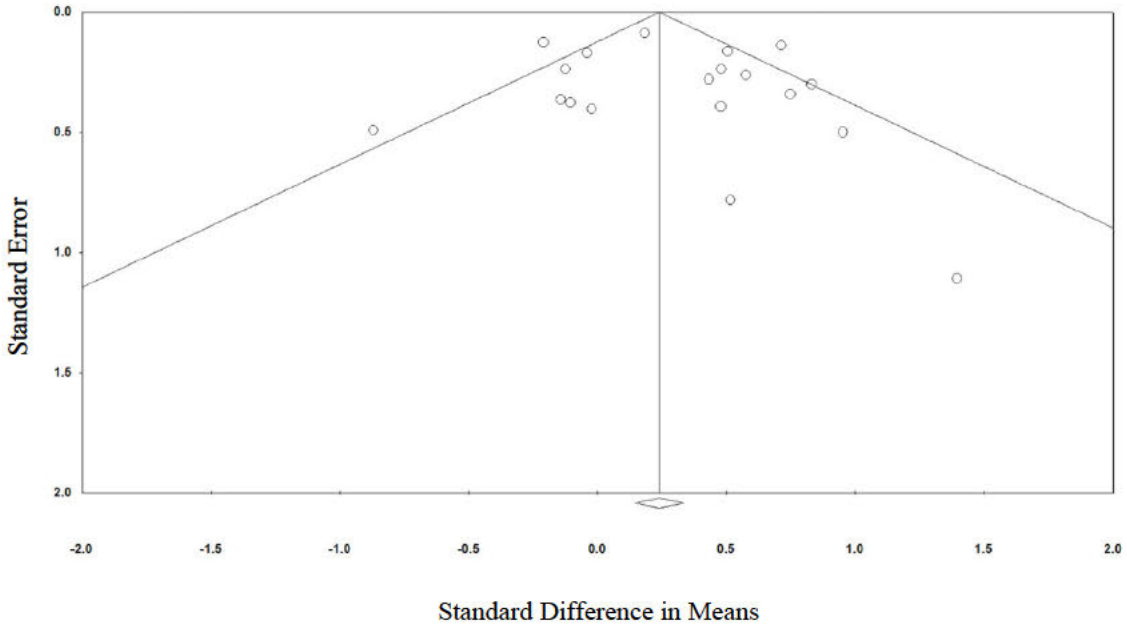


Figure 2.3. Funnel plot depicting the distribution of the effect in the reviewed studies. The plot portrays the standard error by standard differences in means.

2.5 Discussion

Based on the 19 included studies in this meta-analysis, we found a small effect size (d = 0.302) supporting an association between spatial bias and alertness: a rightward bias in attention with declining alertness, and a leftward bias with increasing alertness.

Importantly, the results of four different methods to assess publication bias suggest that the impact of bias on the calculated effect size is modest at best. Duval and Tweedie's trim and fill method implies that the observed effect size might be slightly overestimated by around 10% (adjusted d = 0.279). Similarly, the other publication bias calculations provide no indication of serious bias in the included studies and as a result, it is highly unlikely that the observed overall effect size is a false positive.

A few subgroup analyses were conducted to identify factors influencing the association between alertness and spatial attention. The only factor that was clearly identified was handedness. Significant effects were only observed in studies with right-handed participants, showing the expected rightward bias in attention with decreasing alertness and a leftward bias in attention with increasing alertness. While there was only one study using a sample of non-right-handers (Bareham et al., 2015), it is noteworthy that the Cohen's d value for this sample was negative (i.e., lowered alertness was associated with a leftward bias), however, this was not significant. There is not enough evidence to state that non-right-handers show the opposite pattern of right-handers as the 95% confidence interval crossed zero, nevertheless there is sufficient evidence that the two populations have significantly different effect sizes. This observed difference between right-handers and non-right-handers ties in nicely with a functional magnetic resonance imaging study which examined laterality in right-handers and non-right-handers, showing the typically right-lateralised ventral attentional network (VAN) in right-handers, to be bilateral or even slightly left-lateralised in non-right-handers (Liu, Stufflebeam, Sepulcre, Hedden, & Buckner, 2009). A study by Petit et al. (2015) supports the dorsal frontoparietal network (i.e., the DAN) as showing equal activation in the left and right hemisphere in right-handers, but a strong right hemisphere activation in left-handers. Taken together, these studies suggest differences in lateral neural activity between the DAN and VAN in left- and right-handers. Investigating the differences in lateralisation between right-handers and non-right-handers may provide a promising avenue for refining the current framework of the interactions between spatial attention

and alertness. Differential activations in left- and right-handers suggests that these two groups respond differently to changes in alertness, and if findings were to transfer to real-world scenarios, from a safety perspective, this could indicate that if approaches to combat the consequences of lowered alertness are implemented (e.g., adding more road signs to the right side of the road), these might not be as effective in preventing the effects of lowered alertness on spatial attention in left-handers. Extending these findings to clinical populations could suggest that left-handers (compared to right-handers) might be less affected by spatial neglect after right hemispheric lesions because of their bilateral or slightly left-lateralised VAN (Bareham et al., 2015; Liu et al., 2009). Hence, understanding the differences in neural correlates in left- and right-handers could help construct personalised interventions for neglect patients.

Four other experimental factors were investigated: the experimental design relative to alertness (i.e., time-on-task, sleep deprivation, phasic alerting, or other), direction of alertness manipulation (increase or decrease of alertness), measurement of alertness (subjective or objective), and the nature of the spatial task (detection of appearing stimuli or judgement of spatial stimuli properties), but there was no evidence that any of these modulated the effect size significantly.

The lack of difference between the different experimental designs is interesting as it suggests that similar effect sizes are observed, for example after 28 hours of sleep deprivation (Fimm et al., 2006) and just 40 minutes of time-on-task (Manly et al., 2005). This is potentially an important finding for researchers investigating the link between alertness and spatial attention as it is much simpler to conduct time-on-task experiments than sleep deprivation studies. However, the finding is only based on three sleep deprivation studies included in the analysis, possibly limiting this recommendation. Nonetheless, the provided evidence that time-on-task and sleep deprivation are associated with a rightward shift of attention highlight the need for careful examination of these effects for work safety. For example, the effect of sleep restriction and sleep deprivation have implications for shift-workers, and time-on-task effects can be reflective of jobs involving prolonged task exposure, such as driving and air traffic controlling.

An interesting observation from the comparison between approaches that increased and decreased alertness in this meta-analysis is that, while the two approaches are not statistically different, there is only evidence that decreases in alertness are

associated with attentional shifts. The confidence interval of the estimated effect size for approaches increasing levels of alertness crossed zero and thus an association between an increase in alertness and attentional shifts cannot be confirmed at this stage. All three studies which increased alertness showed a confidence interval which crossed zero, where two of these studies showed a positive Cohen's *d* value, and one showed a negative Cohen's *d* value. This suggests uncertainty regarding the direction of the spatial shift following an increase in alertness in healthy adults, indicating a need for further investigation into the effect of increasing alertness to help uncover this discrepancy.

The analysis examining whether a participant's level of alertness was measured objectively or subjectively, and whether this impacted the alertness and spatial attention relationship, revealing null findings is again interesting from an experimental point of view as it may be logistically simpler and more cost-effective to ask participants than to obtain physiological measures. It might still be advisable to take multidimensional measures of alertness whenever possible as contrasting these measures might provide an avenue for shedding light on which dimensions of alertness are associated with attentional shifts.

The tasks used to measure spatial attention were broadly categorised into detection and judgements tasks. This categorisation is particularly interesting from a work safety perspective. For example, detection tasks are related to job demands that require fast and accurate responses to the environment (e.g., pilots, truck drivers, defence personnel) as one's ability to scan the environment is crucial for job competency, whereas judgement tasks might be more crucial in a setting such as a medical personal deciding on the outcome of an x-ray or scan. However, the review's findings do not support a difference in the effect of these categories: the sub-analysis comparing the two categories suggests that the spatial task employed did not influence the relationship with performance outcomes and alertness.

While this review revealed some interesting findings, it is important to point out that many of the analyses are based on a rather small number of included studies. The results provide an accurate summary of the current evidence; however, the subgroup analyses should be treated as preliminary in nature and more research is needed to draw more definitive conclusions. Further, a caveat of meta-analyses is that important methodological factors may be collapsed when pooling effect sizes. The observed

heterogeneity in the current review suggests indeed that this might be the case. Such possible factors are, for example, line length (Benwell, Harvey, Gardner, & Thut, 2013), and initial bias (Benwell et al., 2013). In the study by Benwell et al. (2013) the length of the Landmark task stimulus influenced whether the spatial bias following a decrease in alertness was statistically significant, as only long (not short) stimuli showed the rightward shift with lowered alertness. This example highlights that potentially important factors modulating the interaction between alertness and spatial attention were lost in the analyses due to collating findings within each study.

Interestingly, almost all studies in this review were behavioural and only one study included in the meta-analysis attempted to uncover the neural mechanisms underlying the interactions between alertness and spatial attention in healthy participants. This study revealed increased alpha absolute power in the right (compared to the left) parieto-occipital scalp regions with decreasing alertness (Newman et al., 2013), potentially supporting literature showing increased alpha power to reflect decreased excitability in these areas (Paus et al., 1997; Zhao, Zhao, Liu, & Zheng, 2012). Furthermore, a study excluded at the last stage of the screening process also examined neural mechanisms, by applying Transcranial Magnetic Stimulation to the left and right posterior parietal cortex (Paladini et al., 2017). This study identified the posterior parietal cortex to be more excitable in the left than the right during low alertness, whereas the right (compared to the left) posterior parietal cortex was more excitable under high alertness (Paladini et al., 2017). As a result, both studies support decreases in alertness to associate with decreases in activation in the right hemisphere, which is proposed to subsequently lead to a hemispheric activation advantage in the left hemisphere, shifting attention towards the right, supporting the dominant VAN/DAN model (Corbetta & Shulman, 2011). However, given the limited number of studies examining the neural mechanism of spatial attention and alertness, there is notably a need for further investigation to confirm the current dominant model.

A critical gap identified in this review was that there was not a single study investigating whether the link between lowered alertness and spatial attention is found outside the laboratory. Even if subtle, information presented on the left side that is neglected may have profound implications for work safety. Yet, it is unclear whether the observed link between alertness and spatial attention in tightly controlled lab

environments have any real-world implications. While testing real-world performance poses significant challenges, it seems paramount that, at very least, designs with higher real-world fidelity are used. For example, tasks involving simulations such as driving or air-traffic control could be used to study real-world applications of alertness on spatial bias. Additionally, it is apparent that none of the reviewed studies were designed to address potential safety implications, hence the relevance of the meta-analysis findings on health and safety remains unclear. The small effect size found in laboratory-based studies may suggest that the impact on safety is likely to be minimal, but this remains to be confirmed. The lack of applied research investigating the effects of lowered alertness on spatial aspects in occupational activities poses a significant knowledge gap.

Age, gender and reading directions are known modulating factors of spatial attentional asymmetries. Males tend to show a slightly more pronounced leftward bias compared to females when bisecting lines under alert conditions (Jewell & McCourt, 2000) and this bias has been shown to be reduced or even reversed in older adults compared to younger individuals (Benwell, Thut, Grant, & Harvey, 2014; Jewell & McCourt, 2000; Schmitz et al., 2011). Furthermore, ageing effects on spatial attention are reportedly stronger in males than females (Barrett & Craver-Lemley, 2008; Varnava & Halligan, 2007). Also, healthy subjects with left-to-right reading pattern generally show a leftward bias, whereas right-to-left readers show a reduced leftward or a rightward bias (Chokron & De Agostini, 1995; Chokron & Imbert, 1993). While neither age, gender and reading directions has been studied in the context of interactions between alertness and spatial attention, such studies might provide an interesting avenue to refine the mechanisms underlying these interactions.

2.6 Conclusions

The meta-analysis revealed a rightward bias in attention with declining alertness and a leftward bias in attention with increasing alertness, albeit with a small effect size. Handedness being identified as a modulator of the relationship suggests a need for further investigation into the variability in the association between alertness and spatial bias in non-right-handers to understand how lowered alertness can impact non-right-handers as this has implications for injury prevention. A critical gap identified in this review was

that there was not a single study investigating whether the link between lowered alertness and spatial attention is found outside the laboratory. Even if subtle, information presented on the left side that is neglected may have profound implications for work safety. Finally, the confirmation of the relationship between alertness and spatial attention in this meta-analysis is strengthening the rationale for implementing targeted interventions aimed at increasing alertness to ameliorate symptoms of spatial neglect in affected stroke survivors (Robertson et al., 1998; Robertson et al., 1995).

Chapter Three: The relationship between alertness and spatial attention under simulated shiftwork

3.1 Abstract

Higher and lower levels of alertness typically lead to a leftward and rightward bias in attention, respectively. This relationship between alertness and spatial attention potentially has major implications for health and safety. The current study examined alertness and spatial attention under simulated shiftworking conditions. Nineteen healthy right-handed participants (*M*=24.6±5.3 years, 11 males) completed a seven-day laboratory based simulated shiftwork study. Measures of alertness (Stanford sleepiness scale and Psychomotor vigilance task) and spatial attention (Landmark task and a detection task) were assessed across the protocol. Detection task performance revealed slower reaction times and higher omissions of peripheral (compared to central) stimuli, with lowered alertness; suggesting narrowed visuospatial attention and a slight left-sided neglect. There were no associations between alertness and spatial bias on the Landmark task. Our findings provide tentative evidence for a slight neglect of the left-side and a narrowing of attention with lowered alertness. The possibility that one's ability to sufficiently react to information in the periphery and the left-side may be compromised under conditions of lowered alertness highlights the need for future research to better understand the relationship between spatial attention and alertness under shiftworking conditions.

3.2 Introduction

Working around the clock is an integral part of a 24-hour society. Approximately 15 to 30 percent of the working population comprise of shiftworkers (Boivin & Boudreau, 2014; Australian Bureau of Statistics, 2010). Shiftwork generally refers to work outside the typical 9am to 5pm hours, such as morning, evening or night shifts. Due to these unusual schedules and poor sleep during the day, these workers often work at times when alertness is low (Rajaratnam, Howard, & Grunstein, 2013) and sleepiness is high (Åkerstedt, 2003). Working outside conventional daytime hours may impact cognitive functioning (Marquié, Tucker, Folkard, Gentil, & Ansiau, 2015). There are also short-term effects, such as reduced productivity, impaired memory and increased safety risk (i.e., more error prone) during a night shift (Meuman, Meer, & Dormolen, 1993; Rouch, Wild, Ansiau, & Marquié, 2005).

Shiftworkers have high levels of subjectively and objectively measured sleepiness during the night shift (Åkerstedt, 2003; Torsvall, Akerstedt, Gillander, & Knutsson, 1989). This is due to shiftworkers being awake when their bodies are programmed to be asleep. A large proportion of shiftworkers work extended hours, and commonly report working consecutive shifts, leading to prolonged exposure to conditions which lower alertness (Santhi, Horowitz, Duffy, & Czeisler, 2007).

Sleepiness and low alertness levels are associated with higher risks for accidents, injury and error (Folkard & Tucker, 2003), and therefore, shiftworkers are at a higher risk of being involved in incidents and accidents than non-shiftworkers (Åkerstedt, 2003). For example, one study reported that medical errors in surgical residents increased by 22 percent with lowered alertness (McCormick et al., 2012). Moreover, reduced efficiency in performance during night shift tends to be pronounced in the early hours of the morning (i.e., 2am-5am; Harrington, 2001), coincident with a peak in incidents and accidents during this time (Folkard, 1997). Working a night shift also increases the likelihood of experiencing a near crash event on the drive home (Lee et al., 2016).

One reason for the increased likelihood of crashes may be related to a narrowing of spatial attention with lowered alertness. Simulated monotonous driving performance in two studies revealed a deterioration in the ability to detect stimuli presented in the

periphery, compared to central presentations, as driving time increased (Rogé, Pébayle, El Hannachi, & Muzet, 2003; Rogé, Pébayle, Kiehn, & Muzet, 2002). This indicates that conditions that lower alertness, such as time-on-task, can narrow attention to the centre of the visuospatial field.

A growing body of literature link lower levels of alertness with a spatial shift of attention towards the right side (Chandrakumar et al., 2019). This rightward shift in attention is characterised by slowed reaction times to left-sided stimuli (Fimm & Blankenheim, 2016), left-sided stimuli misidentified as being on the right (Bareham et al., 2014), and omission of left-sided objects (Manly et al., 2005). A study examined spatial attentional performance in hospital staff at two testing periods: one during a well-rested state (i.e., with an average of 7 hours of sleep in the previous 24 hours prior to testing), and another, during reduced alertness after working a double-shift (i.e., with an average of 3.55 hours of sleep in the previous 24 hours; Manly et al., 2005). The authors found a rightward shift in attention, indicating a neglect of the left side in the reduced alertness condition compared to the well-rested condition. Hence, these findings have safety implications for shiftworkers. For example, highway driving under high-speed conditions whilst operating a large vehicle, such as a truck, requires skilled motor and visuospatial ability (Ting, Hwang, Doong, & Jeng, 2008), and as truck drivers commonly commute during the night and early hours, this places them under monotonous driving conditions which can lower alertness (Zhao et al., 2012). Previous research suggests impaired performance resulting from lowered alertness is linked with vehicular accidents (Harris, 1977; Otmani, Pebayle, Roge, & Muzet, 2005). Currently, the literature examining the spatial attention and alertness relationship is limited, highlighting the need for future research to explore the relationship between lowered alertness and spatial attention under shiftworking conditions, particularly whilst working the nightshift, when alertness is already reduced due to working at a time when the drive for sleepiness is at its greatest (Rajaratnam et al., 2013).

Alertness can be separated into tonic alertness (referring to general alertness) and phasic alertness (referring to moment to moment alertness) and these can differentially influence spatial attention (Sturm & Willmes, 2001). Tonic alertness can be measured via simple reaction time tasks which involve maintaining a state of preparedness to respond to stimuli, for a period of time (Sturm & Willmes, 2001). Phasic alertness can be measured via cued-response tasks and can accelerate and enhance orienting towards a

cued stimulus in healthy adults (Asanowicz & Panek, 2020). In neglect patients experiencing left-sided neglect, a reduction in this neglect under phasic alerting conditions is found (Robertson et al., 1998).

A dominant theoretical framework postulates a rightward shift in attention with declining alertness (Corbetta & Shulman, 2011). This is due to decreasing alertness resulting in an activation advantage in the left hemisphere, which directs attention to the right visuospatial field, and consequently leads to an attentional bias towards the right. Under alert conditions, the right hemisphere is slightly more activated, biasing attention towards the left due to contralateral attentional allocation. Therefore, changes in alertness should demonstrate corresponding changes in attentional biases, where high and low levels of alertness show a leftward bias and rightward bias, respectively.

The current study aimed to investigate the relationship between alertness and spatial attention under simulated shiftwork conditions. The main hypotheses were that (1) lowered alertness will correspond with a rightward bias in attention and high alertness will correspond with a leftward bias in attention, and (2) lowered alertness will be associated with a narrowing of attention.

3.3 Method

3.3.1 Participants.

19 healthy non-shiftworking right-handed participants (11 males) aged between 18 and 39 years ($M \pm SD$: 24.6 ± 5.3 years) were recruited from the general population. Initial eligibility screening involved gathering information regarding age, self-reported height/weight, smoking status, health status, and sleep patterns via telephone screening. Exclusion criteria were the following: presence of medical conditions, psychiatric disorders, sleep disorders, abnormal blood chemistries, habitual sleep duration <7 h or >9 h, BMI outside the normal to overweight range (18.5–27 kg/m^2), regular medication use (oral contraception was allowed), drug and/or alcohol abuse, methamphetamine abuse, more than 2 h of structured high impact activity/exercise per week (to limit the extreme metabolic changes influencing results related to being sedentary in the lab for 7 days), food allergies, pregnancy, and any trans meridian travel in the 60 days prior to the study, or history of shiftwork, to ensure stable sleep/wake patterns and no circadian

misalignment. If deemed eligible, following written informed consent, participants attended two further screening sessions in person to complete questionnaires regarding psychological and physical health, had a blood test completed, and wore an activity monitor for 7 consecutive days prior to the study commencing (Phillips Respironics Actiwatch, Murrysville, PA, USA). Participants also completed a 7-day sleep diary and a 4-day food diary to assess habitual sleeping and eating patterns, respectively. Female participants were only scheduled to participate in the luteal phase of their menstrual cycle, as confirmed by self-report, to control for changes in sleep quality, hormonal factors, and basal metabolism during the menstrual cycle (Baker & Driver, 2007). Participants refrained from over-the- counter medications, caffeine, alcohol, napping, and were instructed to keep a strict habitual sleep schedule (22:00–23:00 to 06:00–07:00), which was verified by actigraphy and a subjective sleep diary during the 7 days prior to study commencement. Urine toxicology was performed to verify the absence of any illicit substances immediately prior to study commencement. These criteria are consistent with the laboratory's previous sleep studies standard exclusion criteria (Grant et al., 2017; Gupta et al., 2017). Handedness was assessed using the Flinders Handedness Survey (FLANDERS; Nicholls, Thomas, Loetscher, & Grimshaw, 2013) and was not used as inclusion or exclusion criteria. Data collection for the present study took place within a wider study, which received approval by the University of South Australia Human Research Ethics Committee (#0000033621) and is registered with the Australian New Zealand Clinical Trials Registry (ANZCTR12615001107516). All procedures were in accordance with the National Statement on Ethical Conduct in Human Research.

3.3.2 Procedure.

The study was conducted at the Sleep and Chronobiology Laboratory at the University of South Australia. Participants spent six nights and seven days consecutively in a laboratory-controlled environment. The laboratory temperature was set to 22±1°C. Light intensity was <100 lux at eye-level during wakefulness and was fixed at <0.03 lux during sleep periods. On the first night, participants had an 8-hour sleep opportunity, which followed a baseline day. Prior to the first night shift, participants were awake for 28 hours to simulate the common pattern observed in shiftworkers prior to their first shift (Åkerstedt, 2003). From days three to six, during the simulated night shifts, participants were given a 7-hour daytime sleep opportunity on each day between 1000h to 1700h. The

last day (day 7) involved recovery sleep, where participants were given an 8-hour sleep opportunity between 2200h to 0600h to adjust their sleep/wake cycle from the shiftwork manipulation. Further information on the protocol can be found from a previously published study (Gupta et al., 2019). Data for the current study was collected at six different time points across six days. Refer to Figure 3.1 for an outline of the testing protocol.

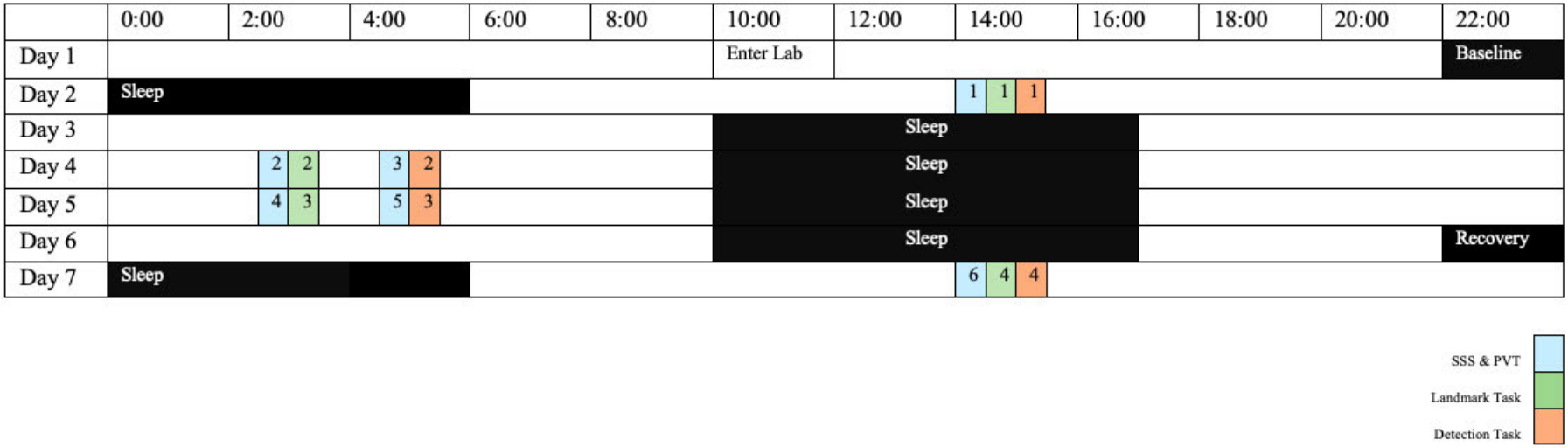


Figure 3.1. Simulated shiftwork protocol with the timepoints of the alertness (Psychomotor Vigilance Task [PVT], Stanford Sleepiness Scale [SSS]) and spatial attention (Landmark Task, Detection Task) measures outlined. The numbers correspond to the order of the tests.

3.3.3 Alertness measures.

Two measures of alertness were employed in the current study, one assessing objective (behavioural) alertness, and the other assessing subjective (self-reported) alertness.

3.3.3.1 Psychomotor vigilance task (PVT).

A 10-minute hand-held PVT device, which is highly sensitive to sleep loss was used to measure alertness in the current study. The PVT is regarded as a reliable and valid assay of alertness (Dinges & Powell, 1985; Dorrian, Rogers, & Dinges, 2005). The PVT required participants to respond as quickly as possible to the presentation of a visual stimulus (i.e., a red circle) which changes to a number as a timer counts from 0 to 500 milliseconds. PVT performance at six time points were obtained in the current study: days two and seven at 1400h, days four and five at 0300h, and days four and five at 0500h were examined. The PVT reciprocal of the mean reaction time (mean RRT) and lapses were used for analysis. Mean RRT was calculated as the mean of the reciprocal of the reaction time (1/RT) in milliseconds. A lapse was counted when reaction time was greater than 500ms (Basner & Dinges, 2011). Lower mean RRT scores and higher lapses indicate poorer performance and lowered alertness.

3.3.3.2 Stanford sleepiness scale (SSS).

A 7-point rating scale was used to assess subjective sleepiness, ranging from 1 "*feeling active, vital, alert, or wide awake*" to 7 "*no longer fighting sleep, sleep onset soon; having dream-like thoughts*" (Hoddes, Dement, & Zarcone, 1972). The SSS has been found to predict performance on tasks that assess alertness, such as reaction time and vigilance tests (Hoddes et al., 1972; Shahid, Wilkinson, Marcu, & Shapiro, 2012). The SSS was used to assess subjective sleepiness throughout the protocol at the same six time points as the PVT (i.e., days two and seven at 1400h, days four and five at 0300h, and on days four and five at 0500h). Higher SSS scores indicate higher levels of sleepiness.

3.3.4 Spatial attention measures.

Two measures assessing spatial attention, more specifically, one assessing judgement and the other assessing detection, were used in the present study. The judgement task entailed judgement of the spatial properties of lines, whilst the detection task required speeded responses to presented stimuli. Stimulus presentation for both tasks were presented using E-prime 2.0 software on a DELL desktop computer with a screen resolution of 1920 X 1080 and a diagonal screen size of 58 cm. Participants were seated approximately 60 centimetres from the centre of the screen, with their heads rested on a chinrest to maintain participants' head position towards the centre of the screen.

3.3.4.1 Landmark task.

A commonly used spatial attention task, the Landmark task (Fimm & Blankenheim, 2016; Manly et al., 2005; Milner et al., 1992) was employed in the current study. In the current study, 108 vertically pre-bisected horizontal lines were presented against a grey background. Each pre-bisected horizontal line contained diagonally opposite pairs of black and white segments on each side of the vertical divider. The top segment on one side was white whilst the bottom segment of the same side was black, and vice versa for the opposite side. Side of longer segment (left/right), polarity (upper left black, upper left white) and deviation from the midline (0.5, 1, or 2 mm) differed between trials. Half the total number of stimuli were pre-bisected towards the left, and half the stimuli contained upper left black polarity. The factors side, polarity and deviation were counterbalanced between the 108 stimuli, such that each factorial combination was presented on nine occasions. Participants were instructed to indicate the side of the pre-bisected line that was longer, responding using the letter 'z' and 'm' on the keyboard to indicate left and right, respectively. Each trial started with a blank screen for 1000ms followed by a stimulus presentation for 500ms and a blank response window for a maximum of 2000ms (see Figure 3.2). If the participants responded within 2000ms, the following trial was presented. However, if participants did not respond within the allocated response time window, the trial was presented again at a later stage, so each participant responded to 108 stimuli before task termination. The task lasted approximately eight minutes. Bisection bias on the Landmark task was calculated as the

number of right responses minus the number of left responses divided by the total number of trials for each participant (Thomas, Loetscher, & Nicholls, 2012). Hence, negative and positive bias scores indicate a bias towards the left and right side, respectively. Landmark task spatial bias on days two and seven at 1400h, and days four and five at 0300h were analysed.

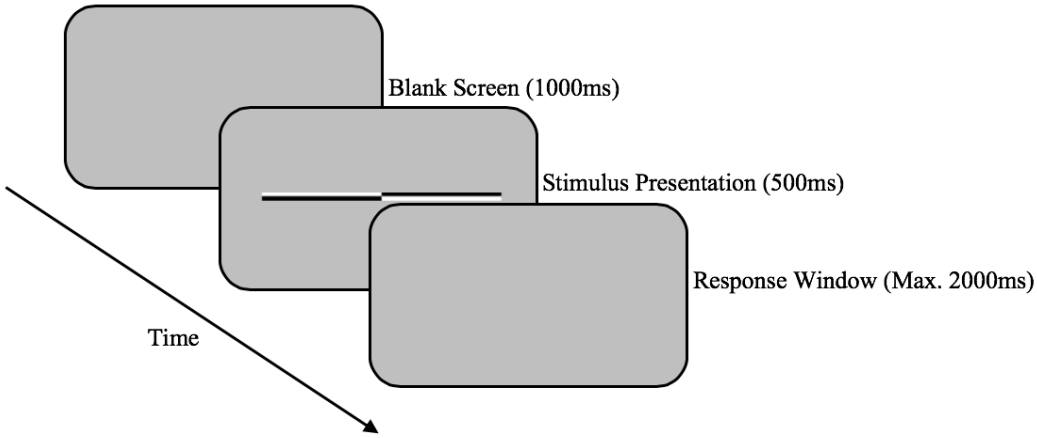


Figure 3.2. Landmark task stimulus train. Prior to stimulus presentation, a blank screen was presented for 1000ms. Stimulus presentation was 500ms and the maximum response window was 2000ms.

3.3.4.2 Detection task.

Participants were presented with 5mm circular dark grey stimuli at varying eccentricities on a light grey screen. Each circular stimulus was presented randomly at one of four eccentricities on each side of the fixation point at 2, 7, 12, and 17 centimetres from the centre of the screen with a height of 28cm and width of 51cm. A total of 120 stimuli were presented, with 15 stimuli at each of the eight screen positions. A fixation cross was presented throughout the trials. Each trial started with the presentation of the central fixation cross for a randomized presentation time ranging between 1500 to 4500ms, followed by the stimulus presentation for 100ms. The response window was set to a maximum of 1500ms (see Figure 3.3). The trial terminated once the participant

responded or if no response was made after 1500ms. If participants did not respond to a stimulus, that trial was considered an omission of response. If participants responded within 100ms of stimulus presentation, this response was deemed an anticipatory response and removed from analysis. The task lasted approximately 12 minutes. Detection task performance was assessed on days two and seven at 1400h, and days four and five at 0500h. The number of omissions (i.e., the trials that participants did not respond to stimuli) and the reaction time following stimulus presentation were used for analysis.

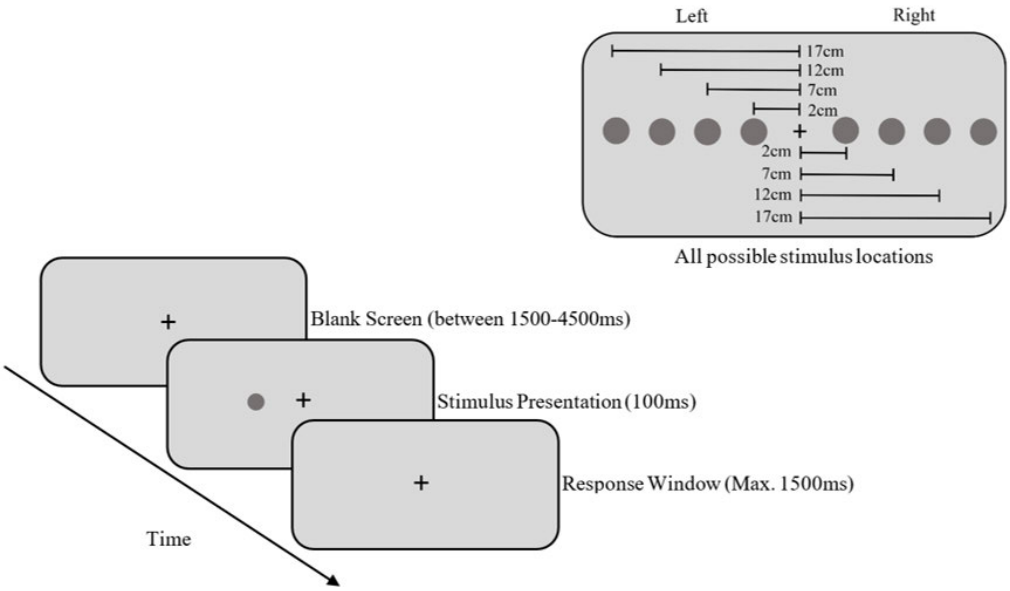


Figure 3.3. Detection task stimulus train. Prior to stimulus presentation, a blank screen was displayed for a duration between 1500 to 4500ms. Stimulus presentation was 100ms with a maximum response window of 1500ms.

3.3.5 Statistical analyses.

3.3.5.1 Data analysis.

Data were analysed using jamovi version 1.0.7.0 (The jamovi Project, 2019). Alertness measures (PVT & SSS) and spatial bias measures (bisection bias on the

Landmark task & reaction time and omissions on the detection task) corresponding to the time of testing (i.e., D2 1400h, D4 0300h, D4 0500h, D5 0300h, D5 0500h, D7 1400h) were used in analysis. Missing data were not imputed or corrected for in the analyses as mixed effects models allow for parameters to be estimated using available data (Field, 2014).

3.3.5.2 Alertness changes with time of testing.

Three mixed effects models with ID as a random intercept were run to determine whether alertness changed across the different time points of the simulated shiftwork protocol. All three models included the categorical variable of time (D2 1400h, D4 0300h, D4 0500h, D5 0300h, D5 0500h, D7 1400h) as a fixed effect. The continuous variables PVT lapses, PVT mean reciprocal reaction time (mean RRT), or SSS were entered as the outcome variable for each model. F-values from fixed effects, degrees of freedom, and post hoc analyses are reported in Table 3.1. Holm corrections were used to account for multiple post hoc comparisons. Partial eta^2 effect sizes were also calculated independently from the mixed effects modelling.

3.3.5.3 Spatial attention changes with time of testing.

Three mixed effects models with ID as a random intercept were run to investigate whether the Landmark task bisection bias, and detection task reaction time and omissions related to time. All models had time as a fixed effect, and the continuous variables bisection bias, reaction time or omissions as the outcome variable for each model. Side and location were further predictors in the detection task models. F values, degrees of freedom, and post hocs comparisons with Holm corrections are reported in Table 3.1.

3.3.5.4 Alertness and spatial attention relationship.

A series of mixed effect models were conducted to investigate the relationship between alertness and spatial attention during the simulated shiftwork. For the Landmark task, two linear mixed effects models with fixed effects of objective alertness, as measured by PVT lapses and PVT mean RRT, were conducted. PVT lapses and PVT mean RRT were predictors in separate models. Bisection bias was the outcome variable

in these models. Another mixed effects model, with subjective alertness, as measured by the SSS, with the same time points as the previous model was conducted, and bisection bias as the outcome variable was run. ID was entered as a random intercept in all models.

For the detection task, six linear mixed effects models with fixed effects of objective alertness (i.e., PVT lapses, PVT mean RRT), or subjective alertness (i.e., SSS), were conducted to determine the relationship between alertness and spatial bias. The outcome variable was reaction time for three models and omissions for the remaining three models. Time, side of stimulus presentation (left/right), and location of stimulus presentation (2, 7, 12 and 17cm) was entered as a fixed effect and ID was entered as a random effect in all models. Post hoc comparisons with Holm corrections were also conducted.

3.6 Results

3.6.1 Alertness changes with time of testing.

PVT lapses (beta=7.32, 95% CI=2.82 – 11.8), PVT mean RRT (beta=4.26, 95% CI=4.02 – 4.50), and SSS (beta=4.66, 95% CI=4.29 – 5.03) differed across time (Table 3.1). The calculated partial eta^2 effect sizes were moderate for PVT lapses (.21) and PVT mean RRT (.30), and large for SSS (.69). Figure 3.4 illustrates these changes in alertness over time, with alertness generally higher during the afternoon testing time points compared to the early morning testing time points.

3.6.2 Spatial attention changes with time of testing.

Spatial bias on the Landmark task did not associate with time of testing (beta=-0.18, 95% CI=-0.27 – -0.09), refer to Table 3.1.

There was an effect of time of testing on detection task reaction time (beta=343, 95% CI=303 – 383) and omissions (beta=2.06, 95% CI=1.09 – 3.03), reflecting generally worse performance in the early morning compared to the afternoon. There was also a significant effect of location, such that performance was better when responding to

stimuli closer to the centre compared to the periphery (Table 3.1). Figure 3.4 depicts the pattern of spatial attention performance with time of testing and Figure 3.5 depicts the pattern of detection task performance relative to stimulus location across time of testing.

Table 3.1

F values, degrees of freedom, p values and holm corrected post hoc comparisons relative to time of testing, for each measure derived from the mixed effects models.

	Predictor	F	df	*p*	Post Hoc Comparisons, $p<.05$
Psychomotor Vigilance Task (PVT)					
PVT Lapses	Time	4.75	5, 90	<.001	D2 1400h > D4 0500h, D5 0500h; D7 1400h > D4 0500h
PVT mean RRT	Time	7.61	5, 90	<.001	D2 1400h > D4 0300h, D4 0500h, D5 0500h; D7 1400h > D4 0300h, D4 0500h, D5 0500h
Stanford Sleepiness Scale (SSS)					
SSS	Time	39.2	5, 90	<.001	D2 1400h > D4 0300h, D4 0500h, D5 0500h, D7 1400h; D4 0300h > D4 0500h, D5 0500h; D5 0300h > D4 0500h, D5 0500h; D7 1400h > D4 0300h, D4 0500h, D5 0300h, D5 0500h
Landmark Task					
Bisection Bias	Time	2.75	3, 53.1	.052	-
Detection Task					
Reaction Time	Time	4.66	3, 546	.003	D2 1400h > D4 0500h
	Side	0.31	1, 546	.576	-
	Location	16.6	3, 546	<.001	2cm > 12cm, 17cm; 7cm > 12cm, 17cm
	Time*Side	0.67	3, 546	.572	-
	Time*Location	0.57	9, 546	.825	-
	Side*Location	0.12	3, 546	.950	-
	Time*Side*Location	0.35	9, 546	.956	-
Omissions	Time	17.3	3, 550	<.001	D2 1400h > D4 0500h, D5 0500h, D7 1400h; D7 1400h > D4 0500h, D5 0500h
	Side	.001	1, 550	.977	-
	Location	29.5	3, 550	<.001	2cm > 12cm, 17cm; 7cm > 12cm, 17cm; 12cm > 17cm
	Time*Side	0.17	3, 550	.917	-
	Time*Location	0.60	9, 550	.794	-
	Side*Location	1.24	3, 550	.293	-

Time*Side*Location	0.17	9, 550	.997	-

Note. D= day. > corresponds to better performance relative to other levels of a factor (i.e., time or location). Locations 2cm, 7cm, 12cm, and 17cm correspond to distance from the centre of the screen.

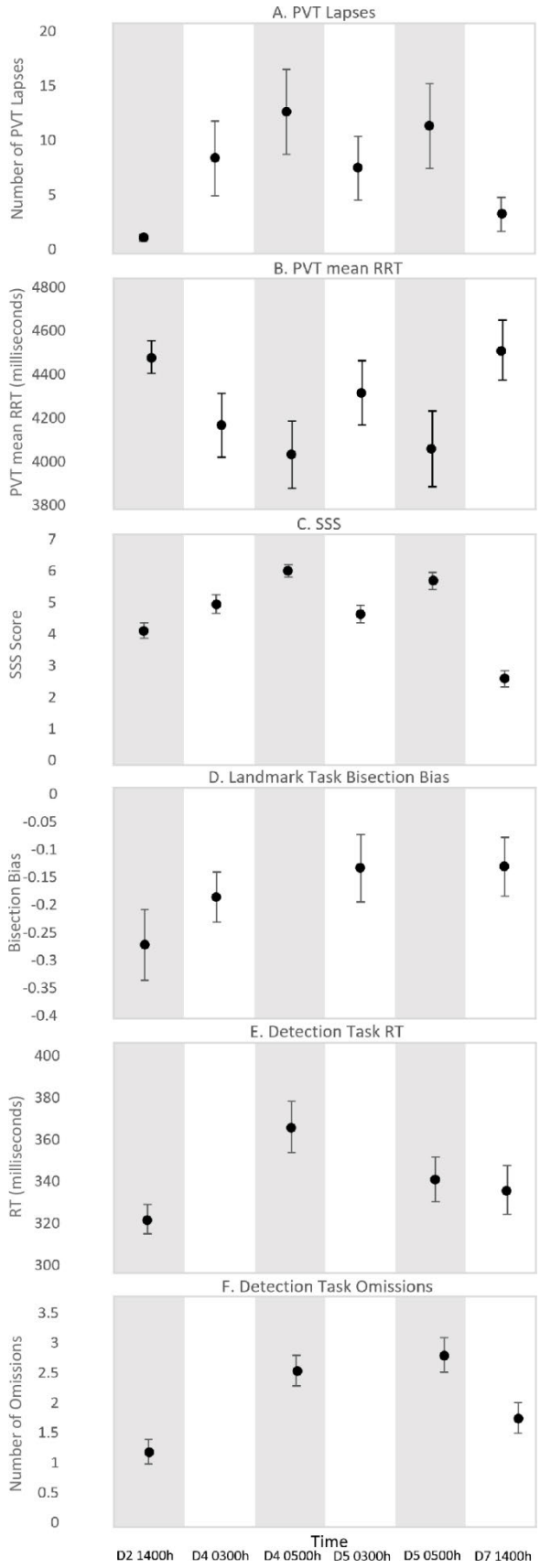

A. PVT Lapses
Number of PVT Lapses
20
15
10
5
0
B. PVT mean RRT
PVT mean RRT (milliseconds)
4800
4600
4400
4200
4000
3800
C. SSS
SSS Score
7
6
5
4
3
2
1
0
D. Landmark Task Bisection Bias
Bisection Bias
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
-0.4
E. Detection Task RT
RT (milliseconds)
400
380
360
340
320
300
F. Detection Task Omissions
Number of Omissions
3.5
3
2.5
2
1.5
1
0.5
0
Time
D2 1400h
D4 0300h
D4 0500h
D5 0300h
D5 0500h
D7 1400h

Figure 3.4. Alertness and spatial bias performance indicators change with day and time. Means and standard errors in alertness (PVT Lapses, PVT Mean RRT & SSS) and spatial bias (Landmark Task & Detection Task) throughout the protocol are depicted. A. High PVT lapses suggest poor performance. B. High PVT mean RRT reflects poor performance. C. High scores on the SSS reflect high levels of sleepiness. D. Negative and positive scores on the Landmark Task bisection bias suggests a leftward and rightward bias, respectively. E. High Detection Task reaction times represent poor performance. F. High Detection Task omissions represent poor perfomance.

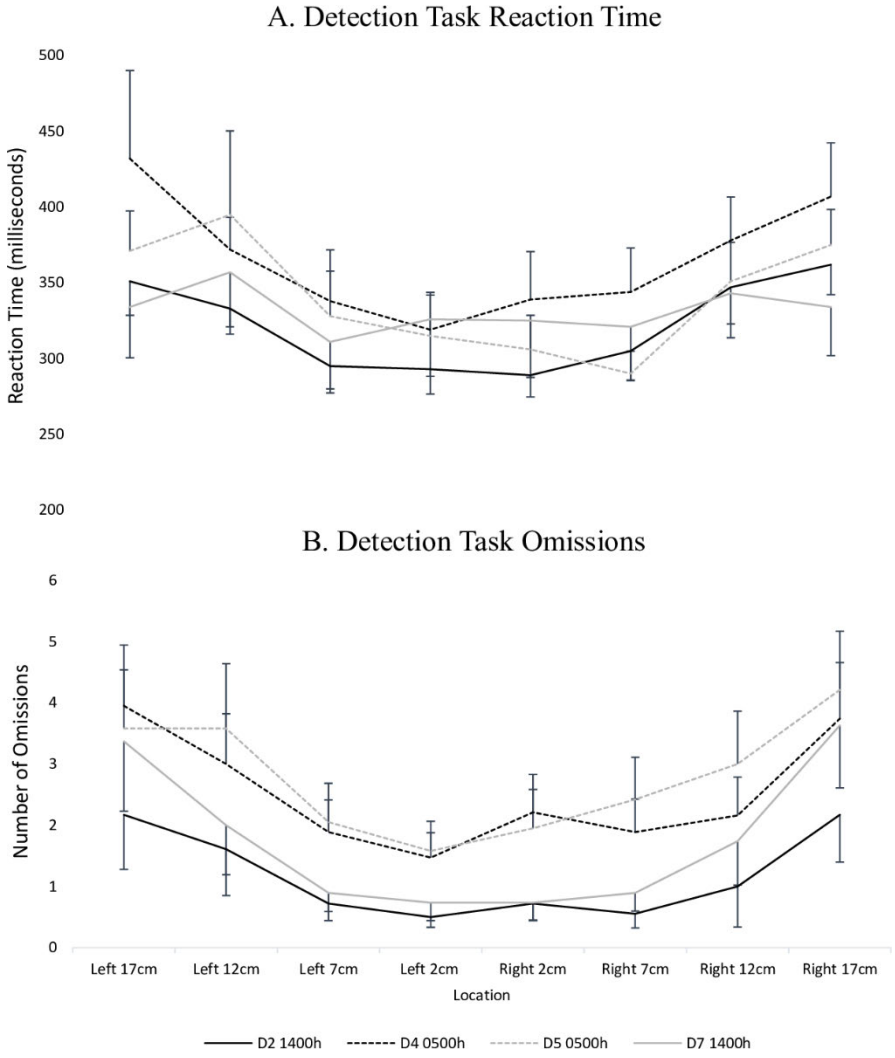


Figure 3.5. Performance in the periphery is worse than in the centre. Detection Task changes in reaction time (A), and omissions (B) with time, relative to stimulus location.

3.6.3 Alertness and spatial attention relationship.

3.6.3.1 Spatial bias in the Landmark task.

Objective measures of alertness: PVT lapses did not associate with bisection bias on the Landmark task (beta=0.001, CI=-0.01 – 0.004), and PVT mean RRT also did not associate with bisection bias (beta=-0.01, CI=-0.12 – 0.10).

Subjective measures of alertness: SSS did not associate with bisection bias on the Landmark task (beta=-0.003, CI=-0.03 – 0.03). Refer to Table 3.2.

3.6.3.2 Reaction time in the detection task.

Objective measures of alertness: PVT lapses were related to reaction time on the Detection Task (beta=2.29, CI= 1.58 – 3.01). That is, for every increase in a PVT lapse, there was a corresponding average increase in reaction time by 2.29 milliseconds on the detection task. Location was a significant predictor of detection task reaction time (p<.001; refer to Table 3.2 for significant post hoc comparisons), indicating that reaction time to stimuli increased with an increase in stimulus distance from the centre. A PVT lapses by side interaction (p=.001) showed left-sided (compared to right-sided) stimuli to have a higher increase in reaction time with increasing lapses. Figure 3.5 (Panel A) portrays this interaction pattern.

PVT mean RRT was related to reaction time on the detection task (beta=-77.7, 95% CI=-95.5 – -60.0). That is, every increase in mean RRT corresponded with a decrease in reaction time by 77.7 milliseconds on the detection task. There was a significant interaction of PVT mean RRT and side, such that the left side had a stronger increase in detection task reaction time with a decrease in PVT mean RRT (p=.030; Panel B in Figure 3.6).

Subjective measures of alertness: Scores on the SSS also related to reaction time on the detection task (beta= 9.77, 95% CI= 4.92 – 14.6), suggesting that every unit increase in subjective sleepiness corresponds with an increase in reaction time by 9.77 milliseconds on the detection task.

3.6.3.3 Omissions in the detection task.

Objective measures of alertness: PVT lapses associated with detection task omissions (beta=0.07, 95% CI=0.06 – 0.09). That is, every increase in lapses related to a .07 increase in an omitted response on the detection task.

PVT mean RRT was predictive of detection task omissions (beta=-2.07, 95% CI=-2.47 – -1.66). The negative association shows every increase in PVT mean RRT to correspond with a reduction in 2 omissions. There was a significant PVT mean RRT by location interaction (p<.001) revealing that the further away the stimulus location, the stronger the effect of PVT mean RRT on omissions. Refer to Figure 3.6.

Subjective measures of alertness: SSS associated with omissions on the detection task (beta=0.32, 95% CI=0.21 – 0.44), such that an increase in SSS corresponded with a .32 increase in an omitted response. Omissions were more likely in the periphery compared to the centre as demonstrated by a main effect of location (p=.009). Refer to Figure 3.6.

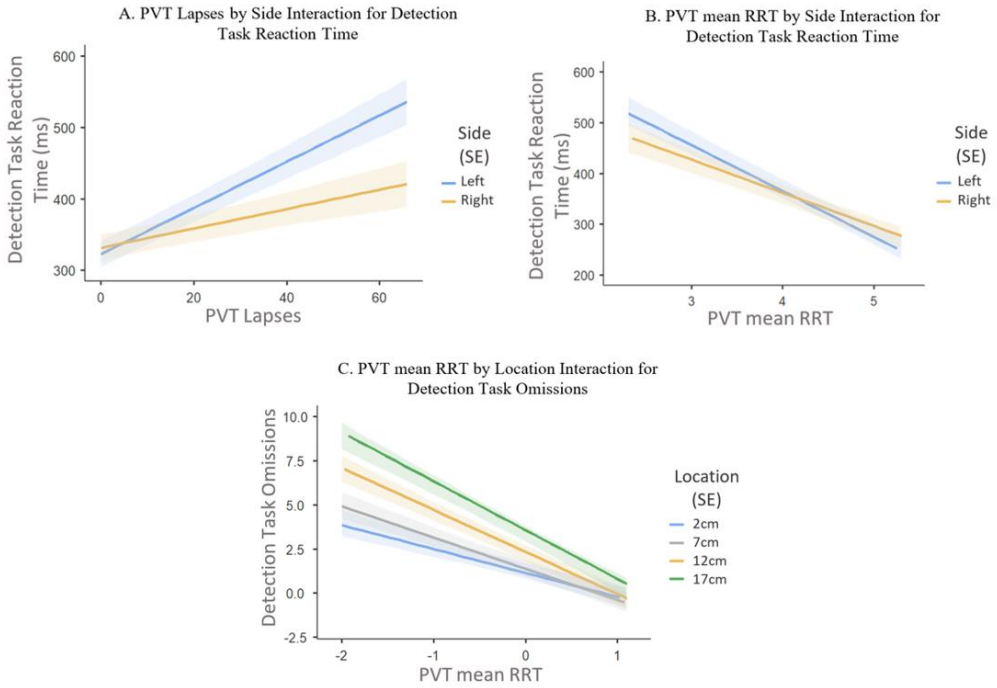


Figure 3.6. Mixed models data show detection task performance decreases with a decrease in alertness. A. Reaction time increases more strongly for left-sided stimuli with an increase in PVT lapses. B. Reaction time decreases more strongly for left-sided stimuli

with an increase in PVT mean RRT (higher mean RRT scores reflect better performance). C. The further away the stimulus, the stronger the effect of PVT mean RRT on omissions. Shaded areas indicate standard error.

Table 3.2

Fixed effect for the relationship between alertness and spatial bias.

Outcome	Predictors	F	df	*p*	Post Hoc Comparisons, *p*<.05
Landmark Task					
	PVT lapses	0.05	1, 68.5	.825	-
	PVT mean RRT	0.03	1, 70.2	.865	-
	SSS	0.03	1, 60.4	.861	-
Detection Task					
1. Reaction Time	PVT lapses	39.4	1, 580	<.001	-
	Side	1.14	1, 562	.286	-
	Location	11.0	3, 562	<.001	2cm > 12cm, 17cm; 7cm > 12cm, 17cm
	PVT lapses*Side	10.9	1, 562	<.001	-
	PVT lapses*Location	1.59	3, 562	.190	-
	Side*Location	0.01	3, 562	.978	-
	PVT lapses*Side*Location	0.91	3, 562	.438	-
2. Reaction Time	PVT mean RRT	73.5	1, 563	<.001	-
	Side	4.99	1, 562	.026	-
	Location	1.83	3, 562	.141	-
	PVT mean RRT*Side	4.72	1, 562	.030	-
	PVT mean RRT*Location	0.99	3, 562	.399	-
	Side*Location	0.29	3, 562	.831	-
	PVT mean RRT*Side*Location	0.26	3, 562	.858	-
3. Reaction Time	SSS	15.6	1, 570	<.001	-
	Side	0.14	1, 562	.713	-
	Location	1.03	3, 562	.378	
	SSS*Side	0.36	1, 562	.547	-
	SSS*Location	0.34	3, 562	.798	-
	Side*Location	0.06	3, 562	.980	-
	SSS*Side*Location	0.11	3, 562	.955	-
4. Omissions	PVT lapses	66.3	1, 584	<.001	-
	Side	0.32	1, 566	.574	-
	Location	19.2	3, 566	<.001	2cm > 12cm, 17cm; 7cm > 12cm, 17cm; 12cm > 17cm
	PVT lapses*Side	1.49	1, 566	.223	-

	PVT lapses*Location	1.68	3, 566	.171	-
	Side*Location	0.37	3, 566	.778	-
	PVT Lapses *Side*Location	1.09	3, 566	.354	-
5. Omissions	PVT mean RRT	99.8	1, 571	<.001	-
	Side	0.0004	1, 566	.984	-
	Location	33.2	3, 566	<.001	2cm > 12cm, 17cm; 7cm > 12cm, 17cm; 12cm > 17cm
	PVT mean RRT*Side	0.33	1, 566	.568	-
	PVT mean RRT*Location	5.71	3, 566	<.001	-
	Side*Location	1.39	3, 566	.244	-
	PVT mean RRT *Side*Location	0.79	3, 566	.502	-
6. Omissions	SSS	32.1	1, 573	<.001	-
	Side	0.34	1, 566	.563	-
	Location	3.91	3, 566	.009	-
	SSS*Side	0.39	1, 566	.533	-
	SSS*Location	0.09	3, 566	.965	-
	Side*Location	0.10	3, 566	.960	-
	SSS*Side*Location	0.33	3, 566	.805	-

Note. When predictors were categorical, all other categories were compared to the first category. Locations refer to distance from the centre of the screen (i.e., 2cm, 7cm, 12cm, and 17cm). "<" refers to direction of performance (i.e., 2cm > 12cm refers to better performance at location 2cm than at location 12cm).

3.7 Discussion

The current study's findings provide some support for a narrowing of attention and a neglect of the left-side with lowered alertness. We observed changes in PVT, subjective sleepiness, and response times and omissions on the spatial attention tasks over time that reflect typical circadian modulation. That is, lower levels of alertness in the night/early morning (0300h, 0500h) compared to the afternoon (1400h; Åkerstedt, 2003; Harrington, 2001). There were also more omissions occurring in the periphery than the centre. However, while there were no significant spatial attentional shifts found in relation to time of testing, there was a relationship between shifts in spatial attention and PVT response times and lapses, which was our assay of behavioural alertness. As PVT response times and number of lapses increased, so did detection task response times, and this relationship was stronger for stimuli presented on the left-side (consistent with the current model by Corbetta and Shulman (2011)), and for those on the periphery (illustrated in Figure 3.6). Put differently, alertness is not reduced uniformly across the whole hemifield, rather a larger reduction is observed in the periphery especially in the left hemifield.

In contrast to the detection task, there were no associations between the spatial performances in the Landmark task and the objective and subjective assays of alertness (see Table 3.2). The lack of associations stands in contrast to the findings from a previous study (Manly et al., 2005). The authors examined Landmark task performance in shiftworkers and reported a leftward bias with high alertness and a rightward bias with low alertness. However, in our study, participants were allowed up to 7h of sleep per 24h (data reported previously in Gupta et al. (2019)), which in terms of sleep opportunity, is more consistent with the 'well-rested' condition in the previous study than their 'sleepy' condition, where participants achieved less than 4h per 24h (Manly et al., 2005).

The objective assays of alertness were only associated with the detection task, but not the Landmark task. The reason for this observed dissociation is not clear. It cannot be ruled out that we were underpowered to detect subtle spatial shifts in the Landmark task. The effect sizes for the Landmark task and PVT assays of behavioural alertness suggests that the effects, although non-statistically significant and very small, were in the expected direction.

It is also possible that the lack of association in the Landmark task is due to the fact that the two spatial tasks tap into different underlying mechanisms. A principal component analysis identified the Landmark and detection tasks as distinct factors contributing to observed variances in spatial tasks (Learmonth et al., 2015). The two tasks differ, for example, in the level they tap into the phasic alertness with higher levels for the Detection task due to the potentially alerting nature of the task's stimuli presentation. They also differ in their cognitive processing demands with one task being a simple detection task and the other task requiring a judgement on spatial properties. However, the degree to which different tasks tap into different underlying spatial mechanisms is a matter of debate (Chen et al., 2019) and our study was not designed to disentangle these mechanisms. Also, a recent meta-analysis did not find evidence that effect sizes for associations between alertness and spatial attention differ between tasks requiring speeded responses to stimuli (i.e., detection of stimuli) and judgement tasks such as the Landmark task (Chandrakumar et al., 2019).

The findings from the detection task revealed that there is a narrowing of attention to the centre from the periphery (with slower responses and more omissions to stimuli in the periphery) consistent with studies that generated alertness reductions through extended time-on-task and sleep restriction (Fimm et al., 2006; Rogé et al., 2003). The current study suggests that even under conditions of relatively common amounts of sleep, attention narrowing may be observed across circadian fluctuations in alertness, particularly as assessed by behavioural assay.

The relationship between spatial attention and alertness measures was stronger for PVT than for subjective alertness. In particular, PVT responses corresponded more strongly to performance decrements to left-sided stimuli (Table 3.2). This was not the case for subjective alertness, suggesting that behaviourally-assessed alertness is a closer reflection of shifts in spatial attention than self-reports.

PVT responses, but not time of the day, were associated with spatial biases. Individual levels of alertness at specific times can vary considerably between participants (Van Dongen & Dinges, 2000). In contrast to PVT measures, individual differences are not captured with the relatively crude measure 'time of the day'. The current study suggests that it is important to consider individuals' alertness levels when investigating the relationship between alertness and spatial biases.

Overall, our findings highlight potential safety risks for occupations requiring a high level of visuospatial ability. While speculative at this stage, our results could have implications for shiftworkers who work unconventional hours. At times when behaviourally-assessed alertness is lower, individuals may be slightly biased towards the right side of their environment and may be more likely to experience attentional narrowing, responding more slowly to, or missing, important information in their periphery. Under conditions, where shiftworkers are required to drive for work (e.g., truck drivers), or drive home after a night shift, their safety might be compromised. Past research into shiftwork and cognitive performance has revealed the detrimental effects of lowered alertness. For example, lowered alertness resulting from shiftwork is linked with an increased risk for accident and injury (Dembe, Erickson, Delbos, & Banks, 2006). Based on our findings, researchers examining alertness should consider the influence of side of space when assessing safety and fatigue management in the future.

Our young, healthy participants in the study underwent a shiftwork manipulation to disrupt circadian timing in a tightly controlled laboratory environment, where they were relatively well-rested following sleep. In the field, shiftworkers tend to be chronically sleep deprived (Rajaratnam et al., 2013), suggesting that narrowing of attention and a neglect of the left-side could be worse in the real world where alertness levels are likely to fluctuate beyond those observed in our study, and may be influenced by many factors (e.g., worker age, health status).

The current study only examined six different time points within the simulated shiftwork protocol. This was a limitation of the study as investigating more time points might have given a clearer indicator of the relationship between spatial attention and alertness. Furthermore, testing both spatial tasks at the same timepoints, as opposed to 3am for the Landmark task and 5am for the detection task, would have helped us assess the potential differential influence of the early morning hours on the spatial measures. Another limitation is that the participant sample comprised of only right-handed participants. This is a limitation as right- and left-handers have been found to show the opposite spatial attention and alertness pattern (Bareham et al., 2015; Chandrakumar et al., 2019).

3.8 Conclusions

To our knowledge, this study was the first to examine whether changes in alertness as a result of a simulated shiftwork protocol is associated with changes in spatial bias. The current study found some evidence for a slight neglect of the left side and a narrowing of attention with lowered alertness. The findings were not definitive and depended on the measures used to assess spatial attention and alertness. Given that our findings suggest the possibility that the ability to sufficiently react to information in the periphery and to the left side may be compromised with lowered alertness, this highlights the need for future research to better understand the relationship between spatial attention and alertness under shiftworking conditions.

Chapter Four: Monotonous driving induces shifts in spatial attention as a function of handedness

4.1 Abstract

Current evidence suggests that the ability to detect and react to information under lowered alertness conditions might be more impaired on the left than the right side of space. This evidence derives mainly from right-handers being assessed on computer and paper-and-pencil spatial attention tasks. However, there are suggestions that left-handers might show impairments on the opposite (right) side compared to right-handers with lowered alertness, and it is unclear whether the impairments observed in the computer tasks have any real-world implications for activities such as driving. The current study investigated the alertness and spatial attention relationship under simulated monotonous driving in left- and right-handers. Twenty left-handed and 22 right-handed participants (15 males, *M*=23.6y, *SD*=5.0y) were assessed on a simulated driving task (lasting approximately 60 minutes) to induce a time-on-task effect. The driving task involved responding to stimuli appearing at six different horizontal locations on the screen, whilst driving in a 50km zone. Decreases in alertness and driving performance were evident with time-on-task in both handedness groups. We found handedness impacts reacting to lateral stimuli differently with time-on-task: right-handers reacted slower to the leftmost stimuli, while left-handers showed the opposite pattern (although not statistically significant) in the second compared to the first half of the drive. Our findings support suggestions that handedness modulates spatial attention and alertness interactions. The interactions were observed in a simulated driving task which calls for further research to understand the safety implications of these interactions for activities such as driving.

4.2 Introduction

Driving safely relies on the ability to sufficiently attend to and navigate the environment (Pierce & Andersen, 2014). When driving, one must complete multiple tasks simultaneously, such as attending to passing cars, pedestrians, traffic signs and react accordingly, whilst also maintaining a speed limit and driving within the designated lane. Prolonged driving durations can lead to lapses in attention and consequently increase the risk of experiencing a traffic accident (Otmani et al., 2005; Thiffault & Bergeron, 2003; Ting et al., 2008). Approximately 10-25 percent of fatal road accidents worldwide result from attentional failure, where the ability to detect and respond to road-traffic information is impaired (Choi, Han, Kong, & Ko, 2016; Dobbie, 2002; European Commission, 2018; Lee, Manousakis, Fielding, & Anderson, 2015). In Australia, such attention-related road accidents are estimated to cost the economy approximately three billion dollars per year (Parliament of Australia, n.d.).

Reduced driver alertness is a common reason for attention-related accidents (Sonnleitner et al., 2014). Alertness is defined as the preparedness to respond to stimuli (Posner & Rafal, 1987; Sturm & Willmes, 2001) and typically decreases whilst engaging in a task for extended durations (Benwell et al., 2013; Matthias et al., 2009; Newman et al., 2014). This decrease in alertness with extended duration is known as the time-on-task effect (Mackworth, 1961). Studies investigating simulated driving performance show decreased alertness with 30 minutes of driving under monotonous conditions. In such instances, the vehicle's position deviates horizontally from the centre of the lane, and the ability to correctly detect signals decreases with time-on-task (Rogé et al., 2003; Rogé et al., 2002).

Studies examining driving performance overlayed with a secondary task, which involves detecting information in the horizontal periphery, report a tunnelling of vision with time-on-task (Rogé et al., 2003; Rogé et al., 2002). These studies reported a reduction in the ability to detect and react to information in the periphery compared to the centre of the visual field with prolonged task exposure. However, it is unclear whether performance decrements in the periphery are uniform with time-on-task under driving conditions, such that both the left and right sides are equally impaired.

Current evidence suggests that the ability to detect and react to information under lowered alertness conditions might be more impaired on the left than the right side of space when assessed with computer and paper-and-pencil spatial attention tasks (Bellgrove et al., 2004; Newman et al., 2013). A recent meta-analysis revealed attention in healthy adults shifts towards the right with lowered alertness in laboratory-based spatial attention tasks (Chandrakumar et al., 2019). This rightward shift is commonly demonstrated by slowed responses to left-sided stimuli (Fimm et al., 2006; Heber et al., 2008) and the misidentification of left-sided stimuli as being on the right (Bareham et al., 2014).

The current theoretical model proposed to account for the relationship between spatial attention and alertness involves two neural networks. One network is the bilateral dorsal attentional network (DAN) and this is responsible for attention allocation to the contralateral visuospatial field. The other is the right-lateralised ventral network (VAN) and this network is involved in detecting unattended stimuli, reorienting attention, and alertness. These two networks are in dynamic interactions with each other and changes to alertness levels (VAN) can influence the interactions between these two neural networks and consequently influence attentional allocation (DAN). These interactions result in higher and lower levels of alertness leading to leftward and rightward shifts in attention, respectively (Corbetta & Shulman, 2011).

One study linked changes in EEG alpha power with changes in spatial attention in a time-on-task paradigm in healthy participants (Newman et al., 2013). Alpha power provides estimates of cortical activation and deactivation, where alpha-indexed deactivation is associated with an active brain state (Pfurtscheller & Da Silva, 1999). Using EEG techniques, the authors showed an increase of pre-target alpha absolute power over the right compared to the left hemisphere with time-on-task. This shift also correlated with a behavioural rightward shift in attention. Lower alpha power in regions contralateral to the attended visuospatial field is apparent during task performance (Sauseng et al., 2005). Previous studies have associated right-lateralised cortical regions with time-on-task (Langner & Eickhoff, 2013; Paus et al., 1997). This suggests that right hemisphere activation associates with increasing time-on-task, and consequently supports the right hemisphere being implicated in alertness.

Research examining spatial attention and alertness has mostly been confined to right-handers, with left-handers being excluded from study participation (Willems, Van der Haegen, Fisher, & Francks, 2014). However, the neural structures postulated for the attentional networks involved in mediating the relationship between alertness and spatial attention may differ (to some degree) between left- and right-handers. A fMRI neuroimaging study by Liu et al. (2009) reported the right-lateralised VAN to be bilateral or left-lateralised in their left-handed compared to their right-handed sample. However, in contrast to these findings, another study suggests the VAN is right lateralised in both a left-handed sample and a right-handed sample, whereas the authors found the DAN to be more pronounced in the right hemisphere for left-handers (Petit et al., 2015). While there are some discrepancies between the findings in these neuroimaging studies, they suggest that the DAN and VAN networks may differ between left-handers and right-handers. If so, the relationships between alertness (VAN) and spatial orienting (DAN) may differ between left- and right-handers. This was indeed confirmed by the only study exploring handedness influences on alertness and spatial attention (Bareham et al., 2015). The study found that left- and right-handers show an opposite behavioural spatial attention and alertness relationship pattern. While decreasing alertness led to a rightward shift in the right-handed group, the alertness decrease led to leftward shift in the left-handed group (Bareham et al., 2015). Hence, handedness may be an important modulator in the relationship between spatial attention and alertness.

The current study sought to examine the relationship between spatial attention and alertness under simulated driving in left-handers and right-handers using both behavioural and physiological measures of alertness. The following research questions were investigated: (1) Are there shifts in spatial attention during simulated driving with time-on-task?; (2) Does handedness influence the spatial attention and alertness relationship with time-on-task?; (3) Do changes in physiological indices of alertness associate with behavioural performance?

We expected handedness to modulate the spatial attention and alertness relationship. Our investigations into left-handers' performance were exploratory given there is only one previous study that investigated this relationship in left-handers. However, we hypothesised the following in our right-handed sample based on previous studies: (1) Physiological and behavioural indices of alertness will decrease in alertness

with time-on-task; (2) There will be slowed response times and more errors on the left side with time-on-task; (3) Alpha power over the right hemisphere will decrease with time-on-task in right-handers; (4) These decreases in physiological alertness will associate with poorer spatial performance on the left than right.

4.3 Method

4.3.1 Participants.

Forty-six healthy participants were recruited with the following inclusion criteria: aged between 18 to 40 years, native English speakers, no hearing or visual impairments that are not corrected for, no history of psychiatric or neurological diagnosis, no current or previous (within one year) history of alcohol or substance abuse, no use of recreational drugs within the last three months, have not taken any medication that targets the central nervous system (e.g., anticonvulsants, antidepressants) in the last month, no history of unconsciousness greater than five minutes, no known intellectual impairments, and a valid driver's licence. Four participants were excluded from analysis due to the following issues: inability to perform the task due to falling asleep (i.e., the participant was woken up by a researcher several times; n=1), technical difficulties with equipment (n=2), and a high proportion of errors (i.e., failure to detect and respond to more than 50% of stimuli; n=1).

The final sample comprised of 42 participants (15 males) aged between 18 and 37 years (mean age 23.6 ± 5 years). Twenty-two participants were right-handed and 20 participants were left-handed, assessed using the FLANDERS handedness survey (Nicholls et al., 2013). Participants in the final sample had an average of 4.6 years of driving experience. Recruitment was via flyers on the University of South Australia's Magill Campus, social media, and through the University's online SONA system (Sona Systems Ltd.) which requires potential participants to be invited to participate if deemed eligible. Separate flyers for recruiting only left-handers were distributed via the same method outlined above.

Participants received reimbursement of $15 (AUD) per hour of participation for their involvement in the study. This study was approved by the Human Research Ethics Committee from the University of South Australia.

4.3.2 Stimuli and apparatus.

4.3.2.1 Behavioural data acquisition.

4.3.2.1.1 Driving simulator task.

Stimulus presentation and behavioural data collection were controlled via a PC running Drivesim 6 software (York Driving Technologies, CA). Logitech (Driving Force G920) wheel and pedals were used to perform the driving task. A custom-built simulator frame (Dominator series 2, Hyperdrive Australia Ltd.) was used in the current study. Participants were seated approximately 120 centimetres from the centre of the screen (29-inch monitor) whilst performing the driving task in the driving simulator (Figure 4.1, Panel A).

The driving course was set-up as an approximately 60-minute drive at 50km through a driving scene with no other vehicles, buildings, or trees in the landscape to maximise the monotonous nature of the environment. The total duration of the drive slightly differed between participants depending on their speed throughout the drive; if a speed of 50km was consistent throughout the drive, the total drive duration would be 60 minutes. This was to ensure that participants had the opportunity to view all the presented peripheral stimuli embedded within the driving course. The driving scene consisted of a blue surface on the top of the screen (i.e., representing the sky), a grey road, and a green untextured surface (i.e., representing grass) outside the road. Participants could view their driving speed and the bonnet of the car whilst driving. Road signs indicating a chicane ahead and speed signs displaying 50km were placed throughout the drive. Participants were given an equal number of left- and right-sided chicanes throughout the drive (see Figure 4.1, Panel B). Whilst driving, 96 circular grey stimuli, appearing sequentially at varying eccentricities to the left and right of the screen, were presented. Stimulus presentation was for 1500ms and the response window was set to a maximum of 2000ms following stimulus onset. Stimuli were presented in a pseudo-randomised order with each half of the drive containing 48 stimuli. Within each half, there were eight repetitions of the six basic factorial combinations deriving from two sides (left and right) and three different eccentricity locations (2°, 4°, 6° from the centre of the screen). Participants responded to stimuli using levers attached to the steering wheel.

The following data were used for analysis: reaction time following correctly identified stimulus presentations, the number of omissions (i.e., the trials that participants did not respond to stimuli), lane variability (calculated as the standard deviation of the road position), and time within 10 percent of the speed limited (calculated as the total time in minutes spent within the speeds 45-55 km). The drive duration was split into two halves for analysis.

4.3.2.1.2 Karolinska sleepiness scale (KSS).

A 9-point rating scale was used to assess subjective sleepiness prior to and following the driving task. The Karolinska sleepiness scale ranges from 1 "*extremely alert*" to 9 "*very sleepy*" (Åkerstedt & Gillberg, 1990). The KSS is a widely used measure of subjective sleepiness and has demonstrated validity for assessing alertness (Shahid, Wilkinson, Marcu, & Shapiro, 2011).

4.3.2.2 Physiological data acquisition.

4.3.2.2.1 Electroencephalography (EEG) recording and data processing.

EEG was recorded using 64 active EEG electrodes using the Biosemi Active two system (Biosemi, Netherlands). Recordings were grounded using common mode sense and driven right leg electrodes (http://www.biosemi.com/faq/cms&drl.htm). Prior to testing commencement, electrode offset was minimised and stabilised. The EEG was recorded at 2048 Hz and downsampled to 512 Hz. The data were cleaned with a high pass of 1 Hz and bad channels were removed based on a Kurtosis threshold greater than five. Bad components were removed using the ICLabel plugin in EEGlab (Pion-Tonachini, Kreutz-Delgado, & Makeig, 2019) with a signal artefact threshold of 0.8 being removed using this method. An independent component analysis (ICA) was run using runica with default settings. Removed channels were interpolated using the spherical spline method. Data were then low-pass filtered at 20 Hz and fast fourier transform (FFT) was conducted using the Pwelch method (Cooley, Lewis, & Welch, 1967) with a window length of 2048. Electrode AFz was used as the reference electrode. FFT was used to extract frequency bands corresponding to alpha activity. The commonly used frequency range of 8-12 Hz for alpha was examined in the current study (Borghini, Astolfi,

Vecchiato, Mattia, & Babiloni, 2014; Zhao et al., 2012). The power was normalised to the average power per channel. EEG processing was performed using the EEGLAB toolbox (Version 14.1.2b; Delorme & Makeig, 2004) in MATLAB (Version 2019b; Mathworks, USA).

EEG alpha relative power for each participant was obtained and temporally split into two halves based on each participant's total drive duration on the driving simulator for statistical analyses. The brain regions were further separated into the left and right hemispheres and separated into frontal and parietal-occipital regions as these areas commonly generate alpha (Nobre, Nobre, & Kastner, 2014; Wascher et al., 2014). The following EEG regions were examined for analysis: P4, P6, P8, PO4, PO8, O2 (right hemisphere parieto-occipital), F2, F4, F6, F8 (right hemisphere frontal), P3, P5, P7, PO3, PO7, O1 (left hemisphere parieto-occipital), and F1, F3, F5, F7 (left hemisphere frontal). Alpha relative power within these EEG regions were collapsed to obtain an average for each region (i.e., the average value of F1, F3, F5, & F7 formed the left frontal region average relative power value).

4.3.2.2.2 Galvanic skin response (GSR) recording and data processing.

Galvanic skin response embedded into the EEG system was used for skin conductance data recording (Biosemi, Netherlands). Two GSR electrodes were placed on the lower portion of the palm on the non-dominant hand (as determined by the FLANDERS; Nicholls et al., 2013). A conductive gel was applied between the electrodes and the skin to improve sensors/skin contact. To obtain good skin-electrode contact, a tape was used to keep electrodes in place. GSR was recorded at 2048 Hz. The measured GSR frequency ranged between 0.01 to 5 Hz, and the calculated sympathetic nervous system (SNS) activity was between 0.05 to 0.24 Hz (Boccia & Roberts, 2000). Skin conductance is widely used to measure autonomic nervous system activity (Lim et al., 1997) and is a sensitive measure of vigilance (Eysenck, 2012). In the current study, normalised SNS range (i.e., .01 to 2 Hz) value was used as the skin conductance measure and the change in power over time was used in the analysis. Similar to the EEG analysis, GSR activity was split into two halves relative to the duration of the drive. The room temperature was maintained at approximately 22 ± 2ºC for all participants.

4.3.3 Procedure.

The study was conducted at the Cognitive Ageing and Impairment Neurosciences Laboratory, located at the University of South Australia Magill Campus. Participants attended the laboratory for testing and provided written informed consent prior to participation. Following consent, participants completed a series of questionnaires which measured handedness and a pre-drive subjective sleepiness scale (i.e., Karolinska sleepiness scale (KSS)). Participants were then set up with an EEG cap and GSR electrodes before completing a driving task in a driving simulator for approximately one hour. Refer to Figure 4.1 (Panel A) for the experimental set-up on a pseudoparticipant who provided informed consent to publish the identifying image. EEG and GSR were recorded throughout the drive.

The height of the driving simulator screen was adjusted for each participant to ensure the centre of the screen was approximately at eye level and participants could see the whole screen clearly. Participants were unaware of the course they were driving through (depicted in Figure 4.1, Panel B). Half the participants started the course at location A and the other half started at B to ensure that the direction of the first chicane was counterbalanced. Participants were given an opportunity to familiarise themselves with the task by completing a practice drive that lasted approximately four minutes. If the participant was unable to complete the practice drive successfully (i.e., they struggled to maintain the speed limit or were unable to detect stimuli), they were given another opportunity to complete the practice drive. Only one participant completed the practice drive twice in the study. Participants were instructed to maintain a speed limit of 50km and remain in the middle of the three-lane road. Whilst driving, participants were also instructed to respond to stimuli appearing on the left and right sides of the screen, pressing a left button when a left-sided stimulus appeared and the right button when a right-sided stimulus appeared. The levers were attached to the steering wheel. Participants were not told to prioritise either aspect of the task.

A webcam was used to monitor whether participants were adhering to task instructions. If participants were speeding excessively (i.e., more than 20km above the speed limit for a duration longer than two minutes, they were asked to adhere to the speed limit). Participants were informed that the total duration of the task was approximately

one hour. Upon completion of the driving task, participants filled remaining questionnaires (e.g., post-drive KSS). Total testing time lasted approximately three hours. All procedures were in accordance with the National Statement on Ethical Conduct in Human Research.

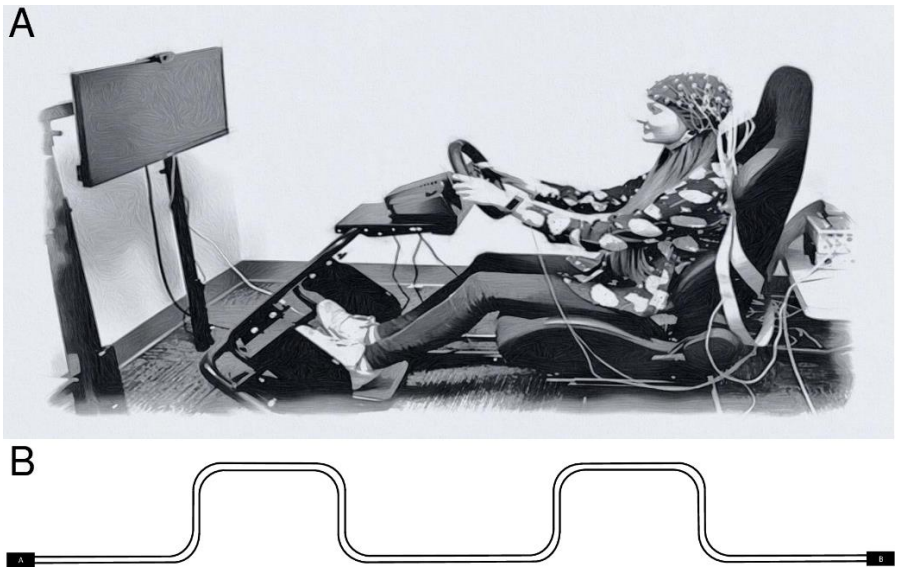


Figure 4.1. Experimental set-up on a pseudoparticipant (A), and the driving course (B). The start and end of the driving course was counterbalanced to ensure the direction of the first chicane.

4.3.3.1 Statistical analyses.

4.3.3.1.1 Data analysis.

Data were analysed using jamovi version 1.1.9.0 (jamovi project, 2018) and R (R Core Team, 2014). First, data were screened for outliers. Outliers were defined as more than three standard deviations above or below the group mean for all measures. One participant was identified as an outlier (more than 3 *SD*s below the group mean for behavioural performance) and excluded (see participant section above). On the driving simulator task, none of the participants responded within 100ms of stimulus presentation, therefore anticipatory responses did not need to be removed.

A series of mixed effects models were conducted to investigate changes in alertness with time-on-task and to investigate the relationship between spatial attention

and alertness. Participant ID was a random effect in all mixed-effects models. Post hoc comparisons with Holm corrections were used to account for multiple comparisons within models. No corrections for multiple comparisons between models were applied.

4.3.3.1.2 Changes in alertness measures (KSS, EEG and GSR) with time-on-task.

A series of mixed effects models were conducted to examine alertness changes with time-on-task. A mixed effects model with an outcome variable of KSS rating and predictors of time (pre-drive/post-drive) and handedness (left-handed/right-handed) was used to determine changes in subjective sleepiness from pre-drive to post-drive. Two mixed effects models with alpha relative power and normalised SNS power as outcomes and a predictor of time (i.e., split by first half and second half of drive) were conducted. Handedness was a predictor in all models, and hemisphere (left/right) and lobe (frontal/parietal-occipital) were further predictors in the alpha model.

4.3.3.1.3 Changes in driving simulator performance with time-on-task.

Two separate mixed effects models with outcome variables lane deviation and time spent within 10% of the speed limit, with a predictor of time (first half/second half), handedness (left-handed/right-handed), and an interaction of time by handedness were conducted.

Two more mixed effects models with reaction time to peripheral stimuli, and omission of stimuli as outcome variables and time (first half/second half), location (left 6°, left 4°, left 2°, right 2°, right 4°, and right 6°) and handedness (left/right) as predictors were also conducted. Reaction time to peripheral stimuli and omissions of stimuli (i.e., the number of omitted responses to peripheral stimuli) were outcome variables in separate models. Another two mixed effects models were conducted to stratify left-handers and right-handers. These models contained fixed factors of time and location and an outcome variable of reaction time.

4.3.3.1.4 The relationship between alertness measures and spatial attention measures.

A series of exploratory Spearman's rho correlations assessed whether changes in physiological variables (GSR and alpha) correlated with changes in spatial performance (i.e., reaction time). Change scores were computed for GSR, alpha, and reaction time to peripheral stimuli at each location identified as statistically significant, by subtracting the first half of the drive from the second half of the drive. No corrections for multiple comparisons between models were applied.

4.4 Results

4.4.1 Changes in alertness measures (KSS, EEG and GSR) with time-on-task.

A main effect of subjective sleepiness (as indexed by the KSS) revealed increased self-reported sleepiness post-drive compared to pre-drive ($p<.001$) in a mixed model. See Figure 4.2. There was a main effect of time for alpha ($p=.005$) with alpha relative power increasing from the first half of the drive compared to the last. There was no main effect of time on GSR ($p=.387$). There was no main effect of handedness or a time by handedness interaction in any of the three models. Refer to Table 4.1 for F values, degrees of freedom, *p* values, and Holm-corrected post hoc comparisons relative to time of testing, for each measure derived from the mixed effects models.

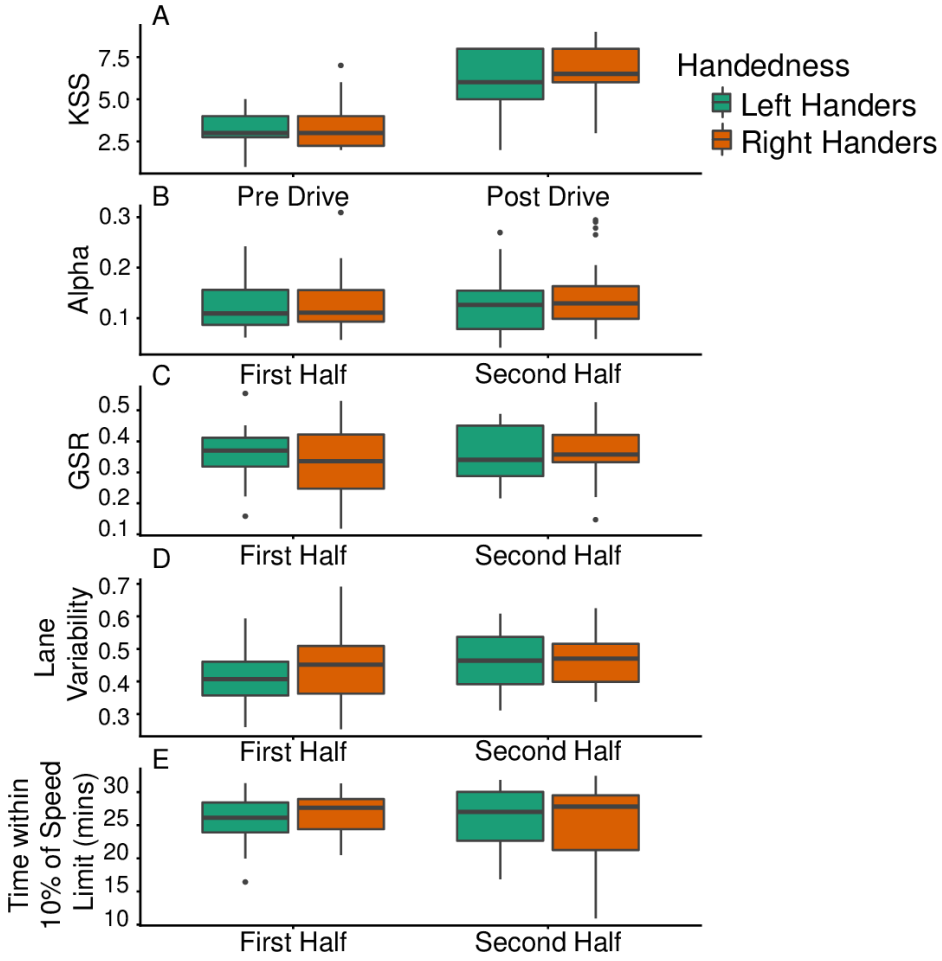


Figure 4.2. Changes in KSS (A), alpha (B), GSR (C), lane variability (D) and time spent within 10% of the speed limit (E), separated by handedness.

Table 4.1

F values, degrees of freedom, p values and holm corrected post hoc comparisons with corrections relative to time-on-task and handedness, for each KSS, Alpha and GSR from the mixed effects models. Hemisphere and lobe are additional predictors in the alpha model.

Outcome Variable	Predictor	F	df	p	Significant Post Hoc Comparisons
KSS	Time (pre-drive and post-drive)	120.7	1, 40	<.001	Pre-drive<Post-drive
	Handedness	2.67	1, 40	.110	
	Time*Handedness	.866	1, 40	.358	
Alpha	Time	7.86	1, 283	.005	$1^{st}<2^{nd}$
	Hemisphere	1.98	1, 283	.161	
	Lobe	178.5	1, 283	<.001	Frontal<Parieto-Occipital
	Handedness	.504	1, 40	.482	
	Time*Hemisphere	.0009	1, 283	.977	
	Time*Lobe	.915	1, 283	.340	
	Time*Handedness	.453	1, 283	.501	
	Hemisphere*Handedness	.205	1, 283	.651	
	Hemisphere*Lobe	3.94	1, 283	.048	Frontal Left<Frontal Right, Parieto-Occipital Left, Parieto-Occipital Right; Parieto-Occipital Left>Frontal Right
	Handedness*Lobe	.627	1, 283	.294	
	Time*Hemisphere*Handedness	.003	1, 283	.956	
	Time*Lobe*Handedness	.646	1, 283	.422	
GSR	Time	.764	1, 40	.387	
	Handedness	.072	1, 40	.789	
	Time*Handedness	1.45	1, 40	.235	

Note. LH=left-handers, RH=right-handers. Pre-D=pre-drive, post-D=post drive. For post hoc analyses < and > indicate the direction of the effect (e.g., $1^{st}<2^{nd}$ refers to lower levels of the outcome variable in the first half compared to second half of drive). Only relevant post hoc comparisons reaching statistical significance ($p<.05$) following corrections for multiple comparisons are reported for interactions.

4.4.2 Changes in driving simulator performance with time-on-task.

Lane variability increased with time-on-task (p=.008). There was no main effect of time for time spent within 10% of the speed limit. There was no main effect of handedness or an interaction of time by handedness in the two models. See Figure 4.2 and refer to Table 4.2 for post hoc comparisons.

Reaction time to peripheral stimuli increased with time-on-task (p<.001). A location by time by handedness interaction reached statistical significance (p=.004). See Table 4.2. The mixed models stratifying left-handers and right-handers revealed a statistically significant location by time interaction for right-handers (p=.023), but not left-handers (p=.146). Refer to Figure 4.3 for the interaction pattern for both left-handers (Panel A) and right-handers (Panel B). See Table 4.3 for mixed models F values, degrees of freedom, p values, and Holm corrected p values.

Omission of responses to peripheral stimuli increased with time-on-task (p=.013). A handedness by location interaction reached statistical significance (p<.001) showing right-handers omitted more stimuli in the rightmost periphery compared to left-handers (Figure 4.4). There was no time by handedness interaction for omissions. Refer to Table 4.2 for post hoc comparisons.

Table 4.2

F values, degrees of freedom, p values and holm corrected post hoc comparisons with corrections relative to time-on-task and handedness, for driving simulator variables derived from the mixed effects models. Location is an additional predictor in the reaction time and omissions to peripheral stimuli models.

Outcome Variable	Predictor	F	df	p	Significant Post Hoc Comparisons
Lane variability	Time	7.81	1, 40	.008	$1^{st}<2^{nd}$
	Handedness	.218	1, 40	.643	
	Time*Handedness	1.40	1, 40	.244	
Time in safe zone	Time	.481	1, 40	.492	
	Handedness	.047	1, 40	.829	
	Time*Handedness	1.31	1, 40	.260	
Reaction time to stimuli	Time	10.2	1, 3397.6	.001	$1^{st}>2^{nd}$
	Location	130.9	5, 3399.4	<.001	L1>L2, L3, L4, L5; L3<L2, L5; L4<L2, L5; L6>L1, L2, L4, L5
	Handedness	2.15	1, 39.8	.150	
	Time*Location	.720	5, 3397.4	.609	
	Time*Handedness	4.31	1, 3397.6	.038	1^{st} RH<2^{nd} RH
	Location*Handedness	.714	5, 3399.4	.613	
	Time*Location*Handedness	3.49	5, 3397.4	.004	
Omissions	Time	6.19	1, 440	.013	
	Location	27.36	5, 440	<.001	L1>L2, L3, L4, L5; L6>L2, L3, L4, L5
	Handedness	.23	1, 40	.632	
	Time*Location	2.41	5, 440	.049	1^{st} L6>1^{st} L2, 1^{st} L3, 1^{st} L4, 1^{st} L5; 2^{nd} L6>L2, 2^{nd} L3, 2^{nd} L4, 2^{nd} L5; 1^{st} L1>1^{st} L3, 1^{st} L4, 1^{st} L5; 2^{nd} L1>2^{nd} L2, 2^{nd} L4, 2^{nd} L5

Time*Handedness	.05	1, 440	.816	
Location*Handedness	7.51	5, 440	<.001	RH L6> RH L3, RH L4, RH L5, LH L6; LH L2 <LH L6
Time*Location*Handedness	.97	5, 440	.432	

Note. LH=left-handers, RH=right-handers. For post hoc analyses < and > indicate the direction of the effect (e.g., LH 1st<LH 2nd refers to left-handers' performance in the first half of the drive is lower than that of left-handers' performance in the second half of drive). L1=location 1, L2, location 2, L3=location 3, L4=location 4, L5=location 5, L6=location 6. Only relevant post hoc comparisons reaching statistical significance (p<.05) following corrections for multiple comparisons are reported for interactions.

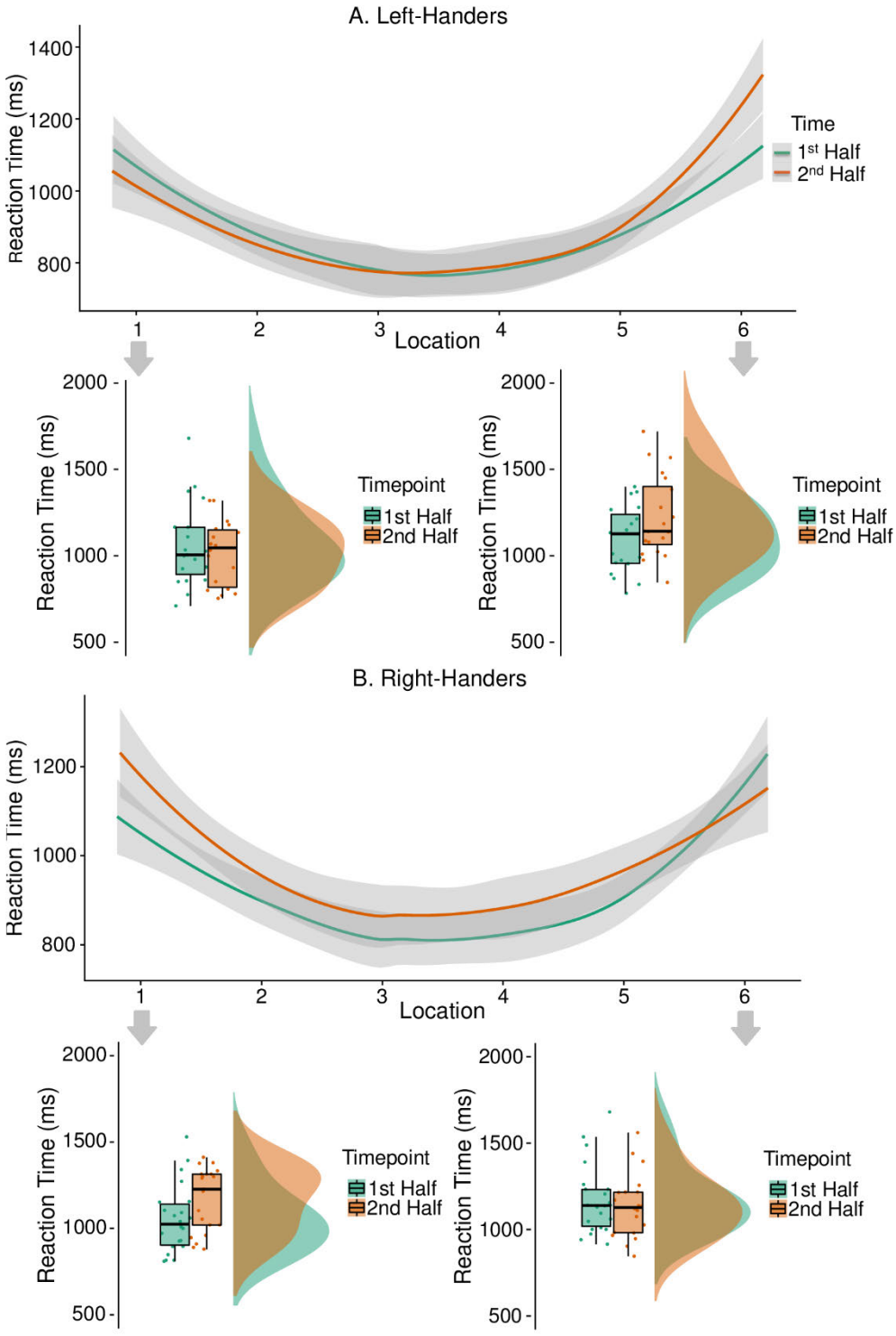


Figure 4.3. Interaction between time-on-task, stimulus location and handedness. Differences as a function of handedness and time-on-task become particularly evident in performance to the most lateral stimulus locations. (A) Reaction time pattern of left-handers with the detailing of performance at locations 1 & 6. (B) Reaction time pattern of right-handers with the detailing of performance at locations 1 & 6. Right-handers show

increased reaction time to the leftmost periphery (location 1) with time-on-task. Shaded area represents 95% confidence intervals.

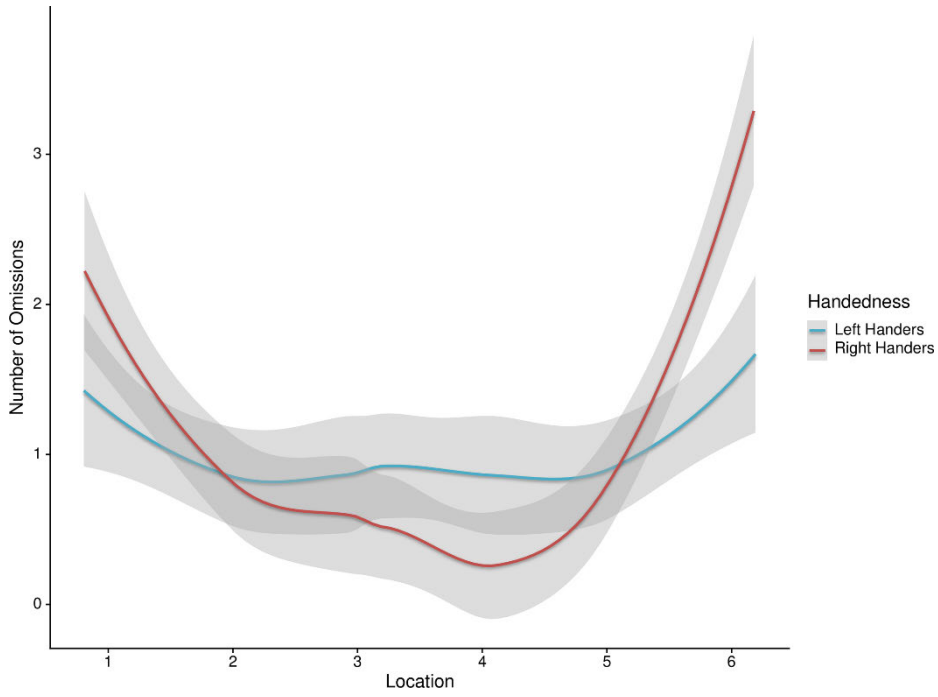


Figure 4.4. A handedness by location interaction revealed right handers show an increased number of omissions in the rightmost periphery compared to left handers. Smoothed means and shaded area representing 95% confidence intervals are displayed.

Table 4.3

F values, degrees of freedom, p values and holm corrected post hoc comparisons with corrections relative to time-on-task and location separated by handedness for models with the outcome reaction time.

Handedness	Predictor	F	df	p	Significant Post Hoc Comparisons
1. Left-Handers	Time	.621	1, 1630	.431	
	Location	68.97	5, 1631	<.001	L2>L3, L4; L6>L1, L2, L3, L4, L5; L1>L2, L3, L4, L5; L5>L3, L4
	Time*Location	1.643	5, 1630	.146	
2. Right-Handers	Time	14.01	1, 1767	<.001	1^{st} Half<2^{nd} half
	Location	64.23	5, 1768	<.001	L1>L2, L3, L4, L5; L2>L3, L4; L5>L3, L4; L6>L2, L3, L4, L5
	Time*Location	2.62	5, 1767	.023	1^{st} half L1<2^{nd} half L1; 1^{st} half L1>1^{st} half L2, 1^{st} half L3, 1^{st} half L4, 1^{st} half L5; 1^{st} half L6>1^{st} half L2, 1^{st} half L2; 1^{st} half L6>1^{st} half L3, 1^{st} half L4, 1^{st} half L5; 2^{nd} half L6>2^{nd} half L2, 2^{nd} half L3, 2^{nd} half L4, 2^{nd} half L5; 2^{nd} half L1>2^{nd} half L2, 2^{nd} half L3, 2^{nd} half L4, 2^{nd} half L5

Note. For post hoc analyses < and > indicate the direction of the effect. For example, L2>L3 reflects higher reaction time at location 2 compared to location 3. Only relevant post hoc comparisons reaching statistical significance (p<.05) following corrections for multiple comparisons are reported for interactions.

4.4.3 The relationship between alertness measures and spatial attention measures.

No evidence for reliable relationships between physiological measures (alpha, GSR) and reaction times to stimuli presented at the six spatial locations was observed. There was one exception, however, between GSR and reaction time to stimuli at location 2 (i.e., the second leftmost peripheral stimulus location) in left-handers, with a moderate effect size. See Figure 4.5 for correlations.

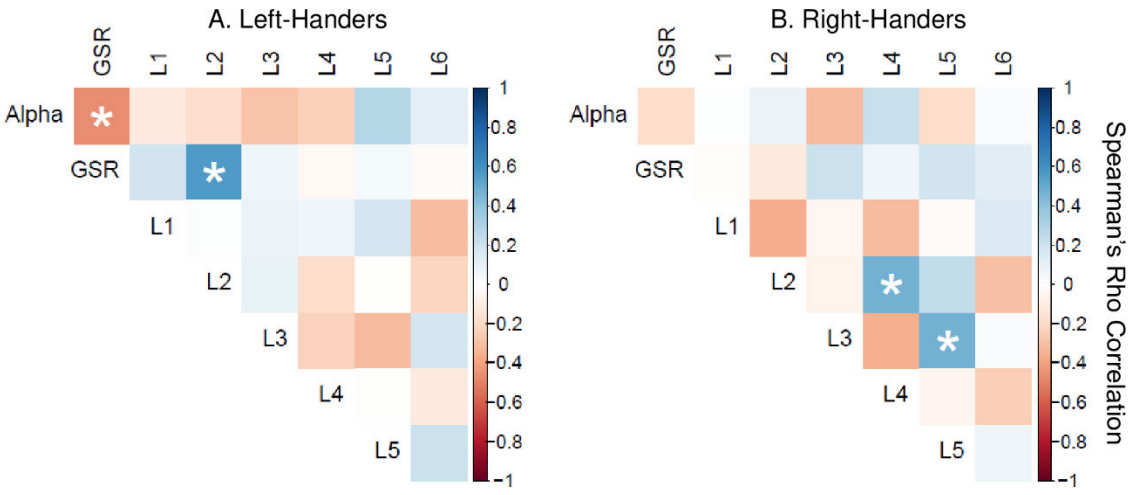


Figure 4.5. Spearman's Rho correlations between physiological alertness (GSR and alpha) and reaction time to all six locations for left-handers (A) and right-handers (B). Correlations reaching significance (p<.05) are highlighted. L1=location 1. Positive values for RT indicate slower RT in the second half than first half of drive (i.e., time-on-task), positive GSR values indicate higher SNS derived alertness with time-on-task, and positive alpha indicates higher alpha power (indicating lower alertness) with time-on-task.

4.5 Discussion

The current study aimed to investigate the relationship between spatial attention and alertness under prolonged simulated driving in left-handers and right-handers. More specifically, we aimed to uncover whether there are shifts in spatial attention during simulated driving and whether handedness influences the spatial attention and alertness relationship with time-on-task.

Before addressing these aims, it is critical to demonstrate the veracity of the driving task employed in this study by replicating typical alertness and driving performance patterns found in time-on-task paradigms.

We observed the expected decrease in alertness as indicated by an increase in subjective sleepiness (measured via KSS) and an increase in alpha relative power with time-on-task. These findings are consistent with previous literature examining time-on-task effects on subjective sleepiness and alpha (Benwell et al., 2019; Newman et al., 2013; Ranney, Simmons, & Masalonis, 1999). Another assay of alertness employed in the current study was sympathetic nervous system (SNS) activity as measured by GSR. No SNS activity changes were observed with time-on-task. While unexpected, our finding aligns with a previous study which also found no changes in GSR with time-on-task whilst performing an alertness decreasing task, which lasted two hours (Huang et al., 2018). A plausible reason for failing to detect changes in SNS activity might be the result of a flooring effect due to the sedentary driving task employed. While there was a lack of changes in SNS activity, the other two measures clearly indicate decreases in alertness. The subjective sleepiness and alpha measures of alertness were not modulated by handedness, revealing that both left-handers and right-handers decreased in alertness with time-on-task.

Decreases in alertness indexed by self-reports and alpha power were mirrored by decreases in driving performance. An increase in lane variability with prolonged task exposure was identified in the current study. This finding is consistent with previous studies using driving simulators (Gupta et al., 2017; Otmani et al., 2005). We found no differences in speed with time-on-task, demonstrating our participants stayed within 10% of the speed limit. This might be indicative of the relatively low speed limit (i.e., 50km) participants adhered to, being easier to maintain than higher speeds, and the nature of the task not requiring speed changes throughout the drive. However, performance

decrements were also found in the detection of stimuli presented within the driving task, where we observed increases in reaction time and omissions in the second half compared to the first half of the drive. Again, these effects are typically found in detection tasks with lowered alertness (Otmani et al., 2005; Rogé et al., 2003; Rogé et al., 2002). Similar to our assays of alertness, measures of driving performance (lane variability and time spent within 10% of the speed limit) were not modulated by handedness. Finally, the pattern of the reaction times across the six locations shows the typical U-shape with slower and faster reaction times in the periphery and centre, respectively (Chandrakumar et al., 2020; Rogé et al., 2002; Staugaard, Petersen, & Vangkilde, 2016). Having established that the prolonged driving task elicited the expected decreases in alertness, driving performance, and slower reaction times, we now turn the discussion to the effects of the prolonged driving task on spatial attention as a function of handedness.

There was clear evidence that prolonged driving affects left- and right-handers' ability to react to stimuli presented in the environment differently. These differences became particularly evident in the detection performance to the most lateral targets used in this study (see Figure 4.3). Right-handers became significantly slower to react to the leftmost peripheral stimulus location in the second compared to the first half of the drive. This finding is in line with previous studies demonstrating a rightward shift in attention with time-on-task and under lowered alertness conditions (Dodds et al., 2008; Jagannathan, Bareham, & Bekinschtein, 2020; Manly et al., 2005; Newman et al., 2013). Left-handers seem to show the opposite reaction time pattern of right-handers: with slower reaction times to right-sided stimuli in the second compared to the first half of the drive. However, the differences at the rightmost lateral stimulus were not statistically significant for left-handers when the analyses were corrected for multiple comparisons (p uncorrected = 0.017).

A three-way interaction of time by location by handedness did not reach significance for the number of omissions to stimuli, suggesting that there were no large differences in omissions of stimuli with time-on-task relative to the stimulus location as a function of handedness. A reason for this null-finding could be that reaction time might be a more sensitive measure than omissions in detecting subtle differences in performance. Our findings revealing more omissions in the rightmost periphery in right-handers might also reflect pseudoneglect. This is in line with a study comparing spatial bias on the Landmark task and a driving task revealing a leftward bias in both tasks,

indicative of the pseudoneglect phenomenon (Learmonth, Märker, McBride, Pellinen, & Harvey, 2018). There was no clear evidence for a tunnelling effect as time progressed and this might be reflective of the small number of stimuli within each location at each half of the drive, and thus not being sensitive enough to detect small changes in performance.

Overall, our handedness findings revealing differences in reaction times to stimuli are in line with findings by a study that showed left-handers and right-handers to differ in their spatial attention and alertness relationship (Bareham et al., 2015).

Correlations examining the relationship between alertness, measured via alpha and GSR, and spatial bias, measured via responses to target stimuli, failed to confirm a reliable relationship between changes in these measures (see Figure 4.5). This finding was unexpected as we predicted that changes in physiological alertness measures would associate with changes in spatial attention (Newman et al., 2013). An explanation for the lack of associations could be the relatively crude physiological measures employed in the current study. While we looked for changes in average alpha power across the two halves of the drive, investigating changes in alpha immediately before target onset might have been more revealing. For example, a study found that changes in pre-target alpha over the right relative to the left hemisphere were associated with a rightward shift in spatial biases (Newman et al., 2013).

We found evidence for differences in alpha across different brain regions (e.g., higher alpha in the parieto-occipital lobe than the frontal lobe and higher alpha in the right compared to the left frontal lobe, see Table 4.1), but these differences across regions were not modulated by time or handedness. Thus, the EEG measures in our study did not provide insights into the interactions between alertness and spatial attention. It cannot be ruled out that our sample of 22 right-handers and 20 left-handers was underpowered to detect small interaction effects. Importantly, however, the EEG measures did confirm that the time-on-task manipulation decreased alertness with time as indexed by an increase in alpha power as has been previously shown (Benwell et al., 2019; Wascher et al., 2014).

Although the EEG findings were inconclusive regarding the mechanisms underlying the interactions between alertness and spatial attention, the differences between left- and right-handers in this study suggest that the dominant model for the

interactions proposed by Corbetta and Shulman (2011) may need some refinement. The direction of the attentional shifts proposed by the model (to the left and right with high and low levels of alertness, respectively) might not necessarily hold true for left-handers. The reason for not showing the same pattern could be related to differences in the lateralisation of the DAN and VAN between left- and right-handers (Liu et al., 2009; Petit et al., 2015) which may consequently influence the spatial attention and alertness relationship differently in these two groups. Hence, it is possible that anatomical differences related to the location and connectivity of the DAN and VAN in left- and right-handers could influence the direction of attentional shift. However, there is a need for further investigation into the localisation of the DAN and VAN to understand the spatial attention and alertness relationship better.

Research on the relationship between alertness and spatial attention has been largely contained to tightly controlled laboratory studies employing paper and pencil or computerised tasks (Chandrakumar et al., 2019). In the current study, we attempted to increase real-world applicability of computerised spatial bias tasks by assessing the interactions between alertness and spatial attention while observing participants' driving behaviours in a safe and controlled environment. Although still based on an artificial task, the current findings confirm the possibility that these interactions could have safety implications for activities such as driving. For example, the right-handers' slowed responses and omission of left-sided compared to right-sided peripheral stimuli could potentially translate to delays in detecting relevant left-sided traffic information and dangers in the real-world. To what degree the stimuli used in this study are reflective of potential real-world dangers (e.g., a pedestrian walking onto the street) is unknown given inconsistencies in real-world applicability of driving simulators (Wynne, Beanland, & Salmon, 2019). However, given the high reliance on driving in today's society, and the increasing number of hours spent commuting (Wilkins, Laß, Butterworth, & Vera-Toscano, 2019), the potential implications resulting from impaired responding to the environment can be significant, on both an individual and economic level. Hence, it is critical to further investigate the factors that influence the ability to respond to the environment. Future research can benefit from investigating whether the effect of asymmetries in attending to the periphery is present in differing road conditions. Here, the simulated driving was conducted in a monotonous environment to decrease alertness,

but busy environments and factors such as light traffic may alert drivers and help counteract time-on-task effects (Thiffault & Bergeron, 2003).

4.6 Conclusions

Our study examined the effect of time-on-task on spatial bias under simulated driving performance. We found evidence of attentional shifts as a function of handedness as time-on-task progressed. Right-handers reacted slowly to the leftmost targets, while left-handers showed the opposite pattern (although not statistically significant) in the second compared to the first half of the drive. As the validity of driving simulators in predicting on-road driving is currently ambiguous, the real-world implications of our findings remain unclear. However, given the potential safety implications for real-world driving inattention, further investigations into the transfer effects of these findings are required.

Chapter Five: General Discussion

The overarching aim of the thesis was to investigate the alertness and spatial attention relationship in healthy adults, as this may provide critical information to assist in the management of human error, to minimise injuries and accidents. The specific aims were to: 1) synthesise the current literature on the relationship between spatial attention and alertness in healthy adults, and 2) identify conditions and modulators that affect the spatial attention and alertness relationship.

In the following sections, findings from the empirical chapters related to these aims are summarised, before discussing limitations and implications of these findings for the theoretical model, clinical population, real-world consequences, and future directions.

Conducting a meta-analysis in Chapter Two resulted in establishing the current state of research whilst pooling the results of all relevant studies to improve the estimate of the effect size due to increased statistical power. The selected papers in the meta-analysis revealed a small effect size of d=.302 (95% CI .125–.480) for a relationship between spatial attention and alertness. Importantly, in the light of the current replication crisis in psychology, there was no evidence for a significant publication bias. However, there was considerable heterogeneity, highlighting the various methodological procedures and outcomes in the studies included in the meta-analysis.

The estimated effect size was based on studies conducted in tightly controlled laboratory conditions and it remained to be seen whether these findings would translate outside of the laboratory into more real-world conditions. Given that the transfer effects of strictly laboratory-based findings were unclear, in Chapter Four, the spatial attention and alertness relationship was explored using a more everyday applicable spatial attention task: a driving simulator task, where we found a rightward shift in attention with time-on-task (i.e., lowered alertness) in our right-handed sample.

The considerable heterogeneity observed in the meta-analysis could, to some degree, be related to a lack of consensus in the literature regarding the definition and construct of ‘alertness’ and on how it is best measured. In this thesis, ‘alertness’ was defined as general wakefulness and readiness to respond to stimuli (Posner & Rafal, 1987). However, this definition might not be used by researchers across the field. A first step could be to conduct a Delphi study to advance the field and to recruit experts across

different fields to systematically establish a consensus on the constructs and terms used to refer to and measure alertness, through employing a controlled feedback process (see Bolger & Wright, 2011). Consensus resulting from a Delphi study could encourage the use of consistent terms and measures across the fields, leading to greater clarity.

As for the different alertness measures, heterogeneity in the meta-analysis was possibly also introduced by the variety of spatial attention measures used in the literature. Different tasks capture different processes as nicely demonstrated by Learmonth et al. (2015). These authors examined four different categories of spatial measures (i.e., size judgements, luminance judgements, stimulus detection, and judgement of global/local features) and reported no statistically significant inter-task correlations between the different measures, although all the measures were found to reliably detect spatial bias through showing good test-retest reliability. Hence, this might indicate various tasks tapping into slightly different aspects of spatial attention, such as endogenous and exogenous attention, and consequently influencing the DAN/VAN differently. Conversely, Chen et al. (2019) established convergent validity across perceptual judgement tasks whilst measuring pseudoneglect. This finding leans towards there being similar mechanisms involved in pseudoneglect and stands in contrast to the findings from Learmonth et al. (2015). The discrepancy between these two studies highlights the need to further evaluate the currently used measures in understanding the underlying processes involved in spatial bias.

Two modulators, specifically spatial task demands and handedness were identified in the literature and investigated in subsequent experimental chapters. Spatial task demands (judgement versus detection tasks) were a modulator of interest in the thesis for a couple of reasons. Firstly, judgement and detection tasks can have different real-world implications. From a work safety perspective, this modulator categorisation is interesting as judgement and detection tasks might tap into slightly different job demands. For example, detection tasks are more likely related to job demands that require fast and accurate responses to the environment such as in the case of pilots, truck drivers, and defence personnel. Judgement tasks on the other hand, might be more vital in a setting such as a medical personal deciding on the outcome of an x-ray or scan. Secondly, judgement and detection tasks capture different attentional processes (endogenous and exogenous, respectively) which may be differently influenced by changes in alertness levels. It is believed that the DAN is involved in endogenous attention processes,

whereby attention is directed intentionally, whereas the VAN is involved in more exogenous processes, and is captured by the appearance of unexpected stimuli for example (Corbetta et al., 2008; Corbetta & Shulman, 2002). Consequently, it seems plausible that spatial detection processes fluctuate more with changes in alertness than spatial judgements. In Chapter Two's meta-analysis, no differences between judgement (endogenous) and detection (exogenous) tasks were found when a subgroup analysis was conducted. This stands in contrast to Chapter Three's findings, where we found a rightward shift with lowered alertness in a detection task, but not the judgement task (although it showed spatial bias in the expected direction).

Hence, the findings in the thesis are not conclusive regarding differences between detection and judgement tasks. It remains to be established whether this effect results from differences in the sensitivity of reaction time tasks over judgement, or whether the close link of detection processes with the VAN results in detection tasks being more affected with lowered alertness.

Handedness was another modulator that was investigated. In Chapter Four, we investigated the notion that left-handers might show the opposite pattern of the spatial attention and alertness relationship to right-handers. A previous study investigated handedness and reported that their left-handed sample showed a leftward bias under lowered alertness (Bareham et al., 2015). Our findings revealed that alertness levels in our sample of left-handers decreased with time-on-task, similar to their right-handed counterparts. However, the left-handed and right-handed participants differed in their responses to lateral stimuli. We found that the right-handers reacted slower to the leftmost stimuli, while left-handers showed the opposite pattern (although not statistically significant) with time-on-task. These deviations in findings for left-handers and right-handers might be indicative of differences in lateralisation based on handedness. These findings will be discussed in more detail below.

5.1 Implications of the thesis findings for the dominant model accounting for spatial attention and alertness

In the thesis, the dominant theoretical framework postulated by Corbetta and Shulman (2011) was tested. It is important to note that this model was proposed as exploratory and was mainly informed by clinical and right-handed populations (Corbetta

& Shulman, 2011). We showed that normal fluctuations of alertness levels over days (Chapter Three) and reduction of alertness through prolonged task exposure (Chapter Four) are sufficient to observe corresponding shifts in spatial attention. Together with the findings of the meta-analysis (Chapter Two), there is now ample evidence to suggest that the dominant framework also holds true for healthy participants, suggesting that it is not restricted to clinical populations with disorders in alertness. In its current form, however, the framework does not explain the observed handedness differences (Chapter Four) and the findings of a stronger interaction effect between alertness and spatial attention in peripheral compared to central vision (Chapter Three & Four).

It is interesting to speculate how the observed differences in handedness could be accounted for by the Corbetta and Shulman (2011) framework. A straightforward explanation is that the VAN in left-handers is not right-lateralised. For example, if the VAN was left-lateralised, a hypoactivation of the left-sided VAN would lead to a dominance of the right-sided DAN and a corresponding leftward shift in attention. In the case of a bilateral VAN, no spatial shifts would be expected because the effects of lowered VAN activity on DAN would be largely symmetrical. In line with this speculation about the attentional networks, a fMRI study by Liu et al. (2009) revealed differences between left- and right-handers in the VAN. They found the VAN to be right-lateralised in right-handers, but bilateral or left lateralised in left-handers. These differences could indeed underlie the opposite direction of spatial shifts with lowered alertness observed between left- and right-handers in Chapter Four. If the findings by Liu et al. (2009) on differences in VAN locations are reflective of true lateralisation in left-handers, then a slight refinement of the Corbetta and Shulman (2011) model might be appropriate based on the findings from Chapter Four and Bareham et al. (2015). That is, it could be clearly stated that the location of the VAN can vary as a function of handedness. It can also be stated that the lateralisation of the VAN will determine the direction of attentional shift with lowered levels of alertness. The shifts will be ipsilateral to the location of the VAN location.

Despite potential differences in the DAN and VAN relative to handedness, it is still too early to suggest that the framework put forth by Corbetta and Shulman (2011) needs to include handedness as a modulator, as more research on how handedness influences the two networks is required. A look into the current literature shows a lack of consensus regarding DAN/VAN differences as a function of handedness. Findings from

Liu et al. (2009), for example, were not replicated in another neuroimaging study, which reported the VAN to be right-lateralised in both left-handers and right-handers (Petit et al., 2015). However, they reported differences in the DAN for left-handers and right-handers, such that left-handers showed a more pronounced DAN in the right hemisphere compared to the left hemisphere (Petit et al., 2015). If the DAN is more pronounced in the right hemisphere in left-handers, then one might expect pseudoneglect to be more pronounced in left-handers than right-handers, as the right DAN is implicated in directing attention contralaterally. However, this is not the case given right-handers are found to exhibit a stronger leftward bias than left-handers (Jewell & McCourt, 2000). Moreover, a right lateralised DAN in left-handers would be a challenge to incorporate into the Corbetta and Shulman (2011) framework to explain the interactions between alertness and spatial attention. It is clearly evident that more research is required to better understand the anatomy of the attention networks in uncovering how exactly the brain responds under lowered alertness conditions.

It is potentially also important to look beyond just the location of the DAN and VAN to understand the relationship between spatial attention and alertness. Findings from a rTMS study suggest that differences in the structure of the corpus collosum could influence the direction and magnitude of spatial attentional biases (Chechlacz, Humphreys, Sotiropoulos, Kennard, & Cazzoli, 2015). A smaller corpus collosum is associated with fewer interhemispheric connections (Bloom & Hynd, 2005) and larger attention shifts compared to individuals with a larger corpus collosum when rTMS is applied to the intraparietal sulcus (Chechlacz et al., 2015).

Interestingly, some early studies have provided support for left-handers having a larger corpus callosum compared to right-handers (Driesen & Raz, 1995; Witelson, 1985). However, Luders et al. (2010) showed that it is not handedness specifically that is associated with the size of the corpus callosum, but rather the degree of handedness lateralisation. The authors showed that strong right-handers and strong left-handers have a similar thickness of the corpus callosum. The authors also showed that the less-lateralised, moderate left-handers had a thicker corpus callosum than strong right-handers. Hence, individual differences in the size of the corpus callosum and the degree of lateralisation may influence the extent of attentional shifts under differing alertness conditions.

In contrast to the predictions arising from the Corbetta and Shulman (2011) framework, our physiological measures of alertness were not related to changes in spatial attention (Chapter Four). Changes in alpha relative power and sympathetic nervous system (SNS) activity did not show correlations with our spatial attention measure. While we demonstrated that time-on-task leads to an increase in alpha power (a proxy for decreases in alertness), we did not detect hemispheric changes in alpha relative power with time-on-task. We were unable to associate the observed shifts in spatial attention with changes in alpha power as predicted by the framework and previously shown by other researchers (Newman et al., 2013).

While unexpected, it is important to note that our null findings for the physiological measures cannot be taken as evidence for an absence of the relationship between the physiological and behavioural measures. As elaborated in Chapter Four, we cannot rule out the possibility that our physiological measures were not ideal to uncover physiological correlates of the interaction between alertness and spatial attention. We looked at changes in the measures from the first half to the second half of the drive. However, comparing averages of 30 minutes are rather crude measures. It is recommended that future research uses more fine-grained measures of physiological changes. For example, investigating changes in alpha immediately before target onset might be more revealing (see Newman et al., 2013). For SNS activity, it might also be worthwhile looking into pre-target measures. Before doing so, however, it might be important to establish whether SNS activity is indeed a good marker for changes in a sedentary driving task, such as that employed in our study. A previous study also found no changes in electrodermal activity with time-on-task whilst performing an alertness decreasing task (Huang et al., 2018). Electrodermal activity is influenced by the intensity of an experience and when an experience does not involve fluctuations in intensity, habituation to stimuli can occur (Leuchs, Schneider, & Spoormaker, 2019). This potentially makes it an unideal measure for a range of relatively uneventful time-on-task paradigms.

In sum, anatomical differences in the DAN and VAN need to be further investigated as there is support for variations in the anatomy of the DAN/VAN differentially influencing the relationship between alertness and spatial attention. A better understanding for how anatomical differences influence function can possibly assist with

identifying individuals who might be more susceptible to attentional shifts resulting from changes in alertness.

5.2 Implications for the clinical population

Application of the thesis findings to the clinical population is limited as our findings were derived from a sample of young and healthy participants. Nevertheless, our findings support the idea to explore approaches that increase alertness as an approach to ameliorate spatial neglect (Robertson et al., 1998; Van Vleet et al., 2020). Moreover, the demonstration that handedness differentially influences the spatial attention and alertness relationship raises the possibility that left-sided neglect following lesions to the right hemisphere might be less severe in left-handed compared to right-handed patients.

Our understanding for differences in how handedness influences neglect recovery in the clinical population is limited. Reasons for the lack of understanding include that handedness is sometimes not a variable of interest, left-handers are often excluded in research studies (Willems et al., 2014), and the small proportion of left-handed (compared to right-handed) neglect patients. Therefore, further investigations are required to identify whether handedness influences the severity of neglect symptoms.

5.3 Implications for healthy adults

The meta-analysis (Chapter Two) provides evidence that lowered alertness shifts spatial attention in healthy participants. A fundamental question is whether this evidence, deriving from tightly controlled laboratory studies and artificial tasks, transfers to real-world settings. If they do, they may have significant implications for health and safety.

In this thesis, we attempted to make a step towards more real-world applicable situations (shift work, see Chapter Three) and tasks (driving, see Chapter Four). It is important to emphasise that this was only a first step towards increasing real-world fidelity, although the employed experiments were still conducted in controlled laboratory settings with unclear real-world relevance. For example, the artificial environment in driving simulators poses no risk to the driver and consequently, drivers may make riskier decisions and may also be unmotivated to enhance safety behaviour (Wynne et al., 2019).

Disregarding the issue of real-world fidelity of our tasks for a moment, it is interesting to think about statistical significance and meaningful real-world differences in our experiments. We found an increase in reaction time by 117ms in detecting the leftmost stimuli in the second compared to the first half of the simulated drive in right-handers. This increase was statistically significant (see Chapter Four), but it is unclear whether such an increase would be relevant in the real-world. One approach to think about whether the increase poses a significant health and safety risk is to calculate the extra stopping distances associated with the slower reaction time. When considering the 117ms delay in responding with time-on-task, if someone drives at 50km per hour and has to ensure a vehicle comes to a complete halt, an extra stopping distance of 1.63m is added (calculated using a stopping distance calculator; Szyk, n.d). This distance changes depending on the vehicle's speed, such that a higher speed increases stopping distance. The observed reaction time increase in Chapter Four would raise the stopping distance by 3.26m if a car driving 100km per hour needs to be brought to a complete halt. To what degree the calculated added stopping distances of 1.63 to 3.26 metres have significant implications in various driving hazard situations cannot be answered at this stage. However, it seems certainly plausible that an increase in stopping distance of more than 3m could in some instances make a difference between a minor or severe traffic accident. Thus, it seems crucial to further investigate the potential real-world consequences of spatial attentional shifts in accidents.

An important next step is to investigate if shifts of attention under conditions of lowered alertness are present in naturalistic conditions. For example, driving in the real-world tends to involve more scanning of the periphery compared to a laboratory-based driving simulator. Hence, examining shifts in attention under controlled real-world conditions via utilising eye tracking can be one step towards determining whether attention shifts with prolonged time driving. Given that a large number of traffic accidents are attributed to driver inattention and decreased alertness levels (Choi et al., 2016), another strategy might be to examine traffic accident data to investigate whether the side of an accident is associated with a rough proxy of alertness (e.g., time of day; Åkerstedt, 2003; Harrington, 2001). Challenges to this idea include the need to control for driving conditions such as traffic, visibility, and weather.

More naturalistic investigations will assist in determining which measures (if any) need to be taken to prevent potential negative safety outcomes related to interactions

between alertness and spatial attention. For example, in instances where one side is more neglected, implementing more road signs or signals on both sides of the road might be beneficial in preventing asymmetry in spatial attention.

5.4 Limitations and future directions

As mentioned previously, the first steps in furthering our understanding for the relationship between spatial attention and alertness is finding a consensus on the taxonomy and constructs to ensure consistency in measuring alertness, investigating the spatial attention and alertness relationship in more real-world applicable conditions, and examining the extent to which findings from tightly controlled laboratory setting apply to meaningful real-world shifts in spatial attention.

Whilst the thesis investigated conditions that decrease alertness (sleep and time-on-task manipulations), there is a particular need to explore countermeasures to the demonstrated spatial shifts in conditions of lowered alertness. For example, warning systems from the haptic modality is one strategy that has gained recognition for its use in alerting individuals (Spence & Gallace, 2007; Spence & Ho, 2008). This haptic modality can be particularly useful under conditions where the visual system is overloaded, such as in the case of attending to stimuli in the environment whilst driving (Meng & Spence, 2015). Additionally, auditory warning cues can be used to increase driver attention (Ho & Spence, 2005). Therefore, utilising a multi-sensory approach which integrates visual, auditory, and haptic modalities might improve safety in individuals with lowered alertness.

A limitation of the thesis was that we did not investigate the influence of motivation on the spatial attention and alertness relationship. Motivation can influence performance such that decreased motivation can reduce attentional allocation and engagement towards a task (Horrey, Lesch, Garabet, Simmons, & Maikala, 2017). Hence, it is plausible to expect the rightward shift in attention observed under lowered alertness to be enhanced, as a lack of motivation can further decrease alertness levels. This is particularly likely to occur in experimental studies where tasks might be highly unmotivating. Previous studies provide support for a reduction in the left-sided neglect experienced by patients when motivation is increased through using rewards (Lucas et

al., 2013; Malhotra, Soto, Li, & Russell, 2013). In these studies, patients who were neglecting the left-side of space were able to attend to their neglected side more fully. Similarly, in healthy participants, Hopstaken, van der Linden, Bakker, and Kompier (2015) showed eye movements directed away from the task decreased when task rewards were increased, whilst performing a task under lowered alertness conditions. This highlights the importance of motivation influencing attentional bias. However, controlling for motivation is a challenge in tightly controlled laboratory studies and it remains to be established how this specifically relates to spatial bias in healthy adults. It cannot be ruled out that the effects of alertness on spatial attention observed in healthy participants are generally higher than they would be in real-world situations due to intrinsic motivation differences.

It is possible that when engaging in high-risk behaviours, motivation is high to focus on a task and maintain high alertness. For example, in a situation where an individual is driving under monotonous conditions that can lower alertness, the individual, whilst likely to experience low levels of alertness, may be highly motivated by the safety consequences of inattention and slowed responses. Hence, they may be able to maintain their alertness levels for a longer period of time compared to if the conditions were low-risk, such as in the case of performing a simulated driving task. In Chapter Four, participants in the study may not have been motivated to perform the task as well as they would have under more naturalistic conditions, such as whilst driving on a real road. Hence, it remains unclear whether these findings would suggest spatial attention is less impaired under on-road driving conditions.

To get a full picture of alertness and spatial attention interactions, it will be important to consider a number of factors that were overlooked in this thesis, such as age, gender, and cognitive load. Age-related changes in visuospatial attention are commonly reported, such that one's ability to attend to the periphery is reduced with age. Studies comparing younger and older adults have repeatedly found older adults perform poorly to the periphery compared to younger adults (Rogé, Pébayle, Campagne, & Muzet, 2005; Rogé et al., 2003; Rogé et al., 2004). When performing line bisection tasks, older adults have been reported as showing more of a rightward bias than younger adults (Jewell & McCourt, 2000). Whilst there is support for age-related differences in spatial attention, findings for gender differences in spatial attention are unclear as findings tend to be mixed, with the majority of studies reporting no differences in gender (Jewell &

McCourt, 2000). In the thesis, age and gender differences were not investigated. However, future studies examining these differences could assist with uncovering this discrepancy as some individuals might be more susceptible to shifts in attention resulting from altered alertness levels compared to others.

Cognitive load, another factor not investigated in the thesis, can be influenced by the details of an experimental procedure, tasks employed, and participant characteristics. A study found spatial bias to be more pronounced towards the right in both healthy and clinical participants under dual-task conditions (Peers, Cusack, & Duncan, 2006). This finding points towards augmentation of spatial biases in conditions with an increased cost to processing capacity, such as when a secondary task is also competing for resources. Increased cognitive load is also associated with decreased alertness levels due to resource depletion (Smit, Eling, & Coenen, 2004). Whilst Peers et al. (2006) showed shifts in attention under dual-task conditions, another study did not find spatial shifts under dual-task conditions (Dodds et al., 2008). An important factor when investigating cognitive load and processing capacity is individual differences (Fitousi & Wenger, 2011). A plausible reason for Dodds et al. (2008) not finding spatial shifts could be due to individual differences, as variation in the direction of bias could have cancelled out on a group level. Hence, further investigations into the influence of load on spatial bias could benefit from untying individual differences in processing capacity influencing the spatial attention and alertness relationship.

5.5 Conclusions

The thesis corroborates evidence that alertness levels influence the allocation of attention in space. Handedness was identified as a critical modulator in determining the direction of attentional shifts with fluctuations in alertness. Handedness is currently not considered in the dominating framework accounting for the relationship between spatial attention and alertness. We established that the spatial attention and alertness relationship can be found in conditions that attempted to simulate more real-world applicable conditions such as shiftwork and driving. However, the extent to which such findings apply to real-world consequences (e.g., slowed reaction times transferring to increased stopping distances whilst driving) is currently unclear. This suggests a need to further investigate the transfer effects under more naturalistic conditions. The limitations of the

thesis findings are acknowledged, and future research suggestions are made to better understand the spatial attention and alertness relationship.

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Appendix A: Overview of authorship contributions

The following section describes the author's contributions to the papers included within this thesis.

Chapter Two

Chandrakumar, D., Keage, H. A., Gutteridge, D., Dorrian, J., Banks, S., & Loetscher, T. (2019). Interactions between Spatial Attention and Alertness in Healthy Adults: A Meta-Analysis. *Cortex*, 119, 61-73. doi: 10.1016/j.cortex.2019.03.016

Study Design and Data Collection

I designed this meta-analysis topic along with my primary supervisor, Dr Tobias Loetscher. This meta-analysis involved me carrying out the literature search of multiple databases using specified search terms. The initial literature search was conducted in March 2017 and I screened 3359 articles for eligibility in this meta-analysis along with a co-author who did the secondary abstract screening. I collaborated with a co-author, Daria Gutteridge, to identify conflicts in abstract screening to selected relevant articles to be included for the review.

Publication of Manuscript

I developed the initial draft of the manuscript and then, with the assistance and input of my co-authors, I refined the interpretation of the literature and re-drafted the manuscript. Following submission and peer-review, I revised the relevant changes for the manuscript, with the assistance of my co-authors, and resubmitted the manuscript for publication. The manuscript was published in *Cortex* in 2019.

Chapter Three

Chandrakumar, D., Dorrian, J., Banks, S., Keage, H. A., Coussens, S., Gupta, C., Centofanti, S. A., Stepien, J. M., & Loetscher, T. (2020). The Relationship between Alertness and Spatial Attention under Simulated Shiftwork. *Scientific reports*, 10. doi:10.1038/s41598-020-71800-6

Study Design and Data Collection

This study took place within a wider study, which was developed by co-authors Prof. Siobhan Banks, Prof. Jill Dorrian, Dr Charlotte Gupta, & Dr Stephanie Centofanti. The smaller study within this study was formulated by myself, Dr Tobias Loetscher, Prof. Siobhan Banks, and Prof. Jill Dorrian.

Publication of Manuscript

With the assistance of my supervisors, I led the analysis and interpretation of research data. I drafted the first version of this manuscript and this was subsequently revised by my co-authors and I. Following submission and peer-review, I revised the relevant changes for the manuscript, with the assistance of my co-authors, and resubmitted the manuscript for publication. The manuscript was published in *Scientific Reports* in 2020.

Chapter Four

Chandrakumar, D., Coussens, S., Keage, H.A.D., Banks, S., Dorrian, J., & Loetscher, T. (Under review). Monotonous driving induces shifts in spatial attention as a function of handedness.

Study Design and Data Collection

I designed this study design along with the assistance of my primary supervisor, Dr Tobias Loetscher. I collected data with the help of two research assistants, and analysed the results with the help of the supervisory panel. The data for this study was collected from February 2019 to July 2019.

Publication of Manuscript

With the assistance of my co-authors, I was involved in the analysis and interpretation of research data. I drafted the first version of this manuscript, and this manuscript was subsequently revised by myself and my co-authors. I was responsible for submitting this manuscript to a peer-review journal, and it is currently under review.

Appendix B: Written permission from co-authors

The co-authors listed below contributed to the publications included within this thesis. The signatures provided below confirm each author's contributions and acknowledge my input into the three empirical chapters described in the overview of the author's contributions. Authors are listed as per the author lists of each publication.

Chapter Two

Dilushi Chandrakumar

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Conceptualisation of study
- Conducted the search of the literature
- Screening of articles
- Data extraction
- Quantitative analysis of data from selected articles
- Writing and drafting of manuscript
- Critical revision of manuscript for important intellectual content
- Completed revisions suggested in the publication process



Hannah Keage

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Interpretation of quantitative analysis data from selected articles
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Daria Gutteridge

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Screening of articles
- Interpretation of articles
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Jill Dorrian

Sleep and Chronobiology Laboratory, University of South Australia

- Interpretation of quantitative analysis data from selected articles
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Siobhan Banks

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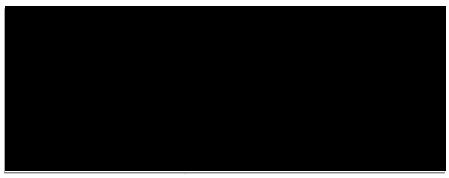
- Interpretation of quantitative analysis data from selected articles
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Tobias Loetscher

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Conceptualisation of study
- Review of data extraction
- Interpretation of quantitative analysis from selected articles
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Chapter Three

Dilushi Chandrakumar

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Contribution to smaller study conception and design
- Data collection
- Data analysis and interpretation of data
- Writing and drafting of manuscript
- Critical revision of manuscript for important intellectual content
- Completed revisions suggested in the publication process



Jill Dorrian

Sleep and Chronobiology Laboratory, University of South Australia

- Contribution to study conception and design
- Contribution to data analysis and interpretation of data
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Siobhan Banks

Sleep and Chronobiology Laboratory, University of South Australia

- Contribution to study conception and design
- Contribution to data analysis and interpretation of data
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Hannah Keage

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Contribution to study conception and design
- Contribution to data analysis and interpretation of data

- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Scott Coussens

Cognitive Aging and Impairment Neurosciences Laboratory, University of South Australia

- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Charlotte Gupta

Appleton Institute, Central Queensland University

- Contribution to the wider study conception and design
- Recruitment
- Data collection
- Wider study coordination
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Stephanie Centofanti

University of South Australia Online

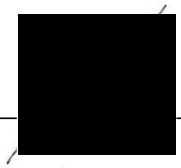
- Contribution to the wider study conception and design
- Recruitment
- Data collection
- Wider study coordination
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Jackie Stepien

Sleep and Chronobiology Laboratory, University of South Australia

- Recruitment
- Data collection
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript

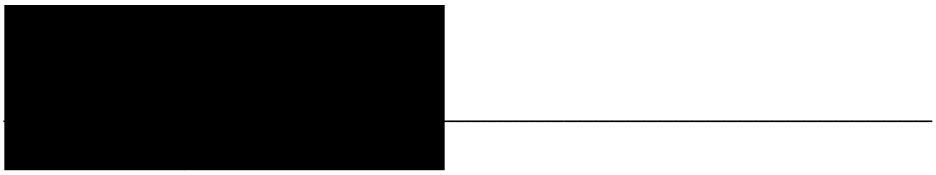


Tobias Loetscher

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- Contribution to smaller study conception and design
- Contribution to data analysis and interpretation of data
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- Final approval of manuscript



Chapter Four

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- Contribution to study conception and design
- Recruitment
- Data collection
- Study coordination
- Data cleaning, data analysis, and interpretation of data
- Writing and drafting of manuscript
- Critical revision of manuscript for important intellectual content



Scott Coussens

Cognitive Aging and Impairment Neurosciences Laboratory, Sleep and Chronobiology Laboratory, University of South Australia

- Contribution to study design
- Contribution to data cleaning, data analysis and interpretation of data
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Hannah Keage

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- Contribution to data analysis and interpretation of data
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Siobhan Banks

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- Contribution to data analysis and interpretation of data
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Jill Dorrian

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- Final approval of manuscript



Tobias Loetscher

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- Contribution to study conception and design
- Contribution to data analysis and interpretation of data
- Drafting of manuscript
- Critical revision of manuscript for important intellectual content
- Final approval of manuscript



Appendix C: Permission for use of published material in thesis

Chapter Two.

Chandrakumar, D., Keage, H. A., Gutteridge, D., Dorrian, J., Banks, S., & Loetscher, T. (2019). Interactions between Spatial Attention and Alertness in Healthy Adults: A Meta-Analysis. *Cortex*, 119, 61-73. Doi: 10.1016/j.cortex.2019.03.016



Chapter Three.

Chandrakumar, D., Dorrian, J., Banks, S., Keage, H. A., Coussens, S., Gupta, C., Centofanti, S. A., Stepien, J. M., & Loetscher, T. (2020). The Relationship between Alertness and Spatial Attention under Simulated Shiftwork. *Scientific reports,* 10. doi:10.1038/s41598-020-71800-6

