Methodological Considerations and Cognitive Factors Underlying Sustained Attention

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Abstract

The active, ongoing maintenance of an adequate level of performance over time on task is an essential cognitive faculty, and has been described in multiple frameworks since the earliest days of cognitive research. Theoretical accounts of performance maintenance focused on the timely fluctuations of attention components, using the partially overlapping constructs of sustained attention, arousal, vigilance and alertness. In this thesis, particular attention is given to sustained attention, arguably the most useful and frequently used construct in a clinical context. Chapter 1 provides an introductory overview of the literature, focusing on the theories and paradigms available to assess sustained attention and other closely related constructs. Chapter 2 introduces a new task for assessing sustained attention, based on a variation of the Continuous Performance Task (CPT), and discusses the contribution of various task factors to performance patterns. In Chapter 3, the newly established paradigm is used to assess sustained attention among stroke survivors and the healthy ageing, and relate task-performance to subjective reports of daily lapses in attention. A detailed discussion is devoted to identifying the task indices that best represent sustained attention capacity, favouring measures incorporating the notion of change in performance over time. Chapter 4 applies the same approach of estimating change in performance over time to studying sustained attention among children with genetic developmental disorders. Chapters 5 and 6 show how performance in a CPT is influenced by the pace at which stimuli are presented in the task. It is argued that individuals are sensitive to varying levels of temporal regularities; consequently, when measuring sustained attention, researchers must account for the rhythmic pattern that the CPT may introduce. Chapter 7 will present an intervention study combining brain stimulation and a spatially-lateralised CPT paradigm, demonstrating changes in components of Selective Attention as defined by a computational model. The thesis is concluded in Chapter 8, which discusses the contributions of the experimental findings to the understanding of sustained attention and associated experimental methods. The thesis proposes a clear mapping of sustained attention with relation to other closely related constructs, and attempts to provide useful tools for improving clinical assessment.

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Dedicated to the memory of my late supervisor, Professor Glyn Humphreys.

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Contents

Chapter 1 : Introduction

Abstract

The following chapter reviews the cognitive literature addressing the fluctuations of performance over time. I will use the term *performance maintenance* when referring to a set of cognitive constructs, all aimed at explaining the temporal dynamics of performance. The first argument that will set the ground for this thesis is that the performance maintenance literature is characterised by a great deal of inconsistency, both theoretical and technical. From a theoretical perspective, I will attempt to disentangle and clarify multiple, partially overlapping constructs of performance maintenance. A more technical discussion will then consider methodological challenges in the cognitive assessment of performance maintenance, focusing on variations of the Continuous Performance Task (CPT). A careful analysis of the various task factors of the CPT will reveal potential confounds in the available assessment tools and will question the various outcome measures that are often used interchangeably in the literature. The introduction will introduce a cohesive framework of performance maintenance and its subcomponents, as well as a detailed analysis of the implicit and explicit factors determining performance in a CPT. I will conclude by presenting the fundamental questions guiding this thesis, revolving around the interplay between sustained

attention (an essential component of performance maintenance) and the way it is assessed and used in clinical and experimental contexts.

Mechanisms Supporting Performance Maintenance

In a constantly changing environment, the ability to continuously monitor our surroundings and react to changes is crucial for adaptive behaviour. This is why the capacity of maintaining adequate performance level over time has been subject to research since the earliest days of modern cognitive sciences (e.g., Head, 1926; Mackworth, 1948). Although Head's notion of Vigilance (Head, 1926) is intuitively appealing, nearly a century after there is still a great deal of inconsistency in attempts to comprehend all the mechanisms underlying performance maintenance, its decrement and its fluctuations. Partially overlapping accounts use different terminology, for example 'Sustained attention', 'Vigilance', 'Vigilant attention', 'Alertness', and 'Arousal'. These concepts have evolved over the years. They can roughly be divided into theories that focus on attention as the central faculty being maintained (sustained attention, vigilant attention and alertness), and theories that refer to the global 'energetic' state of the system (arousal and vigilance). Lacking precise definitions, these terms are often used interchangeably in the literature. In the following section, I will discuss each aforementioned aspect of performance maintenance, focusing on its proposed functions.

Arousal

The first distinction that should be made is between arousal and the other cognitive faculties I wish to discuss. Arousal is an oddball within the literature of performance maintenance. It refers to a general cognitive *resource* rather than a cognitive *function*. First proposed by Hebb (1955), arousal was introduced as a replacement for the behaviouristic notion of 'Drive' (Woodworth, 1918), which roughly corresponds to motivation in its common-sense meaning. While behaviourists theorists thought of Drive as the link between behaviour and learning, Hebb tried to address the possible brain functions and mental faculties linked to performance (Hebb, 1955). Figure 1.1 shows the proposed notion of arousal, according to Hebb.

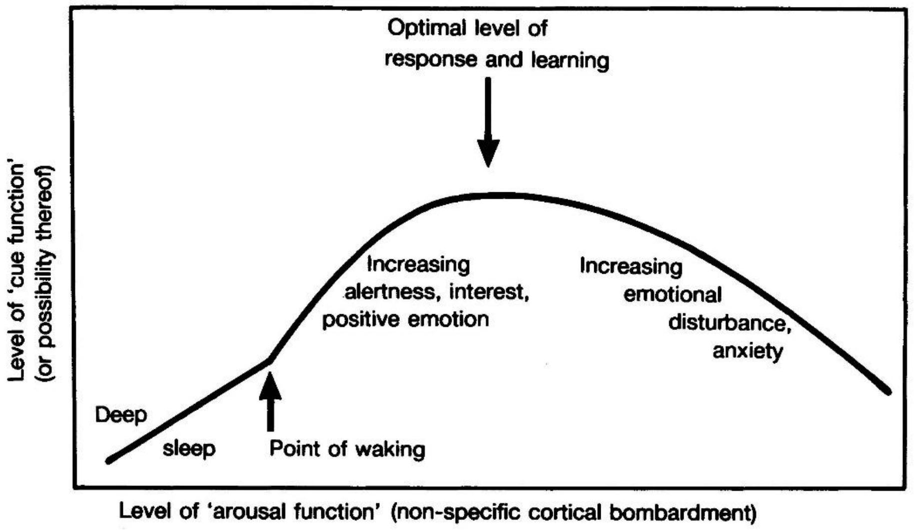

Figure 1.1 The relationships between Hebb's 'arousal function' and 'cue function'. Based on Hebb, 1955, p. 250. Figure is copied in compliance with the APA Permission Policy

As the x-axis title in Figure 1.1 denotes, arousal first appeared as a non-specific function 'whose activity in effect makes organised cortical activity possible' (Hebb, 1955). The inverted U-shaped curve that appeared in Hebb's description became a hallmark of arousal: performance reaches its peak when arousal is at the intermediate level (Aston-Jones & Cohen, 2005; Broadbent, 1971; Hebb, 1955). Following Hebb's work, the inverted U-shaped relationships between arousal and performance were associated with the earlier work of Yerkes and Dodson (1908), in which a similar distribution described how task difficulty affects the learning curve of a discrimination task. This pattern, familiar as the Yerkes-Dodson Law, was only retrospectively applied to arousal (Teigen, 1994). In the years following its introduction, arousal allowed the reinterpretation of many 'classic' theories and findings, including Pavlov's 'strength of the nervous system' in Gray's Optimal Level Theory (Gray & Eysenck, 1964), where motivation was replaced by arousal to describe the 'energetic' capacity of the cognitive system. With the evolution of the cognitive neurosciences, arousal was used to describe the primary function of the Reticular Activating System, a system involving the upper brainstem reticular core that projects to the cortex through synaptic relays in the thalamus (e.g., Steriade, 1996). Within this system, a particular nucleus – the locus coeruleus – was proposed as involved in regulating arousal by distributing noradrenaline (e.g., Foote, Aston-Jones, & Bloom, 1980).

The non-specific nature of arousal is exemplified in Figure 1.1, where it appears as a continuous state ranging between sleep and wakefulness, gradually leading to 'increasing emotional disturbance' and 'anxiety'. Perhaps the most important aspect of arousal in the context of the current discussion is Hebb's speculation about the way in which it is determined. Hebb stated that 'The arousal system can be thought of as representing a second major pathway by which all sensory excitations reach the cortex … but there is also feedback from the cortex and I shall urge that the *psychological* evidence further emphasises the importance of this "downstream" effect' (1955). Hebb describes a bi-directional arousal system changing the energetic state or activation level of the whole system, and regulated by the cortex. With a few adaptations, Hebb's notion of arousal has persisted. The particular role of the locus coeruleus-noradrenergic system and the way it communicates with the forebrain has been articulated in the works of Aston-Jones and Cohen (2005) as part of the Adaptive Gain Theory, which describes how performance is optimised in reward-seeking behaviour. Optimised performance is achieved by the continuous monitoring of task utility (through a system mainly involving the anterior cingulate and the orbitofrontal cortices) and regulating the locus coeruleus-noradrenergic system accordingly. The locus coeruleus firing pattern relates to performance in a U-shaped function, in accordance with the Yerkes-Dodson Law (1908) and Hebb's arousal function (Hebb, 1955). Although the Adaptive Gain Theory is not a theory of arousal *per se*, Aston-Jones & Cohen (2005) use it to 'explain effects conventionally interpreted in terms of arousal'.

Fundamental concepts in Adaptive Gain Theory are the 'exploration' and 'exploitation' modes of operation, which represent a dynamic shift in the locus coeruleus firing pattern, either to optimise utility within the current task set (exploitation) or to seek alternative sources (exploration). Exploitation is associated with phasic, short-lived locus coeruleus firing activity on the occurrence of task-relevant events, which selectively increase neural gain in cortical areas related to the current goal set. Exploration is associated with a tonic increase in firing rate, accompanied by the absence of phasic increases and leading to more distractible behaviour (Aston-Jones & Cohen, 2005; Sara, 2009; Clayton *et al.*, 2004; Rajkowski, Kubiak, & Aston-Jones, 1994; Usher *et al.*, 1999). Consistently with the Adaptive Gain Theory, Yu and Dayan (2005; Dayan & Yu, 2006) describe the locus coeruleus-noradrenergic response by means of adapting to unexpected uncertainty in task gain: low uncertainty will promote exploitation, and high uncertainty will encourage exploration. Arousal is thus the locus coeruleus-noradrenergic response to varying levels of uncertainty.

Importantly for the current discussion, the functions of this arousal system (and in particular the locus coeruleus-noradrenergic system) have gradually become a fundamental element of nearly all theories ascribing performance over time. It is an essential aspect of vigilance (Mackworth, 1968), alertness (Posner & Petersen, 1990), sustained attention (Robbins, 1998), and vigilant attention (Robertson & O'Connell, 2010). It is worth clarifying that performance maintenance is not considered as the primary function of arousal. Instead, arousal supports performance, and the temporal dynamics of arousal are therefore important for understanding performance maintenance.

Vigilance

As mentioned earlier, vigilance and arousal share some features. Both relate to the overall 'energetic' state of the system (Hebb, 1955; Moruzzi & Magoun, 1949). A fruitful way of distinguishing the two is by thinking of arousal as a momentary resource determining activation level, and of vigilance as a non-specific capacity of performance maintenance (Sarter, Givens, & Bruno, 2001). The earliest articulation of vigilance appeared in Mackworth's study of the performance of airborne radar operators during the Second World War, investigating why their efficiency deteriorated over time (Mackworth, 1948). When defining vigilance, Mackworth referred to the works of Head (1926), which defined vigilance as the capacity of readiness to react, stating that 'the present writer also believes that vigilance is a useful word to adopt, particularly in describing a psychological readiness to perceive and respond, a process which, unlike attention, need not necessarily be consciously experienced.' Although attention research has evolved significantly since Mackworth's days, the distinction between vigilance and attention has remained (Robertson & O'Connell 2010). In particular, vigilance (or, more percisely, the lack of it) is thought to represent a 'slow increase in error rate that occurs over periods between 30 minutes and 1 hour, in the context of perceptual detection tasks involving the detection of very rare targets amongst large number of monotonous and homogeneous stimuli' (Robertson & O'Connell, 2010; after Mackworth, 1956). It is therefore distinguished from attention by the time frame of reference and the task requirements in which it is manifested. Mackworth (1968) proposed an explanation for the decrement in vigilance over time in terms of a habituation of the neural response to repetitive, predictable events, alongside a gradual habituation of arousal. She also specified that, while gradual habituation in arousal would lead to a decrement in target detection, the habituation of stimulus-evoked potentials would gradually lead to a general reduction in responses to both targets and distractors. Another strong emphasis that became key to the experimental study of performance maintenance was the rare occurrence of target events within a stream of irrelevant stimuli as a prerequisite for vigilance tasks (Mackworth, 1968).

Researchers often use the term ‘vigilance’ interchangeably with other constructs representing performance maintenance, particularly sustained attention (Parasuramen, Warm, & See, 1998; Robbins, 1998; Robertson *et al.*, 1997; Sarter, Givens, & Bruno, 2001). Other connotations of vigilance refer to specific task properties: a ‘vigilant task’ often denotes a prolonged, repetitive task in which target occurrence is rare and unexpected (e.g., Parasuramen, Warm, & See, 1998; Schroder & Lakatos, 2009). Vigilance could be subdivided into the overall performance level in a prolonged task (termed ‘vigilance level’) and the extent to which it decays (termed ‘vigilance decrement’) (Martel, Dahne, & Blankertz, 2014; Sarter, Givens, & Bruno, 2001). Although the evidence reviewed so far holds vigilance to be a non-specific construct, it provides a useful distinction with respects to the time frames in which attention is typically studied. While vigilance decrement is usually observed after a prolonged period of task performance (over 30 minutes: Mackworth, 1968) attention researchers have noticed that fluctuations in performance maintenance are also seen in shorter durations (e.g., Robertson *et al.*, 1997). To account for changes in performance occurring over shorter time periods, researchers often use the term vigilant attention (e.g., Lim & Dinges, 2008; Martel, Dahne, & Blankertz, 2014; Robertson & O'Connell, 2010).

Vigilant Attention

Vigilant attention is defined as 'the ability to self-sustain mindful, conscious processing of stimuli whose repetitive, non-arousing qualities, would otherwise lead to habituation and distraction by other stimuli' (Robertson *et al.*, 1997 in Robertson & O'Connell, 2010).[1] A complementary definition proposes that vigilant attention is responsible for constantly 'refreshing' the cognitive system in cases where attention is not triggered by external stimuli with novel properties (e.g., Langner & Eickhof, 2013). Vigilant attention is suggested to be supported by a right-hemisphere cortical network that monitors and modulates subcortical

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[1] This citation appears in Robertson and O'Connell (2010) referring to vigilant attention, although the original paper (Robertson *et al.*, 1997) uses it to define sustained attention. The term 'vigilant attention' appears only in later works.

regions governing arousal.[2] This way, the vigilant attention system can promote adequate levels of arousal in the absence of externally arousing signals (Robertson & O'Connell, 2010; Sturm & Willmes, 2001), or in accordance with task demands (Critchley *et al.*, 2003; Foucher *et al.*, 2004). Vigilant attention relies predominantly on the anterior cingulate cortex, the right dorsolateral prefrontal cortex, and the inferior parietal lobule (Robertson & O'Connell, 2010; Sturm & Willmes, 2001). The arousal function is modulated by inputs from vigilant attention regions, and in return supports performance by decreasing signal-to-noise ratio by noradrenaline connections across the cortex (e.g., Berridge & Waterhouse, 2003). Although the original proposal by Robertson & O'Connell (2010) defines vigilant attention as a cortical system, other accounts include sub-cortical connections, including what was previously defined as the arousal system (e.g., Langner & Eickhof, 2013). When contrasted with the notion of vigilance, which directly relates to the individual capacity of performance maintenance, vigilant attention does not account for performance decrement or its maintenance *per se*, but instead provides a mechanistic explanation for momentary

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[2] It is worth noting that the term 'vigilant attention' is often applied retrospectively in literature reviews referring to experimental studies that initially targeted sustained attention, alertness, and arousal rather than vigilant attention (e.g., Coull et al., 1995; 1997; 2004; Sturm & Willmes, 2001).

optimisation of performance. Performance maintenance is therefore achieved by an ongoing ‘collaboration’ or co-activation of arousal and vigilant attention.

Although interrelated, arousal and vigilant attention can be distinguished based on behavioural and neuropsychological dissociations (e.g., Coull *et al.*, 1995; 1997; 2004; Greene *et al.*, 2009; Paus *et al.*, 1997; Smith & Nutt, 1996). In particular, studies have used various methods to selectively influence either sub-cortical structures related to arousal (e.g., the locus coeruleus) or the cortical structures related to vigilant attention. Performance on tasks that measured vigilant attention was impaired when arousal-related locus coeruleus activity was suppressed, and this effect was attenuated when the researchers introduced an exogenous signal (e.g., Bellgrove *et al.*, 2006; Coull *et al.*, 1995; Greene *et al.*, 2009; Smith & Nutt, 1996). Such studies led to a conclusion that vigilant attention can independently compensate for poor performance when arousal (which strongly relies on locus coeruleus activity) is compromised. In a different study, reduced performance caused by interfering with locus coeruleus activity was cancelled in response to an increase in task difficulty, suggesting that vigilant attention can alter arousal in a goal-directed manner (Arnsten & Contant, 1992). A further study used neuroimaging to investigate the degree of association between a decline in task performance and a reduced brain activity in both vigilant attention and arousal substrates. Intriguingly, the course of decrease in activity did not correlate, suggesting that vigilant attention and arousal contributed to task performance independently (Paus *et al.*, 1997). In the same paper, the authors made a further distinction by arguing that the task performance system can reduce its dependency on the arousal system when automatic behaviour is formulated due to learning effects. Finally, arousal and vigilant attention systems are separated in their activity pattern, with the arousal system maintaining unique U-shaped relationships with performance in accordance with the Yerkes-Dodson Law, whereas vigilant attention decays monotonously with performance (Arnsten, 1998).

A major strength of the vigilant attention theoretical framework is that it accounts not only for performance *decrement* (the focus of vigilance research), but also for *fluctuations* in performance over time. Robertson *et al.* (1997) showed that the number of errors occurring along a continuous task (rather than a decrement which is defined as the gradual increase in error rate) correlates with subjective reports of cognitive failures. The authors provided a compelling argument in favour of considering performance dynamics unaffected by vigilance (i.e., behavioural changes that can be observed before the 30 minutes time-on-task). In that respect, the notion of vigilant attention deviates from traditional views focusing on vigilance decrement, and instead considers the momentary fluctuations of attention over time.

A clear difference between vigilant attention and other theories of performance maintenance is the distinction between the cortical (vigilant attention) and the sub-cortical (arousal) systems. This distinction is absent from the influential theory of the networks of attention proposed by Posner and Petersen (1990). The networks of attention theory proposes that attention relies on three distinct functional neural networks, including the alerting network. The alerting network regulates to the momentary level of activation of attention and its maintenance over time (Posner & Petersen, 1990; Petersen & Posner, 2012). The brain structures that underlie the alerting network are the arousal system and right hemisphere cortical systems, which in many ways encompass vigilant attention and arousal within a unified construct.

Alertness

Alertness was introduced by Posner and Boies (1971) as ‘involved in the human ability to perform in long, boring tasks like those that psychologists design to study vigilance’. The authors argued that this capacity to ‘develop and maintain an optimal sensitivity to external stimulation’ builds up rapidly following a warning signal (Posner & Boies, 1971). As opposed to the self-driven nature of vigilance and its prolonged timescales, alertness is a function that responds to external cues and operates on small timescales as part of the process of attentional selection. According to this view, stimulus events within a task provide a ‘miniature vigilance situation’. In their seminal paper presenting the three networks of attention, Posner and Petersen (1990) focused on the operation of the attention network in the context of expectation of and preparation for a single event. Along the same lines, in a task developed to assess the three networks of attention (the attention networks task), alertness was defined as the behavioural benefit of a temporal cue (Fan *et al.*, 2002). A further extension of the notion of alertness included a distinction between ‘phasic’ and ‘tonic’ alertness (Sturm & Willmes, 2001). Sturm and Willmes (2001) argued that alertness, alongside sustained attention (which will be further discussed in the next section), represent the ‘intensity’ aspects of attention, supporting the more complex attentional functions of selection and resource allocation. Tonic alertness is the overall wakefulness and arousal, which determines the response readiness level in the lack of an external cue. Tonic alertness is often mentioned alongside ‘intrinsic’ alertness, which is the capacity of controlling the wakefulness and arousal level. Phasic alertness is the ability to increase response readiness in the presence of an external cue, or based on self-initiated expectations.

The neural basis of both phasic and intrinsic alertness relies on similar regions previously discussed in the context of arousal and vigilant attention. It includes predominantly right-hemisphere frontal and parietal cortices, thalamic and brainstem networks. These structures, as discussed in previous sections, communicate by means of top-down control by the cortex modulating locus coeruleus activity mediated by the thalamus (Sturm & Willmes, 2001; Robbins, 1984; Steriade, Domich, & Oakson, 1986). Intrinsic (and tonic) alertness differ from phasic alertness by the activation patterns observed in the right hemisphere: brain imaging shows a higher activation in the right hemisphere in the presence of a warning signal, reflecting the externally initiated additional neural response (Weis *et al.*, 2000). Nevertheless, based on previous findings, researchers have attributed the different activation pattern to the processing of the external signal, while arguing that the mechanism that supports performance for both phasic and tonic aspects of alertness seems to be shared between the two.

A further distinction is made between alertness and sustained attention. It is important to note that, as opposed to the cognitive constructs mentioned above (arousal, alertness, vigilance and vigilant attention), sustained attention takes different meanings and somewhat harder to pin down. According to Sturm and Willmes (2001), sustained attention represents another aspect of 'intensity' of attention; as opposed to alertness, however, it is not constrained to changes in reaction times (RT) and is also reflected in accuracy level along the task. In that respect, it could be thought of as a general capacity of attention unrelated to 'responsiveness level'. A different approach considers sustained attention as the capacity of endogenously maintaining alertness level while expecting a stimulus (Robertson *et al.*, 1997), thus overlapping with the notion of intrinsic alertness (Sturm *et al.*, 1999). Sustained attention has also been used as a synonym for vigilance (Sarter, Givens, & Bruno, 2001). This association has not been accepted by other researchers, who emphasise the unique time frame and properties that are attributed to vigilance, whereas sustained attention is more of a general capacity that influences performance in any task setting or time frame (e.g., Robertson & O'Connell, 2010). Although sustained attention appears elusive, it will be argued here that it provides a fruitful construct when studying the correlates of performance maintenance and their relation to psychological disorders.

Sustained Attention

An initial point to make about sustained attention is its non-specific nature. Sturm and Willmes (2001) comment that, as opposed to alertness, 'The term sustained attention is used in a more general way, comprising all situations that call for a prolonged state of sticking to a task with considerably more frequent imperative stimuli than under vigilance conditions'. Similarly, in a paper predominantly discussing vigilant attention, Robertson and O'Connell (2010) propose that sustained attention is 'the capacity to maintain accurate responding over time across tasks which can be effortful and demanding, or monotonous and undemanding'. Both accounts agree that sustained attention plays a role in tasks that are unconfined to the strict definition of vigilance tasks (i.e., rare, infrequent targets in a prolonged task). To distinguish sustained attention from alertness, it is proposed to consider the behavioural outcome: alertness level affects RT, and sustained attention affects the equivalent of target detection (Sturm & Willmes, 2001). Others use sustained attention interchangeably with vigilance as the capacity to 'to keep watch for inconspicuous signals over prolonged periods of time', and consider 'vigilance level' and 'vigilance decrement' as components of sustained attention (Sarter, Givens, & Bruno, 2001; see also Clark *et al.*, 2005; Coull *et al.*, 1996; Davies & Parasuraman, 1982; Oken, Salinsky, & Elsas, 2006). Sustained attention has also been proposed as functionally identical to tonic alertness, vigilant attention, and vigilance, differing only from phasic alertness (Sadaghiani & D'Esposito, 2014). One characteristic that seems to be emphasised and shared across different accounts is the endogenous nature of sustained attention: it is an effortful, self-driven capacity of performance maintenance that is required due to the lack of an extrinsic alerting signal (e.g., Robertson & Garavan, 2004; Clayton, Yeung, & Cohen Kadosh, 2015).

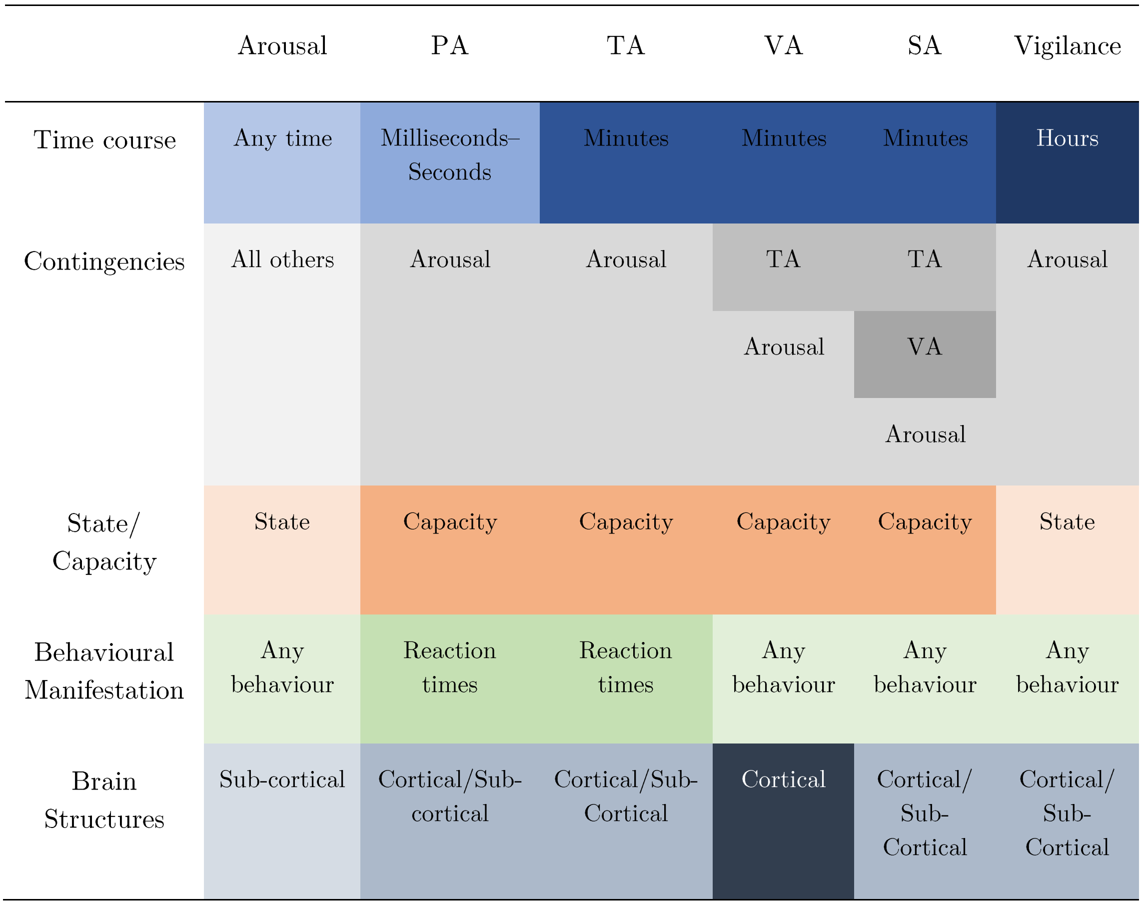
Sustained attention thus seems hard to define, as it contains contradictory elements. Nevertheless, the usefulness of sustained attention is undeniable: it is among the most commonly used terms in psychological literature, particularly when referring to cognitive deficits. For the purpose of this thesis, sustained attention will be defined as the *capacity of maintaining attention-based performance over time on task*. It will be distinguished from phasic alertness (which relates to the effects of a warning signal) and from vigilance (which may reflect a general decay of mechanisms that are unrelated to attention, such as fatigue). While tonic alertness is also often assessed by measuring RT, sustained attention includes all aspects of performance (e.g., accuracy, perceptual sensitivity, RTs, and so forth).

Potentially, one of the main reasons for the dominance of sustained attention in the literature is the association between impaired sustained attention and Attention Deficit/Hyperactivity Disorder, or ADHD. The inattention component of ADHD first appeared in the American Psychological Association's 3rd edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) (APA, 1980). The introduction of inattention as a core symptom of ADHD can be attributed to Douglas (1972), who first proposed that a marked inability to sustain attention over time could account for some of the manifestations of the syndrome, which had previously only been characterised by hyperactivity (Lange *et al.*, 2010). Inattention, as defined by a list of symptoms in the DSM, is often discussed as the behavioural correlate of sustained attention failure (e.g., Barkley, 1997; Bellgrove *et al.*, 2006; Conners, 2000; Swanson *et al.*, 2007). Because of the high prevalence of ADHD (NCHS, 2016), sustained attention and its behavioural correlates have been studied and described extensively. Difficulties in sustained attention are correlated with learning, behavioural and emotional difficulties in adolescence (e.g., Shalev *et al.*, 2015), professional development (e.g., Kalechstein, Newton, & van Gorp, 2003), driving (e.g., Schmidt *et al.*, 2009; Edkins, & Pollock, 1997), everyday cognitive failures (Robertson *et al.*, 1997), medical errors (Taylor-Phillips *et al.*, 2015), lifeguarding errors (Schwebel, Lindsay, & Simpson, 2007), and more. Poor sustained attention is associated with various cognitive disorders other than ADHD, such as autism (Garretson, Fein, & Waterhouse, 1990), learning difficulties (Richards *et al.*, 1990), schizophrenia and affective disorders (Liu *et al.*, 2002), and brain lesions (e.g., Robertson *et al.*, 1997b; Hyndman & Ashburn, 2003). Furthermore, in brain injuries, impaired sustained attention has been found to be an important factor in prognosis of recovery (e.g., Robertson *et al.*, 1995; 1997c). To conclude, although sustained attention may appear as an elusive concept, it is argued that, when properly defined, it is a useful concept in clinical research that summarises the functional aspect of the mechanisms supporting performance maintenance.

Performance Maintenance: an Interim Summary

Some partially overlapping cognitive constructs seem to constitute the individual capacity of performance maintenance. Arousal is viewed as the momentary ‘energetic’ state of the cognitive system, determined by sub-cortical circuits involving noradrenaline transmission across the cortex, and closely related to the reticular formation system. The operation of the arousal system is regulated by inputs from a cortical system that adjusts its operation in accordance with task demands, and its activation level is characterised by U-shaped relationships with performance. Vigilance refers to the ongoing, non-specific energetic state of the system and its decay over time. Some views propose a more specific role of vigilance, identifying it as equivalent to sustained attention. Vigilant attention refers to the cortical systems that maintain the arousal state over time in the absence of alerting signals, and support both accurate and fast response. Alertness can be subdivided into phasic and tonic levels, with the latter monitored and controlled by intrinsic alertness capacity. It is presented as a system that in principle operates at any time scale between seconds to hours through down-regulation of the locus coeruleus-noradrenergic system. It is distinguished from vigilant attention by referring to the entire process of communication between cortical and subcortical systems, and, in that respect, one can view alertness as ascribing the collaboration of vigilant attention and arousal systems.

Alertness is typically measured using RTs during the task, and only rarely related to accuracy levels. Further, sustained attention is presented as a more general term referring to the individual capacity of performance maintenance in durations that are longer than seconds (in which phasic alertness determines performance) and shorter than hours (in which vigilance determines performance). Some accounts consider tonic alertness as the same as sustained attention, although the former is often discussed in the context of response readiness, and the latter is more comprehensive. Finally, it is argued that the notion of sustained attention is highly useful in clinical studies of performance maintenance impairments. Table 1.1 provides an overview of the aforementioned mechanisms, and Figure 1.2 presents an illustration mapping their interrelationships and their time references.



	Arousal	PA	TA	VA	SA	Vigilance
Time course	Any time	Milliseconds–Seconds	Minutes	Minutes	Minutes	Hours
Contingencies	All others	Arousal	Arousal	TA Arousal	TA VA Arousal	Arousal
State/ Capacity	State	Capacity	Capacity	Capacity	Capacity	State
Behavioural Manifestation	Any behaviour	Reaction times	Reaction times	Any behaviour	Any behaviour	Any behaviour
Brain Structures	Sub-cortical	Cortical/Sub-cortical	Cortical/Sub-Cortical	Cortical	Cortical/ Sub-Cortical	Cortical/ Sub-Cortical

Table 1.1 A summary of the various constructs often discussed in the context of performance maintenance. Abbreviations: PA – Phasic Alertness; TA – Tonic Alertness; VA – Vigilant Attention; SA – Sustained Attention. Time-course refers to the time-course in which the mechanism is often discussed; Contingencies refers to other constructs that are dependent or interrelated to the mechanism in question; State/Capacity only marks whether the construct is attributed to a state in which the system can be found, or a cognitive capacity; Behavioural Manifestation refers to the way in which the construct is often measured or appears in behaviour; and Brain Structures refers to the approximate loci of the neural substrates of each mechanism

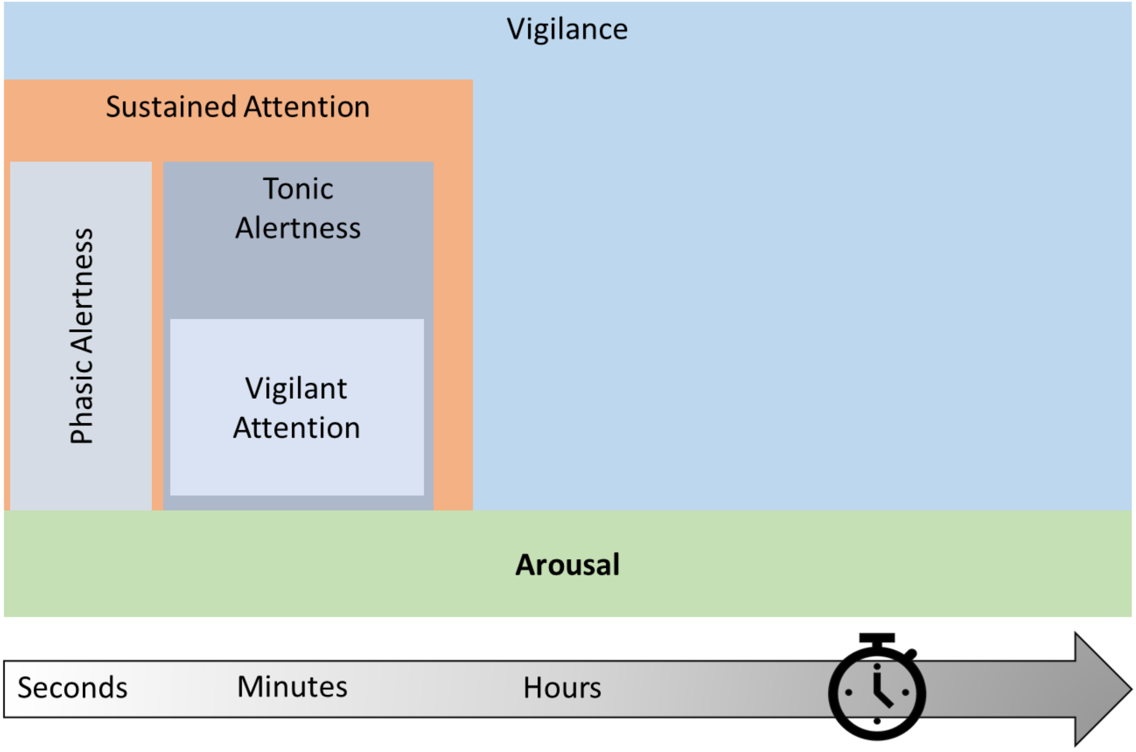


Figure 1.2 A schematic illustration of the aforementioned constructs, emphasising their relationships with respect to the temporal domain. The X-axis represent time on a logarithmic scale, from seconds to hours. The figure is constructed hierarchically, in a way that shows which construct is inclusive of others. Phasic and Tonic Alertness are included within the time scale of attention, and Vigilant attention can be thought as a sub-component of Tonic Alertness. They all fall under the timescale of Vigilance. All the constructs rely on arousal

A brief overview of the literature highlights the contribution of sustained attention to understanding multiple syndromes and symptoms, although it will be argued that a closer inspection reveals many inconsistencies in the way it is measured. For example, in the vigilance literature, two aspects of performance are distinguished: the capacity to maintain performance level over time (‘vigilance decrement’) and the overall performance (‘vigilance level’). Such a distinction is often neglected in the sustained attention literature. Significant task parameters as the target-distractor ratio, the time spent on task, and the rate of relevant events, are also used interchangeably. To comprehend all the possible task indices and the various parameters that may influence performance, the next section will provide a detailed discussion of the central paradigm in sustained attention assessment: the CPT.

The CPT

Sustained attention is typically assessed using different variations of the CPT in which participants are required to monitor an ongoing stream of stimuli and detect a predefined target that appears only occasionally (Conners, 2000; Cornblatt *et al.*, 1988; Esterman, Rosenberg, & Koonan, 2014; Greenberg, 1987; Mackworth, 1948; Klee & Garfinkel, 1983; Robertson *et al.*, 1997; O'Connell *et al.*, 2009; Tsal, Shalev, & Mevorach, 2005; Van den Bergh *et al.*, 2006). The key feature of any CPT is the continuous nature of the task. Most experimental designs in cognitive sciences comprise a sequence of events (such as cues, targets, etc.), which typically terminates when participants are probed to respond. In such cases, a trial is initiated only when the response for the previous trials is provided. Such trial-by-trial designs are therefore profoundly affected by individual responses: the inter-trial intervals are determined by the time between a response (terminating one trial) and its sequential trial. In a CPT design, the stimuli stream and their inter-stimulus intervals remain unaffected by responses: in other words, regardless of whether a response was provided or not, the task progress is determined by stimuli events alone.

The term ‘CPT’ was first introduced by Rosvold *et al.* (1956), although the Clock Test (originally designed to test vigilance; Mackworth, 1948) was probably its first variation. In the Clock Test, individuals are requested to monitor an analogue clock continuously and detect whenever they observe a rare, unexpected event in which the second-hand skips a second. Typically, the detection rate in the task deteriorates as a function of time, with a noticeable decrement after 30 minutes. Experimental manipulations have shown that performance on the Clock Test is strongly affected by the ratio of target events within a given time unit and the irregularity of target intervals (Baker, 1963; Deese, 1955; Jenkins, 1958; Mackworth, 1968). This target ratio, or ‘signal rate’, is defined as the ratio between targets and distractors. Changes in vigilance are sensitive to this ratio, evident in a larger vigilance decrement and a decrease in overall detection rate when targets are less frequent (Deese, 1955; Jenkins, 1958; Mackworth, 1968; Wiener, 1963). In shorter tasks aimed at studying sustained attention, increasing the proportion of targets leads to an increase in false positive or commission errors (e.g., Kolodny, Mevorach & Shalev, 2017). The overall number of events within a given time unit, or ‘event rate’ on a vigilance task (i.e., how many stimuli appeared within a minute), also affects performance whereby the overall detection rate decreases as the event rate increases (McGrath; 1963; Jerison, Pickett, & Stenson, 1965). The irregularity of target intervals was tested in the Clock Test by manipulating the number of distractors appearing in-between targets: performance was worse with fewer distractors appearing between targets (Deese, 1955). In a direct comparison between conditions where the number of distractors appearing between targets was randomised (e.g. ranging between 1–9 distractors) and conditions where the number of distractors was fixed (e.g., a target always appeared after a sequence of six distractor stimuli), researchers found an increase in false alarms (judging a distractor as a target) in cases where there was a random numbers of distractors (Johnson *et al.*, 2007). Nevertheless, it should be noted that the irregularity of targets does not entail a *temporal irregularity* of stimulus-events: in studies where the number of distractors between targets was manipulated, the inter-stimulus intervals (which refer to all stimulus events, targets or non-targets) remained constant. The temporal manipulation was thus only limited to the intervals between targets, whereas the task itself maintained a steady rhythmic pattern (i.e., a stimulus appeared occasionally in fixed intervals). It follows that, when the task contains a rhythmic pattern, the manipulation of the event-rate and the manipulation of the temporal intervals between targets are contingent (this issue will be further discussed in a later section).

CPT: Variations

Notable differences between the CPT and the Clock Test are the stimuli locations and task lengths. On a standard CPT, targets appear in the centre of the monitor, avoiding a potential confound of spatial bias unrelated to Sustained Attention. In contrast with the prolonged duration of the Clock Test (up to two hours), CPTs also typically last for less than 30 minutes. Robertson and O'Connell (2010) suggest that sustained attention differs from vigilance based on the task duration: variations in sustained attention are manifested in any task duration, but vigilance usually only decays after 30 minutes. The deployment of short CPTs can run into problems with performance being at ceiling, evident in low variability in RTs and target detection rate (Robertson *et al.*, 1997; Sarter, Givens, & Bruno, 2001). Ceiling performance on CPTs is an ongoing source of difficulties for cognitive neuropsychologists. To assess individual differences, and relate task-performance to behaviour, some variability in performance is desired. While the Clock Task provides high variability in performance, a prolonged assessment is often unrealistic for clinical populations. This has motivated researchers to introduce different methods to increase inter-individual variability within shorter time frames. These include increasing the working memory load (Parasuraman, 1979; Chen & Faraone, 2000), increasing demands for response inhibition (Robertson *et al.*, 1997), introducing stimulus degradation (Parasuraman, Mutter, & Molloy, 1991), increasing attentional demands (Tsal, Shalev & Mevorach, 2005), and more. Each of these variations manipulates aspects of the CPT, potentially revealing the contribution of different task factors to sustained attention.

Parasuraman (1979) used an auditory CPT to assess sustained attention[3] to investigate decrement in performance over time (referred to as vigilance decrement). He employed Signal Detection Theory (Green & Swets, 1966) to differentiate between two behavioural effects: the change over time in perceptual sensitivity (d'), which corresponds to the ability to distinguish targets from distractors; and the response bias, or the course of change in the Criterion (β), which corresponds to the probability of incorrectly reporting distractors as targets ('false alarm' errors) versus not reporting targets ('miss' errors). When increasing either memory load or event rate in experimental studies, participants demonstrated a decrement in d' with time on task. In a condition where memory load and event rate were lower, a gradual increment in β was observed, indicating the missing of more targets with time (Parasuraman, 1979). A significant contribution of the study was in highlighting the difference between changes in

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[3] In Parasuraman's work, the terms 'vigilance' and 'sustained attention' are used interchangeably.

d' and β. Further studies have shown that a decrement in d' tends to appear when task demands increase, such as through reduction of stimulus saliency, an increase in memory load, or an increase in the event rate (Parasuraman, Warm, & Dember, 1987; See *et al.*, 1995; Parasuraman, Warm, & See, 1998). The gradual change in β has also been considered, and proposed to reflect the gradual shift in strategy as participants form expectations about the low-frequency of targets (Davies & Parasuraman, 1982; Warm & Jerison, 1984). A different account relates the change in β to a gradual change in tonic alertness, or an overall decrease in activation (Van der Meere & Sergeant, 1988). The distinction between d' and β appears continuously in the CPT literature, in which both are estimated separately, although critical views have argued that the two parameters are often correlated, and question their usefulness in estimating different aspects of sustained attention (e.g., Koelega, 1995; Sostek, Buchsbaum, & Rapoport, 1980; Swanson & Cooney, 1989).

Sustained Attention and Response Inhibition

Robertson *et al.* (1997) have proposed an alternative method that does not rely on altering parameters to increase task difficulty for increasing inter-subject variability and prevent ceiling effects in performance. The approach is to maintain the basic task properties of the CPT, but to invert the response task.

They developed the Sustained Attention to Response Task (SART), in which participants are requested to respond only to non-targets and withhold their response to a target (e.g., Fassbender *et al.*, 2004; Johnson *et al.*, 2007; Manly *et al.*, 2003; Robertson *et al.*, 1997). This approach significantly increases the number of responses that can be assessed, while maintaining the essential property of rare target-events on a CPT. The SART design is successful in generating high variability in the response times among participants in approximately five minutes. It is capable of efficiently distinguishing clinical versus non-clinical populations, and results from the SART correlate with self-reports of cognitive failures (e.g., Robertson *et al.*, 1997; Johnson *et al.*, 2007).

It is, however, important to appreciate that the SART design introduces a potential confound by significantly increasing demands for response inhibition. With the requirement to withhold responses to rare targets, accurate performance relies heavily on the ability to inhibit automatic, prepotent responses (Stevenson, Russell, & Helton, 2011; Carter, Russell, & Helton, 2013). The issue of the involvement of inhibitory processes in the CPT is addressed directly in the go/no-go experimental literature (e.g., Casey *et al.*, 1997; Nieuwenhuis *et al.*, 2003; Rubia *et al.*, 2001), where the traditional approach to studying sustained attention is ‘mirrored’: a predefined target appears frequently (‘go’), and participants are requested to withhold their response when seeing a rare non-target ('no-go'). It is evident from the go/no-go literature that various neurological conditions are associated with deficits in inhibitory control (e.g., Drewe, 1975).

It should be noted that the SART is not a classic go/no-go task, as it requires participants to identify a rare target and withhold responding. In contrast, a traditional go/no-go task invokes response inhibition to non-targets by instructing participants to make speeded responses to targets in an ongoing CPT (Donders, 1969). Importantly, the proportion of targets appearing in go/no-go tasks is typically larger than the proportion of non-targets (Casey *et al.*, 1997). The capacity to withhold responses, therefore, relies largely on inhibiting prepotent responses. Response Inhibition is a well-defined cognitive motor construct within the domain of executive functions (MacLeod *et al.*, 2003). It plays a crucial role in typical development (Williams *et al.*, 1999), decays with age (Kramer *et al.*, 1994) and impairments have been associated with a wide range of cognitive disorders, including ADHD (e.g., Barkley, 1997) and Obsessive-Compulsive Disorder (e.g., Tolin, Witt, & Stevens, 2014). The notion of response inhibition has been further developed in the literature, where a distinction was drawn between two complementary aspects of inhibition: restraining a response and cancelling a planned response (Schachar *et al.*, 2007; Verbruggen & Logan, 2008). Whereas the former is often attributed to the task requirement of a go/no-go task, the latter is related to performance on a Stop Signal Task. The Stop Signal Task is a further variation of a CPT: a continuous stream of target stimuli appears and participants are requested to respond to all targets, unless a pre-defined ‘stop signal’ appears, when participants should withhold their response (e.g., Logan, 1994). It is thought to reflect a process of action ‘cancellation’ required for response inhibition (rather than ‘restraining’ which is associated with the go/no-go), as the stop signal appears at a stage in which the appropriate response has been selected and needs to be cancelled. This is in contrast with the notion of response inhibition, which relies on the ability to select the appropriate response and withhold an automatic, pre-potent, competing one.

Although both sustained attention and response inhibition are assessed using variations of the CPT, imaging studies have shown unique activation patterns in go/no-go designs that are unrelated to sustained attention (e.g., Aron, Robbins, & Poldrack, 2014; Criaud and Boulinguez, 2013; Kolodny, Mevorach, & Shalev, 2017; Swick, Ashley, & Turken, 2011). According to some researchers, the SART provides a measurement of response inhibition, since its main requirement is to effortfully withhold responses (e.g., Carter, Russell, & Helton, 2013; Stevenson, Russell, & Helton, 2011; Swick, Ashley, & Turken, 2008; Wilson *et al.*, 2016). The controversy of whether the SART primarily measures sustained attention and/or response inhibition clearly demonstrates the significance of methodological considerations in CPT design.

When studying vigilance, Mackworth (1968) suggested that a vigilance decrement is best observed in a CPT when targets are rare. To increase the demands for response inhibition, researchers have increased the target proportion, making the distractor events a rare event. The involvement of response inhibition demands on the SART (e.g., Swick, Ashley, & Turken, 2008; Wilson *et al.*, 2016), in which target events are rare (10% of all trials), raises the possibility that the *target-distractor ratio* is not the only factor determining the involvement of response inhibition: the proportion of *motor responses* may be equally important. Although only 10% of all trials are defined as targets, in the SART participants are requested to respond to non-targets, and the proportion of motor responses during the task is thus significantly increased when compared with a classic sustained attention task. According to this view, while performing the SART, participants are forming an automatic inclination to respond (as 90% of the trials are non-targets, and therefore require a response). It therefore takes more response inhibition effort to restrain, or inhibit, the response when identifying a target. From a clinical perspective, the difference between tasks that rely heavily on either sustained attention or response inhibition is crucial, as both are associated with multiple cognitive disorders. A good example is the case of ADHD, where both response inhibition and sustained attention are thought to contribute separately, and in a diagnostic way, to the behavioural manifestations of this syndrome (e.g., Barkley, 1997).

A series of studies in which a SART-like task (the ‘gradCPT’) was used to study the neural substrates of sustained attention and ADHD illuminates the potential involvement of inhibitory mechanisms. In the gradCPT, participants are presented with a continuous stream of stimuli and are requested to respond only to nontargets (pictures of cities), withholding their response when identifying a predefined target (a picture of a mountain) (e.g., Rosenberg *et al.*, 2013). One of the key features of the gradCPT is the gradual transition between stimuli, each emerging gradually as the previous fades. Researchers using this task have noted that good performance tasks involve both vigilance and executive functions including response inhibition and distractor suppression (Riley *et al.*, 2016). They have also used it directly to estimate response inhibition capacity (DeGutis *et al.*, 2015). Nevertheless, the gradCPT is most often deployed to measure sustained attention (Esterman *et al.*, 2012; Esterman, Rosenberg, & Noonan, 2014; Fortenbaugh *et al.*, 2015; Rosenberg *et al.*, 2013; 2016). Using the gradCPT in combination with ADHD symptom-scale and brain imaging, researchers have proposed two patterns of network connectivity as relevant to sustained attention: one network associated with high sustained attention (the High Attention

Network), and another predicting poor sustained attention (the Low Attention Network) (Rosenberg *et al.*, 2015). The same group used Methylphenidate (Ritalin), a psychostimulant commonly used to treat ADHD, to manipulate sustained attention and measure the effects on the high and low attention networks (Rosenberg *et al.*, 2016). The study revealed that, under the influence of Ritalin, there was an overlap between brain activity patterns and what was previously identified as the High Attention Network (the connectivity network which predicted high sustained attention). In the unmedicated ADHD group, there was an overlap between brain activity patterns and what was previously identified as the Low Attention Network (the connectivity network which predicted low sustained attention). Importantly, in the same study, the researchers also found the High and Low Attention Networks to be associated with performance on a Signal Stop Task (Rosenberg *et al.*, 2016). Although the study concluded that these network states predict sustained attention, the strong association with the Signal Stop Task could also suggest involvement of response inhibition mechanisms on the task. Such an interpretation is plausible, given that the Stop Signal Task was designed directly to measure response inhibition (e.g., Logan, 1994), and that ADHD symptoms are often associated with response inhibition problems (e.g., Barkley, 1997). In other words, this study demonstrated an association between the characteristic brain activity on a Stop Signal Task and a SART-like task. Consequently, the study associated the SART with response inhibition.

The discussion around the involvement of inhibitory processes is particularly meaningful when considering attentional deficits. Clinical populations such as patients with acquired brain injuries may show specific and dissociable deficits in response inhibition versus sustained attention based on their lesion sites (e.g., Aron *et al.*, 2003; Picton *et al.*, 2006). Individuals with ADHD may suffer either from sustained attention or response inhibition impairments, or both (e.g., Barkley, 1997). Such cases emphasise the need for maintaining response inhibition demands at a minimum when assessing sustained attention, as these two constructs are conceptually dissociable, although they can co-occur in the same disorder.

Manipulating CPT factors other than response mappings can also introduce confounds that complicate interpretations when studying clinical populations. For example, the CPT-AX task increases working memory demands by requesting participants to react only when a target (the letter X) appears after a specific non-target (the letter A) (e.g., Chen & Faraone, 2000; Overtoom *et al.*, 1998; Lee & Park, 2006). Accordingly, when studying sustained attention using the CPT-AX, it is important to verify that individuals have unimpaired working memory capacity to maintain the sequence of two items. In contrast to the explicit demands in tasks requiring working memory maintenance, response inhibition is also affected by implicit task factors. In addition to the implicit factor of response ratio, which has been studied extensively, another task parameter is often neglected: the temporal structure of the task. The temporal regularity and pace for target occurrence is likely to influence performance (e.g., Nobre & Rohenkohl, 2014). How temporal parameters influence performance on a CPT, and how they can be accounted for, is discussed next.

CPT: Temporal Structure

When referring to the temporal structure of a CPT, two aspects should be considered: temporal regularity and ordinal regularity. The temporal regularity is related to the time intervals between task events, and the ordinal regularity is related to the order of stimulus appearance. In tasks with fixed temporal regularity (i.e., when the inter-stimulus intervals remain constant), the two parameters are conflated. A further distinction should be made between the temporal regularities of targets appearance and of stimuli appearance; while the former refers only to the intervals between target events, the latter refers to the temporal regularity of all changes in the task, otherwise known as the ‘rhythmic pattern' of the CPT. In the following section, I will present findings in support of the importance of the temporal structure in determining performance maintenance, although such factors are only rarely considered in a clinical context.

Ordinal regularities of task events have been manipulated when using the SART. Researchers have developed the 'fixed-SART', a task variation in which the order of stimuli presentation was kept in a fixed sequence so that participants could always predict when the target will appear (e.g., Fassbender *et al.*, 2004; Johnson *et al.*, 2007a; 2007b; Manly *et al.*, 2003). Manly *et al.* (2003) compared the performance of patients with frontal lesions to a group of controls in a standard SART (where stimuli order is randomised) and in a fixed version. They discovered that the fixed-SART is better at distinguishing between the two groups, and hypothesised that task difficulty plays a major role: the fixed-SART was considered easier, and therefore showed sensitivity only in the patient group. Although it is possible that the findings were affected by the involvement of response inhibition (given that the patients group had frontal lesions, which is associated with response inhibition; e.g., Garavan, Ross, & Stein, 1999; de Zubicaray *et al.*, 2000), the authors interpreted the findings as evidence for sustained attention impairments, since the fixed-SART allows preparation and the requirement for response inhibition may therefore be lessened (Manly *et al.*, 2003). Fassbender *et al.* (2004) used a similar approach in contrasting the random and the fixed versions of SART to identify neural activity related to executive functions. In the random version of the SART, greater brain activity was attributed to inhibitory mechanisms (particularly the anterior cingulate cortex and the pre-supplementary motor area). Other studies using the fixed versus random SART highlighted further behavioural dissociations, such as differentiating attentional profiles among ADHD children and high-functioning autistic individuals (e.g., Johnson *et al.*, 2007a; 2007b). These studies demonstrated that a manipulation of the ordinal structure of a CPT (i.e., moving from a fixed to a random version of the SART) can influence which cognitive mechanisms are recruited and involved in task-performance. Nevertheless, these findings might be limited for two reasons: first, the use of a SART design where response inhibition and sustained attention cannot easily be distinguished; and second, because the SART manipulates not only the *ordinal* regularity, but also the *temporal* regularity. The original SART design (Robertson et al., 1997), which is frequently used in experimental studies, relies on a stimulus stream occurring at a regular pace (a stimulus would appear every 1500ms), and in such cases any ordinal manipulation would therefore also affect the temporal regularity of targets (i.e., the time interval between targets).

The manipulation of target regularity raised interest when studying vigilance using the Clock Task. Mackworth (1948) aimed to study vigil observers monitoring army radars, a task in which critical events (e.g., army submarines) occur rarely and irregularly. The same properties were applied to the Clock Test, where the infrequent target event (a dial skipping one second) occurred irregularly. A major difference between monitoring a radar and monitoring a clock, however, is the occurrence of irrelevant background events: whereas a radar may contain only relevant signals, most events occurring in the Clock Test are to be ignored. The temporal structure of the task is strongly affected by the appearance of non-targets that can carry task-relevant information. For example, in the Clock Test, a stimulus event (target or non-target) occurs at a fixed rate every second. Although the interval between targets may vary, the rhythmic pattern of targets and non-targets still carries temporal information: participants know when to expect the occurrence of the next event that should be monitored (in the Clock Task, participants should focus their attention every second to detect signal change). Therefore, one should distinguish between observations made in tasks where all events occur irregularly and tasks where only target events occur irregularly within a temporally-structured stream of stimuli. The latter carries more task-relevant information.

The level of infrequency and irregularity of target events is known to be a major factor in determining performance decrement. Typically, when increasing the temporal irregularity of targets (i.e., how predictable a target event is) within the stimuli stream, performance is impaired (e.g., Baker, 1959; 1963; Sanders, 1966; See *et al.*, 1995; Smith, Warm, & Alluisi, 1966). Nevertheless, these manipulations of target 'sparsity' within the CPT fail to account for what will be referred to hereafter as the 'rhythmic pattern' of the task, which is also determined by the regularity of the non-target events. From the original Clock Test (Mackworth, 1948) to the contemporary variations of the SART (e.g., Esterman, Rosenberg, & Koonan, 2014; Robertson *et al.*, 1997), CPTs are often presented in a rhythmic fashion. Arguably, the use of a rhythmic pattern promotes the involvement of entrainment mechanisms and temporal expectations that will be discussed in the following section.

Performance Dynamics and Temporal Expectations

Temporal expectations enhance our analysis of perceived events, either by means of increasing anticipation (Nobre, Correa, & Coull, 2007) or a timely preparation for a predictable onset (Coull & Nobre, 1998). Since the early days of cognitive research, the effects of such temporal predictions (hereafter *temporal expectations*) are known to improve perceptual judgments (Egan *et al.*, 1961;

Lowe, 1967; Lasley & Cohen, 1981; Westhimer & Ley, 1996) and RTs (Woodrow 1914; Bertelson & Boons, 1960). The behavioural benefits of temporal expectations have been observed in studies where perceptual judgments occur on a discreet, trial-by-trial basis (Woodrow, 1914), as well as when presented rhythmically (Newhall, 1923).

Temporal structures within our environment, as in speech and biological motion, are a common source for generating temporal expectations (Henry & Obleser, 2012; Schroder *et al.*, 2010). Such structures are thought to entrain our perceptual system, leading to enhanced performance when stimulus presentation coincides with a rhythmic pattern, and to impaired performance when the stimulus occurs off-beat (Jones *et al.*, 2002). Entrainment is (at least partially) an automatic, stimulus-driven process that occurs whenever the cognitive system is presented with a rhythmic pattern (Jones, 2001; Sanabria, Capizzi, & Correa, 2011; de la Rosa *et al.*, 2012). Temporal predictions can also be driven by memory-guided expectations (Breska & Deouell, 2017), and can be guided by endogenous cues (Coull & Nobre, 1998). In the presence of a temporal structure, a *rhythmic* mode of operation has been proposed to replace a more energy-consuming *continuous* mode that operates in the presence of random events (Schroeder & Lakatos, 2009; Schroeder, Herrero, & Haegens, 2014).

The distinction between *rhythmic* and *continuous* modes was proposed by Schroeder and Lakatos (2009). The scientific inquiry of brain oscillations especially seems key to understanding behavioural adjustments to the presence (or lack) of temporal structures (see Schroeder, Herrero, & Haegens, 2014). In the presence of rhythmic streams, low-frequency brain oscillatory activity (delta and theta bands in particular) entrain to the occurrence of events, whether by means of goal-directed behaviour or stimulus-driven entrainment (Lakatos *et al.*, 2007; 2008). Entrainment leads to enhanced processing of events that are temporally aligned with low-frequency oscillations, and to the relative suppression of events that occur during offset. Schroeder and Lakatos (2009) propose that the rhythmic mode of operation is 'preferred' by the system for purposes of efficiency: it only promotes the full processing of task-relevant events, and allows the system to save energy by reducing ongoing high-frequency oscillations that consume more energy (Mukamel *et al.*, 2005; Niessing *et al.*, 2005). Accordingly, operating in a continuous mode requires the maintenance of a high level of excitability for longer periods. Arguably, such a mode of operation is less energy-efficient and thus accompanied by momentary 'lapses' in performance (Schroeder, Herrero, & Haegens, 2014).

It is likely that many of the available tasks assessing performance maintenance contain sufficient temporal structure to entrain the system. The contribution of a rhythmic mode may question the fully self-driven nature of sustained attention and vigilance (e.g., Robertson & Garavan, 2004; Clayton, Yeung, & Cohen Kadosh, 2015), since entrainment is considered to be an automatic process (Jones, 2001; Sanabria, Capizzi, & Correa, 2011; de la Rosa *et al.*, 2012). A brief overview of available CPT variations used in a clinical context reveals that most tasks present stimuli at a fixed pace (Conners, 2000; Cornblatt *et al.*, 1988; Esterman, Rosenberg, & Koonan, 2014; Greenberg, 1987; Klee & Garfinkel, 1983; Lee & Park, 2006; Mackworth, 1948; O'Connell *et al.*, 2009; Robertson, 1997). Although some CPT variations present stimuli at random intervals (Bekker, Kenemans, & Verbaten, 2004; Rosvold *et al.*, 1956; Tsal, Shalev, & Mevorach, 2005; Van den Bergh *et al.*, 2006), there has been no direct comparison of performance in rhythmic and arrythmic tasks. Considering the findings in the temporal attention literature, the temporal structure of the task is likely to be a key factor in determining performance level in a CPT.

CPT: Performance Indices

CPT studies differ not only in the way they are designed, but also in their performance markers. While traditional studies have focused on the way in which performance changes with time (e.g., Mackworth, 1968), Robertson *et al.* (1997) suggest that sustained attention fluctuations can be observed at any time during the task, and that the mean performance rate might also reflect an important aspect of performance maintenance. Describing performance on a CPT include Signal Detection Theory parameters, mean error rate, and RTs for correct responses. Those parameters are then either presented as markers of an overall performance level by estimating their means or as markers of decrement by estimating the way they change over time. Unfortunately, there is little consistency between studies on the optimal way to estimate sustained attention.[4] The following section highlights a few examples of this inconsistency.

On a CPT, according to the Signal Detection Theory, the process of target detection requires to distinguish between two different stimulus classes: what can be defined as 'noise' (in the CPT context: a 'distractor') from a task-relevant stimulus superimposed on noise (in the CPT context: a 'target'). The Signal Detection Theory presupposes that the strength of the evidence given on each task event (i.e., stimulus presentation) is continuously variable. Therefore, when making a perceptual decision, participants are faced with a distribution value for each possibility (i.e., distractor vs. target). The average distance between the hypothetical distributions of targets and distractors is defined as the perceptual sensitivity (d'). Another component of the Signal Detection Theory, which is

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[4] Many of the studies reviewed in this section refer to sustained attention and vigilance interchangeably.

independent of the perceptual sensitivity, is the decision bias. The decision bias represents the individual cut-off point from which participants will categorize a stimulus as being either target or distractor. Individuals adopt different strategies that lead to different biases. Some may set a ‘conservative’ threshold and categorize a target only when highly confident. In such cases, it is more likely that some targets will be missed, but there will be less cases of ‘false alarms’ categorizing distractors as targets. In other cases, participants may be more permissive and require less evidence to identify a target. In such cases, less targets will be missed but there will be more false alarms. Importantly for our discussion, the two parameters are uncorrelated: for a given perceptual sensitivity, people may adopt different strategies of being more or less conservative. Signal Detection Theory parameters are calculated based on four possible responses: a correct identification of a target; a correct rejection of a non-target; a false alarm, judging a non-target as a target (sometimes referred to as a target ‘commission’); and a miss error, judging a target as a non-target (sometimes referred to as a target ‘omission’). From these, it is possible to derive the response bias (β) and perceptual sensitivity (d’).

Studies have shown that the clinical groups differ from controls in their mean d’ and β in varients of CPTs (e.g., Nuechterlein, Parasuraman, & Jiang, 1983; Oades, 2000; Parasuraman, Mutter, & Molloy, 1991; O'Dougherty, Nuechterlein, & Drew, 1984; Whyte *et al.*, 1995). Training of sustained attention was found to improve mean d' (Egner & Gruzelier, 2001; MacLean *et al.*, 2010); pharmacological intervention for sustained attention increased d' (Sostek, Buchsbaum, & Rapoport, 1980); social competence associated with sustained attention was marked by differences in d' (Bennett-Murphy *et al.*, 2007); and the course of cognitive development of sustained attention capacity was marked by changes in mean d' (e.g., Lin, Hsiao, & Chen, 1999).

Other studies have derived markers of performance decrement by comparing Signal Detection Theory parameters during different periods along CPT variants. Sustained attention among healthy individuals under different task conditions was marked either by a gradual decrement in d' or an increase in β (e.g., Fisk & Schneider, 1981; Parasuraman, 1979; Parasuraman, Warm, & Dember, 1987). The characteristic gradual change in d' or β with time was confirmed as a reliable marker of sustained attention in a comprehensive meta-analysis of vigil performance (See *et al.*, 1995). Individuals with ADHD also showed a similar pattern of increase in β and decrease in d' with time (e.g., Hooks, Milich, & Lorch, 1994; Swaab-Barneveld *et al.*, 2000). Older individuals showed a greater decrement in d' compared with younger controls (e.g., Parasuraman, Nestor, & Greenwood, 1989; Berardi, Parasuraman, & Haxby, 2001), as did patients diagnosed with Alzheimer's disease (Berardi, Parasuraman, & Haxby,

2005) and schizophrenia (e.g., Mass *et al.*, 2000; Nestor *et al.*, 1990). It is worth mentioning that clinical studies have highlighted a dissociation between overall performance and performance decrement, in line with the notions of vigilance level and vigilance decrement (e.g., Parasuraman, Nestor, & Greenwood, 1989; Berardi, Parasuraman, & Haxby, 2001, 2005; Swaab-Barneveld *et al.*, 2000).

Aside from the Signal Detection Theory parameters, studies often discuss specific error types as reliable performance markers, for example presenting only the number of false alarms or miss errors (e.g., Manly *et al.*, 1999; Robertson *et al.*, 1997). It is important to clarify that the prevalence of a specific error type determines the Signal Detection Theory β parameter: β values shift towards positive values as the proportion of missed targets increases and/or false alarms decrease. Reports of differences in error types are therefore an indirect reflection of the response bias, which (according to some theoretical accounts) should gradually shift with time on sustained attention tasks towards missing more targets (e.g., Parasuraman, Warm, & See, 1998). The mean proportion of false alarms in the SART correlates with cognitive failures; this can distinguish patients with a traumatic brain injury from controls (Chan, 2001; Robertson *et al.*, 1997) and characterise ADHD groups (e.g., Bellgrove *et al.*, 2005). Importantly, false alarms in the SART are comparable to missing targets in standard CPTs, as they represent an error related to a target (failing to inhibit response) rather than misjudging a non-target. The proportion of omissions on the CPT has been considered as a marker of sustained attention in ADHD (Seidel & Joschko, 1990) in studies of mindfulness (Schmertz, Anderson, & Robins, 2009) and when studying typical development (e.g., Carriere *et al.*, 2010; Reck & Hund, 2011). The mean number of missed targets and false alarms has also been used to distinguish between subtypes of ADHD by associating omissions with inattention and false alarms with hyperactivity (Egeland, Johansen, & Ueland, 2009). Error types have also been used when describing changes in performance over time, where miss and false alarm errors were assessed in different periods during a SART-like CPT (Esterman *et al.*, 2013).

Another way to assess performance on a CPT is by calculating the mean and standard deviation of RTs for correct responses. There are three approaches to describe RTs during a CPT: calculating the mean RT as a marker of overall performance; calculating changes in mean RT over different periods during the task as a marker of a decrement over time; and estimating the variability of RTs as a marker of consistency and attentional fluctuations during the task. Mean RTs have been used to study sustained attention in bipolar patients in states of mania and euthymia when performing a CPT (Fleck, Shear, & Strakowski, 2005), when studying the effects of using psychostimulants to treat ADHD (Medina *et al.*, 2010), and when associating sustained attention with psychometric schizotypy

(Lenzenweger, 2001). Changes in mean RTs on the task have been used in a study comparing the performance of patients with bipolar disorder and schizophrenia to controls (Fleck, Sax, & Strakowski, 2001), when studying sustained attention within a group with a genetic predisposition to schizophrenia (Birkett *et al.*, 2007), and when describing sustained attention among neurotypical adults (Manly *et al.*, 1999). Variability measures have been used to estimate episodes of inattention during the task among neurotypical adults (Esterman *et al.*, 2012), to assess attention in children with ADHD (Shalev *et al.*, 2011), and to study the course of sustained attention development in young participants (Betts *et al.*, 2006).

The examples provided represent only a small sub-sample of the available research using CPT, and demonstrate a large inconsistency in sustained attention assessment. A possible explanation for the shift from using Signal Detection Theory and error types to relying on RTs is the increased sensitivity of the latter, which helps prevent ceiling performance and low variability often present in accuracy-based measures (e.g., Fleck, Sax, & Strakowski, 2001). Nevertheless, multiple studies have shown that clinical populations are characterised by overall slower responses when compared with neurotypical controls under different conditions that are unrelated to attention (e.g., Birren and Fisher, 1995; D'Erme *et al.*, 1992; Godefroy *et al.*, 2010; Howes & Boller, 1975; Stuss *et al.*, 1989;

Tartaglione *et al.*, 1987). When working with impaired populations, therefore, one should consider the possibility that RT-based measures might be confounded by non-specific slowness. Similar potential confounds to measuring sustained attention may appear when using accuracy-based measures, such as Signal Detection Theory and error rate: ageing and clinical populations may perform worse than control due to sensory differences (e.g., Plenger *et al.* 2015; Ben-David & Schneider 2009, 2010), age-related macular degeneration (Scott, Feuer, Jacko, 2002a; 2002b), and age-related fatigue (Schwarz, Krauss, & Hinz, 2003).

A careful examination of the available parameters is required to distinguish between poor performance on a CPT based on non-specific differences and impaired sustained attention. This thesis proposes to focus on two task indices that are relatively immune to non-specific differences. First is the performance decrement in various task factors: while clinical populations might be characterised by overall lower performance, the extent to which their performance decays is more likely to be related to sustained attention. When reviewing the sustained attention and CPT literature, ceiling effects may conceal subtler group differences, but it is harder to find the opposite effect, because a marked decrement in performance over time is normally attributed to poor sustained attention. A second parameter (not directly related to sustained attention capacity but meaningful in revealing the underlying mechanisms of performance) is the response bias, or β. Higher β values are likely to represent sustained attention effort. Positive β values are associated with missing more targets and committing fewer false alarms. The tendency to miss more targets, even when the sensitivity (d') remains constant, increases with time on task (Parasuraman, Warm, & See, 1998). When contrasted with response inhibition tasks, β values can be viewed as a reflection of the dominant mechanism. Go/no-go tasks are characterised by a greater proportion of false alarms (e.g., Eagle, Bari, & Robbins, 2008; Kolodny, Mevorach, & Shalev, 2017; Schachar *et al.*, 2007), and sustained attention tasks by a greater proportion of miss errors (Carriere *et al.*, 2010; Reck & Hund, 2011; Schmertz, Anderson, & Robins, 2009; Seidel & Joschko, 1990; Young *et al.*, 2004).

CPT: Interim Summary

A few points should be emphasised to conclude the discussion of the CPT. CPT is a general term, referring to experimental designs that require monitoring an ongoing stream to detect occasional targets while ignoring irrelevant non-targets. The task parameters (such as the inter-stimulus intervals) are unaffected by the participant's response. CPT designs can be exploited to assess either sustained attention or response inhibition by manipulating the ratio between targets and non-targets, and the response frequency. Experimental designs differ in many ways: length, demands for sensory or cognitive resources unrelated to sustained attention, response requirements, and temporal structure. The latter factor has remained relatively unexplored. There is a great deal of inconsistency with respect to the way in which performance should be measured in a CPT. This issue seems to derive from the inherent simplicity of CPTs, which may cause low variability in performance and ceiling effects. Three issues – the optimal way of assessing sustained attention, the marked ceiling performance on CPTs, and the effects of temporal expectancies – will be addressed further in the empirical chapters of this thesis.

Summary

In this introductory chapter, I aimed to review the literature on sustained attention and its role in supporting performance maintenance and to provide a critical evaluation of the way in which it is measured in cognitive tasks. I have argued that sustained attention is an intuitively appealing and core construct. It plays a crucial role in guiding adaptive behaviour in extended contexts over time, and its impairments have real-life implications. Much, however, is still unknown. In particular, the literature is fraught with multiple terms and theoretically dissociable concepts that are used interchangeably. measuring sustained attention in cognitive tasks is often entangled with other variables that influence performance. To provide a theoretical framework, I have listed and defined five important constructs for performance maintenance: arousal, vigilance, vigilant attention, alertness and sustained attention. It has been suggested that sustained attention captures the essence of other reviewed mechanisms, and is particularly useful when describing the functional outcomes of performance maintenance and its impairments. Arousal has been described as a basic capacity underlying the temporal fluctuations in behaviour. Vigilance has been distinguished from sustained attention by its longer time course, although in many perspectives it represents the same capacity. Alertness and its sub-categories, i.e., phasic and tonic, are both associated with sustained attention (tonic and intrinsic alertness) and partially dissociated from it (phasic alertness, which strongly relates to a momentary reaction to a warning signal). Alertness and sustained attention have been proposed as distinguished based on their prevailing outcome measures: RTs (alertness) against all aspects of behaviour (sustained attention). With respect to vigilant attention, I have highlighted that this notion has been retrospectively applied to studies of sustained attention, encompassing a relatively narrow scope of the cortical functions that are active in sustained attention.

The second part of this chapter described methodological considerations in assessing sustained attention using the CPT. After a general overview of CPT variations, I have highlighted three factors that may change performance in CPTs other than by tapping into sustained attention capacity: 1) changing stimulus parameters or cognitive demands can lead to contamination of findings by sensory (macular degeneration) or cognitive deficits (working memory); 2) changing response mappings may emphasise response inhibition mechanisms, which in principle are dissociable from sustained attention; and 3) the temporal structure of stimulus presentation and of targets within the stimulus stream could create automatic entrainment and/or facilitate other temporal expectation mechanisms.

In its six empirical chapters, this thesis presents a series of studies examining how different experimental manipulations and performance indices influence the measurement of sustained attention capacity. In Chapter 2, a new task design is developed for assessment of sustained attention. The new design attempts to minimise confounding effects of sensory degradation and cognitive deficits, as well as to increase inter-personal variability in accuracy level. The study also presents a systematic manipulation of the target-distractor ratio on a CPT to better understand how sustained attention and response inhibition can be best distinguished. In Chapter 3 presents a clinical study in which the new task design is applied to stroke survivors. The focus of the chapter is to learn which construct represents best sustained attention effort by learning about the behavioural correlates of various task-markers. The study concludes that the notion of *change* over-time is essential for assessment of sustained attention. In the following chapter (Chapter 4), this approach is applied to a pre-existing dataset of children with developmental disorders. Chapter 4 demonstrates the potential of performance-change markers to distinguish two clinical populations with different etiologies: Down's syndrome and Williams syndrome.

The role played by temporal structuring of stimuli and targets in CPT is explored in Chapters 5 and 6. The chapters will present how performance changes in response to temporal regularities implemented in the task based on behavioural, electrophysiological and computational evidence. It will be argued that the level of stimulus-onset predictability dynamically alters the arousal level in the system in a way designed to optimise performance and cognitive effort. The final empirical chapter (Chapter 7) will be dedicated to studying the interactions between sustained attention and spatial-selectivity, and the hemispheric asymmetry of attention. First, an interventional study will demonstrate a transfer effect between a lateralised sustained attention task and a spatial-attention task. The transfer effect is reflected in the shifting of individuals' spatial-biases, and occurs only when trained to sustain-attention towards the right hemi-field. A second study will replicate the findings and combine a bi-lateral brain stimulation that selectively enhances selection capacity. The two studies in Chapter 7 conclude the empirical part of this thesis with a demonstration of how CPTs can be used in the future for cognitive training. Together, the chapters highlight some major gaps in the sustained attention literature and attempt to reconcile some of the open questions. Hopefully, the findings presented here will provide some of the necessary patches.

Chapter 2 : A New Task for Assessing Sustained Attention

This chapter is based on a published paper: Shalev, N., Humphreys, G.W., & Demeyere, N. (2017). Manipulating perceptual parameters in a CPT. *Behaviour research methods*, 1–12.

Abstract

The following chapter will establish a new task for assessing sustained attention among healthy and cognitively impaired individuals. In light of the theoretical discussion presented in the introduction, the task design was an attempt to respond to some common challenges in CPT assessments. First, the design aimed to prevent ceiling performance in accuracy-based outcome measures by increasing interpersonal variability and allowing a reliable assessment of sustained attention without relying solely on RTs. Importantly, this enhanced sensitivity relied on increasing demands for attention, rather than on other unrelated cognitive constructs (such as memory or response inhibition). In addition, the design diminished the abrupt onset of targets, which may automatically engage attentional mechanisms unrelated to sustained attention. Finally, in contrast to other popular CPT designs, the stimulus stream was presented in jittered time intervals to avoid potential confounds related to temporal expectations or entrainment evoked by the predictable temporal structure of the task. The

resulting new design – the Masked Conjunctive CPT – was contrasted with a non-masked version to demonstrate how masking can selectively impair perceptual sensitivity. The task was subsequently contrasted with a go/no-go design in an attempt to identify cognitive markers of response inhibition and sustained attention. After establishing the task with young, healthy individuals, the task was tested with a neurologically healthy older population and stroke survivors.

Introduction

Sustained attention can be roughly described as the capacity to maintain an adequate level of attention over time, and it is a prerequisite for nearly every aspect of adaptive behaviour in the reality of a constantly changing environment. The introduction to this thesis has raised a few potential confounding factors in the way in which sustained attention is typically measured using CPT. The evolution of the CPT can be traced back to the vigilance studies of Mackworth (1948) and the Clock Test, a task in which participants are requested to attend a prolonged task lasting approximately two hours. Such a design, in a clinical context, seems to be unrealistic both in terms of clinician time, with most tolerable assessment batteries lasting less than 10 minutes (e.g., Blackburn *et al.*, 2013; Sheehan, 2012; Young, Meagher, & MacLullich, 2011), and in the demands placed on the patients. In particular, the effects of general and cognitive fatigue may be unrelated to sustained attention capacity, and yet may cause a decrement in performance (e.g., Ackerman & Kanfer, 2009; Schwarz, Krauss, & Hinz, 2003). The standard CPT, in contrast, requires a shorter duration within a range of a few minutes (e.g., Robertson *et al.*, 1997) to less than an hour (e.g., Parasuraman, 1979). However, unlike performance on the Clock Test, which estimates performance decrement based on a change in detection rate, accuracy on CPTs often reach ceiling (Halperin *et al.*, 1991; Robertson *et al.*, 1997b; Sarter, Givens, & Bruno, 2001). To find a solution to this, the typical outcome measure of most CPT variations is the variability of RT, supposed to represent the overall stability of performance. The lack of discrete outcome measures, however, such as the detection rate as an index for task performance, may pose a problem when applied to some clinical populations that are often generally slower and may suffer from motor difficulties (e.g. Ada *et al.*, 1996; Birren and Fisher, 1995; D'Erme *et al.*, 1992; Howes & Boller, 1975; McCrea & Eng, 2005; Stuss *et al.*, 1989; Tartaglione *et al.*, 1986).

A different way to address the issue of ceiling performance has been suggested by Robertson *et al.* (1997), introducing the SART. In the SART, participants respond to all distractors by pressing a button and withhold their response whenever identifying a target. This task configuration significantly increases the number of commission errors (false alarms), allowing high sensitivity in a non-RT based measurement. Another, different approach is based on increasing memory demands, such as in the case of the CPT-AX (e.g., Chen & Faraone, 2000), in which participants respond to a target – the letter ‘X’ – only if it appears after the letter ‘A’. They therefore have to store in their memory the identity of the target and the pre-target stimulus. Another example of manipulation researchers have used to increase task sensitivity is stimulus degradation (e.g., Parasuraman, Mutter, & Molloy, 1991). It nevertheless seems like these more sensitive CPT variations suffer from a trade-off: to avoid the use of RT-based outcome measurements, they risk being confounded by cognitive constructs unrelated to sustained attention. For instance, many patients with brain lesions suffer from response inhibition problems (e.g., Aron *et al.*, 2003). Given that the outcome measure in the SART is based on failing to inhibit responses to targets, it is difficult to imagine how one can differentiate between poor attention and poor inhibition when testing patients (also see Ballard, 2001). A similar argument can be made with poor memory and performance on the CPT-AX (for more about the involvement of memory in CPT-AX cf. Lee & Park, 2006), and perceptual impairments, such as macular degeneration, influencing performance when stimuli are degraded (Scott, Feuer, Jacko, 2002). The shared feature of all these CPT alternatives is that the increase in task sensitivity is based on factors unrelated to attention.

The second parameter that may influence the measures of sustained attention in a typical CPT is the abrupt onset of targets. Several attentional processes are involved in target discrimination during a CPT: attentional shift and engagement, followed by target selection. The abrupt onset of targets and distractors over a blank screen (or a screen with a fixation point) can cause the mere appearance of either a target or a distractor to act as an exogenous cue, causing attentional capturing in a bottom-up manner. Accordingly, it can be assumed that the process of discriminating a single target which appears abruptly cannot be described by a single process of target selection. Other cognitive process, such as the momentary increase in alertness in response to an abrupt task-relevant event, as well as the spatial selection of the appearing object, are likely to take place. When considering the self-driven nature of sustained attention, researchers have proposed new designs in which the abrupt onset of targets is kept at a minimum. For example, O'Connell and his colleagues (2009) introduced the Continuous Temporal Expectation Task, in which participants observed a continuous stream of squared patterned stimuli flickering on the screen and alternating its orientation every 800ms or 1120ms. Targets were defined as stimuli with longer duration (1120ms exposure time). In the Continuous Temporal

Expectation Task, the stimuli constantly remain on the screen at the same location, and only small alterations mark the shift between stimuli. Similarly, Rosenberg *et al.* (2013) used the gradCPT, in which participants were requested to withhold their response to a rare target. In the gradCPT, each stimulus appeared gradually while overlapping the former one. These two experimental designs, however still elicit concerns of increasing demands for constructs unrelated to sustained attention. The gradCPT, as discussed in the introduction, may increase demands for response inhibition. The Continuous Temporal Expectation Task has been tested with neurotypical subjects who perform very poorly (approximately 65% mean accuracy), and it requires the ability to compare temporal intervals, a task that may be very demanding for clinical populations (e.g., Lackner and Teuber, 1973; Robin, Tranel, and Damasio, 1990).

The issues discussed hitherto (ceiling performance and the abrupt onset of targets in the CPT) have been addressed directly in experimental studies. In contrast, a third aspect of the CPT is often neglected: the temporal structure. Insights from temporal attention literature have highlighted the possible contribution of entrainment mechanisms to selective attention (e.g., Schroeder & Lakatos, 2009). In line with this, a temporally-structured CPT may elicit a stimulus-driven effect of entrainment (e.g., Jones, 2001; Sanabria, Capizzi, & Correa, 2011; De La Rosa *et al.*, 2012). When reviewing the sustained attention literature, it appears that most available CPTs present stimuli in a rhythmic fashion (e.g., Conners, 2000; Cornblatt *et al.*, 1988; Esterman, Rosenberg, & Koonan, 2014; Greenberg, 1987; Lee & Park, 2006; Mackworth, 1948; Klee & Garfinkel, 1983; Robertson, 1997; O'Connell *et al.*, 2009). This raises the possibility that the ceiling effect often observed in CPTs can be partially attributed to automatic processes by decreasing demands for self-driven maintenance of attention.

The aim of the current study was to establish a new task for assessing sustained attention. The CPT design was modified to resolve the challenges raised so far: while maintaining the main properties of the CPT, it should elicit a higher error rate. This will allow deriving measures of sustained attention without relying solely on RTs. The task should also be suitable for various populations (simple, not too difficult); it should not require a high memory capacity; be independent of inhibitory control mechanisms; carry no temporal information that may support performance in a stimulus-driven manner; and be continuous, to avoid the abrupt onset of targets and distractors. With these constraints in mind, the goal was to increase variability in task performance based on individual differences in attention, rather than memory, motor skills, or inhibitory control. When working with clinical populations, there is the danger that other cognitive impairments unrelated to attention could obscure the individual sustained attention capacity when assessed using a cognitive task. Importantly, the tangible aim of this experimental chapter was to develop an assessment tool rather than to test individual differences in sustained attention. The focus was thus to increase variability and sensitivity in error rates, rather than on characterising individual profiles of performance and/or inattention symptoms.

Experiment 2.1 – CPT With/Without Masking

Experiment 2.1 introduced a novel CPT design to derive interpersonal variability in accuracy-based measures in a young, healthy population. The new task allowed a more inclusive assessment by avoiding the use of speeded responses, which in various clinical populations may confound the measure (e.g. Ada *et al.*, 1996; McCrea & Eng, 2005). Typically, young healthy participants perform at ceiling in CPTs, making almost no errors (Halperin *et al.*, 1991), and the standard deviation of RTs (RT-SD) is used to derive a more sensitive measure of sustained attention in these high performing groups (e.g., Shalev *et al.*, 2011).

To increase the number of errors, targets were defined by a conjunction of features, and all stimuli were continually masked (pre- and post-mask). Following previous work showing greater task sensitivity when a conjunctive set of stimuli are presented in a CPT (e.g., Tsal, Shalev, & Mevorach, 2005; Shalev *et al.*, 2011), the target was defined by a conjunction colour and shape, and the distractors shared these features. The new Masked Conjunctive CPT was performed by a group of healthy young volunteers.

Experiment 2.1 compared performance in the new Masked Conjunctive CPT with a non-masked version of the same task (Conjunctive CPT). There were two main reasons to believe that adding a mask to the CPT paradigm would help us create a clearer and more inclusive measure of sustained attention. First, by using a mask in our newly developed task, the abrupt onset of targets and distractors is diminished. During the Masked Conjunctive CPT, there is a continuous stream of visual stimuli, which decreases the spatial cuing to a minimum and requires a continuous engagement at the same location on the screen in a goal-directed manner. Second, by using a mask, the stimulus is degraded without directly impairing its physical properties. This means that if participants fail to attend to the shape while it is presented, they simply miss it and make an omission error. Whereas the introduction of forward and backward masking has an impact on the perceptual evidence that guide target selection by eliminating the abrupt target onset and the restricting information accumulation, the perceptual degradation of the stimulus could be compensated by attention. This assumption is based on the familiar notion that engaged attention enhances perception (e.g., Muller & Humphreys, 1991; Posner, 1980). Hence, the Masked Conjunctive CPT directly increases demand for attention to identify the target and discriminate it from the distractors. Based on previous studies, it is possible to choose appropriate task parameters that ensure sufficient exposure duration for the formation of a full representation of target if attention is engaged: such exposure duration normally falls under 100ms for centrally presented targets in the current physical configuration (e.g., e.g., Vogel, Woodman, & Luck, 2006). Importantly, as opposed to previous tasks in which perceptual degradation was used (e.g., Parasuraman, Mutter, & Molloy, 1991), the degradation in the Masked Conjunctive CPT is achieved without interfering with the physical properties of the stimulus itself. This approach contrasts with a stimulus degradation achieved by blurring or distorting targets, where detection is more likely to be affected by sensory deficits.

The interplay between visual masking and attention has been extensively studied in the past. Within the attention literature, attending a stimulus is thought to reduce the effect of masking (Enns & Di Lollo, 1997). Another experimental tradition, closely related to attention, in which masking is often used to limit stimulus accessibility is the study of Visual Short-Term Memory consolidation. A visual mask is deployed to interfere with iconic memory representation (e.g., Gegenfurtner & Sperling, 1993; Shibuya & Bundesen, 1988). Within this context, researchers have found that the process of consolidating items from their fragile iconic representation into Visual Short-Term Memory occurs within an early time frame following stimulus exposure, ranging between 30 ms (Shibuya & Bundesen, 1988) and 50 ms (e.g., Vogel, Woodman, & Luck, 2006). An integrative perspective of Visual Short-Term Memory encoding and visual attention has been described as part of the Theory of Visual Attention. The Theory of Visual Attention is a mathematical formalisation of the 'biased competition' account of visual attention (Duncan & Desimone, 1995), in which visual categorisations ascribing features to objects compete to be encoded into a limited-capacity Visual Short-Term Memory. The categorisation of a visual element is accomplished once it has been encoded to Visual Short-Term Memory. In line with this perspective, attention could be considered as the mechanism to prioritise elements to be stored in Visual Short-Term Memory. In the context of the current study, it could be viewed as the mechanism that needs to be deployed efficiently as the target appears, to be encoded before the masking will appear and erase iconic traces. This could be achieved as long as the stimulus exposure duration is sufficient to formulate a Visual Short-Term Memory representation.

Increasing error rate by masking is followed by a specific hypothesis about the relationship between performance indices in the task: the standard deviation of RTs and the number of omission errors are likely to be correlated. The reason for this assumption is that they both reflect the same construct: 'attentional disconnections', 'lapses', or 'momentary inattention'. Such lapses in attention typically lead to a delayed analysis of the presented stimuli, reflected in greater RT variability. With the introduction of a visual mask, it is likely that longer disconnection would interfere with the coding of the visual object, leading to a target omission. Importantly, these variables reflect mathematically independent values: omission errors are the number of missed targets, whereas RT-SD relies on RTs for correct target identification only. As opposed to omission errors, the case of commissions ('false alarms') is a bit trickier. While commissions can also result from an 'attentional slippage', they may also appear when failing to inhibit a prepotent response, as often observed in go/no-go tasks (e.g., Nieuwenhuis *et al.*, 2003). Any correlation between commissions and RT-SD should thus be smaller compared to omissions and RT-SD.

One way to incorporate the two error types while controlling for the involvement of response inhibition mechanisms is by using parameters derived from the Signal Detection Theory (Green & Swets, 1966). In Signal Detection Theory, the perceptual sensitivity parameter (d') incorporates the two error types: omissions and commissions. Another parameter derived from Signal Detection Theory is the response bias (or criteria parameter; β), which indicates the bias towards a perceptual decision: participants can be biased either towards missing targets (omissions) or towards responding to distractors (false alarms, or commissions). Here, I propose to use the Signal Detection Theory parameters as two different task indices: d' as the marker of task performance, and β as a control for the dominant error type. The dominance of omission errors can be marked by maintaining the β value either at zero or at a positive value. As will be further verified in Experiment 2.2, the main characteristic of a task demanding response inhibition is a negative β value.

Performance on the new task is compared to performance in a variation of the CPT: the Conjunctive CPT (Tsal, Shalev, & Mevorach, 2005; Shalev *et al.*, 2011). The Conjunctive CPT design was replicated according to the original paper by Tsal, Shalev and Mevorach (2005), and equated in terms of the various the task parameters (e.g., inter-stimulus intervals, set size, stimulus properties etc) to fit the alternative newly proposed masked design. In this variation, participants are required to identify a target shape and ignore distractors, some of which have conjunctive features (either the same colour or the same shape). The use of conjunctive features for distractors has been found to increase demands for attention while maintaining high task reliability (Shalev *et al.*, 2011). In the current study, the use of the Conjunctive CPT as a control allowed to investigate the influence of only one task factor – adding the mask in between stimuli. To make it suitable for various populations, other than adding a mask, the properties of the Masked Conjunctive CPT were preserved as in Tsal, Shalev, & Mevorach, 2005: it was based on shapes and not letters or numbers, and did not require holding more than one target in memory.

Methods

Participants

All experimental protocols were reviewed and approved by the Central University Research Ethics Committee of the University of Oxford. The participants in the experiment were 22 naïve volunteers (10 of whom were female) recruited through an online research participation system at the University of Oxford. All had normal or corrected-to-normal eyesight and reported themselves as right-handed (mean age 28.4, SD=4.95). They were compensated for their time (payment of £10 per hour, inclusive of travel expenses).

Apparatus

A PC with Intel i7 processor and a 2GB AMD video card was used for displaying stimuli and recording data. The task was generated using NBS presentation software (Neurobehavioural Systems, Albany, CA). The stimuli were presented on a ViewSonic V3D245 LED monitor with a screen resolution of 1080X1920 and a screen refresh rate set at 100Hz allowing display times varied in gaps of 10ms. All stimuli were preloaded to memory using the presentation software, to guarantee minimal temporal noise.

Task 1: Masked Conjunctive CPT Sustained Attention

A coloured mask (*Mask*) comprising of four superimposed figures in different colours (square, triangle, circle and hexagon) appeared at the centre of the screen. The total size of the mask occupied three degrees of visual angle, both horizontally and vertically. To avoid habituation effects, minor movements to the mask were generated. The movement was generated by alternating between two mask images every 10–20 milliseconds. One image had thicker outlines for the superimposed figures (the two alternating mask images are illustrated in Figure 2.1a). The mask appeared at the centre of the screen and disappeared only when it was replaced by either a target or a distractor shape for 100ms. The mask then reappeared immediately, generating pre- and post-masking of each target or distractor. The target shape was a red circle, and distractor stimuli were either similar in colour to the target (red hexagon and red triangle), similar in shape (blue circle and yellow circle), or completely different (yellow and blue hexagon). All distractor types appeared with an equal distribution. Distractors and targets appeared at the centre of the screen and occupied a square of three degrees of visual angle. The inter-stimulus interval jittered randomly between 2000 and 5000ms (see Figure 2.1b for a schematic outline of the experimental procedure).

Participants were told that the static shape that appeared at the centre of the screen (the mask) would be replaced every few seconds with another shape, which would appear only briefly. The task was to respond with a button press as quickly as possible whenever they recognised a *red circle* at the centre of the screen. They were instructed to do nothing when they saw any other shape.

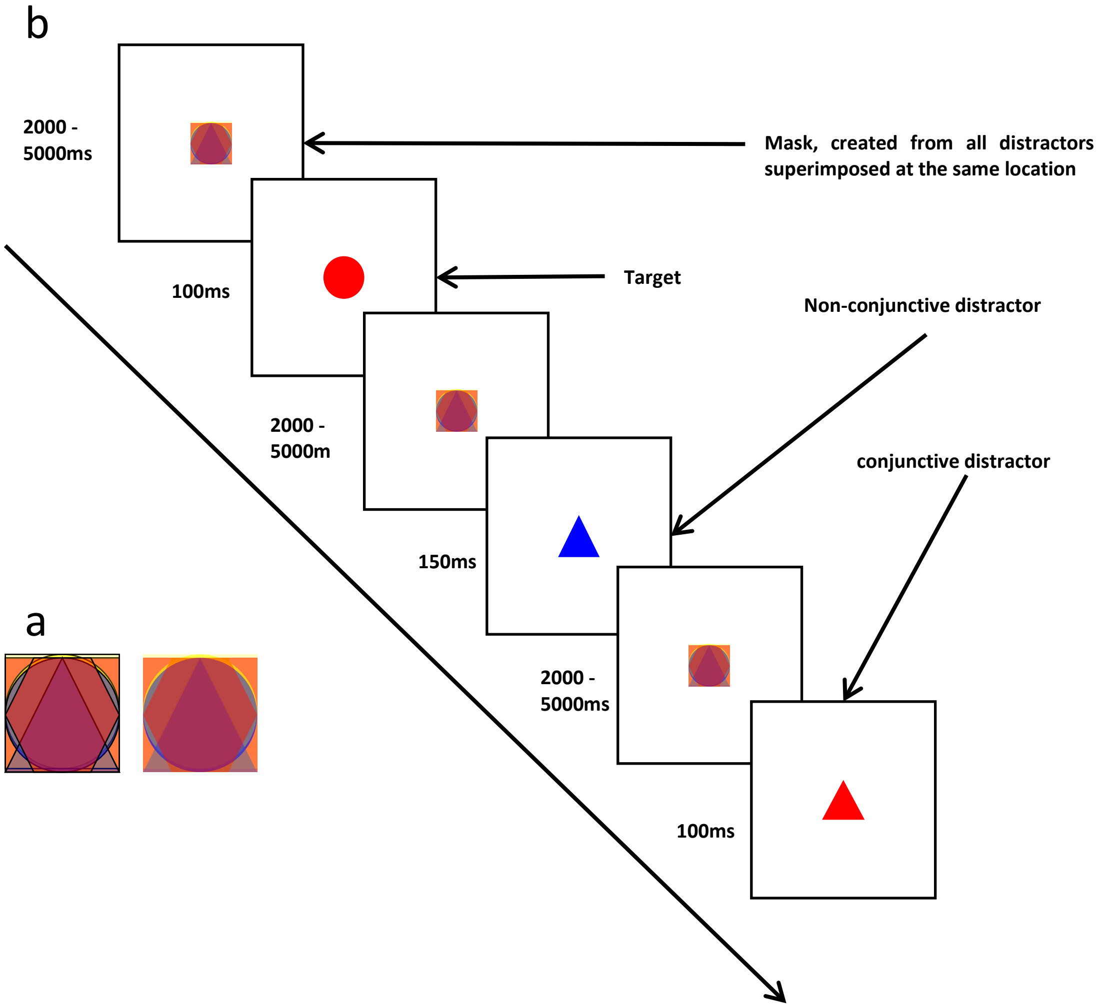

Figure 2.1 a) The two alternating masks; b) the Masked Conjunctive CPT Sustained Attention schematic outline

Task 2: Non-Masked Conjunctive CPT

Task 2 was identical to Task 1, apart from removing the masking condition. There was no mask present at any time. Participants simply focused on the centre of the screen and indicated when they identified a target. All other parameters remained the same.

Procedure

All participants performed both tasks, with a short break in between. The order of administration was balanced across the group. Each task started with a short practice block (15 trials), and the experimenter monitored participants' responses at this stage to ensure the instructions were clear. For each task, after finishing the practice, the participants performed the whole session without a break until the task terminated after approximately 13 minutes. Each task contained 240 trials. The target appeared in 80 trials (33% *target).* There were 160 *distractor* trials (66%)*,* in which one of six possible distractors appeared on the screen in a randomised order. A distractor could share the same colour as the target (*colour-conjunctive-distractor*, 22%); share the same shape (*shape-conjunctive-distractor* 22%); or differ in both shape and colour (*non-conjunctive-distractor,* 22%).

Statistical Analysis

For each participant, the following data was extracted: the number of correct reports of targets, the number of omission errors, and the number of commission errors, and the RT. These measures allowed the estimation of individual performance according to multiple indices: a) the standard deviation of RT; b) sensitivity, or the discriminability of the target from distractors (d'), in accordance with Signal Detection Theory; and c) the criterion for the perceptual decision (β) (also based on Signal Detection Theory).

Whereas the ability to discriminate target from distractor (d') incorporates the two error types – commissions and omissions, the response bias (β) provides a measure of the balance between error types: a positive value means a higher tendency towards omission errors, and vice versa (when β value is zero, there is no bias towards any particular error type). The β parameter will be used as a measure for understanding whether the task facilitates inattention-based errors or inhibition-based errors. As suggested earlier, commission errors can be resulted not only from instances of temporal inattention but also from a failure in response inhibition. Measuring the β parameter allows to estimate which error type is more dominant: presumably, when stressing one's sustained attention, there should be no bias or a bias towards omission errors. Conversely, a bias towards commission errors may indicate that the task involves high requirements for response inhibition. This working assumption will be tested separately in Experiment 2.2.

All the outcome measures were compared to test for consistency within and between the masking and no-masking versions of the tasks, and to determine whether the use of masking indeed increases the sensitivity as predicted.

Results

Multiple methods were applied to verify the reliability of both the Masked Conjunctive CPT and the Conjunctive CPT. Prior to the analysis, one participant was removed due to low performance: accuracy in both tasks was below three standard deviations compared to the rest of the group.

Masked Conjunctive CPT

Based on previous studies using CPT, and since normal young participants with no motor limitations were assessed, the process of task validation commenced by assessing RT related variables. To test for internal consistency in RTs and the RT-SD, the data was split into four quartiles and calculated for each the RT and RT-SD for correct target identifications. Reliability was calculated using Cronbach's Alpha test for the four quartiles, which yielded a high consistency of .948 for RT and .843 for RT-SD.

After verifying internal consistency, the correlations between error types and RT-related measures were assessed. Because the group was smaller than 30 and the calculations are based on discrete variables, the correlation was estimated using Spearman's rho test for nonparametric data. In accordance with the initial hypothesis, the number of omission errors was significantly correlated with RT-SD (Spearman's rho (21)=.74; p<.001). A similar correlation was found between target detection d' and RT-SD (Spearman's rho (21)=-.69; p=.001), demonstrating that a lower ability to discriminate target was linearly related to a high variability in RTs. The correlation between the number of commission errors and RT-SD was not significant (Spearman's rho (21)=.30; p=.18).

Conjunctive CPT

The analysis of Conjunctive CPT data was carried out following the same procedures as for the Masked Conjunctive CPT. When testing for internal consistency, data was split into four quartiles and averaged RT and RT-SD for each. Cronbach's Alpha test for the four quartiles yielded a high consistency of .897 for RT and .794 for RT-SD.

Correlations between RT-SD and error types were estimated once again. As hypothesised, omission errors were significantly correlated with RT-SD (r(21)=.62; p=.002), and no significant correlation was found between commission errors and RT-SD (r(21)=.03; p=.99).

Comparing and Cross-Validating Conjunctive CPT and Masked Conjunctive CPT Sustained Attention

Cross-validation of the tasks was based on the correlation between individual performance on each. A significant correlation was also found between the RT-SD measure of the masked and unmasked CPT (r(21)=.75; p<.001). A similar high correlation was observed for sensitivity (d') (Spearman's rho (21)=.68; p=.001) and for the response bias (β) (Spearman's rho (21)=.77; p<.001).

After confirming that the Masked Conjunctive CPT reliably assessed the same parameters as the Conjunctive CPT, a series of direct comparisons between the two tasks was carried out. A repeated-measures t-test revealed a significantly higher RT-SD in Masked Conjunctive CPT (141ms) compared to Conjunctive CPT (114ms) (t(20)=2.18; p=.04; 95%CI[1.17;50.74]). In addition, sensitivity to target (d') was significantly lower in the Masked Conjunctive CPT (d'=3.64) compared to Conjunctive CPT (d'=4.1) (t(20)=-2.76; p=.012; 95%CI[-.80;-.11]), suggesting that participants had more difficulty in differentiating the target from the distractors in the masking condition. A further analysis of target discriminability was performed by comparing the number of commission errors for conjunctive distractors (e.g., distractors sharing the same colour or shape as the target) versus for non-conjunctive distractors. The comparison showed a significantly higher percentage of errors for conjunctive distractors (t(21)=4.75; p<.001). The response-bias variable (β) was significantly higher in the Masked Conjunctive CPT (β=0.274) compared to the Conjunctive CPT (β=0.089) (t(20)=4.46; p<.001), 95% CI [.098;.270]), demonstrating a higher bias towards omission errors in the masked condition. Importantly, in the masked condition the bias parameter was significantly larger than zero (t(20)=3.98; p=.001; 95% CI [.130;.417]), whereas in the non-masked it did not differ significantly from zero (p=.12). In accordance with the initial hypothesis with respect to the response bias, therefore, participants either had a preponderance of omission errors (Masked Conjunctive CPT) or no specific tendency for one error type (Conjunctive CPT).

Interim Discussion

The results demonstrate how adding a mask in between targets on a Conjunctive CPT increased the general task sensitivity. Participants had a higher RT-SD, showed a preponderance of omissions, and had a lowered target discriminability (d'). Earlier, it was argued that the bias parameter could be used to control for the involvement of inhibitory mechanisms, based on the assumption that in a task with high demands for inhibitory control, one should observe a higher proportion of commission targets (resulting from failure to inhibit prepotent responses; on measuring response inhibition see for example Aron & Poldrack, 2005). In support of this claim, researchers have associated a decrement in performance over time with a gradual increase in β (Parasuraman, Warm, & See, 1998).

In accordance with an earlier discussion, one potential factor affecting the proportion of commission errors (and thus also the bias direction) is the target frequency. Increasing the target frequency should increase the number of responses, which may therefore increase the demands for cognitive control to withhold the prepotent responses in case of irrelevant distractors (see also e.g., Swick, Ashley, & Turken, 2008). The experiment has also shown that the Masked Conjunctive CPT configuration facilitates a positive β value alongside a marked difficulty in target detection. The positive values reflect a general bias towards missing targets. According to the hypothesis, increasing the number of target proportion increases the requirement for inhibitory control, which should be reflected in an increase in commission errors resulting in a modulation of the bias parameters towards negative values (i.e., bias towards false alarms).

A better understanding of CPTs is crucial for improved diagnostics of attentional disorders. There is currently no single convention for an optimal outcome measure for sustained attention, and in many cases commission errors, omission errors and RT-SD are used interchangeably. This experimental investigation attempts to incorporate the different error types using d', while assuring that there is no bias towards commissions.

The aim of Experiment 2.2 is to investigate whether there is a difference in the pattern of performance when a *sustained attention* task is redesigned to act as a *go/no-go* task. The only difference between Experiment 2.2 and the previous Experiment 2.1 is the target-distractor ratio: in a go/no-go task, it is customary to challenge participants with a high frequency of targets, to encourage more responses and more false alarms (Simmonds, Pekar, & Mostofsky, 2008). Experiment 2.2 thus used the same task design as Experiment 2.1, but increased the target probability from 33% to 66%. It is hypothesised that this change will influence mostly the bias parameter in signal-detection theory, reflecting the more probable type of error (commissions versus omissions).

Experiment 2.2 – Inhibitory Control Task, With or Without Masking

The main hypothesis in this experiment is that adapting the Conjunctive CPT and the Masked Conjunctive CPT into a *go-no/go* task by increasing the proportion of targets will lead to lower response bias (β) values. Such a pattern of performance may reflect a greater involvement of inhibitory mechanisms, as false alarm errors are considered to be indices for lapses of inhibitory control in go/no-go tasks (e.g., Aron, Trevor, & Russell, 2004).

Methods

Participants

All experimental protocols were reviewed and approved by the Central University Research Ethics Committee of the University of Oxford. The participants were 22 young and healthy naïve volunteers (nine of whom were female). All had normal or corrected-to-normal eyesight and reported themselves as right-handed (mean age 27.8, STDev=4.6). They were recruited and compensated for their time in the same way as in Experiment 2.1.

Apparatus

The apparatus was the same as in Experiment 2.1.

Task 3: Masked Conjunctive CPT Go/No-Go

The task configuration was the same as in Task 2.1. The *Masked Conjunctive CPT* was repeated, only this time the target/distractor ratio was inverted, with 33% distractors (11% had conjunctive-shape, 11% had conjunctive-colour, and 11% had no conjunctive features) and 66% targets.

Task 2.4: Conjunctive CPT Go/No-Go

The same task configuration as in *Task 2.2. Conjunctive CPT* was repeated, only this time inverted the target/distractor ratio was inverted, with 33% distractors and 66% targets.

Statistical Analysis

To compare the task to our findings from Experiment 2.1, and to try to replicate previous observations, the first analysis procedure targeted the consistency of the various outcome measures. The focus was the task validity across quartiles and the relationship between the error types and RT-SD. This procedure was followed by a direct the comparison between the two experiments to pinpoint how performance on the different measures was influenced by the manipulation of the target-distractor ratio.

Results

Consistently with the validation procedure in Experiment 2.1, task reliability was verified based on RT and RT-SD over four quartiles. In the masked version (Masked Conjunctive CPT), a Cronbach's Alpha test for the four quartiles yielded a high consistency of .942 for RT and .731 for RT-SD. In the non-masked version, a Cronbach's Alpha test for the four quartiles yielded a high consistency of .935 for RT and .826 for RT-SD. Following the analysis procedure in Experiment 2.1, the correlations between the different task indices were calculated. In the Masked Conjunctive CPT, there was a significant correlation between RT-SD and percentage of target omission (r=.642; p=.001) and between RT-SD and d' (r=-.510; p=.015). There was no correlation between the number of commissions and RT-SD (r=.019; p=.932). Similarly, in the Conjunctive CPT design, there was a significant correlation between RT-SD and percentage of target omission (r=.653; p=.001) and between RT-SD and d' (r=-.567; p=.006). Once again, there was no correlation between the percentage of commissions and RT-SD (r=.315; p=.154). These findings replicate the observations made in

Experiment 2.1, suggesting that RT-SD is associated with missing targets rather than committing false alarms.

Comparing Sustained Attention and Go/No-Go Tasks

Descriptive statistics appear in Table 2.1. and an illustration of the perceptual sensitivity (d') and the response bias (β) in four experimental conditions appear in Figure 2.2.

	G/NG Masked Conjunctive CPT	G/NG Conjunctive CPT	SA Masked Conjunctive CPT	SA Conjunctive CPT
% FA	5% ; 8%	4%; 8%	2%; 2%	2%; 2%
% Miss	7%; 7%	1%; 3%	5%; 12%	1%; 8%
β	-0.04; 0.31	-0.30; 0.28	0.27; 0.30	0.09; 0.24
d'	3.14; 0.88	4.02; 0.85	3.64; 0.84	4.10; 0.86

Table 2.1 Descriptive statistics: performance in masked and non-masked variations of the Conjunctive CPT. Acronyms and abbreviations: G/NG: Go/No-go; SA: sustained attention; FA: False Alarms. Data presented in rows represent the mean and standard deviation

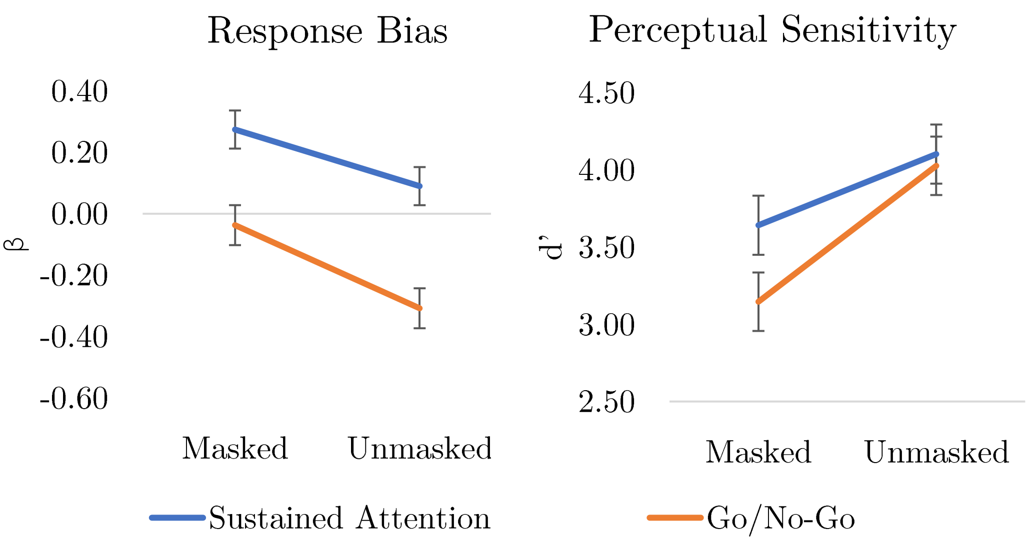

Figure 2.2 Perceptual sensitivity (d') and the response bias (β) in four experimental conditions: Masked/Unmasked X Sustained attention/Go-No-go. Lines represent standard error of means

The next analysis assessed which perceptual task indices were influenced by changing the target-distractor ratio. A series of direct comparisons between the two groups (Experiment 2.1 versus Experiment 2.2, or the sustained attention and go/no-go manipulations) was performed on each of the two conditions (masked versus unmasked). For each of the critical variables, a mixed model 2x2 ANOVA was carried out, with the masked versus unmasked conditions as the within-subjects factor and the low versus high target ratio as the grouping factor.

When applying the 2X2 ANOVA to the percentage of omission errors, there was a significant main effect of masking, with a higher percentage of omission errors whenever the stimuli were masked ($F(1,39)=21.937$, $p<.001$, $\eta^2=.360$). There was also a significant main effect of masking in the perceptual sensitivity parameter (d') with higher perceptual sensitivity in the non-masked conditions ($F(1,39)=22.817$, $p<.001$, $\eta^2=.369$). These observations vindicate the motivation of increasing task sensitivity by adding a mask.

Commission errors increased significantly in the go/no-go conditions ($F(1,39)=14.766$, $p=.001$, partial $\eta^2=.275$). This is in line with the hypothesis that commission errors are sensitive to the involvement of inhibitory control (by increasing proportion of targets), whereas omission errors are not. For the criteria or response bias (β), there was a main effect of masking ($F(1,39)=27.957$, $p<.001$, partial $\eta^2=.418$) with a greater bias towards omitting targets in the masked condition (this replicates the findings in Experiment 2.1). There was also a main effect for condition ($F(1,39)=22.433$, $p<.001$, partial $\eta^2=.365$), with a greater bias towards omitting targets when the proportion of distractors increases. No interaction occurred between the proportion of targets and the use of masking (all p's>.24). This is in line with the argument that the two task parameters influence the perceptual parameters independently.

Evaluating the relationships between mean response times and response variability

Whereas the current chapter focuses primarily on perceptual parameters, there is a broad convention of measuring the response time variability to assess performance on the CPT (e,g., Cho et al., 2008; Shalev et al., 2011; Segalowitz, Dywan, & Unsal, 1997). It is important to appreciate that response time variability provides a significant contribution to estimating sustained-attention. However, as the aim in the current thesis is to develop a reliable method for assessing sustained attention in target population as stroke survivors, there is a concern that such approach will be less reliable due to group differences in reaction times. One of the key characteristics of the RT-SD is that it is highly correlated with overall reaction times. For example, in the current sample, there were correlations of .75 ($p<.001$) and .78 ($p<.001$) in the masked and non-masked versions of the CPT (respectively, across the two versions: Go/No-go and sustained attention). The mean reaction times and standard deviations of reaction times in the four conditions: Go/No-go (masked/unmasked) and Sustained Attention (masked/unmasked) appear in Table 2.2.

	G/NG Masked Conjunctive CPT	G/NG Conjunctive CPT	SA Masked Conjunctive CPT	SA Conjunctive CPT
RT	500ms (74ms)	419ms (87ms)	556ms (106ms)	480ms (85ms)
RT-SD	121ms (52ms)	106ms (58ms)	140ms (77ms)	124ms (67ms)

Table 2.2 Descriptive statistics: reaction times and standard deviations of reaction times in masked and non-masked variations of the CPT. Acronyms and abbreviations: G/NG: Go/No-go; SA: sustained attention. Data presented in rows represent the mean and standard deviation

Taking into consideration the high association between the standard deviation of reaction times and the mean reaction times, the RT-SD index will used primarily to estimate the internal consistency of the tasks and not for group comparisons. The main reason for choosing this approach is that target populations are often characterised by slow responses for reasons that are unrelated to sustained attention, as will be discussed extensively in Chapter 3.

Interim Discussion

Experiment 2.2 successfully established that increasing demands for response inhibition, by adjusting the task parameters to a go/no-go task, changes the response bias towards a higher proportion of commission errors. In other words, the response bias is the main task property that shifts between a sustained attention task and a response inhibition task. It can therefore be considered as a variable dominated by inhibitory mechanisms. Importantly, β did not change as a result of the perceptual manipulation (i.e., masking), which affected the perceptual sensitivity independently. In both experiments, the perceptual sensitivity was correlated with a marker of sustained attention – the RT-SD. This correlation may be indicative of a relationship between d’ and sustained attention. Potentially, the same mechanism that fluctuates over time and underlies the variability in RTs may lead to misidentification of targets when task difficulty is increased. This hypothesis is also supported by the findings showing that adding a mask both increased RTs and decreased d'.

After establishing that the Masked Conjunctive CPT increased sensitivity in accuracy-based measures, and that performance patterns (as reflected in the response bias parameter) were influenced by adjusting the appropriate target-distractor ratio, the next goal was to investigate whether the task is suited for measuring sustained attention impairments in target populations. In Experiment 2.3, an adjusted version of the Masked Conjunctive CPT was used to test sustained attention in a group of healthy, ageing individuals and in a group of stroke survivors.

Experiment 2.3 – Testing Older Adults and Stroke Survivors

The main goal of Experiment 2.3 was to test whether the Masked Conjunctive CPT can be used with healthy ageing and stroke survivors. Success was to be measured on the task being sufficiently simple for these groups to understand and to perform, while still producing informative performance variability. The key question was whether the task could distinguish the populations. The psychometric characteristics of the task when used with 'target populations' were also of interest. In sum, the focus of the current experiment was to develop appropriate methodological procedures, rather than investigating sustained attention deficits in different populations. A detailed study focusing on sustained attention and its correlates will be presented separately in Chapter 3.

Methods

Participants

All experimental protocols were reviewed and approved by the Central University Research Ethics Committee of the University of Oxford. There were 75 participants, 42 of whom were neurotypical adults (26 females; mean age 68.3; SD=8.1), and 33 of whom were stroke survivors (11 females; mean age 63; SD=13.7). The clinical group consisted of chronic stroke survivors who came as volunteers to the Oxford Cognitive Neuropsychology Centre. They were selected for having a minimum age of 40, a brain injury caused by a stroke more than one year ago, and for being in a chronic, stable condition (rather than acute or sub-acute). Lesion site and volume varied, and no exclusion criteria were applied in this regard. As the main goal was to validate the task, no imaging data or questionnaires were presented for the stroke survivors in this chapter, but will be discussed in more detail when the Masked Conjunctive CPT is used to assess sustained attention in the next chapter.

Apparatus

The apparatus was the same as in Experiments 2.1 and 2.2.

Task: Masked Conjunctive CPT Sustained Attention

The same task configuration as in *Task 1: Masked Conjunctive CPT* was used, only this time with an extended stimulus exposure time of 150ms. This change was based on a short pilot study with five individuals aged 65–75, in which three participants reported the 100-ms exposure duration as too brief. The question of whether inter-personal variability can still be obtained in such exposure duration could be answered based on the results of this experiment.

Statistical Analysis

Performance distribution of the two experimental groups focused on accuracy-based outcome measures. The first goal was to try and distinguish a clinical group of stroke survivors from a control group of healthy ageing individuals. A second goal was to make the task simple enough for the stroke survivors, while at the same time avoiding ceiling or floor effects in performance. In addition, the correlation between RT-SD and d' was estimated to learn whether the two variables are related in these groups. Finally, the two groups were also compared to see whether they could be distinguished based on the task.

Results

Descriptive Statistics

Table 2.3 summarises indices of task performance. An illustration of the mean performance indices (d’ and β) and the distribution of individual perceptual sensitivity (d’) in the two groups appear in Figures 2.3 and 2.4.

	d'	β	%miss	%commissions
Controls	4.28; 4.25; .55	.05; 0; .18	2.5; 1.6; .03	1.8; 1.2;.01
Stroke survivors	3.56; 3.77; 1.24	.03; 0.12; .36	7.8; 1.6; .1	7.5; 2.5; .13

Table 2.3 Descriptive statistics of errors made in the task (mean; median; standard deviation)

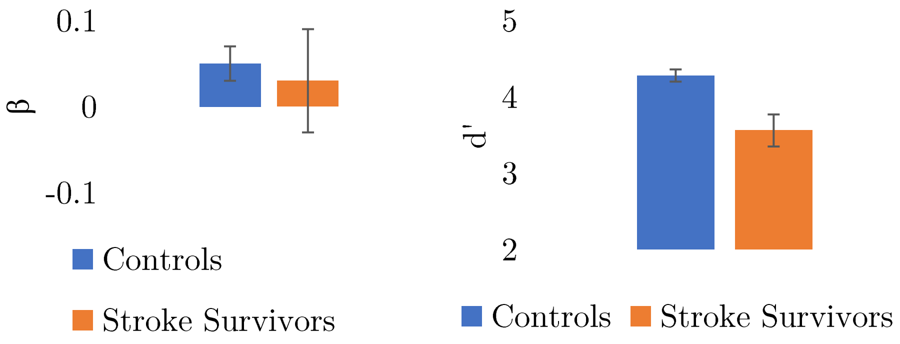

Figure 2.3 Perceptual sensitivity (d’) and descision bias (β) among healthy ageing and stroke survivors. Black lines represent the standard error.

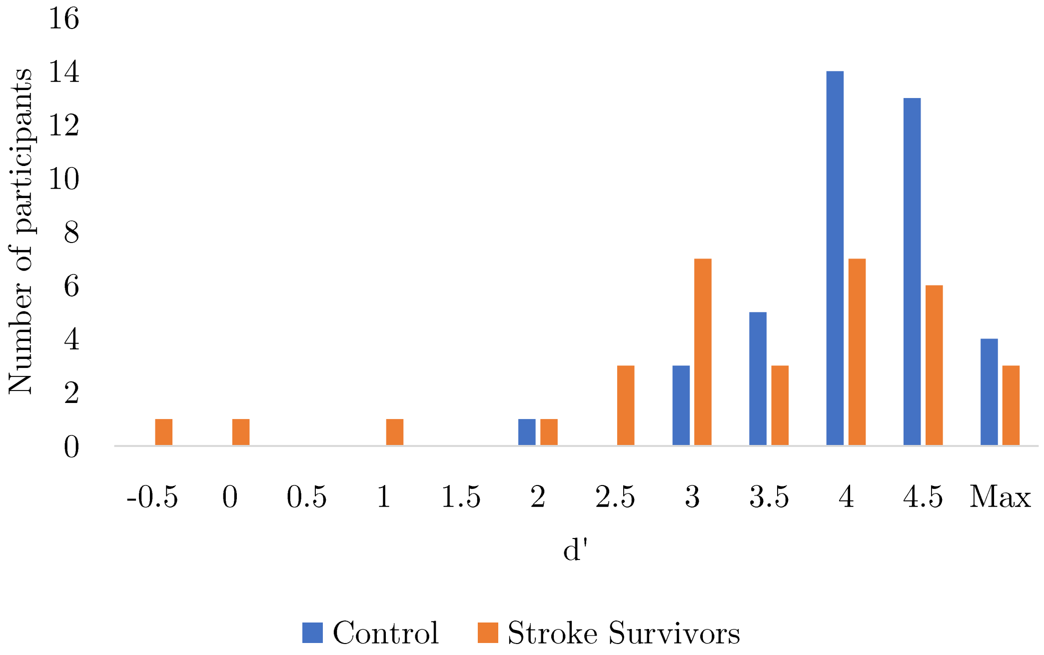

Figure 2.4 Individual perceptual sensitivity (d') among stroke survivors and controls

As with the younger individuals in Experiments 2.1 and 2.2, most of the participants did not reach ceiling performance, even though the stimulus exposure time was extended to 150ms. In line with previous experiments, the mean β value was higher than zero in both groups, suggesting that, at the group level, there was no bias towards committing false alarm errors. When inspecting individual performance, two stroke participants performed at chance level. Both were unable to maintain their heads fixed while seated due to motor limitations.

The histogram in Figure 2.4 shows that the distributions of performance were somewhat skewed in both groups. The skewness of the d' parameter among the healthy ageing control group was negatively skewed (Skewness= -1.3, SE=.374). There is a possibility that this resulted from the limited sample size. Alternatively, the skewness could result from differences within the group, as ageing populations often suffer from sustained attention difficulties, albeit with a large variability within age groups (e.g., McAvinue *et al.*, 2012). A negatively skewed distribution was also observed in the stroke group (skewness = -1.5; SE = .409), although such an observation could result from the small, non-homogeneous, clinical sample. As opposed to the skewed distribution of the d' parameter, the distribution of the bias (β) parameter was symmetrical among controls (skewness = -.041; SE = .374) as well as among stroke survivors (skewness = -.243; SE = .409). These findings converge with the distinction made in this study between the two task indices: β reflects a strategic construct and can be thought as a reflection of the active mechanism within the task (in the context of the CPT, between sustained attention and response inhibition). Conversely, d' appears to be more related to sustained attention capacity.

Estimated Correlation Between Response Variability and Perceptual Sensitivity

Following the findings in Experiment 2.1 indicating an association between RT-SD and d', a similar analysis was carried out for the healthy and stroke groups. First, a single participant was removed from the stroke survivors group due to an extreme RT-SD score (the score exceeded three standard deviations from mean). As each group consisted of a sample larger than 30, the correlation was estimated using the Pearson correlation test. The two parameters were significantly correlated both among healthy old adults (r=-.525; p<.001) and stroke survivors (r=-.638; p<.001). When combining the two groups, the correlation remained significant (r=-.647; p<.001). The scatter plots of the observations, separated according to groups, appear in Figure 2.5.

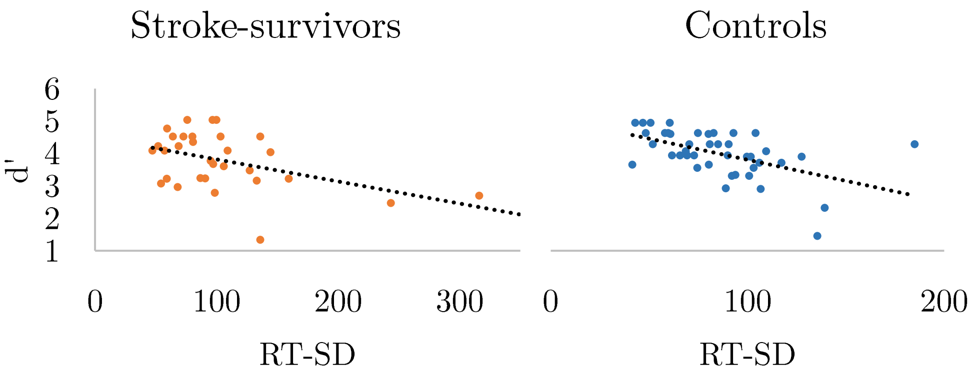

Figure 2.5 Scatter plots, showing the relationships between the perceptual-sensitivity (d') and the standard-deviation of reaction-times (RT-SD) among the healthy ageing control group and the stroke survivors

Group Comparisons

Perceptual sensitivity (d') and response bias (β) were compared between the groups using a t-test for independent samples (equality of variance not assumed). The groups differed significantly in their d' (t(69.27)=3.082; *p*=.004; 95% CI [0.24;1.19]), with an overall higher detection rate among healthy older volunteers. The bias parameter β did not differ between the groups (t(69.27)=.234; p=.816). To ensure that the significant group difference in d' was not driven by the two stroke individuals with performance at chance, they were excluded before repeating the same comparison. The results remained significant (t(64.113)=2.756; *p*=.008; 95% CI [0.13;0.84]). These two comparisons show that the test can, in principle, differentiate a group of participants with and without strokes, and that their overall pattern of performance (or strategy) is similar as reflected in the bias parameter. Nevertheless, it should be clarified that the main purpose of this comparison was to verify the task usability rather than assessing sustained attention directly. As discussed in the introduction, clinical populations are likely to differ from healthy volunteers in their performance, regardless of their sustained attention capacity. The next chapter addresses the question of sustained attention directly by inspecting individual reports of inattention among stroke survivors and healthy ageing controls, and focuses on performance decrement rather than overall performance.

Discussion

This study has successfully established a new reliable method for increasing variability in accuracy in a CPT. Visual masking decreased the perceptual sensitivity to target (d') and was correlated with a well-established parameter of overall sustained attention performance – the RT-SD. Additionally, the change in the response bias parameter (β) marked the difference between a response inhibition task and a sustained attention task. Such a difference is implied when reviewing the literature, and this study directly assessed it. Finally, the task can be performed by older adults and stroke survivors, yielding informative discriminative performance measures.

The increased sensitivity of the task is attributed to the use of a visual mask. According to the suggested theoretical background, the use of masking facilitates a perceptual degradation that can be compensated with attention. This view is in line with findings demonstrating that attention can reduce the effect of masking (Enns & Di Lollo, 1997), and enhance perception (e.g., Muller & Humphreys, 1991; Posner, 1980). In addition, the deployment of visual masking eliminates iconic memory representations in the process of encoding into Visual Short-Term Memory (Smith, Ratcliff, & Wolfgang, 2004). In this respect, while the Masked Conjunctive CPT design aims to avoid load on memory components (as in the case of the CPT-AX), there is a potential that the masking still increases working memory demands. The exposure time used in the Masked Conjunctive CPT is much shorter than the observed mean RTs, and therefore it is likely that the perceptual decision relies on the maintenance of the target in Visual Short-Term Memory. It can, however, be argued that the involvement of memory mechanisms in the Masked Conjunctive CPT does not overshadow the attentional requirements and is not comparable to the CPT-AX for a couple of reasons. First, while the CPT-AX requires the active maintenance of two objects in memory, the Masked Conjunctive CPT requires only one item, and only for the short episode between stimulus onset and perceptual decision. A memory capacity for a single item seems to be a prerequisite for nearly any visual discrimination task where participants need to remember a predefined target. Second, when it comes to the process of encoding the items from iconic memory to Visual Short-Term Memory, it could be argued that this is exactly where attention plays a major part: attention is the cognitive component which 'transfers' visual objects into Visual Short-Term Memory (e.g., Bundesen, 1990; 2005, Desimone & Duncan, 1995, Vogel, Woodman, & Luck, 2001) within a much shorter time frame than the one employed in the exposure times used in the Masked Conjunctive CPT (e.g., Vogel, Woodman, & Luck, 2006). In particular, the Masked Conjunctive CPT relies on the visual presentation of repeating, overlearned, simple stimuli; in such cases, it is likely that early visual processes occur even faster due to effects of learning (e.g., Ahissar & Hochstein, 1997). More compellingly, the empirical findings support this view with the majority of our participants, even within the stroke survivors group, all of whom performed the task adequately.

Keeping in mind the extended discussion in the Introduction chapter to performance indices, there remains a need to verify the external validity of the Masked Conjunctive CPT and its task-markers by directly assessing sustained attention. This will be the main goal of the next experimental chapter, in which a specific attention will be given to self-reports of inattention and their correlates. It is important to clarify that this study has only managed to show that RT-SD and d’ are associated, and has not established any connection between these two parameters and sustained attention capacity. With respect to β, the argument can be more decisive: by contrasting the sustained attention CPT configuration with the go/no-go, the response bias appears to be a good marker for distinguishing the performance pattern among the CPT variations. Following this observation, it is proposed that β can be used to distinguish between response inhibition and sustained attention.

Chapter 3 : Assessing Sustained Attention and Its Impairments

This chapter is based on a published paper: Shalev, N., Humphreys, G., & Demeyere, N. (2016). Assessing the temporal aspects of attention and its correlates in ageing and chronic stroke patients. *Neuropsychologia*, *92*, 59–68.

Abstract

Poor sustained attention capacity is associated with symptoms of inattention and cognitive difficulties. Nevertheless, there is little agreement on how sustained attention is defined when measured using a cognitive task. Whereas traditional approaches have focused on performance decrement, alternative studies have used indices of overall performance or estimation of variability along the task. The aim of the current chapter is to identify the appropriate task indices for sustained attention by using the Masked Conjunctive CPT and subjective reports of cognitive problems with ageing individuals and stroke survivors. It will be argued that a potential challenge in sustained attention assessment is to differentiate between task-contingent fluctuations in phasic alertness and gradual changes in sustained attention. Specifically, the estimation of phasic changes in alertness is critical as they may bias some task indices, although their behavioural correlates are not straightforward. A potential way of assessing occasional phasic changes is by comparing the response times to targets as a function of the preceding stimulus. In the current study, various indices of the Masked Conjunctive CPT were extracted, compared and correlated between themselves and with reports of cognitive problems. The results showed that a) brain lesions are associated with phasic changes in alertness; b) groups of stroke survivors and controls differ in their mean performance; c) the groups differed neither in their subjective reports of cognitive problems, nor in their markers of sustained attention during the task; and d) subjective reports of distractibility correlated only with performance change. In conclusion, the findings suggest a need to revise common methods in sustained attention research.

Introduction

Sustained Attention: Constructs and Measures

In Chapter 1, I suggested that sustained attention should be considered as a general mechanism encompassing multiple time frames and behaviour effects. In view of the available theories ascribing performance maintenance, the construct of sustained attention can be further expanded in two ways that are relevant to the experimental investigation presented in this chapter: first, by disbanding sustained attention according to the time frame in which it operates; and second, by distinguishing between the overall ‘energetic’ state of sustained attention and its decrement over time.

The shortest time frame in which the temporal characteristic of attention is described is milliseconds to seconds, in which phasic alertness plays a part in decreasing signal-to-noise ratio while selecting a single target (e.g., Coull *et al.*, 2001; Posner & Petersen, 1990; Sturm *et al.*, 1999). Although it was initially proposed that such a range could be considered a small-scale model for longer time frames of minutes and hours (Posner & Petersen, 1990), a further expansion of the concept of alertness includes a distinction between phasic and tonic alertness, with the latter playing a role within longer periods of minutes (Posner & Petersen, 2012; Sturm *et al.*, 2000).[5] Accordingly, when performing a continuously ongoing task (e.g. a CPT), tonic alertness relates to performance over a number of events that occur within minutes, as opposed to phasic alertness pertaining to the momentary state of attention. Operationally, phasic alertness is typically defined as the intensity level of the attentional system in a short period following a warning signal (e.g., Sturm *et al.*, 1999; Coull *et al.*, 2001), as opposed to tonic alertness, which is studied by estimating overall performance in a task

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[5] A further time frame of reference is embodied in the concept of vigilance, referring to prolonged tasks lasting a few hours (Mackworth, 1948). As such, timescales may encompass aspects of performance that are unrelated to attention (e.g., general fatigue). This discussion will thus be limited to performance over periods shorter than one hour.

(e.g., Raz & Buhle, 2006; Sturm & Willmes, 2001). As suggested in the Introduction, tonic alertness can be considered a component of sustained attention with respect to its time frame of reference, in which response readiness is measured by RTs (e.g., Robertson & O'Connell, 2010; Sturm & Willmes, 2001). To avoid confusion of terminology between theories of tonic alertness and sustained attention, this chapter will henceforth only refer to sustained attention. This decision is grounded in the theoretical background of performance maintenance, according to which sustained attention is the more inclusive and general mechanism of the two (Sturm & Willmes, 2001).

The way in which phasic alertness and sustained attention manifest themselves within a cognitive task can be distinguished by considering overall performance (sometimes defined as 'vigilance level') versus the decrement in performance over time (sometimes defined as 'vigilance decrement') (e.g., Parasuraman, Nestor, & Greenwood, 1989; Berardi, Parasuraman, & Haxby, 2001; Berardi, Parasuraman, & Haxby, 2005; Swaab-Barneveld *et al.*, 2000). This distinction can lead to a radical view of the way sustained attention is assessed. The momentary availability of phasic alertness might influence fluctuations in response times during a task, as it is the component determining the readiness to detect and respond to each target. Such fluctuations in phasic alertness would be reflected in the variability of response times. In Chapter 2 of this thesis, the variability of response times was found to be closely related to the perceptual sensitivity. Accordingly, the dynamics of phasic alertness within a given task impact on overall performance indices, such as task sensitivity (d') and RT-SD; it is therefore not possible to rule out effects of alertness in overall performance. What follows is that when studies measure tonic alertness (or sustained attention) by estimating mean performance (e.g., Nuechterlein, Parasuraman, & Jiang, 1983; Oades, 2000; Parasuraman, Mutter, & Molloy, 1991; O'Dougherty, Nuechterlein, & Drew, 1984; Whyte *et al.*, 1995), phasic and tonic effects cannot be disentangled. In other words, the vigilance level is determined, at least partially, by phasic alertness.

A potential way of distinguishing phasic alertness from sustained attention is to reintroduce the concept of performance decrement. Logically, phasic alertness and performance decrements must be distinct: if an individual has a lower alertness level at any given moment, this does not imply that his/her performance will also deteriorate more over time. For example, if when playing basketball my performance in shooting the ball is bad or inconsistent, it does not follow that by the end of the task I will perform worse than at the beginning. Conversely, I could be a sharp player and an excellent shooter at the beginning of the play, but, compared to others, my performance might be marked by a decrement over time. In accordance with the distinction suggested here, imaging studies and neuropsychological evidence have demonstrated dissociations between the neural correlates of momentary performance level and its decrement (e.g., Nebes & Brady, 1993; Sturm & Wilmes, 2001; Posner, 2008; Yanaka *et al.*, 2010; for a review see also Oken, Salinsky & Elsas, 2006).

Measuring Phasic Alertness and Sustained Attention

Unfortunately, researchers only rarely account for sustained attention and phasic alertness within the same task. While the latter is typically measured by comparing response times for pre-cued versus non-cued targets (e.g., Callejas, Lupiánez, & Tudela, 2004), sustained attention measures are measured by multiple task indices, either related to mean performance level or performance decrement. A rare exception, Roca *et al.* (2011), used a variation of the task typically used to assess the attentional networks in which performance decrement was assessed separately. The researchers found that overall task indices 'only moderately correlated to a direct vigilance measure' and suggested that 'they could not be used as appropriate of vigilance' (Roca *et al.*, 2011). A conservative approach to assessing sustained attention may pose a further difficulty, as a key property of a sustained attention task is that it should be simple, repetitive and non-arousing (e.g., Roberton *et al.*, 1997). Nevertheless, a task that contains occasional warning signals may not meet such a definition. It seems, therefore, that integrating phasic alertness measurements with traditional ways of assessing sustained attention is challenging, as adding further conditions (such as an exogenous warning signal) to the inherently boring CPT would conflict with the desired non-arousing property of the task. However, being unable to measure phasic alertness in an sustained attention task does not mean that phasic alertness remains uninvolved. Following the theoretical framework of the attentional networks, alertness is a fundamental component of attention, and the warning signal only operates phasically to provoke it.

The question is, therefore, whether (and how) it is possible to find traces of phasic alertness changes in a CPT containing no warning signals. It would be incorrect to assume that uncued conditions selectively tap sustained attention in isolation, ruling out putative contributions from phasic changes in alertness. Conversely, when assessing sustained attention based on a target sensitivity measure (d') (e.g., Corkum, Byrne, & Ellsworth, 1995), it is very likely that the momentary level of alertness (i.e., a phasic change in alertness) contributes to the detection of a target. In line with this, Chapter 2 established that perceptual sensitivity and variability in RTs are associated. It could be explicitly argued that, theoretically, an individual with a momentary lower level of alertness may have a higher probability of missing a target, or in other cases of confusing targets and distractors. Many findings in the attention literature describe task dynamics that can be present and affect performance on traditional CPTs and, in turn, can either influence momentary demands for alertness or phasically modulate alertness. For example, repetition priming is a well-established phenomenon where individuals are better in responding to repeated items within a cognitive task (e.g., Scarborough, Cortese, & Scarborough, 1977). Logan (1990) suggests that repetition priming results from a decrease in attentional demands for the repeated target (Logan, 1990). The attenuation in attentional demands is attributed to the formation of a short-term representation of the repeated target, which makes is easier to categorise by processes of selective attention. Potentially, such repetition can interact with the alerting network: with decreasing attentional demands, repetition priming may decrease the momentary alertness effort. From a different perspective, the response itself can have a modulatory effect on the alertness level in a consecutive trial. A different approach to the modulatory effects of the previous trial is the inter-trial priming effect, where a repetition of task-relevant features benefits performance by means of enhancing both attentional and motor processes (e.g., Lamy, Yashar, & Ruderman, 2010). Although this view has never been discussed in the context of alertness, it also implies that the requirements for alertness can dynamically change within a task: when considering the role of the alerting network in modulating signal-to-noise ratio and enhancing response readiness, it is likely that any change in perceptual and motor demands will somehow interact with demands for alertness.

Hitherto, the discussion has proposed that task contingencies may influence the momentary demands for attention or response readiness. A different perspective suggests that alertness itself can be modulated on a trial-by-trial basis as a result of task contingencies. Cheyne *et al.* (2009) provide a comprehensive account of task engagement and disengagement, and propose that occasional disengagement and inattention can be attributed to an ongoing repetitive structure of a task. In this respect, the high frequency of non-targets on the CPT may gradually evoke task disengagement, and a rare event of a target may reinitiate engagement. This engagement is likely to be followed by a greater sensitivity to subsequent events. As a further development of the engaging properties of a rare target event on a CPT, this chapter will propose a specific prediction with respect to phasic changes in alertness: that the occurrence of an infrequent target event will phasically enhance alertness in a similar manner to a warning signal. As discussed in the introduction, the alerting effect of a warning signal is not merely attributed to temporal expectations *per se,* but also to momentarily increased sensitivity of the attentional system. It is therefore not unlikely that the occurrence of a target event could promote a higher level of alertness to facilitate response-related mechanisms, and this effect can have some ‘spillage’ of increased alertness to temporally proximate events. Although the ‘optimal’ inter-stimulus interval, for a pre-cue serving as a warning signal, is relatively short (approximately 500ms; see Posner & Boies, 1971), under some conditions a pre-cue could have a lasting effect following a warning interval of five seconds (Posner & Wilkinson, 1969 in Posner & Boies, 1971). Such a long-lasting warning interval effect has also been found in many studies of simple RTs following a varying foreperiod (for a review see Niemi & Näätänen, 1981). Accordingly, on a CPT where stimuli appear within a range of a few seconds, a target event could be considered a transient warning signal.

The potential alerting properties of the previous target may have a differential effect on clinical and non-clinical populations. Such speculation relies on previous studies showing marked differences in the temporal course of attention among stroke survivors. For example, Husain *et al.* (1997) have shown that the attentional blink effect, attributed to the temporal allocation of attentional resources, was much longer-lasting among patients with hemi-spatial neglect when compared to healthy controls, demonstrating abnormal temporal dynamics in a disorder often characterised solely by visuo-spatial attentional deficits. It is possible, therefore, that even if healthy individuals do not show a marked benefit from preceding targets, such benefits might appear in patients with an attentional or neurological impairment. Indeed, brain-imaging studies support more widespread activations across brain regions and hemispheres (e.g., Sturm & Willmes, 2001) for alertness, versus the relatively focal loci of sustained attention in the right hemisphere (e.g., Parasuraman, Warm, & See, 1998; Robertson & O'Connell, 2010). The mere probability, therefore, of a disturbance in neural processes underlying the alerting function is higher following a brain lesion.

The aim of the current study was to measure sustained attention while also estimating phasic alertness under similar conditions. The study included a chronic stroke group and a group of age-matched controls. Participants provided subjective reports of cognitive difficulties in four domains: inattention, motor, language, and memory. Particular attention was given to identifying the task indices that correlate with subjective reports of inattention, contrasting markers of overall task indices with markers of performance decrement. Sustained attention was estimated using the Masked Conjunctive CPT presented in Chapter 2 to induce a high variability in accuracy-based outcome measures. Phasic alertness was described based on changes in RTs following a warning signal compared with no cue (here the relevant comparison was based on the preceding trial, i.e., target versus non-target). The sustained attention capacity was assessed based on the RT-SD, the mean perceptual sensitivity and its course of decrement. The extracted indices of sustained attention were correlated with reports of inattention in daily life, attempting to identify a valid marker of sustained attention. Although evidence suggests that phasic changes in alertness are associated with multiple cognitive faculties, such as task switching (e.g., Meiran, Chorev, & Sapir, 2000), executive control (e.g., Weinbach & Henik, 2011), and spatial attention (e.g., Robertson *et al.*, 1998), it is not clear how an impairment or abnormality of phasic alertness might manifest itself in daily activities. The main reason for this is the time frame: phasic alertness operates in milliseconds, as opposed to sustained attention which can be defined in seconds, minutes and even hours. This point is emphasised because, compared to sustained attention, verifying the ecological validity of phasic alertness is not as transparent. Whereas sustained attention can easily be attributed to everyday distractibility, a few milliseconds difference in selecting a target is harder to describe at the symptomatic-behavioural level. There is nonetheless an interesting hypothesis for the current study: given the widespread networks underlying phasic alertness, there is a higher probability that phasic alertness will be influenced by any damage to the brain after a stroke. In contrast, differences at the group level between the stroke and neurologically healthy groups may not be observed in sustained attention, given its relatively focal loci in right frontal and parietal regions (e.g. Molenberghs *et al.*, 2009).

To attribute ecological validity to the measures of sustained attention, people with atypical sustained attention estimates would be expected to experience attentional lapses in real-life situations. Ishigami & Klein (2008) review the existing literature on how attentional capacities are related to self-reports of cognitive difficulties (as defined by the Cognitive Failures Questionnaire; Broadbent *et al.*, 1982). The review includes fourteen studies, of which only three directly assess sustained attention, and, arguably, these tests also involve other cognitive functions (Ishigami & Klein 2008). At least one study, by Robertson *et al.* (1997), identifies a moderate correlation between performance on a sustained attention paradigm (the SART) and self-reports of cognitive failures in a group of 60 participants. However, as Ishigami and Klein (2008) note, the SART introduces requirements for response inhibition, which may confound the results. Furthermore, neither the SART nor any other study has established a connection between sustained attention and inattention symptoms as they appear at the Cognitive Failures Questionnaire. Wallace, Kass, & Stanny (2002) identify four independent constructs in the Cognitive Failures Questionnaire: Distractibility, Memory, Blunders and Naming. In previous studies estimating the relationships between the Cognitive Failures Questionnaire and performance in sustained attention tasks, correlations were found only for the overall questionnaire score. This is surprising: between the four proposed questionnaire factors, only one seems directly related to sustained attention (Distractibility). It is hard to imagine how the Naming factor, for instance, can be related to measures of sustained attention. Accordingly, the present study aimed to identify a *specific* correlation between sustained attention estimations on the Masked Conjunctive CPT and Distractibility.

Current Study

By assessing chronic stroke patients and age-matched controls, this study aimed to 1) identify a marker of sustained attention that correlated with reports of inattention and 2) estimate phasic changes in alertness within the task. Within the first aim, I attempted to differentiate general and non-specific task indices from those that contribute to sustained attention difficulties in daily life. Patients and controls may differ in performance for reasons other than inattention symptoms, such as general slowness, motor problems, or perceptual deficits. Therefore, lower overall performance does not imply necessarily low sustained attention. A careful, theory-driven approach is needed to identify performance variables that isolate inattention. Accordingly, my main experimental prediction was that sustained attention would correlate most strongly with task indices that reflect performance decrement.

Experiment 3.1 – Sustained Attention Among Healthy Ageing and Stroke Survivors

Methods

Participants

All experimental protocols were reviewed and approved by the Central University Research Ethics Committee of the University of Oxford. The participants were 23 chronic stroke survivors and 37 neurologically healthy adults (total N=60). The participants are a sub-sample of the clinical and older controls presented in Chapter 2 (Experiment 2.3).

Stroke Survivors (clinical group): all stroke survivors were at least one-year post-stroke at the time of testing. Their average age was 62.73 years (SD=12.12), and they were all part of a regular pool of volunteers at the Oxford Cognitive Neuropsychology Centre. Stroke survivors were not selected based on their lesion or cognitive deficit, and none of them had an ongoing diagnosis of an attentional disorder.

An overview of the stroke group is given in Table 3.1, and Figure 3.1 provides a lesion overlay in those for whom scans were available.

ID	Sex	Dominant Hand	Lesion Description
#01	F	R	Right Frontal, Parietal Occipital
#02	M	R	Left Frontal, Temporal, Insular, Bilateral Subcortical
#03	F	R	Left Cerebellum
#04	M	R	Left Occipital
#05	M	R	Left Insular, Subcortical
#06	M	R	Right Frontal, Insular, Cerebellum
#07	F	R	Left Cerebellum
#08	F	R	Left Occipital
#09	M	R	Right Cerebellum
#10	M	R	Right Insular, Subcortical
#11	M	R	Left Temporal, Precuneus
#12	M	L	No visible lesion (medical note: right MCA territory)
#13	M	R	Left Brain Stem, Right Precuneus
#14	F	R	Left Insular, Frontal, Parietal, Occipital
#15	M	R	Left Frontal
#16	M	R	Bilateral subcortical
#17	M	R	Left Occipital
#18	M	L	Right Frontal, Insular, Subcortical
#19	M	R	Left Cerebellum, Occipital
#20	M	R	Left Subcortical
#21	M	L	Bilateral Occipital, Temporal
#22	F	L	Bilateral Occipital, Cerebellum
#23	M	L	Left Frontal, Temporal, Insular, Parietal, Occipital, Subcortical

Table 3.1 Brief overview of the lesion descriptions for the patients included. M= male, F= female; R = Right; L = Left; MCA = Middle Cerebral Artery. Brain scans were not available for patients

#10 and #15, and patient #12 did not have any visible lesion in the clinical scan. In these cases, the lesion descriptions were based on the medical notes from the admitting hospital

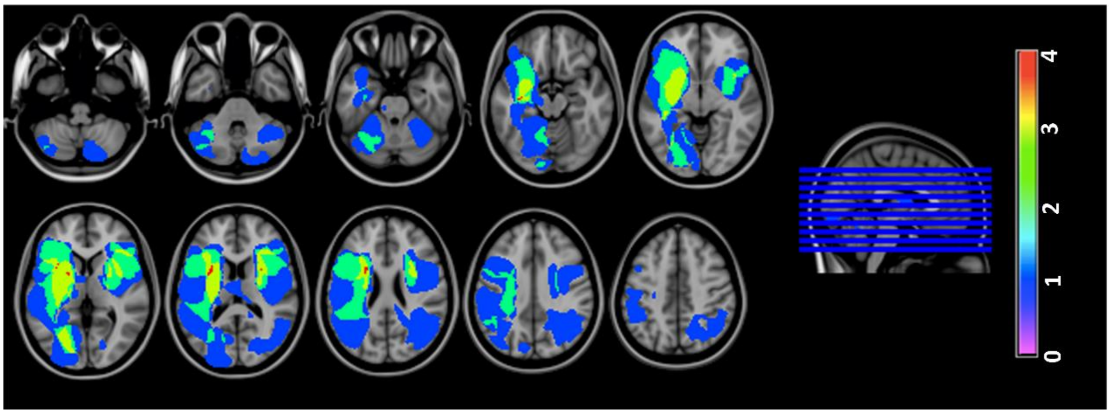

Figure 3.1 Lesion overlay for 19 out of the 23 patients: Four patients were omitted from the lesion overlay. One scan was not available, one scan had no visible lesion and two patients were excluded from the analysis based on their performance (patients #21 and #22; see results section). Patients' anatomical scans were manually delineated slice-by-slice by a trained research technician. The binary delineation was performed using MRIcron (McCausland Center for Brain Imaging, Columbia, SC, USA). Once the lesion masks were generated, a 5-mm full width at half maximum (FWHM) smoothing was applied in the Z-direction. Patients' anatomical scans were linearly registered to a standard template space (i.e., MNI152_T1_2mm) and the resulting registration matrix from this transform was then applied to the binary lesion mask. The processing of the scans and registration was performed using SPM8 (the Wellcome Trust Centre for Neuroimaging, London, United Kingdom) and custom MATLAB scripts (The Math Works, Natick, MA, United States) consistent with the methods described in Gillebert, Humphreys, & Mantini (2014). All patient lesion masks were concatenated to create a conjunction map where intensity values represent the number of patients with a lesion in a given coordinate (max overlay of the sample is 4)

As listed in Table 3.1, only nine patients had right-hemisphere damage, and only three had lesions in either parietal or frontal cortices (with only a small overlap of lesions in these regions). This is particularly important in light of the established relation between right frontal-parietal damage and impaired sustained attention (e.g., Sturm and Wilmes, 2001). Based on the lesion characteristics of this sample, there is a possibility that a large proportion of the clinical sample will have no specific difficulties in sustained attention.

Healthy Control Group (control group): the participants in this experiment were 37 naïve volunteers (22 of whom were women, and 5 of whom were left-handed). All were regular volunteers at the Oxford Cognitive Neuropsychology Centre. All had normal or corrected-to-normal eyesight (mean age 68.21, SD= 7.72). They were compensated for their time (payment of £10 per hour, inclusive of travel expenses). This is a sub-sample of the larger group presented on Chapter 2.

Apparatus, Stimuli, and Procedure

The apparatus, stimuli, and procedures were the same as those described in Experiment 2.3. In addition to performing the computerised task, all participants filled in the Cognitive Failures Questionnaire (Broadbent *et al.*, 1982).

Questionnaire

The Cognitive Failures Questionnaire consists of 25 questions over 2 pages. The scores contribute to four separate factors labelled Memory, Distractibility, Blunders, and Names (Wallace, Kass, & Stanny, 2002). For each question, participants rank, on a scale from zero to five, how often different occasions of cognitive failures have occurred to them over the last six months (Broadbent *et al.*, 1982). The Distractibility factor represents occasional failures of being distracted and non-attentive (e.g., ‘Do you fail to hear people speaking to you when you are doing something else?’); the Memory factors are related to memory problems (e.g., ‘Do you find you forget which way to turn on a road you know well but rarely use?’); the Blunders factor is related to sluggishness or inaccuracy in behaviour (e.g., ‘Do you bump into people?); and the Names factor is related to people’s names (e.g., ‘Do you fail to listen to people’s names when you are meeting them?’).

Statistical Analysis

For each participant, the following data was extracted: the correct reports of targets, the number of omissions (‘miss’) errors, the number of commission (‘false alarm’) errors, and RTs for correct trials, These measures were used to assess individual performance in different conditions, according to multiple indices: a) the RT-SD; b) overall perceptual sensitivity for discriminating the target from the distractors (d’), in accordance with Signal Detection Theory; c) ‘sensitivity change’ (d’-change) reflecting performance decrement, defined as the percentage change in d’ between the first and the second halves of the task; d) previous trial benefit, defined as the difference between RTs for a target when the previous trial was distractor versus when the previous trial was a target. Whereas other studies often focus on the effect of an error on a trial-by-trial adjustments of behaviour (e.g., Danielmeier & Ullsperger, 2011), here the emphasis is on the behavioural benefits of executing a response when contrasted with no response. This approach may allow to identify momentary increases in task engagement that fall in domains that are unrelated to metacognitive processes of error awareness (e.g., Eichele et al., 2010).

Results

Cognitive Failures Questionnaire

Of the 60 participants, 58 completed the questionnaire in full (two participants, one patient and one control, missed items and were removed from this analysis). Questionnaire scores were calculated for each group (stroke survivors and controls) on four factors (Distractibility, Memory, Blunders, and Names), and a general task score was also derived (Wallace, Kass, & Stanny, 2002). The group averages of reported cognitive failures are illustrated in Figure 3.2; the inter-correlations[6] of the questionnaire factors for the full group (N=58) appear in Table 3.2.

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[6] It should be noted that some if the factors described by Wallace, Kass, & Stanny (2002) rely on shared objects. Therefore, while reporting the inter-correlations as they are, any statistical inference based on the inter-correlations will account for the partial overlap.

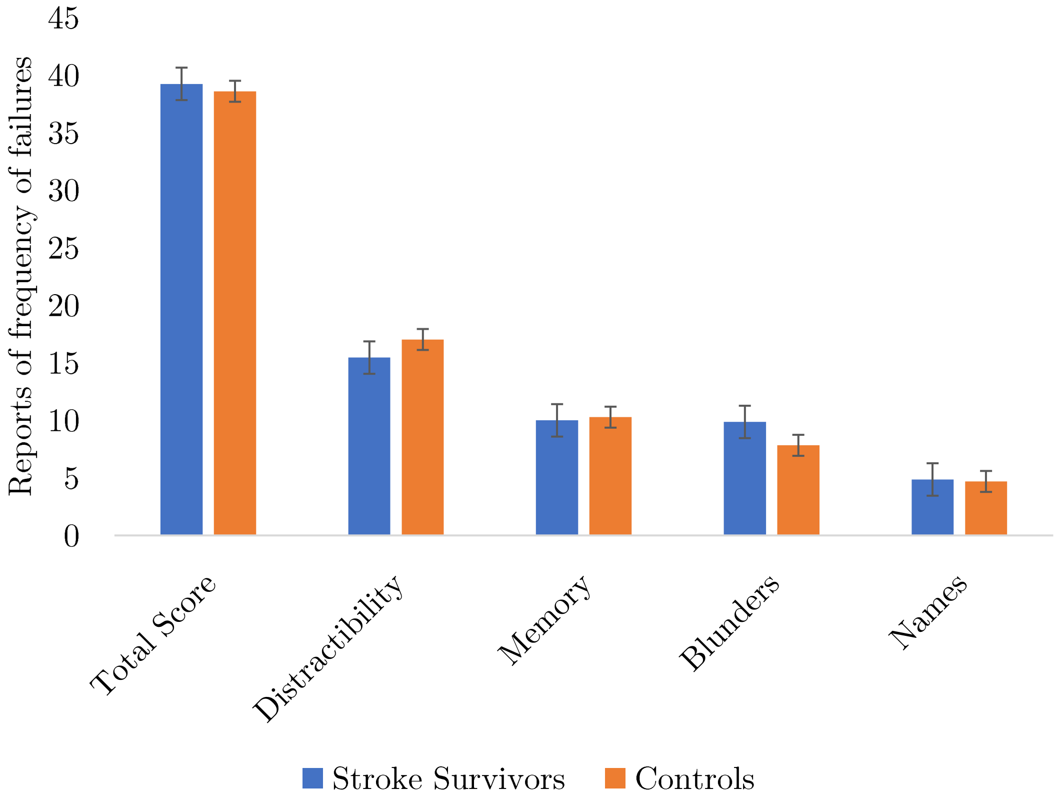

Figure 3.2 Cognitive Failures Questionnaire mean scores (higher values represent a higher frequency of cognitive failures on each domain)

	Distractibility	*Memory*	*Blunders*	*Naming*
Distractibility	1			
Memory	.709**	1		
Blunders	.467**	.636**	1	
Naming	.246	.360*	.438**	1

*Table 3.2 Inter-correlations of Cognitive Failures Questionnaire factors; *p<.01; **p<.001*

A pairwise comparison between the groups on each factor revealed no significant differences in any of the dimensions. A further analysis used a Bayesian t-test (Rouder *et al.*, 2009) to estimate whether there was a similarity between groups. A Prior Scale was set for a medium effect size (0.7071), and the statistical test was based on the Bayes Factor R Package (Version 0.9.12-2, by R Moray). With the exception of the Blunders factor, for which the comparison provided only an anecdotal evidence in favour of H0 (no difference; BF=.49), all other comparisons showed substantial evidence in favour of H0 (all BF<=.30). Therefore, the overall score, as well as individual scores for Memory, Naming and Distractibility, were similar among the groups. The results from the questionnaire have a major implication for the current study: at a group level, in most factors, the clinical sample did not differ in subjective experiences of everyday cognitive failures compared to the neurologically healthy sample. Of particular interest for the cognitive task, the Distractibility factor was well matched, and therefore there is a reason to expect a similar pattern when comparing between the groups the sustained attention indices of the cognitive task (Masked Conjunctive CPT).

Descriptive Statistics

Descriptive statistics for various performance parameters in each group (stroke survivors and controls) are summarised in Table 3.3. Two participants who performed at a chance level on the Masked Conjunctive CPT were removed from the stroke survivors group (P#21, P#22). None of the stroke survivors had lesions that are normally associated with impaired sustained attention: P#21 had damage to the fusiform gyrus, which is often associated with difficulties in processing visual features (e.g., Tyler *et al.*, 2013). P#22 had damage to the cerebellum, which may have caused difficulties in performing a perceptual discrimination task with speeded responses (e.g., Gao *et al.*, 1996).

	RT-SD	*RT*	*Omissions*	*Commissions*	*d'*	*β*
Controls	93.2ms (5.67)	525ms (9.2)	1.3 (0.3)	2.2 (0.3)	4.28 (.009)	.03 (.19)
Stroke survivors	157.7ms (28.26)	548ms (15.9)	2.8 (.65)	3.5 (.71)	3.43 (.28)	.09 (.04)

Table 3.3 Means (and standard errors of means in brackets) of performance indices on the Masked Conjunctive CPT for the stroke survivors and the control group. Abbreviations. RT-SD: Standard Deviations of Reaction Times; RT: Reaction Times

Inspecting the descriptive data revealed that the response bias (β) had a mean positive value in the two groups, suggesting a higher tendency to miss targets. This observation has been reported in Chapter 2, and is here recalculated for the sub-sample included in this study. The positive β is in line with the premise that a sustained attention task should evoke positive bias values.

Correlations Among Performance Indices

The main variables for assessing sustained attention were d', d'-change (change in d' between two halves) and RT-SD. A correlation matrix of the three indices appears in Table 3.4.

	RT-SD	*d'*	*d'-change*
RT-SD	1		
d'	-0.339**	1	
d'-change	-0.092	-.205	1

*Table 3.4 A correlation matrix of the three outcome measures for assessing sustained attention. **p<.01; critical values adjusted according to Benjamini & Hochberg (1995)*

Two variables correlated significantly with one another: RT-SD and d' (r= -.339; p= .009). Interestingly, d'-change did not correlate with the other variables. These results suggest that RT-SD and overall d' may not be (pure) measures of sustained attention (particularly decrements in vigilance over sustained periods, or 'vigilance decrement'). The only variable that reflected a change in performance with time on task appeared to be independent according to the observed correlations.

Comparing Group Performance

The two groups were compared based on the main three task indices: RT-SD, d', and d'-change. These group comparisons revealed a significant difference in two of indices. Descriptive statistics are presented in Table 3.5. Compared to the control group, the stroke survivors group had a greater variability in RTs (t(56)=2.048; p=.45; 95% CI [5.6,5.1]) and lower overall target detectability (d') (t(56)=2.66.; p=.013; 95% CI [0.11,0.87]). The groups did not differ significantly in their d'-change (*p*=.589). A Bayesian t-test with a Prior Scale set for a medium effect size (0.7071) provided confirmatory substantial evidence in favour for the groups being similar in their d'-change (BF=.281).

	Control	*Stroke survivors*
RT-SD	93.21ms (5.67)	157.76ms (28.26)
d'	4.28 (0.09)	3.43 (0.28)
d'-change	4.21(5.01)	8.67 (3.45)

Table 3.5 Descriptive statistics of the group performance. Means (and standard errors of means in brackets). RT-SD: Standard Deviations of Reaction Times

Previous Trial Benefit

As part of the attempt to identify phasic changes in alertness, the RTs for targets were calculated as a function of previous trial type (N-1), comparing target trials that immediately followed either a target or non-target trial.

A 2 (Group) X 2 (previous trial) mixed-design ANOVA revealed a significant main effect for previous trial (target versus no-target) (F(1,56)=5.916; p=.018; partial η2=.096) and a significant interaction (F(1,56)=7.115; p=.01; partial η2=.113). There were no overall group differences in RTs. The results are illustrated in Figure 3.3. Following the ANOVA, the interaction was analysed by performing a set of paired comparisons. The *post hoc* analysis revealed that the source of the interaction was faster RTs in the patient group in cases where the previous (N-1) trial was a target (533ms) compared to non-targets (559ms) (t(20)=2.613; p=.017; 95%CI[5.07;45.91]). There were no significant differences between RTs according to the previous trial within the control group.

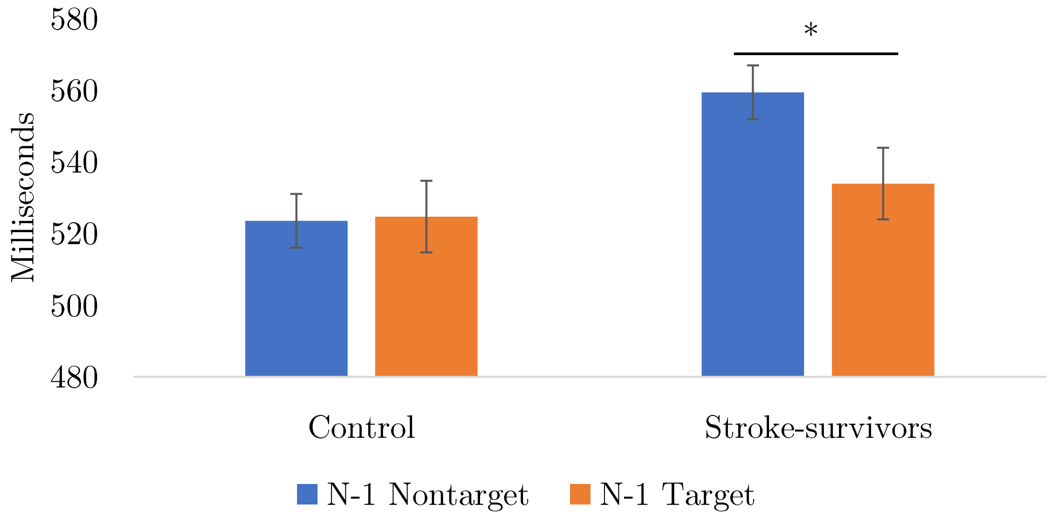

Figure 3.3 Effect of previous trial on RTs for controls and patients (error bars represent Standard Error)

The results revealed group differences in the phasic increase in alertness following a target trial. Whenever a target appeared following another target, RTs were comparable in the two groups. A behavioural benefit resulting from stimulus repetition is often observed when estimating the effect of repetition-priming (e.g., Logan, 1990). Nevertheless, in the current task design, only the stroke survivors group benefitted from a previous trial with a target. Interestingly, the observed benefit only led the reaction times in the clinical group to be equated with controls. Therefore, it could also be proposed that the clinical group had a certain *cost*, associated with the appearance of a target after distractor. Such an effect could result from a confusion caused by a distractor: Huang, Holcombe, and Pashler (2004) reported a comparable effect of slower responses in a visual search task when two subsequent trials had different distractors with shared features. The effect of distractor confusion is often contrasted with the repetition priming (Ásgeirsson & Kristjánsson, 2011). This point should be further verified in future studies, potentially by obtaining a better RT baseline measurement. In the context of the current study, it is important to appreciate that whatever the source of the effect was, it only revealed itself in the clinical group. This observation can be interpreted as a result of the temporal intervals and the simplicity of the task. Potentially, in the control group, the effect of the previous trial was less substantial because of group differences in processing speed. Alternatively, it is possible that performance was already at ceiling among controls.

A secondary analysis assessed whether the previous trial benefit was associated with any of the proposed sustained attention task-markers: the standard-deviation of RTs, the performance-change index (d'-cost) or the overall performance (d'). To this end, a new task marker was derived based on the difference between the RT following a target and the RT following a distractor (previous trial benefit). Table 3.6 shows the Pearson correlations between the previous trial benefit and the sustained attention markers. There were no significant correlations (all ps>.1).

	d'	d'-Change	RT-SD
Previous Trial Benefit	-.14	.21	.14

Table 3.6 Correlations between the previous trial benefit and sustained attention task markers. None of the correlations was significant. The previous trial benefit represents the difference between RTs in trials that follow a target and trials that follow a distractor

Task Performance and Questionnaire Data

Correlations between the three performance indices: d', d'-change and RT-SD; and four questionnaire factors (Distractibility, Memory, Blunders, and Naming) were calculated. To increase statistical power, all participants were first grouped together for the correlation analysis.

	Distractibility	*Memory*	*Blunders*	*Naming*
RT-SD	-.152	-.058	.092	.153

d'	.305	.253	.165	.043
d'-change	-.564**	-.285*	-.201	-.167
Previous Trial Benefit	.253	-.025	-.020	-.172

*Table 3.7 A correlation matrix between Cognitive Failures Questionnaire factors and performance indices. *p<.01; **p<.001; critical values adjusted according to Benjamini & Hochberg (1995)*

The correlation matrix (Table 3.7) shows that the Distractibility factor was correlated with d'-change. As a secondary analysis, the correlation between Memory and d'-change was recalculated while controlling for the Distractibility factor. The reason for doing so is that the two factors were constructed from some overlapping questionnaire items (Wallace, Kass, & Stanny 2002). Therefore, calculating the partial correlation without the Distractibility factor enabled the estimation of any exclusive memory-related items that correlated with the d-prime change. When controlling for Distractibility in a partial-correlation test, the correlation between memory and d'-change disappeared (r=.12; p=.38). Conversely, when repeating a similar procedure while controlling for memory, the correlation of Distractibility and d'-change remained high (r=-.52; p<.001). As a final verification, another *post hoc* analysis was carried out in which the correlations between the questionnaire data and the various task indices were calculated while controlling for the Group factor (Controls/Stroke survivors). The results pattern of this partial correlation remained the same, with a significant correlation between the Distractibility factor and d'-Change (r=-.561; p<.001). A scatter plot of the correlation between d'-change and the Distractibility factor is presented in Figure 3.4.

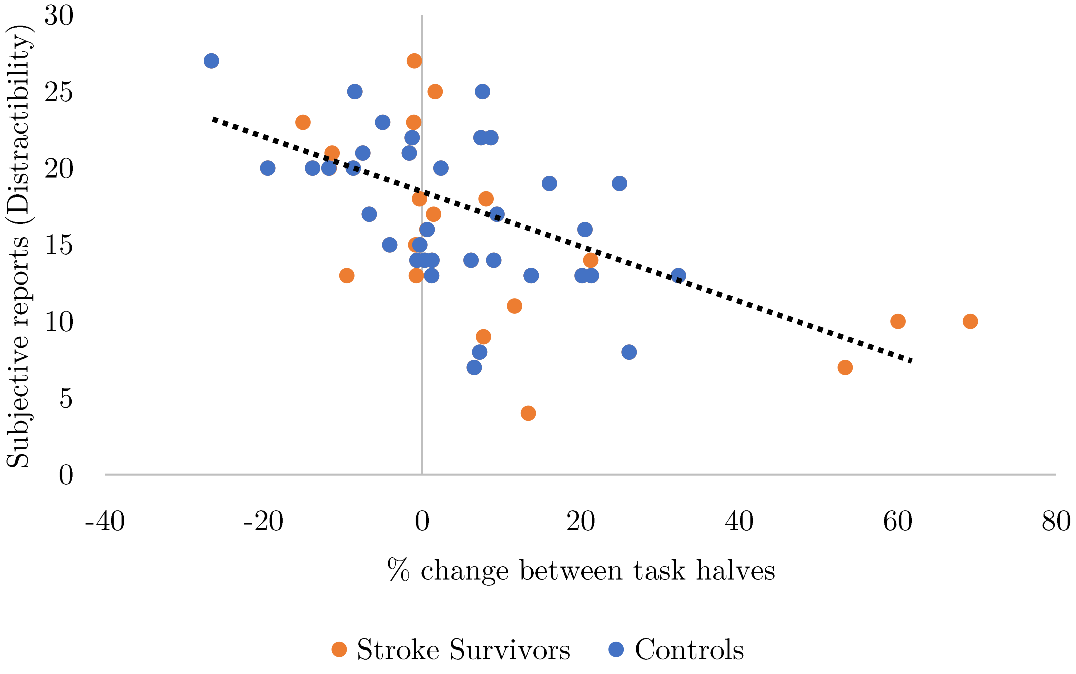

Figure 3.4 A scatter plot and a trend line describing the correlation between the performance change index (d'-change) and the subjective reports of Distractibility

Interestingly, the results show how a large proportion (58%) of the participants had a positive d'-change value, meaning their performance improved between the two halves. These findings nonetheless suggest that the extent to which performance changed, and in some cases improved, is related to symptoms of sustained attention in real life.

Discussion

This study demonstrated that the Masked Conjunctive CPT can provide relevant and selective, accuracy-based markers of sustained attention. Furthermore, the particular measure of d'-change is directly related to self-reported symptoms of inattention in real life. The task was sensitive enough to assess attention with an older adult control-group, and at the same time simple enough to be carried out by most chronic stroke survivors. This is the first study that demonstrates a specific correlation between the Distractibility construct in the Cognitive Failures Questionnaire and sustained attention. In addition, this correlation was found with a very straightforward outcome measure: the extent to which participants maintain their level of performance during the sustained attention task (Masked Conjunctive CPT) was correlated with their subjective reports of lapses in attention in daily activities (the Cognitive Failures Questionnaire Distractibility factor). Previous studies have connected overall mean performance on sustained attention tasks with the general score of the Cognitive Failures Questionnaire, which includes four factors: Distractibility, Blunders, Naming and Memory (e.g., Robertson *et al.*, 1997a). The current findings, however, go further by relating task-performance to the specific Cognitive Failures Questionnaire construct relating to inattention. This external validity supports the conceptualisation of d-prime change as reflecting sustained attention capacity. Furthermore, the findings presented here illuminate the difference between the notion of 'overall vigilance' (mean performance) and 'vigilance decrement' (performance change), implying that the latter is a more useful marker of sustained attention. Another implication of the findings presented here is that focusing on performance *change* rather than performance *decrement* might be useful: there is a possibility that the inability to improve in a simple task as the CPT is also as important for understanding sustained performance, even in the lack of any clear decrement.

An additional contribution of this study is in providing an accuracy-based marker for sustained attention. The importance of this contribution is underscored by the observed differences in RTs according to phasic alertness effects. RT-based outcome measures are likely to reflect such phasic modulations in addition to pure effects of sustained attention. As a clarification, it should be highlighted that the significant differences in RTs that are contingent on the previous trial are likely to determine the group differences in the RT variability index. This measure also appears to be associated with the overall perceptual sensitivity (d'), as shown in this chapter and in Chapter 2. Accordingly, it follows that task indices of overall performance can be biased in populations suffering from brain injuries. The wide distribution of the alerting network increases the likelihood of impairment, which could be manifested in irregular response to task dynamics. Such overall, non-specific group differences in target detection and RTs have also been observed in a study by Rinne and colleagues (2013), in which groups of stroke patients and healthy individuals were assessed using the attentional network task (Fan *et al.*, 2002). Importantly, the authors did not find any group differences in *specific* indices of the attention-networks, but instead reported only overall differences in performance (e.g., patients were slower and less accurate across all conditions).

Interestingly, there were no overall group differences in the proposed sustained attention marker: the d'-change. The absence of such differences, however, followed the lack of self-reported differences in levels or types of cognitive failures. In particular, both groups had equivalent average levels of reported Distractibility. These findings are not that surprising given the sample of stroke survivors. Individuals were selected from a pool of volunteers independently of lesion site or behavioural profile. In fact, the majority of the group had left-hemisphere damage, which is considered to be unrelated to sustained attention. Within the group with right-hemisphere strokes, only three had frontal or parietal damage.

Another intriguing observation was the lack of overall decrement in performance revealed by measures of d-prime change. As noted by Sarter, Givens, and Bruno (2001), practice effects may lead to ceiling performance in target detection. When considering the theoretical implications of the improvement in target detection by approximately half of the group, the straightforward interpretation would be that these individuals simply had enough capacity of sustained attention to allow some improvement. The improvement could be a result of perceptual learning (e.g., Ahissar & Hochstein, 1997) or more general learning (e.g., Shuell, 1986). Taken together, the findings suggest that effects of sustained attention may occur within the context of other, compensatory functions that influence performance. As a whole, therefore, performance may not always decay in CPTs. Nevertheless, comparing performance over time remains informative. Problems in sustained attention, for example, may prevent individuals from improving based on general or perceptual learning over time.

The effect of phasic changes in alertness within the stroke survivors group can be attributed to group differences in the alerting network. Sturm and Wilmes (2001) study the neural substrates of sustained attention and phasic alertness and conclude that phasic alertness relies on similar brain regions as sustained attention, but also recruits left frontal parietal activity. Similar findings have been observed in a study by Rinne *et al.* (2013), where a reduction in alerting indices (defined as the difference in response to target following a cue versus no-cue) was associated with lesions to multiple regions including the bilateral anteromedial thalamus, upper brainstem, and right cerebral peduncle, as well as several small areas across the right hemisphere. These reports support the interpretation that the alerting network subsumes the right-hemisphere system supporting sustained attention, and includes additional brain mechanisms supporting arousal and sensitivity to external cues. Consequently, there is a higher probability that this aspect of attention will be impaired following a brain lesion, which is highly significant when considering the clinical assessment of sustained attention. Phasic changes in alertness may undermine the reliability of RT-based outcome measures: there is an implicit assumption that, on a CPT, responses are unaffected by short-term task-dynamics as the previous stimulus. The findings here reveal that the RT-SD, for instance, incorporates phasic changes that are unrelated to occasional fluctuations in performance, but which rather occur systematically. Nevertheless, none of the Cognitive Failures Questionnaire factors measures were correlated with the phasic changes in alertness. Whether there are everyday subjective activities that do relate to these phasic changes remains an open question for now.

As a final remark for this chapter, it should be re-emphasised that the findings reveal important, but often neglected, methodological considerations.

The main conclusion here is that a simple comparison of mean performance is very likely to distinguish patients from controls, even in a simple task like a CPT, but one should not confuse poor overall performance on a CPT with poor sustained attention. A careful, theory-driven approach is required when selecting the appropriate task indices.

Chapter 4 : Assessing Sustained Attention and its Correlates in Genetic Syndromes

This chapter is based on a collaboration with the Attention, Brain and Cognitive Development lab. I propose a new analysis of a pre-existing dataset that was previously acquired by Dr Ann Steele, and used with the permission of Prof. Gaia Scerif, the project's PI. The analysis and the results content presented here are all original and have never been presented before.

Abstract

Impaired sustained attention is thought to be a key factor in determining the poor functional outcomes of multiple cognitive and behavioural disorders. Williams syndrome and Down's syndrome are genetic disorders causing atypical brain development leading to intellectual disability, and are often associated with attentional disorders. Typically, these attentional disorders are identified based on behavioural symptoms. Nevertheless, when considered from a cognitive perspective, the specific deficits of attention characterising Williams syndrome and Down's syndrome are often unclear and controversial. Potentially, one of the reasons for the difficulty in pinpointing the exact nature of the attentional problems is the difficulty in providing an accurate and reliable assessment when testing individuals with intellectual disabilities and multiple impairments.

Although a deficit in sustained attention is often mentioned among the impairments associated with Williams syndrome and Down's syndrome, close inspection of the available studies reveals many inconsistencies. The present study offers a critical review of the way in which sustained attention has been measured. It will be argued that one shortcoming of previous studies is that researchers have often neglected to consider changes over time during the assessment task. In the current empirical investigation, a novel approach for measuring sustained attention based on performance change was introduced. This approach was able to differentiate between the two syndromes by identifying a decrement in performance characterised only children with Williams syndrome, whereas children with Down's syndrome demonstrated a non-specific poor performance.

Introduction

Sustained attention is thought to be a fundamental factor in determining the efficiency of higher-order cognitive functions (Sarter, Givens, & Bruno, 2002), and a key component in typical development (Scerif, 2010) that helps the child shape and acquire domain-specific skills like reading and numeracy (Steele *et al.*, 2012). In adolescents, lower performance in sustained attention tasks is correlated with poor outcomes in learning and behavioural and emotional difficulties (e.g., Shalev *et al.*, 2015). Difficulties in sustaining attention have been associated with many neurological and psychiatric conditions such as ADHD (Barkley, 1997), Autism (Garretson, Fein, & Waterhouse, 1990), Learning Difficulties (Richards *et al.*, 1990), schizophrenia and affective disorders (Liu *et al.*, 2002), bipolar disorder (Clark, Iversen, & Goodwin, 2002), chronic stroke (Hyndman & Ashburn, 2003), traumatic brain injuries (Robertson *et al.*, 1997), and more.

Poor sustained attention has also been associated with groups of individuals suffering from developmental genetic disorders, such as Williams syndrome and Down's syndrome. Williams syndrome arises from the deletion of some 28 genes on chromosome 7 (Donnai & Karmiloff-Smith, 2000), and Down's syndrome is caused by trisomy on chromosome 21 (Antonarakis *et al.*, 2004). Williams syndrome is associated with poor visuo-spatial abilities alongside slightly better language skills, whereas Down's syndrome is characterised by lower language skills alongside less impaired visuo-spatial skills (e.g. Mervis & John, 2012). At the behavioural level, both groups are reported to be more inattentive, hyperactive, and distractible than neuro-typical children when attention is measured using parent or teacher reports or structured clinical interviews (Porter *et al.*, 2008; Dodd & Porter, 2009). These reports are supported by a high co-morbidity of ADHD with Down (Ekstein *et al.*, 2011) as well as with Williams syndrome (Leyfer *et al.*, 2006). Given that ADHD symptoms are associated with poor sustained attention (e.g., Barkley, 1997), researchers have used cognitive tasks to measure and describe difficulties in sustained attention among children with Down's syndrome or Williams syndrome (e.g., Costanzo *et al.*, 2013; Menghini *et al.*, 2010; Rowe, Lavender & Turk, 2006). A close inspection of the empirical findings reveals that some of the reports of poor sustained attention may be conflicting or anecdotal, perhaps due to inherent difficulties in measuring cognition in individuals with intellectual disabilities. The following section will present a brief overview of the evidence for sustained attention impairments within Down's syndrome and Williams syndrome, emphasising some of the limitations of previous studies.

The previous chapter described the limitations of using the CPT in clinical populations, including the feasibility of performing prolonged tasks and the problem of identifying meaningful performance markers. Typically, individual performance is assessed based on RTs to targets or number of errors (either missing targets or responding to distractors). Traditional approaches influenced by the notion of 'vigilance' emphasise the temporal aspect of sustained attention by targeting performance decrement as the focus of interest (e.g., Parasuraman, 1979). This approach may be inadequate in a clinical context, where assessment is required to be relatively short and therefore a reliable decrement may not be observed. Another way to measure sustained attention in a relatively short time is to estimate the fluctuations of performance over time by measuring the standard deviation of RTs during the task (e.g., Shalev *et al.*, 2011). RT-based indices can, however, be unreliable when assessing clinical populations (see Chapter 3), perhaps even more so with children with underdeveloped motor skills. In accordance with these limitations, researchers have often used discrete outcome measures based on overall accuracy during the task rather than speeded responses, and without focusing on a decrement over time (e.g., Breckenridge *et al.*, 2013).

While relying on accuracy-based outcome measures with unique populations seems intuitive, it is still necessary to ensure that the relevant aspect of cognition (i.e., the performance maintenance over time) is being manipulated. For example, while Costanzo *et al.* (2013) reported unimpaired visual sustained attention among children with Williams syndrome, they assessed it based on performance on a cancellation task primarily aimed at measuring spatial attention. Whereas sustained attention may undeniably influence performance on any cognitive task, cancellation tasks (which are repetitive and non-engaging) do not maintain the key elements that facilitate sustained attention effort (e.g., Robertson *et al.*, 1997a). Scientific evidence has also shown that cancellation tasks provide a poor measure of sustained attention when contrasted directly with a CPT (e.g., Oades, 2000). A valid use of a cancellation task to assess sustained attention would, arguably, require an outcome-measure that allows the estimation of change in performance over time (e.g., number of targets detected at the beginning and at the end of the task). This approach of estimating change in performance was not applied when studying sustained attention in Williams syndrome (Costanzo *et al.*, 2013). In the same study, Costanzo *et al.* (2013) reported poor sustained attention in the auditory modality based on a counting task in which children had to silently count and report ten tones.

The same approach to assessing sustained attention (combining a cancellation task with counting) was applied by Menghini *et al.* (2010) to children with Williams syndrome, reporting poor sustained attention in both the visual and auditory modalities. Rowe, Lavender and Turk (2006) studied a group of children with Down's syndrome and argued for a sustained attention deficit based on a visual search task in which participants searched for a pre-defined target presented among distractors. In another case, Brown *et al.* (2003) assessed sustained attention in toddlers with Williams syndrome and Down's syndrome based on playing intervals (measuring how long the toddlers maintained their interest in a gaming activity). They reported relatively preserved performance among the Williams syndrome children, and poor performance among the children with Down's syndrome. While this approach for measuring sustained attention is common practice when studying toddlers, it lacks some key properties of a sustained attention task such as being repetitive, long and non-engaging (as with the use of cancellation tasks). In contrast with Brown *et al.* (2003), some evidence suggests that sustained attention is likely to be impaired in Williams syndrome children. Mervis *et al.* (2003) and Atkinson *et al.* (2003) found an unusual pattern of ‘sticky fixation’ (a term indicating an intense fixation on specific visual objects in the visual field, which interferes with the ability to process environmental changes). Such a behavioural pattern is thought to be a predictor of abnormal attention maintenance (Cornish & Wilding, 2010).

When highlighting studies which apply a more traditional approach to sustained attention, the results seem to conflict even more. Breckenridge and colleagues (2013) used both auditory and visual variations of CPTs and found no significant differences between Williams syndrome children, Down's syndrome children, and a control group matched for mental age. In the same study, they also reported a significant strength in the auditory sustained attention task among Down's syndrome individuals when compared with Williams syndrome individuals (Breckenridge *et al.*, 2013). In another study using a CPT (alongside an extensive neuropsychological assessment battery), Down's syndrome children were compared to a group of children diagnosed with Fragile-X syndrome and a control group (Munir, Cornish, & Wilding, 2000). Although Down's syndrome children performed worse than the control group in some of the CPT outcome measures (e.g., they had a higher number of false alarms), they were also significantly better than Fragile-X syndrome and comparable to the neurotypical control children who were diagnosed with poor attention. Other studies focus on complementary aspects of attention. For example, Cornish, Scerif, and Karmiloff-Smith (2007) contrasted performance of children with Fragile-X syndrome, Down's syndrome, and Williams syndrome. The researchers demonstrated that Down’s syndrome children were characterised by a ‘global’ impairment affecting performance in multiple tasks. Williams syndrome and Fragile-X syndrome had more distinctive profiles. It was particularly suggested that Williams syndrome children had a specific difficulty in their ability to perform perceptual discrimination in the presence of high attentional demands. Brown *et al.* (2003) presented findings showing a specific difficulty in orienting attention among Williams syndrome individuals when compared with Down's syndrome individuals. In the study, children were presented with two successive stimuli in different spatial locations, and Williams syndrome children often failed to disengage effectively from the first stimulus and orient to the second one. Similar findings highlighted a tendency to a ‘sticky fixation’ towards a visually presented stimulus when performing a spatial re-orienting task (Atkinson *et al.*, 2003). Difficulties in spatial orientation were also observed among toddlers with Williams syndrome (Cornish, Scerif, & Karmiloff-Smith, 2007). In contrast, experimental findings in Down's syndrome children repeatedly report non-specific effects of overall lower performance, often attributed to poor cognitive control rather than to a specific function of attention (e.g., Flanagan *et al.*, 2007; Brown *et al.*, 2003). Accordingly, Cornish and Wilding (2010) propose that ‘there appears to be no one specific area of vulnerability that would indicate a *signature* profile’ of attentional disorders among Down's syndrome individuals.

A potential explanation for what appears to be a non-specific impairment among Down's syndrome can be found in neurophysiological studies. Pinter *et al.* (2001) reported a significantly smaller frontal lobe volume in a group of children with Down's syndrome when compared to neurotypical controls. Accordingly, the authors suggest that the impairments in Down's syndrome individuals derive from underdeveloped frontal-lobe executive functions that are not domain specific. In contrast, the specific problems reported in visuo-spatial abilities in Williams syndrome individuals are supported by the findings of Reiss *et al.* (2004), who identified a reduced grey-matter concentration in the left parieto-occipital region (associated with visuo-spatial construction). In a functional imaging study, Mobbs *et al.* (2007) recorded brain activity among Williams syndrome individuals while performing a go/no-go task. They identified irregular activation patterns of fronto-striatal systems (including the dorsolateral prefrontal cortex, the dorsal anterior cingulate cortex, and the striatum) when compared with the neurotypical control group. These findings are of particular interest as the same brain regions are often associated with sustained attention (e.g., Robertson & O’Connell, 2010; Sturm & Willmes, 2001).

Current Study

The available evidence for a specific sustained attention deficit in either Down's syndrome or Williams syndrome from the CPT literature is inconclusive (e.g., Breckenridge *et al.*, 2013). Studies relying on tasks with high demands for cognitive functions other than sustained attention, as spatial attention (i.e., when assessing sustained attention using the visio-spatial cancelation tasks) either report that Williams syndrome children have intact sustained attention (Brown *et al.*, 2003; Costanzo *et al.*, 2013) or impaired sustained attention (Menghini *et al.* 2010). Similar cases studying Down's syndrome report poor sustained attention (e.g., Rowe, Lavender & Turk, 2006), although these findings are overshadowed by theoretical claims of overall poor performance in multiple tasks (e.g., Cornish & Wilding, 2010).

One possible explanation for this inconclusive evidence is that the available studies all fail to incorporate an important aspect of sustained attention: the capacity to *sustain* attention over time (‘vigilance decrement’ effects). It appears that none of the studies measured how performance changed over time. Instead, researchers have considered overall performance indices as markers of sustained attention. The current study specifically focuses on performance maintenance rather than overall mean differences, using secondary analyses on data collected from cohorts of children with Williams syndrome or Down's syndrome and neurotypical children. Portions of this data were previously published in a paper examining attention among neurotypical children (Steele, *et al.*, 2012) and in a study of Williams syndrome and Down's syndrome, where the focus was on reading skills (Steele, *et al.*, 2013). The remaining data was used in a DPhil thesis by Dr Ann Steele (Steele, 2011). Importantly, the analysis approach presented here has never been applied to this data, or arguably to any published data concerning Williams syndrome and Down's syndrome. Following the findings presented in Chapter 3, the sustained attention measure here is defined as the change in performance between the two halves of a standard CPT that was previously validated with young individuals (Steele *et al.*, 2012.) This performance-change index is used to characterise group differences and to relate individual performance to ADHD symptoms as a behavioural reflection of poor sustained attention in children.

Based on the available evidence, it was hypothesised that 1) children with Williams syndrome are likely to suffer from a sustained attention deficit, 2) children with Down's syndrome are more likely to show overall poor performance when compared with the control group, and 3) the performance-change index will be correlated with reports of inattention, in accordance with the findings in Chapter 3.

Experiment 4.1 – Sustained Attention Among Neurotypical, Down's Syndrome and Williams Syndrome Children

Methods

Participants

Neurotypical Children

All experimental protocols were reviewed and approved by the Central University Research Ethics Committee of the University of Oxford. The neurotypical sample included 103 children aged 3–7, evenly distributed across age and gender. They were recruited from four local state primary schools and three local nurseries in the UK, following procedures set by the relevant research ethics review board. Children were recruited using an opt-in procedure. Following the school's agreement to participate, information letters with consent slips were sent to the parents of children in relevant age groups. Only children who returned a signed consent were included in the study. None of the children had a diagnosed learning disability or a diagnosed attention disorder. Four children did not complete the cognitive task and were excluded from further analysis, therefore leaving a sample of 99 individuals.

Down's Syndrome and Williams Syndrome Children

Children with Down's syndrome were recruited through local support groups including the Downs Heart Group, South Bucks Down's Syndrome Group, and the Swindon Downs Group. Children with Williams syndrome were all recruited through the Williams Syndrome Foundation. The charity organisations posted information sheets and consent forms to all children on their databases between the ages of 4–8. Letters of consent were received back from 27 parents of children in each group. However, one Down's syndrome child was excluded from the study for having mosaic Down's syndrome,[7] and seven Down's syndrome children and one Williams syndrome did not complete the sustained attention task. In all, 19 Down's syndrome children, age 4–8, and 26 Williams syndrome children, age 5–8, participated in the study. The mean age in months and the sample sizes of each experimental group appear in Table 4.1.

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[7] Mosaicism in Downs syndrome means that some cells of the body have trisomy 21, and some have the typical number of chromosomes. This contrasts with the standard presentation of Downs syndrome, in which all cells contain an extra copy of chromosome 21.

	Neurotypical	Down's syndrome	Williams syndrome
Sample size	99	19	26
Age (months) (mean, SD)	85.52; 5.11	86.39; 13.17	79.44; 11.06

Table 4.1 Mean age and sample size of each experimental group

Apparatus

Computerised tasks were presented on an Elo AccuTouch 17” touchscreen monitor using EPrime software. Responses were recorded using the RB-530 Cedrus response box. Children were asked to rest their index finger at a set position at the beginning of every trial and, if necessary, were reminded to do so throughout. They were requested to press the response button whenever identifying a pre-defined target which appeared among non-targets (see details below).

CPT

Children were instructed to press a response button when identifying a pre-defined target within a stream of targets and non-targets. The targets were animal drawings, and the non-targets were drawings of everyday objects, chosen from the Snodgrass and Vanderwart image pool (Rossion & Pourtois, 2004). The testing session began with a short practice block with extended stimulus exposure time, and children were instructed on how to perform the task using verbal instruction and visual aids. During the experimental run, stimulus exposure time was set for 300ms and followed by a fixed inter-stimulus interval of 1250ms, in which a blank screen was presented (stimulus exposure duration and inter-stimulus intervals were chosen following piloting across the age range). A correct 'hit' to a target stimulus resulted in a 'woohoo' reward sound. No sound accompanied a 'miss' response. Incorrect responses following distractor stimuli resulted in a tone indicating an incorrect response. All feedback sounds lasted 450 ms.

As this was a secondary analysis on a pre-existing data set, the use of rewarding signals, fixed inter-stimulus intervals and blank screens between stimuli deviate from the proposed design in Chapters 2 and 3. The main goal, therefore, was to evaluate whether measures of performance change between task halves provided greater sensitivity than the commonly used mean measures, in a design that is commonly used among children. The task lasted approximately four minutes and comprised of 100 stimulus trials presented in a random order, of which 20% presented targets (animals). To estimate overall performance, the following outcome measures were extracted: the percentage of correct responses, the percentage of omitted targets, and the percentage of false alarms. The change in performance, representing the capacity to sustain attention, was based on the percentage change in accuracy over the first and the second halves of the task.

Procedure

All children were tested individually on the computerised CPT. Verbal and non-verbal abilities, as well as ADHD symptoms in the classroom, were also recorded using standardised tests and questionnaires (see details below).

Non-Verbal Ability

Non-verbal ability was estimated using the Pattern Construction Subscale of the British Ability Scales-II (Elliott, Smith & McCulloch, 1996), which measures visuo-spatial ability. Children were requested to copy patterns presented in a book using foam squares (easy), and cubes with patterned sides (hard). The patterns became gradually more complex, and administration was stopped either when a child reached the maximum score, or when they failed to copy four out of five consecutive items. Age-standardised scores, as well as raw scores, were obtained for each child.

Verbal Ability

Verbal ability was estimated using the British Picture Vocabulary Scale II (BPVS-II; Dunn *et al.* 1997), a measure of receptive vocabulary. Children were presented with four pictures and asked to point to the picture named by the investigator. Stimuli were divided into sets of 12 items. The testing session commenced with presenting items deemed appropriate for each age group. The items were then presented in a sequence until a child correctly identified 12 subsequent items with no more than one error, following which they moved up to the next level. The task finished if a child made more than seven errors in a given set (7/12 errors). Verbal mental age was calculated using raw scores.

Teacher-Rated ADHD Symptoms

A measure of ADHD symptoms was obtained from teachers using the Conners Teacher Rating Scale-Revised: Short Version (CTRS-R:S; Conners, 1997). This standardised screening scale consists of 28 items that measure indices of oppositional behaviour problems, hyperactive behaviour, cognitive problems, and attention deficits across the school setting in boys and girls aged 3–17. Items were scored on a Likert scale of 0 to 3. Sub-scales include Cognitive Problems/Inattention, Hyperactivity, Oppositional Behaviour, and an ADHD index (a set of 12 questions based on the Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition; American Psychiatric Association, 1994). The raw scores were standardised based on appropriate age- and gender-matched norm data. The current investigation will only focus on the ADHD index as the dependant variable of interest, for several reasons. First, the Cognitive Problems/Inattention index, which may appear highly relevant as a correlate of sustained attention, comprises item that are more related to academic functioning in the classroom (e.g., ‘not reading up to par’, ‘poor in arithmetic’), and is therefore highly influenced by cognitive problems that are unrelated to attention. Second, empirical findings have shown that of all the CTRS-R:S factors, the ADHD index has the highest correlation with the standard DSM criteria for ADHD inattention symptoms (e.g., McGoey *et al.*, 2007). Although the limitation of using the ADHD index is the inclusion of symptoms that are more related to hyperactivity/impulsivity, it allows the use of age-appropriate standardised t-scores that may be crucial when comparing behaviour across different age, gender and cognitive impairments.

Statistical Analysis

Participants who did not provide any response during the task (i.e., omitted all targets and did not commit any false alarms) were excluded, as this denoted that participants were not engaged in the task. After applying the exclusion criteria, the typically-developing group was divided into three sub-groups based on age (in months). Splitting the data this way allowed comparing the five groups with a relatively similar sample size (Table 4.1), while providing a better aged-matched sample for the Down's syndrome and Williams syndrome groups (i.e., creating control groups to match both mental and chronical age). To assess group differences in sustained attention capacity, the groups were first compared based on the accuracy rate on the first and the second halves of the trial[8] using a repeated-measures ANOVA with the age-group as a between-participants factor. Following the group analysis, a linear regression analysis was conducted to investigate the relationship between ADHD symptoms and performance change. The regression analysis was carried out in two blocks. The first group of predictors only included the estimated verbal and non-verbal mental age, and the second group of predictors added the calculated percentage change in accuracy. The predicted variable was the age-standardised ADHD index based on the CTRS-R:S. Three children (Two Williams syndrome and one Down's syndrome) had missing CTRS-R:S data and were excluded from this analysis.

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[8] A preliminary analysis of the data revealed a considerable difficulty in using Signal Detection Theory parameters, due to the relatively small number of trials alongside a substantial number of individuals with ceiling performance. Signal Detection Theory relies on the estimation of standardized Z-scores of the probability of correctly identifying targets and the probability of committing a false alarm. As probabilities that are at ceiling (i.e., when P(HIT)=1) cannot be transformed into z-scores, a mathematical correction is typically applied as follows: $P=(N-0.5)/N$, where N is the number of the relevant signal trials (Macmillan & Kaplan, 1985). Nevertheless, in cases with a small number of trials, this correction may strongly bias the results. It was therefore decided to focus on accuracy (percentage of correct responses) rather than on Signal Detection Theory data. Accordingly, the previously described ‘d’-change’ was replaced by a new task marker, ‘accuracy change’, which relied on the percentage change in accuracy between the two task halves.

Results

Group Comparisons

Based on the exclusion criteria, three Neurotypical, one Down's syndrome and one Williams syndrome children were removed. Descriptive statistics for the remaining participants, split into five groups (three neurotypical age groups, DS and WS), appear in Table 4.2. Performance on the two task halves on each group is illustrated in Figure 4.1.

	Age	N	VMA	NVA	ADHD score	Accuracy
Young Neurotypical	45.63; 6.59	18	52; 12.71	49.94; 10.46	52.16; 9.85	0.83; .09
Mid Neurotypical	66.06; 6.31	25	71.76; 15.14	63.79; 12.47	57; 14.34	0.92; .08
Oldest Neurotypical	85.52; 5.11	33	89.70; 17.64	87.85; 19.35	52.73; 12.13	0.95; .04
DS	86.39; 13.17	33	42.33; 9.57	40; 9.37	70.6; 9.57	0.74; .13
WS	79.44; 11.06	33	63.08; 19.37	38,56; 6.82	70.8; 11.06	0.75; .18

Table 4.2: Descriptive Statistics (mean; SD). Abbreviations: N: Sample Size; VMA: Verbal Mental Age; NVA: Non-verbal Mental Age; ADHD: Attention Deficit/Hyperactive Disorder; SD: Standard Deviation. Age, VMA and NVA displays age in months units

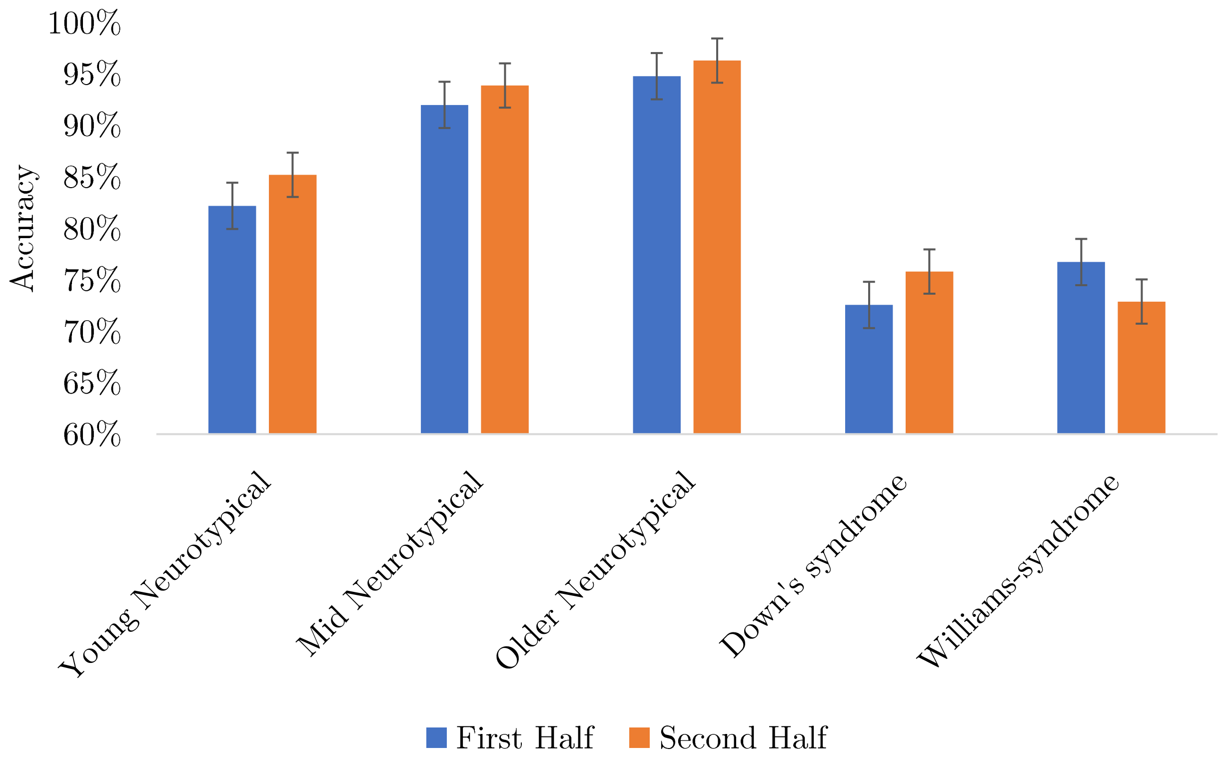

Figure 4.1 performance of the five groups over two task halves

Group differences in sustained attention were assessed using a repeated-measures ANOVA test with the accuracy rate in the first and second halves of the task as a within-subject factor ('task half'), and the experimental group as a group factor. The test revealed a significant main effect for the group factor (F(4,136)=21.907; p<.001; Partial η^2= .390), and no significant effect for the task half factor (p=.092). Crucially, there was a significant interaction between group and the task half (F(4,136)=3.426; *p*=.011; Partial η^2= .091). Another interesting observation is that most groups, with the exception of the WS, had shown an increase in their performance. This is in line with the previous chapter, where most of the clinical and control groups had shown an improvement between two halves of the task.

Further analyses, based on the significant effect of group, were carried out to learn about overall group differences between Williams syndrome, Down's syndrome, and all the other groups. Table 4.3 lists all the paired comparisons.

Group A	Group B	Mean Difference	95% CI (Lower Bound)	95% CI (Upper Bound)
WS	DS	0.006	-0.060	0.073
	Young Neurotypical	-.093*	-0.036	-0.150
	Mid Neurotypical	-.180**	-0.123	-0.237
	Oldest Neurotypical	-.207**	-0.151	-0.264
DS	Young Neurotypical	-.099*	-0.036	-0.162
	Mid Neurotypical	-.187**	-0.124	-0.249
	Oldest Neurotypical	-.214**	-0.151	-0.277

*Table 4.3 Post hoc paired comparisons of overall performance between groups. Abbreviation: DS – Down's Syndrome; WS – Williams-syndrome. *p<.01; **p<.001*

The comparisons table shows that Down's syndrome and Williams syndrome children performed worse than all other groups, including Young Neurotypical. Overall performance for children with Williams syndrome and Down's syndrome was equivalent. As implied in Figure 4.1, all groups but the Williams syndrome had a higher accuracy on the second half of the task when compared with the first half. This effect is also likely to underlie the observed interaction, which was further analysed. A *post hoc* planned comparison confirmed that there was a significant decrement in performance between the two halves of the task in the WS group (t(24)=2.268; p=.033; 95% CI [.003;.073]), with a better performance in the first half (mean accuracy = 76%; SE = 17%) compared to the second half (mean accuracy = 72%; SE = 19%). The significant interaction indicates that there was a pattern of a decrement in performance over time only in Williams syndrome group. This observation is in line with previous reports of poor sustained attention among individuals with Williams syndrome. This observation, when taking into account the significant interaction with the task half factor, indicates that although Down's syndrome children had different patterns of performance compared with Williams syndrome children (i.e., a decrement in accuracy was observed only in the Williams syndrome group), the group was characterised with poor performance (as hypothesised).

Task Performance and Inattention Symptoms

After focusing on group differences in the previous section, the next analysis was designed to investigate how performance decrement (accuracy-change) related to ADHD symptoms. Everyday problems in attention in children is typically estimated by using a standardised questionnaire designed to assess behavioural and cognitive problems by focusing on items related to ADHD.[9] To learn about the relationships, a regression analysis was applied to the age-appropriate standardised ADHD symptom scores (ranked by the teachers) as the dependent variable, and mental age and performance change as predictors. The use of standardised ADHD scores controlled for age-related differences.

A hierarchical regression model was applied to control for differences that can be explained by verbal and non-verbal mental age. The reason for controlling the mental-age variables is to account for symptomatic differences that are related to a 'mismatch' between the biological age and the mental age. The logic of using age-standardised scores as the dependant variable relies on the assumption that inattention and hyperactive/impulsive behaviour varies with age. Accordingly, it is important to account for age differences that are not accounted for within the

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[9] Whereas sustained attention is normally attributed only to the inattentive aspects of ADHD, the Conners questionnaire does not differentiate inattention from other cognitive problems. This study therefore used the age-appropriate standardised ADHD index, which is more representative of the syndrome as a whole.

normative standardised scores. To do so, the first block of predictors included only verbal and non-verbal mental-age. In the second block of predictors, the accuracy-change factor was added (defined as the percentage change in accuracy between the first and second task halves). The regression model and its results appear in Table 4.4.

	β	R^2	R^2 Change	F Change
Model #1		.117	.117	8.870**
Verbal Mental Age	.175			
Non-Verbal Mental Age	-.428**			
Model #2		.150	.034	5.254*
Verbal Mental Age	.134			
Non-Verbal Mental Age	-.399**			
% Change in Accuracy	-.186*			

Table 4.4 Regression table, describing the two models and the change statistics predicting ADHD symptoms.

$^*p<.05$; $^{**}p<.001$

As shown in Table 4.4, the non-verbal mental age measurement significantly contributed to the regression model, whereas the verbal mental age did not. The second model, which incorporates the proposed accuracy-change index, had increased the explained variability of the model by 3%, and proposed that there was a significant contribution of the change measure. The negative relationship proposes that ADHD symptoms were more severe as the decrement in performance on the CPT increased.

Discussion

This study presents a re-analysis of existing data, and by highlighting the notion of change in performance over time reveals new findings. While Down's syndrome and Williams syndrome children had an overall comparable detection rate on the CPT, the groups differed in their ability to sustain performance over time. A significant decrement in performance was observed only within the group of children with Williams syndrome. To validate that the change in performance over time was related to sustained attention, a multiple-regression analysis was applied with ADHD symptoms as the dependent variable and the percentage change in accuracy as a regressor (controlling for mental-age indices). In accordance with the research hypothesis, the results demonstrated that percentage change in performance contributed significantly to the regression model, explaining added variance in subjective reports of ADHD symptoms. These findings suggest that symptoms of ADHD are more closely related to a task involving visuo-spatial abilities, as reflected in the two levels of the regression analysis: the ADHD index negatively correlated with non-verbal mental age, and negatively correlated with the percentage change in performance. There was no association between the ADHD index and verbal mental-age, a finding that resembles previous reports in children (e.g., Cornish *et al.*, 2012).

Although ADHD is often associated with poor academic skills, including verbal skills, such a difficulty is considered to be secondary, with a late onset (e.g., Ek *et al.*, 2010). Verbal mental age was also assessed using a comprehension task, a language skill less likely to be impaired in ADHD (Andreou, Agapitou & Karapetsas, 2007). Non-verbal skills, on the other hand, are thought to be closely related to attention (e.g., Duncan, 1995; Duncan, Burgess, & Emsile, 1995), and arguably there are strong associations between sustained attention capacity and non-verbal measures of intelligence (Stankov, 1988).

This study addressed a major concern in neuropsychological assessment: while clinical populations often exhibit lower performance than controls in cognitive tasks, their performance pattern is not necessarily driven by comparable cognitive factors. To reveal the processes underlying group differences, it is necessary to extract performance indices that have a theoretical meaning. Specifically, it is argued that, although both Williams syndrome and Down's syndrome children may present a poorer performance on CPTs when compared with age-matched controls, it does not follow that both groups suffer from poor sustained attention. While the CPT was originally designed to measure sustained attention, not all task indices reflect the construct of interest; in relying solely on general accuracy, researchers abandon the temporal element, which is key to understanding sustained attention. Keeping in mind this critical view, it is hard to find any evidence in the literature assessing a *decrement* in performance, rather than *overall* poor performance, in Williams syndrome or Down's syndrome children. According to the results, the Williams syndrome group had difficulty in maintaining their attention during the task, as reflected in a significant accuracy decrement over the second half of the task. In contrast, the Down's syndrome group did not show any sign of decrement. Instead, their pattern of performance over time was similar to that of the control groups, with an overall higher accuracy rate over the second half.

Chapter 5 : Temporal Regularities on a CPT

Abstract

The environment often contains useful information about temporal regularities, for example a traffic light changing or an elevator reaching its destination. Many studies have described the way in which temporal expectations benefit behaviour. Nevertheless, the contribution of temporal expectations to regulating behaviour has never been studied directly in the context of an ongoing CPT. Variations in the CPT are typically deployed to estimate the capacity of maintaining adequate performance level over time. As all CPTs are characterised by a rhythmic pattern, this chapter presents an investigation into the effects of temporal expectations on CPT performance dynamics. In this study, behavioural and pupillometry measures were combined to assess the dynamic adaptation of arousal levels in the presence of temporal regularities. Participants performed a CPT in which the levels of temporal predictability of the stimulus onsets were manipulated. Following the existing literature, changes in pupil diameter were considered to reflect changes in arousal. The results showed an improvement in target detection in the presence of temporal regularities. Regular rhythmic context led to lower overall arousal, as revealed by a decrease in mean pupil diameter, punctuated by phasic increases of arousal in preparation for individual stimulus onsets. In

combination, changes in performance and their pupillometry correlates were interpreted as reflecting an adaptive regulation to task requirements, allowing participants to maintain lower levels of arousal and rely on short-lived engagements when stimulus onset was predictable. The findings were interpreted in the context of Adaptive Gain Theory.

Introduction

In a constantly changing environment, predictions of future events are often necessary to adapt our behaviour efficiently and appropriately. Such predictions may shape the way in which individuals interpret their perceptual experiences (Bar, 2007), or allow them to adjust their behaviour and prepare for the occurrence of an event in a timely fashion (Nobre & Rohenkohl, 2014). The latter form of prediction is often associated with the alignment to rhythmic patterns in our environment, leading the cognitive system to prioritise events that occur in predictable timings while filtering ‘off-phase’ events (Schroeder & Lakatos, 2009). In the absence of predictable temporal structure, a continuous maintenance of adequate performance levels is required to detect unpredictable signals (Fries *et al.*, 2001). While the literature proposes a comprehensive understanding of how temporal predictions are generated and benefit behaviour on a trial-by-trial basis, the aim of the current chapter is to determine whether they also influence the way individuals maintain their performance over time. This study describes how temporal patterns may alter levels of arousal, a key factor in determining performance. Pupil diameter was used as a marker for changes in arousal, and the results were interpreted in accordance with the noradrenergic system within the framework of the Adaptive Gain Theory (Aston-Jones & Cohen, 2005). The experimental investigation presents a new approach for relating arousal to temporal expectations in a CPT based on pupillometry data.

Arousal and its Substrates

As previously discussed in the introduction, one way to conceive of arousal is as a reflection of noradrenergic activation patterns (Robertson & O'Connell, 2010; Murphy *et al.*, 2014). The locus coeruleus is a nucleus in the dorsal pons that provides the source of the neuromodulator noradrenaline to a wide network of cortical areas (Berridge & Waterhouse, 2003; Sara, 2009). The noradrenergic system is implicated in regulating task engagement and optimising performance in response to the environmental context (Aston-Jones & Cohen, 2005; Bouret & Sara, 2005; Murphy *et al.*, 2014). The locus coeruleus firing pattern is characterised by different modes of firing rate leading to a distribution of noradrenalin. Phasic, short-lived locus coeruleus firing rates appear in the occurrence of task-relevant events or are elicited by salient stimuli, and selectively increase neural gain in cortical areas related to the current goal set. A tonic or baseline increase in firing rate is accompanied by the absence of phasic increases and leads to more distractible behaviour (Aston-Jones & Cohen, 2005; Sara, 2009; Clayton *et al.*, 2004; Rajkowski, Kubiak, & Aston-Jones, 1994; Usher *et al.*, 1999).

Locus coeruleus noradrenergic activity is particularly associated with performance in an inverted U-shaped relationship, with performance reaching its peak in intermediate tonic locus coeruleus activity operating alongside the phasic firing rate (Aston-Jones, Rajkowski, & Cohen 1999). This U-shaped relationship often appears in the arousal literature and was recognised by Hebb (1955), who suggested the same relationships between arousal and performance, alluding to similar findings by Yerkes and Dodson (1908). Arousal has been associated with vigilance as one of the two factors explaining why individual performance decays over time. Mackworth (1968) argues that, alongside the general habituation that occurs in response to repetitive and unchanging stimuli, a habituation of the 'arousal response' leads to behavioural deficits. Arousal, according to this view, is an ongoing mechanism that 'allows specific potentials to be more clearly distinguished' (Mackworth, 1968). The notion of arousal being a primary resource underlying performance over time has become an essential part of nearly all theories following in Mackworth's tradition.

The concept of arousal itself, however, has often been presented as being vague and non-specific (Aston-Jones & Cohen, 2005; Vanderwolf & Robinson, 1981). First introduced by Hebb (1955), arousal was proposed as a replacement for the behaviouristic notion of ‘drive’, trying to account for motivational changes guided by the internal state of the organism. According to this view, arousal represents a state or otherwise overall level of activation (Schlosberg, 1954; Duffy, 1957) or energy (Barry *et al.*, 2005), which determines the quality of performance, including the maintenance of vigilance (Parasuraman & Davies, 1984). Arousal is also used in a more common-sense manner when contrasted with sleeping (Vanderwolf & Robinson, 1981), and plays a role in shaping attention, stress, anxiety, and motivation (Aston-Jones & Cohen, 2005). It has recently been proposed that arousal is a construct that reflects noradrenergic activation of multiple cortical sites by the locus coeruleus, which ‘both enhances signal-to-noise ratio of neural signals underpinning perceptual and cognitive representations and increases error rate, particularly at high levels of activation’ (Robertson & O’Connell, 2010). This view is in line with multiple studies associating the arousal function with noradrenergic activity (Berridge & Waterhouse 2003; Robinson & Berridge 1993; Wise & Rompre 1989). When considering the functions of the noradrenergic system in arousal, Robertson and O’Connell (2010) emphasise their role as a prerequisite for attention capacity, and in particular sustained attention.

Posner and Petersen (1990) were the first to propose a direct link between arousal and sustained attention by suggesting that arousal is a key component in one of the three networks of attention. The proposed alerting network relies on 'brain stem arousal system along with right hemisphere systems related to sustaining vigilance' (Petersen & Posner, 2012). The original definition focused on the necessity of a mechanism for preparing (and sustaining the processing of) relevant stimuli, based on the behavioural benefit of a warning signal (Posner, 1978). In a revised version of the attentional networks, it has been suggested that the momentary, short-lived effect of 'phasic alertness' should be distinguished from the ongoing state of 'tonic alertness', which is more related to circadian rhythm and affects performance in long, boring vigilance tasks (Petersen & Posner, 2012). Accordingly, phasic alertness plays a role in responding to cues and allowing a short-lived enhancement of processing. In contrast, tonic alertness (sometimes referred to as 'intrinsic alertness') represents overall wakefulness and arousal (Sturm & Willmes, 2001).

Posner and Petersen's alerting network is represented by Robertson and O'Connell (2010) as a near-reflection of the concept of arousal and the noradrenergic system. Posner and Petersen (1990) also discuss the specific involvement of noradrenaline as a key component of the alerting network. They suggest that alertness relies on cortical right hemisphere structures and noradrenaline release at the locus coeruleus, and is associated with arousal functions reflecting the same mechanism (Robertson & O'Connell, 2010). Alternative definitions of the alerting network emphasise the regulatory connections between the locus coeruleus system and right hemisphere cortical structures (Murphy *et al.*, 2011; Sturm & Willmes, 2001; Minzenberg *et al.*, 2008). A similar, sometimes overlapping, definition implicates sustained attention capacity and noradrenalergic circuits (Sturm & Willmes, 2001; Aston-Jones *et al.*, 1994; Schmidt *et al.*, 2009). The relationship between the right hemisphere functions and the noradrenergic systems is supported by evidence from animal studies, where a lesion to the right frontal cortex decreased noradrenalin release in both hemispheres and the locus coeruleus (Robinson & Coyle, 1980). Findings in animals also showed a right hemisphere bias in locus coeruleus-noradrenergic system and the frontal cortex connectivity patterns (Robinson, 1979). Accordingly, neuropsychological and psychopharmaceutical studies have implicated the arousal function with performance in attentional tasks (Coull *et al.*, 1997; 2001; Greene *et al.*, 2009; Minzenberg *et al.*, 2008; Nieuwenhuis *et al.*, 2007).

When associating alertness and arousal, Robertson and O'Connell (2010) distinguish the noradrenergic arousal system from what they call vigilant attention – a cognitive function that supports the ongoing processing of stimuli, the repetitive and non-arousing qualities of which would otherwise lead to habituation and distraction (Robertson *et al.*, 1997;[10] Robertson & O'Connell, 2010). It is proposed that vigilant attention is controlled by a right-hemisphere cortical network, which monitors and modulates subcortical regions governing arousal (Robertson & O'Connell, 2010; Sturm & Willmes, 2001). The inter-connection between the cortical vigilant attention function and the sub-cortical arousal (or alertness) function allows the vigilant system to maintain an adequate level of arousal in the absence of an externally arousing signal. Multiple studies support the distinction between arousal and vigilant attention, proposing a dissociation between cortical (vigilant attention) and the sub-cortical (arousal) structures regulating performance over time (Smith & Nutt, 1996; Paus *et al.*, 1997; Coull *et al.*, 1995; 1997; 2004). As discussed in the introduction, sustained attention can be best described as the sum of the aforementioned cognitive mechanisms (in particular, levels of alertness, arousal and vigilant attention).

The activation pattern at the locus coeruleus has been characterised in a comprehensive framework suggested by Aston-Jones and Cohen (2005): the Adaptive Gain Theory. According to the Adaptive Gain Theory, the locus coeruleus firing patterns correspond to task-relevant processes and 'serve to

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[10] This definition was first proposed by Robertson *et al.* (1997) to describe sustained attention. The concept of vigilant attention only appeared in later work.

optimise the trade-off between system complexity (which can support a broad range of functions) and efficiency of function (optimising performance in the current task)'. Phasic firing of the locus coeruleus facilitates neural responses to the outcome of the task-relevant event while inhibiting irrelevant events. The tonic firing mode appears to correspond to periods in which the system seeks to explore alternative sources of reward when task demands change or task utility decreases. The two modes of firing (phasic and tonic) were accordingly termed the 'exploration' and 'exploitation' modes (Aston-Jones & Cohen, 2005). Although the Adaptive Gain Theory is essentially a theory that describes how performance is optimised in reward-seeking behaviour and does not assert arousal as the specific function of the locus coeruleus, the authors propose that the notion of arousal is highly congruent with the suggested framework (Aston-Jones & Cohen, 2005). Further works of arousal have established a direct link between the Adaptive Gain Theory and the notion of arousal (Murphy *et al.*, 2011; 2014).

A key concept of Adaptive Gain Theory is the dynamic shifts between the exploration and exploitation modes, either to optimise utility within the current task set (exploitation) or to search for alternative sources (exploration). Consistently with Adaptive Gain Theory, Yu and Dayan (2005; Dayan & Yu, 2006) describe the locus coeruleus noradrenergic response by means of adapting to unexpected uncertainty in task gain: low uncertainty will promote exploitation, and high uncertainty will promote exploration. Although the foundations of the Adaptive Gain Theory responses were set in animal studies and pharmacological interventions (Greene *et al.*, 2009; Minzenberg *et al.*, 2008; Nieuwenhuis *et al.*, 2007; Smith & Nutt, 1996), studies of direct recordings of locus coeruleus tonic activity in monkeys have established a strong association between its firing rate and pupil diameter (Rajkowski *et al.*, 1993 in Aston-Jones & Cohen, 2005). These findings have allowed researchers to apply the principles of the Adaptive Gain Theory by recording changes in pupil diameter, and to confirm that switching occurs between the modes of exploration and exploitation in human subjects (Gilzenrat *et al.*, 2010; Jepma & Nieuwenhuis, 2011; Murphy *et al.*, 2011; 2014; Preuschoff, Hart, & Einhäuser, 2011).

Temporal Structure in the CPT

Temporal predictions could provide an important source of information that might affect arousal regulation. Yu and Dayan (2005) argue that the locus coeruleus noradrenergic response can be viewed as an adaptation to the unexpected uncertainty in task gain. Accordingly, if one accepts the common association between the arousal function and the locus coeruleus firing pattern, the temporal structure of a task can be viewed as a key factor in determining the level of ‘unexpected uncertainty’ of stimuli within the task. When discussing the

CPT in the introduction, it was suggested that various factors such as the target ratio, its length and its temporal structure impact performance. Strikingly, when reviewing the CPT literature, it appears that the temporal structure has never been tested directly before. Whereas studies in the past have manipulated the predictability of targets within the stimulus stream (e.g., Fassbender *et al.*, 2004; Johnson *et al.*, 2007a; 2007b; Manly *et al.*, 2003), such studies refer to the ordinal position of the target (i.e., whether a target will appear once in every ten stimulus-events), and neglect the temporally-predictable nature of the task, which is determined by the use of fixed inter-stimulus intervals.

The CPT literature is inconsistent regarding the temporal structure of the task. While some commonly used CPTs are inherently rhythmic, presenting stimuli at a fixed isosynchronous pace (Cornblatt *et al.*, 1988; Esterman, Rosenberg, & Koonan, 2014; Greenberg, 1987; Mackworth, 1948; Klee & Garfinkel, 1983; Robertson, 1997; O'Connell *et al.*, 2009) or at an alternating fixed rhythm (Conners, 2000; Lee & Park, 2006), other tasks present stimuli at a random pace (Bekker, Kenemans, & Verbaten, 2004; Rosvold *et al.*, 1956; Tsal, Shalev, & Mevorach, 2005; Van den Bergh *et al.*, 2006). There is no clear correspondence between studies investigating sustained attention and studies addressing the influence of temporal expectations on performance using trial-by-trial task designs (e.g. Correa & Nobre, 2008; Mehta, Ulbert, & Schroeder, 2000;

Lakatos *et al.*, 2008; Morgan, Hansen, & Hillyard, 1996; Kim *et al.*, 2007). Other studies investigating temporal expectations through a continuous experimental design (e.g., Womelsdorf *et al.*, 2006) strongly deviate from the classic CPT by using rewards, multiple modalities, and occasional breaks. The aim of the current study, therefore, was to provide an integrated account of how temporal structures and arousal contribute to performance in a CPT.

Current Study

In the current study, the degree of temporal regularity was manipulated to test for the interaction between arousal and rhythmic patterns in a CPT. Pupil dilation was used as a readout of arousal, to determine whether it is influenced by the ongoing, dynamic adaptation to temporal regularities. If confirmed, this would suggest that the inter-stimulus interval parameter, which defines the temporal context in a CPT, is a significant factor in determining the arousal level and therefore highly relevant for measuring sustained attention.

Experiment 5.1 –Temporal Regularities in a CPT

Methods

Participants

All experimental protocols were reviewed and approved by the Central University Research Ethics Committee of the University of Oxford. Participants in the experiment were 30 naïve volunteers (19 of whom were female, mean age 26, STDev=2.1). They were recruited through an online research participation system at the University of Oxford. All had normal or corrected eyesight and were right-handed. They were compensated for their time (£10 per hour).

Apparatus

A PC with an i7 processor and a 2-GB video card was used for displaying stimuli and recording behavioural data. The task was generated using Presentation software (Neurobehavioural Systems, Albany, CA). The stimuli were presented on a 24” LED monitor, with a screen resolution of 1080 X 1920 and a refresh rate of 100 Hz. All stimuli were preloaded to memory using the presentation software to guarantee minimal temporal noise. A video-based eye-tracker at 1000 Hz (EyeLink 1000, SR Research, Ontario, Canada) was used to monitor eye movements and blinks and to measure pupil diameter. The recorded data was saved to an eye-tracking PC.

Stimuli

The experimental paradigm was based on the Masked Conjunctive CPT previously presented in Chapters 2 and 3, and adapted for the current aims. Whereas originally the Masked Conjunctive CPT used a visual mask which induced an illusion of a slight motion (by rapidly alternating two masks with and without an outline), the current variation presented a single static mask to prevent it from influencing the pupillometry data. Additionally, the target-distractor ratio was set to 50–50 (i.e., half of the trials were targets, and the rest were non-targets) to reduce the involvement of response inhibition and sustained attention effort. This way, the experimental investigation could focus predominantly on the influence of the temporal structure on the momentary arousal and minimise the effect of sustained attention effort and performance decrement. The stimulus exposure time was also set to 80 ms to increase the task difficulty and reveal individual differences. To diminish any sustained attention effort, a break was provided in the middle of the task, after 210 trials. The inter-stimulus intervals were manipulated according to three experimental conditions: random epoch (Random), alternating epoch (Alternating) or fixed epoch (Fixed). A full description of the experimental conditions appears in the Procedure section.

Procedure

The experiment was conducted in a dark testing room. Participants were seated 50 cm from the monitor, and a chin rest was used to keep their head still. The eye-tracking device was placed near the monitor and set to record the left eye by default. In three cases, participants wore glasses, and the camera did not provide a constant signal during calibration to the left eye due to reflection. In those cases, the right eye was recorded instead. The session began with a short procedure of calibrating the eye tracker. The task instructions then appeared on the screen and were explained to the participant by the experimenter. The participants were told that a visual mask comprising of overlapping geometrical shapes would appear at the centre of the screen and remain constant for the duration of the experiment. They were told that every few seconds the mask would be replaced very briefly by a single shape they should try and recognise. If participant identified a blue hexagon, they should press the space bar; they ignore any other shape or colour. Following these instructions, there was a short practice session (15 trials) with randomised inter-stimulus intervals ranging between 2000ms and 5000ms (generated using a random function in the code). The experimenter monitored the participants' responses at this stage to ensure the instructions were understood and followed.

After completing the practice session, the participants performed the first part of the experiment consisting of four blocks with different conditions of temporal regularities in the following order: Random -> Fixed -> Alternating -> Random. At the end of the first part, the participants were encouraged to take a short break before returning to the same position. The second part of the experiment consisted of an additional four blocks in the following order: Random -> Fixed -> Alternating -> Random. The same epoch order was maintained across participants. The reason for avoiding the randomisation of the epoch type order was to avoid a potential confound of expectations: participants were always introduced with a random epoch type at the beginning and at the end of the block, so they were not biased to search for any temporal 'pattern' as the task began. All experimental blocks consisted of 60 trials (30 targets), except the Random epochs, which appeared before and after the break and consisted of 30 trials each (15 targets). The two short Random epochs were included to erase any temporal expectations after the break (to prevent participants from expecting to find a 'pattern' as the task began). The trial order was randomised, with a limit of three stimulus repetitions in a row. Epochs within each block changed implicitly without providing participants with any feedback. In total, there were 420 trials, and the experiment lasted approximately 30 minutes.

Within each epoch type, stimuli appeared with different degrees of temporal regularity, according to variations in inter-stimulus intervals. During the inter-stimulus interval, participants were presented with a visual mask. In the random epoch type, the inter-stimulus interval was randomised between 2000 ms and 5000 ms (assigned by a random function generating a uniformed distribution), providing a mean inter-stimulus interval of approximately 3500ms. Although the introduction of a uniformed distribution may bias the results due to temporal hazard effects (e.g., Nobre, Correa, & Coull, 2007), the current study is also unique in the use of a continuous task to investigate the effects of temporal expectations. Therefore, a uniformed distribution was chosen at this point to assimilate to other CPT designs with random temporal patterns (e.g., Bekker, Kenemans, & Verbaten, 2004; Rosvold *et al.*, 1956; Tsal, Shalev, & Mevorach, 2005; Van den Bergh *et al.*, 2006).

In the Alternating epochs, which appeared once on each block, two fixed inter-stimulus interval 'pairs' alternated between trials in a constant order. The inter-stimulus interval pairs alternated between a short interval (2500 ms or 3000 ms) and a long interval (4000 ms or 4500 ms), maintaining an overall mean of 3500 ms. In Fixed epochs, the inter-stimulus interval was held constant. Each participant performed one Fixed epoch on each block (two in total), and the inter-stimulus intervals were either 2500 ms in one block and 4500 ms in the other, or 3000 ms and 4000 ms. The experimental design is illustrated in Figure 5.1

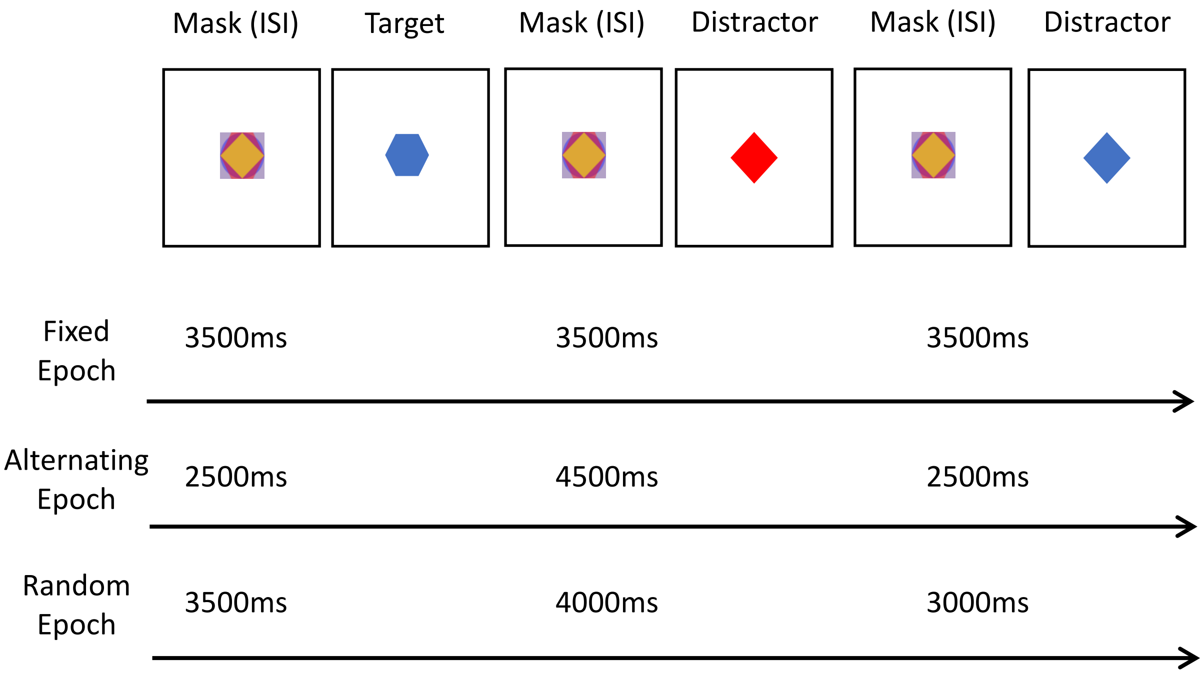

Figure 5.1 Outline of the experimental procedure

Statistical Analysis

Behavioural Data

Experimental conditions were compared based on individual target detection rate (d') and response bias (β). In accordance with the procedure described in Chapter 2, Signal Detection Theory data was calculated based on four possible response types during the task: a correct response to a target, a correct rejection of a distractor, missing a target, or a false alarm when viewing a distractor. RTs were also reported. To maintain an equal number of trials on each condition, the two shortened Random epochs, which appeared at the end of the first block and at the beginning of the second block, were removed from the analysis. As mentioned earlier, the two shortened epochs were only introduced to diminish any expectations for a temporal pattern at the end and the beginning of the experimental blocks.

Pupil Dilation

Pupil dilation was recorded in a 1000-Hz sampling rate, allowing the construction of time series representing pupil size in which every millisecond represented a single sample. The analysis procedure first focused on the changes in pupil size during the one-second period preceding stimulus onset in an attempt to identify markers of rapid changes due to temporal expectations (*Phasic Effects* – a further description appears below). This analysis procedure included only correct responses, to avoid confounding the results with changes that might be associated with errors. A second analysis was carried out to examine overall differences in pupil size between conditions (*Tonic Effects* – a further description appears below). Tonic effects were also examined within the time frame following stimulus onset to try to identify at what point in time tonic differences appear between epoch types.

Missing Pupil Data: before the analysis procedure, missing data was handled by first removing all trials in which participants blinked at onset, or when there were more than 20% of missing pupillometry data during each inter-stimulus interval. The rest of the data was smoothed using a five-milliseconds non-weighted averaging window, and then linearly interpolating the missing data points. This approach was based on previous protocols for handling continuous pupil data (Franklin *et al.*, 2013; Schmidtke, 2014; Van der Meer, 2010).

Phasic Effects: phasic effects were defined as rapid changes in pupil diameter in association with temporal expectations. Based on previous studies showing that a temporal structure leads to temporal expectations, the analysis procedure assessed whether such expectations appeared in the current dynamic task-design (the CPT) and whether they were reflected in pupil diameter. The course of the phasic change in pupil diameter was estimated over the last portion of each inter-stimulus interval, and the mean time series were averaged on epoch type, for each participant, separately. The time frame of interest was the time window 500 ms before stimulus onset (hereafter *Pupil-Change Series*). Choosing a time window of 500 ms was based on previous studies showing a reliable change in pupil diameter in comparable time frames (Kuipers & Thierry, 2011; Naber, Alvarez, & Nakayama, 2013; Wierda *et al.*, 2012; Zylberberg, Olivia, & Sigman, 2012). After extracting the mean Pupil-Change Series for each participant on each epoch type, this data was compared to an appropriate baseline. The baseline was calculated by averaging the pupil size over the 500-ms period that preceded the Pupil-Change Series for each participant on each epoch type. Three analysis procedures were carried out, in which the Pupil-Change Series for each participant was compared to its relevant baseline. The comparisons relied on a permutation t-test based on 50,000 permutation samples. The resulting distribution for each data point (500 observations, representing 500 ms) was compared to a critical t-value ($p<.05$) corrected for multiple comparisons based on the 't-max' method (Blair & Karnisky, 1993; Westfall & Young, 1993). This approach was the same as that used by various previous studies to assess changes in pupil diameter over time (e.g., Silk *et al.*, 2011; Vanderhasselt *et al.*, 2015).

Tonic Effects: tonic differences between conditions were calculated based on a direct comparison of the pupil size (in raw values obtained from the eye-tracker) between conditions, using the permutation test. After identifying time frames that were indicative of tonic changes (see Results), a further *post hoc* analysis was carried out comparing the mean pupil size (in standardised values) within the time frame of interest.

Results

Behavioural Data

Before running the analysis procedure, three participants who performed at chance level were removed from the analysis. The first statistical comparison relied on a repeated-measures ANOVA with two within-subjects factors: the experimental block (Block 1, Block 2) and the three epoch types within the block (Random, Fixed, Alternating). When comparing target detection rate (d'), the ANOVA revealed a significant main effect of epoch ($F(2,52) = 5.556$; $p = .007$; partial $\eta^2 = .176$). There was no significant effect of block ($F(1,26) = 2.038$; $p = .165$) or interaction between block and epoch ($F(2,52) = 1.877$; $p = .163$). When repeating the same procedure to analyse differences in perceptual criteria (β), there was a significant main effect of epoch ($F(2,52) = 3.962$; $p = .025$; partial $\eta^2 = .132$). There was no significant effect of block ($F(1,26) = .275$; $p = .605$), and there was a significant interaction between epoch and block ($F(2,52) = 3.529$; $p = .037$; partial $\eta^2 = .120$). There were no significant differences in RT when comparing either epoch ($F(2,52) = 1.914$; $p = .158$), block ($F(1,26) = 1.931$; $p = .176$), or their interaction ($F(2,52) = 1.029$; $p = .364$). The criterion and perceptual sensitivity data are depicted in Figures 5.2 and 5.3

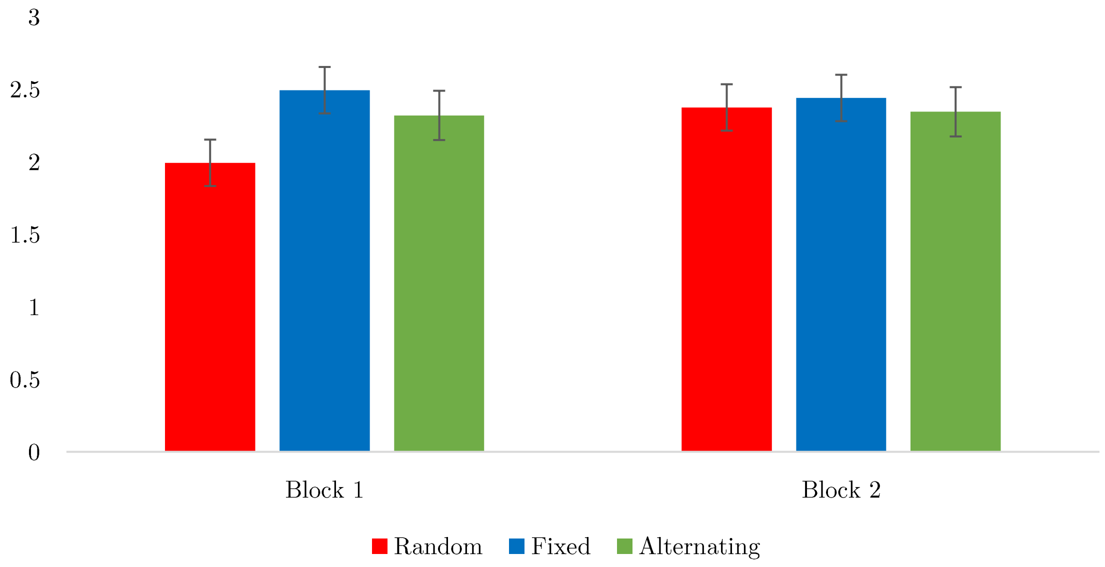

Figure 5.2 Mean perceptual sensitivity on each epoch (error bars represent SE)

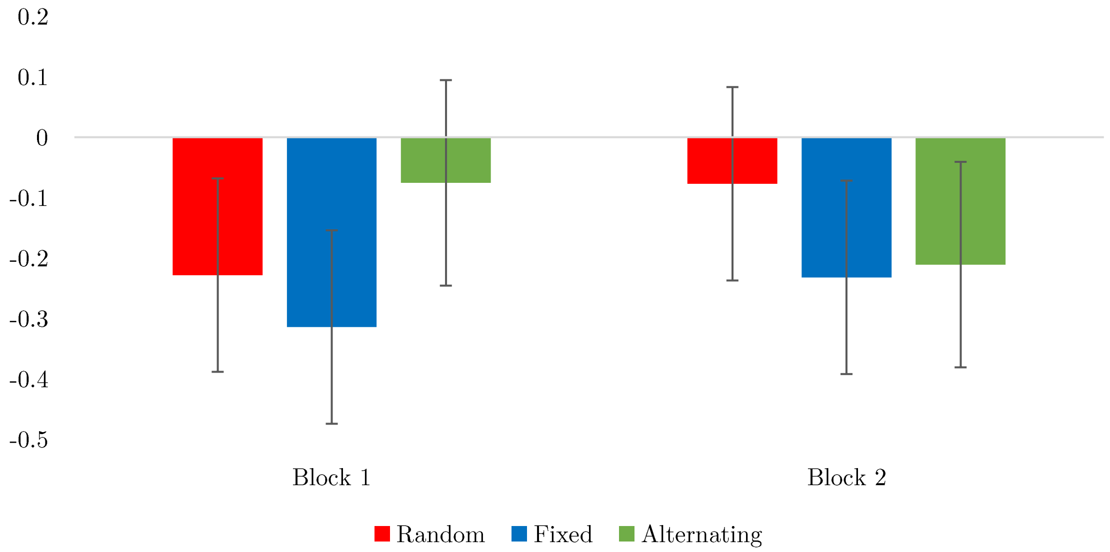

Figure 5.3 Mean criterion on each epoch (error bars represent SE)

To further understand the observed effects, a series of *post hoc* comparisons was carried out. The first comparison focused on the differences between the perceptual sensitivity over different epoch types. The lack of a main effect of block or an interaction between block and epoch allowed the grouping of the data according to epoch types across blocks. Compared to the Random epoch type, sensitivity to detect targets was higher in both Fixed (t(26)=-4.523; p<.001; 95% CI [-.53;-.20]) and Alternating (t(26)=-2.621; p=.014; 95% CI [-.43;-.05]) conditions. Performance in Fixed and Alternating epochs did not differ (t(26)=1.180; p=.249). The mean detection rate on each epoch type, grouped across blocks, is illustrated in Figure 5.4.

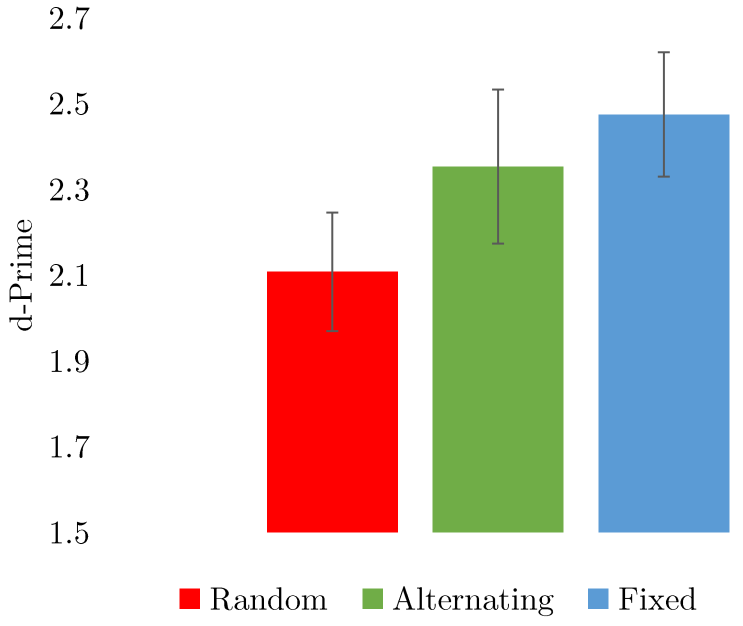

Figure 5.4 Mean perceptual sensitivity on each epoch type (black lines represent standard error of the means)

A second series of *post hoc* comparison was aimed to analyse the main effect of epoch and the interaction between epoch and block observed when comparing the response bias. First, each epoch type was grouped across the two blocks to compare the response bias according to epoch. There was a significant difference in β between the Fixed and Alternating epoch (t(26)=-3.309; p=.003; 95%CI[-.22;-.05]), and between the Random and Alternating (t(26)=-.106; p=.92). The Alternating and Random epoch types did not differ significantly (t(26)=2.163; p=.04; 95%CI[.00;.26]), As illustrated in Figure 5.5, performance in the Fixed epoch type was less conservative when compared with Random and Alternating, characterised by a lower perceptual bias indicating a greater tendency to committing false alarms.

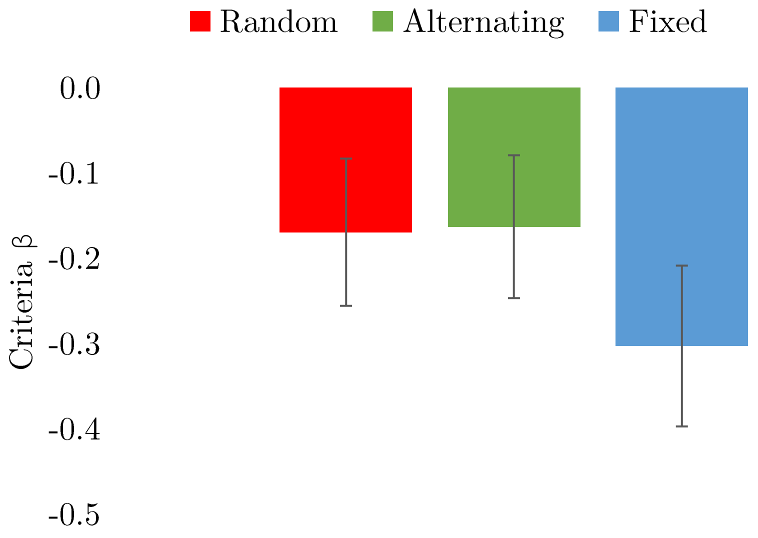

Figure 5.5 Mean response bias on each epoch type (black lines represent standard error of the means)

Finally, the interaction between epoch and block was analysed using a series of paired comparisons. When comparing the epoch types on each block separately, there was a significant difference between the Fixed epoch type and the Alternating epoch type only in the first block (t(26)=-3.639; p=.001; 95%CI[-.37;-.10]), and the two epoch types did not differ significantly on the second block (t(26)=-.362; *p*=.72). The Random epoch type differed from the Fixed only on the second block (t(26)=-2.264; *p*=.03; 95%CI[-.29;-.01]), and the two did not differ in the first block (t(26)=.816; *p*=.42). As illustrated in Figure 5.5, the two significant simple effects were resulted from a lower β value in the Fixed condition.

Phasic Pupil Changes Before Stimulus Onset

To assess whether the temporal predictability of onset affected pupil size before a target appeared, phasic changes in pupil diameter were compared between the 500 ms preceding the target and a baseline based on the preceding 500 ms (between -1000ms and -500ms before onset). The results of three comparisons, based on permutation t-tests, are illustrated in Figure 5.6.

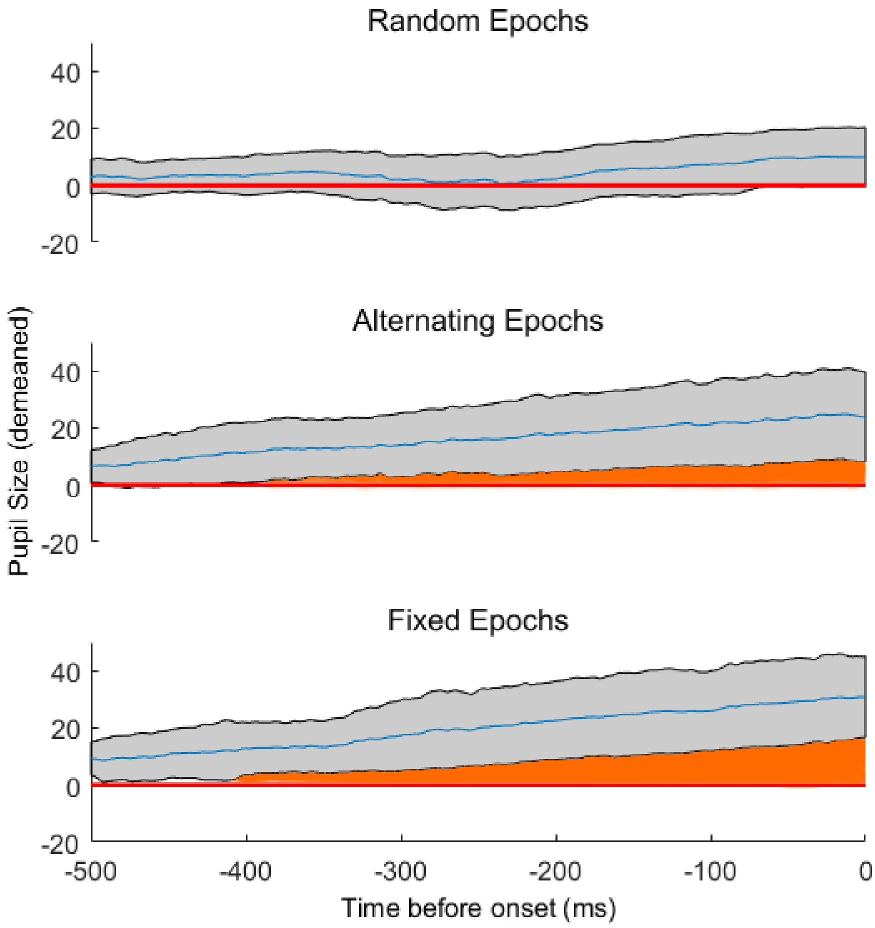

Figure 5.6 Three separate comparisons between mean baseline and mean Pupil Change Series. The red line represents the baseline, the blue line represents the PCS, and the shaded grey area represents the 95% CI obtained in the permutation test. The orange colour indicates periods in which the pupil size during the Pupil Change Series significantly differed from baseline

The comparisons show a reliable difference between baseline and pupil size over the period preceding stimulus onset in the presence of temporal regularities. This data reveals rapid, phasic changes in pupil diameter before stimulus onset in the presence of temporal regularities. There was no significant difference between the baseline and the Pupil Change Series in any of time point of the comparisons.

Tonic/Baseline Differences in Pupil Diameter

To estimate tonic differences between conditions, the mean absolute pupil size was compared between epoch types. A permutation t-test was used to contrast Random, Fixed and Alternating epochs directly. As in the previous section, this analysis focused on the time frame of the one-second period preceding the stimuli, only this time there was no differentiation between the baseline period and the anticipation. Instead, the mean pupil size values were compared directly. The use of a time frame of one second allowed extending the Pupil Change Series and reducing the influence of expectations-related changes, while also allowing at least a one-second period of recovery from changes related to stimulus presentation (the shortest inter-stimulus interval in the task was two seconds). The results are illustrated in Figure 5.7.

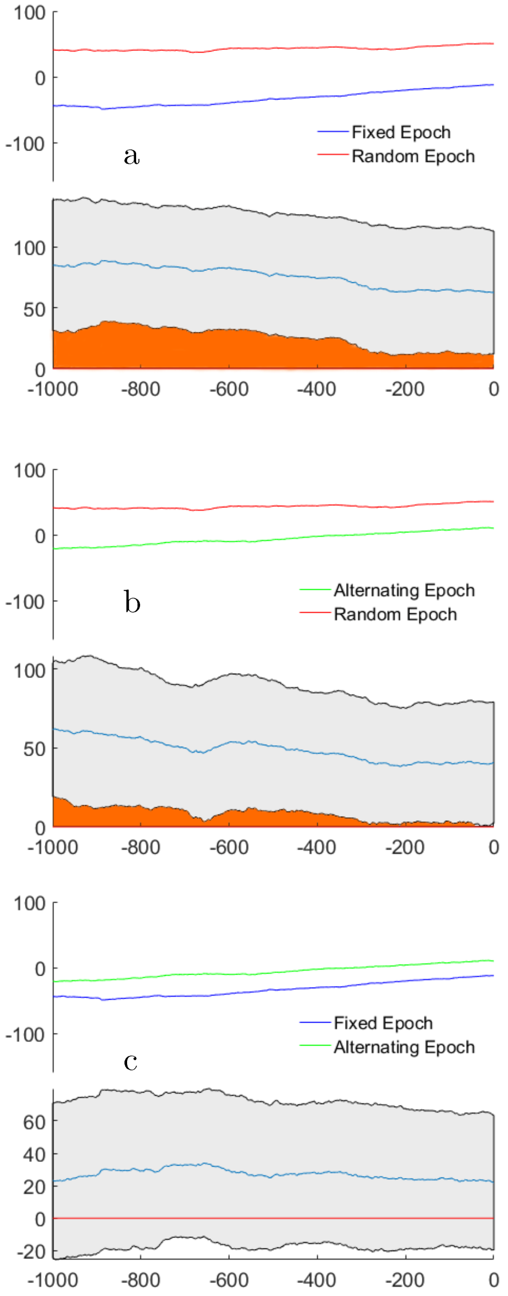

Figure 5.7 Comparing the pupil size in trials with correct responses over a one-second period before stimulus onset in Fixed and Random epochs (panel a), Alternating and Random epochs (panel b), and Fixed and Alternating epochs (panel c). Data is presented in demeaned arbitrary values obtained from the Eyelink 1000 system (subtracting the mean value of each two lines for illustration purposes). The upper graph represents the average value on a ms by ms basis across trials, and the bottom graph represents the permutation t-test comparison: the blue line as the mean difference between conditions, the shaded grey area as the 95% CI of the comparison, and the orange representing points in time in which pupil diameter differed

The comparisons between epochs with a predictable onset time (Alternating and Fixed) and the Random epoch revealed a consistent significant difference in the time-window of interest. This data suggests that temporal predictability tonically decreased the overall pupil size.

Pupil Size at Onset and Task Performance

Pupil diameter is thought to be associated with overall cognitive arousal (Aston-Jones & Cohen, 2005; Murphy *et al.*, 2011; 2014). The next analysis, therefore, used pupil size to determine whether the arousal level at onset time was associated with performance levels. The analysis focused on the pupil size at onset time, as it reflects the added value of two effects: the 'tonic state', or the overall 'baseline' arousal, and any added phasic increase in arousal that precedes onset time. The expected relationship between arousal and performance is thought to be non-linear, following a U-shaped distribution (Dodson & Yerkes, 1908; Hebb, 1955; Aston-Jones & Cohen, 2005). Intermediate levels are optimal for performance, whereas high arousal is thought to lead to high levels of distractibility and low arousal to inattention (Aston-Jones & Cohen, 2005). The relationship between arousal and performance was calculated by first standardising all pupil-diameter values (converting to Z-values), and then splitting the data into ten equally sized bins according to the standardised pupil size. For each participant, the response bias and the perceptual sensitivity were calculated on each bin, and a repeated-measures ANOVA was run with the bin number as a within-subjects factor and performance as the dependent variable. To test whether performance and arousal were related in a U-shaped distribution, the data was fitted to a quadratic contrast. When comparing the perceptual criteria, the ANOVA test for a quadratic contrast was significant (F(1,25)=8.370; p=.008; partial η^2=.251). When reanalysing the data to search for a linear relationship, the effect was not significant (F(1,25)=.114; p=.738). Repeating the same procedure with the detection rate as the dependent variable resulted in no significant effects, either for a quadratic contrast (F(1,25)=.575; p=.455) or a linear contrast (F(1,25)=3.207; p=.085). The data for the detection rate and perceptual criterion as a function of the pupil size bin are depicted in Figures 5.8–5.9.

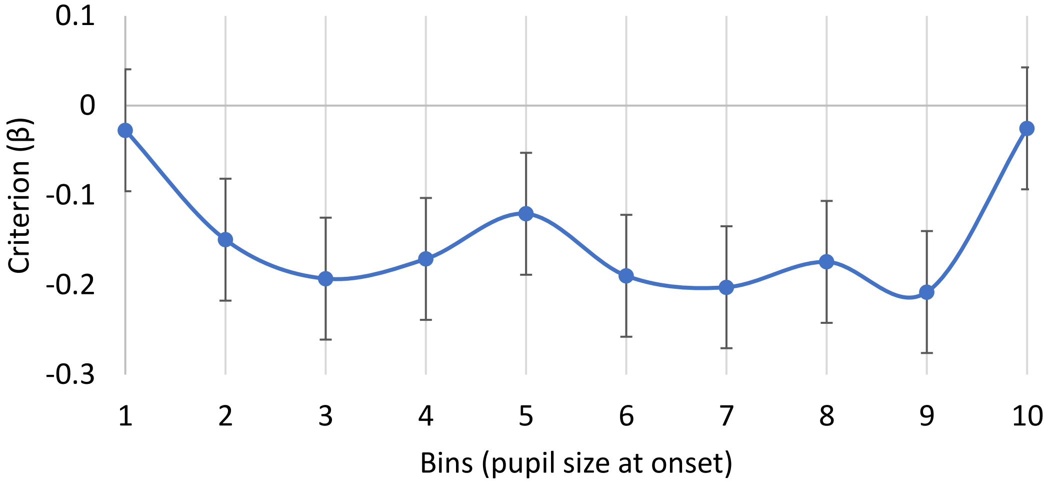

Figure 5.8 The mean response bias as a function of the pupil size bin. Black lines represent standard errors. The data significantly fitted a quadratic contrast

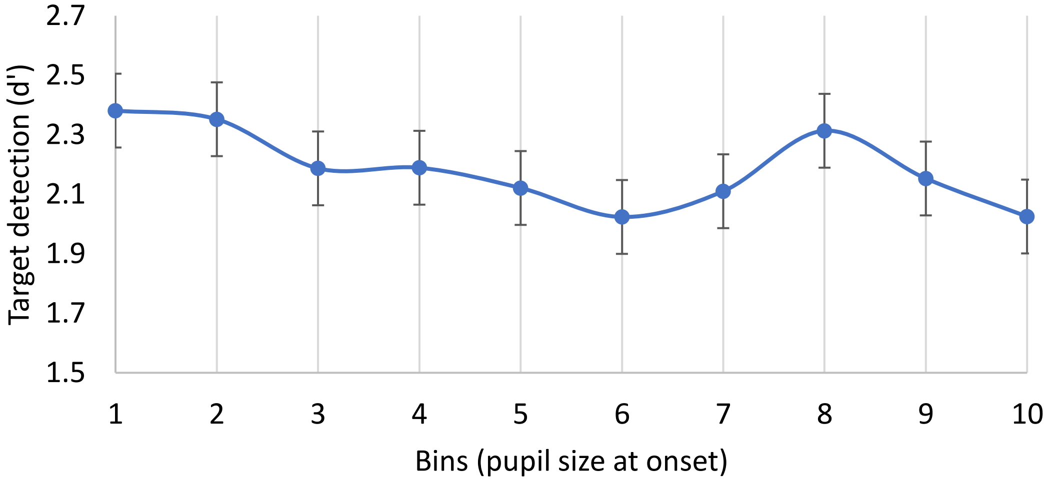

Figure 5.9 The mean perceptual sensitivity as a function of the pupil size bin. Black lines represent standard errors

The data showed that the pupil size in onset time is associated in a U-shaped relationships with the response-bias. Previous works have shown that an increase in the response bias β is associated with a decrease in sustained attention capacity (e.g., Davies & Parasuraman, 1982; Van der Meere & Sergeant, 1988; Warm & Kerison, 1984). According to such view of sustained attenion, the criterion shift towards negative values (in the current study the optimal point was at approximately -0.2) is associated with higher task engagement, leading to a smaller number of missed targets and an increase in false alarms. Sustained attention in the current study was lowest when pupil size was either largest of smallest, in a pattern resembling the predictions of the Adaptive Gain Theory when accounting for arousal and performance (Aston-Jones & Cohen, 2005; Murphy *et al.*, 2011; 2014).

The association reported here between pupil diameter and response bias thus supports the notion of arousal as a fundamental component of sustained attention. The null effect reported when testing the relationships between detection rate and pupil size is in line with previous works, which seldom reflect sustained attention in CPT designs (for a discussion see Parasuraman, Warm, & See, 1998, or the introduction to this thesis).

Discussion

The study revealed dynamic shifts in pupil response and performance level in accordance with the temporal structures introduced in the task. As asserted in the introduction, pupillometry can be considered a reflection of the noradrenergic arousal function. Based on the findings, it can be argued that the inter-stimulus interval factor, which defines the temporal uncertainty level in a CPT, is key to determining performance modes of operation.

The results concur with the Adaptive Gain Theory concept of phasic-tonic, exploration-exploitation modes of operation that are adjusted in accordance with the overall uncertainty to increase task utility. Random epochs represented high uncertainty, whereas alternating and fixed epochs represented low temporal uncertainty. The results showed that temporal expectations (1) improved performance; (2) phasically increased pupil size; and (3) tonically decreased pupil size. During the experiment, the pupil size at onset time was associated with the perceptual criterion parameter (with a bias towards either committing a false alarm or missing target) in a U-shaped relationship. This observation is in line with the familiar interpretation of the arousal function (Aston-Jones & Cohen, 2005; Hebb, 1955; Yerkes & Dodson, 1908).

The results may retrospectively illuminate a fundamental difference between past studies measuring performance maintenance. It appears that the temporal predictability (or uncertainty) strongly affects cognitive arousal. Studies of vigilance, sustained attention, or alertness may, therefore, differ in their results based on the temporal characteristics of the task. In particular, it has been shown here that, in the presence of a temporal structure to entrain to, the indirect measure of the noradrenergic system switches to a more efficient mode of activity, i.e., an overall decrease in pupil diameter, alongside a phasic increase in task-relevant events. The capability of switching to a more efficient mode of operation in the presence of rhythmic patterns might be one explanation for the frequent reports of a lack of performance decrement in short CPTs (Robertson *et al.*, 1997; Robertson & O'Connell, 2010). In the classic Clock Test, Mackworth (1948) reported an evident decrement after only 30 minutes. In view of the findings presented in this study, it should be noted that the Clock Test (Mackworth *et al.*, 1948), the SART (Robertson *et al.*, 1997), the Continuous Temporal Expectation Task (O'Connell *et al.*, 2009), and many more, are CPTs where the stimuli presentation appears rhythmic and shows no evident performance decrement at short task durations (< 30 min).

As illustrated in Chapter 3, when the stimulus stream appeared at random intervals, a subset of a clinical and ageing population showed a decrement in performance in a task lasting approximately 12 minutes. Similarly, in another CPT with random intervals, Van den Bergh *et al.* (2006) reported a decrement in performance in part of their focus group after approximately 24 minutes. Potentially, this decrement observed after a relatively short duration could be attributed to using unpredictable stimulus onset, increasing overall uncertainty and leading the system to operate in a less efficient and more effortful mode. Although a decrement in performance did not occur in the current study, this effect was not expected: the task was intentionally designed to be immune to performance decrement by using a design which is perceptually challenging, with a break between blocks, a relatively high proportion of targets (50%), and alternating between epochs which may challenge the system – all task properties that prevent performance decrement (Robertson & O'Connell, 2010).

It can be speculated that the findings presented here reflect an intersection between two familiar mechanisms: cognitive arousal and its relation to the locus coeruleus-noradrenergic system (Aston-Jones & Bloom, 1981; Aston-Jones & Cohen, 2005; Minzenberg *et al.*, 2008; Rajkowski, Kubiak, & Aston-Jones, 1994; Sara & Bouret, 2012) and behaviour in rhythmic and continuous modes of operation (Newhall, 1923; Schroeder, Herrero, & Haegens, 2014; Schroeder & Lakatos, 2009; Fries *et al.*, 2001). The proposed contribution of this study is that it shows rhythms to be reflected in the arousal function itself (measured indirectly using pupillometry) and not only in the characteristic brain oscillations in response to temporal patterns (Schroeder, Herrero, & Haegens, 2014). Such an interpretation assumes that the interconnectivity between cortical structures and the locus coeruleus allows a modulation of the firing pattern to adjust to the task demands.

An interesting aspect of this study is the use of the alternating epoch, in which temporal predictability was determined by a rhythm based on two alternating intervals. In that respect, the paradigm deviates from the findings showing automatic stimulus-driven effects of entrainment to an isosynchronous rhythm (Jones, 2010; Sanabria, Capizzi, & Correa, 2011; De La Rosa *et al.*, 2012), and present a rhythmic pattern guided by memory for intervals (Breska & Deouell, 2017). The behavioural benefit obtained in the alternating epoch demonstrates that the arousal function not only corresponds automatically to rhythm, but can also be modulated by memory-guided expectations. The involvement of frontal regions and the Anterior Cingulate Cortex in modulating the locus coeruleus firing pattern could explain how memory-guided adaptation can affect arousal (Aston-Jones & Cohen, 2005; Sturm & Willmes, 2001).

To conclude, the temporal-predictability factor in a CPT should be considered as crucial for determining the course of arousal over time. This view of the system behaviour in performance maintenance can account for conflicting results in the literature that may lead to a misunderstanding of functions like sustained attention, vigilance and alertness. Based on the findings, future studies may focus on performance decrement in varying levels of temporal predictability, and imaging and electrophysiological measures might reveal whether entrainment effects that appear in cortical activity are associated with the extent of tonic and phasic differences in pupil diameter and/or locus coeruleus activity.

Chapter 6 : The Theory of Visual Attention Modelling of Temporal Regularities

Abstract

The Theory of Visual Attention is a mathematical model providing a comprehensive account of attention-related processes. The Theory of Visual Attention has previously been applied to describe the way in which temporal expectations and changes in phasic alertness affect information processing. Typically, the results indicate a marked improvement in visual processing speed when the stimulus onset is predictable, or when the system is alerted by an exogenous warning signal. The current study was designed to estimate whether perceptual parameters in the Theory of Visual Attention are sensitive to the temporal regularities implemented in a CPT. In a novel experimental design, participants viewed a continuous stream of arrow-shaped targets, each followed by a visual mask, and were requested to indicate their direction during the inter-stimulus intervals. The inter-stimulus intervals were manipulated across different conditions so that targets appeared in either a fixed, isosynchronous rhythm or unpredictably within a random temporal structure. The task allowed the extraction of two Theory of Visual Attention parameters: the visual processing speed and the perceptual threshold. The results replicated previous findings

showing that temporal expectations improved visual processing speed. Strikingly, random temporal structures also conferred a unique benefit, yielding lower perceptual thresholds. The results are interpreted in line with previous findings in this thesis, and placed within the framework of random versus rhythmic modes of operation and their potential influence on sustained attention.

Introduction

Temporal aspects of attention, such as the capacity of performance maintenance, are typically described within multifaceted frameworks describing how attention is controlled, maintained over time, and operates in space (e.g., Parasuraman, 2000; Posner & Petersen, 1990; Petersen & Posner, 2012). An alternative approach to understanding and describing attention is to focus on the processes underlying its primary behavioural function: selection. While multifaceted models of attention (e.g., Posner & Petersen, 1990; Parasuraman, 2000) propose measuring how attention is maintained over time (alertness/vigilance) and how the selection priorities are determined (control/execution) separately, they share the view that the end goal of attention is an effective selection. One of the most influential models of attentional selection is the Biased Competition Model (Duncan & Humphreys, 1989; Desimone & Duncan, 1995), which rejects one of the key assumptions made by Posner and

Petersen (1990). Whereas Posner's Orienting Network is proposed to control spatial attention in a serial, 'spotlight' fashion (Posner & Petersen, 1990), the Biased Competition Model sees attention as a parallel process of selection in which sensory elements compete for representation in a limited-capacity short-term memory store (Desimone & Duncan, 1995). The Biased Competition Model was formulated mathematically as part of the Theory of Visual Attention (Bundesen, 1990). The Theory of Visual Attention provides a detailed description of the factors determining selection based on a group of equations incorporating the capacity of the short-term memory supporting attention, the minimum time required before processing can begin, the speed at which stimuli are processed once perceived, the attentional weights allocated to perceived elements, and the efficiency of top-down control. Subsequently, the Theory of Visual Attention has been used to characterise attention in the neurologically healthy individuals (e.g., Finke *et al.*, 2005; McAvinue *et al.*, 2012a,b; Chechlacz *et al.*, 2015a) and in various clinical populations (e.g., Bublak *et al.*, 2005; Habekost & Bundesen, 2003; Duncan *et al.*, 2003) to account for inter-individual differences in attention functions and dysfunctions.

The Theory of Visual Attention is normally described by two main equations: the rate equation and the weight equation. The rate equation describes the rate $v(x,i)$ at which a specific categorisation of x as belonging to category i is encoded into Visual Short-Term Memory. The weight equation determines the relative attentional weight allocated to object *x* according to the momentary importance of attending to objects that belong to a specific perceptual category. The sum of all rate values (*v*) across the visual field defines the overall processing speed (*C*). When participants are requested to identify a single target stimulus, the Theory of Visual Attention also provides predictions about the process of target detection. The equation that defines the single-stimulus recognition is a mathematical derivation of the biased-choice model proposed by Luce (1963) (see Bundesen, 1990, 1993; Vangkilde, Petersen & Bundesen, 2013), according to which the probability of making the categorisation '*x* belongs to i' at or before time *t* is given by the formula

$$p(t) = 1 - e^{-v(x,i)(t-t0)}$$

where t_0 is the longest ineffective exposure duration of a masked stimulus, and *v(x,i)* is the processing speed (or the number of visual elements that can be processed within a given time range). Since the rate *v(x,i)* represents the rate value of a single stimulus, it is equal to the aforementioned overall processing speed *C*. The single-target equation can be fitted to experimental data obtained by calculating the mean accuracy in categorisation as a function of the target exposure duration. Figure 6.1 exemplifies the fitting of the single-target categorisation function to a theoretical data set of a single participant.

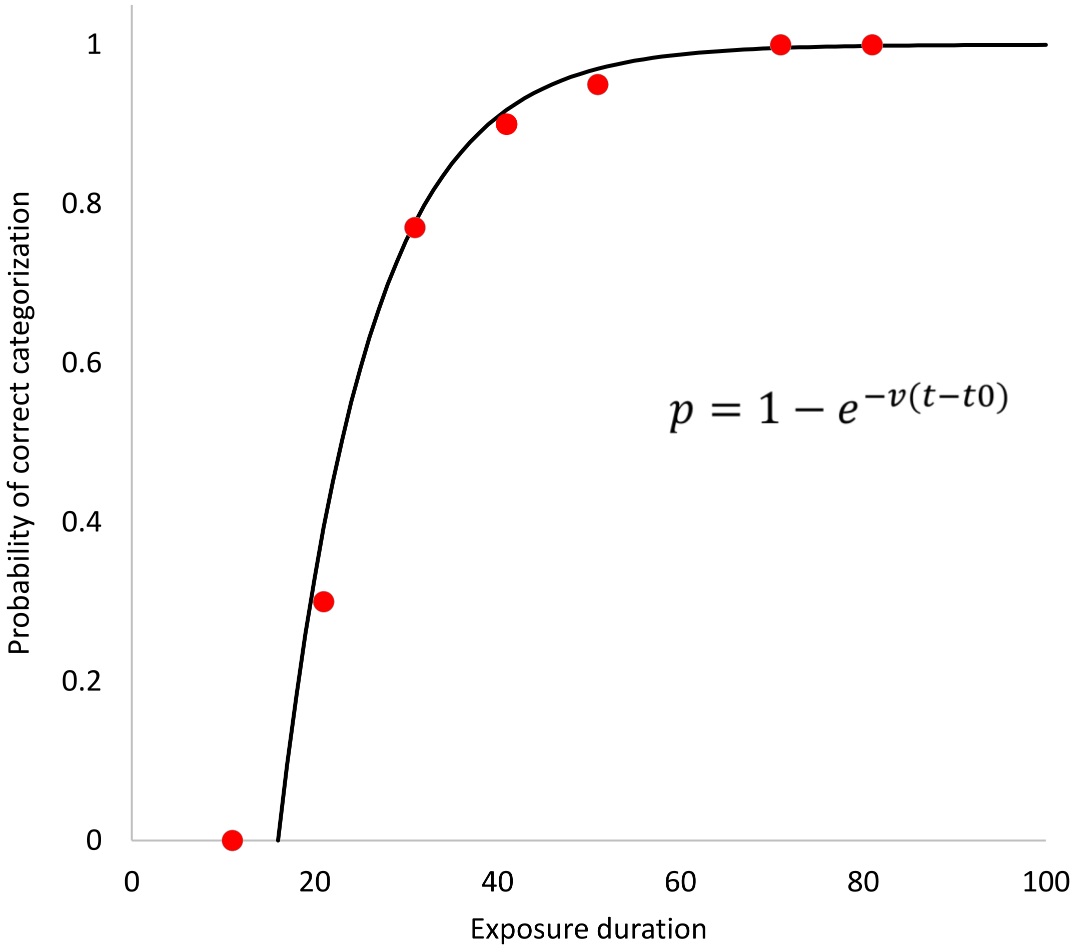

Figure 6.1 Typical results obtained by fitting real observations in performance (red marks) to the single-target identification exponential function (black line). In this example, a single participant identified targets presented in seven possible exposure durations: 10ms, 20ms, 30ms, 40ms, 50ms, 70ms and 80ms. The data was fitted to the function, which is determined by two terms: the perceptual threshold and the processing rate. The results obtained by the fitting procedure predict that the perceptual threshold sufficient to evoke conscious processing is >16ms, and the processing rate is 100 items per second

The single-stimulus categorisation equation has been used in experimental research studying temporal attention. Such studies have discussed the influence of temporal expectations (foreperiods and their hazard rates) on the Theory of Visual Attention parameters underlying the selection of a single target (e.g., Vangkilde, Coull, & Bundesen, 2012; Vangkilde, Petersen & Bundesen, 2013), as well as the benefit of a warning signal evoking phasic alertness (Petersen *et al.*, 2017; Wiegand *et al.*, 2017). Typically, in studies requiring individuals to identify a single target in a fixed location, the findings show a marked increase in the visual processing speed (*c*) accompanying temporal expectations or increased phasic alertness, (e.g., Petersen *et al.*, 2017; Vangkilde, Coull, & Bundesen, 2012; Vangkilde, Petersen & Bundesen, 2013). Comparable findings were also observed when using an isochronous rhythm to entrain the visual system before presenting a single-target (Oderkerk *et al.*, 2016) and when presenting a warning signal in partial- or full-report tasks in which visual stimuli were spatially distributed (Matthias *et al.*, 2010; Wiegand *et al.*, 2017).

Alongside the increase in processing speed in association with phasic alertness, Petersen *et al.* (2017) also identified a lowering of the perceptual threshold parameter (t_0) following a warning signal. Nevertheless, when systematically manipulating the intensity of the warning signal that preceded the target, the only parameter that changed accordingly was the processing speed. The authors concluded that, as opposed to the sensitivity of the processing speed to varying levels of alertness resulted by the warning signal intensity, the perceptual threshold ‘seems to be equally reduced regardless of the level of phasic alerting’ (Petersen *et al.*, 2017). In another study manipulating temporal expectations (rather than phasic alertness), the perceptual threshold remained constant whereas the processing speed increased with elevated expectations (Vangkilde, Petersen & Bundesen, 2013). It appears, therefore, that the processing speed provides a better marker of the enhanced processing effect that accompanies alertness and temporal-expectations. The threshold change might be attributed to a more general change in the cognitive system that follows a warning signal, although more research is needed to establish its role. A further finding, which is highly relevant for the conclusions presented in Chapter 5, is that Petersen *et al.* (2017) found an association between the changes in phasic alertness with a phasic increase in pupil diameter. The authors recorded the pupil dynamics in response to the alerting signal and demonstrated a larger increase in pupil size following a warning signal when compared with the no-cue condition. The extent of the pupil size increase also corresponded to the intensity of the warning signal, and was correlated with the perceptual-speed parameter. Although the study design was different from the one presented in Chapter 5, both studies demonstrated a behavioural benefit associated with a 'short-lived' phasic increase in pupil dilation.

Current Study

A fundamental difference between the approach used to describe the behavioural benefit of alertness and temporal expectations using Theory of Visual

Attention parameters and the experimental studies presented in this thesis is the use of a paradigm providing responses on a trial-by-trial basis. The current study was designed to bridge this gap, and to enable the estimation of Theory of Visual Attention parameters in a CPT design. For this purpose, a new task was designed for modelling the categorisation of a single target appearing in a continuous stream of stimuli. The experimental design allows for the estimation of processing speed in relation to temporal expectations in a continuous, dynamic task, in which a categorisation of a stimulus appearing in a predictable onset is contrasted with that of a stimulus appearing unpredictably. The primary manipulation in this study resembles that of Chapter 5: a rhythmic pattern using fixed inter-stimulus intervals was contrasted with a random-interval pattern. Additional task features involved manipulating stimulus-exposure duration, including more frequent breaks, and presenting only task-relevant stimuli (no distractors or non-targets). These changes further depart from the traditional approach to studying sustained attention to focus instead on the way in which performance is affected by temporal intervals in a CPT.

One motivation was to replicate and extend previous findings of benefits to processing speed by temporal expectations. A further (and speculative) hypothesis was that temporally unpredictable stimulus would lower perceptual thresholds. As argued in Chapter 5, performing a task in which stimulus onset is entirely unpredictable promotes a *continuous mode* of operation (Schroeder & Lakatos, 2009). In such a mode, the cognitive system switches to a less ‘energy efficient’ mode in which constantly attempts to identify environmental changes. Accordingly, it was argued in Chapter 5 that detecting occasional targets on a CPT in which inter-stimulus intervals are randomised is accompanied by a tonic increase in pupil-diameter, which reflects the state of the system in an ‘exploration’ mode. Such an exploration potentially supports performance in a state of an ongoing uncertainty, to allow the detection of unpredictable signals. It is possible that such a tonic or continuous mode of operation might result in an ongoing decrease of the perceptual threshold parameter. According to this hypothesis, an unpredictable event might need a shorter exposure duration to be consciously perceived. Whereas this prediction has never been tested before, it seems intuitively appealing: when we cannot predict when an event will occur, we may likely be more sensitive to environmental changes (i.e., lowering the perceptual threshold), while concurrently being less efficient in processing such unpredictable changes (i.e., showing slower processing speed when compared with a categorisation of predictable events). Such ineffectiveness, if identified, could yield further prediction about attention and performance in a broader context: as the perceptual threshold represents the minimum time required before processing can begin, it might also affect the efficiency of other aspects of attention. For example, the calculation of attentional weights allowing to selectively prioritise it is thought to occur during the time interval between stimulus presentation and the time of perceptual threshold (e.g., Dyrholm, 2011). Therefore, a shorter perceptual threshold duration may also imply ineffective selection. Whereas the current experimental design will not address this issue directly, if the research hypothesis is confirmed it might (theoretically) have further implications on other parameters that should be verified in the future.

Methods

Participants

Participants in this experiment were 30 naïve volunteers (17 of whom were female, mean age 25, SD=2.7). They were recruited through an online research participation system at the University of Oxford. All had normal or corrected eyesight and were right-handed. They were compensated for their time (£10 per hour).

Apparatus

A PC with an i7 processor and a 2GB video card was used for displaying stimuli and recording behavioural data. The task was generated using presentation software (Neurobehavioural Systems, Albany, CA). The stimuli were presented on a 24” LED monitor, with a screen resolution of 1080 X 1920 and a screen refresh rate set at 100 Hz. All stimuli were preloaded to memory using the presentation software to guarantee minimal temporal noise.

Stimuli

One of two coloured masks (*Mask A and Mask B*), comprising of 16 bi-directional arrows circumscribed in two circles coloured in red and blue (see Figure 6.2), appeared at the centre of the screen. The total size of the mask occupied approximately eight degrees of visual angle. Following the presentation of the mask, a single arrow target pointing at one of eight possible directions appeared for a varying duration (10/20/30/50/80ms). The arrow was immediately replaced by a mask. The two masks (A and B) alternated between trials so that one mask always replaced the other. This way, even if participants did not perceive the arrow target, they were informed that a new trial had begun. Participants were instructed to try to identify the target and to respond by indicating its direction using the arrow numpad, in which eight arrows pointing at different directions appeared at a corresponding location (see figure 6.2). The responses were recorded during the inter-stimulus interval in which the mask was presented.

The task consisted of 6 blocks with 120 trials each. The blocks alternated between two conditions. On a Fixed block, a target appeared every 3.5 seconds; on a Random block, the inter-stimulus intervals varied randomly between 2–5 seconds (mean inter-stimulus interval was 3.5 seconds). Fixed and Random blocks always appeared successively. Half the participants commenced with a Fixed block, and the other half with a Random block.

Procedure

The experiment was conducted in a dark testing room. Participants were seated 50 cm from the monitor, and a chin rest was used to keep their head still. The task instructions then appeared on the screen and were explained to the participant by the experimenter. The participants were told that a coloured visual mask would appear at the centre of the screen, to be replaced briefly every few seconds by a single arrow pointing in one of eight different directions, corresponding to the arrows on the numpad. They were also told that the arrow would be replaced immediately by a visual mask with alternating colours. Whenever the new colour mask appeared, they were to indicate the direction in which the arrow-target pointed.

Participants were asked to be as accurate as possible and to keep their eyes fixed on the mask while responding (the compatible spatial organisation of the response mapping on the numpad made it possible to respond while maintaining fixation). They were also told that if they did not observe any arrow, they could simply skip the trial; however, they were encouraged to guess if they if they thought they saw an arrow but were uncertain of its direction. At the end of each experimental block, participants were provided with feedback indicating their accuracy level, and they were asked to try and maintain their performance between 80%–90%. Accuracy was only calculated based on the provided responses, ignoring skipped trials. Therefore, if participants received feedback indicating an accuracy rate lower than 80%, they were told to try and guess less; conversely, if performance was higher than 90%, they were told they should try and guess more. The accuracy range was chosen based on previous works using similar Theory of Visual Attention model-fitting procedure (e.g., Staugaard, Petersen, & Vangkilde, 2016; Vangkilde, Bundesen, & Coull, 2011; Wilms, Petersen, & Vangkilde, 2013).

Before beginning the experimental session, a short practice session with random inter-stimulus intervals (2–5 seconds) consisting of 20 trials allowed participants to learn the task. During the practice block, the first 10 trials presented the targets for an extended duration of 120 ms. The experimenter monitored the participants' responses at this stage to ensure the instructions were understood and followed. The experiment itself consisted of six blocks, each followed by a short break (approximately one minute). In each block there were 120 trials. There were three Fixed blocks and three Random blocks. In all, there were 720 experimental trials (360 for each condition) excluding practice. The five possible exposure durations were evenly distributed and randomised between trials (144 trials of each).

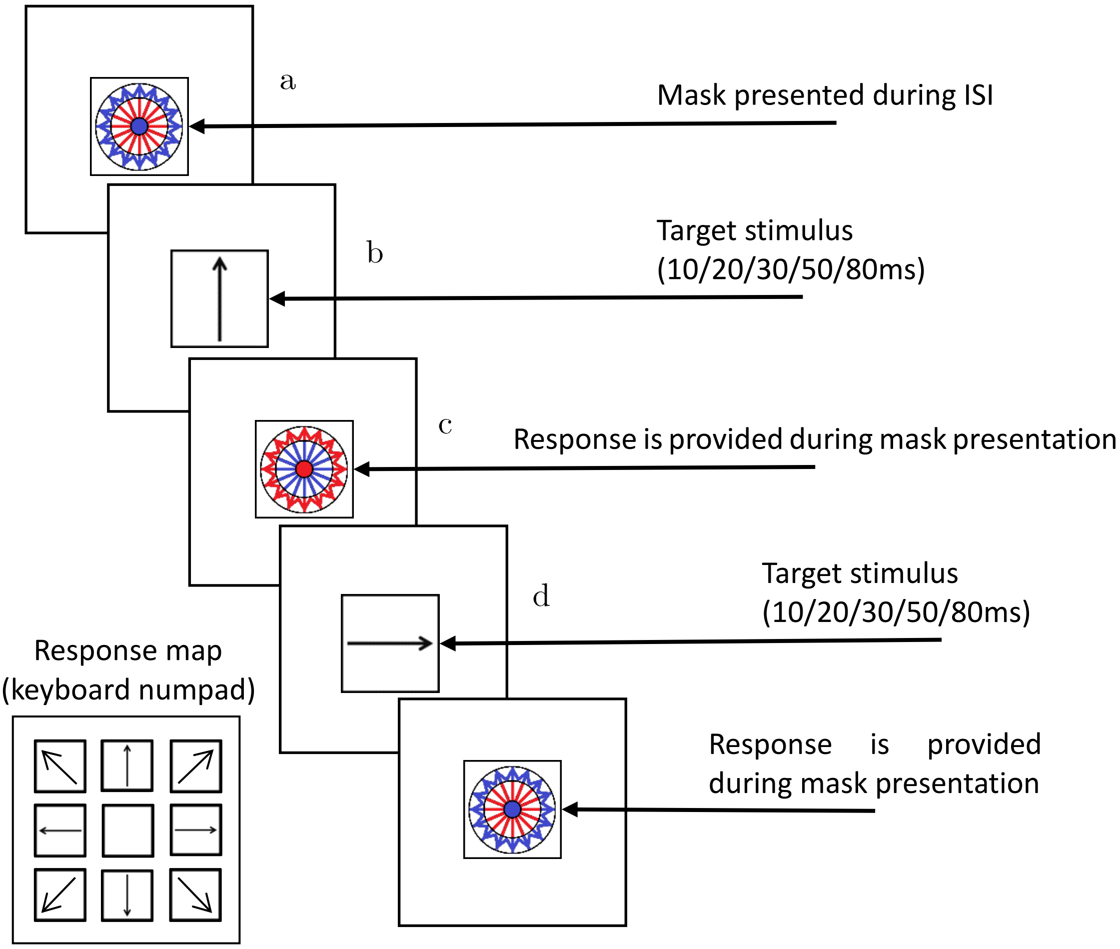

Figure 6.2 A schematic outline of the experimental design and the response mapping: a) a visual mask, made of overlapping arrows in two circles and two colours, appeared at the centre of the screen during the inter-stimulus interval. The inter-stimulus interval was determined according to the experimental condition (with a minimum of 2 sec); b) the mask was replaced by a single arrow, appearing for a varied duration: 10/20/30/50/80 ms; c) the arrow was immediately masked

again, by a mask that had opposite colours compared to the one previously presented. The use of a mask with different colours informed the participants that the stimulus event had terminated, and they were instructed to respond while the mask was presented, or do nothing if they did not perceive the target; d) the mask was replaced by the next trial after the inter-stimulus interval, regardless of whether a response was provided or not; and e) participants used the keyboard numpad, where eight arrows were drawn on stickers to indicate the response mapping. As appears in the illustration, the direction of the arrows corresponded to their locations (i.e., arrow pointing left was located on the left) to assist participants and allow them to response without moving their eyes from the screen

Statistical Analysis

Before running the fitting procedure, the mean accuracy rate was calculated for each individual, to ensure performance was maintained within the range of 80% to 90%. Four participants who failed to meet this criterion were excluded, leaving a sample of 26 participants with valid data. The data extraction and fitting procedures were performed using Matlab (Ver. 2015a; MathWorks, Inc., Natick, MA) and the LibTVA (Dyrholm *et al.*, 2011; Kyllingsbaek, 2006). The calculation of the theoretical attentional parameters (processing speed and
e
perceptual threshold) was based on a maximum-likelihood fitting procedure introduced by Kyllingsbaek (2006) to model the observations based on the Theory of Visual Attention framework. The fitting algorithm output includes two theoretical parameters: (1) Parameter t_0 is the perceptual threshold, defined as the longest exposure duration that does not evoke conscious perception, measured

in seconds; and (2) Parameter C is the visual processing speed, or processing rate, measured in the number of target-letters processed per second.

Results

Descriptive Statistics

Mean performance level was calculated separately for each condition and exposure duration, excluding the practice session. Figure 6.3 depicts the proportion of correct responses for trials in which participants provided a response (skipped trials, in which participants did not perceive the target, were excluded), Figure 6.4 depicts the distribution of the response types (no response, correct response, and incorrect response), and Figure 6.5 depicts the mean RTs.

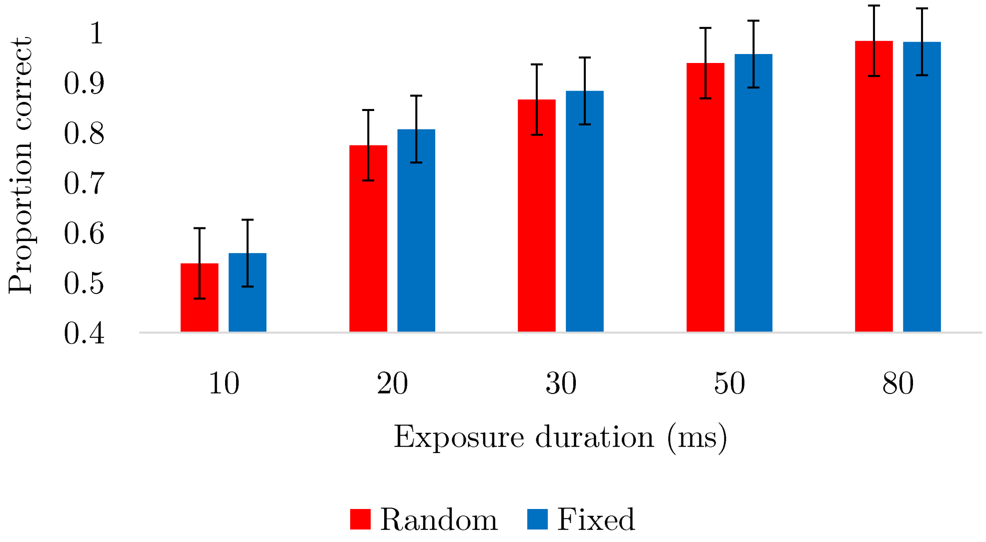

Figure 6.3 The proportion of correct responses on each condition and exposure duration. Black lines represent standard errors. The accuracy rate was based only on responses provided by the participant and excluded all trials that were skipped

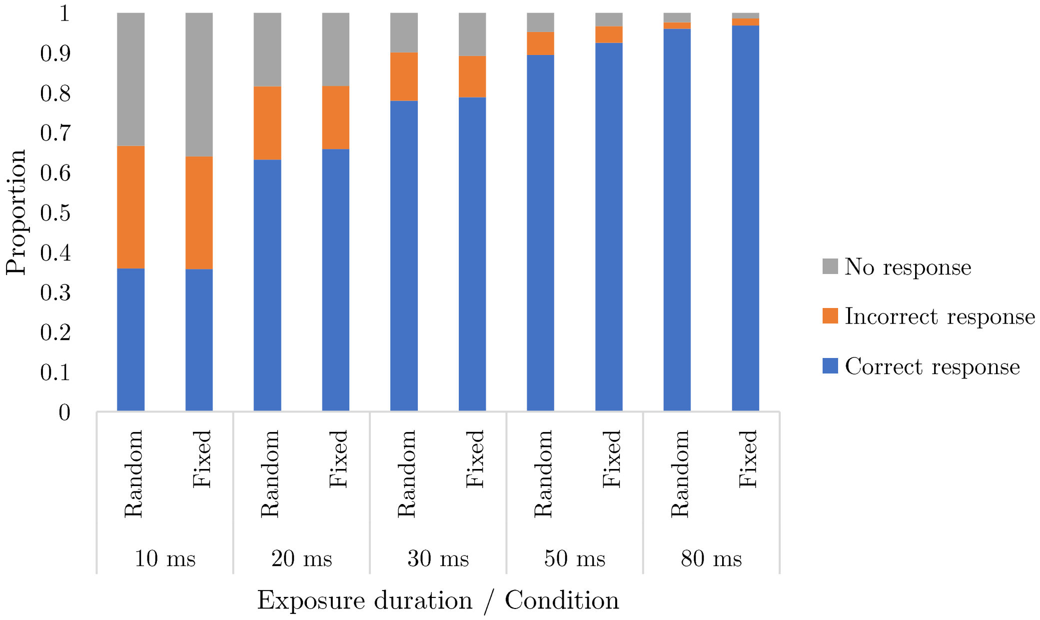

Figure 6.4 The distribution of response types on each exposure time and condition

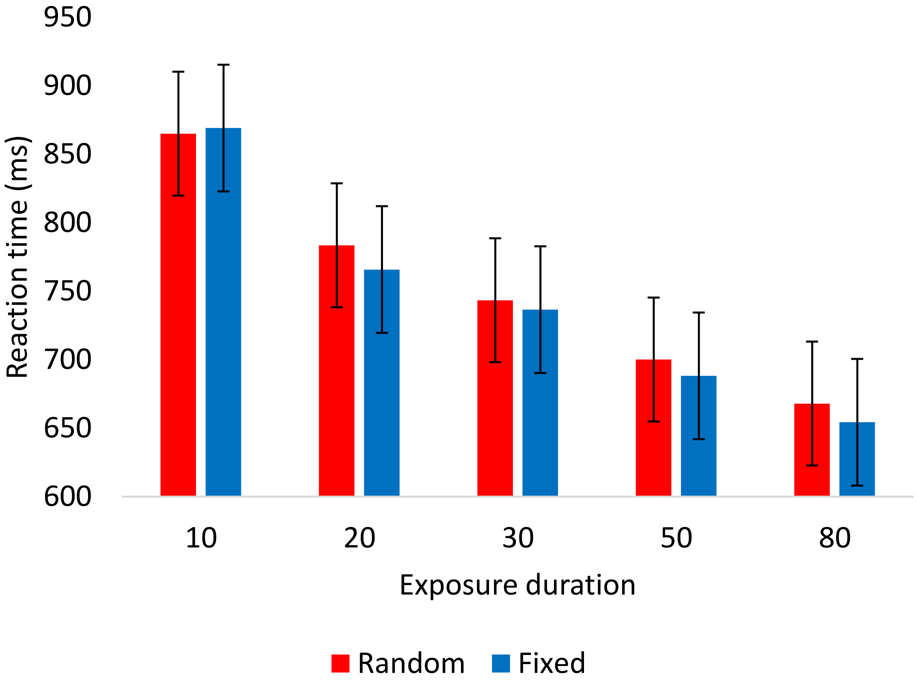

Figure 6.5 Mean RTs for each condition and exposure duration. Black lines represent standard errors

Figures 6.3–6.5 make a few important points. First, performance appears to improve gradually as the exposure duration is extended, and it appears to be generally better in Fixed blocks compared with Random blocks (both in terms of accuracy and response speed). In addition, performance was higher than chance level (%12.5) in all exposure durations, including the shortest 10 ms. Potentially, such high performance was resulted from an ineffective making stimulus which presumably did not eliminate entirely the iconic representation of the target trget and effectively allowed longer processing time. This finding is likely to influence the external validity of the Theory of Visual Attention theoretical parameters: the perceptual threshold, which represents the interaction point of the exponential line with the x-axis, might result in a negative value in some cases. Such values are theoretically possible when fitting data where the shortest exposure time elicited a relatively high performance level. Nevertheless, this limitation does not pose any difficulty when comparing the two conditions in a within-subjects design.

Comparing Performance Indices

Before modelling the data in accordance with the Theory of Visual Attention, the data was compared based on mean accuracy and RTs in different conditions and exposure durations. The first analysis procedure compared the mean accuracy (only for trials in which a response was provided) between two conditions (Random and Fixed) and five possible exposure durations (10/20/30/50/80 ms) using a within-subjects ANOVA. The results revealed a significant main effect of experimental condition (F(1,25)=5.428; p=.028; partial η^2=.178), a main effect of exposure duration (F(4,25)=233.376; p<.001; partial η^2=.903) and no interaction (p=.302). The same comparison was repeated for mean accuracy, with the accuracy rate calculated over all possible responses (including skipped trials, which were counted as incorrect answers). Again, there was a significant main effect of experimental condition (F(1,25)=8.426; *p*=.008; partial η^2=.252), a main effect of exposure duration (F(4,25)=235.135; *p*<.001; partial η^2=.904), and no interaction (p=.254). When using the same factors to compare mean RT as the dependent variable, there was only a main effect of exposure duration (F(4,25)=110.231; *p*<.001; partial η^2=.815). The descriptive statistics relevant for the comparisons appear in Figures 6.3–6.5.

Computational Modelling

Behavioural data was fitted to the single-target categorisation equation, describing the probability of correctly categorising a target arrow at a given exposure duration. The probability is described using two terms: $p(t) = 1 - e^{-v(x,i)(t-t0)}$, where the term *v(x,i)* represent the rate in which a specific categorisation of *x* as being belong to category *i* is encoded to Visual Short-Term Memory. The rate also equals to '*C'*, a parameter representing the sum of all rate values (*v*) and in the case of a single target they are the same. The second term is t_0, the perceptual threshold, standing for the longest ineffective exposure duration of a masked stimulus. The data was split according to the two experimental conditions, Random and Fixed, and were fitted separately. The two resulting exponential functions are illustrated in Figure 6.6.

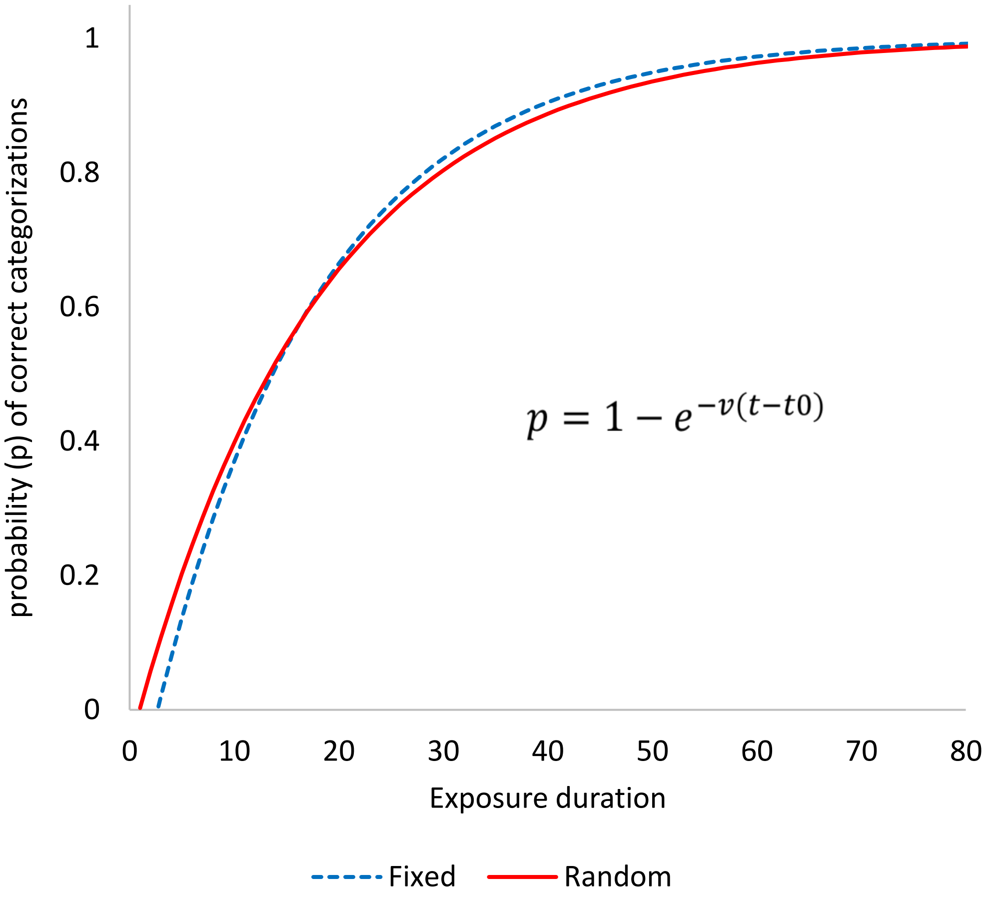

Figure 6.6 The experimental data was split into two separate sets according to the experimental condition (R and F), and fitted to the single-target categorisation equation. The two lines are based on aggregated mean fitting data across all participants.

The two terms defining the function were extracted for each individual in both conditions and compared using a repeated-measures t-test. The results showed a significant difference in both t_0 (t(25)=2.452; p=.022; 95%CI[0.27;3.18]) and in v (t(25)=2.983; p=.006; 95%CI[2.20;12.04]). The differences demonstrate a selective benefit of an increase in the theoretical value of processing speed in the Fixed condition (63.86) compared to the Random condition (56.74), and a decrease in the value of the perceptual threshold in the Random condition (threshold value of -.05) compared with the Fixed condition (threshold value of 1.67). Although the threshold values were unreasonable in a real sense (a negative near-zero value in the Random condition), the within-subjects comparison was significant, allowing it to be interpreted as representing a benefit in performance. A Pearson correlation analysis was used to estimate the reliability of the model by estimating the relationships between the values predicted by the model and the real values in all the exposure durations. The resulting correlation was high in both the Fixed condition (r=.98; p<.001) and the Random condition (r=.98; p<.001). The mean log-likelihood values of the model fit were -144.32 (SD=.29) and -152.49 (SD=.30) in Fixed and Random conditions accordingly.

Discussion

The experiment in this chapter replicated previous findings of enhanced processing speed in the presence of temporal expectations (e.g., Vangkilde, Coull, & Bundesen, 2012; Vangkilde, Petersen & Bundesen, 2013), only here it was extended to a rhythmic structuring of temporal expectation and to an experimental context with a continual stimulation. It also confirmed the speculative hypothesis that perceptual threshold would be lower in the absence of a predictable temporal structure.

The replication of processing speed effects within the context of an ongoing, continuous task provides informative insights, suggesting that rhythmic temporal expectation leads to higher efficiency in visual processing. The prevalence of an isochronous pace in CPT variations is very high (e.g., Conners, 2000; Cornblatt *et al.*, 1988; Esterman, Rosenberg, & Koonan, 2014; Greenberg, 1987; Lee & Park, 2006; Mackworth, 1948; Klee & Garfinkel, 1983; Robertson, 1997; O'Connell *et al.*, 2009), and it is possible that such designs introduce an implicit temporal factor supporting performance. Accordingly, a more tentative speculation would be that CPT designs with a rhythmic pattern may decrease the overall attentional demands, which may contribute to the commonly observed ceiling effect in performance (e.g., Sarter, Givens, & Bruno, 2001).

The finding of a lower perceptual threshold in the absence of temporal regularities is novel. This could be a result of the unique design integrating continuous performance with Theory of Visual Attention modelling. As indicated by the experimental findings in Chapter 5, the use of random inter-stimulus intervals on a CPT could 'switch' the system to operate in a 'random' mode to maximise the detection of unexpected events (Schroeder & Lakatos, 2009). Schroeder, Herrero, and Haegens (2014) propose that, while performing a 'vigilance task', in which events occur randomly and continuously, low-frequency alpha oscillations are continuously supressed to promote the ongoing readiness to unpredictable events. Whereas the current thesis did not focus on brain-oscillatory processes, this suggestion corroborates the findings presented in Chapter 5 showing a dynamic increase in the ongoing tonic arousal level in the lack of a temporal structure. What follows from the findings presented here is that, while attention might be less efficient in a random mode compared with a rhythmic mode (as reflected in the change in processing speed), there may be an overall enhanced sensitivity of the cognitive system (as reflected in the perceptual threshold). Nevertheless, these findings should be treated with some level of caution, as further replications of the current observations should be made. Also, as the actual values that represent the perceptual threshold were negative in some cases (probably due to ineffective masking), future studies should address this issue by assuring the visual mask eliminates any perceptual traces and properly control the exposure duration.

My results on perceptual threshold differed from previous findings by Petersen *et al.* (2017). In their study, both parameters – the perceptual threshold and the processing speed – were improved in the presence of a warning signal. The discrepancy may be explained by differences in task parameters. Inclusion of warning signals in Petersen's study may have elicited heighted phasic alertness, whereas the current experiment did not include any warning signals and relied only on implicit manipulation of temporal expectations. It is therefore possible that different mechanisms were involved in the two studies. The manipulation of temporal expectations in the current study is more similar to classic manipulations of temporal expectations without the potentially additive effect of alerting cues. Potentially, the benefit of the Random condition in perceptual threshold is a unique contribution of the overall *task context*, which is more pronounced when conducting an ongoing CPT. According to this interpretation, operating in task settings with unpredictable onsets elicit a distinctive cognitive adaptation promoting an ongoing elevated alertness to environmental changes.

To conclude, the findings demonstrated the relevance of the temporal structure of the CPT to selective attention parameters. They strengthen the argument that the rhythmic pattern implemented in CPT designs is a meaningful factor affecting performance. Future studies should further contrast performance patterns in CPT designs when testing clinical populations, to establish whether the capacity of performance patterns over time shows different levels of sensitivity to manipulations of the temporal structure. As the modelling results presented here are also somewhat unrealistic (i.e., a negative number in the perceptual threshold), future replications should try and increase the task difficulty by presenting stimuli that remain invisible at the shortest exposure duration.

Chapter 7 : Testing Causal Interactions Between Sustained and Spatial Attention

Abstract

A growing body of evidence indicates that different facets of attention interact and share common neural substrates. The current study aimed to modulate a spatial attentional bias via transfer effects, based on a mechanistic understanding of the interplay between sustained and spatial attention. I adopted the computational framework of the Theory of Visual Attention to investigate (1) whether a single administration of a lateralised sustained attention task could modulate spatial-attention, leading to transferable changes in the Theory of Visual Attention attentional weights parameter (the relative attention assigned to the left versus right hemi-field) and/or other attentional parameters assessed within the framework of the Theory of Visual Attention (Experiment 7.1), and (2) whether the effects of such a lateral sustained attention training protocol could be further enhanced by using biparietal high frequency transcranial random noise stimulation to enhance brain plasticity (Experiment 7.2). The results demonstrated that spatial attentional bias can be modulated by sustaining attention towards the right hemi-field, but this effect does not occur when sustaining attention towards the left visual field. We also showed that the

rightward sustained attention training combined with a bi-parietal high-frequency transcranial random noise stimulation resulted in an increased attentional selectivity. To conclude, we present here a novel, theory-driven method for modulating spatial attention providing important insights into how the spatial and temporal processes in attention interact with attentional selection.

This chapter is based on a paper published in Cortex: Shalev, N., De Wandel, L., Dockree, P., Demeyere, N., & Chechlacz, M. (2017). Beyond Time and Space: The effect of a lateralised Sustained Attention task and Brain Stimulation on Spatial and Selective Attention. Help in data collection was provided by L De Wandel and M Chechlacz. The paradigm development and implementation and all analyses were completed by myself.

Introduction

The Theory of Visual Attention model discussed in Chapter 6 provides a reliable framework to describe the multiple factors that contribute to the process of selection. As a mathematical formulation of the Biased Competition Model, it focuses on selection as the primary, end-goal of attention (Desimone & Duncan, 1995). A key assumption in Theory of Visual Attention is that attention is best described as a competition between sensory elements racing to be encoded in a limited capacity working memory. As a result, the elements that 'win the race' are consciously perceived.

This competition is formulated in a set of equations that describe the working memory capacity; the relative weights that are allocated to each perceived element, according to the current goal set and its relative saliency; the efficiency of top-down control, allowing to filter elements that do not concur with the current goal-set; and the perceptual threshold and processing speed (described in Chapter 6). Based on these five main parameters, the Theory of Visual Attention provides a means to account for individual differences in attention. A Theory of Visual Attention-based assessment has been previously employed to describe changes in attention functions following interventions based on either cognitive-training or brain stimulation protocols. For example, Schubert *et al.* (2015) use a behavioural training paradigm based on video games and show an enhancement in processing speed of visual stimuli at a certain position in the display. In another study, the Theory of Visual Attention framework is used to assess the effectiveness of a meditation-based intervention and demonstrated an increase in various attentional parameters (Jensen *et al.*, 2012). Finally, a recent study by Moos and colleagues (2012) has employed the Theory of Visual Attention model to measure changes in attentional parameters, following application of transcranial direct current stimulation, an emerging approach for cognitive intervention in both healthy and clinical populations (for recent reviews see Filmer, Dux & Mattingley, 2014; Santarnecchi *et al.*, 2015; Harvey & Kerkhoff, 2015).

While behavioural training studies mainly target discrete attentional mechanisms, brain stimulation studies additionally enable the targeting of underlying neural substrates of attention. Attention relies on large-scale neural networks involving cortical and sub-cortical structures sub-serving various components of attention (e.g., Corbetta & Shulman, 2002; Mesulam, 1981; 1990; 1999; Posner & Rothbart, 2007). There is a consensus that the control of spatial attention is achieved by a network involving three inter-connected nodes in the posterior parietal cortex (homologous to the Lateral Intraparietal Area in non-human primates), the dorsal premotor and posterior prefrontal regions (homologous to the Frontal Eye Field region), and the cingulate cortex (Mesulam, 1981). Multiple functional magnetic-resonance imaging studies employing various attention orienting tasks have highlighted the key role of fronto-parietal networks in control of attention (e.g., Corbetta *et al.*, 1993; Nobre *et al.*, 1997; Shulman et al, 2010; Kincade *et al.*, 2005; Doricchi *et al.*, 2010). Further evidence supporting the key role of the frontoparietal regions comes from studies demonstrating strong effects of the brain stimulation applied over the posterior parietal cortex and the frontal eye field (e.g., Duecker & Sack, 2015; Fierro *et al.*, 2000; Nyffeler *et al.*, 2008; Rushworth & Taylor, 2006; Sparing *et al.*, 2009; Taylor, Nobre, & Rushworth, 2006) on the performance in various attentional tasks. In humans, the frontoparietal networks that control spatial attention are functionally lateralised (the allocation of attention to each visual hemi-field is controlled by contralateral hemisphere) and asymmetrically organised, with a right hemispheric dominance.

The empirical evidence supporting functional lateralisation and right hemispheric dominance in attention comes from observations in patients with hemi-spatial neglect syndrome, which is characterised by a difficulty to attend, orient and respond to elements in the contralesional hemi-field. Neglect is more severe and more common following right-hemispheric damage (Luauté *et al.*, 2006; Stone *et al.*, 1991). Additionally, healthy individuals show a small but persistent attentional bias towards the left hemi-field, supported by preferential right-hemisphere activation (so-called pseudo-neglect) (e.g., Bowers & Heilman, 1980; Corbetta & Shulman, 2011; Driver & Mattingley, 1998; Halligan, Fink, Marshall, & Vallar, 2003; Heilman & Valenstein, 1979; Heilman & Van Den Abell, 1980; Jewell & McCourt, 2000; McCourt & Jewell, 1999; Nicholls, Bradshaw, & Mattingley. 1999; Nobre *et al.*, 2004; Shulman *et al.*, 2010; Stone, Halligan, & Greenwood, 1993; Vallar, 1998; Weintraub & Mesulam, 1987). In addition to the evidence provided by neuropsychological and functional brain-imaging studies, the anatomical foundations of the right hemispheric dominance of attention have been linked to the lateralisation of the fronto-parietal networks (e.g., Thiebaut de Schotten *et al.*, 2011, Chechlacz *et al.*, 2015a; Marshall *et al.*, 2015).

In accordance with the hypothesis of the right-hemispheric dominance of attention, researchers applying various behavioural interventions based on a perceptual adaptation have managed to modulate the attentional bias only towards the right, and failed to do so towards the left (e.g., Loftus, Vijayakumar, & Nicholls, 2009; Michel et al, 2003). Similarly, in a brain stimulation study using transcranial magnetic stimulation applied to the right posterior parietal cortex, Hung *et al.* (2005) managed to increase the attentional selectivity in the right hemi-field and decrease the selectivity in the left hemi-field. However, when stimulation was applied to the homologous area in the left hemisphere, no modulation was found. A similar observation was made in a follow-up study using transcranial magnetic stimulation applied to the right and left frontal eye-fields (Hung *et al.*, 2011). Numerous other studies have demonstrated that transcranial magnetic stimulation applied over the right, but not the left, posterior parietal cortex can produce significant shifts in the allocation of visual attention (e.g., Cazzoli *et al.*, 2009; Hung *et al.*, 2005; Hilgetag *et al.*, 2001; Sack *et al.*, 2007; Fierro *et al.*, 2000). Nevertheless, the right-hemispheric dominance in attention remains controversial, with some inconsistent findings from brain imaging studies (e.g., Sommer *et al.*, 2008; Shulman *et al.*, 2010; Doricchi *et al.*, 2010) and lesion studies (Suchan, Rorden, Karnath, 2012), and with reported large inter-individual differences in anatomical lateralisation and lateralised responses to brain stimulation (Szczepanski and Kastner, 2013; Thiebaut de Schotten *et al.*, 2011; Chechlacz *et al.*, 2015a,b; Cazzoli and Chechlacz, 2017).

Brain stimulation studies also support the notion that intra-hemispheric reciprocal connectivity also contributes to top-down attentional biases. For example, by applying transcranial direct current stimulation over the parietal cortex, Sparing *et al.* (2009) managed to alter performance selectively in accordance with the notion of cross hemispheric competition or 'rivalry' (Kinsbourne, 1987; 1993; Reuter-Lorenz, Kinsbourne, & Moscovitch, 1990; Szczepanski *et al.*, 2010). Specifically, they reported a selective modulation of performance according to stimulation polarity (anodal versus cathodal) and site (right versus left hemisphere), demonstrating how inhibiting one hemisphere can enhance performance in the ipsilateral hemispace (by decreasing its inhibitory effect over the contralateral brain hemisphere), and vice versa (i.e., enhancing brain activity in one hemisphere can enhance performance in the contralateral hemi-space: Sparing *et al.*, 2009). In a more recent study, Giglia *et al.* (2011) explore whether dual transcranial direct current stimulation (right cathodal and left anodal) stimulation applied over the posterior parietal cortex compared with unilateral (right cathodal) posterior parietal cortex stimulation might induce greater neglect-like effects in healthy individuals. Based on their findings that the dual stimulation resulted in a stronger rightward bias, Giglia *et al.* conclude that the greater rightward bias triggered by dual transcranial direct current stimulation could be attributed to the modulation of the interhemispheric inhibition (as opposed to unilateral stimulation only affecting right hemisphere activity; see also Benwell *et al.*, 2015).

In summary, the evidence suggests that a bilateral fronto-parietal network supports attention through mechanisms of intra-hemispheric competition (e.g. Szczepanski *et al.*, 2010). However, while some studies report a modulation in attention after application of brain stimulation to both the left and the right hemisphere (e.g., Dambeck *et al.*, 2006; Sparing *et al.*, 2009; Chechlacz *et al.*, 2015b), others only observe attentional shifts when stimulating the right hemisphere (e.g., Fierro *et al.*, 2000; Loftus, Vijayakumar, & Nicholls, 2009; Michel et al, 2003). These observations conflict, reflecting an ongoing debate as to the extent and origin of the right-hemisphere dominance in controlling spatial attention.

By contrast, in the study of sustained attention, a right hemispheric dominance is widely accepted. Sustained attention is sub-served by multiple cortical and sub-cortical structures, including the right posterior parietal cortex (e.g., Coull *et al.*, 1996; Heilman, Schwartz, & Watson, 1978; Pardo, Fox, & Raichle, 1991; Posner & Petersen, 1990; Robertson *et al.*, 1997; Sarter, Givens, & Bruno, 2001; Shulman *et al.*, 2010; Whitehead, 1991). This neural network seems to overlap partially with neural substrates of spatial attention, based on studies reporting an association between neglect symptoms and sustained attention (Husain & Roden, 2003; Husain & Nachev, 2007; Robertson, 2001) and demonstrating an improvement in neglect symptoms after a training targeting sustained attention (Robertson *et al.*, 1995).

Current Study

The first experiment in this chapter capitalised on the partial overlap of the brain networks contributing to sustained and spatial attention, including involvement of the right posterior parietal cortex, to test whether training on one mode of attention (sustained attention) had transferable consequences to the other mode (spatial attention). The Theory of Visual Attention framework (Bundesen, 1990) was used to measure training induced changes in discrete attentional parameters based on the previously reported high sensitivity, reliability and validity of this model (Bundesen *et al.*, 2005; Dyrholm *et al.*, 2011; Finke *et al.*, 2005; Habekost, Petersen & Vangkilde, 2013 Habekost, 2015). In particular, given the right-hemisphere dominance of parietal involvement in sustained attention, we tested the possibility that training in a protocol combining sustained attention and spatial selectivity might lead to changes in attentional weights in the Theory of Visual Attention spatial attention task in favour of processing of items on the left visual hemi-field versus the right hemi-field (Experiment 1). The second experiment in the chapter targeted the overlap in neural systems between sustained and spatial attention directly, and investigated whether applying transcranial random noise stimulation to the posterior parietal cortex, combined with a behavioural training protocol, enhances the training outcomes. The transcranial random noise stimulation protocol was chosen based on its known effectiveness in behavioural training studies (e.g. Fertonani *et al.*, 2011; Cappelletti *et al.*, 2013), and in particular its ability to potentiate neuroplasticity during task performance (Kadosh *et al.*, 2012; Cappelletti *et al.*, 2013; Fertonani *et al.*, 2011; Terney *et al.*, 2008) and to enhance visual sensitivity by increasing action potentials in the visual cortex (van der Groen & Wenderoth, 2016). Again, Theory of Visual Attention-derived parameters were used to quantify changes in attention and transfer effects and to test whether these were enhanced by the application of brain stimulation.

Experiment 7.1: Spatial Biases After Training on a Lateralised Sustained Attention Task

Experiment 1 presents a behavioural intervention protocol targeting the interactions between sustained and spatial attention. Based on the right-hemisphere dominance in controlling spatial attention (e.g., Thiebaut de Schotten *et al.*, 2011, Chechlacz *et al.*, 2015a; Marshall *et al.*, 2015) and sustained attention (e.g., Coull *et al.*, 1996; Heilman, Schwartz, & Watson, 1978; Pardo, Fox, & Raichle, 1991; Posner & Petersen, 1990), it was hypothesised that a lateralised sustained attention training protocol would have a selective modulatory effect on spatial attention biases, depending on the attended visual field. Specifically, sustaining attention towards the left visual field would rely on right hemisphere effort, and was therefore less likely to influence any spatial biases due to the hemispheric role in attending the two visual fields (e.g., Nobre *et al.*, 2004; Shulman *et al.*, 2010; Stone, Halligan, & Greenwood, 1993; Vallar, 1998; Weintraub & Mesulam, 1987). In contrast, sustaining attention towards the right was more likely to bias spatial attention, as the non-dominant left hemisphere does not contribute bilaterally to attention orienting.

This experimental approach differed from traditional methods of modulating attention by a repetitive training protocol with test-retest of the training-task outcome as a marker of training efficiency (e.g., Robertson *et al.*, 1995). Instead, the study was designed to test whether a single administration of a relatively short lateralised sustained attention task could have an immediate effect on attentional bias and/or other attentional-selection factors. For the purpose of the current study, the lateralised sustained attention task was designed based on an adaptation of the Masked Conjunctive CPT described in Chapters 2 and 3. In the modified Masked Conjunctive CPT, participants were requested to monitor *two* lateralised visual streams presented simultaneously. By changing the frequency of the target appearing either in the left versus right visual stream, sustained attention effort was biased towards one side of space. Other task properties were maintained to ensure increased demands for sustained attention (low target frequency in a simple, repetitive and non-arousing task).

Methods

Participants

The participants in this experiment were 60 naïve volunteers (32 of whom were female; mean ± SD age = 25.7 ± 4.9). Participants were recruited through an online research participation system managed by the University of Oxford. Exclusion criteria included any previous history of neurological or psychiatric disorders. Both left- and right-handed participants were recruited for the study, and the hand dominance was assessed according to Edinburgh handedness inventory (Oldfield, 1971; mean handness score ± SD = 80.8 ± 22.69; one participant was classified as left-handed and one as ambidextrous). All participants had either normal or corrected-to-normal vision. All study participants provided written informed consent in compliance with relevant protocols approved by the University of Oxford Central University Research Ethics Committee. The experimental procedures were conducted in accordance with the latest version of the Declaration of Helsinki. Participants were compensated for their time by a payment of £20, inclusive of travel expenses.

Apparatus

A PC with Intel i7 processor and a dedicated 2GB AMD video card was used for displaying stimuli and recording data. The lateralised sustained attention task was generated using NBS Presentation software (Neurobehavioural Systems, Albany, CA), and the CombiTVA paradigm (a Theory of Visual Attention-based task) was generated using E-prime 2 Professional software (Psychology Software Tools, Inc.). The stimuli were presented on a ViewSonic V3D245 LED monitor, with a screen resolution of 1080X1920 and a screen refresh rate set at 100Hz allowing display times varied in gaps of 10ms. All stimuli were pre-loaded to memory using the presentation software, to maximise control over temporal precision.

General Procedure

The 60 participants were divided into four experimental groups, three of which completed the *training* protocol,[11] and one of which acted as a No Training control group: *Right Training* (15 participants; 6 female; mean ± SD age = 24.0 ± 4.6)*, Left Training* (15 participants; 8 female; mean ± SD age = 25.9 ± 4.8), *Neutral Training* (i.e., active control group; 15 participants; 8 female; mean ± SD age = 26.3 ± 4.7), and *No Training* (i.e., static control group, 15 participants; 10 female; mean ± SD age = 26.8 ± 5.6)*.* All participants were invited to the lab on two consecutive days at the same time of day. On the first day, all participants performed the CombiTVA task (see below for details) to assess their baseline attentional bias and other attentional parameters based on the Theory of Visual Attention model. On the following day, participants in the Right Training, the Left Training and the Neutral Training groups performed their version of the sustained attention training task (see below for details), immediately followed by assessment using the CombiTVA task. The participants in the *No Training* group

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[11] For the sake of convenience and clarity, I use the term ‘training’ when referring to the protocol involving the bi-lateral sustained attention task. It should be clarified that this protocol differs from traditional approaches to cognitive training, which typically include a repeated application of the training-protocol and occasional assessment of improvement in the training task. Here, the use of the term ‘training’ denotes only the single administration of the sustained attention task which is aimed to influence selective attention.

were only assessed on the CombiTVA task in this second session, without any prior sustained attention training.

Sustained Attention Training

Stimuli

Two coloured visual masks (*Mask*) acted as placeholders, placed at 10 ° visual angles to the right and left sides of a cantered fixation point (Figure 7.1). They consisted of four superimposed figures in different colours (square, triangle, circle and hexagon) and occupied 3 ° of visual angle. To avoid habituation effects and to decrease the abrupt onset of targets, a minor movement was constantly generated by alternating every few milliseconds between two mask images, one of which had thicker outlines for the superimposed figures (this manipulation of the visual mask appears also in Chapter 2 and Chapter 3). The masks disappeared only when they were replaced by either a target or a distractor shape for 80 ms. The masks then reappeared immediately, generating pre- and post-masking of each target or distractor. The target shape was a red circle, and distractor stimuli were either similar in colour to the target (red hexagon and red triangle), similar in shape to the target (blue circle and red circle), or completely different (yellow and blue hexagon). All distractor types were equally probable, both when appearing concurrently with a target and when appearing with another distractor.

All distractor and target shapes were circumscribed within an invisible square of 3 ° visual angle. The inter-stimulus interval jittered between 1000 and 5000ms (see Figure 7.1 for a schematic outline of the experimental procedure). Participants were told that the static shapes (the mask) appearing at the two sides of the screen (the left and the right hemi-field), would be replaced every few seconds by another shape for a short time. Their task was to press the spacebar as quickly as possible whenever they saw a *red circle* in one of the two locations (i.e., the left or the right hemi-field). They were instructed to do nothing when they saw any other coloured shape.

Participants assigned to the Right Training, the Left Training and the Neutral Training groups performed different versions of the sustained attention training task with respect to the frequency of targets appearing to the left or the right hemi-field. For the Right Training group, targets appeared much more often on the right side (80% of target trials). For the Left Training group, targets appeared more often on the left side (80% of target trials). For the Neutral Training group, the targets were equally distributed between the two sides.

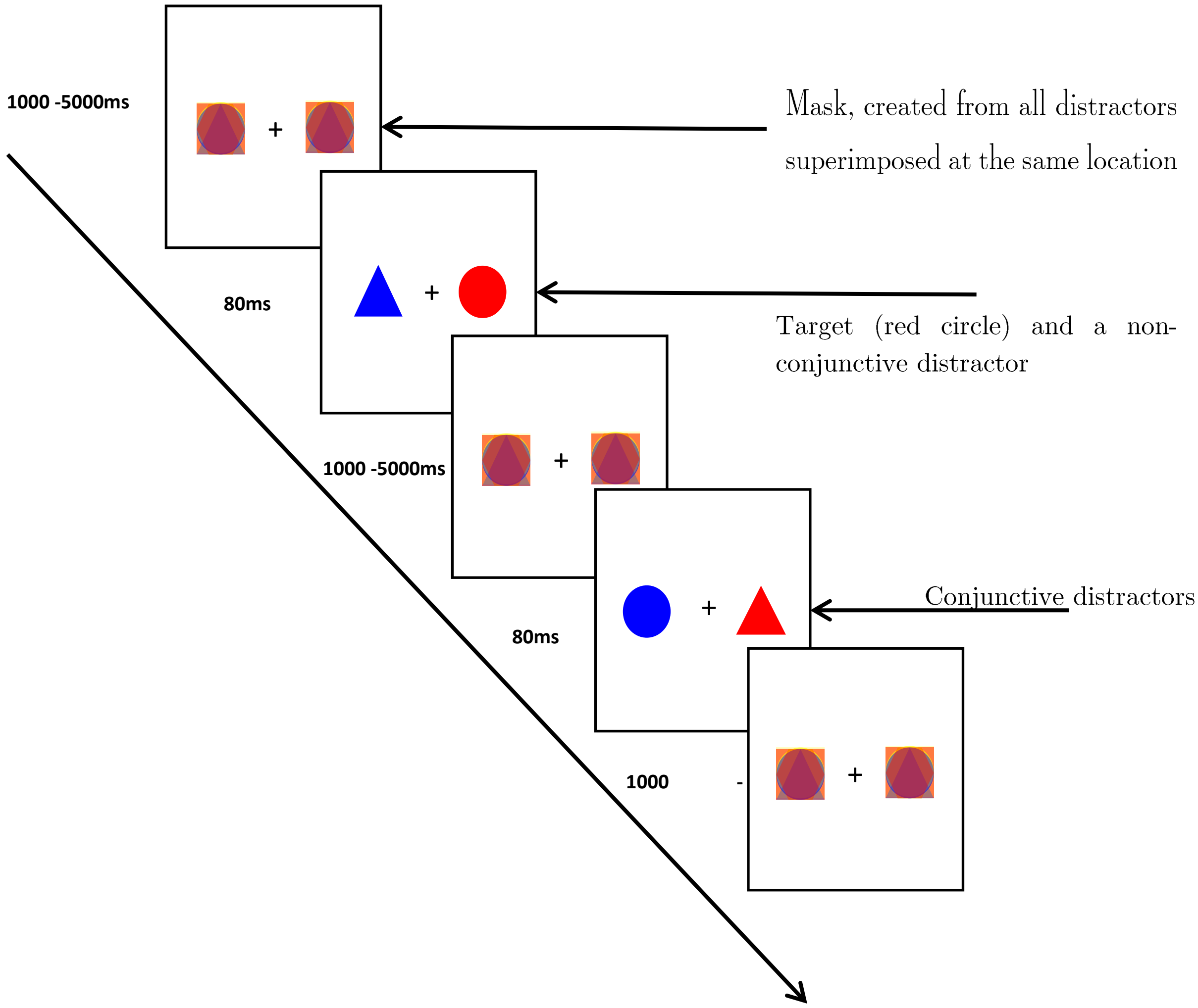

Figure 7.1 A schematic outline of the sustained attention training task

Procedure

The task started with a short practice block (15 trials), and the experimenter monitored subjects' response at this stage to ensure the instructions were clear. After finishing the practice session, the participants performed three experimental blocks each lasting 180 trials with a short break in-between. The whole procedure lasted approximately 40 minutes. The task contained 540 trials, with targets appearing on 180 trials (33% target) and distractors on 360 trials (66%). For the *Right Training* group, 40 targets appeared on the left side, and 140 on the right; for the *Left Training* group, 40 targets appeared on the right side, and 140 on the left; for the *Neutral Training* group, equal numbers of target appeared on the right and the left side (i.e., 90 right and 90 left targets).

CombiTVA Paradigm (Theory of Visual Attention-based task)

Stimuli

The CombiTVA paradigm (Vangkilde *et al.*, 2011) was employed to estimate Theory of Visual Attention-derived attentional parameters. Traditionally, an assessment based on the Theory of Visual Attention framework (Bundesen, 1990) uses two types of task: 1) a partial report task assessing attentional control, and 2) a whole report task assessing attentional capacity. The CombiTVA paradigm employed in the current study implements both full and partial report tasks, which are intermixed on different trials (Vangkilde *et al.*, 2011). On each trial, a centred red fixation-cross appeared at the centre of the screen for 1000ms, followed by a blank screen appearing for 100ms, followed by the stimulus display. The stimulus display could be of one of two random conditions: a *whole report*, where either two or six red letters appeared on the screen, or a *partial report*, where four blue letters and two red letters appeared on the screen. The letters were presented around an invisible centred circle in six fixed placeholders equally distributed on the perimeter ($r=7.5°$ visual angles). The stimulus display presented random letters from a set of 20 capital letters (ABDEFGHJKLMNOPRSTVXZ) with a font size corresponding to $2.7° \times 2.3°$ of visual angles. The display appeared for one of six fixed durations of 10, 20, 50, 80, 140 or 200 ms (randomly assigned and equally distributed), and was followed by a masking noise on each of the fixed placeholders lasting 500 ms. Following the mask presentation, the participants were presented with a response display for unlimited time, and were prompted to recall as many red letters as they could using the computer keyboard, pressing ‘Enter’ when done. The response display appeared for an unlimited time. See Figure 7.2 for a schematic outline of the experimental procedure, adapted from Chechlacz *et al.* (2015a).

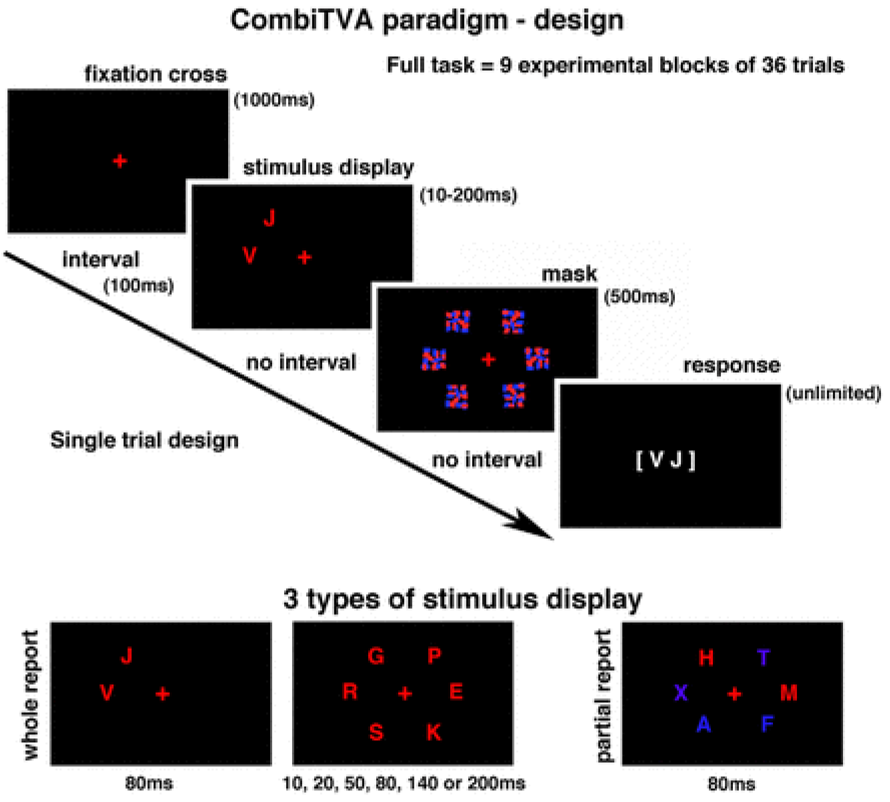

Figure 7.2 CombiTVA Experimental Outline, from Chechlacz et al., 2015. Figure was copied from the Journal of Neuroscience in accordance with the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported License

Procedure

The task started with a short practice block (24 trials), during which the experimenter monitored subjects' responses to ensure the instructions were clear. Following the practice session, participants performed nine experimental blocks consisting of 36 trials each. The exposure times of the stimulus displays, as well as the different conditions and the stimuli letters, were all randomly distributed. The participants were told that their reaction speed was not being monitored, and they should report all the red letters they were 'fairly certain' of having seen and to refrain from pure guessing. Following each experimental block, the participants were informed of their accuracy rate. They were asked to try to maintain an accuracy range of 80%–90%; they were told that if their accuracy was higher, they should try to lower their decision criteria; conversely, if their accuracy was lower, it meant they guessed too many letters and they should try to be more accurate. The whole procedure lasted approximately 45 minutes.

Estimation of Theory of Visual Attention Parameters

The analysis procedure relied on a set of variables extracted from the Theory of Visual Attention framework (Bundesen, 1990). The Theory of Visual Attention model represents a mathematical formalisation of the 'biased competition' account of visual attention, where visual categorisations ascribing features to objects compete to be encoded into a limited capacity Visual Short-Term Memory. The categorisation of a visual element is accomplished once it has been encoded to Visual Short-Term Memory. This race model is normally described by two main equations: the rate equation and the weight equation. The rate equation describes the rate $v(x, i)$ at which a particular visual categorisation 'x belongs to i' is encoded into Visual Short-Term Memory. The rate is determined as a product of three terms: $\eta(x, i)$ which represents the strength of the sensory evidence in favour of categorising x as belonging to category i; β_i which represents the perceptual decision bias associated with category i; and

$\frac{\mathrm{W_x}}{\sum_{\mathrm{z \in S}} \mathrm{W_z}}$ which determines the relative attentional weight of object x divided by the sum of all the attentional weights of all objects within the visual field (S).

$$v(x,i) = \eta(x,i)\beta_i \left\{\frac{\mathrm{W_x}}{\sum_{\mathrm{z \in S}} \mathrm{W_z}}\right\}$$

The sum of all rate values (v) across the visual field defines the overall processing speed (C), formally

$$\mathrm{C} = \sum_{x \in S} v(x) = \sum_{x \in S} \sum_{i \in R} v(x,i)$$

A second key equation is the Weight Equation, which describes the theoretical weights given to the perceived elements according to their pertinence value π_j. The pertinence value is defined by the momentary importance of attending a perceived element x belonging to a category j, where R is the set of all categories $\eta(x,j)$. The Weight Equation is

$$W_x = \sum_{j \in \mathrm{R}} \eta(x,j)\pi_j.$$

Finally, this study used a partial report paradigm where participants were requested to attend and report targets while ignoring irrelevant distractors (defined by a colour feature). Under the assumption that every target on a given display has approximately the same weight, and every distractor has the same weight (different from targets), the α value which defines the efficiency of top-down control was determined as $\alpha = \frac{w_{distractor}}{w_{target}}$

Based on this proposed set of equations, five parameters were calculated (a detailed description appears in the statistical analysis section).

Statistical Analysis

The analysis of the performance on the sustained attention training task was restricted to examining group differences (Right Training, Left Training and Neutral Training) in the accuracy on trials with the target appearing on the right, target appearing on the left, and trials with no target. The performance on the CombiTVA paradigm pre- and post-training were compared to estimate whether the sustained attention training procedure influenced attention parameters estimated based on the Theory of Visual Attention framework.

The CombiTVA paradigm allows the extraction of multiple independent theoretical parameters representing different aspects of attention (Vangkilde *et al.*, 2011). The calculation of the theoretical attentional parameters is based on a maximum-likelihood fitting procedure introduced by Kyllingsbaek (2006) to model the observations based on the Theory of Visual Attention-framework. The fitting algorithm output includes five theoretical parameters. (1) Parameter K is an estimation of the visual short-term memory capacity, measured in number of letters that can be stored. (2) Parameter t_0 is the perceptual threshold, defined as the longest exposure duration that does not evoke conscious perception, measured in seconds. (3) Parameter C is the visual processing speed, or processing rate, measured in the number of letters processed per second. These three parameters, K, t_0 and C, can be visualised when plotting the number of correctly identified letters as a function of the exposure duration, as illustrated in Figure 7.1 (adopted from Habekost, 2015).

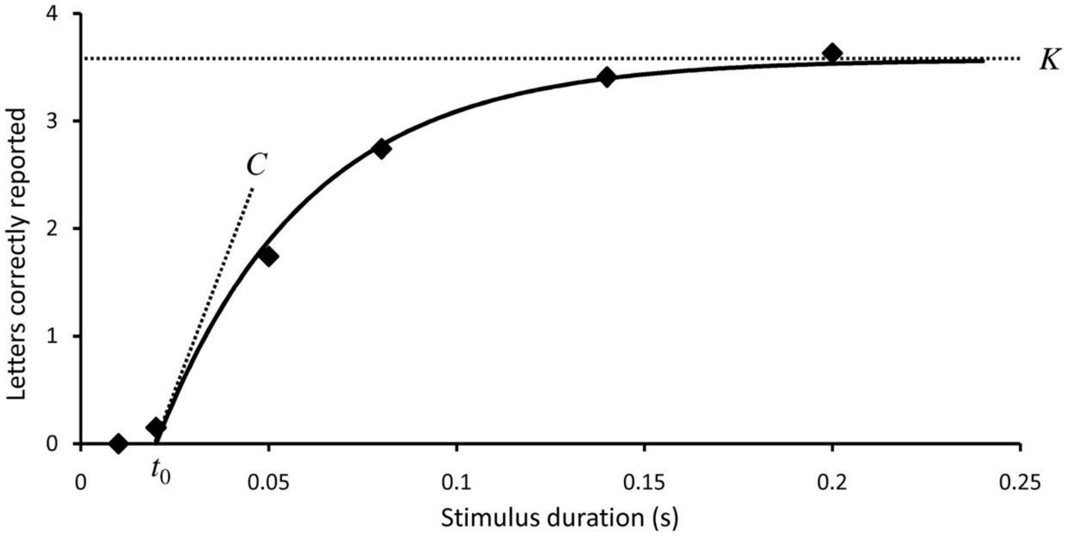

Figure 7.3 A plot describing the probability of correctly categorizing visual stimuli appearing in a memomry array, as a function of exposure time, fitted to an exponential function based on the Theory of Visual Attention framework (Adopted from Habekost, 2015. Figure copied in accordance with the Creative Commons Attribution-Noncommercial-Share Alike 3.0 Unported License)

The other two parameters are (4) the spatial bias parameter ω_{index}, and (5) the top-down selectivity index α. The spatial bias parameter represents the ratio between the sum of the attentional weights assigned to items on the left, and the overall sum of all attentional weights. The parameter ranges between 0 and 1, with a value of 0.5 indicating symmetrical attentional weighting; a value closer to 0 indicates an attentional bias to the right, and a value higher than 0.5 indicates an attentional bias to the left side of the visual field. The top-down selectivity index α is defined as the ratio between the attentional weights allocated to a distractor and to a target. The resulting α value ranges between 0 and 1, with the lowest score indicating perfect selectivity (no attentional weight given to irrelevant distractor). For a detailed overview of the attentional parameters and their correlates, see Habekost (2015). As the attentional weight score (ω_{index}) and the attentional selectivity index (α) are measured on ratio scales with arbitrary values, this data was transformed using a log transformation (a similar approach, of normalising the raw values was also used by Moos *et al.*, 2012). In the new calculated scores (transformed ω and α), the lower the raw score, the lower the transformed value (the transformed values are on a negative scale as they are based on a ratio smaller than 1).

The main analysis procedure focused on whether there was a change in the attentional weight index (transformed ω_{index}) pre- and post- sustained attention training. The research hypothesis was that a significant shift towards the right would only be observed in the Right Training group. However, to explore any other effects of training on attention-related parameters, K, t_0, C and transformed α were also calculated and compared between conditions. The estimated parameters were compared between four groups: Right Training, Left Training, Neutral Training and No Training at two time points. Before analysing the data, one outlier participant whose transformed ω_{index} average exceeded that of the group by more than three standard deviations was removed from the Right Training group. The data extraction and fitting procedures were performed using Matlab (Ver. 2015a; MathWorks, Inc., Natick, MA) and the LibTVA (Dyrholm *et al.*, 2011; Kyllingsbaek, 2006). The statistical analysis was performed using SPSS (Ver 24; IBM Corp, 2016) and the Bayes Factor R Package (Version 0.9.12-2).

Results

Performance on the Lateralised Sustained Attention Training Task

The mean accuracy in the sustained attention task (across three experimental groups: Right Training, Left Training and Neutral Training) was calculated separately for trials in which targets appeared either on the right or on the left. A 2 x 3 repeated-measures ANOVA was carried out, with the target condition as a within-subjects factor (Left Target, Right Target) and the experimental group as a between-subjects factor (Right Training, Left Training, Neutral Training). There were no interactions between the factors, suggesting that the overall performance pattern did not differ between groups when performing the different versions of the sustained attention training task (F(41,2)=1.383; p=.262). There were also no group differences (F(41,2)=.112; p>.8), or overall differences in accuracy when targets appeared on the right or on the left (F(41,1)=1.422; p=.24). A detailed description of the performance is illustrated in Figure 7.4.

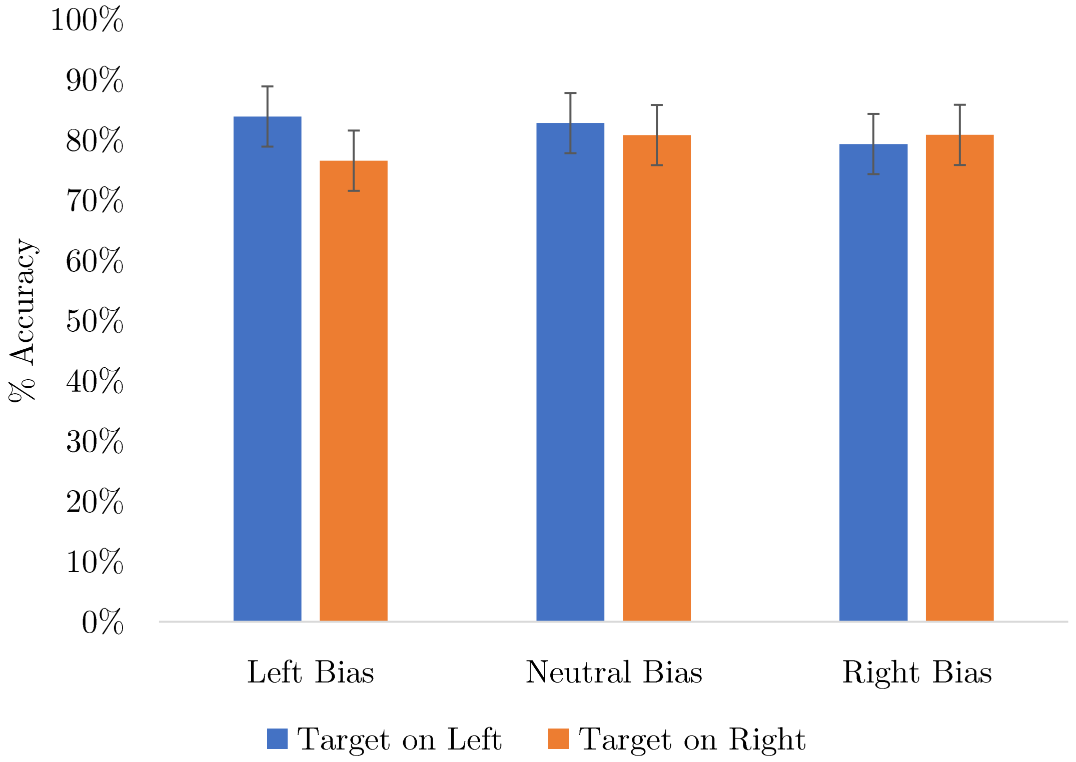

Figure 7.4 Accuracy rate on the lateralised sustained attention task for each experimental group, when target is presented either on right or left. Black lines represent standard error

Theory of Visual Attention Attentional Parameters

Table 7.1 describes the Theory of Visual Attention-based attentional parameters derived from the performance on the CombiTVA paradigm, estimated separately for all experimental groups during the two Theory of Visual Attention assessment sessions.

Group	Theory of Visual Attention Parameters	Training Session 1	Training Session 2
Right Training	ω_{index} *(raw values)*	.47 (.05)	.45 (.07)
	ω_{index} *(transformed)*	-.32 (.05)	-.35 (.07)
	K	3.61 (.90)	3.75 (.69)
	t_0	15.39 (13.22)	12.58 (5.87)
	C	64.54 (21.72)	79.63 (29.06)
	α *(raw values)*	.56 (.21)	.59 (.31)
	α *(transformed)*	-.27 (.16)	-.26 (.19)
Left Training	ω_{index} *(raw values)*	.47 (.08)	.46 (.09)
	ω_{index} *(transformed)*	-.32 (.08)	-.34 (.09)
	K	3.43 (.70)	3.46 (.81)
	t_0	15.27 (5.45)	17.38 (9.12)
	C	59.99 (18.84)	67.66 (22.93)
	α *(raw values)*	.68 (.28)	.57 (.27)
	α *(transformed)*	-.19 (.17)	-.27 (.17)
Neutral Training	ω_{index} *(raw values)*	.46 (.05)	.46 (.06)
	ω_{index} *(transformed)*	-.33 (.05)	-.33 (.06)

	K	3.34 (.67)	3.23 (.77)
	t_0	12.12 (8.69)	17.42 (12.09)
	C	55.25 (20.68)	66.42 (24.78)
	α *(raw values)*	.62 (.24)	.71 (.34)
	α *(transformed)*	-.23 (.17)	-.17 (.22)
No training	ω_{index} *(raw values)*	.46 (.07)	.47 (.06)
	ω_{index} *(transformed)*	-.33 (.06)	-.32 (.06)
	K	3.06 (.67)	3.31 (.57)
	t_0	16.05 (10.73)	18.27 (10.46)
	C	56.85 (26.73)	68.97 (23.10)
	α *(raw values)*	.59 (.26)	.54 (.24)
	α *(transformed)*	-.22 (.15)	-.25 (.13)

Table 7.1 Descriptive statistics of mean group performance (and standard deviation) of each of the estimated Theory of Visual Attention parameters in four experimental groups. α *and* ω*-index values are presented in their raw values and log-transformed*

Changes in Spatial Weights

A mixed-model repeated-measures ANOVA with the CombiTVA session number as a within-subjects factor (First, Second), the experimental group as a between-subjects factor (Right Training, Left Training, Neutral Training, and No Training), and the transformed ω_{index} as the dependent measure, was carried out as the main analysis. The results showed a significant main effect of session (F(55,1)=4.084; *p*=.048; partial η^2=.069) and a significant interaction between Group and Session (F(55,3)=3.220; *p*=.03; partial η^2=.149). There were no between-group differences (p>.9). A *post hoc* analysis revealed that the source of the reported interaction was a significant difference in the transformed ω_{index}

between sessions only in the Right Training group, with a greater bias towards the left in the first session (transformed ω_{index}=-.32) compared to the second session (transformed ω_{index}=-.35) (t(13)=2.573; p=.023; 95%CI[.004;.048]; Cohen's d=0.68).

There were no significant differences in any of the other groups when comparing the attentional bias across sessions (all p's >.18), and no between-group differences when comparing the mean attentional bias (p>.89). To further investigate the change in ω between the two sessions in each group, and to learn whether there was a stronger likelihood of evidence of the null hypothesis when changes were non-significant, a further *post hoc* analysis procedure was repeated with a series of paired-sample Bayesian T tests (Rouder *et al.*, 2009). The statistical test was based on the Bayes Factor R Package (Version 0.9.12-2, by R Moray[12]). The Prior Scale was set to a medium effect size (0.7071). The Bayes Factors for each comparison between the first and second session are reported in Table 7.2.

Group	**Bayes Factor**
Right Training	2.878
Left Training	0.587
Neutral Training	0.269

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[12] Downloaded from https://www.rdocumentation.org/packages/BayesFactor/versions/0.9.12-2

No Training	0.487

Table 7.2 Bayes Factors obtained in four post hoc comparisons, comparing the transformed Bias Score between two sessions

The Bayes Factors obtained in the Bayesian *post hoc* t-tests comparing session 1 and 2 in the Left Training, Neutral Training, and No Training groups can be interpreted as evidence supporting H0, namely that there was no change in ω between the sessions in those three groups. The only Bayes Factor greater than one was in the Right Training group, indicating a weak change in ω between the two sessions. A further interpretation of the Bayes factor, following Jeffreys (1961) and Wetzels *et al.* (2011), would suggest strong evidence in favour of the null hypothesis in the Neutral Training condition (Bayes factor $<1/3$), and therefore it is very likely that the participants' behaviour did not change between conditions. The other effects could be viewed as weaker (in accordance with Wetzels *et al.*, 2011). The Bayes Factors obtained in the Left Training and No Training groups suggest only a slight evidence in favour of the null hypothesis. Finally, the Bayes Factor obtained in the Right Training group suggests a weak support, i.e., approaching the cut-off of a substantial evidence (Bayes Factor = 3) in favour of the alternative hypothesis under the prior assumption of a bias shift with a medium effect size. To verify whether the task reliably changed the attentional bias, therefore, the next experiment attempted to replicate the findings in an independent sample (Experiment 2).

Figure 7.5 illustrates the effect of training for all individual participants plotted as the direction of change in performance (in Theory of Visual Attention parameter ω) in all experimental groups.

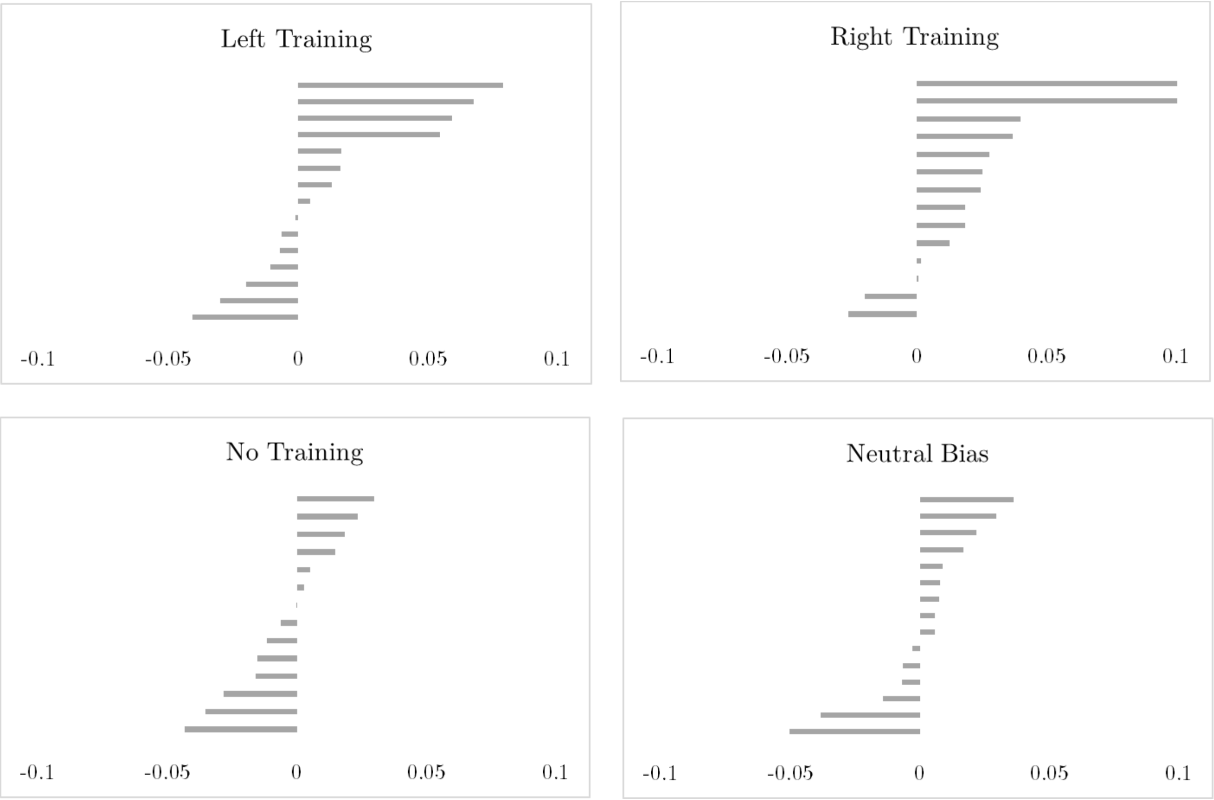

Figure 7.5 Log-transformed values of change in the attentional bias (ω parameter) plotted for individual participants in each experimental group. Positive values represent a shift in bias toward the left; negative values represent a shift in bias towards the right

Changes in Selectivity, Memory, Perceptual Threshold, and Processing Speed

For completeness, separate ANOVAs compared other attentional parameters derived from the CombiTVA paradigm as the dependent variables (K, t_0, C and transformed α). There was a significant main effect of increased processing speed (C parameter) between the two sessions ($F(1,55)=24.359$; $p<.001$; partial $\eta^2=.307$), with no groups differences ($F(3,55)=.727$; $p=.54$) or interaction ($F(3,55)=.423$; $p=.737$). This observation is in line with previous reports of a general increase in processing speed between Theory of Visual Attention sessions (Habekost, Petersen, & Vangkilde, 2014). To further ensure that the change in processing speed can be attributed to an overall practice effect (and was not driven by the three training groups), a *post hoc* comparison of processing speed estimated based on the performance of the No Training group during the first and the second session was carried out. There was a significant difference between the sessions ($t(14)=2.519$; $p=.024$; 95% CI [-22.4;.-1.80]. Memory capacity (K), perceptual threshold (t_0) and selectivity (transformed α) did not differ between sessions, nor there were any interactions or group differences (stats appear in Table 7.3).

	Session 1 X Session 2	Group Effect	Interaction
K	$F(1,55)=1.756$; $p=.191$	$F(3,55)=1.394$; $p=.254$	$F(3,55)=1.722$; $p=.173$
t_0	$F(1,55)=1.3$; $p=.259$	$F(3,55)=.482$; $p=.696$	$F(3,55)=1.228$; $p=.308$
α	$F(1,55)=1.071$; $p=.305$	$F(3,55)=.262$; $p=.853$	$F(3,55)=2.421$; $p=.076$

Table 7.3 ANOVA tests comparing the memory capacity (K), perceptual threshold (t_0) and selectivity (α) between groups over two sessions

Interim Discussion

The findings demonstrate training on sustaining attention to the right visual field influenced the distribution of attentional weights on a subsequent spatial-attention task. A single administration of the bi-lateral Masked Conjunctive CPT, in a condition where a higher proportion of targets appeared on the right, resulted in a significant shift of the attentional bias measured by the CombiTVA. These results were found only when training sustained attention towards the right, and can be explained by a right hemispheric dominance in controlling attention. When increasing sustained attention demands towards the right visual hemi-field, the allocation of spatial-attention predominantly controlled by the non-dominant left hemisphere was enhanced. In other words, the Right Training protocol changed the balance between the hemispheres by triggering increased activation of the non-dominant left hemisphere when participants were trained to sustain attention towards the right hemi-field. This interpretation receives support when contrasting the significant shift rightward with the null effect obtained when applying the left-lateralised sustained attention task (Left Training), as the allocation of attention towards the left is already biased by the preferential activation of the dominant hemisphere. The findings are consistent with previous studies showing that prism adaptation can improve perception only towards the right (e.g., Loftus, Vijayakumar, & Nicholls, 2009;

Michel et al, 2003). Importantly, however, the current study demonstrates a comparable effect triggered by a transfer between two different attention tasks, rather than a perceptual manipulation as in prior prism adaptation studies. Furthermore, in light of evidence that the attentional parameters derived from the Theory of Visual Attention based task are independent of sustained attention (McAvinue *et al.* 2012a, 2012b), the transfer effects appear to reflect a mechanistic change in hemispheric dominance as opposed to a generic effect of task practice.

Another parameter that changed between tasks was processing speed, although the presence of the same effect even in the lack of any training suggests that this was clearly a result of a generalised training effect.

Experiment 7.2: Training Protocol Combined With Brain Stimulation

The aim in Experiment 7.2 was to examine whether brain stimulation targeting the posterior parietal cortex bilaterally could potentiate the effects of training on the sustained attention task. As bilateral parietal transcranial random noise stimulation does not permit precise targeting of a discrete neural substrate of a specific attentional function; the aim of the stimulation protocol was, instead, to modulate the overall function of the posterior parietal cortex (see Beck & Kastner, 2014). Based on prior findings, it was anticipated that both the attentional weight index (ω_{index}) would change due to the training protocol, and that the attentional selection (the top-down selectivity index α) might be affected by parietal stimulation (e.g., Fierro *et al.*, 2000; Hung *et al.*, 2005; Sparing *et al.*, 2009; Moos *et al.*, 2012; Giglia *et al.*, 2011; Benwell *et al.*, 2015). As transcranial random noise stimulation may interact with brain activations involved in task performance and thus potentiate their effects, it was also hypothesised that brain stimulation alone would have a lesser or no effect compared with the combination of training and brain stimulation.

Methods

Participants

The participants in this experiment were 45 naïve volunteers (mean ± SD age = 25.4 ± 4.2; 30 of them were female). They were recruited through an online research participation system at the University of Oxford. Exclusion criteria included previous participation in Experiment 1, any previous history of neurological or psychiatric disorders, or contraindications to transcranial current stimulation (Poreisz *et al.*, 2007). Both left- and right-handed participants were recruited for the study, and the hand dominance was assessed according to Edinburgh handedness inventory (Oldfield, 1971; mean handness score ± SD = 60.2 ± 54.68; six participants classified as left-handed, and one as ambidextrous).

All participants had either normal or corrected-to-normal vision. All study participants provided written informed consent, in compliance with relevant protocols approved by the University of Oxford Central University Research Ethics Committee. The experimental procedures were conducted in accordance with the latest version of the Declaration of Helsinki. Participants were compensated for their time (payment of £25, inclusive of travel expenses).

Apparatus

The same setup was used in this study as in Experiment 7.1, with the addition of a transcranial current stimulation (see the transcranial random noise stimulation section for full details).

General Procedure

Participants were divided into three experimental groups: Right Training with bi-parietal transcranial random noise stimulation (15 participants), Right Training with sham stimulation (15 participants), No Training with bi-parietal transcranial random noise stimulation (15 participants). All participants were invited to the lab on two consecutive days at the same time of day. On the first day, participants performed the CombiTVA task to assess their baseline attentional bias and other attentional parameters based on the Theory of Visual Attention framework. On the second day, the two Right Training groups performed the Right version of the sustained attention training task (with 80% of the right target-trials), while either bi-parietal transcranial random noise stimulation (tRNS Right Training group) or sham stimulation (sham Right Training group) was applied (see below for details). The transcranial random noise stimulation control group was given bi-parietal transcranial random noise stimulation while sitting in the experiment room and not performing any task. Participants in all three experimental groups were assessed on the CombiTVA task immediately following either tNRS or sham stimulation.

Behavioural Paradigm

The task design was the same as in Experiment 1, but only the Right Training version of the task was used (i.e., targets appeared on the right on 80% of the target trials).

Transcranial Random Noise Stimulation

The high-frequency transcranial random noise stimulation was administered by means of a battery-driven, constant current stimulation (neuroConn DC-STIMULATOR PLUS, GmbH, Illmenau, Germany), using 5x5 cm rubber electrodes placed in saline soaked sponges. The saline was used to reduce the risk of skin irritation and the electrodes were secured using an elastic strap to ensure electrical contact with the scalp. The electrodes were placed over left and right posterior parietal cortex, at locations P3 and P4 according to the 10-20 EEG system (Jasper, 1958), and 1mA transcranial random noise stimulation was applied with a frequency of alternating current ranging from 100 to 640 Hz at random. The transcranial random noise stimulation lasted 1200 seconds (20 minutes), while the sham stimulation lasted only 30 seconds; the rest of the time the participants (unknowingly) had no brain stimulation. Both the 1200-seconds and the 30-seconds transcranial random noise stimulation were flanked by a gradual 15-seconds up and 15-seconds down the current ramp. The start of the experimental task was always triggered following the short practice and the subsequent immediate onset of either the sham or the real transcranial random noise stimulation. The sustained attention training task lasted approximately 40 minutes, outlasting the active or sham stimulation.

Statistical Analysis

The changes in Theory of Visual Attention parameters across CombiTVA sessions were compared among groups using mixed-effects ANOVAs with the factors of session (first, second) and group (transcranial random noise stimulation Right Training, sham Right Training, transcranial random noise stimulation No Training). The dependent variables were the five parameters extracted based on the Theory of Visual Attention computational model: transformed ω_{index}, K, t_0, C and transformed α.

Results

Performance on the Lateralised Sustained Attention Training Task

Mean accuracy in the right-lateralised sustained attention task was calculated for the two groups who performed the training task (transcranial random noise stimulation Right Training and sham Right Training), separately for each experimental condition (target appearing on the right, target appearing on the left, and no target). A 2 x 2 repeated-measures ANOVA with the target condition as a within-subjects factor (Left Target, Right Target) and the experimental group as a between-subjects factor (transcranial random noise stimulation Right Training and sham Right Training) revealed no interactions between the factors, suggesting that the overall performance pattern did not differ between groups (F(2,27)=.626; *p*=.543). There were also no group differences (F(2,27)=.067; *p*=.935), nor were there differences between the two sessions across all participants (F(1,27)=2.982; p=.096). As a supplementary analysis, a second ANOVA was carried out with the block number as another within-subject factor to explore if the application of brain stimulation triggered changes in the accuracy rate in the performance on the lateralised sustained attention task. A 3X2X2 repeated measures ANOVA was carried out, with two within-subjects factors: target condition (Left Target, Right Target) and block number factor

(First, Second, Third); and experimental group as a between-subjects factor (transcranial random noise stimulation Right Training and sham Right Training). None of the effects was significant (see results in Table 7.4).

Comparison	ANOVA	p Value
Target Condition	F(1,28)=.735	.399
Block Number	F(2,56)=1.324	.274
Group	F(1,28)=.256	.617
Target Condition X Group	F(1,28)=.034	.855
Block Number X Group	F(2,56)=.017	.983
Target Condition X Block Number	F(2,56)=.1.998	.145
Target Condition X Block Number X Group	F(2,56)=.330	.721

Table 7.4 ANOVA test comparing performance between the two sessions, over three blocks, between the two experimental groups

Theory of Visual Attention Attentional Parameters

Table 7.5 describes the means and standard deviations of all five attentional parameters derived based on the performance in the CombiTVA task in two sessions, calculated separately for every experimental condition.

Group	Theory of Visual Attention Parameters	Training Session 1	Training Session 2
tRNS Right Training	ω_{index} *(raw values)*	.46 (.06)	.44 (.05)
	ω_{index} *(transformed)*	-.33 (.06)	-.35 (.05)
	K	3.55 (.58)	3.56 (.61)
	t_0	11.57 (7.59)	10.85 (7.50)
	C	68.65 (23.97)	73.64 (27.07)
	α *(raw values)*	.62 (.15)	.46 (.15)
	α *(transformed)*	-.22 (.12)	-.34 (.13)
sham Right Training	ω_{index} *(raw values)*	.47 (.06)	.44 (.07)
	ω_{index} *(transformed)*	-.32 (.05)	-.35 (.07)
	K	3.67 (.69)	3.81 (.74)
	t_0	10.10 (5.49)	12.10 (7.25)
	C	69.22 (24.71)	71.85 (24.52)
	α *(raw values)*	.55 (.20)	.55 (.25)
	α *(transformed)*	-.28(.16)	-.29(.18)
tRNS No Training	ω_{index} *(raw values)*	.47 (.05)	.47 (.06)
	ω_{index} *(transformed)*	-.32 (.04)	-.32 (.06)
	K	3.56 (.70)	3.70 (.62)
	t_0	11.23 (7.33)	11.30 (7.41)
	C	62.26 (21.92)	73.13 (23.74)
	α *(raw values)*	.58 (.21)	.56 (.22)
	α *(transformed)*	-.26 (.17)	-.28 (.18)

Table 7.5 Descriptive statistics of mean group performance (and standard deviation) of each of the estimated Theory of Visual Attention parameters in three experimental groups. . α *and* ω*-index values are presented in their raw values and log-transformed*

A 2 x 3 mixed-measures ANOVA with CombiTVA session number as a within-subject factor (Session 1, Session 2), the experimental group as a between-subject factor (transcranial random noise stimulation Right Training, transcranial random noise stimulation, No Training, sham Right Training), and ω_{index} index as the dependent variable, was carried out as the main analysis. There was a significant main effect for the session number (F(1,42)=7.235; *p*=.01; partial η^2=.145), no group differences (F(2,42)=.318; *p*=.729) and no interaction (F(2,42)=2.031; *p*=.144). Although there was no significant interaction, a series of *post hoc* analysis focusing on the change on each group was carried out to verify whether there was a significant shift in all experimental groups. This comparison was meaningful to compare the observed effects in Experiment 7.2 to the equivalents in Experiment 7.1. The significant difference between Sessions 1 and 2 was only observed in the two groups that received the attentional training i.e., the transcranial random noise stimulation Right Training group (t(14)=2.284; *p*=.038; 95% CI [.001;.039]; Cohen's d = 0.58) and the sham Right Training group (t(14)=2.401; *p*=.031; 95% CI [.002;.046]; Cohen's d = 0.61). There was no significant change in attentional weights in the transcranial random noise stimulation control group (t(14)=-.77; p>.9).

As in Experiment 1, the analysis of the simple effects was repeated by using a series of Bayesian T tests (Rouder *et al.*, 2009). The Prior Scale was set to a medium effect size (0.7071), and Bayes Factors were reported for each comparison between the first and the second session (Table 7.6). In accordance with Werzels *et al.* (2011), the Bayes Factor in transcranial random noise stimulation control provided strong evidence in favour of the null hypothesis (Bayes Factor $< 1/3$), and the two other Bayes Factors (transcranial random noise stimulation Right Training and sham Right training groups) provided weak support in favour of a shift in bias with a medium effect size. Although this evidence could only be considered as moderate, the findings observed in these two groups provided two independent replications of the effect demonstrated in Experiment 1, and therefore supported the reliability of the observed change in attentional weights.

Group	**Bayes Factor**
tRNS Control	0.263
tRNS Right Training	1.884
sham Right Training	2.245

Table 7.6 Bayes Factors obtained in three post hoc comparisons, comparing the transformed Bias Score between two sessions

As a final analysis on the attentional weights, we included the participants from all three experimental groups who underwent the right sustained attention protocol (one group in Experiment 1/Right Training Group, and two groups in Experiment 2/transcranial random noise stimulation Right Training and sham Right Training). First, two Bayesian ANOVA tests were used to estimate whether the groups differed in their attentional weights on either the first or the second CombiTVA sessions, with the experimental group as a between-subjects factor, and the ω_{index} as the dependant variable. With a prior scale set to a medium effect size (0.7071), there was substantial evidence in favour of H0, suggesting a similar bias among the three groups (BF=.102). A similar result was obtained for the second session (BF=.108). After establishing that there were no group differences in each session, all the observations were grouped before carrying a within-subjects Bayesian T-Test, with the session number as a within-subjects factor and the attentional weights (ω_{index}) as the dependant variable (now including 45 participants). The results now showed very strong evidence in favour of H1, namely a significant change in the ω_{index} following right sustained attention training (BF=32.745).

Changes in Selectivity

Possible changes in the attentional selectivity parameter (α) as a function of training and stimulation were subsequently assessed. A mixed-measures ANOVA was conducted, with session number as a within-subject factor (Session 1, Session 2), and experimental group as a between-subject factor (transcranial random noise stimulation Right Training, transcranial random noise stimulation No Training, sham Right Training). The analysis revealed a significant main effect for session number (F(42,1)=8.351; p=.006; partial η^2=.166), and a significant interaction between group and session (F(42,2)=4.317; p=.02; partial η^2=.171). A *post hoc* analysis revealed that the source of the interaction was a significant difference in α between sessions only in the transcranial random noise stimulation Right Training group, with an improvement in selectivity as reflected in a higher α value (and therefore lower selectivity) in the first session (transformed α=-.22) as compared to the second session (transformed α=-.34) (t(14)=4.250; p=.001; 95% CI [.063;.193]; Cohen's d = 1.09). There were no significant differences in α between sessions in the transcranial random noise stimulation No Training group (t(14)=.884; p=.391), or in the sham Right Training (t(14)=.303; p=.766). Finally, three Bayesian T tests were used to compare the transformed α between the two sessions for each group. The results (Table 7.7) confirm that 1mA transcranial random noise stimulation applied over the posterior parietal cortex significantly increased selectivity, but only when combined with the sustained attention training. The Bayes Factors suggest that, while in both transcranial random noise stimulation control and sham Right Training groups there was substantial evidence in favour of the null hypothesis (e.g., selectivity did not differ between sessions), the evidence in the transcranial random noise stimulation Right Training group provided very strong evidence (following Wetzels *et al.*, 2011) for increased selectivity when combining transcranial random noise stimulation and sustained attention training.

Group	**Bayes Factor**
tRNS Control	0.269

tRNS Right Training	46.489
sham Right Training	0.273

Table 7.7 Bayes Factors obtained in three post hoc comparisons, comparing the transformed α parameter between two sessions

Changes in memory, processing speed and perceptual threshold.

Finally, the possible effects of training and stimulation on other Theory of Visual Attention parameters (C, t_0, K) were tested with independent ANOVAs using the same factors. Replicating the findings in Experiment 7.1, there was a significant main effect of session on the processing speed parameter (C), with a lower processing speed in the first session (66.71 items per second) compared to the second session (74.19 items per second) (F(1,42)=14.277; *p*<.001; partial η^2=.145).There was no effect of group (F(2,42)=.168; *p*=.846) and no interaction (F(2,42)=.785; *p*=.463). Session also affected memory capacity K (F(1,42)=5.288; *p*=.027; partial η^2=.112), showing overall improved capacity over the second session. As in processing speed, there was no effect of group (F(2,42)=.305; *p*=.739) and no interaction (F(2,42)=1.033; *p*=.365). While such a change did not occur in Experiment 1, a similar effect of increased working memory capacity between repeated sessions has been previously reported (Habekost, Petersen, & Vangkilde, 2014). There were no effects of group or stimulation on t_0: the perceptual threshold did not change between session (F(1,42)=.359; *p*=.552), there was no effect of group (F(2,42)=.003; p=.997), and no interaction (F(2,42)=1.156; p=.324).

Discussion

The results suggest that attentional bias (weights assigned to the left versus right hemi-field, measured by ω_{index}) can be modulated by sustaining attention towards the right hemi-field, but this effect does not occur when sustaining attention towards the left visual field. Interestingly, combining the bilateral parietal high-frequency random-noise stimulation with the rightward sustained attention training protocol did not further increase the shift in attentional bias triggered by the training task alone, but instead resulted in increased attentional selectivity and ability to filter irrelevant distractors.

Experiment 7.1 supports the notion of the right-hemispheric dominance in visual attention (Heilman & Valenstein, 1979; Heilman & Van Den Abell, 1980; Mesulam, 1981; Weintraub & Mesulam, 1987). Consequently, the enhanced bias towards the right, but not the left, visual hemi-field triggered by the sustained attention training can be explained as a result of the inherently lower contralateral activity of the left hemisphere, which perhaps might be easier to modulate or increase. On the other hand, the failure to modulate the attentional bias towards the left hemi-field can be explained by the role of the right hemisphere in directing attention to both visual fields; there should, therefore, not be any shift in the spatial weights when it is trained. Previous studies seeking to modulate spatial attentional biases, by using a perceptual adaptation, have reported similar outcomes, showing successful shifts in pseudo-neglect only towards the right but not the left visual field (e.g., Loftus, Vijayakumar, & Nicholls, 2009; Michel et al, 2003). The interesting and novel finding presented here is that attentional bias can be modulated by applying a right-lateralised sustained attention task, and thus this modulation is a result of transfer effect between two different attentional tasks rather than a perceptual manipulation (e.g., Loftus, Vijayakumar, & Nicholls, 2009) or direct modulation of brain activity (e.g., Giglia *et al.*, 2011). Importantly, this task transfer effect was replicated in Experiment 7.2. It should be emphasised that the approach to training presented in this chapter differs from traditional methods using repetitive training protocols and employing test-retest of the training-task outcome as a measure of training efficiency (e.g., Robertson *et al.*, 1995). In contrast, this study tested whether a single administration of a relatively short task with demanding a lateralised sustained attention towards the left or right visual hemi-fields could have an immediate transferable effect on attentional weights (assigned to the left versus right hemi-field) and/or other attentional functions. Thus, the efficiency of the training task was assessed by the change in Theory of Visual Attention parameters rather than by a test-retest comparison of performance in the training task.

Experiment 7.2 set out to examine whether bilateral parietal transcranial random noise stimulation could further enhance the shift in attentional bias or modulate other attentional parameters. When the right-lateralised sustained attention task was combined with transcranial random noise stimulation, there was an increase in the parameter representing selectivity, measuring the capacity to select relevant stimuli over irrelevant distractors. A Bayesian analysis confirmed very strong evidence for the improvement of attentional selectivity in the group, combining training and transcranial random noise stimulation while providing evidence that selectivity remained unaffected by either transcranial random noise stimulation or sustained attention training alone. It therefore appears that there is unique value in combining transcranial random noise stimulation with sustained attention training.

The enhanced selectivity is in line with the contemporary view of the role of the parietal cortex in charge of attentional control and not just spatial allocation of attention (e.g., Corbetta *et al.*, 1993; Nobre *et al.*, 1997; Shulman et al, 2010; Kincade *et al.*, 2005; Doricchi *et al.*, 2010; for review see Beck & Kastner, 2014). The result broadly agrees with a previous study showing modulation in the

Theory of Visual Attention selectivity parameter after parietal stimulation (Moss *et al.*, 2012). It should, however, be noted that the change in selectivity in the current study was triggered only when stimulation was combined with sustained attention training, and not by stimulation alone (as in the study of Moss *et al.*, 2012). This discrepancy is likely attributable either to the use of a different method of brain stimulation likely operating via distinct neural mechanisms (bi-parietal transcranial random noise stimulation in the current study, as opposed to cathodal transcranial direct current stimulation over the right posterior parietal cortex in Moss *et al.*, 2012; for a recent review contrasting different transcranial current stimulation methods see Santarnecchi *et al.*, 2015), or to differences in study design. A recent study has shown that the introduction of random noise in the neural system (by using high-frequency transcranial random noise stimulation) contributes to overall amplified signal detectability by increasing action potentials across the visual cortex (van der Groen & Wenderoth, 2016). Importantly, prior evidence has suggested that neural enhancement triggered by transcranial random noise stimulation is transferable when the trained and non-trained cognitive domains share common neural substrates (e.g., Cappelletti *et al.*, 2013).

The improvement of selectivity observed only when sustained attention training was combined with transcranial random noise stimulation is worth further consideration. It was potentially the requirement for selective attention in the training protocol (the task required participants to distinguish a target from conjunctive distractors, and therefore had a clear requirement for selection) that contributed to the improvement in selection; the sustained attention task could therefore be understood as requiring both selectivity and spatial attention, and thus affecting the two corresponding Theory of Visual Attention parameters. Nevertheless, such an explanation is insufficient: there is a need to speculate on why sustained attention training applied alone (i.e. without brain stimulation) failed to alter selectivity and affected only the attentional weights. A potential explanation may be related to the nature of the parameters in question: while selectivity *improved*, attentional weights *shifted*. The results of Experiment 7.1 demonstrate how attention can be trained to be spatially biased towards one hemi-field over the other (the right versus the left hemi-field), without demonstrating any overall improvement in task-performance when compared with other conditions. The main influence of the behavioural training alone was not, therefore, the enhancement of the overall attentional capacity, but instead a violation of the balance between the hemispheres. It is possible that *biasing* attention without *increasing* attention may not depend on the enhanced neuroplasticity achieved by using brain stimulation. In contrast, when transcranial random noise stimulation is applied, there is a greater potential for increasing the overall available resource due to the combination of plasticity and focal training of the relevant networks. This observation is also consistent with prior studies showing very small or no effects of stimulation alone as compared to the effects of stimulation combined with cognitive training (e.g. Cappelletti *et al.*, 2013; Filmer *et al.*, 2016; Antal *et al.*, 2007).

In summary, this study indicates that attentional bias can be shifted towards the right hemi-field by a lateralised sustained attention task. When repeating the same paradigm combined with bi-parietal transcranial random noise stimulation, attentional selectivity was also enhanced. Several prior studies indicate that combining transcranial random noise stimulation with cognitive training can improve behavioural performance, and that such an effect can be maintained over time after application of repetitive protocols with multiple sessions spread over several days (e.g. Cappelletti *et al.*, 2013; Fertonani *et al.*, 2011; Popescu *et al.*, 2016). This is of particular interest as it has been suggested that repetitive high-frequency transcranial random noise stimulation, combined with cognitive training, not only increases the activity of the neuronal populations sub-serving the trained cognitive function, but also facilitates brain plasticity (Kadosh *et al.*, 2012; Cappelletti *et al.*, 2013; Fertonani *et al.*, 2011; Terney *et al.*, 2008). It would be interesting, therefore, to explore the longevity of the changes in spatial bias and selectivity observed here in the future, and to test whether lasting effects can be observed after a single session or whether multiple training plus stimulation sessions are required. It would also be worth investigating whether increased amount of training (multiple training session) could enhance the observed effects i.e., changes in spatial bias and/or selectivity. Future work might also investigate the clinical applicability of such protocols in the rehabilitation of visuo-spatial disorders, in particular if their effect is found to be long-lasting (see Harvey & Kerkhoff, 2015).

In the current study, a bilateral stimulation was applied while participants performed a right-lateralised task, but future studies may try to explore whether the effect of enhanced selectivity can also be obtained when combining stimulation with training in the neutral or left-lateralised versions of the sustained attention task. Such an approach could address some interesting questions: whether training the left hemisphere on selectivity without a change in spatial bias could have an effect, and whether the observed change in selectivity was merely the result of performing an attentional selection over time and was completely independent of targeting the rightward attentional shift. Alternatively, it would be interesting to explore whether attention could be biased towards the left hemi-field by a different training protocol alone or combined with brain stimulation, perhaps by a repetitive training protocol conducted over the period of not one but several sessions better suited to trigger changes in the activity/neuroplasticity within the dominant right hemisphere. Finally, a complementary study to the one presented here would explore whether spatial biases of attention can be modulated without the sustained attention component that we have applied. Such a comparison is viable for learning about the specific contribution of sustained attention to the results reported here. Although such a comparison would be beneficial, it should be emphasised that the unique contribution of the current study is its experimental design, which allows the combination of the different attentional functions.

Chapter 8 : General Discussion

From a historical perspective, a few pivotal moments of transition define the scientific inquiry of sustained attention. The seminal work of Norman Mackworth (1948) first formulated the questions of why, how, and to what extent performance deteriorates with time. Jane Mackworth (1968) further extended the study of vigilance, where vigilance was associated with attention, Signal Detection Theory, and neurophysiology. Meanwhile, as the 'cognitive revolution' accelerated, the notion of arousal appeared in Hebb's work (1955) and provided a low-level mechanistic explanation of momentary 'energetic states' of the system. With the appearance of the DSM III, in which ADHD was first associated with poor sustained attention following the works of Douglas (1972), sustained attention capacity became a main focus in clinical research. Further developments by Parasuraman (1979) revealed that cognitive load of many kinds could influence sustained attention capacity, including memory and perceptual degradation. Posner and Petersen (1990) introduced their heterogeneous account of attention in which the alerting network accounts for the changes in attention in the temporal domain. In the clinical field, the works of Ian Robertson (1997) established effective and sensitive ways to assess sustained attention in various populations. Other works attempted to reintegrate the various theoretical frameworks ascribing sustained attention into unified theories and highlighting potential overlaps (e.g., Sarter, Givens, & Bruno, 2001; Sturm & Willmes, 2001).

As articulated in the Introduction, the mere task of defining sustained attention is a challenge. Among the constructs in the human attentional system, it may be the most elusive and poorly defined. From a critical perspective, it could be argued that sustained attention is not a 'pure' component of attention, and should instead be considered as a 'capacity' supported by lower-level functions, such as alertness and arousal. A more flexible approach would be to consider the 'problem' of sustained attention as a Wittgensteinian 'language game' (*Sprachspiel*), its meaning being contingent on the context in which it appears. To some extent, such an interpretation has already been adopted. For example, there seems to be a fundamental gap with no real overlap between the way in which Douglas (1972) and Barkley (1997) use sustained attention to describe the behavioural manifestations of ADHD, and these two accounts share no feature with the way in which Sturm and Willmes (2001) consider sustained attention as a cognitive resource.

Even if one accepts the potential 'multiplicity' of interpretations behind sustained attention, its influence is undeniable. As a defining characteristic of one of the most prevalent developmental disorders in the world (i.e., ADHD; NCHS, 2016), and as a major determinant in how many other conditions across the life-span are characterised (e.g., ageing and neurodegenerative conditions), the way in which sustained attention is defined and measured is crucial. I have therefore tried to propose a few guidelines, or signposts, in this thesis for considering sustained attention. Sustained attention is an effortful and goal-directed aspect of behaviour that captures the ability to maintain an adequate level of attention-based performance over time. Accordingly, its assessment must account for the changes in performance over time, i.e., it should consider not only the *performance level*, but also *performance change*. Any assessment should also aim to manipulate attentional effort, rather that perceptual, motor or mnemonic for instance. Experimentally, sustained attention is best manipulated by introducing non-engaging tasks and avoid facilitating performance in a stimulus-driven manner. As a construct within the cognitive literature, sustained attention is more inclusive than other constructs as alertness (phasic and tonic) and vigilant attention in a few different ways: it refers to a wider time scale than phasic alertness; it relies on wider brain networks (it can be thought as a combination of vigilant attention and alertness); and it is reflected in more behavioural outcomes measures (whereas alertness is typically limited to RTs, sustained attention can also be measured based on accuracy). When contrasted with vigilance, sustained attention refers to a shorter timescale (normally less than an hour). Sustained attention also refers to a specific cognitive capacity within the domain of attention, compared with vigilance which normally refers to the overall decrement in arousal over time. Arousal has been proposed as the sub-cortical function that supports sustained attention.

The findings presented in this thesis raise many issues that should be addressed in future studies of sustained attention. For example, I have argued that, during the transition towards clinical assessment of sustained attention, the practical requirements for tasks that increase inter-subject variability in a short time have led researchers to increase demands for cognitive resources that are unrelated to sustained attention. This led to memory-based CPT designs (e.g., Chen & Faraone, 2000) and (arguably) the increasing demands for response inhibition (Robertson *et al.*, 1997). In Chapter 2, I addressed the involvement of response inhibition mechanisms in CPTs by manipulating target-distractor ratios. Strikingly, a very similar manipulation appeared a few decades ago, when it was explicitly argued that vigilance is best observed when the target ratio is kept to a minimum (e.g., Mackworth, 1968). Mackworth (1948) set the tradition of facilitating vigilance decrement by introducing rare target events within a prolonged continuous task. Such designs are, by definition, inefficient in terms of the amount of data that can be extracted per time unit, as most of the trials cannot be analysed: participants do not provide a response when they are (frequently) introduced with a non-target. Nevertheless, an increase in the number of target events could lead to misleading interpretations. For example, researchers have used the Stop-Signal Task when studying the neural substrates of sustained attention (e.g., Rosenbreg *et al.*, 2013; 2016). Although the Stop-Signal Task is more informative and robust in terms of the number of trials that can be analysed, such reports could be viewed critically in light of the findings presented in Chapter 2. In Chapter 2, different performance patterns were observed when contrasting experimental designs aimed to measure sustained attention versus response inhibition. It was demonstrated that when increasing the proportion of the response-relevant events, individuals are less likely to miss targets and more prone to commit false alarms. It was then argued that such a shift in the perceptual-bias criteria (according to the Signal Detection Theory) could be thought of as marking the cognitive mechanisms involved in the task, with sustained attention effort marked by a greater proportion of missed targets.

Another discussion in this thesis addressed the adequacy of task indices in use for clinical assessment of sustained attention and called for the questioning of some well-established findings. In Chapter 3, by presenting differences in RTs that linked to dynamics occurring within a task (i.e., phasic increase in alertness following a target-trial), I questioned the utility of relying on RT-based indices when assessing clinical populations. With respect to the way in which sustained attention is estimated, I argued that researchers have gradually shifted from the use of task indices that mark performance *decrement* in favour of a new approach of performance *averaging* (e.g., Bennet-Murphy *et* al., 2007; Egner & Gruzelier, 2001; Lin, Hsiao, & Chen, 1999; MacLean *et al.*, 2010). Although some assessment batteries do evaluate the course of change over time in a clinical context (e.g., Conners, 2000), it is less frequent in experimental studies. Chapters 3 and 4 provide a compelling argument against this transition, by demonstrating that, in two different CPT variations, the extent to which performance changed over time is closely associated with subjective reports of distractibility and inattention. Correlations between different task indices showed that performance change is independent of the overall detection rate and RT variability. I have thus argued that the transition towards cognitive assessment based on mean performance, rather than performance change, is not justified. It appears that, within the sustained attention literature, the issue of the appropriate performance indices is rarely discussed.

In Chapter 3, a group of stroke survivors was compared to an age-matched control group. The two groups had many similarities in their subjective reports of distractibility, as well as in their sustained attention markers, which were estimated based on the change in task performance over time. It was also demonstrated that across all participants, the sustained attention task markers and subjective reports of distractibility were highly correlated. When comparing the two groups based on mean performance alone (without accounting for the change in performance), the two groups differed significantly, with the stroke survivors showing an overall lower performance. It was argued that poor performance (e.g., low accuracy or slower responses) can be derived from many cognitive factors unrelated to sustained attention, such as phasic fluctuations in alertness or motor difficulties. Perhaps the most provoking aspect of the study is the notion that, although the groups did not differ in their sustained attention capacity (based on subjective reports and performance decrement indices), the simple averaging approach could have easily led to an opposite conclusion.

In Chapter 4, a critical evaluation was applied to two clinical groups that are often described as having sustained attention difficulties (Williams syndrome and Down's syndrome children). With a slight modification of the task indices in use, I showed that children with Down's syndrome are more similar to controls in terms of their capacity of maintaining performance over time. What follows from these results is that individuals with Down's syndrome may not suffer from a selective impairment in sustained attention; instead, they may tend to perform poorer than controls. Both Chapters 3 and 4 lead to the same conclusion: that measuring performance on a CPT is insufficient for identifying sustained attention difficulties. A large number of studies rely on the averaging approach (i.e., reporting mean performance) when reporting poor sustained attention among other clinical groups such as patients with schizophrenia (e.g., Liu *et al.*, 2002), bipolar disorder (e.g., Clark, Iversen, & Goodwin), and Alzheimer's disease (e.g., Perry, Watson, & Hodges, 2000). Such groups, and others, might benefit from a systematic comparison between markers of *mean performance* and markers of *performance change*.

Whereas the first three experimental chapters (Chapters 2–4) presented and discussed manipulations that can be traced in the sustained attention literature, Chapters 5 and 6 discussed the implicit parameter related to the rhythmic pattern often implemented within the CPT. The contribution of temporal factors to selective attention has not been considered in the context of CPT, but has been investigated by manipulating the foreperiod preceding targets (e.g., Niemi & Näätänen, 1981), orienting attention to a predictable onset (e.g., Coull & Nobre, 1998), and increasing sensitivity in the time that follows a warning signal (e.g., Posner & Boies, 1971). The influence of a warning signal on performance has largely influenced the networks of attention framework (Posner & Petersen, 1990) and resurfaced in the performance maintenance literature in the form of momentary, phasic changes in alertness (for example Sturm & Willmes, 2001). A different perspective focused on the contribution of entrainment to selective attention by generating temporal expectations towards specific onset-times that coincide with the current rhythmic pattern (e.g., Henry & Obleser, 2012; Schroder *et al.*, 2010). Such temporal expectations can either be driven by an automatic process that occurs whenever the cognitive system is presented with a rhythmic pattern (Jones, 2001; Sanabria, Capizzi, & Correa, 2011; De La Rosa *et al.*, 2012), or guided by memories in a goal-directed manner (Breska & Deouell, 2017). In view of the evidence, I reconsidered the CPT to be a particular case where entrainment is likely to occur if the task carries a rhythmic pattern. Accordingly, I provided evidence showing marked differences in the performance pattern in association with temporal regularities.

Using pupillometry data in Chapter 5, I showed dynamic shifts in the arousal level that corresponded to the rhythmic pattern: in the presence of temporal regularities, a phasic increase in pupil size preceded onset time, alongside an overall tonic decrease. This unique behaviour pattern of the arousal function was accompanied by an improvement in the perceptual sensitivity. When performing the same task in the absence of a predictable rhythmic structure of intervals between stimuli, phasic effects disappeared, and performance decayed. In contrast, there was an overall increase in the tonic pupil size. This marked sensitivity and automatic adjustment of the arousal system to the level of temporal predictability was explained using the principles of the Adaptive Gain Theory (Aston-Jones & Cohen, 2005). According to the Adaptive Gain Theory, the operation of the locus coeruleus-noradrenergic system (corresponding to 'arousal') can be described by means of adapting to unexpected uncertainty in task gain (Yu & Dayan, 2005; Dayan & Yu, 2006). I argued that the temporal predictability of stimulus onset can be thought of as a factor determining uncertainty level within the CPT, and facilitates changes in the arousal level accordingly.

In Chapter 6, I relied on the notion of different performance patterns that are sensitive to the rhythmic pattern. Using computational modelling, I showed that participants are more efficient in processing a predictable stimulus (i.e., elevated processing speed), and that they require shorter exposure duration to perceive stimuli when the onset time is unpredictable (i.e., lower perceptual threshold). As in Chapter 5, the results were explained in terms of dynamic adaptation of the arousal system to the level of predictability within the task. It was argued that when stimulus onset is predictable on a CPT (when the inter-stimulus intervals are fixed), individuals can prepare for the target and be more efficient, as reflected in the enhanced processing speed. When stimulus onset is unpredictable, the cognitive system is calibrated to maximise its sensitivity to unpredictable environmental changes, as reflected in the lowered perceptual threshold. The significance of the studies in Chapters 5 and 6 is highlighted when considering the high prevalence of CPT designs using fixed inter-stimulus intervals (e.g., Conners, 2000; Cornblatt *et al.*, 1988; Esterman, Rosenberg, & Koonan, 2014; Greenberg, 1987; Klee & Garfinkel, 1983; Lee & Park, 2006; Mackworth, 1948; O'Connell *et al.*, 2009; Robertson, 1997). In such studies, researchers might unknowingly decrease demands for the goal-driven maintenance of sustained attention by entraining the cognitive system to the rhythmic pattern (e.g., Jones, 2001; Sanabria, Capizzi, & Correa, 2011; De La Rosa *et al.*, 2012). Given the findings presented in this thesis, such rhythmic facilitation also modulates arousal, which is a fundamental aspect of sustained attention. Even if such rhythmic facilitation of performance is desired, any discussion of why an isochronous pace is being used in the available CPT literature is virtually non-existent. It also seems as though using random inter-stimulus intervals may benefit future clinical assessment tools by increasing the continuous load on the intrinsic maintenance of arousal over time.

The last experimental chapter provided a preview of the possible interactions between the mechanisms supporting sustained-, spatial- and selective-attention, which may serve as a basis for future interventional studies. The study exploited the cognitive and neurophysiological overlap between mechanisms of attention, demonstrating how sustaining attention towards the right hemi-field can bias spatial attention, and how a combination transcranial random noise stimulation with a lateralised sustained attention task can enhance attentional selectivity. The spatial biasing protocol relied on a variation of the CPT paradigm, in which participants constantly monitored two lateralised stimulus streams. The proportion of target events on each side was manipulated between groups to facilitate an attentional bias towards either the right or left, or to maintain a balance between the visual fields. The study showed that the sustained spatial biasing manipulation was effective only in shifting attention to the right. These findings were replicated in a second experiment combining lateralised sustained attention training with bilateral parietal transcranial random-noise stimulation. In this experiment, the combined behavioural training and brain stimulation regime also improved attentional selectivity (the capacity of filtering irrelevant distractors). The findings were interpreted based on the notion of a right-hemisphere dominance in selective attention, which was counteracted when using the sustained attention lateralised protocol. It was hypothesised that only the less dominant left hemi-field could be spatially biased, as it only directs attention towards the right; this is in contrast with the right hemi-field, which controls attention orienting bilaterally. Importantly, these findings show that sustained attention effort can systematically modulate other attentional capacities through shared substrates. Concerning the sustained attention literature, the findings highlight the potential of using a CPT experimental design in intervention studies.

In a series of theoretical considerations and experimental investigations in this thesis, I have tried to introduce some new perspectives into how sustained attention is defined and measured, and how it can be placed in relation to other aspects of attention. Sustained attention is hard to define, and yet it is an essential aspect of human cognition. To some extent, sustained attention can be perceived as one of the most common-sense answers to the question 'What is attention?'. The answer, in that case, is 'Attention is how long one can "maintain concentration"', which is perhaps the intuitive meaning of attention familiar to the general population. Intuitive as it may be, it is also described analytically as a fundamental, essential, low-level construct in multiple theoretical frameworks. Perhaps more than any other construct in the attentional research, it plays a part as a primary function while being heavily considered in a clinical context or day-to-day functioning. This duality potentially underlies the difficulty that accompanies the evolution of sustained attention. I propose that there is still much to be explored and reconsidered in the scientific inquiry of sustained attention. This suggestion applies to the theoretical aspect, which needs to be better refined and placed alongside other closely related constructs (alertness, arousal, vigilance and so forth) to form a unified and cohesive terminology. It also applies to the paradigm in use, which needs to be further standardised to account for all the contributing factors involved.

This thesis has its limitations, but perhaps its main contribution is in highlighting concerns that should be further inquired with larger sample sizes and experimental manipulations. Methodological considerations I have raised, such as the involvement of inhibitory mechanisms when target events on a CPT are frequent, can be verified further using imaging data and neuropsychological studies. A sensible prediction would be that right-hemisphere lesions might lead to a greater difficulty when target events are rare, as this requires more sustained attention effort. Experimentally, future research could explore the course of change in the response bias derived parameter from the Signal Detection Theory by gradually adjusting the target-distractor ratio, transitioning from a sustained attention task to a response inhibition task. The distinction I have described here between 'general performance' and ‘performance decrement’ could also benefit from a more dynamic description of performance, such as by describing data on a trial-by-trial basis and viewing the momentary fluctuations in performance. The phasic alternations in alertness identified in Chapter 3 as contributing to the changes in RT variability should be contrasted and correlated with more standardised measures of phasic alertness, i.e., by using an alerting signal.

Whereas the aforementioned methodological considerations can, to some extent, be deduced based on the available sustained attention literature, the potential influences of rhythmic patterns within the CPT require additional experimental inquiries. It is necessary to further integrate new findings from the temporal attention literature with the CPT's experimental and clinical traditions. Such work should consider the notions of cognitive entrainment, rhythmic facilitation, temporal orienting and temporal expectations and their influence on performance patterns on the CPT. Particular attention should be given to rethinking the unwanted involvement of bottom-up, stimulus-driven facilitation of attention when rhythmic tasks are in use. As a potential extension of the studies presented in this current thesis, it would be interesting to learn about the time course of adapting the arousal level by the rhythmic patterns on a CPT (as used in Chapters 5 and 6). The time it takes for individuals to implicitly identify a change in the rhythmic pattern and adapt their behaviour accordingly may correlate with levels of task engagement and sustained attention, and could provide a further method for assessing individual differences in performance. A final proposal for future studies would be further expanding the cognitive training protocol I presented in Chapter 7. Forthcoming studies could compare the effectiveness of the training protocol to tasks that demand either only sustained attention, or only spatial-orienting. The effectiveness of the brain stimulation could be tested when combined with sustaining attetnion towards the left or the centre, to test whether the effect of enhanced selectivity could be obtained under different lateralised conditions.

As the final chapter reaches its conclusion (as does the thesis), I would like to briefly recapture some key points and 'take-home' messages. I learned through writing this thesis that, although numerous studies have discussed and manipulated sustained attention, there is still good reason to stop for a moment and wonder about its nature. As often happens in Cognitive Psychology, the construct is never independent of the task being used to measure it. Sustained attention, for example, has been defined by Ian Robertson as 'the ability to self-sustain mindful, conscious processing of stimuli whose repetitive, non-arousing qualities, would otherwise lead to habituation and distraction by other stimuli' (Robertson *et al.*, 1997). In that case, the way in which sustained attention can be measured is included in the way it is defined. Another implication is that it might be hard to identify sustained attention when performing a task that is stimulating and arousing. It is possible that, although sustained attention can influence performance on any task (whether a prolonged memory test or linguistic assessment), there is no straightforward way of predicting the way it will manifest itself in a complex task. Just as a thought experiment, one could imagine how a complex memory task will occasionally re-engage attention or elevate arousal in cases of effortful trials, error awareness, or semantic effects evoking a happy memory. This is why I believe sustained attention is inseparable from the simple, boring and non-engaging CPT. Accordingly, in many ways, the CPT has been the main focus of this thesis as a proxy for sustained attention.

I have argued for the existence of a few main obstacles, which repeatedly reappear in the literature. When increasing target proportion, sustained attention demands clear space for response inhibition. This notion is strongly supported by empirical findings in the go/no-go literature, which is practically a mirror image of a classic sustained attention CPT introducing more targets than non-targets. When measuring sustained attention, a simple averaging of overall performance is insufficient to capture the gradual decrement in performance. The temporal structure of the task, in other words its rhythmic pattern, carries meaningful information which determines the overall level of task uncertainty. The cognitive system is sensitive to the overall level of uncertainty, and dynamically adapts accordingly in a way that influences sustained attention. Any attempt, therefore, to measure sustained attention must account for the possible influence of rhythm within the task. Finally, the CPT provides a unique opportunity to exert sustained effort of the cognitive system, and can therefore be a practical tool for cognitive training and modulation. Thank you for sustaining your attention. With these guidelines in mind, there is still much to be done.

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