Attentional Control of Goal Directed Behaviour



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The ability to modulate behaviour in a goal directed manner, is fundamental to all aspects of life. To become goal directed, attention must be configured to bias perception and action in favour of the current directive. This competitive process allows expansive possibilities to be moulded into coherent purposeful behaviour. It allows intention to become action.

The following thesis can be broken down into two parts. The first part is comprised of three empirical chapters that examine the functional consequences and neural underpinnings of impaired attentional control following stroke. The second part is comprised of two empirical chapters aimed at more specific experimental questions. These chapters propose novel paradigms aimed at answering finer grained questions regarding the structure of attentional control.

Part I: Chapter 2 examines the functional consequences for patients with impaired attentional control. Chapter 3 takes a subset of patients from the previous chapter and uses a voxel-based lesion-symptom mapping approach to examine damage associated with impaired attentional control. Chapter 4 utilises a BiFactor model to examine whether executive dysfunction manifests differentially after frontal and posterior damage.

Part II: Chapter 5 proposes a novel paradigm that allows better dissociation of errors associated with the break down of goal directed behaviour. Chapter 6 examines how attention is distributed during concurrent processing and maintenance activities.

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Chapter 1

Introduction

The ability to adapt behaviour to ensure goal attainment, is one of the most complex, yet fundamental cognitive abilities (Duncan, 1986; Shallice & Burgess, 1991; Diamond, 2012; Miller & Cohen, 2001). Without it behaviour becomes chaotic, unconstrained by relevance, rendering even the simplest of tasks extremely difficult (Luria, 1966; Bianchi, 1922). The following thesis is dedicated to how goal representations utilise attention to guide encoding, maintenance and action in favour of current objectives. Using stroke as a model of impairment, it is aimed that this abstract concept be grounded in context by examining the neural underpinnings and functional impact on every day life.

The idea of being "goal directed" is somewhat misunderstood. The term lends itself to the interpretation of the pursuit of long-term complex goals. However, behaviour needs to be modulated to achieve even seemingly simple and mundane tasks (e.g. making tea). To successfully perform a task an individual needs to know their goal state (e.g. a hot cup of tea) and the sequence of sub-goals which will lead them effectively to the goal state (e.g. select cup from cupboard) and have the stored knowledge required to undertake each sub-goal (e.g. what a cup looks like and how to grasp it). This goal representation needs to guide behaviour by filtering incoming stimuli based on relevance (e.g. identify the correct cup), selectively maintaining relevant information (e.g. guests' tea preferences) and produce relevant actions in an appropriately timed sequence (e.g. pour water until cup is full). The ability to represent goal states and effectively use them to bias behaviour is fundamental to most daily activities, especially if they are novel or require adaptation (e.g. making tea in an unfamiliar kitchen).

To illustrate the consequences of impairment I draw upon an example of a stroke patient whom I assessed. SB is an extremely intelligent man, who before suffering a large stroke, worked in a highly prestigious field. The consequence of the stroke was primarily cognitive, and in particular SB experienced executive dysfunction. Despite being able to understand and recall task requirements, he became quite unable to enact his intention.

The testing session chosen to illustrate contained the torch task from the Birmingham Cognitive Screen (Humphreys, Bickerton, Samson, & Riddoch, 2012). In this task a set of objects are placed in front of the patient, including a torch and 2 batteries (in addition to distractor items). The examiner asks the patient to light the torch and proceeds to gesture to the objects whilst informing them that everything they need is in front of them. A typical response to this task is to try to switch on the torch, only to discover it is not working. After which the participant will deduce the batteries are missing, replace them and light the torch.



Figure 1.1: Images from the recorded testing session, to illustrate the test set up and give some examples of both irrelevant and relevant behaviour.

During the session SB demonstrated that he understood and remembered the task instructions, he could name the items in front of him and was physically capable of performing the necessary actions. However, his behaviour was chaotic and distractable. He would use task irrelevant items (e.g. matches, glue stick), he would perseverate (e.g. trying to light matches or opening and closing the match box). He would start a goal directed action and then abandon it before completion (e.g. opening the torch with intent to add the batteries, only to close it again) and would try unusual actions (e.g. trying to balance the batteries on the end of the torch). During the session SB repeated the task instructions with accuracy and demonstrated intent to undertake them. Despite this being the third time he had attempted the torch task, it took him over ten minutes and without prompting the task would have been abandoned well before completion.

Overall, the testing session demonstrated some of the fundamental behaviours attributed to executive dysfunction (Duncan, 1986; Luria, 1966; Milner, 1963) and highlighted how detrimental a breakdown of goal directed behaviour could be for daily functioning. In essence his behaviour was unconstrained by relevance, inappropriate actions intruded, relevant actions were omitted and the goal was intermittently and almost completely abandoned before completion (Duncan, 1986; Luria, 1966; Milner, 1963). There was disconnect between his intention, knowledge and action. This is a phenomenon known as goal neglect: the disregard for task requirements despite them being understood and remembered (Duncan, Emslie, & Williams, 1996).

1.1 Cognitive Theory

The occurrence of goal neglect following brain injury can be quite striking (Luria, 1966; Konow & Pribram, 1970). In the general population goal neglect manifests more subtly, but can be measured using experimental tasks (e.g. Duncan et al., 1996, 2008; De Jong, Berendsen, & Cools, 1999; Iveson, Della Sala, Anderson, & MacPherson, 2017; Towse, Lewis, & Knowles, 2007). These normally require multiple cognitive component processes which need to be switched between. The original task used to measure goal neglect was a letter monitoring task (Duncan et al., 1996; Iveson et al., 2017). It required participants to monitor one of two streams of onscreen character presentations and read the letters, whilst ignoring the numbers. A cue was presented at the beginning of the trial indicating which side to pay attention to. A secondary cue was presented midstream, indicating whether they needed to switch and report from the other side or stay (for alternative designs see Duncan et al., 2008; Bhandari & Duncan, 2014). Goal neglect was observed as complete neglect of the second side cue when it indicated a switch, despite the participants being able to recall the side cue instruction. In parallel with the patients, there was a disconnect between intention and behaviour (Duncan et al., 1996).

The phenomenon of goal neglect can also be observed on conventional executive tasks (e.g. Stroop De Jong et al., 1999). However, true instances of goal neglect are hard to dissociate from other types of mistakes. The reason for this is that goal neglect is symptomatic, an umbrella term describing a failure of top-down control of behaviour. This failure can manifest as many different types of error. For example, goal neglect could be displayed as a failure to shift attention (e.g. Duncan et al., 1996), but also could be a failure to effectively deploy inhibitory resources (e.g. De Jong et al., 1999). Moreover, each of these types of error could arise from poor goal representation, but may also be a result of a more specific type of error (e.g. failure to monitor, poor working memory or delayed task configuration). Therefore, goal neglect is difficult to dissociate from other more specific sources of error when measured experimentally. The idea that goal directed behaviour may fail either due to a less than optimal goal representation or a failure of a more specific executive function is central to the problem of task impurity when measuring executive control (Friedman & Miyake, 2017).

It has long been debated whether there is a central executive controlling goal directed behaviour or whether executive control can be fractionated into multiple separate functions (Logie, 2016; Stuss & Alexander, 2007; Friedman & Miyake, 2017; Miyake et al., 2000; MacPherson, Sergio, Simon, Alessandra, & Matthew, 2015), such as, planning (e.g. assembly of goal representation and sequencing of sub-goals), updating (monitoring and changing the working memory contents), shifting (changing between task-sets/sub-goals) and inhibition (override pre-potent responses, Miyake et al., 2000; Ravizza & Carter, 2008; Smith & Jonides, 1999). Although it appeared clear that these functions are separable, it is also observed that they share something in common, leading to the definition of executive function in terms of both "unity" and "diversity" (Teuber, 1972; Miyake et al., 2000; Miyake & Friedman, 2012; Friedman & Miyake, 2017).

Evidence now suggests that executive function encapsulates both superordinate control and additional subdivisions (Niendam et al., 2012). Factor analysis has demonstrated that executive functioning is best modelled when both separate factors and the correlation between them are estimated (Miyake et al., 2000; Friedman & Miyake, 2017). This observation has lead researchers to use a "BiFactor" Model, which allows a separate common executive latent variable to be estimated (unity), in addition to independent and orthogonal latent variables for more specific contributions (diversity, Friedman et al., 2008; Friedman & Miyake, 2017). The concept of executive functioning being an amalgamation of both the superordinate control and more specific sub-divisions can be likened to calling pre-programmed functions (e.g. update working memory contents) from a main processing script.

The main processing script (superordinate/unity) first sets the environment by calling relevant information from knowledge stores (production rules and target infomation) and biases relevant new information in perceptual buffers. It then calls on stored functions (subordinate/diversity) that provide the temporal progression, linking the available information to the desired action. Some examples could be "While A is not encoded, update working memory contents" or "If A encoded, then do B". These functions allow relevant information to be linked to the appropriate action, creating a task guided loop between perception and action (Fuster, 2002; Fuster, Bodner, & Kroger, 2000; Quintana & Fuster, 1999). On the following page is a visual schematic of how superordinate and subordinate control processes could work together in the acquisition of goal directed behaviour (Figure 1.2).

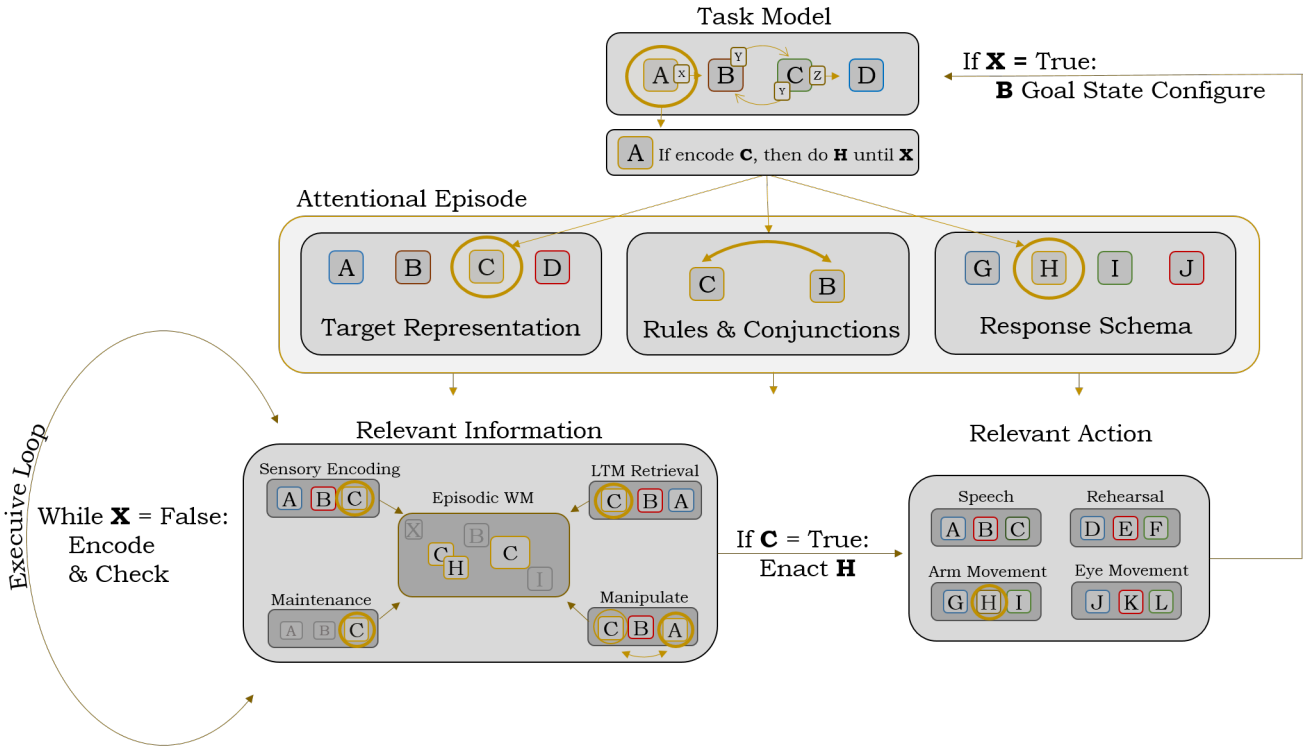


Figure 1.2: A simplified visual representation of top-down goal directed modulation of behaviour. It is an interpretation based upon models such as the working memory architecture set out by Barrouillet and Camos (2015), which draws upon the ACT framework (Anderson, 1993) and the concept of an episodic buffer (Baddeley, 2000). This representation also draws on the concept of an attentional episode set out by Duncan (2013). The first step is setting up the goal model (also known as task model or goal list). 1) This is stored in a stable form of working memory and organised into sub-goal (task-sets) (Duncan et al., 2008). 2) Attention selects a sub-goal for processing and configures an attentional episode, in which attention biases relevant information, action and production rules. 3) The executive loop monitors the contents of working memory against the desired end state (X) for that sub-goal, whilst preforming the designated production rules. In this example these rules are to **encode** and **update** working memory contents until the end state is detected and if C is encoded to **initiate action** H. 4) When the end state X is detected a shift to the next sub-goal is initiated and the process begins again.

In Figure 1.2, it is proposed that goal directed behaviour is achieved in two steps. First pertains to superordinate control (constructing the script and target information selected) and the second subordinate control (the script is run, calling upon stored functions and production rules). It is conceived that the task model is constructed by combining different types of stored knowledge (e.g. declarative, procedure and outcomes) and optimised into a sequence of sub-tasks (Duncan, 1986). This task model (also conceived as a goal buffer or control programme) contains task requirements such as target stimuli, stimulus-response mapping, action and desired end-state (Anderson, 1983; Duncan, 2013; Barrouillet & Camos, 2015). When a sub-task is selected it creates an attentional episode which biases the selection of goal relevant information and action (Duncan, 2013).

After this initial construction and attentional configuration, the second stage is more automatic. The sub-goal script is run, selecting subordinate executive functions to run in conjunction with the previously loaded target information (see Chapter 6 in Barrouillet & Camos, 2015). One of these subordinate control processes has been conceived as an "executive loop", which is in charge of updating or maintaining the contents of working memory (Barrouillet & Camos, 2015; Oberauer, 2002). This loop checks the contents of working memory against the sub-goal model, triggering specified production rules and actions as conditions are met (Barrouillet & Camos, 2015; Anderson, 1993). The simple example given in Figure 1.2 demonstrates how this could be conceived in the instance that a participant must monitor the environment until a C is identified, on successful encoding they must produce action H (for example a button press). X is representative of the end-state (e.g. completed action) or shift trigger (cue for a different sub-goal) and when identified attention shifts to the next or specified sub-task. Although this schematic is simplified it gives a basic representation of how goal directed behaviour can be achieved via a combination of superordinate and more automatic subordinate control processes. These processes will now be discussed in greater detail, under the headings of superordinate and subordinate control.

The "Unity" of Executive Function: Superordinate Control

All goal directed behaviour requires the representation of task requirements, sometimes referred to as a task model (also called goal list or task set, Duncan et al., 2008; Duncan, 1986). A task model is a stable working memory trace in which task rules are represented, organised and maintained until goal completion (Duncan et al., 2008). It is comprised of a sequence of chunks (sub-tasks); each of which configure an attentional episode to bias perception and action in favour of effective task completion (Duncan, 2001, 2013). This representation contains a series of parameters responsible for elements such as orienting attention to relevant environmental information, applying correct categorisation rules and representing response-mapping (Logan & Gordon, 2001; Vandierendonck, 2012). A task model can be conceptualised as a self-written code which configures an attentional filter to bias an individuals thoughts and actions to the current directive. Therefore, it can be conceived as superordinate control, the unity shared by executive function.

How effective superordinate control of behaviour is depends on whether this attentional configuration effectively gives target information the competitive edge compared to other sources of attentional bias (Bisley & Goldberg, 2010; Duncan, 1986; Thompson, Biscoe, & Sato, 2005). It has been proposed that this configuration is achieved by deploying attentional resources selectively based on task relevance (defined in the task model, Duncan, 2013). The additional resources cause disproportionate sensory activity in response to target compared to non-target information (Reynolds, Chelazzi, & Desimone, 1999). The increase in attentional resources gives relevant items a head start in the perceptual race into the limited resources of working memory (Bundesen, 1990), shaping what is encoded and available for use during task completion. Other influences of this process originate from the efficiency of the task model (Duncan, 1986; De Jong et al., 1999; Munakata, Morton, & Yerys, 2003) and from bottom-up processes such as salience or previous stimulus-response mapping (Ptak, 2012; Vandierendonck, 2012).

How efficiently a task model can bias attention is influenced by two main factors: the complexity of the task rules and the availability of necessary stored knowledge. It has been observed that increasing task complexity results in higher instances of goal neglect (Duncan et al., 2008; Roberts & Anderson, 2014). This effect is regardless of whether the additional instructions are used in the task block (Duncan et al., 2008; Dumontheil, Thompson, & Duncan, 2011). Furthermore, a similar effect has been seen regarding the complexity of the stimulus-response mapping; increasing complexity resulting in more instances of goal neglect (Houghton, Pritchard, & Grange, 2009). Interestingly, this effect is primarily concerned with the complexity of the sub-tasks, rather than the overall complexity of task instructions (Bhandari & Duncan, 2014). Two more important elements regarding complexity are: the structural relationship between rules (Badre & D′Esposito, 2009; Oberauer, Süß, Wilhelm, & Wittmann, 2008) and how effectively the task model has been chunked into separate sub-tasks (Halford, Cowan, & Andrews, 2007; Diamond, Carlson, & Beck, 2005; Sacerdoti, 1974). The effect of task complexity on goal neglect suggests that task rule working memory is a limited resource (e.g. Oberauer, 2002; Duncan et al., 2008; Kane & Engle, 2002). With decreasing fidelity of the representation rendering it less able to bias behaviour (Munakata et al., 2003).

Another strongly influential factor is the availability of task appropriate stored knowledge (Baddeley & Hitch, 1974; Barrouillet & Camos, 2015; Buckner, Andrews-Hanna, & Schacter, 2008; Anderson, Bothell, Byrne, & Lebiere, 2004; Vandierendonck, 2012). This is the information required to complete the task and the means by which to execute it (Oberauer, 2009, 2010). This stored knowledge spans declarative memory (e.g. what is cup?), procedural memory (e.g. how to pour water) and conditional rules (If cup is full, stop pouring, Vandierendonck, 2012). It has been suggested that working memory traces can be enhanced by previously stored knowledge about the item to be remembered (Brady, Stormer, & Alvarez, 2016) and previously learnt stimulus-response pairing remains influential on task performance (Bichot & Schall, 1999; Allport, Styles,

& Hsieh, 1994; Allport & Wylie, 2000; Pashler & Baylis, 1991; Teskey & Masson, 2017). Perhaps this accounts for why familiar cue-response pairing (e.g. arrow) is associated with less goal neglect (Towse et al., 2007; van't Wout, Lavric, & Monsell, 2013).

In line with this, it has been observed that the use of overlearnt stimuli or task rules affects the robustness of the task model. For example, using more familiar tasks or items produces a smaller, but more robust and effective neural task representation (Rainer & Miller, 2000; Asaad, Rainer, & Miller, 1998). When task rules are received they must be transformed into a control programme (e.g. Anderson, 1983; Duncan, 1986). Relevant information and action must be chosen and used to create a course of behaviour which allows the participant to reach the goal state (Duncan, 1986). With task practice this task model can be updated and refined, perhaps underlying why novelty impacts goal neglect (Bhandari & Duncan, 2014). One may consider that for a familiar task, the task model may be stored like a pre-programmed function requiring more or less adaptation depending on differences in the context of application. However, it will be far less resource/time consuming than writing a script from scratch. Therefore prior knowledge and task familiarity may result in a more effective and concise task model.

In addition to the clarity of the task model, bottom-up processes (e.g. salience and speed of onset) also influence the distribution of attention (Ptak, 2012; Bisley & Goldberg, 2003; Gottlieb, Kusunoki, & Goldberg, 1998). For example, stimulus directed attention toward task irrelevant items detrimentally effects encoding of relevant information (e.g. Anticevic, Repovs, Shulman, & Barch, 2010; Majerus et al., 2012). It has also been suggested that stimulus directed attention can result in enhanced encoding of the task irrelevant information (Ravizza & Hazeltine, 2013) or salient items (Bays & Husain, 2008; Bays, Gorgoraptis, Wee, Marshall, & Husain, 2011), demonstrating how these sources of attentional biasing compete for resources and subsequent encoding. In the visual spatial domain it has been suggested that these competing processes are combined

to calculate a "priority map"; an amalgamation of expectations, goals and perceptual features (Treisman, 1998; Koch & Ullman, 1985; Bisley & Goldberg, 2010; Ptak, 2012; Zelinsky & Bisley, 2015). The item within the map location that has the highest priority value becomes the focus of attention (Koch & Ullman, 1985), thus demonstrating how bottom-up (e.g. cue salience) and the top-down (e.g. task requirements) compete during attentional configuration.

The "Diversity" of Executive Function: Subordinate Control

In addition to superordinate executive control (unity), distinct diverse executive functions have also been proposed (Friedman & Miyake, 2017; Niendam et al., 2012; Miyake et al., 2000). Some consider these to be subordinate processes (also known as production rules) which are called upon dependent on relevance to goal attainment (Barrouillet & Camos, 2015; Anderson et al., 2004). These subordinate processes provide the means to represent current events internally and integrate them with existing relevant knowledge (episodic working memory) while monitoring the contents for task relevant events (executive loop). Based on the contents of working memory, production rules are activated such as updating working memory, producing an action or shifting between sub tasks (Barrouillet & Camos, 2015; Fuster, 2002; Anderson et al., 2004). These distinct processes can be thought of as previously saved functions, called upon by the main superordinate processing script whilst orchestrating goal directed behaviour.

The first important subordinate function required for successful goal directed behaviour is an internal representation of task relevant information: working memory. It has been argued that this internal space allows the transient and adaptable integration of different sources of relevant information into a multimodal code (Baddeley, 2000; Oberauer, 2002; Repov & Baddeley, 2006; Langerock, Vergauwe, & Barouillet, 2014; Barrouillet & Camos, 2015). It can contain new information consolidated from transient

sensory stores (e.g. visual spatial and verbal buffers) or previously learnt information via the retrieval from long-term memory stores (Barrouillet & Camos, 2015; Anderson et al., 2004; Baddeley, 2000). The store provides a region of direct access in which task relevant information can be utilised efficiently for the current goal.

As previously mentioned, working memory can be considered as a limited resource, thus making the attention selection for representation a competitive process (Bundesen, 1990; Bays et al., 2011; Bays & Husain, 2008; Alvarez & Cavanagh, 2004). Previous work has suggested that this limited capacity was governed by the number of items to be remembered (e.g. 7 or 4, Miller, 1956; Cowan, 2010). An alternative view is that working memory is a representational medium which can be flexibly and unevenly distributed between to be remembered items (Ma, Husain, & Bays, 2014). Continuous-resource accounts suggest that there is no fixed upper limit to the number of items that can be stored, but an incremental decrease in the resolution with increasing set-size (Bays & Husain, 2008; Bays et al., 2011) and/or a trade-off in allocation based on attentional prioritisation (Gorgoraptis, Catalao, Bays, & Husain, 2011; Bays et al., 2011). Prioritised items are maintained with greater precision than other items (Bays et al., 2011; Bays & Husain, 2008; van den Berg, Shin, Chou, George, & Ma, 2012). Moreover, this prioritisation can occur before encoding into working memory (pre-cue) or subsequently (retro-cue) by shifting attention within working memory (Pertzov, Bays, Joseph, & Husain, 2013; Bays et al., 2011; Gazzaley & Nobra, 2012; Ma et al., 2014).

A second important subordinate function in the pursuit of goal attainment is the ability to monitor and compare the current working memory contents to the desired sub-goal from the goal model (Barrouillet & Camos, 2015; Anderson et al., 2004). This continuous monitoring allows production rules to be activated at the appropriate time when conditions are met (e.g. If relevant item is encoded, then produce action). This process has been termed the executive loop. It has been estimated to cycle at a rate of ap-

proximately 50 milliseconds, running appropriate production rules as required (Anderson et al., 2004; Barrouillet & Camos, 2015). These production rules could include: external processing/encoding, attentional refreshing of the contents of working memory, activation of an appropriate action or finally shifting from one sub-goal to another (Barrouillet & Camos, 2015). These functions are similar to the independent executive functions suggested in BiFactor analysis (updating working memory and task-set shifting, Friedman et al., 2008; Friedman & Miyake, 2017), with inhibition and activation of actions accounted for primarily by the effectiveness of the task representation to configure a successful attentional episode (perhaps explaining why inhibition tends to load solely on the common executive functioning factor, Friedman et al., 2008; Friedman & Miyake, 2017).

Goal directed behaviour is generally complex, comprised of multiple and often overlapping elements (e.g. remembering task relevant information whilst simultaneously performing another task component). Both of these activities are suggested to draw on the same attentional resource with a trade-off in performance when performed simultaneously (e.g. Case, Kurland, & Goldberg, 1982; Pashler, 1984). Originally researchers envisaged this trade off was due to simultaneous capacity sharing, performing two tasks meant there was less resource available for each component (e.g. Case et al., 1982). More complex concurrent tasks used up more available resources and thus had a greater impact on concurrent working memory maintenance (Case et al., 1982; Daneman & Carpenter, 1980; Turner & Engle, 1989). However, harder concurrent tasks took longer to complete and it appeared that this extended retention interval was more predictive of concurrent working memory performance than task complexity (Towse & Hitch, 1995; Towse, Hitch, & Hutton, 1998). Therefore it was proposed that attention was sequentially shared between processing and maintenance activities. The trade off in performance occured because whilst attention was captured by the concurrent task, working memory traces were liable to temporal decay (Towse & Hitch, 1995; Towse et al., 1998).

Based on these accounts the Time Based Resource Share (TBRS) model was proposed (Barrouillet, Bernardin, & Camos, 2004; Barrouillet & Camos, 2015). Unlike the previous absolute task switching model proposed by Towse et al (1995), the TBRS model suggests that attention may be rapidly switched back to maintenance during brief pauses in the processing task (Barrouillet et al., 2004; Camos et al., 2018). More complex tasks would take longer to complete within the retention interval as compared to easier processing tasks. Therefore, the ratio of time the task captured attention, compared to time attention was available for working memory refreshing, would be greater for more complex tasks. This ratio was conceptualised as a time based cognitive load of the concurrent task and found to have a linear relationship with concurrent working memory performance (Barrouillet et al., 2004; Barrouillet & Camos, 2015; Barrouillet, De Paepe, & Langerock, 2012). The contribution of time based cognitive load was found to have a greater impact on concurrent performance than retention period or the number of processing items (Barrouillet et al., 2004; Gavens & Barrouillet, 2004; Barrouillet, Portrait, Vergauwe, Diependaele, & Camos, 2011; Plancher & Barrouillet, 2013). Overall the findings suggest that executive functions (e.g. updating or maintaining working memory) share attention via rapid switching (Barrouillet & Camos, 2015).

To conclude, the breakdown of goal directed behaviour is hard to measure experimentally because the same behavioural errors may occur from a failure of different processes. Goal directed behaviour is dependent on both superordinate (e.g. task model implementation) and subordinate control (e.g. working memory updating and maintenance). A Limited attentional resource must be distributed between these subordinate processes dynamically and rapidly to manage multiple demands. The following section will give an overview of the proposed neural mechanisms underlying top-down control.

1.2 Neural Mechanisms

One influential theoretical proposal for the neural mechanisms of goal directed attentional control of behaviour is the adaptive coding model (Duncan, 2001, 2013; Duncan & Miller, 2002; Miller & Cohen, 2001; Everling, Tinsley, Gaffan, & Duncan, 2002). This proposes that neurons in the prefrontal cortex are highly adaptable and have the ability to rapidly and efficiently re-program to selectively respond to current task demands. The change of neuronal firing creates a task representation that acts as a global attention system. A domain general and task directed attentional episode is created; focusing on information and actions of relevance and thus filtering out irrelevant information. The attentional episode acts in a top-down manner to bias perception and action selection in lower order brain regions, providing a neuronal basis for the superordinate control of goal directed behaviour (Desimone & Duncan, 1995; Duncan, 2013).

The first proposal of the adaptive coding model is that neurons can be programmed to respond based on current task relevance (Duncan, 2001; Duncan & Miller, 2002). Recordings of LPFC neurons in non-human primates support this assumption. Neurons can be adaptively modulated by task context; firing preferentially for target as compared to non-target information (Everling et al., 2002). Dependent on task specification neurons can become selective for target features such as colour or shape (Bichot, Schall, & Thompson, 1996; Janssen, Srivastava, Ombelet, & Orban, 2008) or for object category (Freedman, Riesenhuber, Poggio, & Miller, 2001). Neurons can also become selective for a combination of features, for example the link between visual and auditory cues (Watanabe, 1990, 1992; Fuster et al., 2000). Moreover, neurons can be selective for item-reward associations (Watanabe, 1990, 1992), stimulus-response mapping (Asaad et al., 1998; Bichot et al., 1996; Toth & Assad, 2002) and task context/rules (White & Wise, 1999; Wallis, Anderson, & Miller, 2001). DLPFC selectivity for abstract rules has also been demonstrated in single cell recordings of human participants (Mian et al., 2012).

This neuronal adaptation is rapid with selectivity being quickly updated as the task context changes (Duncan & Miller, 2002; Toth & Assad, 2002). Distinct neuronal firing rates and profiles can be observed as non-human primates transition between tasks (Asaad, Rainer, & Miller, 2000). Neurons responsive for a particular cue can become unresponsive to it in an alternative task context (Asaad et al., 2000; Sigala, Kusunoki, Nimmo-Smith, Gaffan, & Duncan, 2008). Dynamic and rapid shifts in selectivity have been observed for changes in relevant category boundary (Roy, Riesenhuber, Poggio, & Miller, 2010), visual feature (Sakagami & Niki, 1994), or even between two types of information such as item identity or location (Rao, Rainer, & Miller, 1997). There are quick population shifts with change in strategy or preference (Durstewitz, Vittoz, Floresco, & Seamans, 2010; Karlsson, Tervo, & Karpova, 2012). These findings suggest that this neural programming is not only flexible, but adjusts rapidly depending on the current task specification.

In compliment with single cell recordings of non-human primates, studies using multivoxel pattern analysis (MVPA) have observed adaptive coding of task relevant information in human FMRI studies (Woolgar, Jackson, & Duncan, 2016). Interestingly, this dynamic neural coding can be observed not only in the PFC, but also in a wide range of interconnected brain regions (Woolgar et al., 2016). This network of brain areas has previously been identified in activation based FMRI studies as involved in domain general cognitive control (e.g. Duncan, 2010; Fedorenko, Duncan, & Kanwisher, 2013; Cabeza & Nyberg, 2000; Cole & Schneider, 2007). Activation is observed in response to a wide variety of executive tasks, including working memory, inhibition, sustained attention and multiple forms of task switching (Müller, Langner, Cieslik, Rottschy, & Eickhoff, 2015; Brass, Derrfuss, Forstmann, & von Cramon, 2005; Ravizza & Carter, 2008).

This collection of brain regions has been named the multiple demands (MD) network due to its domain general involvement in a variety of tasks (Duncan, 2013; Fedorenko

et al., 2013), also known as the cognitive control network (Cole & Schneider, 2007), the superordinate control system (Niendam et al., 2012), the fronto-parietal control system (Vincent, Kahn, Snyder, Raichle, & Buckner, 2011) or the task-positive network (Fox et al., 2005). The MD network has been suggested to include the dorsolateral prefrontal cortex, medial frontal cortex (e.g. anterior cingulate and insula cortex), the inferior parietal cortex (IPS), pre-supplementary motor area (pre-SMA) and the cerebellum (CB) (Duncan, 2001; Fedorenko et al., 2013). Recently an extended MD network was proposed, including the basal ganglia and thalamus (Camilleri et al., 2018).

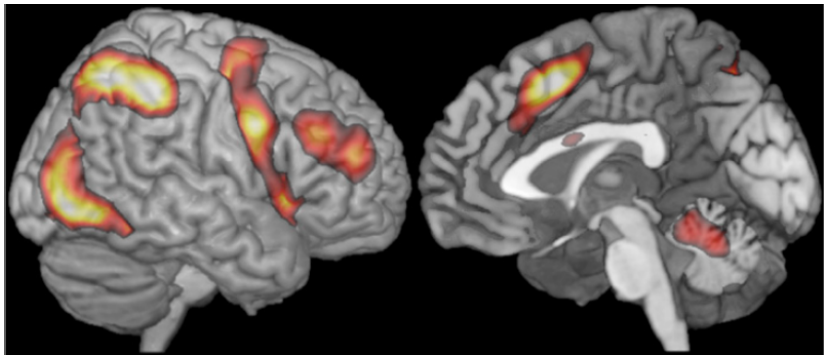


Figure 1.3: A helpful visualisation of the MD network reproduced from Fedorenko et al (2013). This image displays MD activity averaged across hemispheres and thresholded at $t = 1.5$.

The type of task coding found throughout the multiple demands network is very similar to the sort of selectivity demonstrated by single cell recording (Woolgar et al., 2016). In contrast to lower order sensory regions, the coding in the MD network discriminates target information in visual, auditory and motor domains (Woolgar et al., 2016). For example, colour (Bode & Haynes, 2009), stimulus orientation (Kahnt, Grueschow, Speck, & Haynes, 2011), visual cue (Reverberi, Gorgen, & Haynes, 2012), pitch and loudness (Giordano, McAdams, Zatorre, Kriegeskorte, & Belin, 2013), spoken words (Boets et al., 2013) and item category (Li, Ostwald, Giese, & Kourtzi, 2007; Linden, Oosterhof, Klein, & Downing, 2012; Clarke & Tyler, 2014; Simanova, Hagoort, Oostenveld, & van Gerven, 2014) have all been discriminated.

This selectivity is based on task requirements; with regions discriminating strongly for the relevant features, but not for irrelevant features of the same item (Jackson, Rich, Williams, & Woolgar, 2016). Coding has also been identified for selected motor responses. For example, discriminating between which of two fingers were selected to execute a response (Carp, Park, Hebrank, Park, & Polk, 2011; Woolgar, Hampshire, Thompson, & Duncan, 2011). This MD network also contains higher order coding of task rules and representations, for example, stimulus response mapping (Bode & Haynes, 2009), intended task operation (Haynes et al., 2007), current rule (Zhang, Kriegeskorte, Carlin, & Rowe, 2013) and task context (which of two delay periods Nee & Brown, 2012). Overall, demonstrating multi-modal coding of task relevant information and requirements.

In the previous cognitive section, theory was discussed that suggested that the goal model configured attention, creating an attentional episode that biases perception and action based on relevance (Duncan, 2013). This top-down modulation is also suggested by neuroimaging and electroencephalogram (EEG) research (Miller & Cohen, 2001; Duncan, 2001; Gazzaley, 2011; Gazzaley & Nobra, 2012). For example, using EEG selective attention has been found to modulate the early phase of stimulus identification (e.g. P1 ∼100-200ms, Hillyard, Vogel, & Luck, 1998; Schoenfeld et al., 2007, 2003; Zanto & Gazzaley, 2009; Rutman, Clapp, Chadick, & Gazzaley, 2010). This attentional modulation (of P1 or N1 amplitude) has also been related to subsequent working memory performance (Rutman et al., 2010; Zanto & Gazzaley, 2009; Berry, Zanto, Rutman, Clapp, & Gazzaley, 2009).

Functional neuroimaging has demonstrated a trade-off with activity for the target stimulus upregulated and that for the non-target stimulus downregulated (Higo, Mars, Boorman, Buch, & Rushworth, 2011; Gazzaley, Cooney, Rissman, & D′Esposito, 2005). A similar effect was also found to amplify with expectation of a reward (Gazzaley et al., 2005). Interestingly, when task demands make perceptual discrimination hard, there

is reduced representation in visual areas, but increased coding in frontal-parietal areas (Woolgar, Williams, & Rich, 2015). This suggests that more attentional resources can be given to support weak environmental input. Overall, these results demonstrate how top-down attentional configuration acts to boost perceptual processing of task relevant information and thus supports entry into working memory (Gazzaley & Nobra, 2012).

The MD network has previously been segregated into the frontal-parietal (FP) and the cingulo-opercular (CO) sub-networks (Dosenbach et al., 2007; Power & Petersen, 2013). The FP network is comprised of IPS, IFJ and the pIFS. The CO network is comprised of the ACC/pre-SMA, AI/FO and the aIFS. Although these two sub-networks can be dissociated they both have been found to carry information regarding both target information, action and current rule (Woolgar et al., 2016), with significantly more motor representation within CO sub-network. Previously, these networks have been interpreted as the FP executive and CO salience networks (Seeley et al., 2007). Within this distinction the FP executive network has been hypothesized to be responsible for adaptive transient configuration of the task model and the CO for implementing and sustaining control processes (Dosenbach et al., 2007). Together these sub-networks are suggested as a core system for the initiation and implementation of task set (Dosenbach et al., 2006; Charlton & Morris, 2015).

It was briefly mentioned above that an extended MD network has recently been proposed which also includes subcortical brain regions (Camilleri et al., 2018). The basal ganglia (BG) has strong connections with the PFC and its role in executive function is increasingly recognised (Duffau, 2012a; Krause et al., 2012; Cools, Ivry, & D′Esposito, 2006; Thoma, Koch, Heyder, Schwarz, & Daum, 2008). For example a meta-analysis of 193 imaging studies reported superordinate executive control to be related to frontal, parietal, premotor, caudate, puteman and cerebellum activation (Niendam et al., 2012).

The role of the basal ganglia has been attributed to selective gating of action and information (Van Schouwenburg, Den Ouden, & Cools, 2015; Hazy, Frank, & O′Reilly, 2007). At first this mechanism had been suggested to gate the selection of action (Mink, 1996; Yin, 2014), however, more recently a similar process has been conceived for cognition. For example, it was found that the BG can modulate connectivity between frontal and visual regions during attention shifting (van Schouwenburg, den Ouden, & Cools, 2010). It is also proposed that the BG are involved in the gating of working memory, either allowing updating, or preventing it so that traces can be maintained (Frank, Loughry, & OReilly, 2001; OReilly & Frank, 2006). In the TBRS working memory architecture the interaction between the PFC and the BG is said to play a prime role in the executive loop, attributing the BG with the procedural knowledge of the production rules (e.g. how to make an action or perform an operation) proposed in the ACT-R theory (Anderson, 1993; Barrouillet & Camos, 2015).

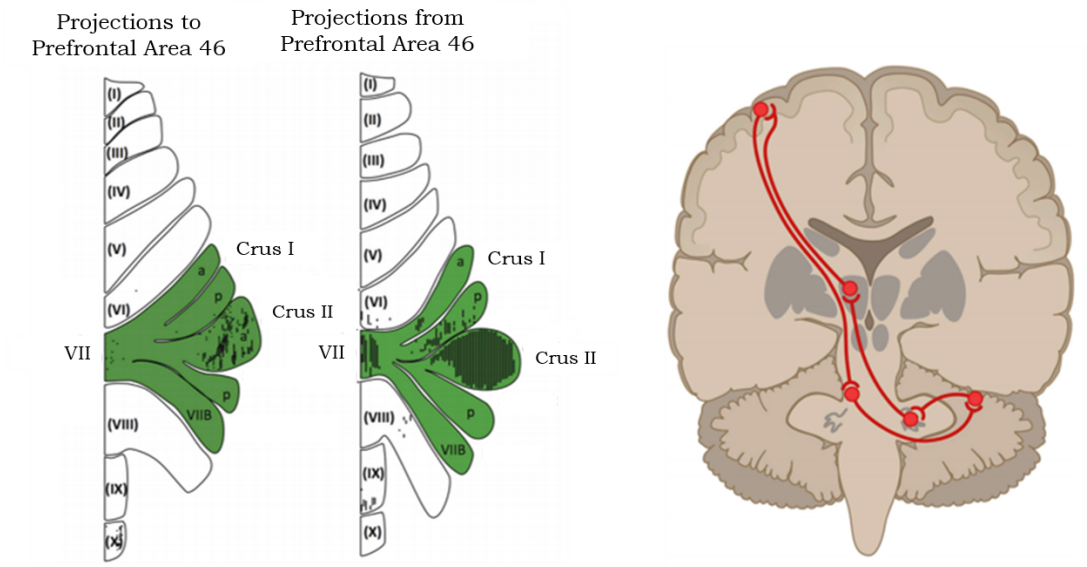


Figure 1.4: Helpful visualisations of the cerebrocerebellar connectivity. On the left is an image depicting the output and input between the cerebellum and DLPFC (BA:46), modified from Bostan et al (2013). On the right is an image depicting the major input and output cerebrocerebellar circuits modified from Bucker et al (2014).

The cerebellum (CB) has often been identified as part of the MD network (e.g. Fedorenko et al., 2013) and observed in investigations of executive function (Niendam et al., 2012). The lateral cerebellum (primarily crus I/II) has bidirectional connectivity loops with the PFC, premotor and parietal cortices (Heyder, Suchan, & Daum, 2004; Middleton & Strick, 1994; Strick, Dum, & Fiez, 2009; Buckner, 2013), in addition to the BG (Bostan & Strick, 2010). Co-activation of these regions is obsered during tasks requiring the implementation of a task model (Dosenbach et al., 2006, 2007). Resting state connectivity analysis has demonstrated substantial inter-individual variability in CB structure, over two fold the representation of the frontal-parietal network (compared to the cortex) and a temporal lag between cortex and CB bold response (Marek et al., 2018). These observations are suggested to support the CB role in supervised learning, adaptation and error signalling (Dosenbach et al., 2006). Overall it is hypothesized that the CB and BG support adaptive control of behaviour via experience based plasticity (Caligiore et al., 2017; Doya, 2000; Ito, 2008).

To conclude, there is evidence for a large distributed network of both cortical and subcortical brain regions which work together to provide effective top-down control of goal directed behaviour. It has been proposed that this network integrates superordinate control processes such as task/goal representation and attentional configuration, with subordinate functions such as working memory gating and experience based feedback.

1.3 Lesion Neuroanatomy

The beginning of this introduction started with an example of SB, a stroke patient who had impaired executive control of goal directed behaviour. The occurrence of stroke often leads to localised cell death, producing a brain lesion. This brain damage is caused by lack of blood supply resulting from a blockage (ischemic) or rupture of a cerebral blood vessel (haemorrhagic). The consequences of stroke depend on the type, location, shape and volume of damage, but are also effected by individual differences in brain structure, demographics (Cipolotti et al., 2015; MacPherson et al., 2017), lifestyle and other protective factors (e.g. education Kalaria, Akinyemi, & Ihara, 2016; Mirza et al., 2016). Although whether protective factors such as education influence performance on more specific executive tests in frontal patients has been questioned (MacPherson et al., 2017). Subsequent to stroke, cognitive impairment occurs in over 50% of patients (e.g. Douiri, Rudd, & Wolfe, 2013; Tatemichi, Desmond, Stem, & Paik, 1994; Paker, Bugdayc, Tekdos, & Dere, 2010). Executive dysfunction is one of the most common cognitive deficits (Zinn, Bosworth, Hoenig, & Swartzwelder, 2007; Nys et al., 2007; Leśniak, Thomas, Seniów, Wojciech, & Członkowska, 2008). Therefore, stroke provides a valuable window to study the link between structural damage and impaired executive function.

Executive dysfunction has long been thought of as a disorder of the frontal lobes (Luria, 1966; Bianchi, 1922; Duncan, 1986; Stuss, 2011). Damage to the frontal cortex has been linked to impaired planning (Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Shallice, 1982), response initiation and suppression (Burgess & Shallice, 1996; Godefroy, Cabaret, Petit-Chenal, Pruvo, & Rousseaux, 1999; Picton et al., 2007; Aron, Fletcher, Bullmore, Sahakian1, & Robbins, 2003), sustained attention (MacPherson, Turner, Bozzali, Cipolotti, & Shallice, 2010; Rueckert & Grafman, 1996; Robertson et al., 1998), working memory (Milner, Broadbent, & Weiskrantz, 1982; Baddeley, Della Sala, Papagno, & Spinnler, 1997) and cognitive set switching/flexibility (Milner, 1963; Milner

et al., 1982; Yochim, Baldo, Nelson, & Delis, 2007; Varjai et al., 2017; Gläscher et al., 2012; Ravizza & Ciranni, 2002). Interestingly, different elements of rule learning have been attributed to different frontal regions, for example learning and remembering rules (ACC), forming appropriate plans (right DLPFC) and the ability to follow plans (left SFG) (Burgess, 2000). Lesions to the lateral frontal cortex have also been observed to negatively impact higher level functions such as decision making (MacPherson et al., 2010; Fellows & Farah, 2005).

It was observed that frontal patients were more severely impaired than patients with damage to posterior brain regions (Cipolotti et al., 2017; Owen et al., 1990; Shallice, 1982), although this is not always the case (Andrés & Van der Linden, 2002; Vilkki, Levnen, & Servo, 2002). Executive dysfunction can also be experienced by non-frontal patients (e.g. Godefroy, 2003). For example, deficits in executive functioning and attentional selectivity have been related to damage to the parietal lobe (Collette et al., 2005; Koenigs, Barbey, Postle, & Grafman, 2009; Vandenberghe, Molenberghs, & Gillebert, 2012; Gillebert et al., 2011), the anterior temporal lobes (Hornberger, Geng, & Hodges, 2011), subcortical regions (Kramer, Reed, Mungas, Weiner, & Chui, 2002; Eslinger & Grattan, 1993; Godefroy et al., 1992; Godefroy, Rousseaux, Pruvo, Cabaret, & Leys, 1994; Mendez, Adams, & Lewandowski, 1989; Thoma et al., 2008) and the cerebellum (Schmahmann & Sherman, 1998; Manto & Mariën, 2015; Stoodley, MacMore, Makris, Sherman, & Schmahmann, 2016; Bellebaum & Daum, 2007). The link between the frontal lobes and executive function is more complex than originally conceived.

A network approach of how executive and attentional disorders manifest has started to become prominent (e.g. Thiebaut de Schotten & Foulon, 2017; Mandonnet et al., 2017; Thiebaut de Schotten, Urbanski, Duffau, Volle, Lévy, et al., 2005). This approach takes into account interactions between brain regions by considering white matter disconnection. For example, it has been observed that dysexecutive syndrome can

occur following damage to a distributed network of both frontal and posterior regions (prefrontal cortex, parietal lobes, basal ganglia, thalamus and the cerebellum) and the white matter that connects them (Rabinovici, Stephens, & Possin, 2015; Bettcher et al., 2016). In line with this view a study examining the link between damage to the MD network and fluid intelligence (closely related to rule working memory), reported that the extent of damage to this network correlated with level of impairment following stroke (Woolgar et al., 2010).

Several studies have used voxel based symptom lesion mapping approaches to examine executive function globally using a composite score (superordinate), in addition to looking at individual executive tasks or factors (subordinate). A small scale VLSM examined executive functioning in 62 patients (37 frontal and 25 non-frontal patients of mixed aetiology). The authors reported that global executive functioning composite score was associated with bilateral DLPFC, superior mesial frontal cortex, right supramarginal gyrus and superior/middle temporal gyri damage. They also ran a 3 factor model looking at working memory, cognitive control and verbal fluency. The working memory factor was associated with lesions involving the bilateral DLPFC, left mesial frontal cortex and the right angular gyrus and temporal lobe. The cognitive control factor was associated with damage to the bilateral superior frontal cortex, the right anterior cingulate and the right DLPFC (Robinson, Calamia, Gläscher, Bruss, & Tranel, 2014).

The second study was larger (Gläscher et al., 2012), including 344 patients with focal lesions. The global executive composite score was associated with the ACC, left precentral gyrus, middle orbital frontal cortex, putamen and right globus pallidus damage. They found that the Trail Making Task (TMT) was associated with left rostral ACC. The Wisconsin Card Sorting Task (WCST) was also associated with lesions involving the left rostral ACC and the medial frontal gyrus, in addition to right damage to the superior/posterior middle temporal lobe, the angular gyrus, precentral gyrus and subcor-

tically the head of the caudate. Poor performance on the Stroop task was associated with DLPFC damage. The Controlled Oral Word Association Test (COWAT) was associated with damage to the left frontal-parietal regions, anterior PFC and insula (Gläscher et al., 2012). Overall, these studies demonstrated a link to multiple demands regions (e.g. DLPFC, ACC). They also displayed both overlap and segregation in support of both superordinate and subordinate control functions.

Superordinate control of behaviour requires the ability to configure an attentional episode to bias perception and action (Duncan, 2013). The link between stroke and visual spatial selective attention has been extensively studied due to the striking consequences of hemispatial neglect, a condition in which patients have difficulty orienting their attention to the contralesional side of space. Hemispatial neglect has frequently been linked to lesions in the inferior parietal lobe/temporal parietal junction (Bays, Singh-Curry, Gorgoraptis, Driver, & Husain, 2010; Mort et al., 2003; Friedrich, Egly, Rafal, & Beck, 1998; Chechlacz et al., 2010; Rengachary, He, Shulman, & Corbetta, 2011) and the superior/middle temporal cortex and underlying insula (Mort et al., 2003; Corbetta, Kincade, Lewis, Snyder, & Sapir, 2005; Committeri et al., 2007; Chechlacz et al., 2010; Rengachary et al., 2011). A specific focus has been drawn to the intraparietal sulcus which is suggested to be the neuroanatomical location of the hypothesized priority map (Bisley & Goldberg, 2003; Gillebert et al., 2011; Vandenberghe et al., 2012; Bays et al., 2010).

In addition to these posterior regions neglect has also been observed after frontal lesion (Vallar & Perani, 1986; Husain & Kennard, 1996, 1997) and focal lesions to the basal ganglia and/or thalamus (Vallar, 2001; Perani, Vallar, Cappa, Messa, & Fazio, 1987; Karnath, Himmelbach, & Rorden, 2002; Kumral, Evyapan, & Balkir, 1999; Caplan et al., 1990). Although, it is suggested that these subcortical strokes may lead to abnormal perfusion in cortical regions that have previously been associated with neglect (inferior parietal lobe, superior/middle temporal lobe and ventrolateral prefrontal cortex, Hillis

et al., 2002; Karnath et al., 2005).

These observed frontal, temporal and parietal brain regions are linked forming the perisylvian neuronal network (Karnath & Rorden, 2012; Karnath, 2009). This network is connected by a range of white matter tracts including the superior longitudinal fasciculus II/III (SLF), the superior and inferior occipitofrontal fasciculus (SOF/IOF), the arcuate fasciculus (AF) and the extreme capsule (EmC) (Karnath, 2009). Visual spatial neglect has also been observed after disconnection of these white matter tracts (e.g. He et al., 2007; Thiebaut de Schotten, Urbanski, Duffau, Volle, Lvy, et al., 2005; Urbanski et al., 2008, 2011; Shinoura et al., 2009; Karnath, 2009). These deficits are usually most prominently demonstrated after damage to the right hemisphere, with the left perisylvian network suggested as more important for language (Suchan & Karnath, 2011).

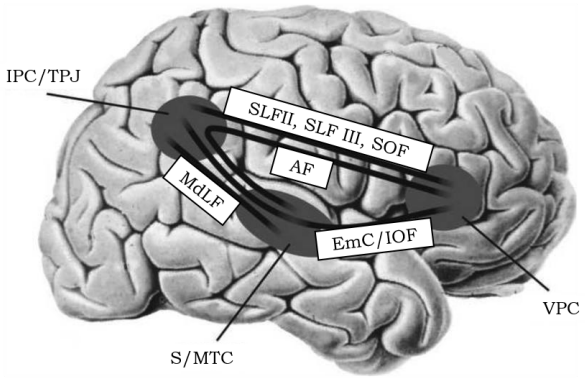


Figure 1.4: Visualisation of the perisylvian network modified from Karnath & Rorden (2012). Demonstrates the connections between the inferior parietal lobe, ventrolateral prefrontal cortex and the superior/middle temporal gyrus. SLF: superior longitudinal fasciculus; SOF: superior occipitofrontal fasciculus; AF:arcuate fasciculus; EmC: extreme capsule; IOF: inferior occipitofrontal fasciculus; MdLF: middle longitudinal fasciculus; IPC: inferior parietal cortex; TPJ: temporo-parietal junction; S/MTC: superior/middle temporal cortex; VPC: ventrolateral prefrontal cortex.

Interestingly the neglect syndrome is both multi-faceted (can include deficits in attention, working memory and motor responses) and multi-dimensional (can present with both spatial and temporal deficits)(for a review see Husain & Rorden, 2003). Damage within the perisylvian network can result in non-spatial attentional deficits both independently and in conjunction with hemispatial neglect (Husain & Rorden, 2003; Husain & Nachev, 2007). For example right frontal lesions can result in impaired sustained at-

tention (right frontal lesions, Robertson, Ridgeway, Greenfield, & Parr, 1997; Hjaltason, Tegner, Tham, Levander, & Ericson, 1996; Maguire & Ogden, 2002) while parietal lesions can result in extended attentional dwell times on attentional blink paradigms (Husain & Kennard, 1997; Shapiro, Hillstrom, & Husain, 2002; Hillstrom, Husain, Shapiro, & Rorden, 2004). Neglect patients can also display impaired visual spatial working memory finding it difficult to keep track of previously searched locations (Wojciulik, Husain, Clarke, & Driver, 2001; Husain et al., 2001; Driver & Husain, 2002), perhaps suggesting that it might also apply to more generalised selective attention deficits and difficulties with binding information in working memory (Correani & Humphreys, 2011).

The lesion correlates of non-spatial attention have also been examined. For example, instances of commission errors on a visual sustained attention to response task have been linked to damage to the inferior frontal cortex (Molenberghs et al., 2009; Aron et al., 2003). Moreover, it has been found that left lateral and medial lesions can result in poorer auditory sustained attention perfromance (MacPherson et al., 2010; Shallice, Stuss, Alexander, Picton, & Derkzen, 2008). This observation is complimented by EEG studies which have examined the link between damage and impaired selective auditory attention. It has been observed that DLPFC lesions are associated with a global decrease in frontal negative polarity, a ERP component which facilitates top-down selective attention (Bidet-Caulet et al., 2015; Knight, Hillyard, Woods, & Neville, 1980).

In the previous section it was also observed that fronto-striatal and fronto-cerebellar circuits might also be important for executive functioning (Heyder et al., 2004). The basal ganglia have multiple loops associating them with frontal motor regions (SMA, FEF) and prefrontal cortices (DLPFC, LOC, ACC) via the thalamus (Alexander, DeLong, & Strick, 1986). BG lesions have been found to result in executive dysfunction, such as poor set shifting on the WCST (Eslinger & Grattan, 1993), increased susceptibility to interference (Godefroy et al., 1992, 1994; Mendez et al., 1989) and impaired

inhibition (Rieger, Gauggel, & Burmeister, 2003). Interestingly, a study comparing PFC lesions to BG lesions reported that PFC lesions were related to attenuation of extrastriate visual activity and visual working memory activity on the contra-lesional side, whereas, BG lesions resulted in global visual working memory deficits independent of hemisphere, with retained extrastriate visual activity (Voytek & Knight, 2010). These findings are in line with the concept of selective gating of action and working memory proposed in the preceding section.

The cerebellum also has closed loops with the PFC, superior temporal lobe and the parietal cortex via the thalamus (Schmahmann & Pandyat, 1997). CB damage has been considered to produce similar symptoms in the cognitive domain as in the motor domain: a "dysmetria" of thought and behaviour termed Cerebellar Cognitive Affective Syndrome (CCAS Schmahmann, 1998; Schmahmann & Sherman, 1998; Schmahmann, 2004). It has been suggested that PFC and CB patients share similar executive deficits. For example, they can display difficulties in working memory span (Ilg, Giese, Gizewski, Schoch, & Timmann, 2008; Gottwald, Wilde, Mihajlovic, & Mehdorn, 2004), divided attention (Gottwald et al., 2004), verbal fluency (Richter et al., 2007; Hubrich-Ungureanu, Kaemmerer, Henn, & Braus, 2002), spatial fluency (Gottwald et al., 2004), attention/executive difficulties (Stoodley et al., 2016; Schmahmann, 1998; Bellebaum & Daum, 2007; Gottwald et al., 2004; Tedesco et al., 2011; Gottwald et al., 2004) and even in decision making (Cardoso et al., 2014). Interestingly, although working memory and divided attention appear to be impaired, these patients do not appear to have a deficit in selective attention (Gottwald, Mihajlovic, Wilde, & Mehdorn, 2003).

To conclude, there is evidence for a large distributed network of both cortical and subcortical brain regions which work together to provide effective top-down control of goal directed behaviour. Damage to different regions within this network can cause deficits in superordinate and subordinate control of goal directed behaviour.

1.4 Functional Impact

In the previous sections executive control of goal directed behaviour has been discussed in terms of theory and its neural underpinnings. At the beginning of this chapter a patient example was given, which demonstrated how even a seemingly simple task could become profoundly disrupted due to executive dysfunction. Stroke has been suggested to have the larger functional impact on an individuals' life compared to any other chronic disease (Adamson, Beswick, & Ebrahim, 2004; Kneebone & Lincoln, 2012). It is considered to be one of the leading causes of complex disability (Stroke Association, 2017) and known to have a detrimental impact on quality of life (Ayerbe, Ayis, Salma, Crichton, Rudd, Anthony, & Wolfe, Charles, 2015; Raju, Sarma, & Pandian, 2010). One factor that contributes to poorer functional outcome is cognitive dysfunction (Barker-Collo & Feigin, 2006; Mole & Demeyere, 2018; Nys et al., 2007).

It is suggested that cognitive impairment may exacerbate functional dependency both directly (e.g. forgetting appointments, disorganisation, difficulties with paperwork, getting distracted) and indirectly (disrupting rehabilitation and recovery strategy/adaptation) (Whyte, Skidmore, Aizenstein, Ricker, & Butters, 2011; Skidmore et al., 2010). Global cognitive impairment (across multiple domains) has been linked to poorer basic (e.g. personal care) and complex (e.g. shopping, cleaning) functional independence (Patel, Coshall, Rudd, & Wolfe, 2002; Oros, Popescu, Iova, Mihancea, & Iova, 2016; Heruti et al., 2002). Global impairment is also predictive of the extent of motor improvement at discharge (Özdemir, Birtane, Tabatabaei, Ekuklu, & Kokino, 2001; Heruti et al., 2002) and related to the likelihood of requiring either home or institutional care (55%-impaired, 32.7%-unimpaired, Tatemichi et al., 1994). In the long term, global cognitive impairment is linked to reduced community ambulation six months post stroke (Paker et al., 2010) and predicts outcomes such as survival, disability and institutionalisation four years post stroke (Patel et al., 2002).

As previously mentioned executive dysfunction is one of the most common forms of cognitive impairment following stroke (Nys et al., 2007; Barker-Collo & Feigin, 2006; Leśniak et al., 2008), particularly for patients with left cortical damage (Nys et al., 2007). Moreover, executive dysfunction (as measured by the TMT) is also prevalent in patients with transient ischemic attack (37%-40%, Sörös, Harnadek, Blake, Hachinski, & Chan, 2015). Executive dysfunction is also one of the most common and robust cognitive domains to be linked to functional dependency (Barker-Collo & Feigin, 2006; Mole & Demeyere, 2018; Leśniak et al., 2008; Nys et al., 2007).

Executive dysfunction in the subacute phase of stroke recovery has been linked to poor functional outcomes. Subacute patients with cognitive impairment (including executive, reasoning, verbal memory or visual spatial neglect) have a higher proportion of functional impairment as compared to those without (N=190, Nys et al., 2007). For example, executive and memory performance (measured by WASI, HVLT-R) predict discharge motor scores and need for supervision (N=44, Stewart, Gale, & Diamond, 2002). On a larger scale, executive impairment (measured by a composite executive score) has been linked to significantly worse ratings of independence on basic and instrumental activities of daily living (ADL) (N=262, Pohjasvaara et al., 2002). Some of these activities affected include intermediate functional disabilities in self-care, such as shopping, house/garden maintenance, transport and games/hobbies (N = 339, Stephens et al., 2005).

Executive dysfunction is also associated with poorer longer term recovery. For example, it is suggested as a strong predictor for recovery from disability from 3 months to a year post stroke (adjusted OR .47), with patients who improved demonstrating significantly better executive functioning, memory, visual spatial and language performance (N=182, Park et al., 2015). A study in 2008 screened eighty patients two weeks post-stroke and followed them up a year later. It reported that the presence of executive dys-

function (composite score) on the initial assessment was a significant predictor of poor basic functional outcome at follow up (OR 6.94, Leśniak et al., 2008). However, a similar study found that only inattention and perceptual difficulties were predictive of continued functional impairment, whereas continued executive dysfunction was predictive of continued cognitive impairment (N=111, Nys et al., 2005). Overall, it is suggested that patients with executive dysfunction are more likely to experience lasting impairment.

Moreover, it has been reported that executive function predicted engagement with inpatient stroke rehabilitation (Skidmore et al., 2010) and chronic rehabilitation (Cirstea, Ptito, & Levin, 2006). Executive dysfunction has also been seen to relate to poorer physical performance during physiotherapy. For example, performance on the Stroop task was associated with lower scores on the Berg Balance Scale, Times up and Go test, Six Minute Walk Test and Stair Climbing in a sample of 63 chronic stroke patients (Liu-Ambrose & Pang, 2007). An association has also been found between executive dysfunction and poorer balance and lower levels of physical activity one year post-stroke (Páhlman, Marianne, & Elisabeth, 2012; Páhlman, Gutiérrez-prez, Svborg, Knopp, & Tarkowski, 2011). Poorer performance on executive tasks (e.g. TMT, Stroop and frontal behaviour assessment) is significantly negatively correlated with the complex gait tasks (e.g. 10 metre: gait while counting, obstacle gait, busy gait) (Hayes, Donnellan, & Stokes, 2013) and balance (Hayes, Donnellan, & Stokes, 2016). These findings demonstrate that executive dysfunction is associated with poorer rehabilitation gains and linked to physiotherapy outcome measures.

The link between impaired selective attention and functional independence has begun to be investigated. Although the association between visual spatial neglect and poor functional recovery has been established (e.g. Jehkonen et al., 2000; Paolucci, Antonucci, Grasso, & Pizzamiglio, 2001), there have been few studies examining auditory selective attention and functional outcome. A small pilot study of 14 patients found a

relationship between poorer auditory attention and balance in the subacute phase of recovery (Stapleton, Ashburn, & Stack, 2001). A larger study of 122 patients reported that auditory sustained selective attention was linked to subacute ADL. Furthermore, balance and ADL was correlated with sustained attention at a one year follow up, while discharge attention scores were related to functional outcome (Hyndman, Pickering, & Ashburn, 2008). A relationship between sustained and divided attention, chronic ADL and fall incidents has also been demonstrated (N=48, Hyndman & Ashburn, 2003a). In line with this, sustained attention performance at 2 months post stroke has been found prognostic for ADL performance 2 years later (N=47, Robertson et al., 1997). These results show that impaired selective attention may be related to poorer functional outcomes for stroke patients.

To conclude impaired executive functioning and more specifically impaired attentional selectivity has been linked to worse independence following stroke and in some instances poorer performance on physiotherapy assessment and rehabilitation outcome.

1.5 Summary and Overview

It has been demonstrated that several lines of cognitive research and neuroimaging research have suggested that goal directed behaviour is achieved from a combination of both superordinate and subordinate executive control functions. There is substantial evidence to suggest that these processes are controlled by a distributed network of both cortical and subcortical brain regions. Brain damage to this network resulting from stroke is linked to impaired executive function and attentional selectivity. This impairment is linked to poorer functional outcomes during recovery.

This thesis is divided into two sections. The first aims to address the functional impact and neural correlates of impaired top-down attentional configuration in a stroke population. The second is aimed at more focused experimental questions in a healthy population. This section addresses the dissociation of different types of goal activation errors and examines how attention is distributed between external processing and internal working memory maintenance during goal directed behaviour.

Part I: Attentional Control in a Stroke Population

Functional Impact of Impaired Selective Auditory Attention.
The first empirical chapter aims to address the real life consequences of when a task model fails in its ability to configure an attentional episode which is effective in biasing attention in favour of task relevance. Although executive function in general has been linked to functional independence, relatively little work has addressed selective attention specifically, especially in the auditory domain. This is an important area of research due to the fundamental need to pay attention to speech during the recovery process and in day to day activities. There is also a need for more research in this area which includes control for both stroke characteristics (e.g. lesion volume) and demographics (e.g. age

and education). Therefore, this investigation aimed to add a targeted and controlled investigation of the link between impaired selective auditory attention and functional independence, firstly, in overall ability to selectively attend and secondly, separately looking at errors of omission, commission, sustained attention and recall of target information.

Lesion Neuroanatomy of Selective Auditory Attention.

In the following chapter a subsection of patients from previous chapter were examined using a voxel based symptom lesion mapping (VLSM) approach to investigate the neuroanatomical underpinning of impaired selective attention. This analysis was run on the overall selective attention score and subsequently in the segregated scores mentioned above. Although there is previous work pertaining to selective attention in the visual domain (in particular pertaining to visual spatial neglect) there is very few studies specifically addressing the neural underpinning of selective auditory attention, especially using a larger scale VLSM methodology.

Executive Dysfunction: Beyond the Frontal Lobes.

The framework of unity and diversity of executive functioning was utilised to examine whether executive impairment experienced by frontal and posterior patients differed. This was achieved by running a BiFactor model on several executive tasks to segregate the variance into a common executive functioning factor and several more specific executive factors. The patients were compared on performance and examined for consistencies in the type of lesion location that resulted in impairment. Although some VLSM work has been performed using this framework (albeit using composite scores rather than a BiFactor model), a direct comparison between patient groups had not hitherto been performed. This allowed a more detailed investigation of whether lesions throughout the attentional control network differ on their effect on superordinate compared to subordinate elements of executive control.

Part II: Attentional Control in a Healthy Population

Dissociating Errors of Goal Activation.

Although goal neglect happens more frequently in a brain-damaged population, such as patients with stroke, it can also occur in the general population and can be measured experimentally. In traditional goal neglect paradigms it is hard to dissociate different types of goal activation error. In this chapter a novel goal neglect paradigm is developed to dissociate different types of goal activation errors (e.g. failure to monitor the environment, delayed task reconfiguration and pure goal neglect). The link between task switching and the perceptual difficulty of the cue was then re-examined and the effects compared across different types of goal activation error.

Attention in Processing and Maintenance.

In the last empirical chapter a more specific question is addressed regarding how attention is shared between the external processing of the environment and the internal refreshing of working memory traces during goal directed behaviour. In this chapter the Time Based Resource Share Model of working memory (Barrouillet et al., 2004; Barrouillet & Camos, 2015) was adopted and applied to non-sequential working memory maintenance of a single item feature. A novel paradigm adopted a delayed response task that allowed the precision with which the item feature could be remembered to be measured on a continuous scale. Until now the literature base was built on complex span tasks which required sequential recall of items (e.g. letters or digits). Therefore, this chapter aimed to extend their findings by examining the model assumptions under a different memory context, using a more sensitive graded measure of recall.

Part I

Attentional Control in a Stroke Population

Chapter 2

The Functional Impact of Impaired Selective Auditory Attention.

2.1 Abstract

Introduction: Stroke is the leading cause of complex disability in the UK, with over half of stroke survivors experiencing disability, and over a third becoming dependent on others in their daily lives. It has previously been observed that cognitive impairment, and in particular executive dysfunction, is linked to a higher likelihood of being functionally dependent following stroke. A key component of executive function is selective attention; the ability to bias perception and action based on goal relevance.

Method: This study aimed to establish the prevalence and functional impact of impaired selective attention in the subacute (M=24 days post-stroke, SD=21 days, N=410) and chronic (M=308 days post-stroke, SD= 31 days, N=188) stages of stroke recovery.

Results: Impaired selective attention (as measured by the Auditory Attention Task, BCoS), was not only prevalent in the subacute stage (52%), but also persistent into the chronic stage of recovery for many patients (45%). The relationship between selective attention and functional status (Barthel Index and Nottingham Extended Activities of Daily Living) was examined using robust linear regression. A forced entry method was used to explore the impact of selective attention above that of age, years in education, instruction comprehension, lesion volume and whether there had been a previous instance of stroke. It was found that selective attention was negatively associated with subacute and chronic functional independence. Interestingly, a prognostic analysis found that difficulty in sustaining selective attention in the subacute stage was predictive for functional dependence in the chronic stages of recovery. Model testing demonstrated that attentional indices explained unique variation in functional independence above that of covariates (e.g. demographics and stroke characteristics).

2.2 Introduction

In the UK, stroke is not only prevalent but also resides as the leading cause of complex disability (Stroke Association, 2017). It is suggested that stroke has a greater disability impact on an individual than any other chronic disease (Adamson et al., 2004; Kneebone & Lincoln, 2012). Of the ∼1.2 million stroke survivors living in the UK, it is estimated that over half are living with disability and over a third are dependent on others during daily living (Stroke Association, 2017). The loss of functional independence can cause great psychological distress for the individual; relating to higher instances of depression and decreased quality of life (Ayerbe et al., 2015; Raju et al., 2010). Besides the personal burden, functional dependency has a large economic cost for society (∼9 billion per year; Saka, McGuire, & Wolfe, 2009). Therefore, understanding factors which may exacerbate functional dependence is of great importance.

One of the factors shown to exacerbate functional dependence following stroke is cognitive impairment (Barker-Collo & Feigin, 2006; Mole & Demeyere, 2018; Nys et al., 2007). Cognitive impairment can influence functional dependence not only by directly impacting daily living (e.g. forgetting to take medication), but also indirectly by disrupting rehabilitation (e.g. difficulty concentrating during rehabilitation sessions) (Whyte et al., 2011; Skidmore et al., 2010). Global cognitive impairment has been linked to more dependence on basic and instrumental activities of daily living (Oros et al., 2016), in addition to poorer motor functioning (Özdemir et al., 2001) and less rehabilitative gains at discharge (Heruti et al., 2002). This relationship appears persisitent, with cognitively impaired patients more likely to require home or institutional care three months post stroke (Tatemichi et al., 1994), participating in less community ambulation six months post stroke (Paker et al., 2010) and performing worse on a variety of outcome measures (e.g. institutionalisation & disability) up to four years post stroke (Patel et al., 2002). It is well established that global cognitive impairment can impact poorly on functional

independence. However, the examination of global cognitive impairment comes with some inherent weaknesses. For example, global measures make no distinction between specific cognitive deficits leading to the patient reaching the impairment cut-off, therefore leading to inconsistencies and general variability in the literature (Mole & Demeyere, 2018). To understand the link between cognitive impairment and functional independence an in depth analysis of individual elements of cognition is advantageous because it yields more robust and informative results.

Of the work that has examined specific cognitive deficits, the most common and robust predictor of functional dependency is executive function (Barker-Collo & Feigin, 2006; Mole & Demeyere, 2018; Leśniak et al., 2008). Executive function is an umbrella term for high level control processes which utilise goal and task set representations to achieve goal directed behaviour (e.g. Friedman & Miyake, 2017). A fundamental element of executive function is selective attention: the ability to bias perception and action in favour of task relevant information (e.g. Bosman & Womelsdorf, 2009; Duncan, 2010, 2013). Without the ability to preferentially focus on and respond to information that is relevant, behaviour can become unstructured and maladaptive (Duncan & Miller, 2002). Consequently, deficits in executive function, and more specifically selective attention, are critically placed to disrupt the ability to live independently.

Executive dysfunction is prevalent following stroke, with over 50% of patients demonstrating impairment (Zinn et al., 2007). In the subacute phase of recovery, executive and attentional dysfunction have been linked to poor functional outcome (Stewart et al., 2002; Mysiw, Beegan, & Gatens, 1989), difficulties in self-care (Stephens, et al., 2005) and need for supervision on discharge (Stewart et al., 2002). Moreover, executive dysfunction has been shown to impact negatively on the level of participation in acute rehabilitation (Skidmore et al., 2010) and has also been associated with less kinematic gains during repetitive movement practice a year post-stroke (Cirstea et al., 2006).

As was previously observed with global cognitive impairment, the impact of executive dysfunction appears to endure into the chronic stages of recovery predicting poorer functional outcome years following stroke (e.g. Bennett et al., 2002; Leśniak et al., 2008; van Zandvoort, Kessels, Nys, de Haan, & Kappelle, 2005).

Very few studies have investigated the link specfically between auditory selective attention and functional status, despite impairment being reported in over 50% of stroke patients (Barker-Collo, Feigin, Lawes, Parag, & Senior, 2010). A small study of 13 subjects found that poorer auditory selective attention correlated with measures of balance in the subacute stage of stroke recovery (Stapleton et al., 2001). Another examination of subacute attention and functional status observed that selective auditory attention (as measured by a mixed auditory and visual continuous performance task) did not correlate with BIADL, whereas multimodel performance did (N=96 Barker-Collo et al., 2010). A larger analysis of 122 patients found that auditory selective and sustained attention correlated with ADL and balance scores in the subacute stage of recovery (Hyndman et al., 2008).

In the same investigation, it was observed that discharge sustained attention scores correlated with ADL scores at a one year follow up, whereas, none of the discharge attention measures were prognostic of outcome (Hyndman et al., 2008). Another investigation of 49 patients found an association between sustained and divided attention and ADL in the chronic stage of recovery (46 months post stroke; Hyndman & Ashburn, 2003b). Additionally, sustained attention performance at 2 months post stroke has been reported to predict ADL at 2 years post stroke (N=47; Robertson et al., 1997). Therefore, there is some indication that selective auditory attention may be related to functional status in the subacute phase of recovery and that the ability to sustain attention may influence more longer term recovery. However, at present these results remain inconclusive.

Although it has been indicated that executive dysfunction can impact functional independence following stroke, it is still unclear which elements of executive function contribute to this relationship. Selective attention contributes to goal directed behaviour by biasing perception in accordance with the current task and thus, impairment has the potential to disrupt activities of daily living. Despite this potential, relatively few studies have investigated whether selective attention impacts on functional independence. Moreover, very few studies control for lesion volume and most have small sample sizes. Therefore, the following investigation aimed to address these weaknesses by adding a targeted examination of the impact of auditory selective attention on functional independence following stroke in the subacute ($\sim$3 weeks, N=410) and chronic stages ($\sim$10 months, N=188) of recovery.

Auditory selective attention will be measured using the auditory attention task from the Birmingham Cognitive Screen (Humphreys et al., 2012). This task requires the patient to remember and make selective tapping responses to target information (3 target words) whilst ignoring distracting information (3 related words). Therefore, examining executive functioning by means of working memory, selective and sustained attention. There are two aims: firstly to establish the prevalence and persistence of impairments in selective attention and secondly, to examine the impact deficits have on functional dependency. Importantly, this examination intends to extend previous findings by providing evidence in a large sample, using less confounded measures and controlling for elements of stroke severity (e.g. lesion volume and previous instance of stroke) and demographics (e.g. age and education).

2.3 Method

Sample

This was a retrospective analysis using data from the BCoS study, a 5 year clinical study run in 10 hospitals across the west-midlands. All participants provided written informed consent according to the UK National Research Ethics Committee approved procedures. The inclusion criteria for this study was (i) confirmed stroke (ii) BCoS completed within 100 days (iii) complete data on the Auditory Attention Task and (iv) access to a clinical CT scan (see Appendix A.1, p.330 for an overview of data selection).

Procedure

After giving informed consent, patients underwent a full cognitive assessment using the Birmingham Cognitive Screen (BCoS; Humphreys et al., 2012) and filled out Barthel Index Activities of Daily Living (BIADL; Mahoney & Barthel, 1965). The task battery took approximately one hour to complete. The assessment took place in a quiet room situated in the hospital and patients were given breaks as required. Patients were followed up approximately nine months later. During the follow-up appointment, each patient completed an alternative version of the BCoS, the BIADL and the Nottingham Extended Activities of Daily Living scale (NEADL; Nouri & Lincoln, 1987).

The Auditory Attention Task

The Auditory Attention Task (AAT) measures selective attention to verbal information through time (see Appendix A.4.1, p.333). The aim of the task is to make selective tapping responses to three previously learnt target words (hello, please, no), whilst withholding responses to non-target words (goodbye, thanks, yes). The task is comprised of 54 pre-recorded (pseudo-randomised) word presentations, administered over a continuous three minute duration. The task is comprised of three blocks of eighteen word presenta-

tions (six words presented three times each with a jittered inter-stimulus interval of two, three or four seconds). Before the task is started, there are up to three practice trials. Each practice starts and ends with a free recall of the target words (prompted if incorrectly recalled) and includes six word presentations to practice the tapping response. If the patient recalls all the target words or completes the practice with 100% accuracy the task is started. If the patient is unable to reliably complete the task (e.g. due to motor or language difficulties), it is discontinued. After the task, patients were asked to recall the target words. In order to support patients with expressive aphasia short familiar words were chosen and visual multiple choice options were provided during recall.

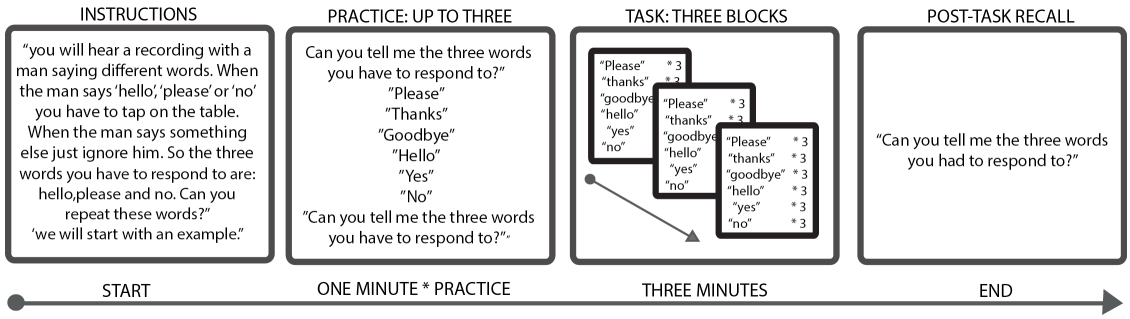


Figure 2.1: Schematic Overview of the Auditory Attention Task.

Several attentional indices are derived from the AAT: Overall task performance, number of omission errors, number of commission errors, sustained attention and target word recall. Overall task performance (0-54) is the sum of correctly initiated and withheld responses and serves as an index of general *selective attention* efficiency. This score can be broken down into the ability to withhold a response (*commission errors*, 0-27) and the ability to initiate a response (*omission errors*, 0-27). High scores denote worse performance. *Sustained attention* can be measured by looking at whether there has been a decrement in performance over the duration of the task (block1-block3). If the patient made more than 8 errors in the first block the task was discontinued. Therefore, the minimum score was -8 (10-18) and the maximum score was 18 (18-0). A higher score indicates a greater decrement in performance. Target word recall at the end of the task

(0-3) indicates the ability to maintain task relevant information.

Functional Measures

Barthel Index of Activities of Daily Living (BIADL; Mahoney & Barthel, 1965). The BIADL measures basic activities of daily living; including items referring to grooming, feeding, transferring, mobility, dressing, bathing, continence and the use of toilet and stairs. The scale primarily measures physical dependence (Quinn, Langhorne, & Stott, 2011) and has good psychometric properties (Novak, Johnson, & Greenwood, 1996; Hertanu, Demoposalos, Yang, Calhoun, & Fenigstein, 1984). There are 10 questions, with scores ranging from 0 to 20. Items are on a 3 or 4 point scale (0-2 or 0-3), with higher scores indicating greater independence.

Nottingham Extended Activities of Daily Living (NEADL; Nouri & Lincoln, 1987). The NEADL measures complex activities of daily living; including items referring to mobility, feeding, housework, food preparation, shopping, written and verbal communication, social interaction and driving. The NEADL has good psychometric properties and is unaffected by ceiling and floor effects (Sarker, Rudd, Douiri, & Wolfe, 2012). The scale includes 22 questions, with scores ranging from 0-22. Each item has 4 possible responses referring to the level of independence (not at all, with help, on my own with difficulty, on my own). The first two options (marked as 0) are classed as dependent, the second two options (marked as 1) are classed as independent.

Additional Neuropsychological Assessment

Performance on the AAT is reliant on the ability to remember (short-term memory capacity) and selectively respond to target information (attentional control). To help dissociate the contribution of short term memory and attentional control, two additional tasks were selected.

Immediate Story Recall (ISR; Humphreys et al., 2012), has been chosen because it primarily examines short-term memory. In this task the examiner reads the patient a short story with 15 key elements. The patient must immediately recall as many details as possible (score range 0-15; see Appendix A.4.2, p.334). The patient is required to comprehend, indiscriminately pay attention to and retain verbal information without selectivity biasing perception and action. Therefore, the examination of the relationship between ISR performance and functional independence will provide a clearer understanding of the role of short-term memory capacity, independent of attentional control.

Rule Finding and Concept Switching (RFCS; Humphreys et al., 2012), was chosen because it requires high level attentional control in the visual domain. In this task the patient predicts where a dot will move on a grid, based on the moves it made before (score range 0-18; see Appendix A.4.2, p.334). The patient is required to monitor changing visual information in order to successfully assemble and use an appropriate rule set to bias action. The additional assessment of the RFCS task is intended to give a clearer picture of whether functional independence is associated with "domain general" attentional control.

Table 2.1: Overview of Measures

Indices	Range	Optimal Score	Measures
Selective Attention	0-54	High	Task model implementation
Omission Errors	0-27	Low	Initiating appropriate response
Commission Errors	0-27	Low	Withholding inappropriate response
Sustained Attention	-8-18	Low	Sustaining selectivity.
Target Word Recall	0-03	High	Maintenance of target information
Immediate Story Recall	0-15	High	Immediate non-selective recall.
Rule Finding & Switching	0-18	High	Task model implementation
Barthel Index ADL	0-20	High	Basic functional independence.
Nottingham Extended ADL	0-22	High	Complex functional independence.

Please see appendices for examiner sheets and cut-off scores. ADL = Activities of daily Living

Neuroimaging

Lesions were delineated from CT scans using an automated procedure (Gillebert, Humphreys, & Mantini, 2014). See Chapter 3 (p.82) for details. Lesion volume was calculated using a script written in python (2.7.3), using the module NiBabel (2.1.0, Brett et al., 2016).

2.4 Results

Data Handling

First the data were filtered on the completeness of the variables of interest (see Appendix A.1, p.330). There was missing data for years in education for 2% of patients, which was imputed based on education level or the grand mean if unavailable. As recommended by the authors of the BCoS manual (Humphreys et al., 2012), patients who did not complete the AAT were considered impaired on the sustained attention index and the worst score was imputed (for details see Appendix A.2, p.331). The results are reported before and after imputing. The analysis was run using the statistical package R (3.0.3), using packages stats (R Core Team, 2014a) and robustbase (Maechler et al., 2016).

Sample Characteristics

Table 2.2: Sample Characteristics

		Subacute N=410		Chronic N=188	
Gender	Male	224	57%	103	55%
	Female	186	43%	85	45%
Handedness	Left	40	9%	26	14%
	Ambidextrous	8	2%	4	2%
	Right	362	89%	158	84%
Stroke Instance	First	293	72%	135	72%
	Previous	110	27%	44	23%
	Unknown	7	2%	9	5%
Stroke Type	Ischemic	284	69%	136	72%
	Haemorrhagic	52	13%	24	13%
	Unknown	74	18%	28	15%
Lateralisation	None	18	4%	12	6%
	Left	142	35%	65	35%
	Bilateral	78	19%	16	15%
	Right	163	40%	81	43%
	Unknown	78	19%	0	0%
Coarse Location	Frontal	285	70%	132	70%
	Posterior	125	30%	56	30%

Frontal = including frontal cortex, Posterior = excluding the frontal cortex

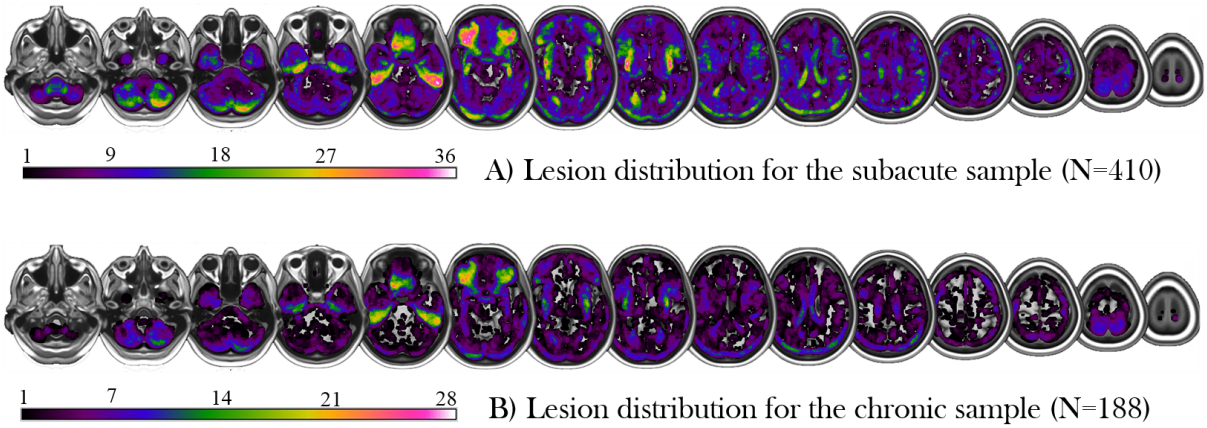


Figure 2.2: Lesion Overlap. A) Lesion overlap in the full sample of 410 patients. B) Lesion overlap in the chronic sample of 188 patients.

At the subacute time point, there were 410 patients with an average age of 70.56 (SD=13.39). They had spent an average of 11.53 (SD=2.85) years in education and had an average lesion volume of 32.53 cm^3 (SD=58.08 cm^3). Time from stroke to assessment was available for 398 patients. On average the assessment was given 24 days post stroke (SD=21 days). As can be seen from Figure 2.3 A, 326 (82%) patients were tested within 6 weeks post stroke, whereas the other 72 (18%) patients were tested outside of this critical time period (Stapleton et al., 2001).

A subset of patients (188, 46%) took part in a follow up assessment. The sub-sample had an average age of 69.69 (SD=12.46), had spent an average of 11.89 years (SD=3.13) in education and had an average lesion size of 32.94 cm3 (SD=60.69). Of the sub-sample 159 (87%) patients had data available for the time between the initial and follow-up assessment (M=282 days from initial assessment, SD=27 days, see Figure 2.3 B). Patients were on average 308 (SD=31) days post stroke at the follow up assessment.

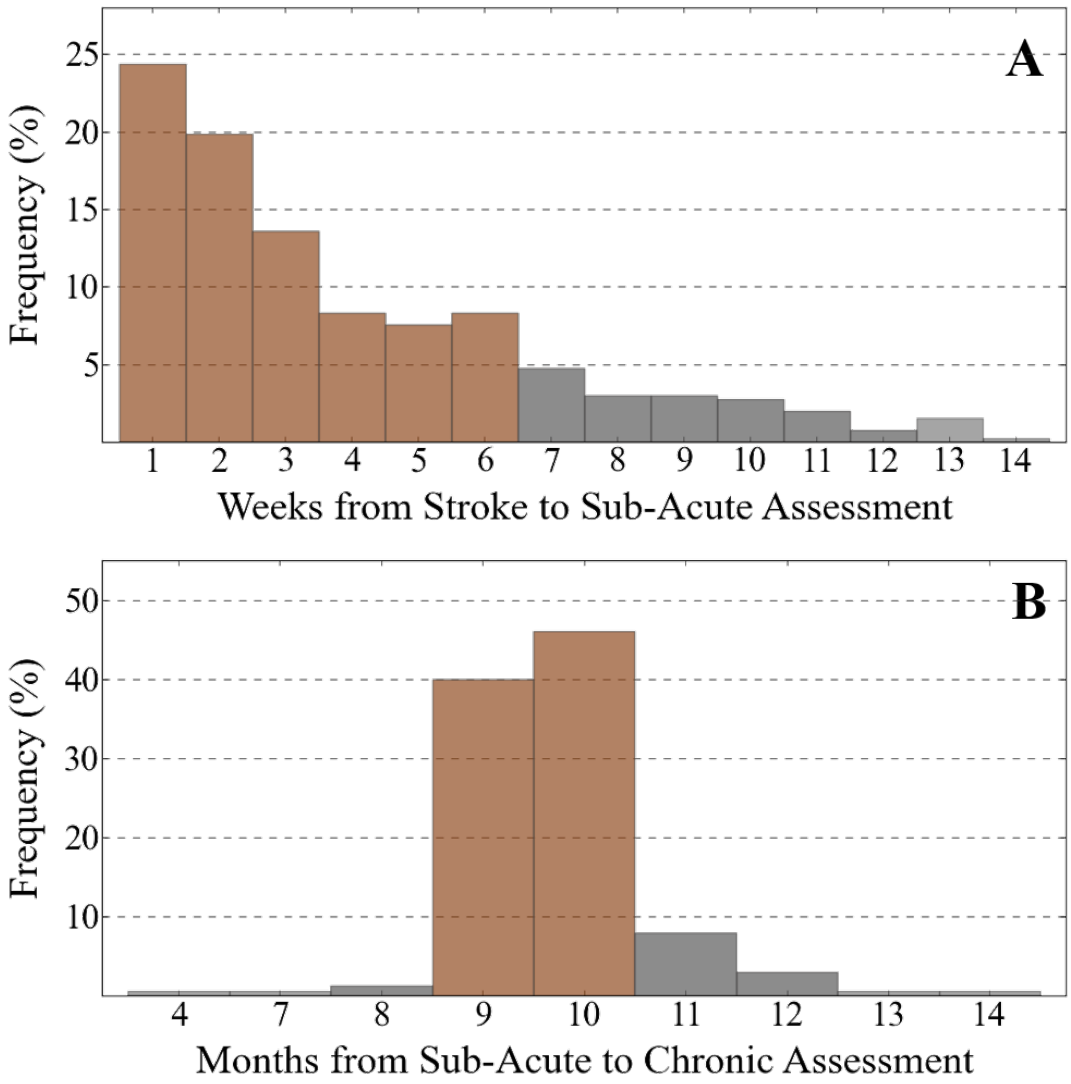


Figure 2.3: A) Percentage of patients split by how many weeks the subacute assessment was performed following the stroke. B) Percentage of patients split by how many months the chronic assessment was performed following the subacute assessment.

Follow-up Sample Representativeness

In order to examine the representativeness of the follow-up sample, patients who had agreed to take part in a follow up were compared to those who were unable to take part on their sub-acute performance. A series of uncorrected Welch's two samples t-tests (Chi-Square/Friedman tests for frequency data) were run. As can be in Table 2.3, there were no significant differences between the groups on demographics, stroke characteristics or BIADL. However, on average patients who took part in the follow-up assessment were impaired on fewer tasks overall, had better instruction comprehension and performed significantly better on the AAT. This suggests that although the follow-up sample was representative in terms of demographics and stroke characteristics, they were less cognitively impaired as compared to those unable to take part at follow-up.

Table 2.3: Comparison of Follow-Up Sample

	Declined M (SD)	Agreed M (SD)	Difference P-Value
N	222	188	–
Age	71.01 (14.32)	70.02 (12.21)	n.s.
Barthel Index	13.30 (05.65)	12.95 (05.72)	n.s.
Lesion Volume cm3	30.17 (49.27)	35.34 (67.12)	n.s.
Frontal Overlap cm3	8.28 (17.26)	9.94 (19.52)	n.s.
Days To Assessment	24.44 (22.19)	23.87 (19.72)	n.s.
Years in Education	11.19 (02.56)	11.75 (03.14)	n.s.
Tasks Impaired	09.48 (07.09)	08.00 (06.25)	.03*
Selective Attention	39.59 (15.84)	43.55 (13.07)	.01*
Commission Errors	03.53 (15.84)	03.48 (05.36)	n.s.
Omission Errors	04.34 (04.74)	03.79 (05.06)	n.s.
Sustained Attention	02.76 (03.81)	02.01 (03.20)	.03*
Target Word Recall	02.37 (00.88)	02.55 (00.76)	.03*
Immediate Story Recall	05.85 (02.97)	06.42 (03.25)	n.s.
Instruction Comprehension	02.83 (00.44)	02.91 (00.29)	.01*
Gender female/male	55%/45%	54%/46%	n.s.
Stroke Instance first/prev	30%/66%	23%/73%	n.s.
Stroke Type isch/heamo	66%/12%	72%/13%	n.s.
Coarse Location front/post	69%/31%	70%/30%	n.s.
Lateralisation none/left/bi/right	5%/37%/36%/21%	7%/32%/43%/18%	n.s.

Results considered significant at * <0.05 uncorrected

Prevalence and Persistence

Aim 1: To establish the prevalence of selective attention deficits and their persistence into the chronic stages of recovery.

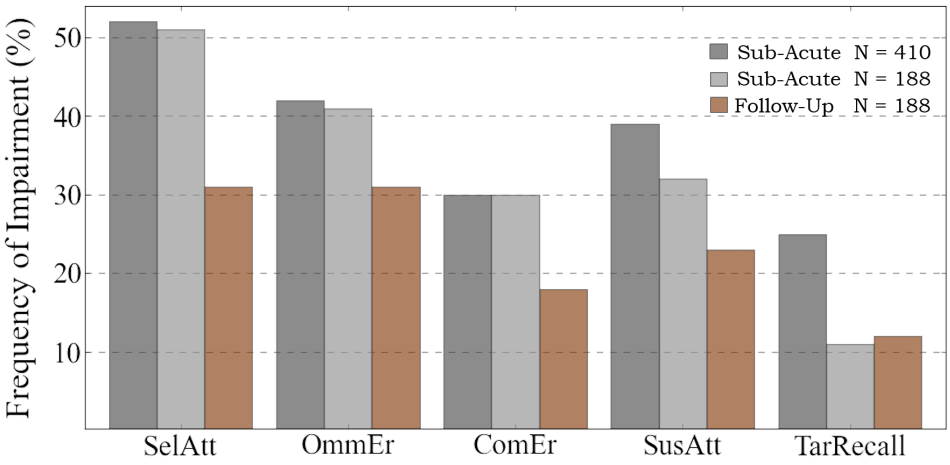


Figure 2.4: Frequency of impairment in the full subacute (N=410) and follow up sample (N=188) as indicated by the 5th percentile cut-off (see Appendix A.5, pp. 336). SelAtt = Selective Attention, OmmEr = Omission Errors, ComEr = Commission Errors, SusAtt = Sustained Attention, TarRecall = Target Word Recall.

Patients were classified as impaired or unimpaired based on whether they performed outside the normal range (5th or 95th percentile cut-off score adjusted for age, Humphreys et al., 2012). As seen in Figure 2.4, deficits in selective attention were prevalent in the subacute and chronic phase of stroke recovery. This was particularly apparent for the overall selective attention score, with 52% of patients at the subacute phase and 31% of patients in the follow-up performing below the 5th percentile cut-off score. After breaking down the total score into individual error types it was observed that in the subacute phase 42% of patients were impaired on omission errors and 30% on commission errors. At follow up 31% of the sample were impaired on omission errors and 18% on commission errors. The prevalence was also high for problems sustaining selectivity throughout the task and the ability to retain the target words, with 39% and 25% of patients reaching the cut-off retrospectively. At follow up 23% of patients were impaired on the sustained attention index and 12% were impaired on target word recall.

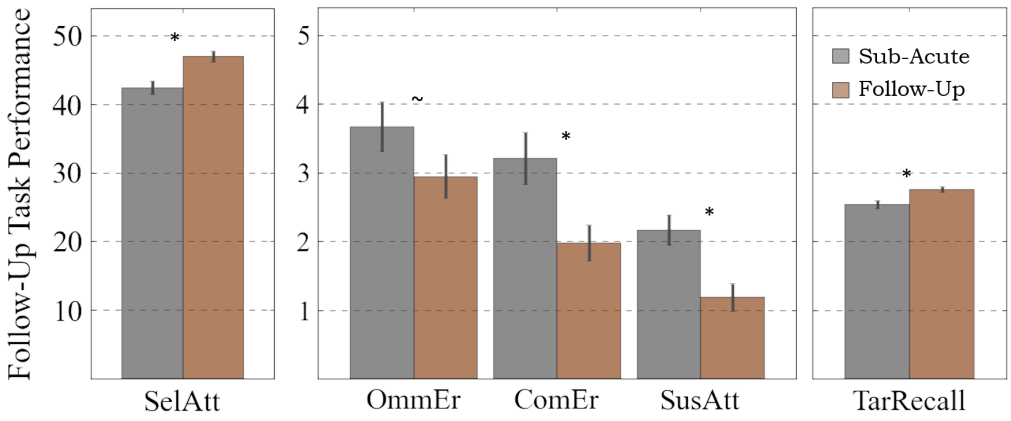


Figure 2.5: Average task performance in the subacute and chronic stages of recovery for the follow up sample (EB = 1* SEM). SelAtt = Selective Attention, OmmEr = Omission Errors, ComEr = Commission Errors, SusAtt = Sustained Attention, TarRecall = Target Word Recall. * = p <.05, $\sim$ = p=.05.

A series of repeated measures t-tests were run in order to examine whether there was a significant improvement in attentional performance between the subacute and chronic assessments in the follow up sample (N=188). A significant improvement [$t(187)$= -4.169, p <.001, d=.28, CI=0.08:0.48] was seen in selective attention (overall task performance). This was subsequently reflected in a significant decrease in the number of commission errors [$t(187)$=3.26, p=.001, d=-.21, CI=-0.41:-0.004] and a trend towards a decrease in omission errors [$t(187)$=1.96, p=.05, d=-.14, CI=-0.34:-0.07]. There was also a significant improvement in the ability to sustain selectivity throughout the task [$t(187)$=3.93, p <.001, d=-.27, CI=-0.47:-.006] and in the post-task target word recall [$t(187)$=-3.60, p <.001, d=.23, CI=0.03:0.44]. Overall it is suggested that attentional performance significantly improved between the subacute and chronic assessments.

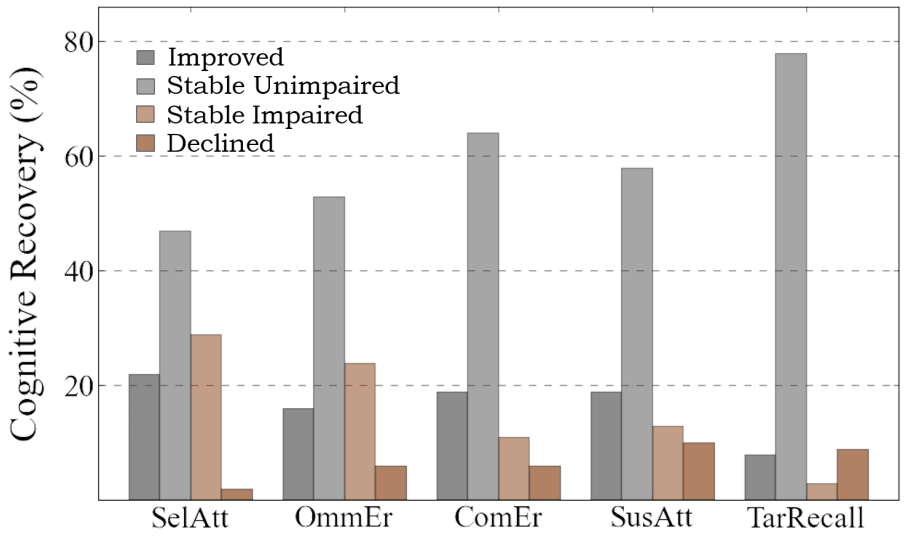


Figure 2.6: Percentage of patients in the follow up sample (N=188) who recovered, decline or stayed stable as indicated by the 5th percentile cut-off score. SelAtt = Selective Attention, OmmEr = Omission Errors, ComEr = Commission Errors, SusAtt = Sustained Attention, TarRecall = Target Word Recall.

To examine whether this improvement translated into significant recovery of attentional function the change in classification as impaired or unimpaired (as denoted by the cut off scores) were examined across time points in the follow up sample (N=188). Figure 2.6, demonstrates the percentage of patients who improved (moved from impaired to unimpaired), were stable between time points (either stayed unimpaired or impaired) and those who declined (moved from unimpaired to impaired). There were relatively few patients (between 8%-22%) who successfully recovered as denoted by the cut-off score. There were also between 3%-29% of patients who remained impaired and between 2%-10% of patients who declined between the assessments. Overall this pattern indicates that although many patients improved, many of them did not make a full recovery. This suggests that attentional difficulties may persist into the chronic stages of recovery.

Attentional Indices by Stroke Location and lateralisation

Table 2.4: Subacute Task Performance and Prevalence by Stroke Characteristics

			Left	Bilateral	Right
SelAtt	Frontal	M (SD)	36.84 (16.29)	39.73 (15.09)	43.48 (13.42)
		Impaired	61 (64%)	36 (59%)	57 (44%)
	Posterior	M (SD)	41.44 (15.68)	40.47 (17.00)	45.65 (10.63)
		Impaired	23 (45%)	12 (63%)	17 (50%)
OmmEr	Frontal	M (SD)	5.82 (5.82)	4.18 (4.65)	3.18 (4.16)
		Impaired	52 (55%)	26 (43%)	46 (36%)
	Posterior	M (SD)	4.65 (5.31)	4.79 (4.80)	3.56 (4.43)
		Impaired	48 (44%)	11 (58%)	13 (38%)
ComEr	Frontal	M (SD)	3.57 (4.01)	3.89 (5.20)	3.71 (5.62)
		Impaired	30 (32%)	16 (26%)	36 (28%)
	Posterior	M (SD)	2.67 (3.79)	4.05 (5.16)	3.21 (5.40)
		Impaired	14 (29%)	7 (37%)	10 (29%)
SusAtt	Frontal	M (SD)	3.22 (4.12)	3.07 (3.75)	2.11 (3.18)
		Impaired	44 (46%)	28 (46%)	44 (34%)
	Posterior	M (SD)	2.08 (3.55)	2.95 (4.31)	1.50 (2.54)
		Impaired	16 (33%)	8 (42%)	13 (38%)
TarRecall	Frontal	M (SD)	2.25 (0.96)	2.31 (0.79)	2.60 (0.74)
		Impaired	35 (37%)	12 (20%)	23 (18%)
	Posterior	M (SD)	2.52 (0.80)	2.21 (1.08)	2.5 (0.75)
		Impaired	14 (29%)	6 (32%)	23 (32%)

Frontal = Includes a lesion overlapping with the frontal cortex. Posterior = Lesion excluding the frontal lobe.
Impaired = N<5^{th} percentile cut-off score.

Next the effect of lesion lateralisation and coarse location on attentional indices was examined using a 2(location)x 3(lateralisation) factorial design. For overall selective attention performance there was a significant main effect of lesion side [$F(2,380)= 6.553$, p=.002]. A posthoc Tukey test of lesion lateralisation demonstrated that participants with a right unilateral lesion performed significantly better than those with a bilateral (p=.05) or left unilateral (p=.002) lesion. Although participants with lesions sparing the frontal cortex did perform slightly better on average, this difference was not significant and did not interact with the the main effect of lesion side.

The overall score was split into errors of commissions and omissions. As before, there was a significant main effect of lesion lateralisation [$F(4,760)=3.88$, $p=.003$], but not for coarse lesion location. Follow up tests revealed the effect was driven solely by a significant difference in the number of omission errors [$F(2,380)=7.60, p<.001$]. A posthoc Tukey analysis found that patients with unilateral right lesions performed significantly better than those with unilateral left lesions ($p<.001$).

Next the ability to sustain selective attention throughout the task was examined. Once again there was a significant main effect of lesion lateralisation [$F(2,380)=3.65$, $p=.03$], but no main effect or interaction with coarse lesion location. The posthoc analysis revealed a non-significant trend towards patients with right unilateral lesions performing better than patients with left unilateral ($p=.06$) and bilateral ($p=.07$) lesions.

Finally, the same analysis was performed for the number of target words recalled at the end of the test session. Once again there was a significant main effect of lateralisation [$F(2,380)=4.75$, $p=.001$). The posthoc analysis demonstrated that patients with right unilateral lesions recalled significantly more words than those with bilateral ($p=.03$) and left unilateral lesions ($p=.03$). Overall, these results are in keeping with the verbal nature of the task, damage to the left hemisphere is associated with poorer task performance.

The relationship between the extent of lesion overlapping with the frontal cortex and the attentional indices was examined using Pearson's correlation. None of the measures were significantly associated with the extent of overlap, although the number of omission errors did show a non significant negative trend (β= -0.07, $t(283)$= -1.88, $p=.06$). The same analysis was run for the overall lesion volume, demonstrating no relationship.

Impact on Functional Status

Aim 2: To Examine the Relationship Between Selective Attention and Functional Independence Following Stroke.

The linear relationships between the variables of interest were examined using Pearsons correlation. All the measures were correlated, with the exception of commission and omission errors. Due to potential problems of multicollinearity, a series of separate regression models were run. These models included: a separate model for overall selective attention, a combined model for commission and omission errors and a separate model for sustained attention (for details see Appendix A.3.1, p.331). A series of robust linear regressions were run using a forced entry method. In all cases, age, years spent in education, overall instruction comprehension, lesion volume and instance of previous stroke were entered as covariates of no interest. First target word recall was entered into the model and compared to the model containing only the covariates using a test of deviance. The model containing target word recall was then used to compare all subsequent models. This method allowed an indication of how much unique variance each of the attentional indices were adding above the covariates and the influence of target word recall.

The model comparison and change in R^2 is reported in Table 2.5, alongside the main regression results (α= .05 FDR corrected). The analysis was run in the subacute stage, in the chronic stage of recovery and finally a prognostic analysis was run predicting chronic functional status using subacute attentional performance. In the prognostic analysis the chronic attentional score was also included in the model and model comparison was performed to the chronic model. This allowed a better understanding of whether the subacute performance had an effect over and above the continued immediate impact of any remaining deficits. The results were further analysed in a more stringently controlled analysis which also included stroke type (ischemic or haemorrhagic) and lesion lateralisation (left, right or bilateral) and reported in the text.

Table 2.5: Relationship between attention and functional status (N=410).

		β	CI 2.5%:95%	T	P	R^2	Model Deviation X^2 P R^2 change
Subacute	Target Recall	1.05	0.40:-1.70	3.18	.00*	.12	11.53 (1) .00* .03
	Selective	1.33	0.57:-2.10	3.44	.00*	.15	13.55 (1) .00* .03
	Commission	-0.90	-1.51:-0.28	-2.86	.00*	.15	05.61 (1) .00* .01
	Omission	-0.90	-1.59:-0.20	-2.54	.02*		04.65 (1) .06 .01
	Sustained	-0.95	-1.66:-0.24	-2.62	.02*	.14	07.63 (1) .03* .02
Chronic	Target Recall	0.04	-0.90:-0.98	0.08	.93	.20	00.01 (1) .94 .00
	Selective	1.78	0.68:-2.87	3.20	.00*	.24	10.38 (1) .00* .04
	Commission	-1.28	-1.33:-0.22	-2.39	.02*	.23	04.18 (1) .06 .02
	Omission	-0.56	-1.75:-0.64	-0.92	.49		01.18 (1) .32 .01
	Sustained	-0.28	-1.53:-1.00	-0.42	.73	.20	00.20 (1) .69 .00
Prognostic	Target Recall	0.59	-0.74:-1.91	0.87	.49	.20	01.30 (1) .30 .00
	Selective	1.02	-0.27:-2.32	1.56	.18	.22	03.26 (1) .10 .02
	Commission	-0.58	-2.10:-0.91	-0.78	.49	.23	01.55 (1) .27 .01
	Omission	-0.96	-1.99:-0.07	-1.86	.11		04.25 (1) .07 .02
	Sustained	-1.90	-3.06:-0.74	-3.24	.00*	.26	13.71 (1) .00* .06

Subacute refers to the time point within 100 days post stroke. This analysis is looking at the relationship between BIADL and Attentional indices. Chronic refers to the follow up time point approximately 9 months post stroke. This analysis is looking at the relationship between NEADL and attentional indices. Prognostic refers to the prediction of chronic NEADL using subacute attentional indices. In all cases age, education, instruction comprehension, lesion volume and instance of previous stroke were included in the comparison model using a forced entry approach.

Subacute BIADL

In the subacute phase of stroke recovery, lesion volume (R^2 change = 1%, X^2=5.04, p=.03), instance of previous stroke (R^2 change = 1%, X^2=6.09, p=.02) and age (R^2 change = 5%, X^2=24.39, p <.001) were significant predictors of BIADL. As can be seen in Table 2.5, target word recall and all attentional indices were also predictive of the subacute BIADL. Each measure uniquely explained between 1% and 3% of the variance above that accounted for by the covariates. However, for omission errors the model comparison did not reach significance after correction (p=.06).

A stricter analysis was run (N=287), including stroke type (ischemic or haemorrhagic) and lesion lateralisation (left, right or bilateral). Stroke type was a significant predictor of BIADL, with haemorrhagic patients experiencing higher functional dependency (R^2 change = 2%, X^2=10.78, p <.001) and a non-significant trend for lesion lateralisation (R^2 change = 1%, X^2=2.88, p=.09). The cognitive results were replicated for selective (β=0.24, p < .001, R^2change = 4%, X^2=12.43, p <.001) and sustained attention (β=0.17, p=.02, R^2change = 2%, X^2=6.17, p=.01). Omission errors were also a significant predictor of BIADL (β=0.14, p=.05) and as demonstrated in the full sample and this analysis also explained a significant amount of variance (R^2change = 2%, X^2=4.12, p=.04). However, this was no longer the case for commission errors, which no longer significantly predicted subacute BIADL.

To examine whether the imputation of the worst SAI score for those unable to complete the test affected the analysis those individuals were removed and the analysis run again. After exclusion, the results were comparable with the sustained attention index still significantly predicting BIADL (β=-1.47, p=.01, R^2change = 1%, X^2=6.96, p <.001).

Overall the results demonstrate that selective attention explains a small but significant amount of variation in post stroke functional status, even after controlling for multiple demographic factors and stroke characteristics. However, the relationship was less robust for individual instances of omission and commission errors.

Chronic NEADL

In the chronic stage of recovery, age was a significant predictor of NEADL (R^2change = 5%, X^2=16.01, p <.001) and lesion volume demonstrated a non-significant trend (R^2change = 2%, X^2= 3.05, p=.08). Of the cognitive variables, selective attention performance was predictive of complex activities of daily living (NEADL, see Table 2.5). However, no relationship was found between functional independence and any of the other attentional indices. In the stricter analysis (N=152) controlling for stroke type and lesion lateralisation, the findings were further replicated with chronic selective attention solely predicting functional status (β=1.70, p <.001, R^2change = 5%, X^2=8.83, p <.001). Neither stroke type or lesion side significantly predicted NEADL performance at this stage. Therefore, it is suggested that continued difficulties with selective attention may impact on chronic functional independence.

Prognostic NEADL

In the prognostic analysis, it was observed that subacute sustained attention performance was prognostic of chronic NEADL. However, this was not the case for any other measure. In the stricter analysis also controlling for stroke type and lesion lateralisation the result was replicated with subacute sustained attention solely predicting chronic functional independence (β=5.19, p=.02, R^2change = 5%, X^2=6.71, p=.01). To assess for the influence of imputing the worst sustained attention score for those unable to complete the test, the analysis was run again whilst excluding those patients with imputed scores. Subacute sustained attention remained prognostic of chronic NEADL (β=4.60, p=.01), explaining 3% of the variance (X^2=8.78, p <.001). This observation indicates that difficulties with sustaining selectivity in the subacute stage of recovery may be related to continued functional dependency in the chronic stages of recovery.

Control Task Analysis

Table 2.6: Relationship between control tasks and functional status.

		β	CI 2.5%:95%	T	P	R^2	Model Deviation X^2 P R^2 change
Subacute	ISR	-0.07	-0.72:0.59	-0.20	.84	.12	00.04 (1) .84 .02
	RFS	1.00	0.32:1.68	2.89	.01*	.13	08.52 (1) .00* .03
Chronic	ISR	00.6	-1.16:1.28	0.10	.92	.21	00.01 (1) .91 .01
	RFS	1.85	0.62:3.07	2.99	.01*	.25	12.01 (1) .00* .05
Prognostic	ISR	-0.02	-1.39:1.35	-.03	.98	.20	00.00 (1) .97 .00
	RFS	0.00	-0.21:0.21	0.00	.99	.25	00.00 (1) .99 .00

Subacute refers to the time point within a 100 days post stroke. This analysis is looking at the relationship between BIADL and the control tasks. Chronic refers to the follow up time point approximately 9 months post stroke. This analysis is looking at the relationship between NEADL and attentional indices. Prognostic refers to the analysis in which attentional indices at the subacute phase are being used to predict performance on the NEADL at the chronic phase. In all cases age, education, instruction comprehension, lesion volume and instance of previous stroke were included in the comparison model using a forced entry approach. ISR = Immediate Story Recall, RFS = Rule Finding & Switching.

In order to better understand the relationship between performance on the AAT and functional independence two additional tasks were examined. Performance on the AAT is dependent on both high level attention and short-term memory capacity (the ability to remember the three target words). To better understand the potential influence of short-term memory capacity, the Immediate Story Recall (ISR) task was chosen because it measures short-term memory capacity independent of attentional selectivity. In the ISR, the patients must pay attention indiscriminately and immediately recall information without the requirement for active memory maintenance. Therefore, if short-term memory capacity is driving the association between AAT performance and functional independence, the ISR might be expected to show a similar association.

As can be seen from Table 2.6, the ISR was not associated with functional independence at any time point. In order to test the null hypothesis a top down Bayesian analysis was run to assess whether there was moderate evidence in favour of removing ISR from the predictive model. In the subacute assessment, evidence was found in favour of removing ISR from the predictive model ($BF_01 = 4.15 \pm 0.0\%$, N = 386). This was also evident in the chronic assessment ($BF_01 = 3.43, \pm .01\%$, N=176) and for the prognostic analysis ($BF_01 = 2.89 \pm .01\%$, N=172). Therefore, suggesting that short-term memory capacity is not associated with functional independence as measured by the BIADL (in the subacute phase of stroke recovery) and the NEADL (in the chronic phase of recovery).

In consideration that high level attentional control is suggested to be domain general a secondary executive task was chosen, this time in the visual domain. The Rule Finding and Concept Switching (RFS) task was chosen because it required the active assembly of task rules and the use of this task set to bias action. If the association between performance on the AAT and functional independence is driven by high level attentional control, it might be expected that a similar relationship exists for the RFS task. As can be seen by Table 2.6, performance on the RFS task was a significant predictor of functional independence in the subacute and chronic stages of stroke recovery. However, subacute RF performance was not found to be prognostic of chronic NEADL scores. Therefore, corroborating the findings for the AAT task and suggesting a link between attentional control and reduced functional independence following stroke.

2.5 Discussion

The aim of the present study was to provide a targeted examination of the relationship between selective auditory attention and the level of functional independence following stroke. This aim was approached in two parts: first to establish the extent of the problem (i.e. prevalence and persistence) and second to examine whether attention was predictive of functional dependence (whilst accounting for factors such as age and lesion volume).

Prevalence and Persistence

Very high prevalence rates were observed with over 50% of patients experiencing impairment on the overall task performance. Although the prevalence was slightly less after breaking down the overall measure into different error types the prevalence rates were still notable (25%-42%). Furthermore, these deficits were still prevalent in the chronic stages of recovery (11%-31%), with many patients remaining impaired (3%-29%) and a small group declining (2%-10%). The continued high levels of attentional difficulties are noteworthy, especially when considering the follow-up sample was significantly less impaired than those who declined or were unable to take part in a follow-up assessment. The high levels of prevalence noted in this analysis corroborate past research (Barker-Collo & Feigin, 2006; Nys et al., 2007; Zinn et al., 2007) and act to highlight the importance of understanding the impact deficits may have on functional independence.

Attentional scores were explored in relation to lesion lateralisation. It was found that patients with left lesions performed worse than those with right lesions. Although, importance has been given to the right hemisphere in previous investigations, this difference may be influenced by the verbal nature of the task. Due to attentional control previously being associated with the frontal cortex, the patients were split by whether or not their lesion extended into the frontal cortex. In general scores were slightly poorer for patients with frontal lesions, but this difference did not reach significance.

Although this appears contradict some of the past literature, several points must be considered. The lesion overlap was only explored in relation to grey matter and thus did not take into account disconnections of frontal white matter. Secondly, the frontal lobe was taken as a whole and it could be that certain regions of the frontal cortex are more important for attentional control (e.g. DLFPC or AI). It is also of note that other more posterior lesions also play a role in selective attention (e.g. IPS, Gillebert et al., 2011). With these considerations in mind, perhaps only a small difference between these groups is to be expected. A more detailed analysis of lesion location with behavioural outcome is required and will be addressed in the following chapter by means of voxel-based symptom lesion mapping.

To further this point, no relationship was found in regards to lesion volume or frontal lobe overlap and attentional measures. It could be expected that larger lesions lead to more widespread impairment, however when investigating specific cognitive impairment perhaps only the extent of damage to a specific network is important. Additionally, overall lesion volume may have differential effects for a patient with one large lesion as compared to a patient with multiple distributed small lesions. Therefore, although lesion volume is a useful measure to control for, perhaps it is not unusual that no direct relationship was found with the attentional measures.

Relationship with Functional Independence

The relationship between selective attention and the level of functional independence was first examined in the subacute (∼24 days post-stroke) stage of recovery. At this time point, it was observed that all attentional indices were associated with functional independence (as measured by the Barthel Index). The model comparison demonstrated that all of the measures, excluding omission errors, explained a significant amount of unique variance (1%-3%) above that explained by the covariates (e.g. demographics and stroke characteristics). Excluding commission errors, these results were further replicated in

a stricter model also including stroke type and lesion lateralisation. The model comparison demonstrated that attentional indices continued to explain between 2% and 4% of variance. Therefore, these data demonstrate a robust association between functional independence, overall selectivity and the ability to sustain selectivity in the subacute stage of stroke recovery. On the other hand, the relationship between specific errors of omission or commission and functional independence appear less reliable.

These findings corroborate past research, which has demonstrated a link between global cognition (e.g. Oros et al., 2016; Stephens et al., 2005), executive function (Stewart et al., 2002; Mysiw et al., 1989; Stephens et al., 2005) and the ability to sustain attention (i.e. Robertson et al., 1997; Stephens et al., 2005) with reduced functional independence following stroke. Importantly, this examination extends these findings by providing evidence in a large sample, using more sensitive and less confounded measures and controlling for elements of stroke severity. Overall past research suggesting a link between selective and sustained auditory attention and NEADL at discharge is corroborated. Furthermore, the present analysis extends their finding by demonstrating a similar association between verbal (monitoring verbal information rather than tones) auditory selective and sustained attention with a measure of more basic functional independence (BIADL). Furthermore, it demonstrates this link whilst also controlling for stroke characteristics and demographic information.

To further address aim two, the link between attentional performance and functional independence was examined in the chronic stages of recovery (∼9-10 months post-stroke). At this time point functional independence was measured using the Nottingham Extended Activities of Daily Living scale. Although the BIADL was available, over 40% of the sample were at ceiling and therefore it was considered unsuitable for examination (also see Sarker et al., 2012). In the chronic stages of recovery, overall selective attention performance was exclusively a significant predictor of the level of functional independence

(as measured by the NEADL). The model comparison indicated that overall selective attention performance uniquely explained 4% of the variance above that explained by the covariates. This result was replicated in the stricter analysis also controlling for stroke type and lateralisation; with the selective attention performance continuing to explain 3% of the variance. It is suggested that a disruption in the ability to selectively bias action and perception continued to impact functional independence in the chronic stages of stroke recovery. This finding substantiates past research linking global cognitive impairment and executive dysfunction to poorer long term functional outcome (Patel et al., 2002; Bennett et al., 2002; Leśniak et al., 2008; van Zandvoort et al., 2005) and lower levels of community ambulation (Paker et al., 2010). It is worth noting that Parker et al (2010) found no difference in modified BIADL between patients with and without global cognitive impairment six months post stroke. Perhaps this discrepancy can be explained by the specific cognitive measurement and use of a more sensitive measure of functional status in the present study.

Finally, the prognostic value of attentional capacity in the subacute phase, for predicting functional independence in the chronic stage was investigated. It was found that the ability to sustain selectivity throughout the task was predictive of reported functional independence in the chronic stage; uniquely explaining 6% of the variance above that of the covariates. This result was further replicated in the stricter analysis including stroke type and lateralisation, with sustained attention continuing to explain 5% of the variance. These findings suggest that the ability to sustain selectivity may interfere with the recovery of functional independence. This result corroborates past research suggesting attention as an important contributor to functional recovery (van Zandvoort et al., 2005; Bennett et al., 2002; Robertson et al., 1997). However, the results are not in keeping with past work which has demonstrated that multiple elements of cognition are prognostic for future functional status (e.g. van Zandvoort et al., 2005). The origin of this discrepancy is unknown, but is perhaps due to the current study controlling for

stroke severity, the larger sample size or using a different measurement of functional independence. Indeed, another study which controlled for stroke characteristics (Nys et al., 2005), found that following correction, only visual spatial selective attention (hemispatial neglect) had prognostic value for chronic functional independence. The results from the present study extend this finding to temporal auditory selective attention.

Interestingly, in the chronic stage of recovery neither incidence of previous stroke or stroke type predicted NEADL. Lesion volume also had a diminished impact as compared to the subacute phase. The discrepancy in the impact of stroke characteristics between the time points could be due to the motor based focus of the BIADL or perhaps due to the extended time period allowing patients even with severe stroke time to regain a certain level of independence. Although the lesion lateralisation had been seen to influence cognitive performance (left lesions resulting in greater impairment), it did not predict functional independence at either time point. Therefore, these data did not lend support for the importance of the right hemisphere in regards to the impact of attention on functional independence (e.g. Robertson et al., 1997). These data are more cohesive with the results which displayed a trend towards left unilateral lesions producing greater deficits in auditory selective attention in the subacute phase of recovery (Hyndman et al., 2008). Additionally, the absence of predictive power of lesion lateralisation supports Hyndman et al (2008), who also found that side of lesion was not an important predictor of outcome at 12 months post stroke.

Control Task Analysis

One of the difficulties with studying selective attention is that target information also needs to be maintained to allow for the biasing of perception and action. Therefore, performance is also dependent on short term memory capacity. In this study we included the post task recall of target information within the regression models and tested the

addition of attentional indices against a model already including recall. This approach allowed better understanding of whether attentional indices explained variance above that of simply forgetting the target information. In addition, the relationship between a separate short-term memory task (ISR) and functional independence was also investigated. Interestingly, no association was found between the control short-term memory task and functional independence. However, there was a significant association between functional independence and a second task involving executive function. These findings suggest the link between functional status and selective attention may be influenced more primarily by domain general, executive processes, as opposed to short-term verbal memory capacity. This corroborates past research placing executive dysfunction as particularly influential on activities of daily living (e.g. Barker-Collo & Feigin, 2006; Mole & Demeyere, 2018).

The importance of being able to focus attention on only items of importance is necessary if behaviour is to be successfully goal directed. It follows that the break down in the capacity to use attention to shape the selection of perception and action, may lead to disorganisation and distraction. Whether the resulting disorganisation leads to impaired independence is reliant on multiple other factors, such as environmental and life style demands. For example, if the consequence of the disorganisation is that the individual finds shopping difficult factors such as shop proximity, layout familiarity, novelty of the shopping items and relationships with the shop staff may all influence whether or not the impairment truly impacts on their level of independence.

Furthermore, someone who regularly entertains guests or has a family to cook for may experience a greater impact on their independence because of increased lifestyle demands as compared to someone who has to shop solely for themselves. Attentional impairment is is more likely to impact some activities covered in the functional questionnaires more so than others. Thus, the observation that attentional indices explain

3-5% of the variance is noteworthy and may even be greater if a more targeted analysis of daily activities was approached. Strikingly, this amount of explained variance is comparable with other more widely accepted influences such as age (5% Jongbloed, 1986; Kwakkel, Wagenaar, Kollen, & Lankhorst, 1996) and lesion volume (1% Schiemanck, Kwakkel, Post, & Prevo, 2006). The understanding of how selective attention impacts independence certainly deserves further investigation and clinical consideration during assessment and treatment of stroke.

Limitations

Overall, these data support the assertion that difficulties with selective attention influences functional dependence following stroke. However, there are a few considerations that should be kept in mind when interpreting the results. First is the verbal nature of the task; paying attention to spoken language is particularly important in many facets of daily living and may be particularly well placed to have a negative impact on functional status. Therefore, caution should be taken when generalising these findings across modalities. The current analysis kept the sample as inclusive as possible, with the aim of being clinically relevant and thus, includes patients suffering from co-morbid cognitive deficits (e.g. mild aphasia). Although the AAT had been designed to minimise the effect of confounding cognitive difficulties, the influence cannot be ruled out completely. Another weakness of the current analysis is that the functional assessment was purely self-report. Using self-report measures can be problematic due to a general lack of awareness or due to differences in the subjective experience of functional impairment (e.g. it could be masked by family support or due to reduced environmental demands). Future research should aim to include direct functional measures (e.g. requirement for institutional support or occupational assessment). Finally, further work should include a functional measure which is appropriate for both the subacute and chronic phases in order to directly examine whether attentional deficits disrupt recovery.

In this study, stroke characteristics were included, which is a strength compared to the majority of previously published studies. However, it should be noted that only clinical CT scans were available. Clinical CT scans are acquired as part of normal clinical practice during the process of diagnosing stroke and thus are obtained for speed rather than resolution. Furthermore, an automated lesion delineation process was used, which may be less reliable than manual delineation (Gillebert et al., 2014). It would be desirable to use higher resolution scans and manual delineation to increase accuracy for the calculation of lesion size. Nonetheless, this approach supports inclusivity and opens up the opportunity to analyse large samples. Although, high quality MRI scanning and a manual delineation process would allow for a more reliable measure of lesion volume, it is still fairly difficult to obtain large sample sizes due to cost and the frequency of MR contraindications.

Conclusions

To conclude, these data indicate that impaired selective attention performance is prevalent following stroke and can persist into the chronic stage of recovery. Furthermore, it is suggested that poor selective attention performance is associated with lower levels of independence both in the subacute and chronic stages of recovery. Interestingly the ability to sustain selectivity in the subacute phase was prognostic for higher levels of chronic functional dependency. Most importantly, attentional indices were found to explain unique variance in functional independence over and above that explained by the covariates (demographics and stroke characteristics).

Further research is needed to illuminate the specific daily activities affected by impaired auditory selective attention, and to fully examine whether this impact is direct or indirect via a disruption in rehabilitation. However, these findings highlight the importance of cognitive assessment and the integration of cognitive rehabilitation in optimising functional independence following stroke. It is hoped that better understanding of exacerbating factors of functional dependence, such as cognitive impairment, will help towards achieving the best possible outcome for stroke survivors.

In this chapter it was observed that auditory selective attention has a negative impact on functional outcome following stroke. It was also observed that left hemispheric or bilateral lesions resulted in poorer performance on the auditory attention task. Lesion overlap with the frontal cortex was not seen to influence performance. To better understand the relationship between lesion location and impaired selective auditory attention, Chapter 3 will utilise a voxel-based lesion symptom mapping approach in a sub-set of the current sample.

Chapter 3

Lesion Neuroanatomy of Selective Auditory Attention

3.1 Abstract

Introduction: The ability to selectively pay attention and respond to verbal information is fundamentally important to daily living. However, there have been very few lesion studies have examined selective attention in the auditory temporal domain.

Method: The following analysis aims to address this imbalance by providing a large scale (N=334 stroke patients) voxelwise lesion symptom mapping analysis of damage associated with selective auditory attention. The auditory attention task (Birmingham Cognitive Screen) was utilised to examine the capacity of remembering target words and using this information to make selective tapping responses. Overall accuracy, omissions, commissions and the ability to sustain selectivity throughout the task was examined in the full sample and again in a reduced sample of 205 patients with perfect recall of the target words.

Results: In the full sample impaired selective attention was associated with damage to the lateral and medial frontal cortex (e.g. IFG, AI), the middle temporal gyrus, SLF III, arcuate, fasciculus and fronto-insula tracts. There were no associations with isolated commission errors. Omission errors was associated to damage to the SMA. The ability to sustain selectivity was associated with damage to the lateral and medial frontal regions (e.g MFG, IFG, AI/FO), superior and inferior parietal regions (angular gyrus, precuneus), superior and middle temporal gyri and occipital fusiform gyrus.

In the sub-group of patients with perfect word recall, selective attention was again associated was lateral and medial frontal regions (MFG, IFG, AI and PreCG) and white matter damage to the unicate fasciculus and fronto-insula tracts. In this sample there were no lesion sites associated with omission errors or the sustained attention index. However, commission errors were associated with damage to the lateral and medial frontal lobe (e.g. MFG, IFG), subcortical regions (putamen, external capsule), the medial/posterior insula, the precuneus and white matter (e.g. frontal inferior longitudinal, arcuate fasciculus).

Conclusions: Impaired auditory selective attention is associated with damage to a range of regions previously implicated in the initiation and implementation of task set.

3.2 Introduction

Selective attention is the term given to the ability to preferentially pay attention and respond to information relevant to the current task goal. It can be conceived as mental programming that biases perception and action based on relevance (Bundesen, 1990; Bosman & Womelsdorf, 2009; Duncan, 2013; Driver, 2001; Ptak, Schnider, & Fellrath, 2017; Gallivan & Culham, 2015). In essence, selective attention allows us to filter a chaotic influx of stimuli, to shape the environment to our own internal directive and importantly to bias behaviour in a goal directed manner (Duncan, 2010, 2013; Driver, 2001). Therefore, selective attention fundamentally underpins behavioural autonomy.

Given the importance of selective attention in daily living, it is unsurprising that the search for its neural origin has received much attention. One important tool used in this endeavour has been patient studies which aim to link lesion location to behavioural impairment. These types of studies can be combined with neuroimaging work to extend understanding beyond what regions are involved, into the realms of what regions might be essential (Bates et al., 2003; Rorden & Karnath, 2004). Although the neural correlates of visual spatial attention have been widely studied in this manner, far less focus has been given to auditory selective attention. This is particularly the case when selective attention must be distributed in time, rather than space. Considering some neuroimaging studies have suggested the main mechanism of selective attention to be domain general in nature (e.g. Fedorenko et al., 2013; Shomstein & Yantis, 2004, 2006), this is an important gap in the literature to address. Therefore, the following study aims to extend our current understanding by providing a large scale voxel-based symptom lesion study specifically examining damage associated with selective auditory attention to temporally distributed events.

Underlying the behavioural phenomenon of selective attention is the ability of individual neurons to dynamically modulate their firing profile, and rate, in preference for task relevant information (The Adaptive Coding Model Duncan, 2001; Duncan & Miller, 2002; Duncan, 2013; Everling et al., 2002). Frontal neurons become adaptively selective for stimuli features that are important for the current task. For example they may preferentially fire for a stimulus of a particular colour (Bichot et al., 1996), shape (Janssen et al., 2008) or category (Freedman et al., 2001). Moreover, some neurons respond selectively for specific combinations of features, such as the link between different cue types (e.g. Fuster et al., 2000) or stimulus-response mapping (e.g. Bichot et al., 1996). These firing patterns are distinct between tasks and highly adaptive, with neurons observed to change their selectivity between task contexts (Asaad et al., 2000; Sigala et al., 2008). These findings suggest that this neural programming is not only flexible, but adjusts rapidly depending on the current task specification.

These patterns of activity can be conceptualised as task representations that act in a top-down manner to modulate lower level perceptual processing (Miller & Cohen, 2001). For example, if the lateral PFC activity of a monkey is disrupted during the presentation of a relevant cue, the corresponding activity in the visual cortical neurons is diminished (Chafee & Goldman-Rakic, 2000). As is suggested by single cell recordings, human research also demonstrates both high level adaptive task coding (Li et al., 2007; Haynes et al., 2007; Woolgar et al., 2015, 2016) and the modulation of sensory processing by higher order regions (Bauer, Kennett, & Driver, 2012; Driver, 2001; Woolgar et al., 2011; Buschman, Denovellis, Diogo, Bullock, & Miller, 2012; Salazar, Dotson, Bressler, & Gray, 2012). For example, goal directed top-down modulation has been found to enhance cortical responses to task-relevant sounds and reduce responses to task-irrelevant sounds (Bidet-Caulet et al., 2007; Chait, de Cheveigne, Poeppel, & Simon, 2010; Giard, Fort, Mouchetant-Rostaling, & Pernier, 2000). In summary, it has been observed that task dependent firing patterns bias perception by modulating sensory activity.

Selective attention is not a modular function, but a mechanistic process resulting from interactions within a network of highly adaptable brain regions. This neuronal system has been termed the multiple demands network (Duncan, 2010, 2013) and includes regions such as the

middle and inferior frontal gyri (MFG, IFG), precentral gyrus (PreCG), supplementary motor area (SMA), anterior insula/ frontal operculum (AI/FO), the intraparietal sulcus (IPS) and anterior cingulate cortex (ACC, Duncan, 2010, 2013; Fedorenko et al., 2013). However, it is also worth noting that this network is also suggested to include regions within the cerebellum (Fedorenko et al., 2013) and recently suggested to involve the basal ganglia (Camilleri et al., 2018). The primary focus of this network is initiation and maintenance of task representations (Dosenbach et al., 2006; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Crittenden, Mitchell, & Duncan, 2016). Broadly speaking this network is responsible for domain general configuration of attentional episodes, which act to bias perception and action in favour of current demands (Duncan, 2013; Scolari, Seidl-Rathkopf, & Kastner, 2015; Szczepanski, Konen, & Kastner, 2010; Rishel, Huang, & Freedman, 2013; Swaminathan & Freedman, 2012).

Damage to locations within this network have previously been associated with impaired executive functioning (e.g. Gläscher et al., 2012; Robinson et al., 2014) and lower fluid intelligence (Woolgar et al., 2010; Barbey, Koenigs, & Grafman, 2012). Moreover, similar damage has been associated with impaired visual spatial attention (e.g. Corbetta & Shulman, 2002, 2011; Gitelman, 2003; Chechlacz, Rotshtein, & Humphreys, 2012; Verdon, Schwartz, Lovblad, Hauert, & Vuilleumier, 2010). For example hemispatial neglect has been associated with damage to the temporal parietal junction/ inferior parietal lobe (Carter et al., 2010; Critchley, 1953; Mort et al., 2003; Karnath, Rennig, Johannsen, & Rorden, 2011; Rengachary et al., 2011), the superior/middle temporal cortex and insula (Chechlacz et al., 2010; Corbetta et al., 2005; Karnath et al., 2011), the intraparietal sulcus (Gillebert et al., 2011; Vandenberghe et al., 2012) and the ventrolateral prefrontal cortex (Husain & Kennard, 1996; Committeri et al., 2007; Rengachary et al., 2011).

These frontal, temporal and parietal brain regions are linked forming the perisylvian neuronal network (Karnath & Rorden, 2012; Karnath, 2009). These deficits are usually most prominently demonstrated after damage to the right hemisphere, with the left perisylvian network suggested as more important for language than spatial orienting (Suchan & Karnath, 2011). This network is connected by a range of white matter tracts including the superior

longitudinal fasciculus II/III (SLF), the superior and inferior occipitofrontal fasciculus (SOF/ IOF), the arcuate fasciculus (AF) and the extreme capsule (EmC) (Karnath, 2009). In addition to grey matter damage, disconnection of these white matter that connects these regions is also been associated with impairment (He et al., 2007; Thiebaut de Schotten, Urbanski, Duffau, Volle, Lvy, et al., 2005; Urbanski et al., 2008, 2011; Shinoura et al., 2009; Karnath, 2009).

Damage within the perisylvian network can result in non-spatial attentional deficits both independently and in conjunction with hemispatial neglect (Husain & Rorden, 2003; Husain & Nachev, 2007). For example a recent review article examined the abnormal temporal dynamics of visual attentional processing in stroke patients, concluding that ventral areas of the frontal-parietal network were important in the prolongment of attentional deployment thresholds (Low, Laycock, & Crewther, 2017). Some examples are impaired sustained attention subsequent to right frontal lesions (right frontal lesions Robertson et al., 1997; Hjaltason et al., 1996; Maguire & Ogden, 2002) and extended attentional dwell times on attentional blink paradigms after parietal lesions (Husain & Kennard, 1997; Shapiro et al., 2002; Hillstrom et al., 2004). Moreover, patients can also have difficulties with visual spatial working memory demonstrated by difficulty in keeping track of previously searched locations (Wojciulik et al., 2001; Husain et al., 2001; Driver & Husain, 2002). These multifaceted symptoms have lead researchers to suggest that some of the impairment displayed by neglect patients could be due to a more generalised selective attention deficits (Correani & Humphreys, 2011).

Relatively few studies have addressed the ability to sustain selectivity to auditory information through time. Attentional allocation has been examined in terms of processing speed and compared between visual and auditory domains. Interestingly, only parietal patients were significantly impaired in the visual domain, whereas both frontal (n=12) and parietal (n=13) patients were impaired in the auditory domain (Peers et al., 2005). Another study examined the effects of different types of frontal lesion (n=55) and posterior lesions (n=18) on auditory sustained attention as measured by the elevator counting task (MacPherson et al., 2010). This task requires patients to track and keep a running count of a series of tones (Robertson, Nimmo-Smith, Ward, & Ridgeway, 1994). Overall, they found that medial and lateral left hemispheric

damage resulted in impaired performance. Moreover, the pattern of results suggested that more medial damage resulted in competition from task irrelevant schemas, whereas lateral damage resulted in reduced ability to keep track of tones. These result were similar to another examination of a sustained counting task which also implicated superior medial and right lateral damage in disrupting performance. In particular, they suggested that superior medial damage disrupted energising processes, whereas right lateral damage disrupted monitoring processes (N=43, Shallice et al., 2008).

The effect of specific lesions on the EEG component Nd (negative difference) relating to selective auditory attention has also been examined. The Nd compoenent is said to facilitate top-down selection by modulating the amplitude of ERP components (N1, N100) involved in sensory processing (Hansen & Hillyard, 1980). Previous work has demonstrated that lesions to the lateral prefrontal cortex disrupt attention-related negativity. Interestingly, patients with left lateralised lesions displayed reduced amplitude to tones presented in either ear, whereas right unilateral lesions only demonstrated attenuation to tones presented in the left ear (Knight et al., 1980; Knight, Hillyard, Woods, & Neville, 1981). Another more recent study found similar effects, with poorer performance and a global decrease in facilitatory component of frontal negativity in a sample of 9 patients with DLPFC lesions (Bidet-Caulet et al., 2015). Interestingly, the Nd component has also been observed as reduced in both hemispheres for patients with lesions in the temporal/parietal junction, whereas it was only reduced in the lesioned hemisphere for patients with inferior parietal lesions (Woods, Knight, & Scabini, 1993). Overall these results suggest that lesions to the DLPFC and perhaps also the TPJ result in impaired goal directed modulation of perception.

The past literature strongly suggests that damage to the lateral prefrontal cortex will result in impaired selective auditory attention. The majority of current research studying selective auditory attention has been focused on specific patient populations (e.g. with frontal lesions). The current study hoped to offer a large scale VLSM analysis to better understand the network of regions associated with impaired selective auditory attention following stroke.

3.3 Method

Sample

This was a secondary analysis using data from the BCoS study, a large 5 year clinical study run across 10 hospitals in the west-midlands. All participants provided written informed consent according to the UK National Research Ethics Committee approved procedures. The inclusion criteria for this study was (i) confirmed stroke (ii) BCoS completed within 100 days (iii) complete data on the Auditory Attention Task, (iv) access to a high quality clinical CT scan and high quality lesion delineation and (v) visible lesion. The sample retained after filtering on this criteria consisted of 334 stroke patients. The relationship with the sample in the previous chapter is as follows: 68 of the patients included in the functional chapter were not included in the current sample due to having no visible lesion, the remaining 8 were removed for technical reasons. The reason for removing patients with no visible lesion is due to the acute nature of the CT scans. When scans are performed early following a stroke, the lesions may not yet be visible on the image.

Procedure

After giving informed consent, patients underwent a full cognitive assessment using the Birmingham Cognitive Screen (BCoS; Humphreys et al., 2012). The task battery took approximately one hour to complete. The Auditory Attention Task is the 11th of 22 tasks in the test battery. It is administered approximately half an hour into testing. The assessment took place in a quiet room situated in the hospital and patients were given breaks as required.

The Auditory Attention Task

The Auditory Attention Task (AAT) measures selective attention to verbal information (Appendix A.4.1, p.333). The task description was given in Chapter 2 (p.45-46). Several attentional indices can be derived from the AAT: Overall task performance, number of omission errors, number of commission errors, sustained attention index (block1-block3) and target word recall. Please see Table 3.1 for an overview.

Table 3.1: Auditory Attention Task Measures

Indices	Range	Optimal Score	Measures
Selective Attention	0-54	High	Task model implementation.
Omission Errors	0-27	Low	Initiate an appropriate response.
Commission Errors	0-27	Low	Withhold an inappropriate response.
Sustained Attention	-8-18	Low	Sustain selectivity.
Target Word Recall	0-03	High	Maintenance of target information.

Image Acquisition

The Computerised Tomography (CT) images were obtained as part of the routine clinical assessment during hospital admission following stroke. The average time between the stroke and the CT acquisition was 3 days (Range = 0-67 days, SD=7.11, N=269). Image acquisition was done using a Siemens Sensation 16, GE Medical System Light Speed or Light Speed plus cover. Similar CT acquisition protocols (adult head routine axial slicing) were used across sites: all images covered the whole brain with slices aligned along the AC-PC, an in-plane resolution of 0.5*0.5 mm and a slice thickness that varied between 4 and 5mm. CT images with substantial noise, visible shunts or a slice thickness larger than 5 mm were excluded from the analysis.

Image Pre-processing

Pre-processing and lesion delineation was performed using a fully automated toolbox (Gillebert et al., 2014). The toolbox was written in MATLAB (The MathWorks, Natick, MA, USA), utilising SPM8 (Statistical Parametric Mapping, Welcome Department of Cognitive Neurology, London, UK) and the clinical toolbox for SPM (Rorden, Bonilha, Fridriksson, Bender, & Karnath, 2012). The images had irrelevant signals removed from the head and neck using threshold based clustering (0.1% maximum intensity). The resulting image was spatially aligned to the CT template (Rorden et al., 2012) using the coregistration tool in SPM8. The Hounsfield intensity values were then transformed using an invertible formula in order to emphasize the contrast between brain matter and cerebrospinal fluid. The CT image was then warped into MNI space using a age relevant CT template (Rorden et al., 2012). This action was achieved in two steps. First a 12-parameter affine transformation was performed and the image was stripped of CSF and skull (using a ventricle and brain mask). Secondly a spatial deformation was calculated from the skull stripped image to a skull stripped version of the template and subsequently applied to the unmasked CT image. Finally, the image was resliced at 1 mm isotropic resolution and smoothed using a Gaussian filter.

Lesion Delineation

Following the pre-processing, the lesion was automatically delineated for each patient. In this process, each voxel was compared against 116 control CT scans using a Crawford-Howell single-case control comparison (Crawford, Garthwaite, & Howell, 2009). This gave a t-score, which reflected to what extent the intensity of the voxel deviated from the normal range indicated by the control scans. The resulting t-score map was thresholded (Bonferroni corrected $p < 0.05$) to obtain binary lesion maps which contained values of -1 (ischemic stroke), 0 (no lesion) and 1 (haemorrhage). This method of delineation has been proven reliable (please see Gillebert et al., 2014).

Analysis Methodology

Voxel Based Lesion Symptom Mapping

An in-house MATLAB script was used to prepare the data and run the VLSM analysis. The lesion maps were binarised (1 = lesion, 0 = no lesion). The images were used to calculate lesion volume, which was combined with the participants behavioural data to create the design input for the subsequent VLSM analysis. The behavioural data included the dependent variable and a set of covariates (lesion volume, age, gender, handedness, orientation in time/space). The VLSM parameters were set to only include voxels where at least 10 patients had a lesion (Sperber & Karnath, 2016). Next a parametric VLSM analysis was run using the vlsm2 function from the toolbox by Bates et al. (2003). The VLSM analysis uses ANCOVA to compare the behavioural performance of patients with and without a lesion for each voxel. The resulting statistical maps were thresholded to correct for multiple comparisons using the false discovery rate $\alpha < .05$ (Benajmini & Hochberg, 1995) and clusters over 100 voxels were reported.

Extent of White Matter Damage

An in house script was used to calculate the extent of damage to specific white matter tracts. The script was written in MATLAB and called upon SPM8. For each patient the binary lesion map was overlaid with each of the available white matter tracts from the Cantani atlas (Thiebaut De Schotten et al., 2011). The number of overlapping voxels was used to calculate the percentage of overlap with the total tract size. Forced entry linear regression was then utilised to investigate whether the extent of damage to each tract could predict the attentional indices. The same covariates were used as in the VLSM analysis and the results were corrected for multiple comparisons (FDR, $p < .05$).

3.4 Results

Sample Characteristics

The sample included 334 stroke patients (153 male, 29 left handed), with an average age of 72 (SD=13) and an average of 11 years (SD=3) spent in formal education. Of the sample 266 patients had an ischemic stroke, 46 had a intracerebral haemorrhage, 4 had a subarachnoid haemorrhage, 5 had a transient ischemic attack, 4 were classified as other (e.g. subdural hematoma) and 9 were unknown. Included in the sample were 231 (70%) patients for whom it was their first instance of stroke and 103 (30%) patients who had previously had a stroke. The average Barthel Index of Activities of Daily Living of the sample was 12.81 (SD=5.67) and average Hospital Anxiety and Depression scores were 6.59 (SD=4.87) and 6.33 (SD=4.42) retrospectively. As can be seen in Figure 3.1, a good proportion of the brain had at least 10 patients with damage. The average performance and percentage of patients impaired for each of the attentional indices and covariates is presented in Table 3.2. For an overview of average task performance on the complete BCoS assessment please see Appendix B.1 (p.338).

Table 3.2: Sample Characteristics

		Mean(SD)	Range	Impairment(%)
AAT	Selective Attention	41.00(14.84)	5:54	184(55%)
	Omission Errors	04.20(04.91)	0:27	142(43%)
	Commission Errors	03.58(05.04)	0:27	100(30%)
	Sustained Attention	02.34(03.59)	-7:09	125(38%)
	Target Word Recall	02.44(00.84)	0:03	80(34%)
Covariates	Orientation	05.44(00.98)	0:06	110(33%)
	Lesion Volume cm^3	77.31(104.25)	4:709	-
	Age	71.88(13.00)	27:93	-
	Gender	F/M	181/153	-
	Handedness	L/R	29/305	-

For BCoS manual cut-off scores see Appendix A.5, pp. 336 (Humphreys et al., 2012).

Main Analysis (N=334)

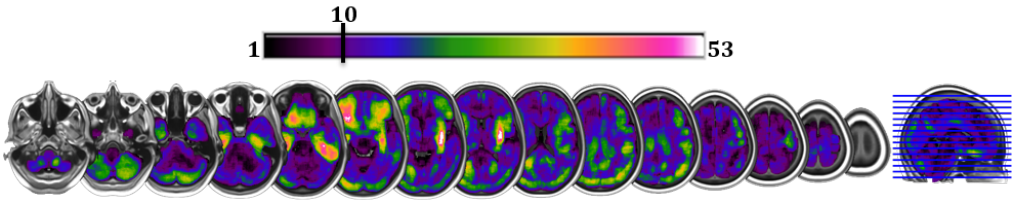


Figure 3.1: Lesion Distribution: Please note that only voxels for which a minimum of 10 patients had damage were included in the analysis (N=334).

VLSM Results

Parametric voxel-based Lesion Symptom Mapping (VLSM; Bates et al., 2003) was run on each of the AAT indices. Voxels in which patients with a lesion had significantly worse performance than those who did not (p <.05, FDR corrected) were identified and clusters of 100 significant voxels or above were reported. Covariates included age, gender, handedness and orientation in time and space.

Selective Attention performance was associated with lesions to the left inferior frontal gyrus pars opercularis (IFGpo), precentral (PreCG) gyrus, the insula and the posterior middle temporal gyrus (MTG). Higher instances of **Omission Errors** were associated with damage to the left superior frontal gyrus (the supplementary motor area). Increased instances of **Commission Errors** were not associated to any lesion site.

Sustained Attention was associated with lesions within a large network of brain regions. In the left hemisphere these regions included the IFGpo, middle frontal gyrus (MFG), frontal operculum, PreCG, post central gyrus, the insula, MTG and the superior temporal gyrus (STG). In the right hemisphere the regions included the MTG, angular gyrus (AG), occipital fusiform gyrus (OFG), the precuneus, cuneal cortex and the parietal operculum cortex. **Target Word Recall** was associated with the left parietal operculum, frontal pole, middle temporal gyrus, planum polare and superior/inferior occipital fusiform gyrus and the right cingulate gyrus and precuneus (Table 3.3/Figure 3.2).

Table 3.3: Grey Matter Lesions Associated with Selective Attention Performance

	Cluster	Region	Side	Max *T*	Damaged *N*	MNI *XYZ*	Cluster *Extent*
Selective	1	Inferior frontal gyrus pars opercularis	L	5.18	56	-42 5 11	1064
		Precentral gyrus					
	2	Posterior middle temporal gyrus	L	5.93	24	-54 -33 -04	434
	3	Precentral gyrus	L	5.53	35	-33 -14 32	535
	4	Insula cortex	L	4.39	46	-26 10 12	329
Omissions	1	Superior frontal gyrus	L	5.67	19	-15 -8 60	248
	2	Superior frontal gyrus	L	5.37	19	-12 -8 66	223
Sustained Attention	1	Inferior frontal gyrus pars opercularis	L	5.29	145	-33 -14 32	15537
		Anterior supramarginal gyrus					
		Middle frontal gyrus					
		Frontal operculum					
		Postcentral gyrus					
		Precentral gyrus					
		Insula					
	2	Middle temporal gyrus	L	4.35	23	-54 -16 -11	719
		Superior temporal gyrus					
	3	Middle temporal gyrus	R	3.87	22	52 -45 2	430
		Angular gyrus					
	4	Occipital fusiform gyrus	R	4.39	24	21 -81 3	256
	5	Precuneus	R	4.30	41	19 -68 21	193
		Cuneal cortex					
	6	Middle temporal gyrus	L	4.51	18	-50 -34 -8	146
	7	Parietal operculum cortex	L	4.01	27	-54 -26 18	119
Target Recall	1	Parietal operculum cortex	L	5.6	69	41 15 26	4596
	2	Superior occipital fusiform gyrus	L	6.21	71	-29 -78 -05	1630
	3	Frontal pole	L	3.90	15	-35 47 19	232
	4	Cingulate gyrus	B	4.95	42	01 -51 27	225
		Precuneus					
	5	Planum polare	L	4.04	24	-44 -08 -10	139
		Insula					
	6	Inferior occipital fusiform gyrus	L	4.43	31	-29 -75 -18	138
	7	Middle frontal gyrus	L	5.12	37	-38 16 38	136

Results thresholded using 0.05 FDR correction for multiple comparisons. Clusters of voxels above that threshold were identified using FSL cluster tool and reported if they were a minimum of 100 voxels in size. Brain regions were identified using the Oxford Harvard atlas. Max T: the maximum t-value in that given cluster. Damaged N: number of patients who have damage within the identified cluster. The MNI coordinates reported refer to the voxel with the highest t-score. Cluster extent: number of voxels that comprise the cluster.

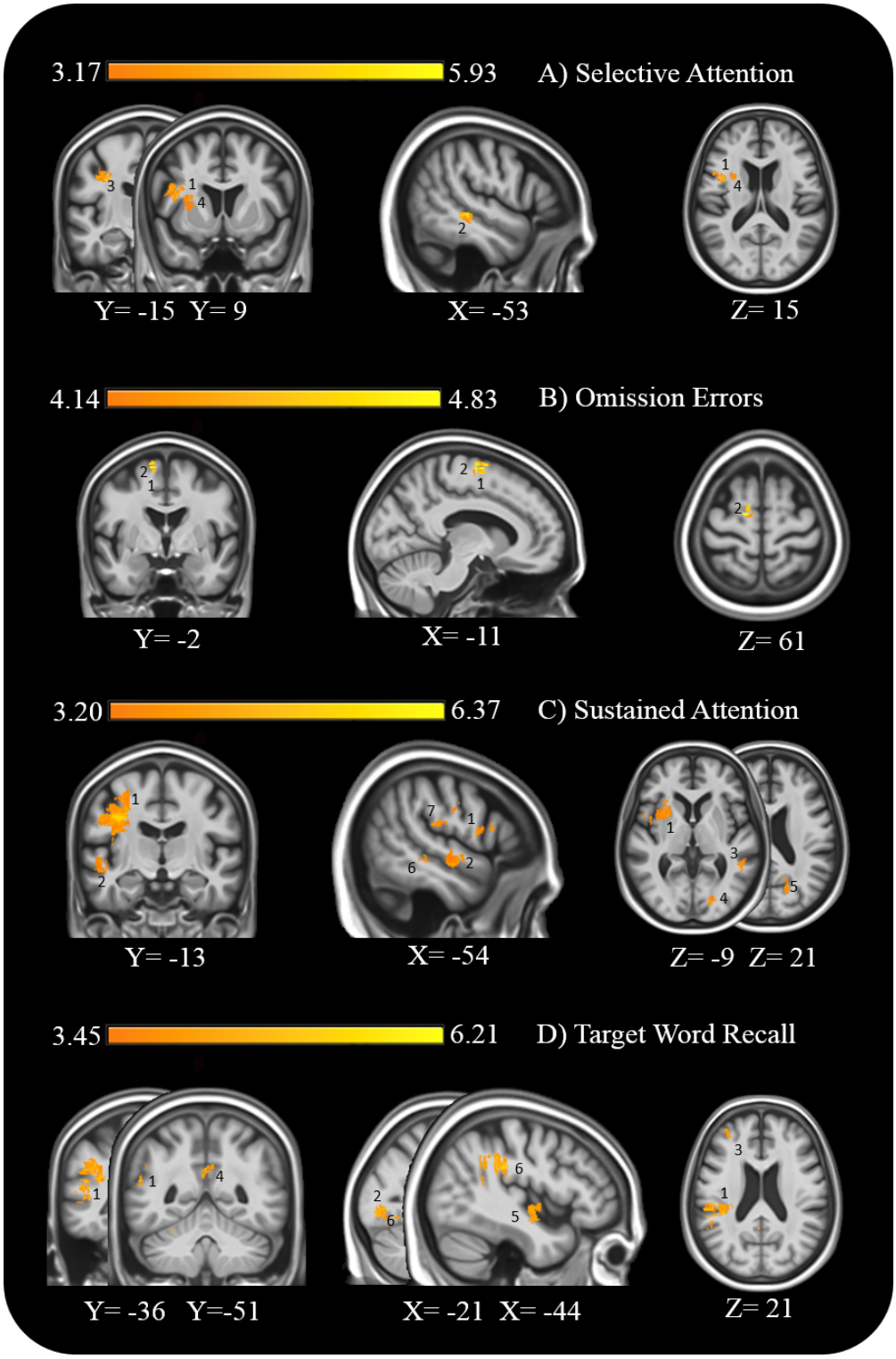


Figure 3.2: Significant clusters associated with AAT performance A) Clusters associated with selective attention. B) Clusters associated with increased number of omission errors. C) Clusters associated with sustained attention D) Clusters associated with Target Word Recall. All results reported are corrected for multiple comparisons (FDR correction: 0.05) and cluster thresholded (100 voxels). The cluster numbers refer to the cluster numbers in Table 3.3.

Extent of White Matter Damage Results

In order to examine the relationship between white matter damage and impaired task performance an extent of damage analysis was run. In this analysis the percentage of damage to each white matter tract was calculated for each patient. Linear regression was run, whilst controlling for age, gender, handedness and orientation in time and space. Tracts for which the extent of damage significantly predicted task performance(p <.05, FDR corrected) were reported.

Table 3.4: White Matter Damage Associated with Selective Attention Performance

	Tract	Side	N[1] *Lesion*	Max %[2] *Lesioned*	β	T	P[3]	CI 2.5−95
Selective Attention	Superior longitudinal fasciculus 3	L	175	73%	-2.70	-3.23	0.02	-4.34:-1.05
	Arcuate long segment	L	158	88%	-3.58	-4.19	0.00	-5.26:-1.90
	Frontal insula tract 1	L	82	99%	-2.36	-2.91	0.04	-3.95:-0.77
	Frontal insula tract 3	L	98	98%	-2.95	-4.00	0.00	-4.40:-1.50
	Frontal insula tract 4	L	93	99%	-2.58	-3.45	0.02	-4.04:-1.11
	Frontal aslant tract	L	138	54%	-2.35	-2.81	0.04	-4.00:-0.70
	Arcuate fasciculus	L	116	95%	-2.30	-2.97	0.03	-3.83:-0.77
	Posterior segment	L	85	97%	-2.37	-2.97	0.03	-3.93:-0.80
Omissions	Corpus callosum	L	245	35%	1.19	3.58	0.00	0.54: 1.84
Target Recall	Superior longitudinal fasciculus 3	L	175	73%	-0.17	-3.47	0.01	-0.27:-0.07
	Arcuate Anterior Segment	L	110	76%	-0.16	-3.24	0.01	-0.25:-0.06
	Arcuate Posterior Segment	L	114	87%	-0.20	-3.58	0.00	-0.30:-0.09
	Arcuate Long Segment	L	158	88%	-0.21	-4.13	0.00	-0.31:-0.11
	Arcuate fasciculus	L	116	95%	-0.20	-4.33	0.00	-0.28:-0.11
	Posterior Segment	L	85	97%	-0.14	-3.02	0.03	-0.23:-0.05

White matter tract defined by Catani White Matter Atlases 181-217-191 (NAT). Age, gender, orientation in time and space, handedness and lesion volume included as covariates are of no interest in all regression models. 1) N lesioned refers to how many patients have damage within that tract. 2) Max lesioned is the largest percentage of tract damaged. Note that the minimum is always 0%. 3) FDR corrected P values reported.

As can be seen in Table 3.4, worse **Selective Attention** performance was predicted by the extent of damage to intralobar tracts connecting frontal regions and interlobar tracts connecting frontal and posterior regions. Intralobar frontal tracts included: the frontal aslant tract (connecting the IFG with the SMA/pre-SMA; Kronfeld-Duenias, Amir, Ezrati-Vinacour, Civier, & Ben-Shachar, 2014) and frontal insula tracts 1,2 and 4 (which connect the anterior insula with the IFG pars orbitalis, IFG pas opercularis and the pre-central gyrus retrospectively; Catani et al., 2012). Interlobar association tracts connecting frontal and posterior regions include, the superior longitudinal fasciculus 3 (connecting the IFGop and PreCG to the supramarginal gyrus (SmG) Wang et al., 2016) and the long segment of the arcuate fasciculus (which connects IFG, MFG and PreCG to the STG and MTG; Catani, Jones, & ffytche, 2005; Catania & Thiebaut de Schotten, 2008; Rilling et al., 2008). Furthermore, damage to the posterior segment also predicted impairment (posterior interlobar tract connecting MTG to the SmG and AG; Catani et al., 2005).

The number of **Omission Errors** was predicted by the extend of damage to the corpus callosum (commissural tract, Catania & Thiebaut de Schotten, 2008). There were no tracts associated with **Commission Errors** or with **Sustained Attention**.

Target Word Recall was predicted by the extent of damage to the interlobar association tracts connecting frontal and posterior regions. These included: the left anterior arcuate fasciculus (connecting the IFG, MFG and PreCG to the SmG), the arcuate long segment (connecting the IFG and MFG to the STG and MTG, Catania & Thiebaut de Schotten, 2008; Catani et al., 2005) and the superior longitudinal fasciculus 3 (connecting the IFGpo and PreCG to the SmG, Wang et al., 2016). Additionally, damage to two interlobar association tracts connecting posterior regions were predictive of damage. These included the arcuate posterior segment (connecting the AG to the STG and MTG) and the posterior segment (connecting MTG to the SmG and AG, Catani et al., 2005).

Relationship with Target Word Recall

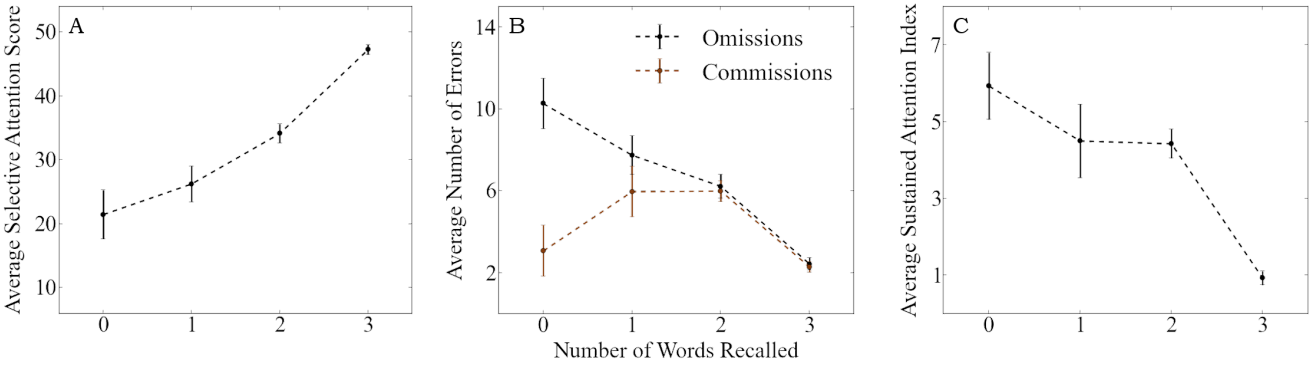


Figure 3.3: Relationship between target word recall and attentional indices (EB=SEM).

An important element that contributes to AAT task performance is the ability to remember and utilise the target words throughout the duration of the task. Therefore, impaired performance has multiple origins: attentional difficulties and short-term memory capacity. Poor recall of the target words affect the attentional measures differentially. As can be seen in Figure 3.3 A, there is a significant positive correlation between selective attention (overall task performance) and target word recall (r= -.56, p=.00). This is echoed in the error scores, with an increase in errors as more words are forgotten for both omission errors (r= -.48, p=.00) and commission errors (r= -.23, p=.00). However, as can be seen from Figure 3.3 B, the relationship between target word recall and commission errors is more complex.

In the instance that no target words are recalled there are less commission errors than if only one or two words were forgotten. The pattern of increased omission errors and decreased commission errors for these patients may indicate that they have stopped responding. An explanation for the increase in commission errors made for patients only able to recall one or two words could be that they consistently identify a non-target word incorrectly remembering it as a target word.

As can be seen in Figure 3.3 C, sustained attention demonstrated a significant negative correlation with target word recall (r= -.46, p=.00). This relationship highlights how forgetting the target information is related to a greater decrement in task performance. Although poor sustained attention may lead to both poorer task performance and poor maintenance of the target information, there may be a dissociation between sustained attention in terms of external attentional monitoring and internal working memory refreshing and thus this relationship should also be taken into consideration. These confounding factors highlight the importance of controlling for target word recall in this analysis of selective attention and therefore the analysis was run again in a sub-sample of participants who achieved perfect target word recall.

Target Word Recall and Language Performance

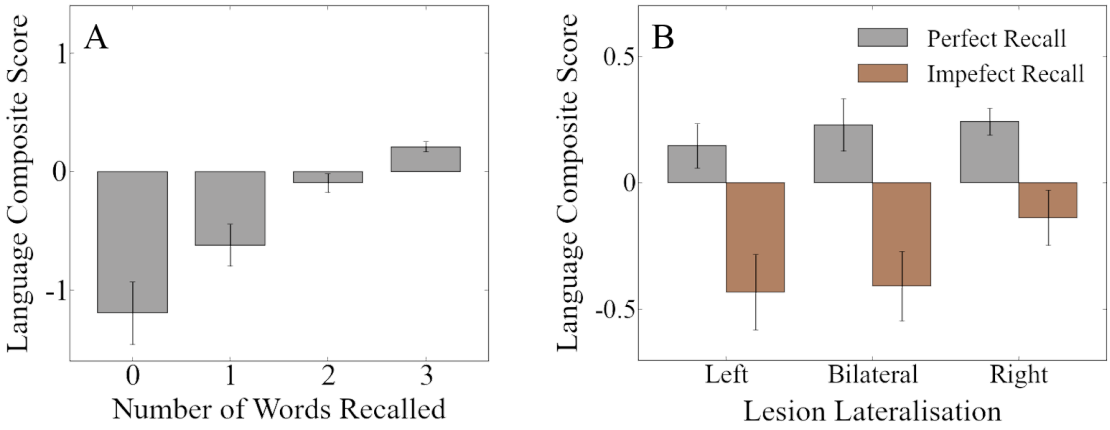


Figure 3.4: A) Relationship between the number of target word recalled and a language composite score. B) Comparison of patients with and without perfect word recall, split by lesion lateralisation.

Another important consideration in this analysis is the use of verbal information. Although patients with severe aphasia were filtered out during the task practice, patients with subtle deficits will have been retained. Subtle language deficits may interfere with sub-vocal rehearsal of the target words and therefore the relationship between target

word recall and language performance was investigated. A composite score of language performance was computed for picture naming, sentence construction, sentence reading and overall instruction comprehension to give an overview of language ability and to use in a comparison between patients with and without perfect target word recall.

As can be seen in Figure 3.4 A, there is a significant relationship between target word recall and average language ability (r=.41, p=.000). If patients with perfect target word recall (M=.65, SD =1.98) are compared to those without (M= -1.04, SD= 2.98) they perform significantly better on tests of language [$F(1,331)$=38.42, p=.000, η^2=.10]. This suggests that subtle language difficulties may contribute to poor target word recall. Because of the dominance of the left hemisphere for language, patients were further split by lesion lateralisation and the relationship was re-examined. On average patients with left or bilateral lesions perform worse on both tests of language [$F(1,288)$=7.644, p=.006, η^2=.03] and also on target word recall [$F(1,289)$=11.13, p=.001, η^2=.04]. As can be seen from Figure 3.4 B, patients with left or bilateral lesions, who also have imperfect target word recall perform the worst on language tests. This analysis gives further support to the importance of running the analysis again in a sub-section of patients with perfect target word recall.

Therefore a control analysis was run aiming to further isolate the lesion anatomy associated with impaired selective attention, above that of impaired target word recall and subtle language difficulties.

Control Analysis in Patients with Perfect Target Word Recall

Sub-Group Sample Characteristics

The sub-group was comprised of 205 patients, 59 (29%) of which had a previous instance of stroke. Of the sample, 161 patients had an ischemic stroke, 29 had an intracerebral haemorrhage, 6 had a TIA, 4 had a stroke labelled as other and 5 were unknown. The sub-sample had an average BIADL of 13.89 (SD=5.35) and an average HADS anxiety and depression score of 6.12 (SD=4.81) and 6.18 (4.40) retrospectively. See Table 3.5 for an overview of average performance and impairment on attentional indices and covariates. As can be seen in Figure 3.5, there was still a large proportion of the brain in which at least 10 patients had damage. Date from stroke to CT was available for 173 of the patients. The average time from stroke onset to CT scan was 2.97 days (R=0-67, SD=7.24).

Table 3.5: Sub-Group Characteristics

		Mean(SD)	Range	Impairment(%)
AAT	Selective Attention	50.01(5.75)	28:54	56(27%)
	Omission Errors	02.07(3.54)	0:23	52(25%)
	Commission Errors	01.93(4.24)	0:26	28(14%)
	Sustained Attention	00.39(1.61)	-5:09	39(19%)
Covariates	Orientation	05.73(00.66)	3:6	46(22%)
	Lesion Volume cm^3	78.14(112.32)	4:709	-
	Age	70.17(13.04)	30:92	-
	Gender	F/M	114/91	-
	Handedness	L/R	13/192	-

Impairment indicated using 5th percentile cut-off scores. Cut-off scores given in Appendix A.5, p.336.

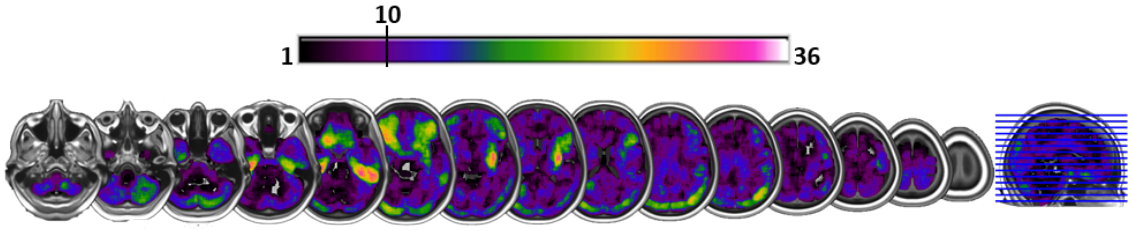


Figure 3.5: Lesion Distribution in the Sub-Group of Patients.

VLSM Results

As can be seen in Table 3.6, **Selective Attention** was associated with lesions to the right IFGpo, MFG, PreCG and the left insula cortex. When the full score was broken down into error types it was observed that increased instances of **Commission Errors** were associated with lesions to the right IFGpo and MFG, and left IFG pars triangularis (IFGpt), putamen, external capsule, precuneus, medial and posterior insula. However, the number of **Omission Errors** and overall **Sustained Attention** performance were not associated with any lesion sites.

Table 3.6: Grey Matter Lesions Associated with Selective Attention in the Sub-Group

	Cluster	Region	Side	Max T	Damaged N	MNI X Y Z	Cluster Extent
Selective Attention	1	Insula cortex	L	4.80	35	-38 -15 -4	1519
	2	Inferior frontal gyrus pars opercularis Middle frontal gyrus Precentral gyrus	R	4.46	37	46 20 29	1338
	3	Insula	L	5.36	29	-32 9 10	671
	4	Inferior frontal gyrus pars opercularis	R	4.70	32	52 15 9	349
	5	Middle frontal gyrus	R	4.30	20	36 11 35	316
	6	Insula	L	4.91	32	-24 17 -4	185
Commission Errors	1	Inferior frontal gyrus pars opercularis Middle frontal gyrus	R	5.29	55	39 13 29	4207
	2	Inferior frontal gyrus pars triangularis Putamen External Capsule	L	7.63	67	-25 16 -3	3512
	3	Precuneus	L	4.63	28	-12 -63 21	651
	4	Medial Insula External Capsule	L	4.53	31	-36 1 -3	382
	5	Posterior Insula	L	3.83	24	-37 -21 3	237

Results thresholded using 0.05 FDR correction for multiple comparisons. Clusters of voxels above that threshold were identified using FSL cluster tool and reported if they were a minimum of 100 voxels in size. Brain regions were identified using the Oxford Harvard atlas. Max T: the maximum t-value in that given cluster. Damaged N: number of patients who have damage within the identified cluster. The MNI coordinates reported refer to the voxel with the highest t-score. Cluster extent: number of voxels that comprise the cluster.

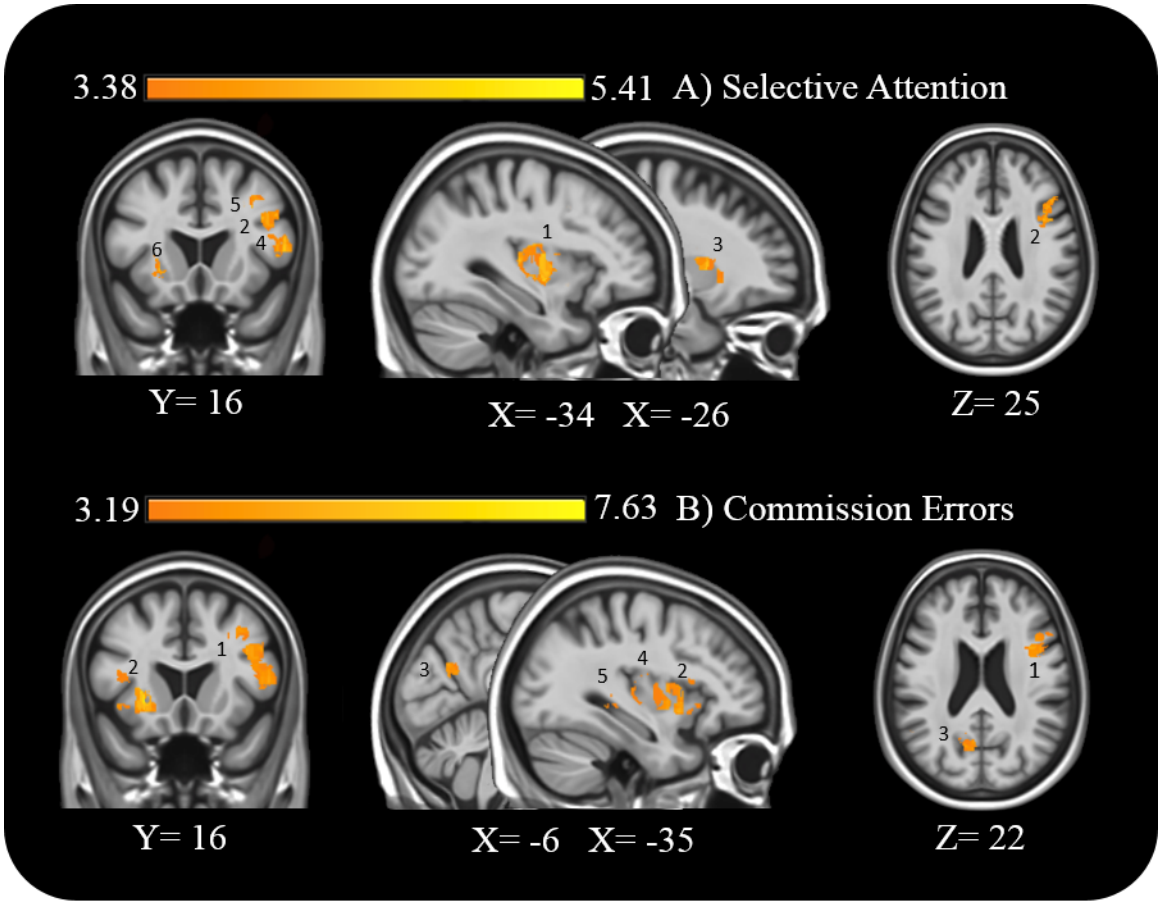


Figure 3.6: Significant clusters associated with AAT performance A) Clusters associated with selective attention. B) Clusters associated with increased number of commission errors. All results reported are corrected for multiple comparisons (FDR correction: p=.05) and cluster thresholded (100 voxels). The cluster numbers refer to the cluster numbers in Table 3.6.

Extent of White Matter Damage Results

The extent of damage to white matter tracts analysis found that poorer **Selective Attention** performance was predicted by the extent of damage to left uncinate fasciculus (connecting anterior temporal gyrus to parts of the orbital frontal cortex, Catania & Thiebaut de Schotten, 2008), frontal insula tracts 1 and 2 (connecting the anterior insula to IFG pars orbitalis and the IFG pars triangularis retrospectively, Catani et al., 2012). It was observed that increased **Commission Errors** were predicted by the extent of damage to the left arcuate fasciculus (connects IFG, MFG and PreCG to the superior and middle temporal gyri, Catania & Thiebaut de Schotten, 2008; Catani et al., 2005), posterior segment (MTG to the supramarginal and angular gyri, Catania & Thiebaut de Schotten, 2008), frontal insula tract 1 (connecting the anterior insula to the IFG pars orbitalis Catani et al., 2012) and the right frontal inferior longitudinal (projects from the precentral gyrus to the MFG and IFG, Catani et al., 2012). There were no tracts associated with **Omission Errors** or **Sustained Attention**.

Table 3.7: White Matter Damage Associated with SA in the Sub-Group

	Tract	Side	N[1] *Lesion*	Max %[2] *Lesioned*	β	T	P[3]	CI 2.5–95
Selective	Uncinate fasciculus	L	95	82%	-5.19	-3.34	0.03	-8.25:-2.13
	Frontal insula tract 1	L	51	91%	-3.41	-3.92	0.00	-5.12:-1.69
	Frontal insula tract 2	L	51	89%	-2.85	-3.09	0.04	-4.67:-1.03
Commissions	Frontal inferior longitudinal	R	74	85%	0.90	3.09	0.03	-0.73: 1.11
	Arcuate fasciculus	L	55	34%	2.19	3.14	0.03	0.81: 3.56
	Posterior segment	L	44	60%	1.76	4.12	0.00	0.92: 2.61
	Frontal insula tract 1	L	51	91%	1.17	3.32	0.03	0.47: 1.86

White matter tract defined by Catani White Matter Atlases 181-217-191 (NAT). Age, gender, orientation in time and space, handedness and lesion volume included as covariates are of no interest in all regression models. 1) N lesioned with refers to how many patients have damage within that tract. 2) Max lesioned is the largest percentage of tract damaged. Note that the minimum is always 0%. 3) FDR corrected P values reported.

Reduced Power in the Sub-Group Analysis

In the full sample **Selective Attention** was associated with lesions to the MTG, however no relationship was found in the sub-group analysis. In the full sample there were 24 patients with lesions that overlapped with the cluster in the MTG. In the sub-group there were only 11 patients with overlap in this area. Of those patients, 7 had lesions with less than 25% (106/434 voxels) overlap with the previously identified cluster and 4 of them had under 5% overlap (21/434 voxels). Therefore, it is likely that many of the voxels in the cluster were not examined due to having less than 10 patients with lesion overlap.

In the full sample **Omission Errors** were associated with lesions to the SMA, however no relationship was found in the sub-group analysis. However, only 8 participants remained who had damage in the area of the cluster found in the full analysis. Therefore, this region would not have been included in the sub-group analysis. Furthermore, in the full analysis the extent of damage to the CC, was predictive of the number of omission errors. However, this relationship no longer remained in the sub-group analysis. In the sub-group there were 147 patients that had lesions which extended into the CC (compared to 245 in the full sample). However, on average damage was minimal (M=3.56, SD=5.11 cm^3). On average that is just under 4% of the total volume of the tract ($\sim$3554/91084 voxels). On further examination only 13 patients had tract overlap above 10% of the overall tract volume (27 in full sample). Therefore, there may not have been a sufficient number of patients with substantial overlap to find the relationship. In addition, of the 142 patients who were impaired on the omission error score, 86 (61%) were also impaired on target word recall and therefore only 52 of the patients remained in the sub-group analysis.

Another discrepancy in the analyses was the large scale association found between **Sustained Attention** and damage in the full sample, as compared to no association in the sub-group. There were 127 patients with overlap with the clusters associated with sustained attention within the full sample (178 in the full sample). The largest cluster

associated with SA was located in the left frontal cortex, The amount of patient overlap reduced from 145 patients in the full analysis to 71 in the sub-analysis. Of the 71 patients with overlap (15 who were impaired), there was on average only 7.54 % overlap with the cluster (∼1172/15537 voxels). Sixty-five of these patients had under 25% overlap. Therefore, there may be the possibility of some voxels within the cluster losing power, although the majority of voxels are likely to retain power.

The second largest cluster located in the left superior and MTG had 23 patients with overlap in the full sample, however this number reduced to only 8 (none of which were impaired) patients in the sub-group. Therefore, it is likely that this closer location was excluded from the analysis. The third cluster was located in the right MTG and AG, in the full sample there were 22 patients with damage, this reduced to 11 in the sub-group (6 of whom were impaired). Of the 11, there was an average of 36% overlap (153/430 voxels). Two patients had ∼1% overlap, with only 2 or 5 voxels overlapping. Therefore, it is likely that voxels within this cluster lacked sufficient overlap to be included.

In the fourth cluster in the right occipital fusiform cortex, there was a reduced overlap from 24 to 7 patients (1 who was impaired). The fifth cluster situated in the right precuneus reduced from 41 patients to only 14 with overlap (3 of whom were impaired). Within the 14 patients, there was an average of 34% overlap with the cluster(∼64/193 voxels). Nine of these patients had less than 50% overlap and there were 4 patients with less than 10% overlap (1-15 voxels overlapping) making it likely that voxels contained in the cluster may lack sufficient overlap to be included in the analysis. The sixth cluster located in the MTG, reduced from 18 to only 4 patients (1 impaired). The seventh cluster in the parietal operculum reduced from 27 to 5 patients with overlap (0 impaired).

3.5 Discussion

The current study aimed to examine lesion locations associated with impaired selective auditory attention to temporally distributed events. This aim was addressed firstly in a large sample of 334 stroke patients and subsequently in a sub-group of 205 patients with perfect target word recall. The results are supportive of the role of the medial and lateral PFC in selective auditory attention (MacPherson et al., 2010; Shallice et al., 2008; Bidet-Caulet et al., 2015). They also share similarities with studies examining visual temporal attention (IFG, IPL: Hillstrom et al., 2004; Molenberghs et al., 2009; Shapiro et al., 2002) and visual spatial neglect (MFG, AI, MTG, IPL: Chechlacz et al., 2012; Verdon et al., 2010; Husain & Kennard, 1996; Husain & Rorden, 2003). Overall the pattern of results suggest that poor selective attention can result from damage to a core system responsible for the initiation and implementation of task set (Dosenbach et al., 2006; Duncan, 2013; Fedorenko et al., 2013; Shomstein & Yantis, 2004). The results will now be discussed for each of the attentional indices investigated.

Selective Attention

The first index under investigation was general selective attention performance (sum of correctly initiated and withheld responses). This measure was taken to represent the patients general ability to bias perception and action. In the main analysis it was found that left lateralised lesions to the IFGpo, PreCG, AI and the pMTG were associated with selective attention impairment. The IFGpo, PreCG and AI have previously been identified as part of the MD network (Fedorenko et al., 2013; Duncan, 2010). Moreover, the IFG has been associated with impaired visual temporal selective attention (Molenberghs et al., 2009; Aron et al., 2003) and the AI with attentional switching on the trail making task (Varjai et al., 2017). The MTG is a auditory association area involved in speech comprehension (Dronkers, Wilkins, Van Valin, Redfern, & Jaeger, 2004; Vorobyev et al.,

2004), therefore damage to this region may be related to poor performance for reasons other than selective attention deficits. Although it is worth noting that it has previously been identified in studies examining hemispatial neglect (e.g. Chechlacz et al., 2010; Corbetta et al., 2005; Karnath et al., 2011).

These results were partially replicated in the control analysis with poor performance still associated with damage to the left insula. Interestingly, in this sub-group with perfect recall, poor performance was now associated with right lateralised lesions to the IFGpo, preCG and MFG. These results are supportive of past lesions studies which have observed the medial and lateral PFC as important in auditory selective attention (MacPherson et al., 2010; Knight et al., 1980; Bidet-Caulet et al., 2015; Shallice et al., 2008). It is also complementary of work that suggests damage to the DLPFC results in a top-down executive deficit in visual spatial neglect (Rinne et al., 2013). The change in lateralisation was of interest because of the previous suggestions that the right lateral PFC is important for sustaining attention (Robertson et al., 1997). The pattern of results is suggestive that left hemispheric lesions results in language deficits and impaired phonological rehearsal, whereas right frontal lesions are associated with temporal selective attention (in line with the proposed functional lateralisation for the perisylvian network Suchan & Karnath, 2011). In this sub-group analysis selective attention performance was no longer associated with the MTG, however it is unclear whether this absence was due to reduced power.

In the full sample, it was found that damage to the left SLF III, AF, the frontal insula short U tracts (1,3 & 4), the frontal aslant tract and the posterior segment were predictive of selective attention performance. These tracts connect frontal, parietal and temporal regions (e.g. Wang et al., 2016; Catani et al., 2005; Catania & Thiebaut de Schotten, 2008; Rilling et al., 2008). In particular, the SLF III and AF join regions in the perisylvian network (Karnath & Rorden, 2012; Karnath, 2009) and disconnection of

these tracts have previously been associated with hemispatial neglect (He et al., 2007; Thiebaut de Schotten, Urbanski, Duffau, Volle, Lévy, et al., 2005). The SLF III in particular has previously been implicated in persistent signs of visual spatial neglect (Verdon et al., 2010; Bartolomeo, Thiebaut de Schotten, & Chica, 2012). In the left hemisphere damage to the AF and SLF has previously been associated with deficits in both sentence processing and verbal working memory (Bernal & Ardila, 2009; Galantucci et al., 2011). Considering that these tracts were also associated with target word recall, it could be suggested that these associations are primarily driven by patients with poor verbal working memory.

In the control analysis damage to SLF III or AF was no longer observed as predictive of poor performance. However damage to the left fronto-insula tracts (1 & 2) and the uncinate fasciculus were associated with poorer task performance. The left uncinate fasciculus connects the anterior temporal gyrus to parts of the orbital frontal cortex (Catania & Thiebaut de Schotten, 2008) and is suggested to have a key role in associative learning, error monitoring and retrieval of correct pairing (Von Der Heide, Skipper, Klobusicky, & Olson, 2013). Therefore, damage to this tract may be important due to the requirement of pairing verbal information to the response. The continued importance of the frontal insula connections is interesting considering the proposed role of the insula in task set switching (Varjai et al., 2017).

Omission Errors

In order to explore deficits in greater detail the overall selective attention score was split into the two error types: omissions and commissions. In the full sample, omission errors were associated with lesions within the superior frontal gyrus, more specifically the supplementary motor area (SMA). The SMA has been found to selectively code for sequences of motor actions (Bednark, Campbell, & Cunnington, 2015; Mushiake, Inase, & Tanji,

1990; Woolgar et al., 2015) and past research has highlighted the importance of the SMA in goal directed action and learning new stimulus-response associations (for a review see Nachev, Kennard, & Husain, 2008). Therefore, lesions within the SMA may be associated with omission errors because of the role it plays in initiating and maintaining relevant responses to target information. Although the association between the extent of CC damage and the number of omission errors was unexpected, there is some previous work linking the integrity of the CC to attention deficit hyperactivity disorder (Hutchinson, Mathias, & Banich, 2008) and mental processing speed/rapid problem solving in multiple sclerosis (Rao, Leo, Haughton, St. Aubin-Faubert, & Bernardin, 1989). There were no lesion sites associated with omission scores in the control analysis, however it is worth noting that the previous cluster location had less than 10 patients with overlap and thus, was excluded from the analysis.

Commission Errors

There was no link between lesion site and commission errors in the full patient sample. Unlike the other error types commission errors do not have a linear relationship with target word recall. Patients who forget all the target words had high numbers of omission errors and low instances of commission errors, perhaps indicating that they stopped responding. Therefore, fewer commission errors could reflect more optimal response inhibition or a failure to respond due to poor target recall. This dual aetiology may underlie why commission errors did not relate to any specific damage in the full sample. In the sub-group analysis lesion sites associated with higher commission errors included multiple attentional control regions (right IFG pars opercularis, right MFG, left IFG pars triangularis and the left insula cortex) in addition to the precuneus and putamen.

Once again these results highlight the importance of lateral and medial frontal regions in selective temporal auditory attention (MacPherson et al., 2010; Shallice et

al., 2008; Bidet-Caulet et al., 2015; Robertson et al., 1997). Moreover, it further complements past visual selective attention research which had suggested that damage to the IFG increases instances of commission errors (Aron et al., 2003; Molenberghs et al., 2009). Interestingly, lesions to both the right and left IFG were linked to increased commission errors. This contradicts past research that had suggested the link between the IFG and response inhibition to be right lateralised (Aron & Poldrack, 2006; Aron et al., 2007) and supports research demonstrating a bilateral association (e.g. Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). The left IFG has been linked to rehearsal and monitoring of verbal information (Menon, Adleman, White, Glover, & Reiss, 2001; Wagner, Par-Blagoev, Clark, & Poldrack, 2001) and research demonstrating bilateral activation normally also involves verbal tasks (e.g. counting silently and verbal report, Hampshire et al., 2010). Therefore, the bilateral associations may be influenced by the verbal nature of the task.

Recently, a proposal has been made to extend the MD network to include the basal ganglia and thalamus (Camilleri et al., 2018). The basal ganglia is strongly connected with the PFC and has formerly been implicated in attentional control processes (Duffau, 2012a; Krause et al., 2012; Cools et al., 2006; Thoma et al., 2008). It is suggested that the putamen works with the frontal cortex during the attentional gating of information and action (focally releasing inhibition of task-relevant representations and inhibiting task-irrelevant representations, Van Schouwenburg et al., 2015; Bednark et al., 2015; Mink, 1996; Yin, 2014; Frank et al., 2001; OReilly & Frank, 2006). Damage to the putamen has previously been associated with impaired visual spatial attention (Karnath, Fruhmann Berger, Kker, & Rorden, 2004; Ringman, Saver, Woolson, Clarke, & Adams, 2004) as well as impaired set shifting (Eslinger & Grattan, 1993), increased susceptibility to interference (Godefroy et al., 1994; Mendez et al., 1989) and impaired inhibition (Rieger et al., 2003). Therefore, the observed association in the current sample could be suggestive of an impaired attentional gating mechanism.

In addition to these task active MD regions, there is another set of commonly identified regions (medial temporal and frontal lobe, posterior cingulate and precuneus) which commonly show a pattern of deactivation during cognitively demanding tasks (Fedorenko et al., 2013). These regions are thought to be important for internally directed cognition, such as episodic retrieval, the division of personal plans and mind wandering (Spreng, 2012; Spreng, Mar, & Kim, 2009; Cavanna & Trimble, 2006; Mason et al., 2007). It is suggested that the control network mediates internal and external cognition during goal directed behaviour, combining current information with predictions and past knowledge (Cavanna & Trimble, 2006; Spreng, 2012). Previous work has found that activity in the precuneus reflects previously learnt stimulus-response mapping (Hartstra, Kühn, Verguts, & Brass, 2011; Woolgar et al., 2015, 2016). It could be suggested that damage to the precuneus in the current sample could impaired the ability to retrieve the previously learnt mapping between target words to the selective tapping response. Or perhaps difficulty in modulating the balance between internal and external attention in the form of mind wandering.

In the sub-group there were also four white matter tracts that were predictive of the quantity of commission errors. Two of these tracts are short connections between frontal attentional control regions: left fronto-insula tract 1 (connecting the anterior insula to the IFG pars orbitalis) and the right frontal inferior longitudinal (projects from the precentral gyrus to the MFG and IFG, Catani et al., 2012). The other two tracts included the arcuate fasciculus (which connects frontal regions with the MTG, Wernickes territory and supramarginal gyrus, Catani et al., 2005) and the posterior segment (connects the supramarginal gyrus to the Wernickes territory, Catani et al., 2005). These results complement the VLSM analysis, with connectivity between regions involved in task set representation, action control and monitoring of verbal information predicative of commission errors.

Sustained Attention

Finally, task performance was examined in terms of the ability to sustain selective responding throughout the task (overall performance on block one minus block three). In the full sample, worse sustained attention performance was associated with a selection of left lateralised attentional control regions (IFG, IFJ, MFG, PreCG, FO, and AI), the right precuneus and the MTG. These results replicate the observations that lateral/medial frontal and inferior parietal lesions are associated with poor auditory selective attention (Woods et al., 1993; Bidet-Caulet et al., 2015; Knight et al., 1980; MacPherson et al., 2010; Shallice et al., 2008). Additionally, these observations share many similarities with damage associated with impaired visual spatial attention (e.g. LPFC, AI, M/LTG and IPL, Chechlacz et al., 2012; Corbetta et al., 2005; Varjai et al., 2017). Overall it is suggested that poor sustained attention performance on this task may result from the ineffective initiation or implementation of task set (Dosenbach et al., 2006).

Interestingly, there were no regions of damage associated with the sustained attention index in the sub-group. Although, lack of power may have contributed for 6/7 of the clusters it may also reflect the strong relationship between target word recall and sustained attention performance. In the full sample, the pattern of results was similar to target word recall. The origin of this overlap is ambiguous and most likely bidirectional. Forgetting target words can lead to errors in selection, but impaired attention could also lead to poor working memory maintenance. Moreover, it has been suggested that both external processing and internal refreshing share the same attentional resource (e.g. Barrouillet & Camos, 2015; Barrouillet et al., 2004). Therefore, it could be suggested that an impairment in top-down attention could lead to both impaired processing and working memory refreshing, or alternatively an impairment in the ability to shift attention between the two processes.

Limitations

Before concluding, the strengths and weaknesses of the approach utilised in this study should be carefully considered. The use of CT scans (given as standard clinical practice), allowed the collection of a large and representative sample with homogenous lesion aetiology (de Haan & Karnath, 2018). However, there are caveats to this approach: the scans were of relatively poor resolution (4-5mm slices) and were taken soon after the stroke. Therefore, there is a possibility that some small or hard to identify lesions may have been missed. In line with this, an automated lesion delineation process was employed, allowing feasible lesion delineation of a large sample (without hours of manual delineation) and preventing inter-rater differences. Although this methodology has been proven reliable, it is not yet as effective as manual delineation (Gillebert et al., 2014).

One of the main strengths of lesion analysis is that it allows us to start understanding which regions are necessary for cognitive functions. The VLSM approach employed avoids some of the caveats of previous lesion mapping techniques (Bates et al., 2003), such as the requirement to categorise based on lesion type or behavioural cut-off scores. Moreover, the use of whole brain voxel by voxel analysis avoids erroneously excluding potentially important areas (unless there isnt sufficient lesion coverage). The use of this approach also affords the examination of continuous data and the use of covariates and thus, the effects of lesion volume and other influential factors (e.g. age, handedness etc.) can be controls for. Despite these strengths, there are some substantial weaknesses. The first pertains to the use of mass univariate analysis, which can give rise to the potential of erroneously attributing cognitive functions to regions that are commonly damaged alongside regions of importance (Price, Hope, & Seghier, 2017; Mah, Husain, Rees, & Nachev, 2014). The second is diaschisis, in which impairment occurs not directly due to the lesion, but indirectly because of disrupted perfusion to distal regions of importance (Carrera & Tononi, 2014).

Conclusions

In summary, the pattern of results demonstrated in the current analysis is consistent with the idea that auditory selective attention can be disrupted from damage to regions responsible for initiating and implementing task sets during the pursuit of goal directed behaviour (Fedorenko et al., 2013; Duncan, 2013; Dosenbach et al., 2006). The current observations support the previously reported association between damage to the lateral/medial frontal lobe (MacPherson et al., 2010; Shallice et al., 2008; Bidet-Caulet et al., 2015; Peers et al., 2005) and inferior parietal lobe (Woods et al., 1993; Peers et al., 2005) and impaired auditory selective attention. Interestingly, after controlling for poor target recall the results were dominated by frontal cortical (MFG, IFG, AI, PreCG) and subcortical regions (putamen), whereas, in the full sample there were more associations within the temporal (S/MTG), occipital (S/IOFG) and parietal (PO, AG) lobes. The only parietal region to be found in both the full and control analysis was the precuneus, which is of particular note due to its involvement in the default mode network. The similarities demonstrated between the current analysis and past investigations of visual spatial attention were suggestive that these deficits can arise from a domain general impairment in the top-down control of attentional resources.

The current analysis observed that impaired selective attention can result from a wide range of damage throughout a distributed network of brain regions. Both shared and distinctive neural correlates were observed between the different attentional scores. Chapter 4 aims to examine the contribution of impaired task model implementation in greater detail and compare this contribution between different regions of damage.

Chapter 4

Executive Dysfunction: Beyond the Frontal Lobes

4.1 Abstract

Introduction: Executive dysfunction has long been considered a disorder of the frontal lobes. However, evidence is beginning to suggest that posterior damage may also result in impairment. The present investigation aimed to address 3 questions. Can posterior lesions influence executive dysfunction? Can posterior patients experience executive dysfunction similarly to frontal patients? Are there lesion-behaviour associations?

Method: The Oxford Cognitive Screen + was used to assess elements of executive function (rule finding, task switching and attentional selectivity) in a sample of 150 controls and 40 stroke patients (7 frontal-subcortical(SC), 17 frontal/posterior, 18 posterior lesions). A BiFactor analysis was used to extract both a general executive factor and the more specific sub factors (temporal attention/working memory, spatial attention and updating/shifting). Case control comparisons were made individually and average factor scores compared across groups.

Results: The individual analysis demonstrated that all patient groups were impaired, although impairment was more prevalent in the frontal-SC and posterior groups. Both the frontal-SC and posterior patients significantly differed compared to controls on the executive factor. Whereas, only the frontal-SC group differed to controls on the temporal attention and working memory factor. The group analysis demonstrated that both frontal-SC and posterior groups performed significantly worse than controls on all factors, but did not significantly differ from each other. It was observed that lesions to the basal ganglia and cerebellum were most consistently associated with impairment on the executive, shifting/updating and spatial attention factor scores.

Conclusions: The results suggest that posterior patients experience general executive dysfunction similarly to frontal-SC patients. The examination of lesion location corroborates the idea that subcortical nuclei and their connectivity with the cerebral cortex are important in contextual control of behaviour.

4.2 Introduction

Executive function is the term given to describe higher order processes which bias behaviour in favour of the current task or goal. Executive control processes have long been considered as frontal lobe functions (e.g. Stuss, 2011; Stuss & Knight, 2002). However, this conceptualisation is beginning to be replaced by a network oriented view of executive control (e.g. Duncan & Miller, 2002; Miller & Cohen, 2001; Duncan, 2013). This view postulates that the control of goal directed behaviour is the result of competitive and integrative process spread across a network of both frontal and posterior brain regions (e.g. Kennedy & Raz, 2009; Kramer et al., 2007; Sasson, Doniger, Pasternak, Tarrasch, & Assaf, 2013). Throughout this network there are neurons that modulate their firing patterns to adaptively represent information important to the current task (Woolgar et al., 2015) and network activity has been implicated in the domain general control of goal directed behaviour (Duncan, 2013). Given this evolving understanding, two questions are under debate: Can executive dysfunction result from damage purely located in posterior brain regions and if so, is this executive dysfunction dissociable from that experienced following frontal lobe damage?

In the last few decades there has been much debate over the "unity" and "diversity" of executive function (e.g. Friedman & Miyake, 2017; Miyake et al., 2000). It has been suggested that executive function can be dissected into specific processes, such as response inhibition, resisting distraction/interference from irrelevant information (internal and external), switching between task sets, working memory, dual tasking, planning, monitoring and verbal and design fluency (Friedman & Miyake, 2017). However, it is also observed that there is a central element to executive function driven by goal attainment (Duncan et al., 1996) and related to fluid intelligence (Duncan, 2010; Duncan et al., 1996).

It appears likely, that both of these views are correct. The unity of executive functioning can be considered as the requirement to construct an effective task representation. If the task set was insufficiently represented or incorrectly constructed it would result in a multitude of different "executive" errors due to weak or incorrect top-down control (Friedman & Miyake, 2017). However, the same errors could occur in a more specific presentation if a problem occurred subsequent to task representation. A practical example to demonstrate this concept could be an observed deficit in attentional visual selective attention. This type of deficit could result from incorrectly or unsuccessfully representing task set, the inability to maintain the task until goal completion or simply due to insufficient integration of top-down control signals with saliency maps. Unfortunately, many executive errors have multiple potential origins, making them complex and confounded to study (Friedman & Miyake, 2017). This complexity may also explain some of the inconsistencies in past work examining the neuroanatomy of executive function.

There are multiple ways in which to study the neuroanatomy of cognitive functions. Each has its own strengths and weaknesses. Whilst newer techniques can give insight into which brain regions are involved and hold information regarding the attainment of goal directed behaviour, more traditional techniques such as studying the consequences of brain damage can give us greater insight into which of these regions might be necessary (Rorden & Karnath, 2004). Just as with other techniques (e.g. Woolgar et al., 2015; Fox, Corbetta, Snyder, Vincent, & Raichle, 2006), lesion studies have also begun to adopt the network approach to executive dysfunction (e.g. Thiebaut de Schotten & Foulon, 2017). Recently it has been suggested that although dysexecutive syndrome was originally attributed solely to frontal lesions, it can occur following damage to a distributed network of both frontal and posterior regions (prefrontal cortex, parietal lobes, basal ganglia, thalamus and the cerebellum) and the white matter that connects them (Rabinovici et al., 2015; Bettcher et al., 2016).

It has long been understood that frontal regions in this network can result in executive dysfunction. Some examples include problems with response initiation and suppression (Burgess & Shallice, 1996; Godefroy et al., 1999; Stuss et al., 2000), difficulties with switching cognitive set rules (e.g. Delis, Squire, Bihrle, & Massman, 1992; Milner, 1963; Varjai et al., 2017), bizarre nonsensical strategies and a tendency to prematurely abandon the correct rule (Burgess & Shallice, 1996; Stuss et al., 2000). It has been suggested that frontal patients are more severely impaired on executive tasks compared to patients' with posterior lesions (e.g. Cipolotti et al., 2017; Owen et al., 1990; Shallice, 1982). In some instances it has even been reported that posterior patients do not differ from control participants on measures of executive function (e.g. Stuss et al., 2000). However, it should also be noted that frontal patients do not always have executive dysfunction (Baddeley et al., 1997) and that they do not always perform significantly worse as compared to posterior patients (e.g. Andrés & Van der Linden, 2002; Vilkki et al., 2002).

In addition to the inconsistencies reported above executive dysfunction has also been reported following focally posterior damage. For example, deficits in abstraction and cognitive flexibility have been found following non-frontal brain injuries (Godefroy, 2003). More specifically, executive dysfunction can occur following lesions to the parietal cortex (Collette et al., 2005; Koenigs et al., 2009), the anterior temporal lobes (Hornberger et al., 2011) and specific regions of the cerebellum (VII-VIII) (Manto & Mariën, 2015; Stoodley et al., 2016; Bellebaum & Daum, 2007). Moreover, it has been observed that electro-stimulation of posterior cortical (and subcortical) regions can generate executive dysfunction (Duffau, 2012b). Although, whether there is dissimilarity in the way this dysfunction is displayed depending upon lesion location is vague in the literature.

Returning to the concept of unity and diversity of executive dysfunction, the question now remains as to whether posterior lesions result in a"general" executive impairment that is comparable to frontal patients or whether the impairment is more specific and dissociable. Some voxel-based symptom lesion mapping studies have begun to address this question indirectly. For example, a study in 2012 examined which brain regions were important for multiple executive tasks. First, raw performance on the tasks was examined. It was found that performance on a variety of these tasks was related to frontal, posterior and subcortical damage. Secondly, the authors examined a single executive functioning factor, and found associations with damage to the anterior cingulate, left precentral gyrus, middle orbital frontal cortex, putamen and the right globus pallidus (Gläscher et al., 2012).

Another study in 2014, administered a large battery of executive tests and used factor analysis to reduce the data into three executive factors: verbal fluency, working memory and cognitive control. All factors were associated with damage to the DLPFC, although each had additional associations. Verbal fluency was associated with damage to the insula and superior temporal gyrus, working memory with the anterior temporal lobe and angular gyrus and cognitive control with anterior cingulate and mesial frontal lobe. The authors further explored general executive functioning, demonstrating an association with the bilateral superior mesial frontal region, right supramarginal gyrus, and right superior/middle temporal gyri (Robinson et al., 2014). Therefore, deficits in a general executive factor may be associated with a range of frontal, subcortical and posterior brain regions. This is suggestive of frontal and posterior patients both experiencing deficits in general executive function (for a review see Friedman & Miyake, 2017). However, a more direct comparison using a BiFactor model is required to truly examine whether the presentation of executive dysfunction is different between lesion localisations.

In the current examination there are three research questions to be addressed. "*1) Can damage to posterior brain regions lead to executive dysfunction?". 2) "Do posterior patients display executive dysfunction similar to frontal patients".* Particularly this question is focused on understanding whether posterior damage can lead to a impairment in global executive functioning (representing and utilising task set), or if it is due to a more specific executive difficulty (e.g. task switching or spatial selectivity). The final more exploratory question is *3) "Are there any specific lesion locations within posterior brain regions that result in executive dysfunction?*". Overall it is aimed that taking on the framework of unity/diversity of executive functioning and using a BiFactor model to dissociate these elements will extend our current understanding of executive dysfunction resulting from posterior damage.

4.3 Method

Sample

The sample consisted of 40 stroke patients and 150 control participants. Inclusion criteria for the control sample included being aged twenty-eight or above, fluent in the English language and being neurologically healthy. Stroke patients were sampled at least 6 months post stroke and did not have receptive aphasia or severe motor deficits.

Computerised Neuropsychological Assessment

The Oxford Cognitive Screen Plus (OCS+) is a computerised neuropsychological assessment comprised of 11 tasks. The assessment examines a range of cognitive functions, including language, praxis, memory, attention and executive function. The assessment battery was delivered on a surface tablet running Windows 8 and responses are made using a stylus pen. The screen was 10.6 inches with a resolution is 1920x1080. The testing session begins with a practice which allows the participant to become familiar with the use of the stylus for drawing on the screen and making tapping responses. Subsequently the tasks are run in a predetermined order. For each task the instructions are displayed on screen for the examiner to read aloud verbatim. The assessment takes approximately 30 minutes to complete. For a overview of the assessment tasks see Appendix C.1 (p.340).

Executive Measures

The four tasks of predominant interest for the current study are rule finding, the trail making task, visual selection and the auditory attention task. These tasks were chosen because they each require the representation and use of a task model to guide goal directed behaviour, thus each relies on high level attentional control.

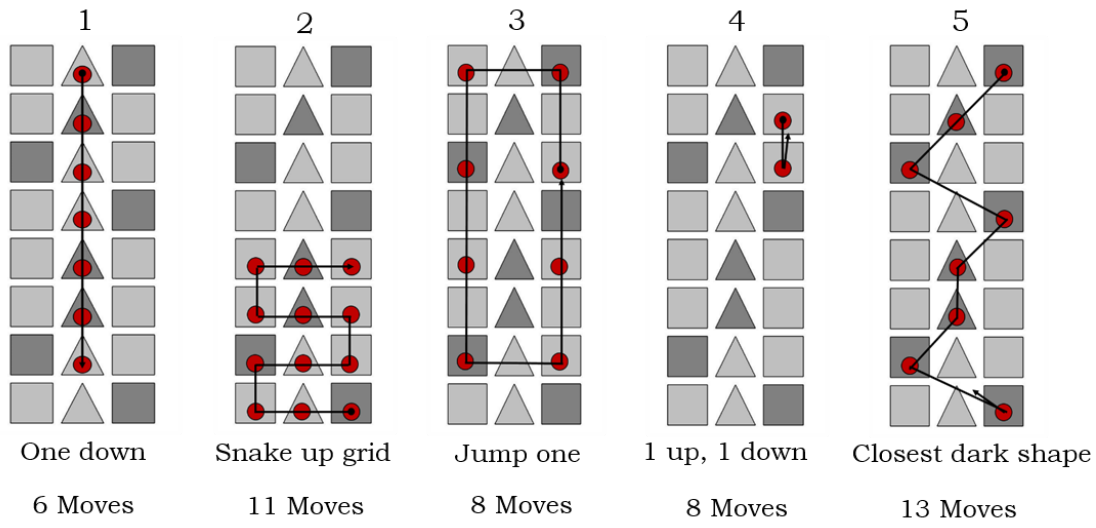


Figure 4.1: Rule Finding and Switching. The Figure above demonstrates the five rules of the rule finding task, presented in order 1-5 without a break. The black dot represents the start of the rule and the arrow head the last move. A slanted arrow (rule 4, 5), indicates the rule repeats in the opposite direction.

The rule finding and switching task is designed to measure the participants ability to successfully deduce an unknown task set and then use it to successfully guide behaviour. Therefore, it measures cognitive skills normally associated with executive functioning. The participant is given instructions verbatim:

"In the next task you will see a pattern of squares and triangles. A red dot will appear on one of the shapes. The dot will move around the shapes following certain rules. It's previous position will be highlighted to help you remember. Your task is to predict where the dot goes next based on the previous moves. Sometimes the rule will change without notice. When that happens, please try and pick up on the new rule. Because the rules change without notice, it is impossible for you to correctly predict the moves every time. Just try to do your best".

The participant is then presented with a 3*8 grid of 24 shapes. Of the three columns presented, the outer two are comprised of squares and the middle triangles. There are 16 light shaded shapes and 8 pseudo randomly placed dark shaded shapes. A red dot is positioned in the top middle shape. The instructions *"Guess where the dot may go next"* are printed on the top of the screen and are read aloud by the examiner. On the next screen the previous location is highlighted in blue and the dot has moved onto the new position. The examiner reads "*This is where the dot went (points). It came from the position highlighted in blue*" and prompts the participant to predict where the dot will move to next. The task then continues at the participants pace for 46 moves. During the task there are five rules for the participant to deduce (Figure 4.1). The first four rules are based on position (e.g. move one shape down), whereas the final rule is based on the intensity of the shading. The number of moves per rule is different to make the change unpredictable. The task is scored as number of correct responses (0-46).

Trail Making Task

The trail making task is a measure of the participants ability to use and switch between task set. The examiner reads aloud the following instructions *"I will ask you to use the pen to draw lines on the screen to connect some shapes. I will demonstrate how to do it as we go along"*. On the demonstration screen target shapes are displayed in order. The examiner reads aloud the instructions on the top of the screen, for example *"Connect the circles going from small to large"* and demonstrates using the stylus (Figure 4.2 A). The practice screen includes a small set of mixed shapes (Figure 4.2 B) and the path drawn can be erased if required. The final test screen has no instructions and a larger quantity of shapes (Figure 4.2 C). The participant repeats this process three times, once for each single rule trial (circles ascending, squares descending) and once alternating between these rules (largest square to smallest circle). The task measures include single rule accuracy 0-7, mixed accuracy 0-14 and the executive score (Mixed/(Circles + Squares)*100).

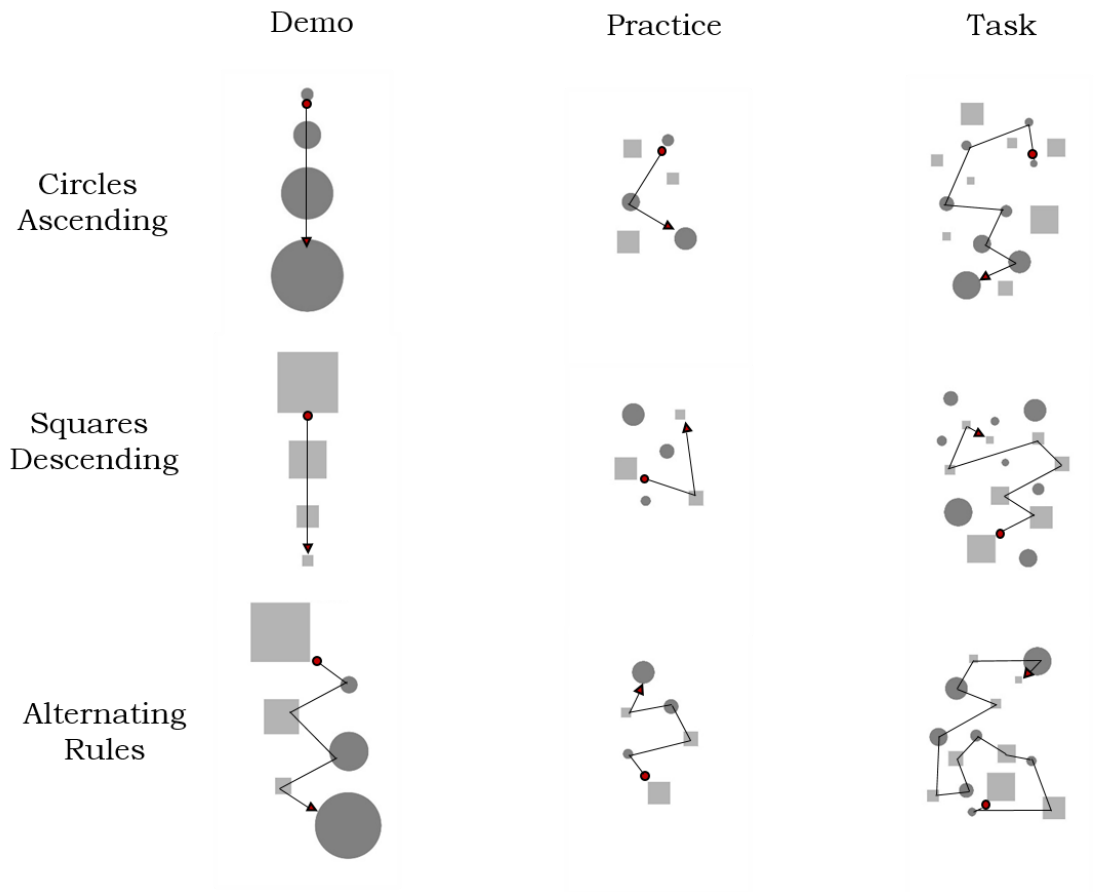


Figure 4.2: Trail Making Task. Test stimuli and optimal completion path for the 3 rule conditions (circles ascending, squares descending and alternating rules) are given above. First the researcher demonstrated the rule on a simple shape layout (first column). For each condition, the demonstration (column 1), reduced practice stimuli (column 2) and final test layout (column 3) are given. The use of shapes reduces the language requirement making the task more assessable for aphasic patients.

Visual Selection Task

The selection task is a measure of visual spatial selective attention. The participant is required to select pictures of fruits, whilst ignoring vegetables. The instructions are read: *"You will see a set of drawings on the screen. Your task is to use your pen to select the fruits"*. The tablet is positioned in front of the participant directly in the mid line. For the practice six images are displayed (3 targets, 3 distractors) and the participant is given time to practice selecting using the stylus.

On the test page there are 60 drawings in a pseudo randomised order which positions 15 targets and 15 distractors on each side (see Figure 4.3). When the participant selects a fruit feedback appears on-screen and remains there until the the task is complete. The second version of the task follows the same procedure, however now the visual feedback will no longer remain on screen to remind the participant of which fruits they have already selected. The aim is to select all the fruits without revisiting the same fruit twice, giving a measure of spatial working memory. The second instructions are read: "*You will see a similar set of drawings. The task again is to use your pen to select the fruits, but this time you'll have to remember the ones you have already selected and try not to select them more than once*". A second practice is given to demonstrate the feedback disappearing. The three task measures utilised from this task are visual $d'z$(probability of correct hit)-z(probability of false positive), asymmetry (left accuracy - right accuracy) -12:12 and the number of revisits from the no feedback version of the task.

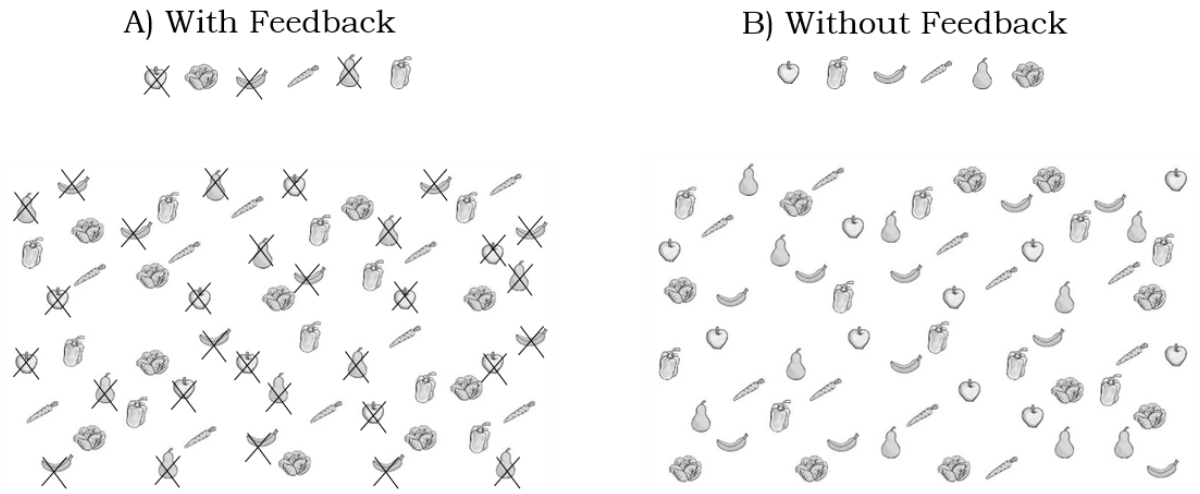


Figure 4.3: Visual Selection Task. A) Visual section with feedback, that appears appears after the participant taps the screen with the stylus and remains until the task is complete. B) Visual selection without feedback, the feedback appears briefly on-screen before disappearing.

Auditory Attention Task

The auditory attention task is a measure of auditory-temporal attention. The participant is required to remember three target words and make a selective tapping response to these words throughout the task. The instructions are read verbatim:

"*You will now hear a recording with a series of words. Your task is to tap the screen with the pen after each word. There are three target words which you have to remember: GOODBYE PLEASE NO (points). When you hear any of these words, tap the top blue button. When you hear any other words, tap the bottom yellow button.*

We will start with some practice".

The task begins with a free recall of the target words followed by a practice of 6 recorded word presentations. After the practice the patient must select the target words from a list. If the patient cannot remembering the words up to three practice trials can be given. The task contains 81 word presentations, split into 3 blocks. In each block there are 3 presentations of each of the 9 potential words. These words include targets (goodbye, down, no), related distractors (hello, up, yes) and unrelated distractors (today, and, drink). The task runs as a continuous stream given in a pseudo random order with a varying inter-stimulus interval. The target word presentation times were $94ms$ (goodbye), $80ms$ (down) and $85ms$ (no). The related distractor presentation times were $75ms$ (hello), $50ms$ (up) and $72ms$ (yes). The unrelated distractor presentation times were $75ms$ (today), $8ms5$ (and) and $76ms$ (drink). The inter-stimulus interval was 1, 2 or 3 seconds, each randomly selected 9 times within each block. At the end of the task the patient is asked to select the target words from a list (see Figure 4.4).

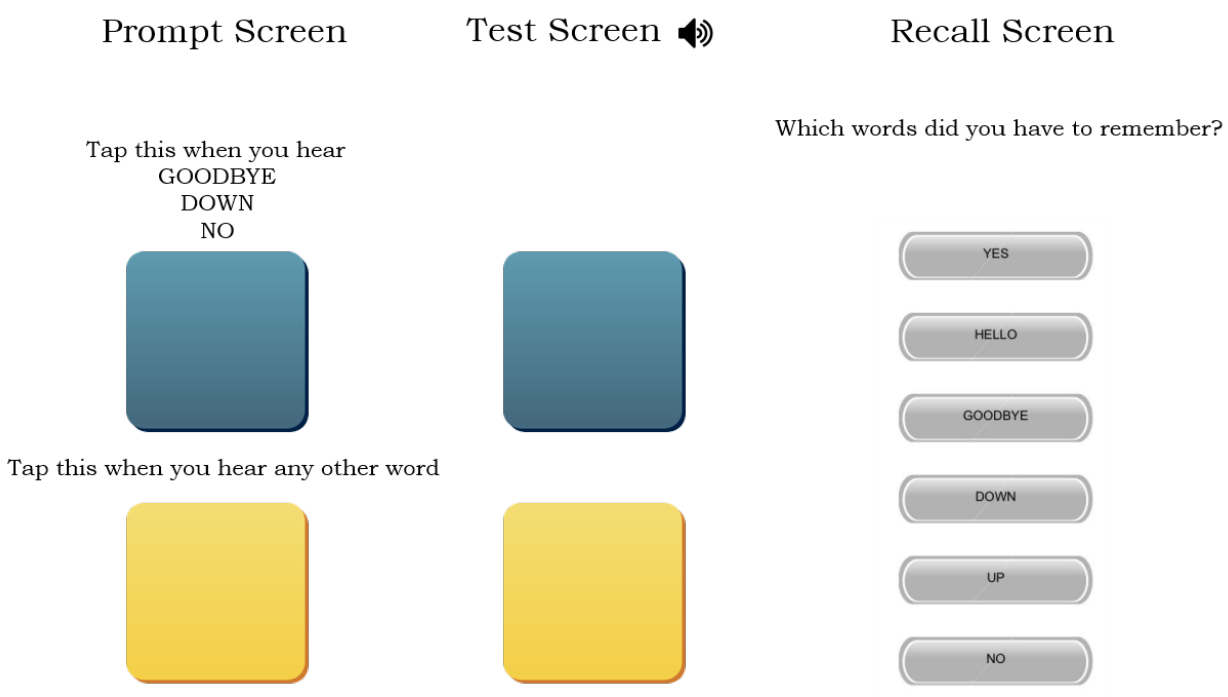


Figure 4.4: Auditory Selection Task. The prompt screen was displayed during the test instructions and kept on screen during the practice. However they were removed during the task. The participants' received visual feedback when their tap had been registered, indicated by a slight expansion of the pad. Participants are asked to recall the target words by tapping on the words provided during recall.

The task measures include: Correct target selection 0-27, the number of commissions 0-54 or omission errors 0-27, sustained attention index (correct targets in block 1 - block 3) −9-9 and the number of target words recalled 0-3. To measure attentional selectivity d' is calculated as z(probability of correct hit)-z(probability false positive). Please note that 0.5 was added to both the hit and false positive rate and 1 to the number of trials in both instances in order to address the difficulties faced when the probability is 1 or 0 in the calculation (see Stanislaw & Todorov, 1999)

Lesion Delineation

The lesions were manually delineated onto the native CT (n=12) or MRI (n=28) scans using the MRIcron software (Rorden & Brett, 2000). This process was undertaken by JL and AV researchers in the department who had been specifically trained. The images were subsequently evaluated for correctness by CG an experienced associate professor.

Image Processing

Image processing was performed in MATLAB (R2014a) using SPM8. The normalisation process was completed using the clinical toolkit package (Rorden et al., 2012). The clinical toolbox comes with age appropriate template scans and similar processing pipelines for both CT and MRI modalities, thus making mixed modality studies feasible. All the images were checked for alignment and the origin was set to the anterior commissure. Manual adjustments were performed using SPM's display if required.

The CT normalise function was used for CT scans, which implemented the following steps. First an invertible intensity transform was used on the Hounsfield units to match the template intensity range by emphasising the contrast between CSF and parenchyma (Rorden et al., 2012). Normalisation was run, with the inclusion of a dilated lesion mask to ensure the normalisation process is driven by intact brain tissue (Brett, Leff, Rorden, & Ashburner, 2001). The image was then transformed back to Hounsfield units.

In the case of MR scans the "MR segment-normalise" function was used. Unified segmentation-normalisation was run (Ashburner & Friston, 2005) including a dilated binary lesion mask. In some instances the lesion had been drawn on a "pathological scan" (FLAIR or T2 image), rather than the T1. In this case the pathological scan is used to co-register the lesion map to the T1 before processing. In all cases a bounding box of -90 -126 -72 90 90 118 was used and the voxels were resliced to 1x1x1mm resolution.

Lesion Classification

The lesions were then classified by calculating the percentage of overlap the normalised binary lesion map had with the Harvard-Oxford grey matter atlas and Cantani (2011) white matter atlas. This was performed using an in house script. Furthermore, masks were made for each lobe by summing together atlas regions in order and the percentage of overlap calculated in order to produce a coarse lesion summary. Patients were then split on the basis of whether their lesion was focally located in the frontal lobe, overlapped with both frontal and posterior regions or was focally located in the posterior brain. See Appendices C.2 (p.339) and C.3 (p.342) for an overview.

Statistical Analysis

All statistical analyses were run in R (3.0.3, R Core Team, 2014b), utilising packages Johnson (Fernandez, 2014), lmer4 (Bates, Mächler, Bolker, & Walker, 2015) and BayesFactor (Morey & Rouder, 2015; Rouder, Morey, Speckman, & Province, 2012). The Bayes factor is a ratio of the probability of the null and the alternative hypothesis, it ranges from 0 to infinity, with larger numbers indicating stronger evidence. Bayes factor values can be reported as evidence in favour of the alternative hypothesis (BF_10) or in favour of the null hypothesis (reciprocal of $BF_10 = BF_01$). Strength of evidence can be coarsely interpreted as: <3 (anecdotal), 3-10 (moderate), 10-30 (strong) >30 (very strong) (Kass & Raftery, 1995; Wagenmakers, Wetzels, Borsboom, & van der Maas, 2011; Nuijten, Wetzels, Matzke, Dolan, & Wagenmakers, 2015).

4.4 Results

Sample Characteristics

Table 4.1: Demographic Overview and Group Comparison

	Controls Mean(SD)	Patients Mean(SD)	Difference $t/X^2(df)$	P
Age	63.85(14.07)	64.30(14.42)	t (63)= -0.18	p=.86
Ed Yrs	16.62(4.24)	13.64(3.59)	t (67)= 4.31	p=.00
Gender F/M	80/70	12/28	X^2 (1)= 5.98	p=.02
Hand L/R/A	3/131/2	3/35/0	X^2 (2)= 0.78	p=.68
Ethnicity C/A/O	125/3/2	29/1/2	X^2 (2)= 2.50	p=.29

Missing Data Overview: Handedness(C=9, P=2) Ethnicity (C=20, P=8)

The sample consisted of 40 stroke patients (after removal of 2 patients due to confounding sensory deficits and poor alignment during normalisation) and 150 control participants. On average the control group had spent more years in education and had a more even distribution of gender than the patient group (Table 4.1). The average lesion volume for the patient group was 42.79 cm^2 (SD= 53.58 cm^2). There were 21 patients with left unilateral lesions, 13 with right unilateral lesions and 6 with bilateral lesions. The localisation of the lesions fell into three coarse groups, sub-cortical frontal lesions (n=7), focal posterior lesions (n=18) and lesions that were distributed across both frontal and posterior regions (n=17, Figure 4.5).

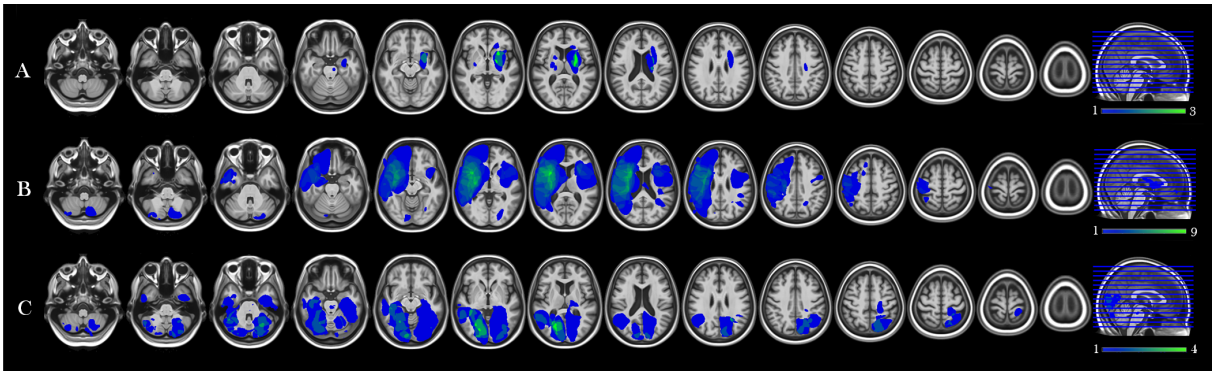


Figure 4.5: Lesion Distribution Split by Group. A) Frontal Sub-Cortical Group. B) Frontal and Posterior Group. C) Posterior Group.

Individual Patient Impairment on Raw Scores

The first step in understanding whether posterior damage can lead to executive dysfunction was to compare the raw performance of each patient to that of control participants within the same age range. The control data was examined and utilised to make age appropriate 5^{th} percentile cut-off scores and to run Crawford-Howell case control t-tests (Crawford & Howell, 1998). Table 4.2 provides an overview of task performance split by age group (<50, 50-69, =>70). The case analysis is summarised in Table 4.3, with ⊛ indicating that the patient was in the 5^{th} percentile or below and the significance level from the t-test represented as *(p <.05), **(p <.01) and ***(p <.001). In the following analysis only the results from the executive tasks are presented, for a full overview with additional OCS+ scores please see Appendix C.5 (p.345).

Patients in all lesion classification groups demonstrated impairment across the executive tasks (Table 4.3). No obvious differences in patterns of impairment were observed between the groups. Many of the patients with lesions to the posterior cortex were impaired on multiple tasks, including the trails executive score (n=7) and rule finding accuracy (n=4), thus suggesting posterior infraction may influence executive dysfunction.

In order to better understand whether there may be differences in the way that posterior patients are impaired a BiFactor analysis was run and the factors compared across patient groups. The purpose of this analysis is to help isolate the constructs. In this way, it can be seen whether posterior patients are impaired on general executive functioning (general ability to construct and utilise task sets to guide behaviour) or whether their impairment has a more specific origin (e.g. selective attention in space).

Table 4.2: OCS+ Overview for 150 Control Participants

		Age <50 (N=24)					Age 50-69 (N=61)					Age > 70 (N=65)				
	Measure	Mean	SD	Range	N	Cut-Off	Mean	SD	Range	N	Cut-Off	Mean	SD	Range	N	Cut-off
RF	Overall Accuracy	32.68	7.31	15-42	22	**20**	28.25	8.68	5-43	61	**11**	24.65	8.40	9-41	65	**12**
TMT	Executive Index	91.76	18.26	29-100	23	**53**	84.55	21.24	25-100	58	**41**	81.22	26.33	07-100	65	**29**
AAT	d-prime	3.87	0.65	1.71-4.46	24	**2.90**	3.66	0.87	1.05-4.46	58	**1.70**	3.69	0.72	1.40-4.46	58	**1.41**
	Sustained Index	1.11	0.07	1-1.25	24	**1.25**	1.11	0.20	.75-2	58	**1.53**	1.11	0.17	.75-2.75	58	**1.75**
	Target Recall	3.00	0	3-3	24	**3**	2.91	0.43	0-3	58	**2**	2.97	0.18	2-3	58	**2**
VST	d-prime	4.16	0.26	3.32-4.28	24	**3.80**	4.11	0.28	3.06-4.28	60	**3.80**	4.02	0.36	3.06-4.28	64	**3.25**
	Asymmetry	0.04	0.20	0-1	24	**0**	0.06	0.41	⁻1-1	60	**0-1**	⁻0.13	0.63	⁻2-1	64	**⁻1-1**
	WM Revisits	0.92	1.10	0-3	24	**3**	1.63	2.40	0-11	60	**6**	1.45	1.82	1-7	65	**6**

Overview of varying sample size. Auditory Attention (2-insufficient capacity on the practice trials, 2-auditory difficulties, 2-technical, 1-ran out of time). Visual Selection (2-technical). Visual Selection No Feed Back (1-technical). Trail Making Task (2-Interruption, 2-comprehension). Rule finding (1-comprehension, 1 examiner error).

Table 4.3: Patient Task Impairment Overview

Group	PID	Side	Volume	Lobe	RF	TMT	Auditory Attention			Visual Attention		
							d'	SAI	WM	d'	Asym	WM
Frontal-SC	P3174	L	0.96	SC				⊛***		×	×	×
	P4051	R	0.3	SC		⊛***				⊛**		
	P4019	L	1.5	SC	⊛	⊛**	⊛**	⊛**				
	P3046	R	2.02	F/SC	⊛*	⊛**				⊛***	⊛***	⊛***
	P3076	R	4.15	F/SC			⊛					
	P3001	R	27.76	FL	⊛	⊛**				⊛**		
	UO21	R	21.50	FLT						×	×	×
Frontal/Posterior	P3180	L	6.78	F/I/T/CB		⊛*		⊛*		⊛**		
	P3030	R	70.22	F/I/T								
	P3104	R	33.57	F/I/T/CB			⊛*			⊛***		
	UO26	L	31.24	F/I/T								
	P3012	L	65.07	F/I/L/T								
	P3043	L	30.11	F/I/P/T		⊛**						
	P2003	L	121.11	F/I/P/T			⊛*			⊛*		
	P4042	L	91.58	F/I/P/T	⊛		⊗	⊗	⊗	×	×	×
	P4046	L	172.04	F/I/P/T			⊛***	⊛***				
	P2046	L	184.13	F/I/P/T			⊛*					
	P3277	L	168.28	F/I/P/L/T			⊛*		⊛***			⊛***
	UB11	L	131.29	F/I/T/P/O		⊛*						
	P3239	B	19.09	F/I/T/P/O	⊛*	⊛**				⊛**		⊛***
	P2027	B	15.38	F/I/T/P/O/CB			⊛*		⊛**			
	P3178	L	20.50	T/L/F		⊛***				×	×	×
Posterior	UO23	R	0.47	L							⊛***	
	P4037	R	1.48	O/P	⊛*	⊛**	⊛**					
	P3222	L	25.36	O/T	⊛*	⊛**	×	×	×		⊛**	⊛***
	UO05	L	18.67	T/L/O								
	UO01	R	146.99	O/P			⊛					
	P3053	B	64.55	O/L/P				⊛***		⊛*		
	P4041	L	39.22	O/P/T	⊛*	⊛**	⊗	⊗	⊗	⊛*	⊛**	
	P4097	L	88.92	CB/O/T/L		⊛*	⊛*	⊛**	⊛**			
	UO24	L	32.54	CB/T/O								
	P3057	B	1.77	CB/O		⊛**	⊛*					
	P3101	L	17.28	CB/O	⊛*							
	P3102	R	9.48	CB		⊛***	⊛	⊛*				
	P3108	L	8.93	CB		⊛*		⊛*		⊛**		
	P3122	L	2.46	CB								
	P3089	B	28.97	CB			⊗	⊗	⊗			⊛***
	P3173	R	4.55	CB			⊛**	⊛***		⊛* ⊛***		
	P3163	R	0.76	BS								
	P3118	B	0.62	BS						⊛*	⊛***	
	Impairment Total				9	16	17	12	5	12	6	5

× = Not Run ⊗ = Aborted due to inability to meet criteria on practice task
* p <.05** p <.01*** p <.001 Crawford-Howell case control t-test
⊛ = 5^{th} percentile or below.

Bi-Factor Analysis

The four neuropsychological tasks examined were chosen because they require executive functioning in the form of representing a task set and using that task set to bias perception and action. However, they also have more individual aspects, for example being able to sustain attention through time, distribute it in space or use it internally to refresh working memory traces. Therefore, a BiFactor analysis was run to examine both the shared variance (unity) and the more unique variance (diversity).

There were 8 observed variable scores entered into the analysis: trails executive score, rule finding total accuracy, auditory d', sustained attention index, target word recall, visual d', spatial asymmetry and number of revisits (spatial selection without feedback). Cases with missing data were not included, which resulted in a sample of 172 (participant to variable ratio of 1:21). Three of the scores (absolute asymmetry, sustained attention index and number of revisits) were reversed so that high scores consistently represented better performance. For this procedure the highest possible score was subtracted from participants observed score.

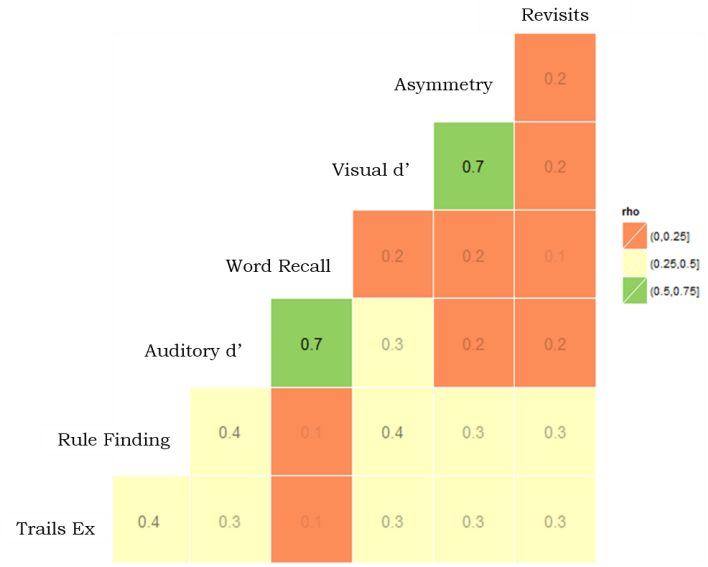


Figure 4.6: Correlation Matrix.

First the correlation matrix was examined. The Kaiser-Meyer-Olkin (KMO) measure verified the sampling adequacy for the analysis as .75 ('good' Kaiser & Rice, 1974). The individual KMO scores were above the .5, apart from the SAI (.33). Due to this inadequacy, the sustained attention index was removed from the subsequent analysis. The participant to variable ratio was updated to 1:24.57. The Barlett test was significant ($\chi^2(21)$ 337.65, p <.001), suggesting that the correlations between variables were sufficient to run factor analysis. The determinant of the correlation matrix was .13 indicating that multicollinearity is not a problem (Field, Miles, & Field, 2012).

A very simple structure analysis was run suggesting that three factors were optimal (VSS=.84). This was also corroborated by parallel analysis screen plots. The exploratory BiFactor model was run using the omega function from the psych package for R (Revelle, 2015). The omega function runs hierarchical factoring using the Schmid-Leiman (SL) transformation to create orthogonal factors. The SL procedure first extracts the number of primary factors using maximum likelihood extraction and subsequently runs an oblique (oblimin) factor rotation. Next, the second order factor is extracted from the primary factor correlation matrix and a SL orthogonalisation is performed on the second order factor solution to obtain the loadings for each item on the uncorrelated general and grouping factors. Therefore, the contribution of the general executive factor is statistically independent of the more specific executive factors (Revelle, 2015; Schmid & Leiman, 1957; Reise, Moore, & Haviland, 2010; Costello & Osborne, 2005; Osborne, 2014).

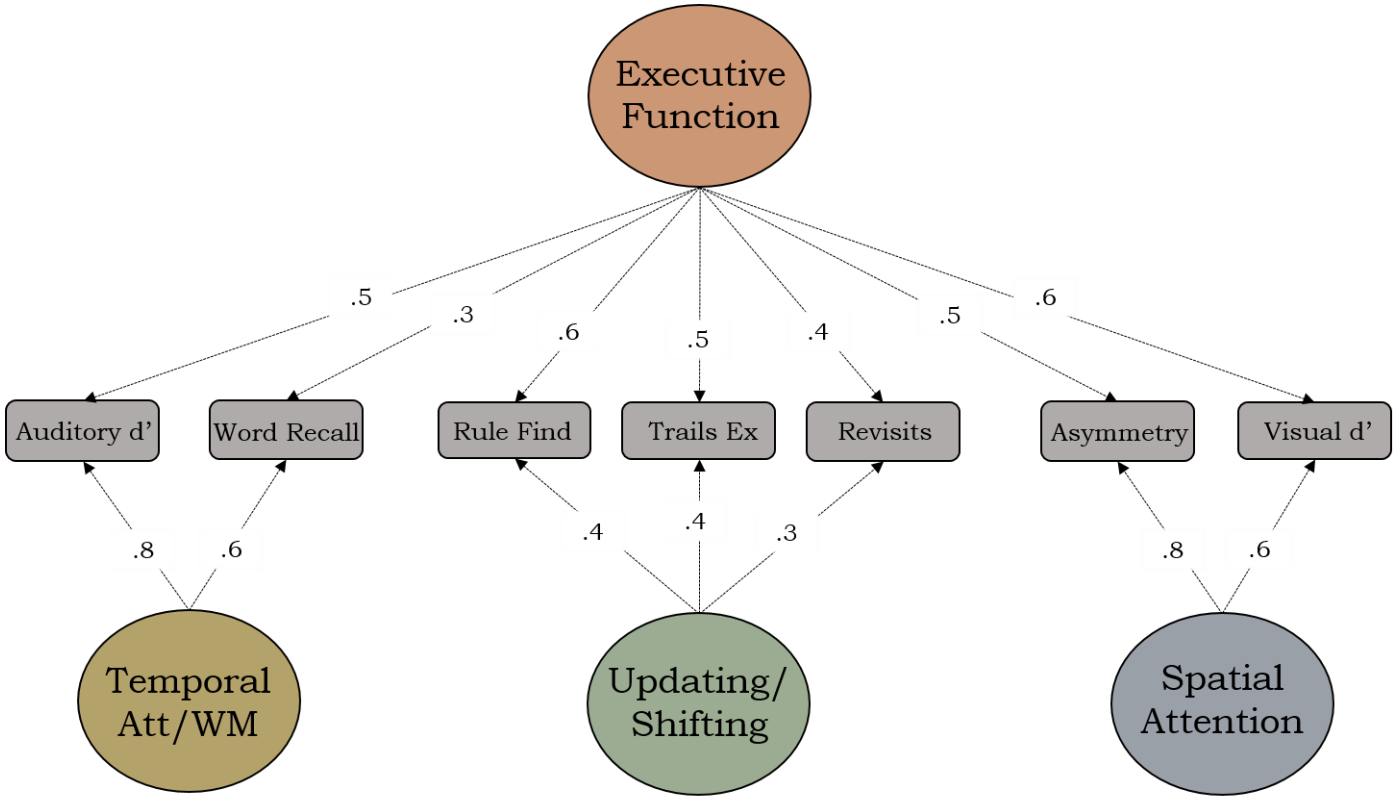


Figure 4.7: Schmid Leiman Transformed BiFactor Analysis Results.

Naming the Factors

The general factor on which all tasks loaded was named "Executive Function" and will be considered to represent the shared requirement to a use task model to guide goal directed behaviour. The Raven's progressive matrices total score correlated with the general executive factor (r=.5, $t(15)$=2.10, p=.05, N=17). The following factors are created after accounting for this shared variance, making them orthogonal to the general Executive Function factor. The first factor comprised of shared variance between auditory d' and word recall. This factor was labelled "Temporal Attention/Working Memory" because of the requisite of attentional tracking of externally relevant stimuli and the maintenance (refreshing) of the target words through time. The second factor comprised of shared variance between the selection asymmetry score and visual d'. This factor was labelled "Spatial Attention" because of the requirement to orient and select in space. Finally, the last factor which is comprised from the rule finding, trail making task executive score and number of revisits has been labelled "Updating/Shifting". These three visual tasks all require working memory to be updated and attention to be shifted to keep track.

Reliability of the Model

The reliability of the model was assessed. Cronbach's $\alpha = .75$ (Cronbach, 1951), McDonald's ω hierarchical = .54 and ω total = .85 (McDonald, 1999). The overall reliability of the model is good, but the common factor is not as reliable (mostly due to the smaller loadings of the two working memory measures). The RMSEA index (.04, CI.13) was below .05 and the χ^2 (3.86, p=.28) was above .05 indicating good fit. The eigenvalues are EF:1.59 (R^2=.58, ω_t=.85), TA/WM:1.10 (R^2=.83, ω_t=.84), SA:.93 (R^2=.65, ω_t=.85) and US:.44 (R^2=.32, ω_t=.61). The explained common variance (ratio of the general factor eigenvalues to the sum of all eigenvalues) of the general factor is 39%. Despite the third factor being under the Kaiser's criteria of 1, retaining it improved model fit and therefore it was kept in the model.

Individual Impairment on Factors

To address whether posterior patients also demonstrated executive dysfunction on the factors from the BiFactor analysis their factor scores were compared individually to age matched controls in the same manner as the raw data. An overview of control performance is given in Table 4.4 and patient impairment is given in Table 4.5.

Table 4.4: Factor Score: Overview for 138 Control Participants

	Age <50 (N=21)				Age 50-69 (N=57)				Age > 70 (N=60)			
	Mean	SD	Range	Cut-Off	Mean	SD	Range	Cut-Off	Mean	SD	Range	Cut-off
EF	27.85	2.70	21.13-30.68	**22.81**	25.33	4.52	12.39-30.89	**15.62**	24.17	5.0	10.28-30.63	**13.31**
TA	-16.15	2.27	-19.25- -10.65	**-12.87**	-14.37	3.19	-19.25- -6.58	**-7.24**	-13.65	3.91	-19.53- -3.93	**-4.80**
SA	-4.81	1.46	-6.25- -0.77	**-2.16**	-3.51	2.51	-6.35- 4.00	**-2.02**	-3.07	2.79	-6.16- 5.22	**-3.21**
US	36.32	4.45	24.88- 41.22	**28.42**	32.31	7.22	12.32- 40.85	**16.03**	30.63	8.21	8.20- 40.86	**12.53**

Control participant performance on factor scores derived from BiFactor model. EF = Executive function factor. TA = Temporal attention and working memory factor. SA = Spatial attention factor. US = Updating and shifting factor.

As can be seen from Table 4.5, impairment on the factor scores demonstrates more obvious patterns of impairment across the three patient groups. The frontal sub-cortical patient group most consistently demonstrates impairment (80%, 4/5) across all four factors. There are also three patients with frontal/posterior lesions and five purely posterior patients who display impairment as compared to age matched controls. It was considered that perhaps posterior patients might display impairment differently across the factors as compared to the frontal patients. The frontal patients may have been impaired on the general executive function factor, whereas the posterior patients impaired primarily on one of the other factors. However, this pattern was not observed. The only difference of note at this stage is that on an individual level more frontal patients appear to be also impaired on the temporal attention/working memory factor. The average performance of patient groups will now be examined.

Table 4.5: Patient Task Impairment Overview For Factor Scores

	Case	Age	Gen.	Lat.	Vol.	Lesion	Ex.	Tem.	Spa.	Sh/Up.
Frontal	P4051	68	F	R	0.31	SC	⊛**	⊛***	⊛**	⊛**
	P4019	86	M	L	1.47	SC	⊛***	⊛*	⊛***	⊛**
	P3046	84	F	R	2.02	F/SC	⊛**	⊛***	⊛*	⊛*
	P3076	65	M	R	4.15	F/SC				
	p3001	70	F	R	27.76	F/I/SC	⊛***	⊛**	⊛***	⊛**
Frontal/Posterior	P3180	79	M	L	6.781	F/I/T/CB	⊛*			
	P3030	70	M	R	70.215	F/I/T				
	P3104	70	F	R	33.567	F/I/T/CB				
	UO26	49	M	L	31.237	F/I/T				
	P3012	47	F	L	65.068	F/I/L/T				
	P3043	58	F	L	30.106	F/I/P/T		⊛*	⊛*	
	P2003	35	M	L	121.109	F/I/P/T				
	P4042	71	M	L	91.575	F/I/P/T				
	P4046	30	F	L	172.04	F/I/P/T				
	P2046	63	M	L	184.133	F/I/P/T				
	P3277	44	M	L	168.284	F/I/P/L/T				
	UB11	44	M	L	131.285	F/I/T/P/O	⊛**	⊛**	⊛***	⊛***
	P3239	86	M	B	19.086	F/I/T/P/O	⊛***	⊛**	⊛***	⊛***
	P2027	77	F	B	15.383	F/I/T/P/O/CB				
	P3178	50	M	L	20.494	T/L/F				
Posterior	UO23	43	M	R	0.47	L				
	P4037	66	M	R	1.48	O/P	⊛***	⊛**	⊛***	⊛***
	UO05	60	M	L	18.67	T/L/O				
	UO01	59	M	R	146.99	O/P				
	P3053	56	M	B	64.55	O/L/P				
	P4097	70	F	L	88.92	CB/O/T/L	⊛*		⊛*	
	UO24	52	M	L	32.54	CB/T/O				
	P3057	75	M	B	1.77	CB/O	⊛*		⊛**	⊛*
	P3101	81	M	L	17.28	CB/O				
	P3102	69	M	R	9.48	CB	⊛**		⊛**	⊛*
	P3108	80	M	L	8.93	CB	⊛*			
	P3122	73	M	L	2.46	CB				
	P3089	72	F	B	28.97	CB				
	P3173	67	M	R	4.55	CB				
	P3163	69	F	R	0.76	BS				
	P3118	48	M	B	0.62	BS				
	Frequencies of Impairment						12	8	11	9

Please note that patients with missing data were not included in the factor analysis N=172
⊛ $< 5^{th}$ percentile $p < .05$* $p < .01$** $p < .001$*** Crawford-Howell t-test

Group Analysis

To better understand whether there are differences in the way frontal and posterior patients display executive dysfunction a group analysis was run. The assumptions of normality (Anderson-Darling test) and homogeneity of variance (Levene's test) were broken for most measures and therefore the Johnson power transformation was applied to the data. Although this transformation produced univariately normal data, the assumption of multi-variant normality (as tested by the Shapiro test) and homogeneity of covariance matrices (Box test) were not met. The data were nested within groups. Therefore the need for a multilevel analysis was examined by comparing the intercept model with a model including a random intercept for group. In all instances the Log Likelihood test was significant at $p < .001$, thus indicating the observations within groups are dependent and there is a requirement for multilevel modelling.

Two important additional cognitive elements to control for are processing speed (Leskel et al., 1999) and language ability (Wall, Cumming, & Copland, 2017). Factor analysis was run for two processing speed measures (visual search time and average time on the two single rule conditions on the trails task) and separately for two language tests (picture naming and semantics). In each case one factor was extracted and Barlett factor scores were estimated and included as covariates. Two demographic elements that are also important to control for are age (Knoflach et al., 2012) and years in education (Mirza et al., 2016) and therefore they were also included in the model.

Therefore, a mixed multilevel analysis was run for each factor separately examining the main effect of group (control, frontal sub-cortical, frontal/posterior and posterior) whilst controlling for age, education, processing speed and language performance. This was followed by planned Tukey contrasts (FDR corrected p values were reported).

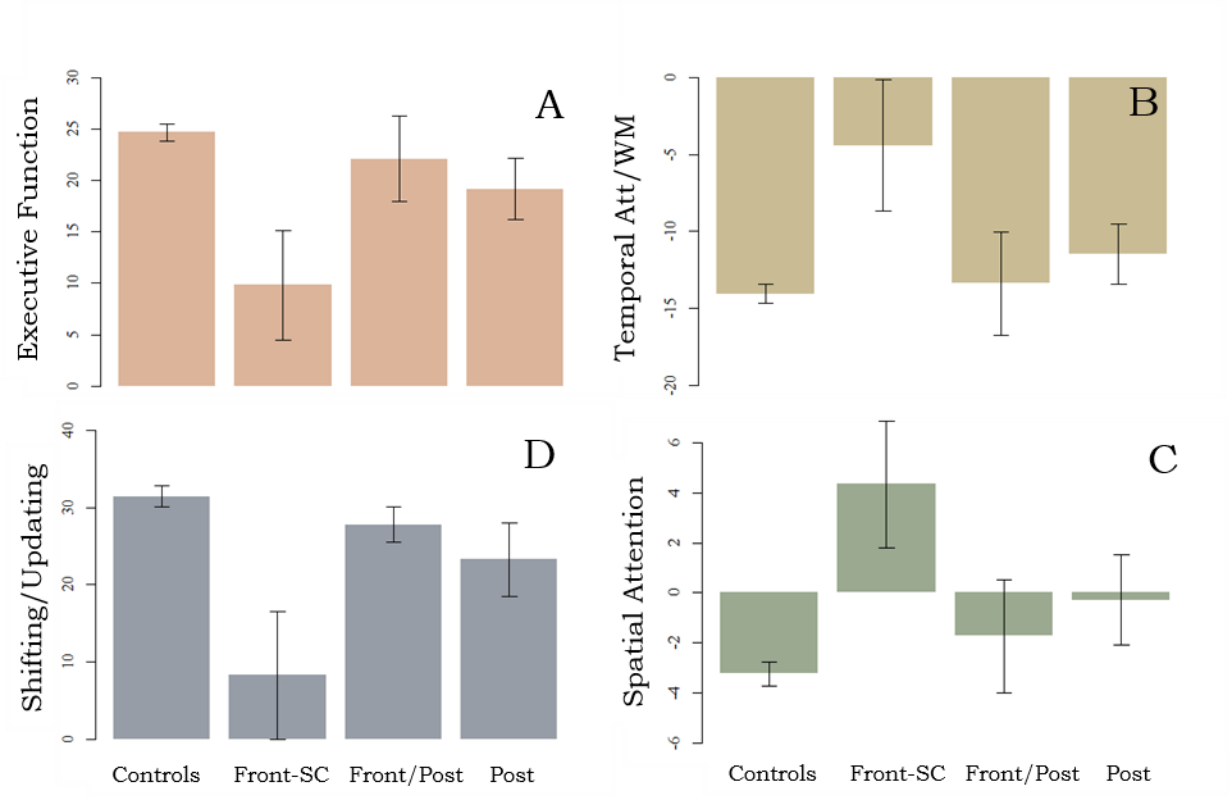


Figure 4.8: Average Factor Scores by Group. A) Executive Function B) Temporal Att/WM C) Spatial Attention D) Updating/Shifting. Error bars = 2*SEM

Figure 4.8 displays the average factor scores for each group and Table 4.6 gives an overview of the statistical analysis. There was a significant main effect of group for all factors. Follow up contrasts found that for all factors frontal sub-cortical and posterior patients performed significantly worse than control participants. When the patient groups were compared it was observed that for all factors on average posterior patients did not significantly differ from either frontal group. The frontal sub-cortical group consistently performed worse than the frontal/posterior distributed group, whereas the posterior group did not. In all models age was a significant covariate at $p < .001$. Education was a significant covariate at $p < .01$ for all models apart from temporal attention. Processing speed and language were not significant covariates. Overall there was no indication that posterior patients experienced executive difficulties differently to frontal patients.

Table 4.6: Group Comparison on Factor Scores

Factor Score	Wald χ^2 test	Contrast		Estimate	SE	Z	P
Executive Function	$\chi^2(3)$=17.10***	F	C	-1.57	.38	-4.11	***
		F/P	C	-0.45	.25	-1.82	*n.s.*
		P	C	-0.76	.23	-3.22	**
		P	F	0.81	.41	1.98	*n.s.*
		P	F/P	-0.31	.31	-1.02	*n.s.*
		F/P	F	1.13	.43	1.97	*
Temporal Att/WM	$\chi^2(3)$=17.14***	F	C	1.59	.44	3.62	**
		F/P	C	0.03	.28	0.11	*n.s.*
		P	C	0.67	.27	2.49	*
		P	F	-0.92	.50	-1.93	*n.s.*
		P	F/P	0.64	.35	1.84	*n.s.*
		F/P	F	-1.60	.50	-3.20	**
Spatial Attention	$\chi^2(3)$=19.70***	F	C	1.50	.39	3.87	***
		F/P	C	0.45	.24	1.81	*n.s.*
		P	C	0.61	.24	2.55	*
		P	F	-0.89	.42	-2.13	*n.s.*
		P	F/P	0.16	.31	0.50	*n.s.*
		F/P	F	-1.05	.44	-2.40	*
Updating/ Shifting	$\chi^2(3)$=21.00***	F	C	-1.57	.40	-3.90	***
		F/P	C	-0.33	.26	-1.29	*n.s.*
		P	C	-0.74	.25	-3.00	**
		P	F	0.83	.44	1.91	*n.s.*
		P	F/P	-0.41	.32	-1.28	*n.s.*
		F/P	F	1.24	.45	-2.73	*

F = Frontal/Subcortical, F/P = Frontal/Posterior, P = Posterior, C = Control
Significance codes: *** <0.001 ** <0.01 * <0.05 . =.05

Control Analysis: Lesion Volume and Side

The group differences between posterior and frontal patients were further examined, whilst controlling for two extra sources of inter-subject variability lesion volume (cm^3) and lesion lateralisation (Price et al., 2017). Only one of the frontal-subcortical patients had a left lateralised lesion, therefore the frontal groups were combined (17 with and 17 without frontal damage). The need for multilevel modelling was assessed by examining whether the addition of a random intercept for group or side significantly improved model fit. The χ^2 test was not significant and therefore a regular linear model was run examining the between subject effects of Group(frontal, posterior)* Side(left, bilateral, right). To better examine the null hypothesis a general Bayesian factor analysis was performed.

Table 4.7: Patient Comparison on Factor Scores

Factor	Effect	F test	P	η^2	BF_ 01
Executive	Group	F(1,23)=0.28	$^{n.s.}$	.01	0.00 ± 0.00%
Function	Side	F(2,23)=0.72	$^{n.s.}$	.06	3.17 ± 1.72%
	G*S	F(2,23)=1.03	$^{n.s.}$	.08	2.59 ± 2.58%
Temporal	Group	F(1,23)=0.04	$^{n.s.}$	.00	2.06 ± 1.63%
Att/WM	Side	F(2,23)=1.11	$^{n.s.}$	.09	2.85 ± 2.25%
	G*S	F(2,23)=0.85	$^{n.s.}$	.07	2.76 ± 2.09%
Spatial	Group	F(1,23)=0.69	$^{n.s.}$	.03	2.33 ± 2.64%
Attention	Side	F(2,23)=1.16	$^{n.s.}$	.09	3.28 ± 2.58%
	G*S	F(2,23)=0.78	$^{n.s.}$	.06	2.45 ± 2.64%
Updating/	Group	F(1,23)=0.11	$^{n.s.}$	.01	2.37 ± 1.64%
Shifting	Side	F(2,23)=0.84	$^{n.s.}$	.07	3.04 ± 1.97%
	G*S	F(2,23)=0.98	$^{n.s.}$	.08	2.50 ± 2.42%

Significance codes: *** <0.001 ** <0.01 * <0.05
Partial η^2 is reported

As can be seen in Table 4.7, there were no main effects of or interaction between group and lateralisation. Age was a significant covariate (p <.01) in all cases. Lesion volume was a significant covariate for temporal attention (p=.05). In all cases the Bayesian model only including age was preferred. There was weak evidence to suggest both the main effect of side and interaction between side and group should be removed from the model. This was also true for the main effect of group, for all but the executive factor.

Factor Overlap Analysis

In order to start examining the third research question regarding consistencies in lesion sites that lead to executive dysfunction, overlap maps were created for each factor regardless of patient group.

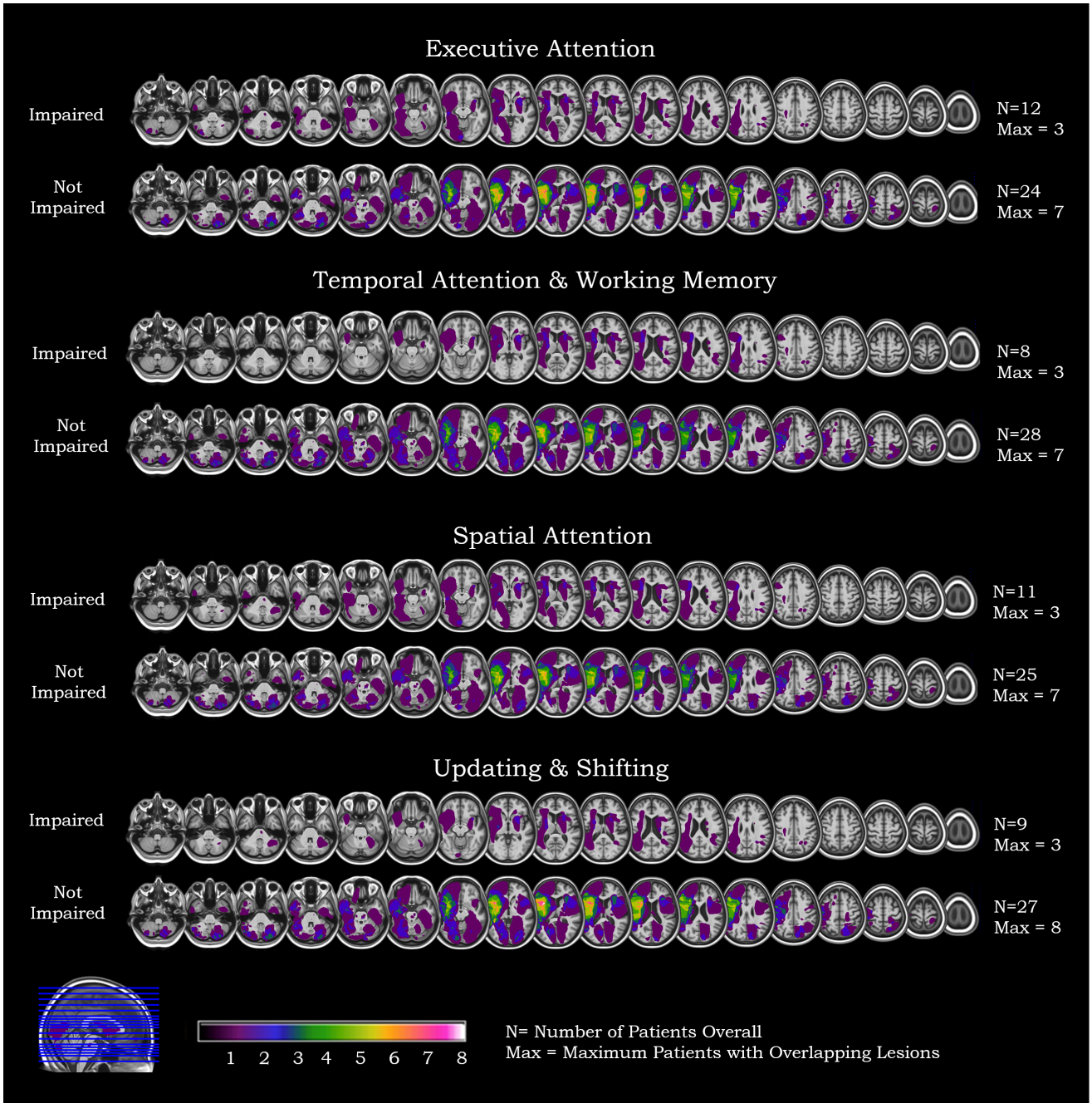


Figure 4.9: Lesion Overlap Maps Split by Impairment on Factors

As can be seen in Figure 4.9, frontal sub-cortical lesions were most consistent for all factors. For the executive function factor the point of maximum overlap (n=3) was located over the left puteman/globus pallidus. However, there are multiple points in which two patients overlap such as the right basal ganglia, crus I/II of the left cerebellum and the left posterior occipital cortex.

For temporal attention/working memory, there were two points in which three patients overlapped. The first was the same location as the general executive factor. The second was more anterior in the left putamen. There were multiple regions where two patients overlapped bilaterally in the BG. There were also two locations (one left and one right) in the posterior parietal cortex (precuneus), bordering the occipital lobe where two impaired patients overlapped. For spatial attention, the same two locations in the left basal ganglia had 3 patients with overlap. Regions were 2 patients' overlapped were the posterior occipital cortex (junction where occipital pole, lingual and occipital fusiform gyrus meet, see Appendix C.7, p.348) and bilateral points in the posterior parietal cortex (precuneus). There was also overlap of two patients in the superior temporal lobe. The results for the updating/shifting factor resembled the general executive function, with 3 patients overlapping in the left putamen. The locations where 2 patients overlapped were bilaterally in the basal ganglia.

The results of this analysis overall suggest that the basal ganglia are particularly important for executive dysfunction (as already indicated in the group analysis). For a visualisation of individual frontal-subcortical patients lesions overlaid on a subcortical atlas please see Appendix C.6 (p.347). The involvement of posterior regions appears less consistent across the factors. However, posterior lesions do appear (despite not overlapping) for all the factors. Another important observation is that many unimpaired patients have lesions overlapping with the impaired group.

Posterior Patients

The posterior group will now be examined in greater detail to see if there are any consistencies between patients experiencing impairment. When examining the patients within the posterior group in greater detail, several subgroups are present. As can be seen in Table 4.8, two of the patients have brain stem lesions, five patients have lesions solely to the cerebellum, two patients have both a cerebellum lesion and damage to the posterior cortex and the remaining 7 have damage solely to the posterior cortex. Patients displaying impairment were spread over the cerebellum, posterior cortex and mixed groups.

For each of the factor scores, impaired patients were compared to unimpaired patients on age, education, lesion volume, processing speed and language. For the general executive factor the only observed difference between groups was in age [$t(13.87)$= -2.37, p=.03], with impaired patients being significantly older (M=72, SD=11.67) on average than unimpaired patients (M=62, SD=5.52). There were no observed differences on any of the measures for temporal attention/working memory (case control t-tests run) or spatial attention. For the updating/shifting factor, there was a trend [$t(12.97)$=2.23, p=.04] towards the impaired patients having a smaller average lesion volume (M=4.24 cm^3, SD=4.53), as compared to the unimpaired patients (M=31.98 cm^3, SD= 43.82).

In Table 4.8, a detailed overview of demographics, cognitive impairment and lesion characteristics is given for each patient. Patient scans were also examined for signs of subcortical cerebrovascular disease (SCD). Please see Appendix C.7 (p.348) for a visualisation of scans showing signs.

Table 4.8: Posterior Patient Detailed Overview

		Demo					Cognitive Impairment					Lesion Overview				
	Case	Age	Gen.	Ed.	Hand.[1]	BADL[2]	Ex.	Temp.	Spac.	Shif.	Other	Lat.	Vol.	Teri.	Lobe	White Matter	SCD
BS	P3163	69	F	18	0	-[3]					ImRC2	B	0.76	PICA/BA	Pontine	CPC/CS/IC	
	P3118	48	M	12	0	20					ImRC2	B	0.62	PICA/BA	Pontine	CPC/CS/IC	X
CB	P3108	80	M	10	0	20	⊛*					L	8.93	PICA/SCA	Crus I/II VII VIIIa/b		
	P3102	69	M	11	0	20	⊛**		⊛**	⊛*	ImRC1 PN PS	R	9.48	SCA	Crus I VI IV V	CPC	X
	P3122	73	M	10	1	16					Ori DelRC	L	2.46	SCA	VI V	SCP/ICP/CPC	
	P3173	67	M	23	0	20					SM	R	4.55	SCA/PICA	Crus I/II VIIb VIIIa		X
	P3089	72	F	12	-	20					SM	B	28.97	PICA/SCA/LLA	Crus I/II VI VIIIa/b IX Pons	CPC/SCP/ICP/CS	
CB+	UO24	52	M	16	-	-						L	32.54	SCA/PCA	CrusI/II VI V T/O	CPC ICP SCP	
	P4097	70	F	10	1	17	⊛*		⊛*		Ori ImRC1 PN	L	88.92	SCA/PCA	CrusI V VI /O/T/L/P	CPC Cing CC IFOF ILF OR	X
	P3053	56	M	12	1	20					Ori DelRC PN PS	B	64.55	SCA/PCA/ MCA	O/T/L/P	CPC Cing ILF Stri OR IFOF AF SLF	
Cortical	P3057	75	M	15	1	20	⊛*		⊛**	⊛*		B	1.77	PCA	O/Pontine	IFOF IC ILF CS	X
	P4037	66	M	15	0	17	⊛***	⊛**	⊛***	⊛***	Im &DelRC PS	R	1.48	PCA MCA	O/P	SLF AF IFOF ILF IC	
	UO01	59	M	18	-	-					OR	R	146.99	PC5	O/P/T/L	CPC S/I CP IC Cing multiple Ass$^{s/l}$	
	UO05	60	M	-	-	-					Im& DelRC	L	18.67	PCA	L/T/O	Cing IFOF OR ILF	
	P3101	81	M	10	0	18						L	17.28	PCA	O	IFOF OR ILF	X
	UO23	43	M	-	-	-						R	0.47	PCA	L	Cing IC	

⊛ < 5^{th} percentile p <.05* p <.01** p <.001*** Crawford-Howell case control t-test, 1) Hand. indicates a change of hand dominance 1= yes 0 = no,

2) Barthel Index Activities of Daily Living at 6 month follow up 3) BADL missing but scored at ceiling on Stroke Impact Scale ADL and mobility

Territory: SCA= Superior Cerebellar Artery, BA= Basilar Artery, PICA= Posterior Inferior Cerebellar Artery, LLA= Lateral Lenticulostriate Arteries, PCA= Posterior Cerebral Artery

White Matter: PC= Cortico Ponto Cerebellum, CS= Cortico Spinal, SCP= Superior Cerebelar Pedunculus, ICP= Inferior Cerebelar Pedunculus, IC= Internal Capsule, Cing= Cingulum, Stri= Striatum

AF = Arcuate fasciculus, IFOF= Inferior Fronto Occipital Fasciculus, ILF= Inferior longitudinal Fasciculus, SLF= Superior longitudinal Fasciculus, OR= Optic Radiations, S/I = Superior and Inferior

CC= Corpus Callosum, Lobe: O= Occipital, T= Temporal, L= Limbic, CB lobes = IX, CrusI, Crus II, VIIa/b VIIIa/b, VI, V IV

OCS+ Assessment Abbreviations: IMRC1 = Immediate recall after first presentation of five words, ImRC2 = Immediate Recall after second presentation of five words, DelRC = Delayed recall of five words

PN = Picture Naming, SM = Semantics, PS = Processing speed, Ori = Orientation in time and space, OR = object recognition, For future task details please see Appendix C.1, pp.341

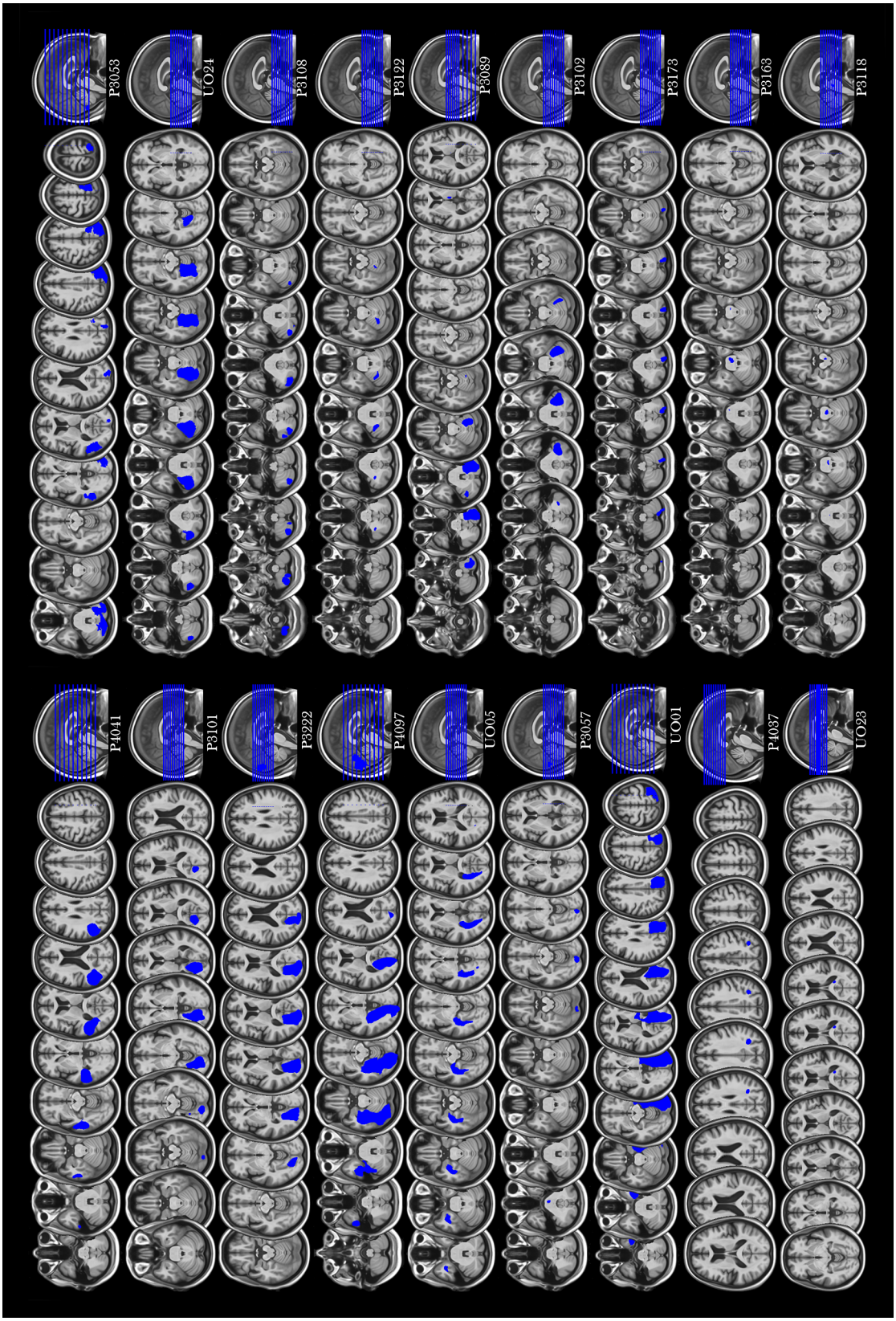


Figure 4.10: Patient Lesions in Posterior Group

Lesion Location in the Posterior Group

Table 4.8, gives an overview of the location of damage for the posterior patients. The lesion locations for impaired patients will now be discussed. Three impaired posterior patients had cerebellar lesions. For two of these patients the lesion was isolated to the cerebellum (P3102, P3108) and for the remaining patient there was damage to both the cerebellar and the inferior posterior cortices (P4097). All three of these patients had damage overlapping with crus I and/or crus II (previously associated with cognitive impairment Tedesco et al., 2011; Stoodley et al., 2016). It is also worth noting that P3180 (an impaired frontal/posterior patient) also has a cerebellar lesion in the crus II region. This lesion overlaps with P3108 (their lesions extend through both the crus I and crus II regions) and these two patients are the only two solely impaired on the general executive factor (see Figure 4.11). P3102 has an additional impairment in processing speed, whereas P3108, P4097 and P3180 do not.

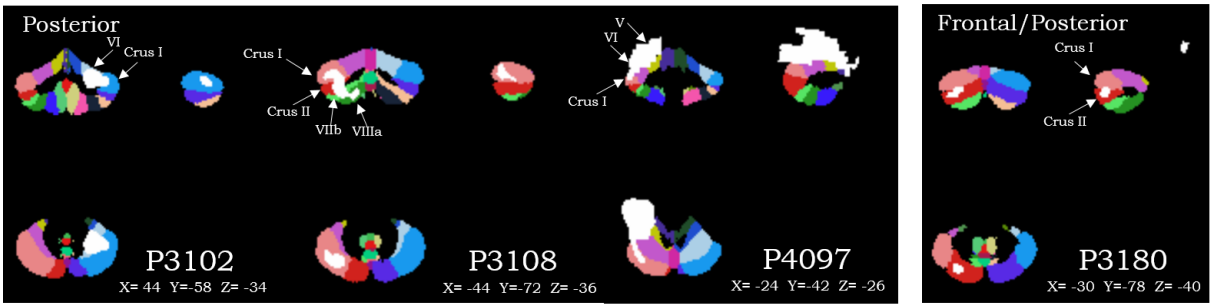


Figure 4.11: Lesion visualisation for impaired patients with cerebellum infarction. Lesions are displayed in white on top of a CB atlas (Diedrichsen, Balsters, Flavell, Cussans, & Ramnani, 2009; Diedrichsen et al., 2011).

However, please note that there are patients in this sample that have lesions that overlap with these CB lobes that do not display impairment in both the posterior (P3173, P3089, UO24) and frontal/posterior groups (P2027, P3104). Moreover, there was only one patient who had a purely anterior CB lesion (P3122). They were not impaired on any factor or any of the raw neuropsychological measures.

Impaired Posterior Patients Without Cerebellum Damage

The were two posterior patients without cerebellum damage who were also impaired on the general executive factor (P3057 and P4037). P3057 had a lesion to the occipital lobe, this lesion was on the junction between the occipital pole, occipital fusiform gyrus and the lingual. This region overlapped with the additional cortex damaged displayed by P4097 (CB patient). Both patients were not impaired on the raw scores of the the visual selection task making it unlikely that a visual deficit such as hemianopia was present. Additionally, P2027 (frontal/posterior group) has a lesion overlapping with this area and has no impairment.

Given the information above it could be suggested that the impairment displayed by P4097 is more likely to be related to the CB lesion, than the damage to the occipital lobe. Moreover, P3057 also has an additional lesion to the pons. Although both other patients P3163 and P3118 with pons lesions were not impaired, P4097's lesion was situated more anterior and may have contributed to the impairment. Therefore, the impairment may also have had a different origin than the occipital damage.

Finally, the only patient in this group to display impairment on all factors was P4037 (including processing speed). They had a smaller lesion to the lateral occipital superior division, extending into the precuneus. It is worth noting that this lesion was primarily white matter (e.g. SLF I/II, arcuate, IFOF, Inferior Longitudinal, internal capsule). It could be suggested that disconnection may have contributed to the more extensive impairment displayed.

White matter disconnection will now be examined to see whether it indicates why some patients may be impaired after damaging a particular region, whereas others do not display impairment.

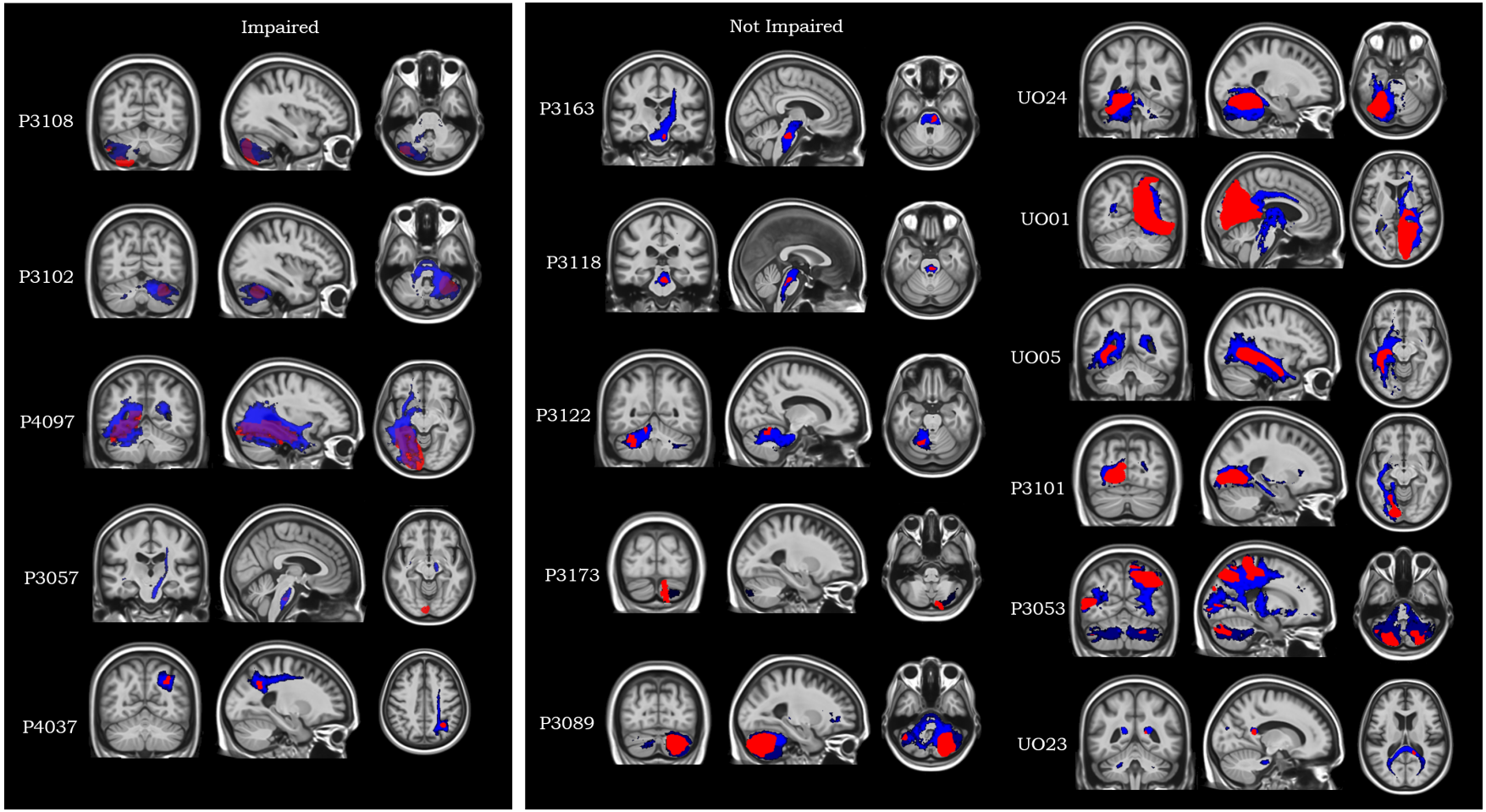


Figure 4.12: Lesion location and white matter disconnection (disconnectome maps set to .8 probability of disconnect, Foulon et al., 2018) for posterior patients. Lesions are displayed in red and white matter disconnection in blue. Please note that a visualisation for impaired patients in the frontal/posterior group can be found in Appendix C.7 (p.348).

White Matter Disconnection in the Posterior Group

In order to see whether white matter disconnection might have contributed to the impairment displayed by these patients the BCB toolbox was utilised to make disconnectome maps for each of the posterior patients. For this analysis the threshold was set to 80% probability of disconnect. See Figure 4.12 for a visualisation of the results (blue), with the lesion map overlaid (red) for each posterior patient. The results displayed in Figure 4.12 should help illustrate the potential distal effects that may occur due to posterior damage. Please see Table 4.8 for a written overview.

The two impaired cerebellum patients (P3108 and P3102) both have damage to the Cerebellum-Ponto-Cerebral (CPC) tract. P3102 has additional damage to the superior and inferior cerebellar pedunculus. Interestingly, damage to the superior CB pedunculus is also shared by P3180 (frontal/posterior group). This patient has previously been noted for the overlap with CB damage displayed by P3108, considering both patients are impaired solely on the main executive factor. The patient who had both CB and cortical damage P4097 had quite substantial white matter disconnection, including the CPC tract as with the other two patients, but also including damage to the inferior fronto-occipital fasciculus (IFOF), the inferior longitudinal fasciculus, the posterior cingulum, the corpus callosum and optic radius. Therefore, making damage to the CPC tract fairly consistent amongst impaired patients.

The white matter disconnection for P3057's occipital lesion was minimal, although a small amount of damage was done to the IFOF. There was quite substantial disconnection resulting from the lesion in the pons. This included the white matter connection from the pons, the cortico-spinal tract and the internal capsule.

Finally, it is observed that patient P4037 also has some damage to the IFOF and some to the inferior longitudinal and the arcuate. However, the primary disconnection was of SLF I and SLF II, thus the impairment may be accounted for by a disconnection of the Frontal parietal attentional control network. Also of note is that the impaired patients P3239, UB11 and P3043 from the frontal/posterior group also had damaged to the SLF tracts, the striatum and internal capsule (see Appendix C.7, p.348, for visualisation). Therefore, it seems that damage to the SLF, IFOF and striatum is also demonstrating some consistency amongst impaired patients.

In summary, it seems that damage to the cerebellum or surrounding white matter (e.g. CPC, SCP) is linked to executive dysfunction in the posterior patient group. Furthermore, some consistencies were seen in damage to the IFOF, SLF and striatum.

4.5 Discussion

There were three research questions addressed in the current investigation: Can damage to posterior brain regions lead to executive dysfunction? Is the type of dysfunction experienced fundamentally different from that of frontal patients (do they both experience impairment in general executive functioning)? Are there any specific posterior lesion locations that lead to impairment? For each research question, the current findings will be summarised and discussed.

Executive Dysfunction in Posterior Patients: Raw Scores

To first address the question of whether posterior damage can influence executive dysfunction individual patients' performance on raw scores was compared to age matched controls. Several posterior patients were impaired across the selected tasks including the rule finding task, executive set switching and both auditory and visual selection tasks. Secondly, a BiFactor analysis was run in order to examine the overall executive factor in isolation from the other more specific factors. When the individual factor scores were compared to age matched controls it was once again seen that some of the posterior patients were impaired on multiple factors, including the general executive factor. The results demonstrate that on an individual level patients with purely posterior damage can display executive impairment against age matched controls.

The patient groups were then compared on a group level. On average both frontal-subcortical and posterior patients performed significantly worse on all the factors compared to healthy controls. However, this was not the case for the frontal/posterior group. It was also observed that the posterior group was not significantly different to the frontal-subcortical group. These group effects were observed after controlling for the effect of age, education, processing speed and language. Therefore, both the individual and group data gives support for the assertion that executive dysfunction can arise following poste-

rior damage. Importantly, this difference was observed on the general executive factor, even after controlling for the influence of processing speed. Another important point to note, is that the group differences between posterior patients and controls are observed despite the heterogeneity of the the posterior group of patients.

On this surface level of investigation, the results suggest that posterior patients can display executive dysfunction. This observation compliments the growing body of literature that suggests that goal directed behaviour is produced by a network of frontal, subcortical and posterior brain regions (e.g. Godefroy, 2003; Stoodley et al., 2016; Manto & Mariën, 2015; Schmahmann & Sherman, 1998). It also corresponds with the VLSM work that has demonstrated a connection between posterior and subcortical regions on a global executive function factor (Gläscher et al., 2012; Robinson et al., 2014). Furthermore, it stands in opposition of research which has found that posterior patients do not significantly differ from controls on measures of executive dysfunction (e.g. Stuss et al., 2000).

Executive Dysfunction in Posterior Patients: Factor Scores

The second question addressed was whether executive dysfunction displayed in posterior patients was different to that displayed by frontal patients. This question was the reason why a BiFactor analysis was performed to explore whether the patients were impaired on the general factor which is meant to represent the "unity" of executive dysfunction or whether they only displayed impairment on specific executive factors ("diversity" of EF). For example, it could have been that posterior patients only displayed impairments on spatial attention, rather than the general executive factor. However, this pattern was not observed and both frontal and posterior patients demonstrated impairment on the general executive factor.

First the individual scores were examined and compared to age matched controls. It was observed that there were both frontal and posterior patients that were impaired on the general executive measure. The only dissimilarity observed was that the majority of posterior patients were not impaired on the temporal attention/working memory factor, whereas, frontal sub-cortical patients were impaired on all factors. Next the group analysis was performed and average factor scores compared. As previously mentioned both frontal-subcortical and posterior patient groups were impaired in comparison to controls (but not the frontal/posterior group). When the patient groups (frontal-subcortical to posterior) were compared to each other, it was observed that they did not significantly differ on any of the factors.

These group differences were examined again, comparing solely the patient groups whilst controlling for lesion lateralisation and lesion volume (note that frontal subcortical and frontal/posterior groups were collapsed for this analysis). There were no group differences observed. Evidence for the null hypothesis was tested using a Bayesian top down analysis. Only weak evidence at best was observed in support of the null hypothesis (no differences between groups). Therefore, no firm conclusions should be drawn regarding the differences between frontal and posterior groups. Taken together, these results suggest that posterior lesions can result general executive dysfunction which is similar to that observed in frontal patients. Although, further investigation with a larger sample is desirable.

The present findings suggest that frontal and posterior patients do not differ substantially in the way they display executive dysfunction. This result is in line with past studies suggesting that frontal and posterior patients do not consistently differ on tests of executive dysfunction (e.g. Andrés & Van der Linden, 2002; Vilkki et al., 2002). Additionally, these results are compatible with the VLSM studies that found frontal, subcortical and posterior lesion locations associated with the overall general executive

factor (Gläscher et al., 2012; Robinson et al., 2014). Whereas, it does not support the view that frontal patients are significantly more impaired than posterior patients (e.g. Owen et al., 1990; Shallice, 1982; Cipolotti et al., 2017).

Lesion Locations Associated to Executive Dysfunction.

Despite the exploratory nature of the final analysis (due to a small sample size), some consistencies were observed in which lesion locations were associated with impairment. Firstly, it was apparent in the frontal-subcortical and to some extent in the frontal/posterior group that damage to the basal ganglia was related to executive dysfunction. These findings are in line with VLSM work that has found that an overall EF factor is linked to the putamen and globus palladus (Gläscher et al., 2012).

The involvement of subcortical regions in executive dysfunction has become increasingly recognised (e.g. Duffau, 2012b; Krause et al., 2012; Damasio, Damasio, & Chui, 1980; Cools et al., 2006; Thoma et al., 2008). One of the leading theories is that the basal ganglia are involved in attentional gating of information based on task relevance and in the updating of higher order hierarchical contexts in working memory (Nee & Brown, 2013). In particular, it is posited that these structures are responsible for modulating the degree of flexibility verses stability of working memory representations (e.g. Braver & Cohen, 2000; Reynolds & OReilly, 2009). This sort of modulation is very important for successful executive functioning because stability can lead to preservation and flexibility can lead to distractibility.

It was expected that the frontal/posterior group would show a putative effect of difficulty, especially considering the prevalence of large MCA strokes that damaged a large portion of the fronto-parietal network. Previous work has suggested that damage to the PFC is associated with impairments in executive dysfunction (e.g. Burgess & Shallice, 1996; Godefroy et al., 1999; Stuss et al., 2000; Delis et al., 1992; Tsuchida & Fellows,

2013) and specifically on a global executive factor (Gläscher et al., 2012; Robinson et al., 2014). However, this pattern was not observed in the current sample with only one of the large MCA patients demonstrating impairment on the factor scores (the other impaired patients had smaller lesions distributed through both frontal and posterior regions).

Overall the absence of impairment in some of these patients is intriguing in itself considering the very large lesion volumes (e.g. 168, 184 cm^3). Although it is worth noting that more patients demonstrated impairment on the raw scores. There are multiple variables that can lead to protection against cognitive decline following stroke (e.g. education, age, cognitive reserve, Price et al., 2017). So the absence of these expectations in such a small heterogeneous sample is perhaps not so unusual. However, it does once again demonstrate that not all frontal patients are impaired on executive functioning (Baddeley et al., 1997).

Regarding the posterior group, it was initially expected that damage to, or disconnection of, the fronto-parietal network would lead to executive dysfunction. This was based on multiple studies that have demonstrated the importance of this network in executive functioning and attentional control (e.g. Rabinovici et al., 2015; Collette et al., 2005; Duncan, 2013). Although some patients had disconnection of the IFOF and the SLF, in general this was not the primary observation with the results aligning more with research suggesting the importance of the cerebellum in executive dysfunction (Schmahmann & Sherman, 1998; Schmahmann, 1998; Manto & Mariën, 2015; Stoodley et al., 2016). Taken together these findings compliment Rabinovici et al (2015) who highlighted the importance of subcortical regions, along with cerebellum and white matter connectivity in executive dysfunction.

Cerebellar Involvement in Executive Dysfunction

The conclusion that cerebellar damage can lead to executive dysfunction is based on observed impairment for several patients with isolated cerebellar lesions and several with cerebellar lesions and additional cortical damage. Although the lesions were heterogeneous with minimal overlap, the commonality between them was that they all had damage (of varying extent) to crus I and/or crus II. The damage was also associated with disconnection of the cerebellar-ponto-cerebral tract and/or the superior and inferior cerebellum peduncles. This suggests that damage to, or disconnection of, the cerebellum with the cerebral cortex may lead to executive dysfunction.

These results compliment previous research which suggest that damage to the lateral posterior cerebellum can lead to "dysmetria of thought" (e.g. Schmahmann, 1996, 2004; Middleton & Strick, 2001; Dum & Strick, 2003; Strick et al., 2009). The cognitive control difficulties associated with this phenomon can affect both cognitive and affective functions and thus, have been termed Cerebellar Cognitive Affective Syndrome (CCAS Schmahmann & Sherman, 1998; Stoodley et al., 2016). It is now well documented that the cerebellum is indirectly connected to locations throughout the association cortices, including the frontal and parietal lobes (Strick et al., 2009; Middleton & Strick, 2001).

Of particular importance for the present findings is that crus I/II are interconnected to lateral prefrontal cortex (broadman area 46) and that these connections are distinct from motor control (Middleton & Strick, 2000; Strick et al., 2009; Kelly & Strick, 2003). There are connections that project from the lateral cerebellum, via the dentate nucleus and the thalamus to the PFC and projections back to the cerebellum via the pontine nuclei (Heyder et al., 2004; Schmahmann & Pandyat, 1997; Middleton & Strick, 1994; Daum & Ackermann, 1997). See Buckner 2013 for an extensive review and helpful visulisation (Figure 1.4, p.21). Overall this connectivity pattern demonstrates that the cerebellum is well placed to influence executive computations in the association cortices

(Clower, Dum, & Strick, 2005; Middleton & Strick, 2001; Strick et al., 2009).

The exact role of the cerebellum in these cognitive tasks has been debated. One of the main hypotheses is that the cerebellum is involved in the creation of internal models (Ito, 2008). These internal models are suggested to facilitate adaptive control of mental activity (Doya, 1999; Ito, 2008). This conceptualisation of cerebellum function integrates results from studies that have found the cerebellum to be important to prediction, timing, sequencing and adaptation following error (for a review see Sokolov, Miall, & Ivry, 2017). The notion that the cerebellum plays a role in representing internal models of behaviour might be considered as consistent with the findings of the current observation that cerebellum lesions can result in global executive impairment. It may also account for the regular identification of the cerebellum in the multiple demands network (e.g. Fedorenko et al., 2013; Duncan, 2013) and recent account of its involvement in the dorsal attention network (Brissenden, Levin, Osher, Halko, & Somers, 2016).

Functional neuroimaging has also corroborated these links with cognitive tasks found to activate posterolateral cerebellar hemispheres (e.g. Stoodley, 2012; Keren-Happuch, Chen, Ho, & Desmond, 2014). One particular cognitive function repeatedly implicated to involve the lateral posterior cerebellum is working memory (Hautzel, Mottaghy, Specht, Mller, & Krause, 2009; Marvel & Desmond, 2010; Stoodley & Schmahmann, 2009, 2010). Interestingly activity is seen bilaterally and non-modular, with similar activations for both verbal and visuo-spatial tasks (Hautzel et al., 2009). Activation in the cerebellum during working memory tasks has been found to be load dependent in the same manner as the parietal and lateral PFC cortices (Salmi et al., 2010; Kirschen, Chen, Schraedley-Desmond, & Desmond, 2005). Of particular importance for the current observations is that Crus I (and sometimes Crus II) has previously been implicated in attention (Townsend et al., 1999; Baier, Dieterich, Stoeter, Birklein, & Müller, 2010; Striemer, Cantelmi, Cusimano, Danckert, & Schweizer, 2015) and working memory tasks

(Allen, Buxton, Wong, & Courchesne, 1997; Chen & Desmond, 2005a, 2005b; Kirschen et al., 2005; Ilg et al., 2013; Ravizza et al., 2006).

The present investigation compliments past lesion studies which have suggested that damage to the lateral posterior regions of the cerebellum can lead to cognitive deficits (Gottwald et al., 2004; Schmahmann & Sherman, 1998; Fiez, Petersen, Cheney, & Raichle, 1992). Some of the observed difficulties span working memory (Ilg et al., 2013), attention (Gottwald et al., 2004), rule based memory tasks (Fiez et al., 1992), verbal fluency (Richter et al., 2007; Hubrich-Ungureanu et al., 2002), spatial fluency (Gottwald et al., 2004), problem solving (Hallett & Grafman, 1997) and attention/executive difficulties (Stoodley et al., 2016; Schmahmann & Sherman, 1998; Bellebaum & Daum, 2007; Gottwald et al., 2004; Tedesco et al., 2011).

One suggestion is that the cerebellum is part of the central executive of a working memory model (Hautzel et al., 2009). In the current study, one consistency across tasks is that task rules and relevant target information need maintaining on line to guide behaviour. Therefore, the current findings could be considered as compatible with this view. Interestingly, impaired working memory following cerebellar infarction has been reported to produce differences in BOLD response across the cortico-cerebellar network (e.g. DLPFC, parietal cortex, SMA and anterior cingulate) during an n-back task. This finding suggests that localised cerebellar lesions may result in disruption of the attentional control network overall (Ziemus et al., 2007).

Subcortical Nuclei to Cerebral Connections

Another interesting consideration given the observations made in the current analysis is that subcortical nuclei including both the dentate of the cerebellum and the basal ganglia have closed loops with association regions in the cortex (Middleton & Strick, 2001), as well as being interconnected with each other (Bostan & Strick, 2010). For example, transneu-

ral transport HVS1 (herpes simplex virus type 1) was utilised to examine both basal ganglia-thalamocortical and cerebellar-thalmocortical pathways, injections into DLPFC (BM 46/9) labelled neurons in dentate nucleus and globus palldus (this connectivity was observed as bidirectional Middleton & Strick, 2000, 1994). Both of these sets of nuclei have connections with frontal regions involved in higher level cognition and working memory (Middleton & Strick, 2000). Therefore, these closed loops between the nuclei and the cortex may be important in setting context for achieving goal directed behaviour. This observation perhaps provides an explanation for why frontal-subcortical and cerebellar lesions are both associated with impaired general executive functioning.

Time Since Stroke

One additional observation in this study is that executive dysfunction was found in patients in chronic stages of recovery (>6 months post stroke). Studies in the past have found that elements of executive dysfunction were transient in cerebellar patients, subsiding in the chronic phase of recovery (e.g. Neau, Anllo, Bonnaud, Ingrand, & Gil, 2000; Heyder et al., 2004; Richter et al., 2007), or that only specific deficits remain (e.g. response control and verbal fluency, Alexander, Gillingham, Schweizer, & Stuss, 2012). Here it is shown that for some patients with a cerebellar lesion executive dysfunction can remain in the chronic phase of recovery. This compliments previous findings that executive dysfunction can be present in a sample of mixed subacute and chronic patients (Tedesco et al., 2011).

Covariates

Both age and education were found to be significant covariates. This compliments past research that has found that age (Knoflach et al., 2012) and education (Mirza et al., 2016) can affect outcome following stroke (Price et al., 2017). Two other covariates of interest were language performance and processing speed. By controlling for them in the group

analysis it allowed assessment of whether executive dysfunction was seen after controlling for the relationship between these variables and the executive factors. Interestingly, for the frontal subcortical group only the patient who was unimpaired on the executive measures demonstrated impairment on the processing speed measure. These results conflict with some past results which suggest that frontal stroke was mainly related to slowed mental speed (Leskel et al., 1999). In the posterior group there were three patients impaired on the processing speed factor, two of which were also impaired on the executive factors. However, it was also observed that three of the patients were impaired solely on executive factors, without an additional processing speed deficit. Therefore, it can be suggested that some posterior patients display executive dysfunction which cannot fully be explained by slowed processing speed.

In the group analyses no main effect of lesion lateralisation was found. Our current understanding of lateralisation of cognition in the cerebellum is inconclusive; some studies demonstrate that right side lesions cause greater impairment (Gottwald et al., 2004; Alexander et al., 2012) and others find no significant differences (Ravizza et al., 2006). It can be noted that the projection from the cerebellum to the different association cortices is fairly symmetrical (Buckner, 2013). Therefore, if there are differences found it could be driven by lateralisation of function in association cortices it projects to (e.g. right cerebellum being more involved when verbal tests are used, Gottwald et al., 2004). Furthermore, it has been noted that stronger cerebral functional asymmetries are accompanied by stronger cerebellar asymmetries (Wang, Buckner, & Liu, 2012) and thus small sample sizes with particular patterns of asymmetries could influence lesion lateralisation results.

There was also no main effect of lesion volume on all but the temporal attention/working memory measure. In general a trend was seen towards smaller lesions resulting in worse impairment. However, this could due to small lesions being more com-

mon in the subcortical brain regions. It is not inconsistent to find no effect of lesion volume in the literature and there are multiple other confounding factors that must be kept in mind when considering it as a contributing factor. For example, lesion volume probably should not be considered to have the same influence for patients with one large lesion as compared to patients with multiple small lesions. Equally, the shape of the lesion can be seen as important, a lesion with the same volume as another may have different effects depending on how it is oriented. For example, the same size lesion could lay across a tract so that it completely disconnects it, or lay along it so that it is damaged but still connected. Another important factor to consider is the relationship between the size of the lesion and the region it overlaps with. For example, a small lesion may not have a large effect when situated within a large cortical lobe, but could totally destroy one of the small nuclei (e.g. substantia nigra). Moreover a small lesion that disconnects a white matter tract may cause widespread network dis-regulation which is more substantial than the volume would suggest. Although it is an important factor to consider, how meaningful it is without additional information should be questioned.

Limitations

There are several limitations in the current study that must be taken into consideration when interpreting the results. Firstly, the sample size is fairly small and consists of patients with heterogeneous lesion types and locations and therefore larger scale work is required to determine generalisability. In the current analysis sources of individual variability have been included as covariates wherever possible, however, there were many left uncontrolled for (e.g. depression, premorbid cognitive status, differences in neuronal and vascular network, fatigue, Price et al., 2017). In the present analysis a less traditional set of tests was used in the BiFactor analysis. Subsequent work could aim to use more commonly utilised tests (see Friedman & Miyake, 2017) so that the results can be easily integrated with existing literature.

The scans utilised to perfrom lesion delineation are of mixed modality (CT and MRI). It should be taken into account that patients with CT scans will have lesions that were defined at much worse resolution than those with MRI available. If further examination is to be done, high resolution scans would be desirable considering the regions of interest in this particular study are small and close together. The compact organisation of these regions also becomes problematic because lesions tend to cover more than one location which may produce co-morbid and confounding cognitive difficulties such as ataxia (Strick et al., 2009).

Another important factor to consider is the potential of diaschisis, in which changes in connectivity cause hypometabolism in a distal brain region (Carrera & Tononi, 2014; Saita et al., 2017). Damage to the cerebellum can be accompanied by hypometabolism in contralateral cerebral regions that it projects to (Beldarrain, Garca-Monc, Quintana, Llorens, & Rodeo, 1997; Saita et al., 2017). Future work may consider including additional measures such as perfusion imaging or cortical thickness to control for these effects. Finally another consideration to take into account when working with this type of population is signs of additional degeneration not relating directly to the lesion. In the present analysis all comparisons have been made to an age matched control group. This step was taken to try and assure that the impairment seen was that above normal age related decline. The scans were examined and in some cases some evidence of subcortical cerebral vascular disease were apparent. For individuals caution should be taken when interpreting the results as it is difficult to establish whether they were experiencing dysfunction prior to the stroke. In large scale investigations, adding this element to the inclusion criteria would be ideal.

Conclusions

The present investigation once again gives support for executive dysfunction following posteriorly located lesions. Interestingly, both posterior and frontal-subcortical patients displayed impairment on a general measure of executive function (unity of executive functioning). Both posterior and frontal-subcortical patients demonstrate similar executive dysfunction. These findings are compatible with the idea that executive control of behaviour is the result of a network of frontal, subcortical and posterior brain regions. Although in the current sample, lesions to the basal ganglia and cerebellum were most consistently associated with impairment. This corroborates the idea that these subcortical regions and their connectivity with the cerebral cortex are important in contextual control of behaviour. Overall, it is hoped that this work has added and supported our current understanding of executive dysfunction resulting from posterior damage by utilising a BiFactor analysis to compare patients on both general executive functioning and its more specific elements.

In the current chapter the use of a BiFactor model allowed previously hidden patterns of impairment to be examined. This highlights the importance of considering task impurity and its confounding effects when studying higher level processes such as executive function. In the next chapter a novel experimental task will be presented which aims to better dissociate errors that can occur when the task model fails to successfully bias behaviour.

Part II

Attentional Control in a Healthy Population

Chapter 5

Dissociating Goal Activation Errors

Revisiting the impact of task switching and perceptual difficulty of the instructional cue on goal neglect.



5.1 Abstract

Introduction: Goal neglect is "the disregard of task requirements, despite them being both understood and remembered". Goal neglect is hard to measure because it can manifest as multiple types of error. The current investigation aimed to develop a novel paradigm that could dissociate neglect of environmental monitoring (failure to bias perception), from neglect of behaviour (failure to bias action). The paradigm was then utilised to revisit the impact of infrequent task switching and the perceptual difficulty of the instructional cue for these dissociated goal activation error types.

Method: The experiment had three parts: presentation of a previous learnt instructional cue indicating response rule (clockwise or anticlockwise), a secondary task (immediate recall of an orientation), in which the instructional cue is applied (direction to turn the dial during recall) and a trial rule recall. The rule recall provided a measure of errors in monitoring and the use of a response mode that allowed correction of errors made due to delayed configuration. A mixed design was used to examine the within subject effect of switch type (repeat or switch) and the between subject effect of cue type (colour or symbolic) in a sample of 60 healthy participants (Age: M=50, $\pm$ 23).

Results: It was observed that both switching and the use of a perceptually harder cue increased the proportion of trials in which the participant incorrectly recalled the trial rule (monitoring errors). Whereas, both manipulations did not influence the proportion of delayed task configuration or goal neglect (delayed or failed action selection). The repetition of response rule had an immediate benefit for the proportion of incorrectly recalled rules, suggestive of attentional lapses subsequent to switching when using a perceptually difficult cue. Whereas, higher repetitions were required before any benefit was observed for delayed configuration or goal neglect. The results demonstrate dissociable errors related to goal activation and show how these manipulations may have a differential impact on each error type.

5.2 Introduction

The ability to be goal directed is fundamental to nearly all aspects of daily living (Barker-Collo & Feigin, 2006; Mole & Demeyere, 2018; Leśniak et al., 2008). Without the capacity to turn our internal directives into physical action, behaviour becomes disorganised, chaotic and inert. Behaviour can become fragmented and unconstrained by relevance; inappropriate actions intrude on performance, relevant actions are omitted and the goal state is often abandoned before completion (e.g. Duncan, 1986; Duncan, Burgess, & Emslie, 1995; Luria, 1966; Milner, 1963). In both frontal patients (e.g. Duncan, 1986) and to a lesser extent in a healthy population (e.g. De Jong et al., 1999; Duncan et al., 2008) sometimes a total disconnect between understanding, intention and behaviour is observed. This phenomenon is known as goal neglect: a total disregard for task requirements despite them being understood and remembered (Duncan et al., 1996). A clear example of goal neglect is given by Luria (1966) who describes a patient who when required to squeeze a "squeeze" bulb when a light comes on, would on seeing the light say "I must squeeze" without actually performing the action. In essence, goal neglect is the failure to enact goal directed behaviour despite both knowledge and intention.

Although the definition of goal neglect is clear, it is difficult to measure with clarity. The reason being that it is symptomatic; a behavioural consequence of a failure somewhere in a highly diverse and domain general attentional mechanism (Duncan, 2013). This mechanism is the product of a highly adaptable control system in the brain, which preferentially focuses on information which is relevant to the current epoch of behaviour (e.g. relevant stimuli, responses, rewards, rules and working memory contents, Duncan, 2001; Duncan & Miller, 2002; Duncan, 2010; Stokes et al., 2013; Woolgar et al., 2011, 2016). This pattern of activity can be thought of as a task model, which configures an attentional episode giving priority to information and action of current relevance (Duncan et al., 2008; Duncan, 2013, 2001). Behaviour is influenced in a top-down manner by

biasing perception and action based on task relevance (Haynes et al., 2007; Duncan, 2001; Woolgar et al., 2011). Goal neglect can be conceived as the failure of this task model to successfully exert top-down control (De Jong et al., 1999; Duncan, 1986; Norman & Shallice, 1986).

Giving additional attentional weight to items of relevance makes it more likely they will be encoded into working memory (Bundesen, 1990; Klink, Jentgens, & Lorteije, 2014). However, this process is competitive and the priority of an item is calculated by combining attentional weighting from multiple sources. In particular, these top-down signals are combined with bottom-up influences such as salience, speed and familiarity (e.g. Bisley & Goldberg, 2010; Duncan, 1986; Thompson et al., 2005; Ptak, 2012). In order to be successful in this competition for behavioural control the task requirements need to be represented with clarity and strength (e.g. Munakata et al., 2003). For example, if the complexity of the task instructions is manipulated (by adding extra but irrelevant information), instances of goal neglect increase (Bhandari & Duncan, 2014; Duncan et al., 2008). Overall, a clear and concise task model will be more competitive and thus more likely to successfully modulate behaviour in favour of current task demands.

In addition to the characteristics of the task representation, the success of attentional control is also influenced by the physical properties of the task relevant stimuli (e.g. Klink et al., 2014; Ptak, 2012). In the instance that there has been weak or incomplete goal activation of the appropriate task schema, strong environmental cues can compensate for weak top-down attentional prioritisation (De Jong et al., 1999; Woolgar et al., 2011). Experimentally this is demonstrated with instances of goal neglect being influenced by the explicitness (ease of stimulus response mapping) or perceptual difficulty (how easy it is to process and dissociate from other cue types) of the instructional cue (e.g. De Jong et al., 1999; Duncan et al., 1996; Towse et al., 2007). In existing goal neglect paradigms the manipulation of the strength of externally relevant information

has frequently been utilised to increase instances of goal neglect (Duncan et al., 1996; Towse et al., 2007; Iveson et al., 2017). For example in Bhandari et al. (2014) they state *"We designed critical trials to be especially sensitive to goal neglect. First, they were less frequent than regular trials. Second, the two symbols used to signal regular and critical trials were visually similar. Therefore, participants had to closely monitor the symbols to detect changes in context".* However, it is yet to be examined whether these environmental manipulations differentially impact on the presentation of goal neglect (e.g. failure in control of perception verses action).

It could be suggested that these bottom-up manipulations of environmental support may be more likely to influence a failure to bias perception rather than action. For example, weak top-down control could interact with the availability of attentional resources rendering the participant unaware of the change in instructional cue (Dockree, Kelly, Foxe, Reilly, & Robertson, 2007). If the cue has not been processed it could be argued that the participant did not know what to do on the current trial. These types of errors are harder to reconcile with the definition of goal neglect because the participant lacks the current knowledge to guide behaviour. To return to the patient example given by Luria (1966), if the patient had not seen the light, the observation that they failed to squeeze the button would seem less remarkable. However, this type of error is still of great interest and could indicate the ineffectiveness of the task model to bias environmental monitoring for pertinent information. These types of errors may represent tonic fluctuations in the effectiveness of the task model (De Jong, 2000; Dockree et al., 2007).

The dissociation of different goal activation errors can go further. If the instruction cue has been encoded there could still be either a partial or full failure for the task model to bias action. A partial failure would simply represent delayed action selection due to incomplete task configuration, whereas a total failure would be representative of the task model being ineffective (akin to the patient example given by Luria 1966). The

main difference in these types of error is that delayed configuration will result in the enactment of goal directed behaviour if given sufficient time to do so, whereas a total failure is unlikely to resolve unless further support is provided.

Delayed configuration can result from a sub-optimal but still effective task model (De Jong et al., 1999; De Jong, 2000), but could also be modulated by the speed with which relevant information is encoded from the environment. Any experimental manipulation that may increase the time course of perceptual identification of the instructional cue, could theoretically impact on subsequent speed of task configuration. To illustrate, single cell recordings in non-human primates have observed that the initial activity of neurons in the lateral prefrontal cortex is associated with the physical properties of the cue (∼90ms), subsequently transitioning to stimulus invariant encoding of context and relevance (∼140ms), before settling into a low activity state representing the choice decision (∼500ms Stokes et al., 2013). The idea that delayed perceptual identification can postpone subsequent task configuration is consistent with the observation that goal neglect is more frequent when a smaller inter-trial interval is used (200ms-160ms Iveson et al., 2017) and could provide clarity for the observed relationship between processing speed and goal neglect (Iveson et al., 2017). Goal neglect as a result of delayed task configuration may be conceptually different from that of a complete failure and further work is required to try and dissociate these sources of error.

In the following investigation a novel paradigm was developed in order to better dissociate poor environmental monitoring and delayed task configuration from pure instances of goal neglect. To achieve this dissociation two important design features were utilised: trial by trial rule recall (to dissociate monitoring errors) and a response mode that allowed correction (to dissociate delayed task configuration). This paradigm was used to revisit the impact of infrequent switching and perceptual difficulty of the cue.

5.3 Method

Sample

A sample of 60 participants (30 in each group), were recruited from the Cognitive Neuropsychology Centre control database or via the online Oxford Recruitment Participant system. Inclusion criteria included having normal or corrected to normal vision, having no history of neurological or psychiatric conditions and being over the age of 18. All participants were reimbursed £10 per hour for their time.

Experimental Design

The following paradigm was designed to dissociate goal activation errors by including a trial by trial rule recall (to check for monitoring failures) and a response mode that allowed correction (to dissociate delayed configuration). The experiment had three parts: presentation of a previous learnt instructional cue indicating response rule (clockwise or anti-clockwise), a secondary task (immediate recall of an orientation), in which the instructional cue is applied (direction to turn the dial during recall) and a trial rule recall. The perceptual difficulty of the cue is examined between groups (colour vs symbolic cue) and switching response rules was examined within subjects (performance on switch as compared to repeat trials).

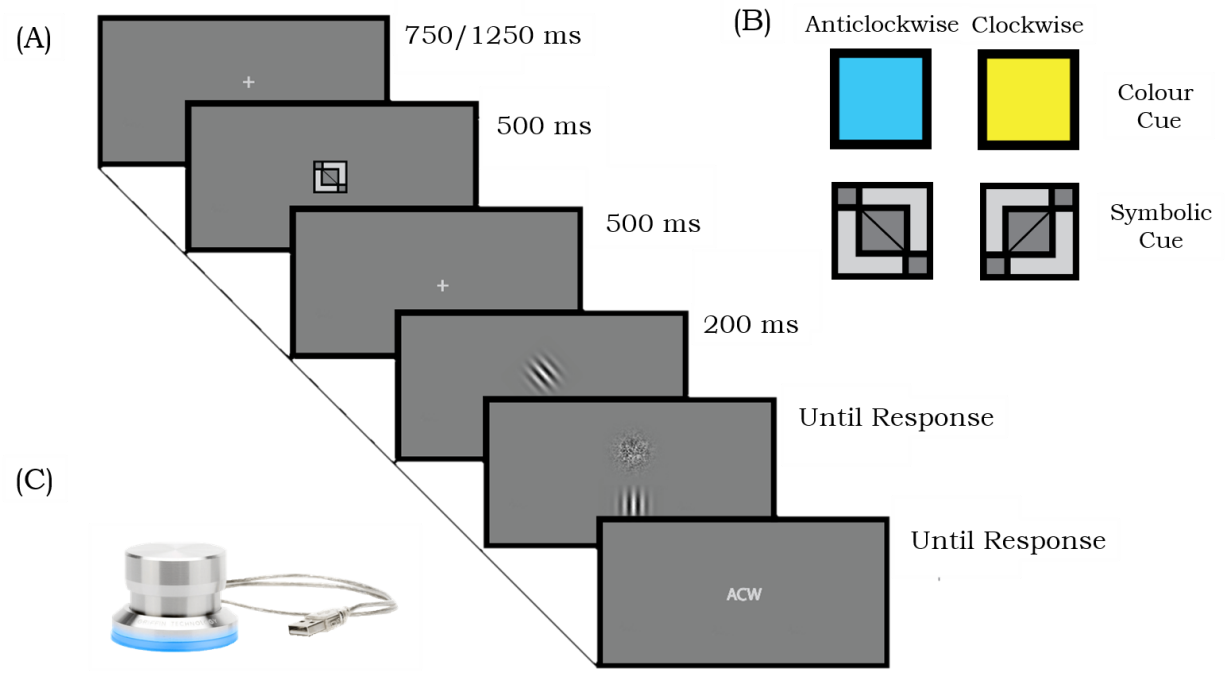


Figure 5.1: (A) Experimental Design. A cue was presented indicating the response rule (clockwise or anti-clockwise). The orientation memorandum was displayed and then masked. The participant had to recall the orientation using a dial. During recall they had to turn the dial in the direction indicated by the cue. The participant then had to recall the current response rule by selecting one of two keys. **(B)** Cue - Response Rule Associations for Both Colour and Symbolic Cue Types **(C)** Response dial.

The stimuli were presented on a 21 inch LED monitor (BenQ XL2411) at a resolution of 1,920 x 1,080, with a vertical refresh rate of 100Hz. Experiments were programmed in Python 2.7, using the PyGaze toolbox (Dalmaijer, Mathôt, & Van der Stigchel, 2014). The background colour was grey (RGB 127,127,127). First a white fixation cross was presented in the centre of the screen, at a visual angle of 0.67°, 0.67°, for 750 or 1250 milliseconds. The cue was then presented at the same location (2.48°, 2.48°) for 500 milliseconds. The cue was followed by a second fixation for 500 milliseconds, with the intention for this period to act as a preparatory interval for response rule retrieval and task configuration (times chosen based on Stokes et al., 2013).

The next stage required the participant to remember a briefly presented orientation. A gabor (7.62°, 7.62°, spatial frequency 0.5 cycles per degree) was presented centrally for 200 milliseconds. The gabor acted as a memorandum, illustrating an orientation to be remembered. This orientation was chosen randomly from 0-180°, non-repeat and with the constraint of being at least 5° different from the target orientation in the previous trial. To minimise after image, the gabor was immediately masked for 500 milliseconds using a noise patch (7.62°, 7.62°). The orientation recall screen followed. The noise patch was retained onscreen at the same location. A probe gabor was displayed below the noise patch (Eccentricity of 24.22°, visual angle of 7.62°, 7.62°, orientation was always 0°). This gabor provided a visual analogue of the powermate dial, and allowed the participant to recall the target orientation (see Figure 5.1 C). The participant submit their response by pressing down on the top of the dial.

In the final stage of the trial, the participant was presented with a sentence asking which rule the cue had indicated at the beginning of the trial. They gave their answer by selecting one of two keys on the keyboard, one had been labelled CW (clockwise) and the other ACW (anticlockwise). When they entered their answer CW or ACW would appear on the screen. They could use the delete key to adjust the answer if required. The participant then pressed on the top of the dial to begin the next trial.

Study Procedure

The participant was seated in a small windowless room, which was dimly lit with a lamp positioned at the back (time was given to allow their eyes to adjust to the change in illumination). The participant was provided with an information sheet and consent form and given the opportunity to ask questions. After taking informed consent, the researcher explained the task instructions with help from a printed visual aid (for instructions see Appendix D.1, p.350). These instructions included an explanation of the response rules, an opportunity to learn the cue-response rule pairs and a step by step walk through of

the experimental procedure. Before starting the practice trials the participant was given pictures of the two cues and asked to freely recall the associated response rules.

Participants were seated 60 centimetres from the computer screen and a chin rest was used to ensure viewing distance was kept constant. The chair, monitor and chin rest were adjusted to ensure the participant was comfortable and viewing the screen centrally. A practice of eight trials was given, which consisted of four of each cue type. This allowed the participant to get used to the speed of the stimulus presentation, familiarise themselves with the mode of response and allow the researcher to assess whether they had understood task procedure. The cue types are presented in blocks, to give the participant the best chance of learning the cue response pairing. In the instance that the participant was not following the correct task procedure they would be asked to repeat the task requirements (if incorrect the rules were repeated).

Experimental Procedure

The experimental task was comprised of 304 trials, which were split into 4 blocks of 76 trials and separated by a self-paced break. The participants were split into two groups: one group were given an instructional cue that was perceptually distinct (colour) and the second group were given a perceptually similar, more complex instructional cue (symbolic, Figure 5.1 B). This was a manipulation of environmental support, with the more distinct cue types (colour) providing greater support. The participant had to learn to pair these cues with two alternative response rules: turn clockwise (CW) or turn anticlockwise (ACW). The rule indicated the direction they were required to turn a dial (Figure 5.1 C) during the upcoming trial.

The response rule was repeated on 80% of trials and switched on 20% of trials (a similar frequency used for goal neglect sensitive critical trials in Bhandari & Duncan, 2014). The type of switch employed is associated with the response mode (clockwise

or anticlockwise), rather than a switch in rule or attention shift. This type of switch has been found to be sensitive to preparation effect, in which time to prepare reduces the impact of switching (Monsell, 2003; Meiran & Marciano, 2002). The random cueing paradigm employed (Sudevan & Taylor, 1987; Meiran, 1996) allowed preparation time for task configuration (Rogers & Monsell, 1995), and thus is likely to produce "residual" switching cost (Monsell, 2003).

Each block was a randomized sequence containing 60 repeat trials (30 of each repeat type ACW-ACW and CW-CW), 1 initial cue presentation (2 blocks started clock-wise and 2 blocks anti-clockwise) and 15 switch trials (8 of one switch type and 7 of the other, counter balanced for frequency across the four blocks, CW-ACW or ACW-CW). The number of subsequent repeats was constrained to five (six of one cue in a row). The cue could repeat 1, 2, 4 or 5 times and order was randomised within each block for each response rule, thus there was an equal number of repeats for each rule, for each possible number of repeats within each block. A 2x2 mixed design was utilised to examine the between-group effect of cue type, the within-group effect of switch type and the interaction between them.

Task Measures

Performance on the orientation recall was measured in speed and accuracy. Speed was measured as reaction time (time from screen onset to response onset in milliseconds). The median reaction time was reported because it lessened the influence of outliers on the results (Ratcliff, 1993). Accuracy was measured in two ways, the raw angular error from the response to the target orientation (degrees) and secondly as the "precision", the reciprocal of the circular standard deviation of the error, which has been corrected for random guessing (Bays, Catalao, & Husain, 2009; Fisher, 1993).

Incorrect Rule Recall	Percentage of Trials	If the rule recall is **incorrect**
Goal Neglect	Percentage of Trials	If the rule recall is **correct** The direction of trial completion is **incorrect**. The first direction turned was **incorrect**
Delayed Task Configuration	Percentage of Trials & Distance Travelled.	If the rule recall is **correct** The direction of trial completion is **correct**. The first direction turned was **incorrect**
Switch Cost	Decrement in Precision & Speed	If the rule recall is **correct** The direction of trial completion is **correct**. The first direction turned was **correct**

Figure 5.2: Classification of error types, including the proportion of trials in which the participant made a goal activation error and residual switch cost measured by a decrement in performance in orientation recall on switch as compared to repeat trials.

Goal Activation Errors: Incorrect rule recall was defined as a trial in which the participant incorrectly reported the trial rule. If the rule was reported correctly and the participant turned the dial in the incorrect direction, this was taken to indicate a goal neglect error. If the rule was correct, the participant started turning the dial in the incorrect direction, but corrected themselves, this was classified as delayed task configuration. For this measure there was two indices, proportion of errors and distance travelled (degrees) before correction.

Residual Switch Cost: For trials that were completed correctly the residual switch cost was calculated, by looking at the decrement in both precision and speed for switch trials as compared to repeat trials. Moreover, the proportion of different goal activation errors were compared between switch and repeat trials.

Overshoot: It was noted that participants had a tendency to slightly pass their intended orientation and make a small adjustment back. This was seen as a attempt to follow the instruction to report the orientation as precisely as possible and was not considered a type of error (unless over 30° was travelled). See Appendix D.4, p.353.

Analysis Methods

The impact of response rule switching and cue type on orientation recall: The first analysis aimed to establish whether switching response rules (CW-ACW) is sufficient to illicit switching costs (speed and accuracy) in task performance in a manner comparable to more traditional task switching paradigms. This analysis is performed after removing trials that the participant made goal activation errors on and thus is hoped to represent residual switch costs on correctly performed trials. It was hypothesised (H1.1) that participants will be slower and less precise on trials that required a switch between response rules, as compared to trials with a repetition. Furthermore, it is hypothesized (H1.2) that this switch cost will be greater for perceptually similar cues, as compared to perceptually dissimilar cues. This hypothesis was further examined by splitting the trials by number of repeats.

The impact of response switching and cue type on goal activation errors: The second analysis examined the impact of switching on the occurrence of goal activation errors. It was hypothesised that (H2.1) there would be significantly more errors on switch as compared to repeat trials. Furthermore, it was expected that (H2.2) this effect would be greater when using a perceptually similar symbolic cue, as compared to a more salient and easier to discriminate colour cue. This analysis was examined in further detail by splitting by repetition number. For instances of goal neglect these hypothesis were re-examined after using different classification criteria. This criteria did not control for incorrect rule recall or delayed configuration and acted as a proxy for traditional measures of goal neglect.

The impact of goal activation errors on orientation recall: Because of the unique set up of the current experimental task the impact of goal activation errors on task performance (speed and accuracy on orientation recall) can be compared in an exploratory analysis.

5.4 Results

Software and Analysis

Data processing was performed using python 2.7. The precision of recall was modelled using a toolkit translated into python from the available matlab scripts (provided by Bays et al., 2009). All statistical analyses were run in R (3.0.3 R Core Team, 2014b), utilising packages Johnson (Fernandez, 2014), lmer4 (Bates et al., 2015) and BayesFactor (Morey & Rouder, 2015). A 2x2 mixed ANOVA (lmer) was followed up with a Bayesian factor analysis (anovaBF) (for information on default priors and methods used by this function please see Rouder et al., 2012). The Bayes factor is a ratio of the probability of the null and the alternative hypothesis (ranges 0 - ∞). Bayes factor values can represent evidence in favour of the alternative hypothesis (BF$_-$ 10) or evidence in favour of the null (the reciprocal, BF$_-$ 01). Coarsely they can be interpreted as 1-3 weak evidence, 3-20 positive evidence, 20-150 strong evidence and $>$ 150 very strong evidence (Kass & Raftery, 1995).

Sample Overview

Table 5.1: Sample Characteristics

Group	N	Age M (SD)	Education M (SD)	Gender F/M	Handedness R/L
Symbolic	30	52.33 (23.67)	16.91 (4.02)	60%/40%	90%/10%
Colour	29	49.04 (21.63)	17.50 (3.86)	48%/52%	90%/10%
Total	59	49.77 (22.66)	16.75 (4.38)	54%/46%	90%/10%

Data Handling

Trials for which the reaction time was ± 3 standard deviations from the participants' average RT score were removed. On average 3.16 (SD=2.37) trials were considered outliers and removed, with a maximum of 9. One participant was removed from the analysis based on having unusually slow average reaction (2866 ms) and response (5879 ms) times which resulted in only completing 167 trials. As can be seen from Table 5.1, the groups did not significantly differ in age or years spent in education.

Switching Costs: Speed and Accuracy

The following section aims to examine whether switching response rules and the perceptual difficulty of the cue impacts on orientation recall performance. The statistical analysis was performed on Johnson transformed data.

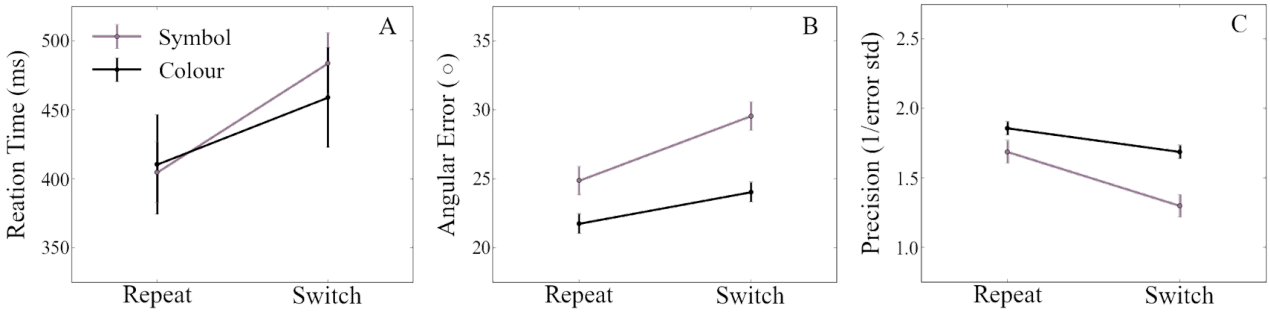


Figure 5.3: Decrement in performance on switch as compared to repeat trials. (A) The average median reaction time on switch compared to repeat trials. (B) The average degree of error between the response and the target orientation on switch as compared to repeat trials. (C) The reciprocal of the standard deviation of the angular error (corrected for random guessing) on switch as compared to repeat trials. Error Bars = 95% confidence intervals.

As can be seen from Figure 5.3 A, a significant main effect was found for switch type [$F(1,57)$=10.80, p=.002, η^2=.16] for median reaction time. Participants were significantly faster on repeat trials, regardless of the type of cue used. The Bayes factor analysis supported this finding favouring the model that solely contained the main effect of switch type ($BF_10 = 8.25 \pm 0.96$).

As can be seen in Figure 5.3 B, there was a significant main effect of switch type [$F(1,57)$=28.92, p <.001, η^2=.33] on average raw angular error. Although there was no main effect of cue type, there was a significant interaction between switch type and cue type [$F(1,57)$=5.73, p=.02, η^2=.09]. The symbolic cue group displayed greater switching cost as compared to the colour cue group. The Bayes factor analysis corroborated these results favouring the model including solely the main effect of switch type and the interaction term ($BF_10 = 7615.26 \pm 1.19\%$).

As seen in Figure 5.3 C, the analysis of recall precision was repeated this time using the reciprocal of the circular standard deviation, corrected for chance. The results were replicated; finding a significant switching cost [$F(1,57)$=33.05, p <.001, η^2=.36] and an interaction with cue type [$F(1,57)$=6.14, p=.02, η^2=.10]. The Bayes factor model complemented these findings favouring the model containing the main effect of switch type and the interaction ($BF_10 = 28779.32 \pm 2.62\%$).

Overall, the current observations support H1.1, by suggesting that participants are slower and less precise on switch as compared to repeat trials. In partial support of H1.2, use of a symbolic cue led to greater costs in precision, but not in speed.

Impact of Repetition Number on Speed and Accuracy

The impact of repetition number was examined to see whether the results were similar to past accounts of repetition priming (Dreisbach & Haider, 2006; Altmann, 2005). Mixed linear models were run looking at the impact of repetition number and cue type on orientation recall performance. Please note that Satterthwaite degrees of freedom approximation reported.

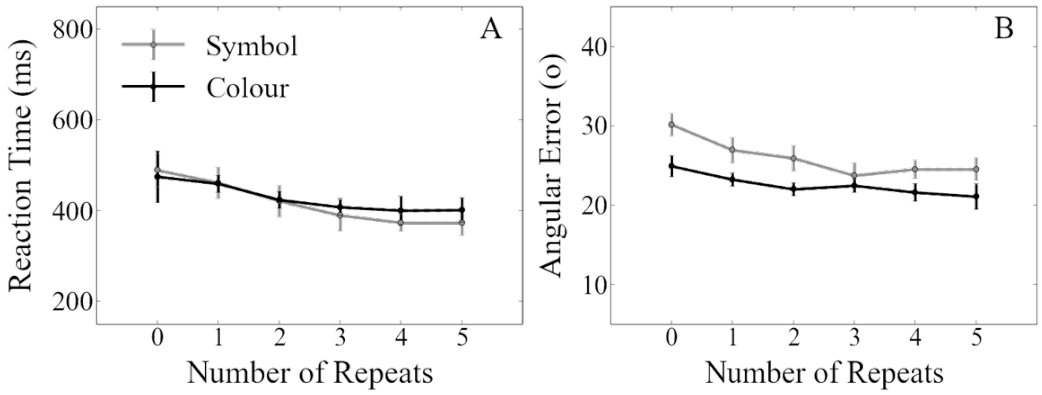


Figure 5.4: Orientation recall performance by number of cue repetitions (0 refers to a switch trial). (A) Average median RT by repetition number. (B) Average angular error by repetition number. EB = 95% CI.

For the reaction time, there was a significant main effect of repetition number [$F(5,295)$= 11.76, p <.001], but no main effect of or interaction with cue type. Planned contrasts were utilised to compare each number of repeats to the switch condition. No difference was found in RT between switch trials and trials with only 1 repetition. However, participants were significantly faster following 2 repetitions (Z=3.72, p=.003), 3 repetitions (Z=5.21, p <.001), 4 repetitions (Z=5.43, p <.001) and 5 repetitions (Z=5.92, p <.001).

A similar pattern was observed for raw angular error, with a significant main effect of repetition number [$F(5,295)$=13.29, p <.001], but no main effect of or interaction with cue type. Planned contrasts were run comparing each number of repeats to the switch condition. As can be seen in Figure 5.4 B, switch trials did not significantly differ from trials with one repetition. However, participants were significantly more error prone on switch trials as compared to trials with 2 repetitions (Z=3.01, p=.003), 3 repetitions (Z=2.54, p=.01), 4 repetitions (Z=3.42, p <.001) and 5 repetitions (Z=3.96, p <.001). Overall, it is suggested that the benefits of response repetition can be observed after two or more repetitions.

Impact of Switching and Cue Type on Goal Activation Errors

The following section aims to examine the impact of switching response rule and perceptual difficulty of the instructional cue on the proportion of goal activation errors. Statistical analysis was performed on Tukey transformed data.

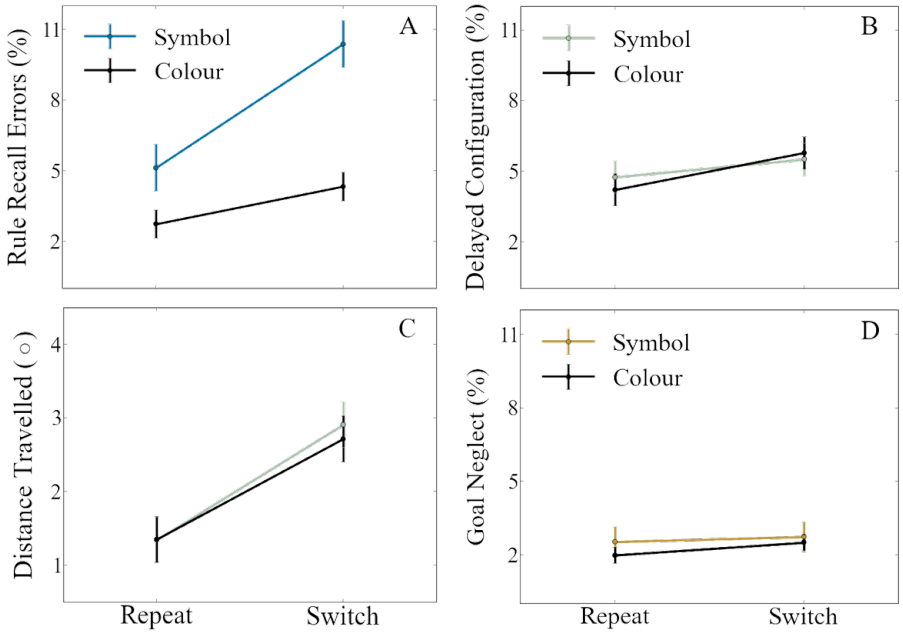


Figure 5.5: Proportion of errors on switch as compared to repeat trials. (A) The percentage of trials in which the participants incorrectly recalled the trial rule on switch as compared to repeat trials. (B) The percentage of trials in which the participant made an inhibition error (started the trial in the incorrect direction, before correcting themselves) on switch as compared the repeat trials. (C) The average distance travelled before correction during the delayed task configuration (N= 48). (D) Proportion of goal neglect errors. Error Bars = 95% CI.

The examination of incorrect rule recall (Figure 5.5 A), observed a significant main effect of switch type [$F(1,57)=40.49$, p <.001, $\eta^2=.41$], with a higher proportion of incorrectly recalled rules on switch trials. There was a significant main effect of cue type [$F(1,57)=6.981$, $p=.01$, $\eta^2=.11$], with the symbolic cue group demonstrating higher instances of incorrect rule recall. There was also a significant interaction [$F(1,57)=8.992$, $p=.004$, $\eta^2=.14$], with switching costs more pronounced in the symbolic cue group. A Bayes factor analysis corroborated these results with the full factorial model favoured over the other models ($BF_10 = 288929.3 \pm 5.24\%$).

As seen in Figure 5.5 B, switching and cue type were not found to have a significant effect on the proportion of delayed configuration errors. The Bayes factor analysis observed no strong support for any model. A top-down analysis found some weak support for removing the main effect of switch type ($BF_01 = 1.53 \pm 3.15\%$), the main effect of cue type ($BF_01 = 2.91 \pm 2.86\%$) and the interaction ($BF_01 = 2.14 \pm 2.72\%$).

Although no difference was found for the proportion of delayed configuration errors (Figure 5.5 C), there was a significant effect found for the distance travelled before correction [$F(1,48)= 15.98$, $p < .001$, $\eta^2= .26$], with participants travelling further on switch trials. There was no main effect of or interaction with cue type. These results were corroborated by a Bayes factor analysis that favoured the model solely including the main effect of switch type ($BF_10 = 206.50 \pm 1.0\%$). A top-down analysis found that there was weak-moderate support in favour of removing both the main effect of cue type ($BF_01 = 3.22 \pm 2.66$) and the interaction ($BF_01 = 3.52 \pm 3.01\%$) from the model.

As can be seen from Figure 5.5 D, switching and cue type were not observed as having a significant impact on the proportion of goal neglect errors. The Bays Factor analysis corroborated these findings, there was no support found for any of the models (Bayes Factors < 1). There was some weak evidence in favour of omitting the main effect of switch type ($BF_01 = 3.13 \pm 5.63\%$), the main effect of cue type ($BF_01 = 1.73 \pm 4.62$) and for the interaction ($BF_01 = 3.39 \pm 5.63\%$).

In summary, H2.1 and H2.2 were only supported in relation to the proportion of incorrect rule recall. No evidence was found in favour of either manipulation affecting delayed configuration or goal neglect. On trials with delayed configuration errors, participants were observed to travel further before correction. This is perhaps due to the additional residual switch costs in speed. These results tentatively suggest that these manipulations primarily affect failures to monitor the environment effectively.

Classification of Goal Neglect

The following control analysis aimed to examine whether switching and cue type might have been observed to affect goal neglect if the additional controls (trial rule recall and response correction) were not included in the classification. The analysis was run once without controlling for trial recall or delayed task configuration and then twice more while controlling for them individually. The change in classification is outlined below.

1) Unfiltered goal neglect is classified as a trial completed in the incorrect direction.

2) Goal neglect filtered on delayed task reconfiguration is classified as a trial completed in the incorrect direction, without correction.

3) Goal neglect filtered on trial rule recall is classified as a trial completed in the incorrect direction, with correct trial rule recall.

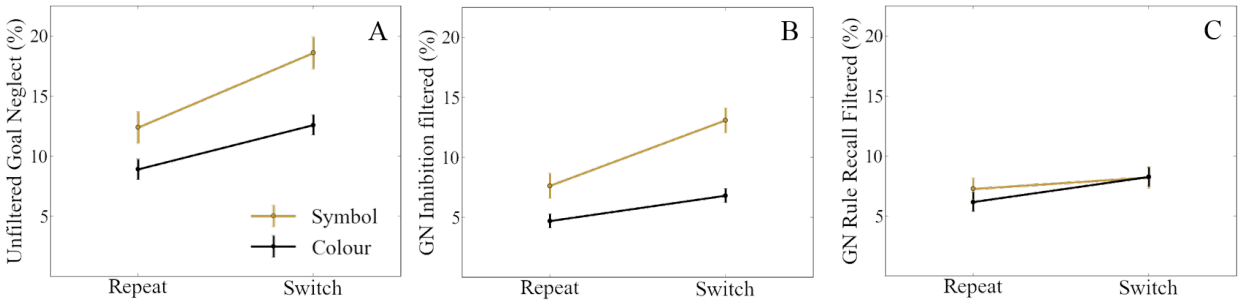


Figure 5.6: Instances of goal neglect on switch as compared to repeat trials before and after filtering confounding error types. (A) Goal neglect without controlling for incorrect rule recall or delayed configuration errors. (B) Goal neglect with incidences of delayed configuration errors filtered out. (C) Goal neglect with incorrect rule recall filtered out. Error Bars = 95% CI.

As can be seen from Figure 5.6 A, for unfiltered goal neglect there was a significant main effect of switch type [$F(1,57)$=34.90, p <.001, η^2=.38], with a higher proportion of goal neglect on switch trials. There was also a non-significant trend for the main effect of cue type [$F(1,57)$= 3.15, p=.08, η^2=.05], with a higher proportion of errors for the symbolic cue group. The Bayes factor analysis preferred the model including both main effects ($BF_10 = 104307.10 \pm 2.72\%$). Weak evidence was found in favour of removing the interaction ($BF_01 = 2.52 \pm 6.75\%$).

As seen in Figure 5.6 B, for goal neglect filtered on delayed configuration (but not incorrect rule recall) there was a significant main effect of switch type [$F(1,57)=52.05$, $p<.001$, $\eta^2=.47$] and a trend towards a main effect of cue type [$F(1,57)=4.08$, $p=.05$, $\eta^2=.07$]. Moreover, there was a significant interaction between cue type and switch type [$F(1,57)=6.74$, $p=.01$, $\eta^2=.11$], with greater switch costs seen in the symbolic cue group. The Bayes factor analysis corroborated these findings favouring the full model ($BF_10 = 284152.3 \pm 4.45\%$).

As seen in Figure 5.6 C, for goal neglect filtered on incorrect rule recall (but not delayed configuration) there was a trend towards a main effect of switch type [$F(1, 57)= 4.18$, $p=.05$, $\eta^2=.07$], however, there was no main effect or interaction with cue type. The Bayes factor analysis favoured the model only containing the main effect of switch type ($BF_10 = 2.72 \pm 0.92\%$). A top-down analysis indicated some weak evidence in favour of removing the effect of cue type ($BF_01 = 1.90, \pm 4.11\%$) and the interaction ($BF_01 = 2.60 \pm 4.47\%$), but not for removing switch type ($BF_01 = 0.31, \pm 4.53\%$).

Overall this pattern of results is suggestive that the incorporation of multiple types of error into one classification may have contributed to the observation that goal neglect is influenced by perceptual difficulty of the cue and is more frequent on switch trials. Here it is suggested that the manipulation of environmental support may interact with the effect of monitoring for target information, whereas it may not influence errors associated with action selection in the same manner.

Repetition Number: Goal Activation Errors

It was expected that the repetition of response rules could produce practice effects given time. Therefore, the proportion of goal activation errors was examined split by the number of repetitions and the pattern of results compared across error types. Mixed linear models were run looking at the impact of the within subject factor of repetition number and between subject factor of cue type for proportion of goal activation errors.

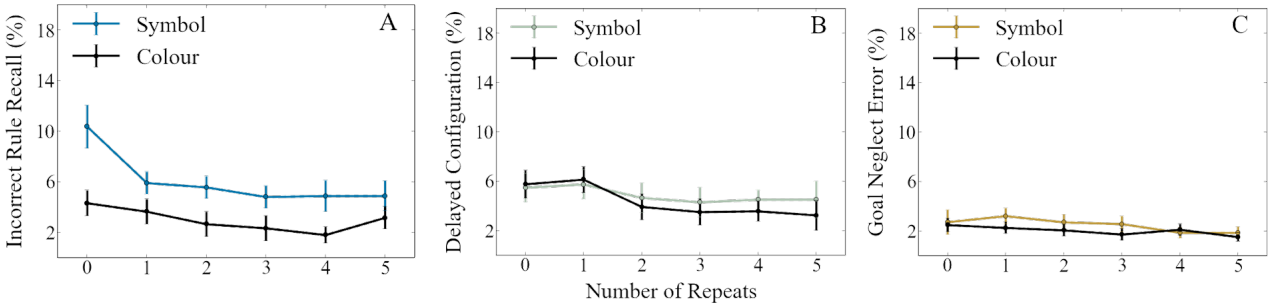


Figure 5.7: Proportion of errors by number of cue repetitions. (A) Proportion of incorrectly recalled rules by repetition number. (B) Proportion of delayed task configuration errors by repetition number. (C) Proportion of goal neglect errors by repetition number. Error Bars = 95% CI.

As seen in Figure 5.7 A, there was a significant main effect of repetition number [$F(5,295)$= 19.25, p <.001] for incorrect rule recall. Moreover, there was also a significant interaction with cue type [$F(5,295)$=3.02, p=.01]. Planned contrasts comparing each repeat to switch trials were run for each cue type. In the symbolic group there was a significantly higher proportion of incorrect rule recalls on switch trials as compared to 1 repetition (Z=5.18, p <.001), 2 repetitions (Z=5.71, p <.001), 3 repetitions (Z=6.75, p <.001), 4 repetitions (Z=7.52, p <.001) and 5 repetitions (Z=7.04, p <.001). Whereas, for the colour cue, there was no difference observed between switch trials and 1 repetition. However, there was a significant difference compared to 2 repetitions (Z=2.87, p=.004), 3 repetitions (Z=3.67, p <.001), 4 repetitions (Z=4.77, p <.001) and 5 repetitions (Z=2.88, p=.004).

As seen in Figure 5.7 B, for delayed task configuration there was a significant main effect of repetition number [$F(5,295)=6.43$, $p < .001$], but no main effect or interaction with cue type. Planned contrasts demonstrated that there was no difference in the proportion of delayed task configuration errors between switch trials and 1 cue repetition. However, there was a higher proportion of trials with delayed task configuration on switch trials as compared to 2 repetitions ($Z=2.59$, $p=.01$), 3 repetitions ($Z= 2.842$, $p=.01$), 4 repetitions ($Z= 3.35$, $p=.003$) and 5 repetitions ($Z=3.35$, $p < .001$).

As seen in Figure 5.7 C, there was also a small but significant main effect of repetition number [$F(5, 295)= 7.41$, $p < .001$] for proportion of goal neglect error. However there was no main effect or interaction with cue type. Planned contrasts demonstrated no difference in the proportion of goal neglect errors between switch trials and trials with 1 or 2 repetitions. However, there was a higher proportion of goal neglect on switch trials as compared to 3 repetitions ($Z=2.38$, $p=.02$) and 5 repetitions ($Z=3.82$, $p < .001$).

It was observed that the impact of repetition number differed for errors in incorrect recall as compared to the other two error types, primarily for the symbolic cue. For the symbolic group there was a large decrease in incorrectly recalled rules on all repeat trials. This pattern is suggestive that the use of a perceptually harder cue may result in higher instances of monitoring failures, in which participants failed to notice the change in cue. On the other hand, it took at least two repetitions before a repetition benefit was observed for configuration errors and even more before a small decrease was seen in the proportion of goal neglect errors. Overall, this suggests that multiple repeats of the response rule may gradually strengthen it, making it more effective in the competition for behavioural control.

Differential Impact of Goal Activation Errors on Performance.

Because of the unique set up of the current experimental task the impact goal activation errors on concurrent orientation recall could be examined. Because error proportions were low for many participants the data were pooled over groups. Only participants who had made more than one error were considered. Therefore, sample size differs per type of error. In order to handle the impact of missing data a multilevel linear model was run. Overall, this analysis is exploratory and should be considered as descriptive.

The following analysis examined the main effect of error type followed by a set of planned contrasts. Error type has five factors which correspond to baseline trials (errorless repeat trials), switch trials (errorless switch trials), delayed task configuration errors, goal neglect errors and incorrect rule recall. The planned contrasts firstly compared performance on the repeat trials to trials with each of the error types and secondly, performance on switch trials to trials with each of the error types.

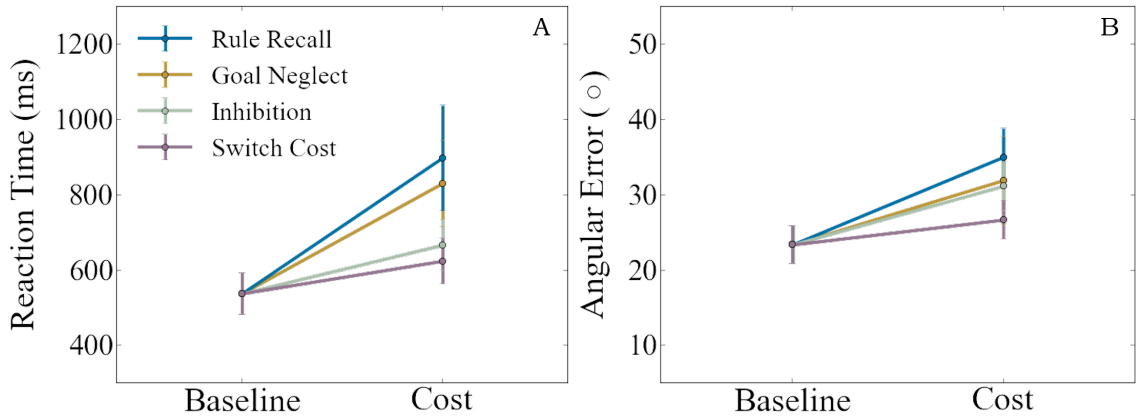


Figure 5.8: The impact different types of error had on task performance. In this instance baseline refers to repeat trials on which there has been no error. It represents the average error experienced whilst recalling the orientation without extra influence of switching or the occurrence of an error. Plotting on costs is first the average impact on task performance depending on the type of error experienced. Each type of error is looked at in only the participants who demonstrated at least 2 of that particular error type and thus N differs slightly between error types. (A) The impact of switching response rules, delayed task configuration, goal neglect and incorrect rule recall on reaction time. (B) The impact of switching response rules, delayed task configuration, goal neglect and incorrect rule recall on the average orientation recall error. Error Bars = 95% CI.

As seen in Figure 5.8 A, for reaction time there was a significant main effect of error type [$F(4)$=7.23, p <.001]. Participants were faster on repeat trials as compared to switch trials (p <.001), trials with delayed configuration (p=.001) and trials with incorrect rule recall (p <.001). Goal neglect trials did not significantly differ (perhaps influenced by a large amount of variability). Participants were also significantly faster on switch trials as compared to trials with incorrect rule recall (p <.001).

As seen in Figure 5.8 B, for raw angular error there was a significant main effect of error type [$F(4)$= 4.83, p <.001]. Participants were less error prone on repeat trials as compared to switch trials (p <.001), trials with delayed task configuration (p <.001), trials with goal neglect errors (p=.009) and trials with incorrect rule recall (p <.001). Participants were also significantly less error prone on switch trials as compared to trials with incorrect rule recall (p=.003).

Overall these results are suggestive that these error types can have a greater impact on concurrent task performance than residual switch costs. Furthermore, it appears that errors have an incremental impact on concurrent performance depending on which element of attentional control they disrupt.

Impact of Task Novelty

An important factor when considering attentional control is novelty (Duncan et al., 1995). In the current design the participants only have to learn and assemble the task rules once at the beginning of the experiment. It is likely that practice effects will occur through the experiment as the task becomes more automatic. Therefore, task novelty will be explored by examining performance split by the four task blocks.

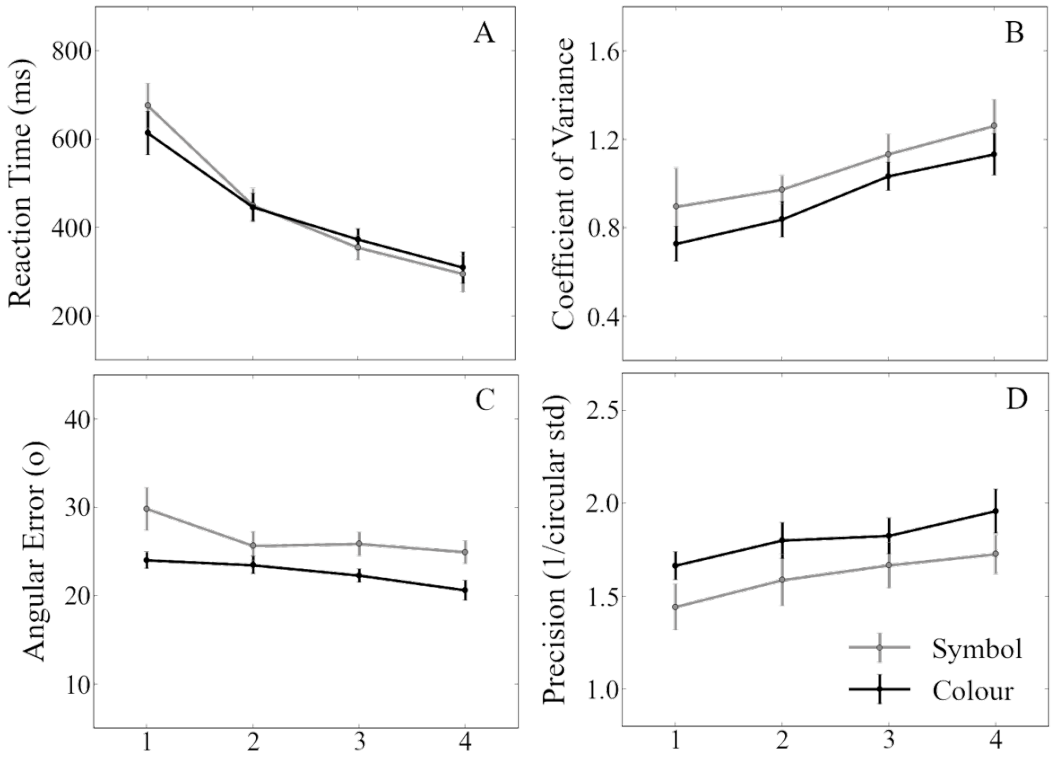


Figure 5.9: Average task performance split by block. (A) Average median reaction time. (B) Reaction time coefficient of variation (standard deviation / mean). (C) Average absolute angular error on orientation recall (degrees). (D) Average precision of recall (reciprocal of the circular standard deviation). Error bars = 95% CI.

As can be seen in Figure 5.9, on average participants in both groups were quicker (A) and more precise (C & D) over the course of the experiment. However, their reaction time variability increased over the course of the experiment (B). For reaction time, there was a significant main effect of block [$F(1,56)=120.39$, $p<.001$], but no differences or interaction with cue type. Bonferroni corrected follow up contrasts demonstrated that reaction time in block 1 was significantly slower than block 2 ($Z=$ -4.60, $p<.001$), block 3 ($Z=$ -12.29, $p<.001$) and block 4 ($Z=$ -13.32, $p<.001$). The coefficient of variation also demonstrated a significant main effect of block [$F(1, 56)=23.68$, $p<.001$], with no indication of a main effect of or interaction with cue type. Bonferroni corrected contrasts found that block 1 was significantly less variable than both block 3 ($Z=3.4$, $p=.004$) and block 4 ($Z=$ -6.16, $p<.001$).

For raw angular error, there was also a significant effect of block [$F(1,56)$=13.91, p=.001] and a non-significant trend for the main effect of cue type (p=.08). Follow up contrasts demonstrated significantly more error during orientation recall on block 1 as compared to block 2 (Z= -3.818, p=.001), block 3 (Z= -10.81, p <.001) and block 4 (Z= -12.40, p <.001). A similar trend was seen in the precision of recall, with a significant main effect of block [$F(1,36)$=18.38, p <.001], but no main effect or interaction with cue type. Contrasts demonstrated that participants were significantly less precise on block 1 compared to block 2 (Z= -5.33, p <.001), block 3 (Z= -8.73, p <.001) and block 4 (Z= -10.39, p <.001).

Impact of Novelty on Goal Activation Errors

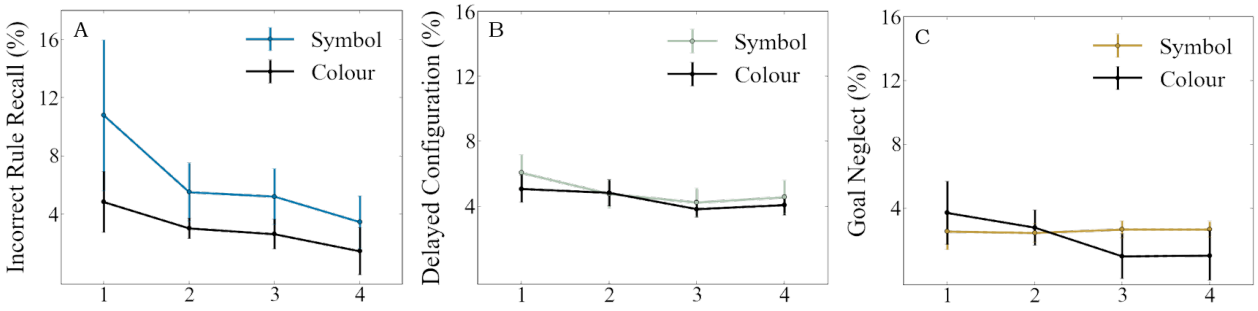


Figure 5.10: Effect of block on (A) delayed configuration, (B) goal neglect and (C) incorrect rule recall.

A series of mixed ANOVAs were used to investigate the proportion of goal activation errors across blocks and between cue types. As can be seen in Figure 5.10 A, for the incorrect rule recall there was a significant main effect of block [$F(1,172)$=13.52, p <.001] and a significant main effect of cue type [$F(1,56)$=5.80, p=.02]. Contrasts demonstrated that block 1 had a significantly higher proportion of errors as compared to block 3 (Z= -5.27, p <.001) and block 4 (Z= -7.25, p <.001). Furthermore, block 2 has a higher proportion compared to block 3 (Z= -3.31, p <.01) and trend as compared to block 4 (Z= -2.54, p=.07).

As seen in Figure 5.10 B, for the proportion of delayed task configuration there was a significant main effect of block [$F(1,172)=7.17$, $p=.01$], but no main effect of or interaction with cue type. There was a small decrease in the frequency of errors across blocks. As seen in Figure 5.10 C, for the proportion of goal neglect errors there was also a significant main effect of block [$F(1,172)=8.11$, $p=.01$] and a significant interaction with cue type [$F(1,172)=6.83$, $p=.01$]. The frequency of goal neglect errors decreased across blocks solely for the group using the colour cue.

In summary, participants demonstrate practice effects in both speed and accuracy over the course of the experiment. Moreover, there is a decrease in all types of goal activation error, apart from goal neglect when using the symbolic cue. The largest reduction is seen in incorrect rule recall, particularly for the symbolic group.

5.5 Discussion

The current investigation aimed to develop a novel paradigm that can dissociate different types of goal activation errors and re-examine the influence of infrequent task switching and perceptual difficulty of the instructional cue. The current paradigm and the results will be considered in context with the existing literature and implications discussed.

Residual Switch Costs

In line with other task switching paradigms, a cost of switching response rules was observed in both speed and the precision of orientation recall (e.g. Monsell, 2003; Petersen & Posner, 2012; Meiran, 1996). Moreover, this observation was made after filtering out trials in which participants made goal activation errors (i.e. incorrect recall, delayed task configuration or goal neglect). The investigation of repetition number demonstrated a predictable benefit of response rule repetition similar to investigations of repetition priming (Altmann, 2005). Interestingly, switching costs in precision were greater when using a symbolic cue, despite there being no difference in reaction time. This dissociation could suggest a greater working memory load associated with the symbolic cue.

In terms of past goal neglect paradigms the current task switching design is most comparable with Bhandari et al (2014). Both experimental designs required participants to continuously monitor the cue for infrequent (20%-25%) and unpredictable switches in response rules. In contrast, letter monitoring paradigms used intermittent but predictable cue presentation, which indicates a shift of attention to the alternative stream 50% of the time (Duncan et al., 1996; Towse et al., 2007; Iveson et al., 2017). Similar to these letter monitoring tasks, the current paradigm used a temporally separate cue and therefore in contrast to Bhandari et al (2014) attentional monitoring does not require attentional selection during competition with simultaneously presented (and relevant) stimuli. An important difference in the current design is that the cue was always presented for 500ms

(followed by a 500ms ISI). In the letter monitoring tasks the second instructional cue is only presented for 200ms (200ms ISI), making it more vulnerable to lapses in attention and providing a greater opportunity for switching to impact on the subsequent trial.

The Impact of Switching and Cue on Goal Activation Errors

The impact of task switching on occurrences of goal activation errors was examined. Firstly, it was observed that there were significantly higher proportions of incorrect rule recall on switch as compared to repeat trials. Moreover, this manipulation was stronger when using a perceptually more difficult cue. These results mirrored past investigations of goal neglect (Duncan et al., 1996; Bhandari & Duncan, 2014). For the symbolic cue group, the analysis of repetition number demonstrated significantly greater performance on repeat trials, regardless of repetition number. The large difference in performance between switch trials and trials with only one repetition is suggestive of monitoring errors, in which the participant failed to notice the change in cue. The use of a continuous cueing paradigm, temporal separation of the cue and extended time for cue processing all should have reduced the impact of monitoring errors compared to past paradigms. Overall, these observations suggest that infrequent switching and perceptual difficulty of the cue can influence the effectiveness of top-down control to bias attentional monitoring for task relevant information.

Unlike incorrect rule recall, the proportion of delayed configuration errors did not differ between switch or cue types. This was unexpected because it was considered that task reconfiguration on switch trials would make a delay more likely and that the use of a perceptually harder cue may extend processing times. The long processing and preparation time given in the current design may contribute to this observation. However, it was observed that the distance travelled before correction was significantly longer for switch trials, perhaps due to the additive effect of residual switch costs. The

analysis of repetition number demonstrated a dissimilar pattern of results as compared to incorrect rule recall. This perhaps suggests that although switching may influence incorrect rule recall more immediately (due to inattention to the cue change), it may also influence delayed task configuration in a more subtle fashion by slowly strengthening the task representation and thus, making it easier to bias perception and action (Petersen & Posner, 2012).

It had been predicted that the proportion of goal neglect errors would be significantly higher on switch trials as compared to repeat trials (e.g. Duncan et al., 1996; Iveson et al., 2017; Bhandari & Duncan, 2014), particularly when using a perceptually difficult cue (Bhandari & Duncan, 2014). However, using the current definition of goal neglect (that is distinct from monitoring errors and delayed configuration), switching and cue type were not found to impact the proportion of goal neglect errors. The analysis of repetition number demonstrated that it took multiple response rule repetitions to result in a small reduction in the proportion of goal neglect errors. This perhaps suggests that repetition may enhance how competitive action selection is over time. Interestingly, if goal neglect was examined using a classification which did not utilise the control afforded by the current paradigm, a different pattern of results was observed. Now the results were consistent with past literature, demonstrating higher proportions of goal neglect errors for the symbolic cue and on switch trials compared to repeat trials (Duncan et al., 1996; Iveson et al., 2017). These results suggest that task switching and cue type may primarily impact on goal activation errors in monitoring rather than goal neglect when defined using a stricter classification.

Overall it is suggested that perceptual difficulty of the cue and infrequent switching may be more sensitive to failures in environmental monitoring as compared to goal neglect errors (action selection). This perhaps suggests that the previously observed relationship between these manipulations and goal neglect was influenced by monitoring errors (e.g.

Duncan et al., 1996; Bhandari & Duncan, 2014). However, there are some important differences in task design to consider. For example, in traditional monitoring tasks the secondary instructional cue is presented subsequent to 10 repeat trials (Duncan et al., 1996). It has been found that after repeat practice, errors can occur due to this more practiced or salient behaviour being selected and interfering with performance (Norman, 1981; Roca et al., 2018; Reason, 1990). Therefore, it could be that a more consistent difference would be revealed if the design constantly used a high number of repetitions. In line with this, goal neglect proportions were also slightly lower after multiple repeats. Further work is required to more specifically address this relationship.

One substantial difference between the current paradigm and traditional measures of goal neglect is the criteria used in classification. Past paradigms assessed goal neglect based on sub-block performance (2 repeat and 2 switch trials). Participants could pass a sub-block if they correctly completed at least one stay and one switch trial. It is still ambiguous to how individual goal neglect errors measured on the current task relate to goal neglect as measured by the traditional criteria. Moreover, the majority of analysis in the original paradigm was performed on participants who had complete neglect for the secondary cue. In the present paradigm many participants demonstrated frequent instances of incorrect rule recall, however only one participant demonstrated a high frequency of goal neglect (42% of trials). Firstly, it is important for further work using this paradigm to try to modulate the frequency of goal neglect to allow a more detailed analysis (perhaps by modulating novelty or by sampling from individuals with low fluid intelligence). Secondly, further work is required in order to better understand the relationship between these differential approaches to measuring goal neglect.

In order to incorporate the requirement of enough trials to model precision for infrequent switch trials (>40), the experiment needed to be at least 304 trials long (plus 8 practice runs). Furthermore, the addition of the trial by trial recall also meant that

trials took approximately 8 seconds to complete. In total the whole experimental session (including set up, consent, instructions, practice and experiment) took approximately 90 minutes. Therefore, it is likely that this design relies more heavily on the ability to sustain attention than previous designs with fewer trials (e.g. Duncan et al., 1996). Therefore, the effect of tonic attention on goal reactivation may be more influential in the current design (Dockree et al., 2007).

In the current investigation goal neglect has been dissociated into three different manifestations. The first, incorrect rule recall, is considered as a failure in monitoring the environment for task relevant information. This could be due to an ineffective task model or could be a result of fluctuations in its effectiveness due to alertness. It has been suggested that the task model is stored as a long term working memory trace, with greater stability as compared to normal working memory representations (Duncan et al., 2008). However, successful tonic sustained attention is said to require intermittent re-activation of the task model (Dockree et al., 2007; Petersen & Posner, 2012; Sturm et al., 1999). It could be suggested that the clarity and strength of the task model may influence the frequency of how often it needs to be refreshed in order to remain effective. During piloting for the current paradigm, the data was split into individual epochs of within and outside of the participants median RT range. It was found that incorrect recall was significantly higher in epochs outside of the individuals normal reaction time range (for further details on the analysis used see Esterman, Noonan, Rosenberg, & DeGutis, 2013). This relationship between tonic attention and goal activation errors would be interesting to explore further.

A substantial weakness of the current study is the way in which the perceptual difficulty of the cue was manipulated. The cues differed on multiple perceptual qualities, including salience, complexity, similarity and support from stored semantic knowledge. Moreover, the symbolic cue contained more explicit response mapping (direction of slant). The explicitness of the cue-response mapping is suggested to modulate instances of goal neglect (e.g. Towse et al., 2007). It would be interesting to separately modulate the similarity of the cue and the directness of mapping, comparing the impact on the different types of goal activation errors.

Differential Task Impact

The impact of goal activation errors on concurrent orientation recall demonstrated an incremental cost in both speed and accuracy above that of observed residual switch costs. This increment started with delayed configuration, through goal neglect to incorrect rule recall. Tentatively, this is suggestive of the goal activation approach (De Jong et al., 1999; De Jong, 2000, 2001). It appears that where the error occurs in the sequence of task configuration, can have a greater or lesser impact on a participant's ability to prepare for the coming trial. However, this analysis will need further investigation before interpretations can be made. Of particular importance will be changing the paradigm or sample to ensure greater frequency and consistency of goal activation errors. In line with the proposed importance of task novelty on the frequency of goal neglect (Duncan, Schramm, Thompson, & Dumontheil, 2012), a decrease in activation errors was observed across blocks. Further work could utilise novel task requirements at the beginning of each block in order to address this concern (similar to Bhandari & Duncan, 2014).

Other Experimental Influences on Task Performance

The response rules were examined to see whether there was any underlying bias. The use of the anticlockwise cue produced a small response time decrement ($\sim$ 35ms) regardless of the cue type used (please see Appendix D.2, p.351). This could perhaps reflect the additional time required for internal articulation of anti-clockwise over clockwise and/or a slight motoric bias. There was no observed impact on absolute angular error demonstrating that this impact on response time did not necessarily substantially impact performance. Interestingly, there was a divergence between cue types in regards to the influence of response rules on the occurrence of configuration errors. Participants using the colour cue had a higher proportion of trials ($\sim$2% more) with delayed task configuration when turning anti-clockwise as compared to clockwise. This effect was not shared by the symbolic group, perhaps suggesting that the explicit response information (slant in direction of turn) in the cue may protect against this small bias. Overall, there was a slight bias in speed, and for the colour group, delayed configuration errors (in favour of turning clockwise). However, this bias had a very minimal impact on task performance.

Another potential source of bias in the current design is the distance from the probe to the target orientation. When examined, a significant positive relationship was found between the probe to target distance and both reaction time and raw angular error. However, the results in the main analysis remained the same when controlling for this influence (see Appendix D.3, p.352). It was observed that on some trials participants would overshoot the target orientation and then make a small adjustment back towards it. A proportion of participants appeared to use overshoot as a strategy to improve the report of orientation. The participants using over shoot consistently demonstrated quicker reaction times, slower response times and more precise recall. For the participants that had infrequent occurrences of overshoot the pattern was different, with slower reaction times, slower response times and more error on orientation recall (see Appendix D.4,

p.353). The proportion of overshoot did not appear to differ between groups or between switch and repeat trials and therefore is unlikely to influence the results. However, it is suggested that future research using this response mode should aim to control for this source of variability by giving explicit instructions.

Conclusions

The present investigation aimed to develop a novel paradigm that could dissociate goal activation errors (incorrect rule recall, delayed configuration and goal neglect). The impact of perceptual difficulty of the cue and task switching on the proportion of goal activation errors was examined. It was found that these manipulations had a significant impact on instances of incorrect trial rule recall (which is taken to suggest a failure for the task model to bias perception of relevant information). Interestingly, these manipulations had little effect on the occurrence of delayed task configuration or goal neglect. Splitting the results by repetition number demonstrated an immediate impact on incorrect rule recall, compared to a gradual impact on delayed task configuration and to some extent goal neglect. It is suggested that the effect of perceptual difficulty of the cue and task switching may differentially impact types of goal activation error. Overall, this study has provided a novel way to dissociate errors resulting from sub-optimal goal activation and has demonstrated that commonly used experimental manipulations may affect the task models ability to bias attention and action differentially.

In the current chapter it has been observed that a failure in top-down modulation of goal directed behaviour can manifest in multiple ways depending on interaction with the environment. One factor that has consistently been found to affect the efficiency of this process is concurrent task demands. The following chapter will address how attention is shared between internal and external requirements during the pursuit of goal directed behaviour.

Chapter 6

Attention in Processing and Maintenance

A Test of the Time Based Resource Share Model on the Precision of Feature Recall.

6.1 Abstract

Introduction: Goal directed behaviour often requires concurrent processing and working memory maintenance. These two processes have been theorised to require the same attentional resource and how this resource is shared has been widely debated. The Time Based Resource Share (TBRS) model proposes that attention is shared via rapid sequential attentional switching. It is suggested that the trade-off in concurrent performance is a function of the ratio of time attention is captured by external processing, compared to being available for maintenance activities. Given that harder tasks take longer to complete, this ratio of attentional capture has been conceptualised as cognitive load. Past research has investigated the impact of cognitive load using complex span tasks, which require the maintenance and sequential recall of items under dual task conditions. The current analysis aims to examine the TBRS assumptions in a different memory context, using a delayed adjustment task to investigate the impact of cognitive load on the precision with which a single item feature (orientation) can be recalled.

Method: Three experiments were run in young adults and teenagers, implementing two different research designs. These designs were adaptations of the strictly timed complex span task, but employed the recall of an orientation, either with or without an intervening interference task. This interference task required a series of shape match judgements, which came at different paces to carefully control time based cognitive load.

Results: In three experiments a significant interference effect was observed, with the addition of the processing task negatively impacting the precision of orientation recall. However in contrast to the results of complex span tasks, the cognitive load did not modulate the interference effect. The manipulation of cognitive load was observed as stronger for low span individuals, who had poorer recall overall (particularly for the condition with the highest cognitive load).

Conclusions The current investigation suggests that cognitive load may not modulate the precision of one item feature recall in the same manner as sequential recall on complex span tasks. These results raise questions regarding how attention is used to refresh working memory contents during brief maintenance pauses.

6.2 Introduction

In order for behaviour to be successfully goal directed, it is important for attention to bias both the perception and maintenance of relevant information. In doing so, not only will relevant information be encoded, but it will be maintained on line until goal completion. It has been argued that both goal directed processing and maintenance share a limited attentional resource (Anderson, 1993; Baddeley, 1986; Barrouillet, Lepine, & Camos, 2008; Cowan, 1999, 2005; Engle, 2002; Engle & Kane, 2004). Research has demonstrated that there is a trade-off in performance when external processing and internal maintenance happen simultaneously (e.g. Anderson, Reder, & Lebiere, 1996; Barrouillet & Camos, 2001; Baddeley & Hitch, 1974; Duff & Logie, 2001). However, how this resource is shared between these competing processes is still a matter of debate. One important question remaining is the contribution of time. Is the trade-off caused by simultaneous sharing of a limited resource (Anderson et al., 1996; Case, 1985, 1992; Daneman & Carpenter, 1980), or due to a bottle neck during sequential attention allocation (Barrouillet et al., 2004; Barrouillet & Camos, 2015; Towse & Hitch, 1995; Pashler, 1984)?

One of the current models which aims to address this question is the Time Based Resource Share (TBRS) model of working memory (Barrouillet et al., 2004; Barrouillet & Camos, 2015). In line with previous theory, the TBRS model also assumes that both goal directed processing and maintenance compete for the same limited attentional resource (Barrouillet, Bernardin, Portrat, Vergauwe, & Camos, 2007; Barrouillet et al., 2008). The TBRS model assumes a central bottle neck, which prevents the simultaneous distribution of attention between these two processes (Pashler, 1984). Therefore, the TBRS model proposes that attention is sequentially shared, using rapid switching between processing and maintenance activities. Unlike the previous task switching model (Towse & Hitch, 1995; Towse et al., 1998), the TBRS model assumes switching can happen dynamically during brief pauses in external processing (Barrouillet et al., 2004).

The proposed temporal nature of attentional sharing becomes fundamental to the trade-off between processing and maintenance, when another important assumption of the TBRS model is introduced. The assumption that working memory traces suffer temporal decay (Anderson, 1993; Barrouillet, Gavens, Vergauwe, Gaillard, & Camos, 2009; Cowan, 1995; Camos et al., 2018; Lovett, Reder, & Lebiere, 1999; Pertzov et al., 2013; Zhang & Luck, 2009). It is also suggested that temporal decay can be counteracted by swiftly switching attention back to reactivate (refresh) the working memory trace (Cowan, 1995; Cowan, Saults, & Elliott, 2002; Raye, Johnson, Mitchell, Greene, & Johnson, 2007; Camos et al., 2018; Vergauwe & Cowan, 2015). The longer a concurrent processing task captures attention, the less time attention is available to maintain the contents of working memory. Therefore, the working memory contents is liable to greater temporal decay. Based upon these assumptions the TBRS model proposes that the ratio of time between attentional capture and time available for working memory maintenance will govern the trade-off in performance (Barrouillet et al., 2004). This ratio is conceptualised as the "Cognitive Load" of the concurrent processing task (Barrouillet et al., 2004; Barrouillet & Camos, 2015).

The conceptualisation of cognitive load in time based parameters was significantly different from the views put forward by previous theories. In capacity sharing models, cognitive load had primarily been defined by task difficulty (e.g. Case, 1985) or the number of items to be processed (e.g. Anderson et al., 1996). However, this conceptualisation ignored the temporal cost of task difficulty (Barrouillet & Camos, 2015; Kahneman, 1973; Towse & Hitch, 1995). It became evident that in self-paced complex span tasks, harder interference tasks (or tasks with more processing items) took longer to complete confounding the effects of cognitive load with the length of the retention interval (Towse & Hitch, 1995; Towse et al., 1998). After controlling for this confound, it was concluded that the increased retention period was more informative than the difficulty of the concurrent task (Towse & Hitch, 1995). However, this assumption was based on the idea

that attention was switched to the processing task for the extent of the retention period; thus failing to account for the possibility that attention could have been switched back intermittently during concurrent processing. Working under the notion that attention could be rapidly switched back during brief pauses in the concurrent processing task and that harder processing tasks would take more time to complete, careful temporally constrained experiments were designed in order to disentangle the effects of cognitive load and retention interval in complex span tasks (Barrouillet et al., 2004; Barrouillet & Camos, 2015).

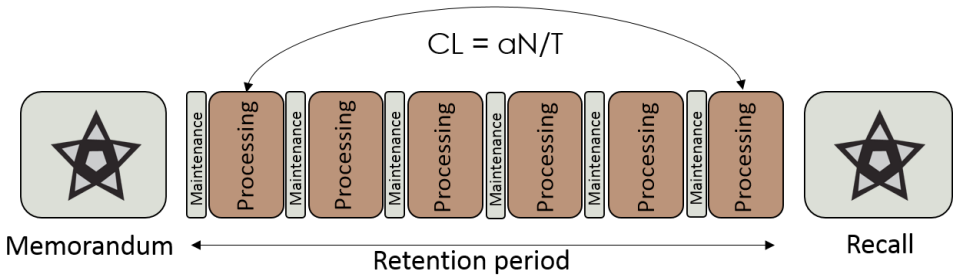


Figure 6.1: Visual representation of cognitive load. Temporal cognitive load can be thought of as the ratio of time within the retention period that attention is free for working memory maintenance compared to the time an internal processing task captures attention. This can be summarised as cognitive load is equal to "a" the time each processing task component takes timed by the number of components (N), divided by the total duration of the retention period (T).

Complex span tasks provide the participant with an increasing number of items (e.g. digits, letters, visual pattern cubes) to be remembered and alternate with an attentional demanding interference task (e.g. reading, operations or counting, Daneman & Carpenter, 1980; Turner & Engle, 1989; Case et al., 1982). Figure 6.1 gives a pictorial representation of the parameters that interact during an interference task to produce the temporal cognitive load. 1) "a" the amount of time a processing task element takes to complete (e.g. time taken for one operation), 2) "N" the number of task elements (e.g. the number of operations) and 3) "T" the overall retention period. Cognitive load is equal to the amount of time the concurrent processing task occupies attention (a*N), divided by the total amount of time available (T) (Barrouillet et al., 2004; Barrouillet &

Camos, 2015). Therefore, the cognitive load of a concurrent task can be manipulated as follows: changing the amount of time required to complete a task element, manipulating the amount of time available between task elements for maintenance activities and by manipulating the overall retention period (Barrouillet & Camos, 2015).

Using these careful controlled manipulations there is now a strong evidence base to support the impact of time based cognitive load on concurrent maintenance (for a review see Barrouillet & Camos, 2015). For example, the 4th experiment in Barrouillet et al's (2004) seminal paper used a design in which participants were required to maintain letters in memory, whilst reading aloud a series of numbers presented on a screen at either a fast or slow pace. The retention period was held constant (6 seconds). In the fast paced condition the numbers appeared onscreen for 450ms, followed by a 150ms pause. In the slow pace conditions, numbers were presented for 700ms, followed by a 300ms pause. Therefore, the cognitive load was higher in the fast paced condition (.75), as compared to the slow paced condition (.70). There was a significant impact of this manipulation. The average verbal span in the slow paced condition was 4.28 (1.01), dropping to 2.77 (0.92) letters in the fast paced condition. In this paper they also demonstrated (experiments 5 & 6) that if the number of items to be processed remains the same, but the pace is manipulated, the fast pace condition which has the higher cognitive load still results in a significantly lower span as compared to the slow pace condition with a larger retention interval (Gavens & Barrouillet, 2004; Barrouillet, Portrait, et al., 2011; Plancher & Barrouillet, 2013).

This evidence base includes a variety of complex span tasks using different memorandum, different processing tasks and different domains (Barrouillet & Camos, 2015; Barrouillet, Portrat, & Camos, 2011; Barrouillet et al., 2012). Firstly, of importance the impact of temporal based cognitive load has been found to transfer to visual spatial domains (Barrouillet et al., 2007; Barrouillet, Portrait, et al., 2011; Barrouillet &

Camos, 2015; Vergauwe, Barrouillet, & Camos, 2009). For example, when using visual pattern recall, or indicating movement direction (Vergauwe et al., 2009). Moreover, it is suggested that attentional capture can effect performance across domains (Vergauwe et al., 2009; Vergauwe, Barrouillet, & Camos, 2010).

Although this model has been extended to different domains the literature body is firmly grounded in the slot model approach to working memory (Cowan, 2005; Luck & Vogel, 1997; Pashler, 1998). This approach considers that working memory holds several independent memory "slots" (Cowan, 2005). However, this approach to memory performance is limited, with correct responses not providing information regarding the resolution of the item maintained (e.g. Ma et al., 2014). An alternative model has been proposed that suggests working memory is a limited representational medium, which can be flexibly allocated between items (Bays & Husain, 2008; Bays et al., 2009; Ma et al., 2014). Rather than there being a limited number of slots, the addition of more items simply effects the resolution with which the others items are stored (Ma et al., 2014).

The resolution with which items are stored is measured using delayed adjustment tasks (e.g. Bays & Husain, 2008). These types of tasks allow the recall of features such as orientation, movement or colour on a continuous scale, providing a more sensitive index of working memory (Zokaei, Burnett Heyes, Gorgoraptis, Budhdeo, & Husain, 2014). Using this approach it has been observed that temporal decay gradually effects the fidelity with which items are stored (Pertzov et al., 2013; Zhang & Luck, 2009) and how holding working memory items in the focus of attention can protect against this decay (Pertzov et al., 2013; Wang, Yan, Wang, Olivers, & Theeuwes, 2017; Zokaei et al., 2014).

Examining the assumptions of the TBRS model within the framework of a resource based approach to working memory lends itself to more detailed analysis, especially when dealing with a small number of items to be retained. Although previous complex span tasks have suggested that 1 or 2 items can be retained whilst simultaneously completing the interference task, no research to date has examined the fidelity of these items. It could be that these items are effected by cognitive load, but not enough to go below the threshold for accurate recall. Using an index of precision would allow smaller decrements to be detected and will give a detailed investigation of the TBRS model.

Therefore, the following investigation aims to test the assumptions of the TBRS model on the precision of recall of one single item feature. Because precision measures of working memory can examine smaller decrements in the resolution with which an item is stored (e.g. degrees away from an orientation or location or steps away from a certain shade of colour), it was hypothesized that cognitive load would directly impacts on the precision with which we can recall an item: the higher the cognitive load, the worse recall precision. The reasoning behind this is that in higher load conditions more time would be available for the item to be held in the FoA and therefore, the item would spend less time when it is liable to gradual temporal decay. In line with previous research it was expected that the addition of an interference task would impair recall precision in comparison to a matched retention interval. Furthermore it was expected that the cognitive load of the interference task would modulate the trade-off in working memory performance.

6.3 General Method

Sample

Inclusion criteria for all studies included: aged 30 or below, fluent in the English language and normal or corrected to normal eyesight.

Procedure

Participant recruitment differed between experiments and details will be provided individually below. The experiment room was dimly lit using a lamp which was positioned behind the participant. The participant was seated in the room at least 15 minutes prior to starting the experiment to allow their eyes time to adjust. In this time they were given the task instructions and any questions were answered. The participant was positioned comfortably and centrally in front of the experimental computer by making adjustments to the chin rest, chair and screen height. The chin rest was set up to keep the viewing distance at 60 centimetres. The experiments were programmed in Python, using the PyGaze toolbox (Dalmaijer et al., 2014). The stimuli were presented on a 21 inch LED monitor (BenQ XL2411) at a resolution 1,920 x 1,080, with a vertical refresh rate of 100Hz. The researcher stayed present for a sequence of practice trials to ensure the participant understood and was able to complete the task.

Experimental procedure

In the following three experiments two differing experimental designs were used and more specific details will be given below. The two designs primarily differ on the interference task used, although the experimental presentation remains the same.

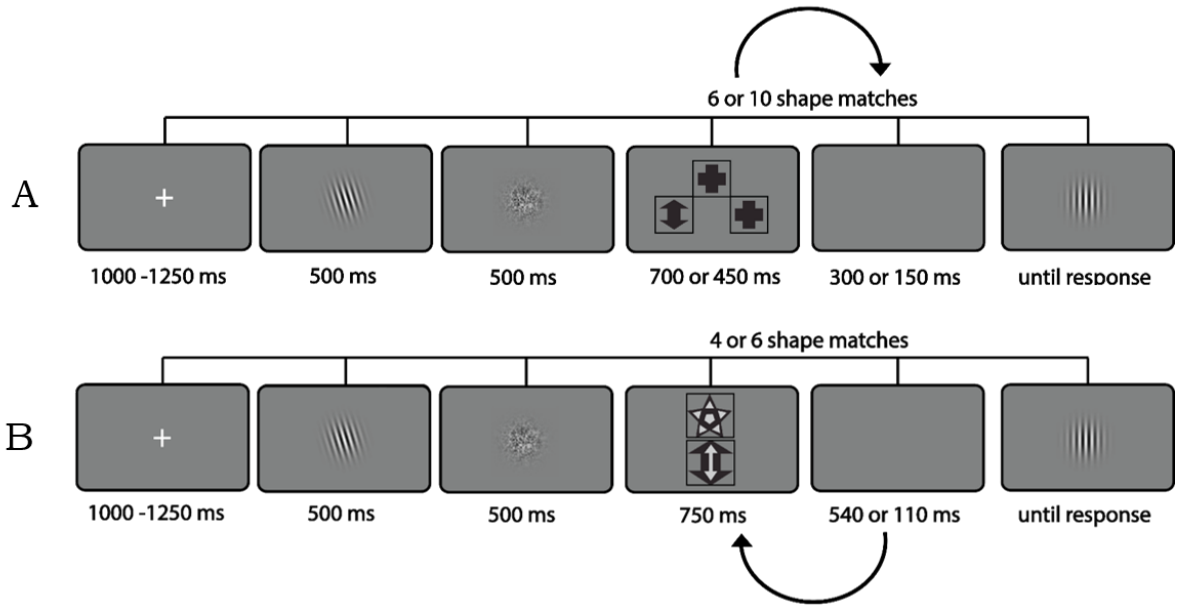


Figure 6.2: Experimental Procedure Overview. A) Experiment 1 design. B) Experiment 2 & 3 design. The two designs differ only on the interference task. In experiment 1 participants have to select which of the bottom shapes match the top shape. In the second design the participants have to indicate whether the two shapes match or do not match.

Memorandum Presentation: First, the participants attention was brought to the center of the screen using a white fixation cross (0.67^o, 0.67^o), which was displayed for 1000 or 1250 milliseconds. Next they were presented with a memorandum. The memorandum chosen was a gabor (7.62^o, 7.62^o, spatial frequency 0.5 cycles per degree) which was slanted to display an orientation between 1^o -180^o degrees from vertical. The gabor was displayed centrally for 500 milliseconds. To help control after image a noise patch (7.62^o, 7.62^o) was presented subsequently for 600 milliseconds. A gabor presented orientation memorandum was chosen for two reasons. First visual processing of a gabor stimuli is well understood (e.g. Boynton, 2005) and secondly the use of the orientation feature is more simple than the use an object stimuli in which interactions with other memory systems would take place (e.g. prior semantic knowledge, Brady et al., 2016).

Interference Task: There was then a retention interval of varying lengths (dependent on condition). Within this interval participants were either required to do nothing, or complete an interference task. Both designs utilised a choice reaction time task in which judgements about whether shapes matched were made and responses given by selecting one of two keyboard buttons. This design took elements from a visual choice reaction task previously found successful in manipulating cognitive load (Barrouillet, Portrait, et al., 2011). These shape match choices came in a sequence, with a brief pause between each shape match judgement. The manipulation of the number of shape matches to be performed and the pause times allowed the manipulation of cognitive load. The timing and stimuli used for the interference task vary between experiments and detail will be given more specifically below. Both the reaction time and accuracy of each shape match was recorded.

Orientation Recall: Following the interference task, a second gabor was presented centrally on screen (7.62^o, 7.62^o, spatial frequency 0.5 cycles per degree). The orientation of the target stimulus was recalled using a powermate dial, which provided a physical analogue of the on-screen gabor. The reaction time (screen onset to first dial turn), response time (first dial turn to final orientation submit) and the absolute angular error (difference between orientation selected and correct orientation in radians) were collected. The recall had no time limit and the participants submitted their answer and moved onto the next trial by pressing the space bar.

Conditions

The manipulation of cognitive load provided five conditions: *baseline short, slow pace short, fast pace short, slow pace long and baseline long.* In the baseline conditions there was no interference task. However, non-relevant visual information was still displayed on screen to include the general disruption of visually presented information on the

concurrent maintenance of visual information (Logie, 1986; Quinn & McConnell, 1996). The baseline short condition had the same retention interval as the slow and fast paced short condition. The slow and fast paced conditions included the interference task, but differed on the number of shape match judgements to be completed. This manipulation meant that the fast pace condition had a significantly higher cognitive load as compared to the slow pace condition. Because the fast pace condition had a higher number of shape match judgements than the slow pace condition, the slow pace long condition was designed. This condition had the slower pace, but the same number of shape matches as the fast pace condition. This extended the length of the retention period. Therefore, a second baseline condition was made to match the retention period of the slow pace long condition.

Measures

Interference Task: The binary accuracy of the interference task was scored, summed per trial and the percentage correct calculated. To be considered correct the participant had to answer correct within the presentation time of the shape match. Any answers given in the maintenance pause were not considered. The reaction time of each shape match was also taken and the average per trial calculated.

Orientation Recall: For the orientation recall the primary measure taken was the precision of orientation recall. This was measured using the absolute error between the target orientation and the recalled orientation in radians between 0 (perfect recall) and -0.5π or 0.5π (largest possible error). This allowed average error within conditions to be calculated and compared across conditions. Furthermore, reaction time was recorded in milliseconds. This measure was taken as recall screen onset to first dial and indicated how quickly they began to make a response. A secondary time measure, response time was also recorded. This was first dial turn to the space bar press that indicated response

submission. The reason for segregating these two measures is that response time is also contingent on the distance between the start orientation of the probe gabor and the target recall orientation.

Experimental Questions/Comparisons

1) First decay was indexed by comparing the baseline short to baseline long condition.

2) Next the interference effect was examined by comparing baseline short to the slow and fast paced short conditions and the baseline long condition to the slow pace long condition. The TBRS model would suggest that in all cases the interference task should negatively impact on orientation recall performance.

3)Next the manipulation of cognitive load was examined by comparing the slow pace short and long to the fast paced short condition. The TBRS model would suggest that orientation recall would be more error prone on the fast paced condition.

4)Finally, impact of cognitive load over that of retention interval and number of items was investigated. To examine the impact of retention interval the slow pace long was compared to the slow pace short condition. These conditions differed in retention interval length but not cognitive load. The TBRS model would suggest that the slow paced conditions should not differ in working memory performance. Secondly to examine the impact of number of items the slow pace long condition was compared to the fast paced condition. These conditions differed in retention interval, but were matched for the number of items. The TBRS model would propose that the fast paced condition would be significantly more error prone than the slow pace long condition.

Analysis

Data processing was performed using python 2.7. All statistical analyses were run in R (3.0.3 R Core Team, 2014b) using package lmer4 (Bates et al., 2015) and lmerTest

(Kuznetsova, Bruun Brockhoff, & Haubo Bojesen Christensen, 2014). This allowed a linear model to be run, looking at the within effects of condition. In the final experiment a 5*3 mixed design was run looking at the within effect of condition and the between effects of digit span group. LmerTest was used to run FDR corrected Tukey contrasts.

6.4 Experiment 1

Sample

Ten participants were recruited from the Oxford Participant Recruitment (OPR) system. All of which were neurologically healthy and fluent in the English language. The average age of the sample was 23.59 (SD=4.97). The sample was 60% female, 60% had corrected to normal vision, 70% students, 60% white and education was distributed from secondary to postgraduate (10% secondary school, 10% college, 60% university and 20% post graduate).

Procedure

Participants were invited into the Cognitive Neuropsychology Centre (CNC) and shown into the experimental room and seated at a desk. They were given time to read through the participant information sheet, ask questions and give informed consent. The seat, chin rest and screen was then adjusted to ensure the participant was positioned so that they viewed the screen centrally. Participants were then asked to give some demographic information. After the questions had been answered, the task instructions were given verbally using printed experiment task screen shots to illustrate the process. The participant was then given up to 10 practice trials to ensure they understood the task and to become familiar with the speed, response buttons and use of the dial. Subsequent to the practice the experiment task was started.

Experimental Design

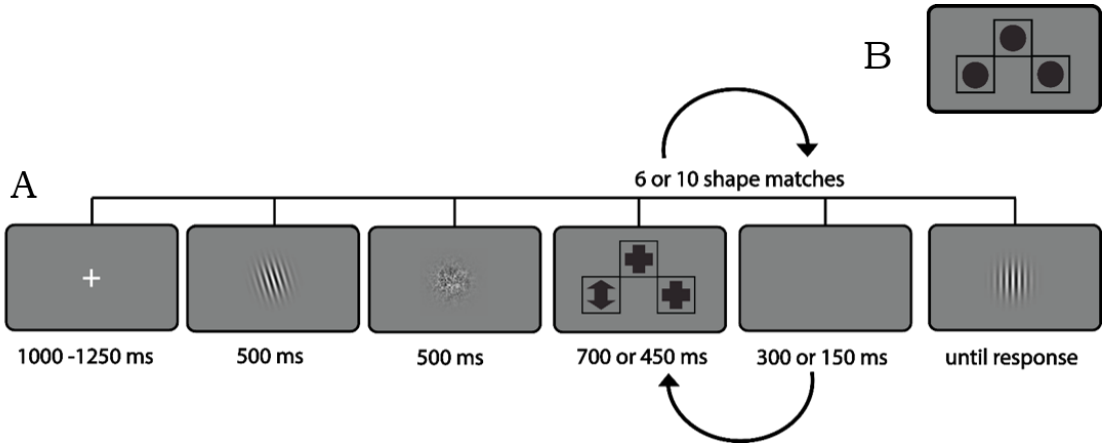


Figure 6.3: Experimental design overview. A) Experimental task procedure. Showing the orientation memory task, with the shape match interference task in the retention period. The varying number of shape match judgements and timing during the interference task was used to manipulate cognitive load. B) Baseline screen, shown when no interference task is to be completed.

Interference Task Design: The participant was presented with three boxes, each containing a solid black shape (see Figure 6.3 A). One box was presented centrally towards the top of the screen (5.00^o) at a visual angle of 5.25^o, 5.25^o. This box contained the target shape. The other two boxes were presented lower down, situated to the left and right of the screen (8.30^o, 5.00^o). One of the boxes contained the target shape and the second a distractor shape. The task was to indicate which, out of the bottom two boxes, contained the matching shape. Participants made their selection by pressing the left or right arrow keys on the keyboard. In order to be counted as correct the participant had to make the choice within the time the shapes were still presented on the screen. After the shapes had been presented a blank screen would appear, after a pause the next shape match screen would appear for a sequence of 6 or 10 shape match judgements. On baseline conditions, the participant did not have to make a response, however, the same three boxes would appear all containing a black circle (see Figure 6.3 B). The reason for the baseline display is that passive visual interference has been suggested to impact working memory recall (e.g. Logie, 1986; Quinn & McConnell, 1996).

There were 200 trials in total (40 in each of the five conditions). The participants have a self timed break after each block of 40 trials. In each block there were 8 of each condition type presented in a randomised order.

Manipulation of Cognitive Load: In the present design the manipulation of cognitive load was firstly approached by manipulating both the shape match presentation and pause times. This manipulated the pace at which shape matches were given in a fixed retention interval. The retention interval was also manipulated in order to provide a control for the number of items. There are five conditions in total, summarised below. The timing for this experiment was taken directly as a replication of experiment 4 from Barrouillet & Camos (2004). Please see Table 6.1, for a summary.

Table 6.1: Experiment 1 Conditions Overview

Condition	Shape Judgements	Pause	Retention Interval	Cog Load
Baseline			6000	
Slow Pace Short	06 * 700 ms	300	6000	.70
Fast Pace	10 * 450 ms	150	6000	.75
Slow Pace Long	10 * 700 ms	300	10,000	.70
Baseline Long			10,000	

Data Filtering

The data were filtered individually for correctness on the interference task. It would have been desirable to filter on 100% correct in the interference task, however there were very few trials where this criteria would have been met (slow pace: 61%, fast pace: 4%, slow pace long: 47%). Therefore, the data was filtered using a less conservative criteria of achieving at least 50% correct shape matches on a given trial. To be considered correct the shape match answer had to be submitted before the pause period, this was to ensure attention was free for working memory refreshing. Using this criteria an average of 32 trials (SD=4.08) were retained in each condition.

Results

Cognitive Load Manipulation

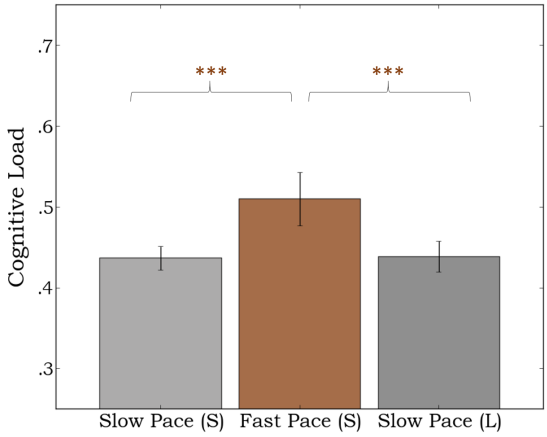


Figure 6.4: Average Cognitive Load by Condition (EB= 95% CI)

In order to calculate the average cognitive load per condition, for each trial the reaction times on the interference task were summed and divided by the total duration of the interference task (p.65, Barrouillet & Camos, 2015). This gave the trial cognitive load ($\sum a_i \; N_i/\mathrm{T}$), which was then averaged within each condition. There was a significant effect of condition on cognitive load [$F(2,30)=11.63$, $p <.001$]. Tukey contrasts demonstrated that the cognitive load was significantly higher in fast pace condition as compared to the slow pace condition ($Z=$ -4.24, $p <.001$) and compared to the slow pace long condition ($Z=$ -4.11, $p <.001$). The two slow paced conditions were comparable.

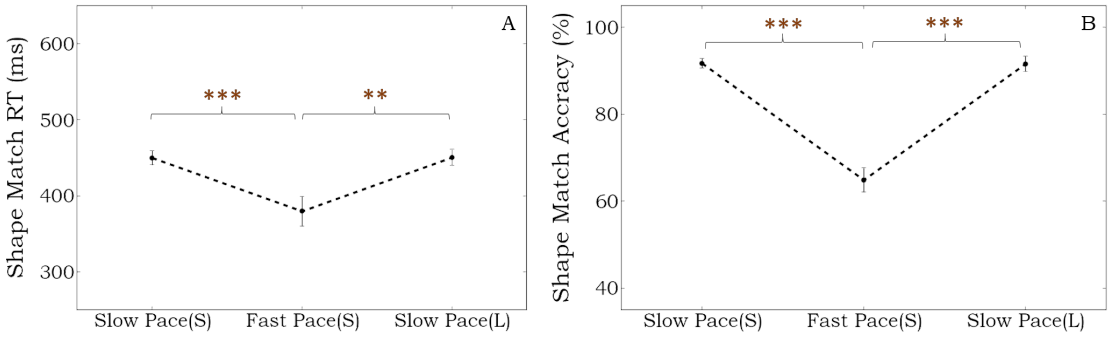


Figure 6.5: Interference Task Performance by Condition. A) Average RT (ms). B) Average Percentage of Correct Shape Matches. (EB= 95% CI)

As can be seen in Figure 6.5 A, there was a significant effect of condition on average shape match reaction time [$F(2,20)=24.35$, $p<.001$]. FDR corrected Tukey contrasts revealed that fast pace condition had a significantly quicker average shape match reaction time as compared slow pace ($Z=6.02$, $p<.001$) and to the slow pace long condition ($Z=2.08$, $p<.001$). No difference was found between the two slow paced conditions.

As can be seen in Figure 6.5 B, there was a significant main effect of condition on average shape match accuracy [$F(2,20)=167.47$, $p<.001$]. FDR corrected Tukey contrasts found that fast pace condition had a significantly lower percentage of correct shape matches as compared to slow pace condition ($Z=15.89$, $p<.001$) and the slow pace long ($Z=15.81$, $p<.001$). There were no differences observed between the two slow paced conditions for accuracy. These results suggest it was difficult to response correctly within the 450ms presentation time of the fast paced condition.

Furthermore, the number of times the participant had to switch between left or right hand shape match was examined. A significant effect of condition was found [$F(2,20)=53.74$, $p<.001$]. FDR corrected Tukey contrasts found that there was a significantly lower number of switches on average in the slow pace (M=3.0, SD=.22), compared to the fast pace condition (M=4.78, SD=.66, $Z=9.0$, $p<.001$) and the slow pace long condition (M=4.77, SD=.70, $Z=8.95$, $p<.001$).

Orientation Recall Performance

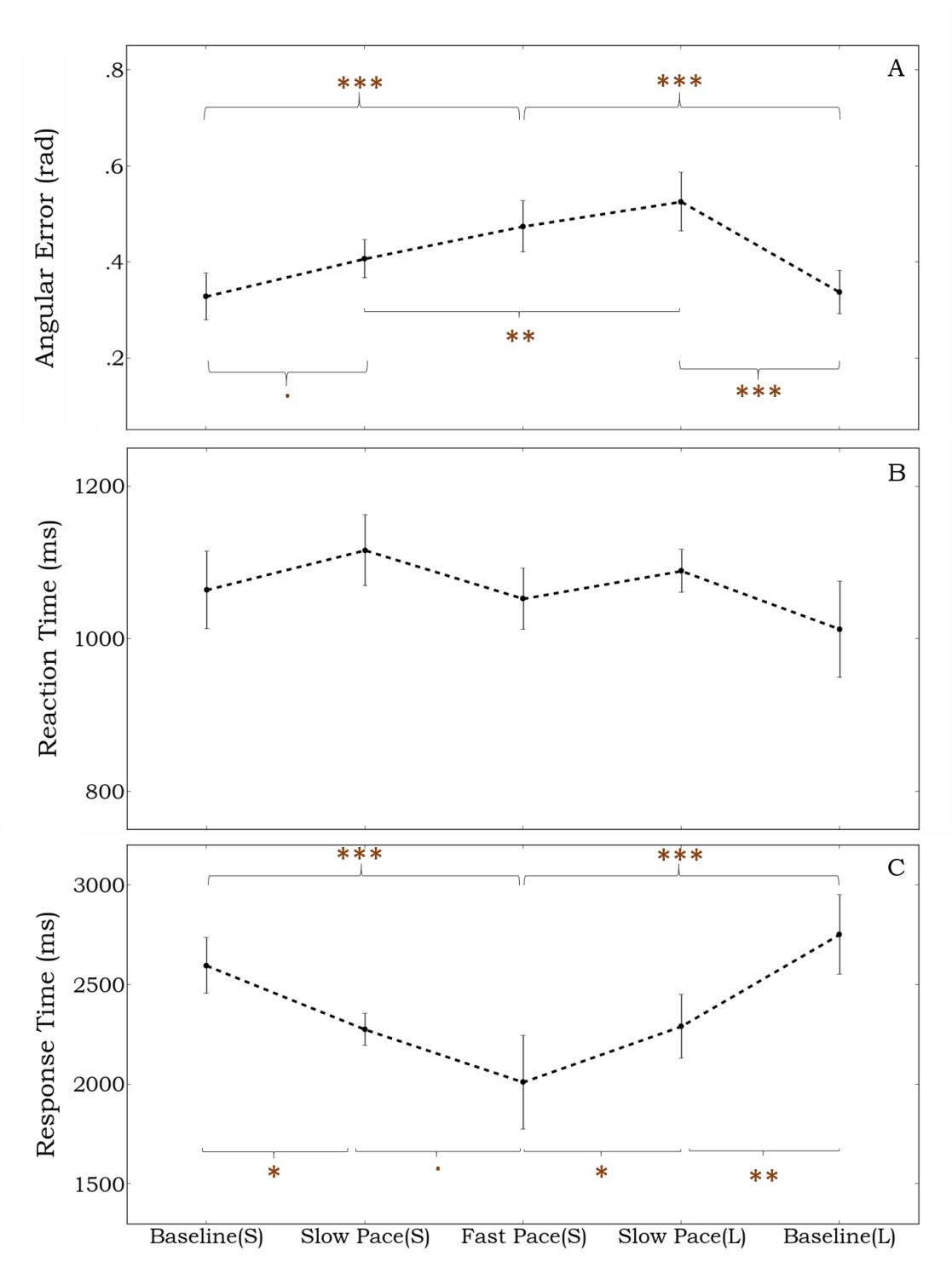


Figure 6.6: Orientation Recall Performance. A) Angular Error (radians between answer and target orientation). B) Average RT (screen onset-first dial turn). C) Average Response Time (first dial turn-response submission). (EB= 95% CI)

As can be seen in Figure 6.6 A, there was a significant effect of condition on absolute angular error [$F(4,40)=9.97$, $p<.001$]. FDR corrected Tukey contrasts revealed: **1)**There was no significant difference in error (angular deviation from true orientation of the item) of recall when comparing the two baseline conditions. **2)** There was however, significantly more precise recall on the baseline condition as compared to the fast pace condition ($Z=3.80$, $p<.001$) and a trend when compared to the slow pace condition ($Z=2.04$, $p=.07$). Participants were also significantly more precise on the baseline long condition compared to slow pace long ($Z=4.91$, $p<.001$) and fast pace conditions ($Z=3.57$, $p<.001$). **3)** There were no differences seen between the fast and slow paced conditions. **4)** Participants were significantly more precise on the slow pace short as compared to the slow pace long condition ($Z=3.10$, $p=.004$). There was no difference between the slow pace long and fast paced conditions.

As can be seen in Figure 6.6 B, condition did not significantly impact reaction time. However, as demonstrated in Figure 6.6 C, there was significant impact of condition on response time [$F(4,40)=9.93$, $p<.001$]. FDR corrected Tukey contrasts demonstrated: **1)** There was no difference between the two baseline conditions. **2)** However, in comparison to the baseline short condition, participants were significantly faster responding on the slow pace condition ($Z=2.45$, $p=.03$) and the fast pace condition ($Z=4.47$, $p<.001$). In comparison to the baseline long condition, participants were significantly slower on slow pace long condition ($Z=3.52$, $p=.002$) and the fast pace condition ($Z=5.67$, $p<.001$). **3)** There was a trend for the fast paced condition to be completed significantly faster as compared to the slow pace condition($Z=2.02$, $p=.054$). **4)** There was no difference found between the two slow paced condition, however the fast paced condition was completed significantly faster than the slow pace long condition ($Z=2.14$, $p=.046$).

Experiment 1: Discussion

In experiment 1 the TBRS model was tested to examine whether the assumptions also hold true for the precision of recall for one item. The modulation of cognitive load was significant, with a higher load in the fast paced condition.

First of all the presence of temporal decay was examined. Although recall error was slightly worse in the longer baseline condition as compared to the shorter baseline condition, this difference was not significant. This suggests that in this design when attention is not occupied by a concurrent processing task participants are able to maintain the orientation over the extra 4 seconds with relatively little extra decay (orientation recalled within 20^o). Within the model framework, this would suggest that attentional refreshing (Raye et al., 2007; Camos et al., 2018) was enough to prevent decay.

Interestingly, the slow pace long condition was found to be significantly more error prone than the slow pace short condition. This finding is in conflict with previous observations in which it was suggested that if cognitive load remains constant increasing the retention period should have little or no affect on working memory performance in adults (Plancher & Barrouillet, 2013; Barrouillet et al., 2004; Barrouillet & Camos, 2015). A small impact of renetion interval has previously been noted in children (Gavens & Barrouillet, 2004) and it has been postulated a similar effect could occur in adults due to factors such as fatigue (Barrouillet & Camos, 2015). Although, it is important to consider that in the current design it was observed that the number of switches was significantly higher in the slow pace long condition. Task switching has been shown to effect storage during working memory span tasks (Liefooghe, Barrouillet, Vandierendonck, & Camos, 2008). Therefore, this parameter could have impacted the difference between the slow pace conditions and should be kept constant in further work.

It was observed that the addition of an interference task impacted poorly on the precision with which the orientation could be recalled. This result is in line with the past complex span literature (e.g. Barrouillet & Camos, 2015; Towse & Hitch, 1995; Barrouillet et al., 2004), but extended the finding to include the precision of one item recall. However, it was not found that cognitive load impacted significantly when comparing the fast and slow paced conditions. This finding suggests temporal cognitive load may be less important when considering the precision of recall for one item. Perhaps this is because the bottle neck only interacts with time, when attention is required to shift between working memory traces in sequential memory (Barrouillet & Camos, 2015). Alternatively, it could indicate that cognitive load is important more generally when binding of information in time or space is required (Humphreys, 2016; Wolfe, 2014; Manohar, Pertzov, & Husain, 2017). It could however, simply be that a stronger manipulation of cognitive load is required to impact detrimentally on the recall of only one item. The modulation of cognitive load in the current experiment was not particularly strong (.44 vs .51). A large percentage of time was not occupied by the concurrent task and may have provided enough time for sufficient refreshing in both conditions. Therefore it would be beneficial to test this relationship with a stronger cognitive load manipulation.

In addition to the working memory error, reaction and response times were also examined to see whether the conditions impacted on speed. Although there was little effect on the speed with which the orientation recall began, there was a modulation of response time (time from first dial turn to response submitted). The participants were significantly faster in conditions with the interference task. This is perhaps a strategy employed to improve orientation recall, with the participants speeding up to prevent further working memory decay. Alternatively, it could represent a speed accuracy trade off, with faster responding and worse precision.

An alternative could be that the pace of the interference task entrains the pace with which the participants respond on the recall task. It was observed that both the reaction and response times were faster in the fast pace condition. This could have been due to the additional requirement of faster responding on the shape match task carrying over into the secondary task (i.e. only having 450 ms to make the judgement in rather than 700 ms). Allowing the participants equal time to respond on the shape match judgements may change this relationship.

The difference in time allocated to make the shape match judgements between the conditions may also be the reason for such poor task performance. This is illustrated by the average reaction time being significantly quicker in the fast pace condition, but the accuracy being significantly lower. This pattern suggests that participants found it hard to complete the judgement within the 450 ms. The difference in time allowed for responding in the interference task has also previously been criticised for changing the time pressure requirement in addition to the cognitive load. It has even been suggested that this time pressure difference is the main reason for recall differences between conditions (Oberauer & Lewvandowsky, 2013). In the following design the shape judgement time will be kept constant and only the pause time adjusted in order to try and equalise these differences between conditions.

A related difficulty arising from such poor performance on the interference task (especially in the fast condition) is that it is ambiguous as to whether the participants were paying attention. Poor task performance could be caused by the task difficulty being too high or the speed being too quick. However, it could also be affected by poor attention (e.g. mind wandering). Alternatively, participants may have been sacrificing interference task performance in favour of maintaining the orientation. Therefore, the manipulation may not have been working in the manner it was intended to.

In addition to equalising the time available to make the shape match judgement, the task will be slightly modified to make it easier to complete within the time. The requirement to shift attention between two stimuli will be removed and replaced with a single shape match judgement (match or no match). This change will also address another problem, which is that there could possibly be competition between the two task response sets (i.e. left or right may be in the same or different direction to the slant of the gabor orientation). In addition the stimuli will also be modified to make them more distinct and they will be moved closer together (previously found to modulate task difficulty, Barrouillet et al., 2007).

Experiment 2 was designed to readdresses the current questions with a new task design which accounts for some of the current weaknesses. This new design has a stronger modulation of cognitive load, the time for the shape match response is equalised between conditions, shape match task was adjusted to make it easier to complete in the time limit to allow better filtering and finally the number of switches was equalised between conditions.

6.5 Experiment 2

Sample

A sample of 10 participants (60% female). The mean age was 24.7 (5.03). Of the sample 80% was right handed, education distribution is 10% secondary school, 10% college, 60% university and 20% post graduate. 50% of the participants were students. The same participants recruitment and procedure was used as experiment 1.

Experimental Design

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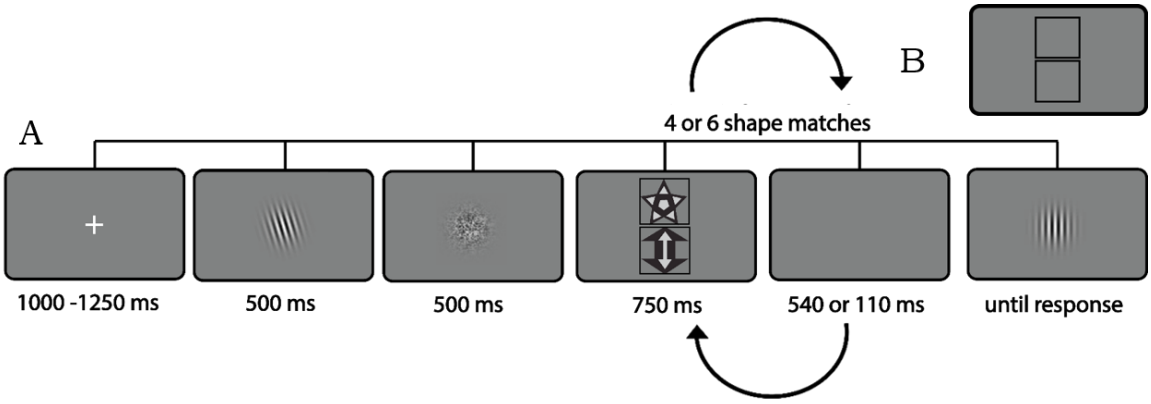


Figure 6.7: Method Overview for Experiments 2 and 3. A) Experimental task procedure. The orientation memory task, with shape match interference task in the retention period. The number of shape matches (4 or 6) and pause duration (540ms-110ms) was manipulated to create conditions with varying cognitive load. B) Screen displayed during baseline conditions without an interference task.

Interference Task Design: The new interference task consisted of making a singular shape match judgement: match or no match. Two boxes were presented above and below the central line (both visual angle of 5.25^o, 5.25^o). Inside each box was one of 8 shapes (Figure 6.7 A, Appendix E.1). If the two shapes matched the participant pressed the "M" key and if they didn't match they pressed the "N" key.

Table 6.2: Experiment 2 and 3 Overview

Condition	Shape Judgements	Pause	Retention Interval	Cog Load
Baseline			5160	
Slow Pace Short	4 * 750 ms	540	5160	.58
Fast Pace	6 * 750 ms	110	5160	.87
Slow Pace Long	6 * 750 ms	540	7740	.58
Baseline Long			7740	

For a visualisation of the design please see Appendix E.4, p.357

Cognitive Load Manipulation: In all instances the shape match pairs were presented for 750 ms, whereas the length of the pause between shape match judgements was 110 ms on the fast pace condition and 540 ms on the slow pace conditions. On the slow pace condition there were 4 shape match judgements and on the fast pace and slow pace long condition there were 6 shape match judgements (see Table 6.2 for an overview). In all conditions the number of switches between match and no match was constrained to two. Empty boxes were displayed on the baseline condition (see Figure 6.7 B).

Experimental Procedure: There were 200 trials (40 in each condition). A self timed break was given after each set of 40 trials. Each block was comprised of 8 trials of each condition type, presented in a randomised order.

Data Filtering

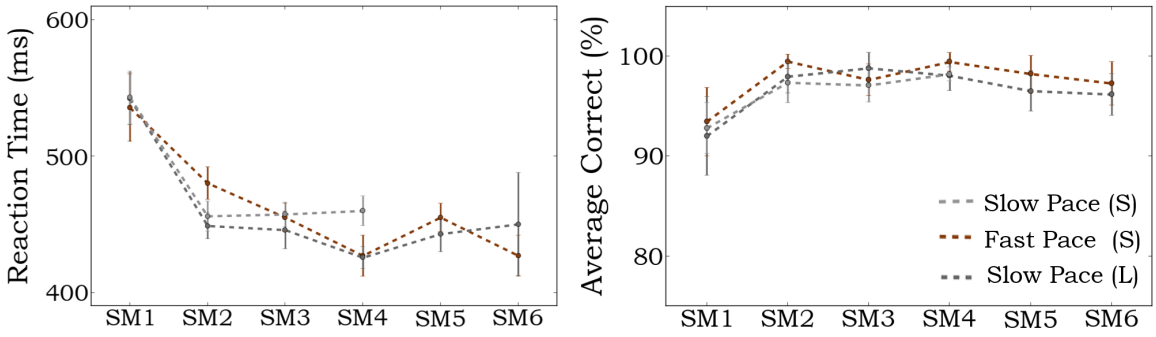


Figure 6.8: The Effect of Shape Match Number on Average Performance. SM = Shape Match. Error bars = 95% CI

Trials on which the reaction time for the precision recall task was ± 3 MAD were taken to indicate attentional lapses or other forms of error and removed (Leys, Ley, Klein, Bernard, & Licata, 2013). The percentage of correctly complete trials was much higher in the new design, but still not as high as expected. The interference task performance was examined split by the order of shape matches (Figure 6.8). It was observed that the first shape match choice was both slower and had a lower percentage of correct trials. The same effect has previously been observed and was attributed to a task switching cost (Jarrold, Tam, Baddeley, & Harvey, 2011; Vergauwe & Cowan, 2014), rather than the participants being inattentive to the task. Therefore, only trials on which the interference task was completed with at least 75% accuracy were retained. This cut off allowed for only one mistake on both the shape match short condition (3/4 = 75%, 2/4=50%) and other two conditions (5/6=83%,4/6=67%). After filtering on average there was 32.08 trials (SD=7.40) per condition.

Results

Cognitive load Manipulation

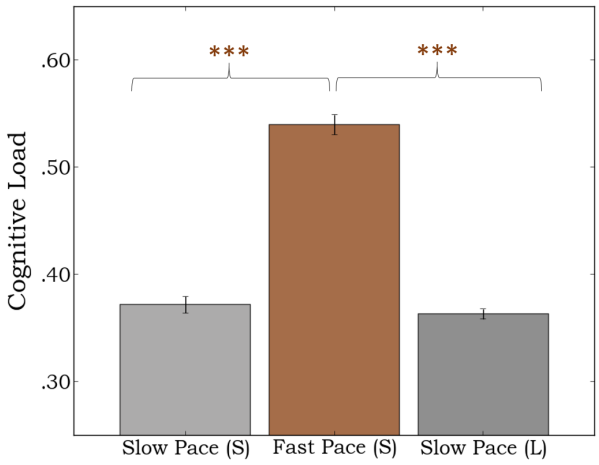


Figure 6.9: Average Cognitive load by Condition.

Next the effectiveness of the manipulation was examined by looking at the effect of condition on average cognitive load ($\sum\ a_i\ N_i$/T). There was a significant main effect of condition on cognitive load [$F(2,20)$=505.13, p <.001]. The cognitive load was significantly higher in the fast paced condition as compared to the slow pace short (Z= -26.80, p <.001) and the slow pace long condition (Z= -28.20, p <.001). The manipulation of cognitive load was successful with participants spending on average 866 ms more on external processing in the fast paced condition as compared to the slow pace short condition. The cognitive load was similar between the two slow pace conditions.

Interference Task Performance

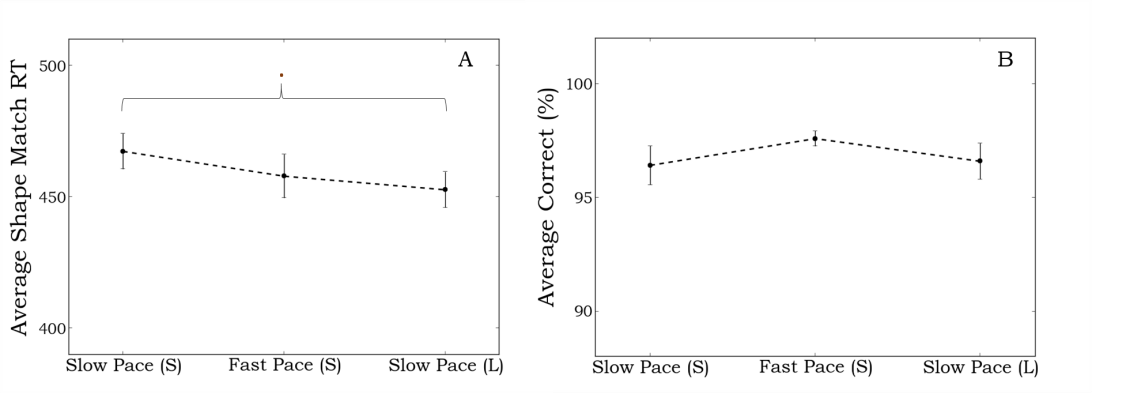


Figure 6.10: Average interference task performance. A) Average reaction time. B) Average percent correct. Error bars = 95% CI.

The performance on the interference task was compared across conditions. There was a trend towards condition having an impact on average shape match RT [$F(2,20)$=2.91, p=.08]. FDR corrected contrasts demonstrated a trend for the average RT to be slightly quicker on the slow pace long condition as compared to the slow pace short condition (Z= -2.38, p=.05). As seen in Figure 6.8, shape match reaction time got quicker with practice. The smaller number for shape matches in the slow pace condition meant this benefit wouldn't have had the same impact on the average. The percentage of correct shape matches was similar between the conditions.

Precision Performance Split by Condition

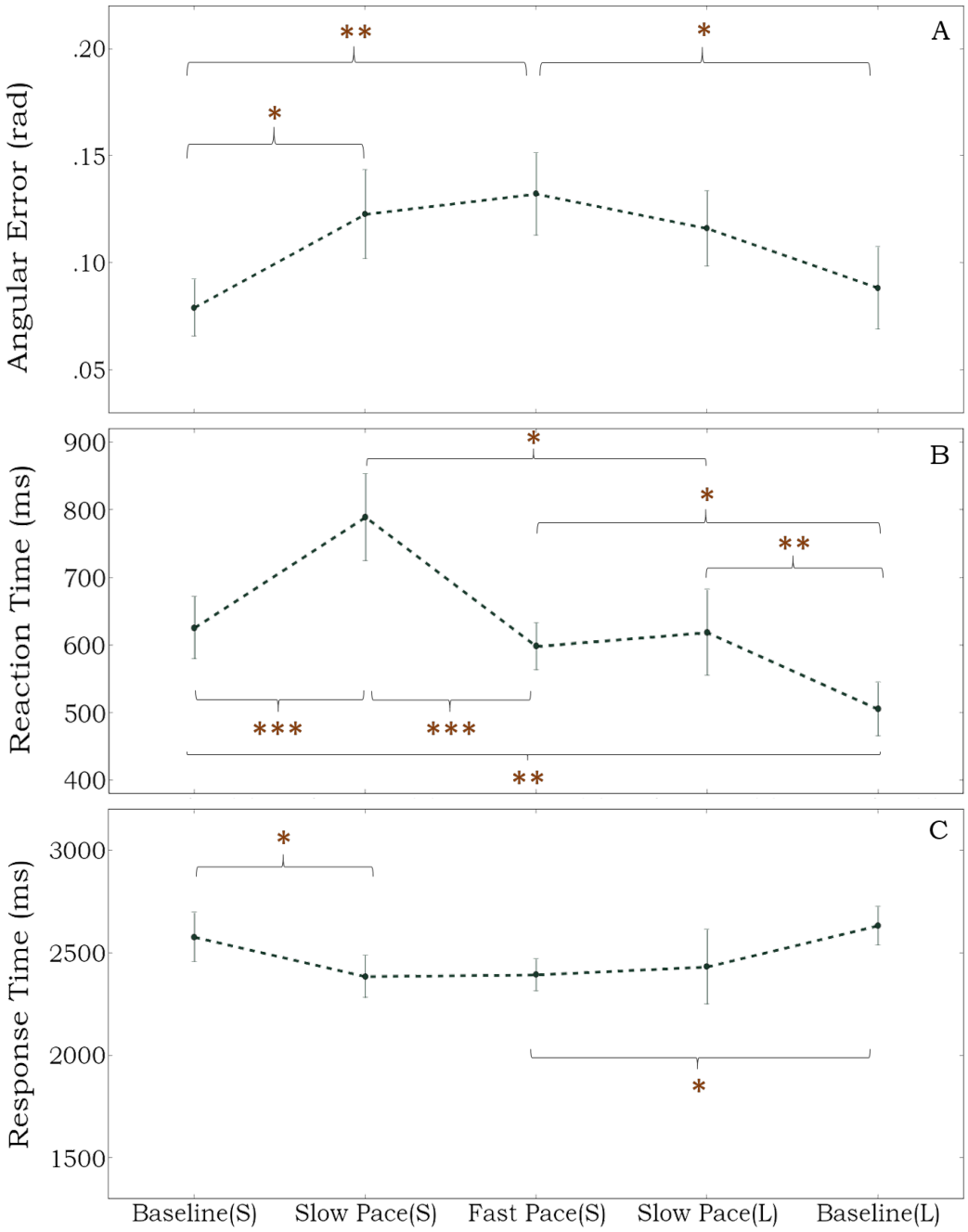


Figure 6.11: Orientation Recall Performance. A) Absolute Angular Error (distance between answer and target orientation). B) Reaction Time (screen onset- first dial turn). C) Response Time (first dial turn to answer submission). Error Bars = 95% CI.

As seen in Figure 6.11 A, there was a significant effect of condition on absolute error [$F(4,40)=4.67$, $p=.003$]. FDR corrected contrasts demonstrated: **1)** There was no significant difference observed between the two baseline conditions. **2)** In comparison to the baseline short condition, there was more error on the slow pace short condition ($Z= 2.88$, $p=.01$) and the fast pace condition ($Z= 3.13$, $p=.006$). In comparison to the baseline long condition, there was significantly more error on the fast pace condition ($Z=2.92$, $p=.01$). **3)** There were no differences observed between the fast and slow paced conditions. **4)** There were no differences observed between the two slow paced conditions. Overall, there was a significant interference effect, but no effect of cognitive load.

As seen in Figure 6.11 B, there was a significant main effect of condition on reaction time [$F(4,40)=13.04$, $p <.001$]. Contrasts demonstrated: **1)** Participants' had significantly faster reaction times in the baseline long condition as compared to the baseline short condition ($Z= -3.03$, $p=.005$). **2)** The baseline short condition was significantly faster than the slow pace short condition ($Z= 4.05$, $p <.001$), but not the fast pace condition. The baseline long condition was significantly faster than the slow pace long ($Z= 2.85$, $p=.007$) and fast pace ($Z=2.33$, $p=.03$) conditions. **3)** The fast pace condition was significantly quicker compared to the slow pace short condition ($Z=4.75$, $p <.001$), but not the slow pace long condition. **4)** Moreover, the slow pace short condition was significantly slower than the slow pace long condition ($Z= -4.23$, $p <.001$).

As seen in Figure 6.11 C, there was a significant main effect of condition on response time [$F(4,40)=3.81$, $p=.01$]. Contrasts demonstrated: **1)** There was no difference between the two baseline conditions. **2)** In comparison to the baseline short condition the slow pace condition was completed significantly faster ($Z= -2.77$, $p=.03$), but no the fast pace condition. In comparison to the baseline long condition, the fast pace condition was completed faster ($Z=2.45$, $p=.05$), but not the slow pace long condition. **3)** There were no differences observed between the fast and slow pace conditions. **4)** There were also no differences observed between the two slow pace conditions.

Discussion for Experiment 2

The experimental design changes implemented in experiment 2 were for three main reasons: to make the manipulation of cognitive load stronger, to equalise the time available to make shape match judgements and to improve the accuracy on the interference task. The modulation of cognitive load was now stronger between the slow (.37) and fast paced (.54) conditions. Overall the new task design was easier, the average reaction time was faster and average accuracy was much higher. Furthermore, these parameters were no longer significantly different between the conditions. Therefore, suggesting that the time pressure between the conditions was now matched more effectively. The data could now be filtered on 75% correct, allowing much greater control over the efficiency of the cognitive load manipulation.

As with the previous design there were no differences observed between the two baseline conditions. This suggests that attentional refreshing was good enough to prevent significant decay in the extra 2580 ms between the two retention intervals (Camos et al., 2018). After equalising the time pressure and number of switches between response modes (match-no match), there was no longer a significant difference between the two slow pace conditions. Therefore, the results from the new design compliment the idea that when cognitive load remains constant, the length of the retention period has little effect (Barrouillet & Camos, 2015; Barrouillet et al., 2004).

In correspondence with the previous design there was a significant interference effect, with the interference tasks impacting negatively on the precision of orientation recall. However, once again there was no significant impact of cognitive load found. This again suggests that time based cognitive load may not impact on the precision of one item feature recall. However, it was noted that there was a large amount of variability on how the slow and fast paced conditions impacted recall. Previous work had demonstrated individual differences in working memory capacity to impact on TBRS

complex span performance, particularly in the fast pace condition (Barrouillet et al., 2008). Therefore, a third experiment will be run with a larger sample of participants including additional measures of working memory capacity. This inclusion should address some of the variation and allow the investigation of whether the impact of cognitive load may differ depending on baseline working memory capacity.

6.6 Experiment 3

Sample

A sample of 41 Psychology A Level students were recruited from Farnham College. It was the first time any of them had participated in a psychology experiment. Two participants were removed due to their performance on the interference task being exceptionally poor (below 30% of trials with 100% accuracy in all experimental conditions). Therefore, all subsequent results are reported for a sample of 39 students. Within the remaining sample, one student had myalgic encephalomyelitis (ME) and another had dyslexia. However, both performed within the average range on the experimental task and had good GCSE results. Therefore, were retained in the sample.

Procedure

A letter was sent to the students giving some preliminary information about the study for them to share with their parents. If they were interested in taking part they informed their A level teacher. An information sheet and consent form was then given to them to take home and to read through with their parents and sign if they were happy to take part. Once the consent form was returned, they were sent a link to a set of on-line questionnaires to be completed before the experimental session.

Over the course of one week, the researcher visited the college and set up a testing room in a spare office. Three computers were set up, each faced away from each others to ensure the other participants were not in sight. Sheets were hung at the windows and a lamp was used to try and maintain consistent illumination throughout the day. For pictures see Appendix E.2, p.356.

Students booked appointments in lots of three. On arrival the students were sat at their desks and the chairs, screen and chin rests were adjusted so the participant's eye line was central with the screen. Instructions for the experimental task were given as a group, using a power point to illustrate (Appendix E.3, p.357). The participants then completed the practice and were given time to ask any questions if anything was unclear. The eye tracker was calibrated (EyeTribe, 60HZ). The experimental task was started. After the experimental task was complete, the visual digit span task was completed.

The participants were only partially debriefed at this time point to ensure the subsequent participants remained naive. On the last day a full debriefing was given via a presentation. All participants were entered into a prize draw in return for participation. The winners were given their prizes during this session.

Experimental Design

The experimental design was the same as experiment 2, however this time there were 50 trials in each condition. This meant that there were 250 trials in total. There was a self timed break after each 50. Each block was comprised of 10 of each of the conditions presented in a randomised order.

Sample Characteristics

Table 6.3: Sample Characteristics

	Mean (SD)		Frequency
Age	17.08(00.96)	Gender$^{Female/Male}$	69%/31%
GCSE Average	05.80(00.70)	Education $^{AS/A2}$	67%/43%
Mind Wandering	17.85(04.26)	Vision $^{Normal/Corrected}$	56%/44%
Cognitive Failures	40.87(20.35)	Ethnicity $^{White/Asian}$	82%/18%
Impulsivity Scale	63.95(08.32)	Handedness $^{Left/Ampi/Right}$	15%/3%/82%
DASS Depression	08.16(08.62)	MEG $^{A/B/C/D}$	10%/23%/44%/23%
DASS Anxiety	08.24(07.67)	Current Grade $^{A/B/C/D/E/U}$	10%/31%/28%/18%/5%/8%
DASS Stress	12.47(09.92)		
Digit Span FW	05.80(01.59)		
Digit Span BW	06.62(02.89)		

MWF = Mind Wandering Frequency (Mrazek, Phillips, Franklin, Broadway, & Schooler, 2013)
CFQ = Cognitive Failures Questionnaire (Broadbent, Cooper, FitzGerald, & Parkes, 1982)
DASS = Depression, Anxiety and Stress Scale (Lovibond & Lovibond, 1995)
BIS = Barratt Impulsivity Scale (Patton, Stanford, & Barratt, 1995)
MEG = Minimum Expected Grade

Data Handling

The data for the final analysis was filtered on three parameters: extreme reaction times in the precision recall (±3 MAD, Leys et al., 2013), 75% accuracy on the interference task and whether the participants gaze was close to the center of the screen during the memorandum presentation. These parameters were used as filters to ensure the participant was paying attention and performing the task as expected.

First of all the interference task was examined split by the order of the shape match judgement (Figure 6.12). As in experiment 2, the same pattern of results was observed. Both accuracy (A) and speed (B) was worse on the first shape match considered to indicate a task switch cost (Jarrold et al., 2011; Vergauwe & Cowan, 2014). Therefore, the shape match accuracy filter was set once again to 75% to retain trials on which participants made one error.

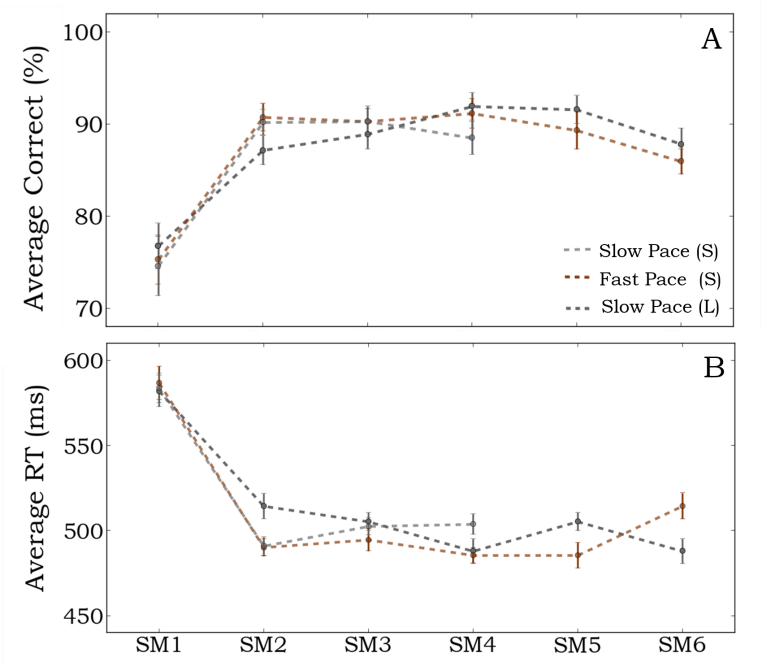


Figure 6.12: Interference task performance split by the order of presentation. A) Average percentage correct split by order position. B) Average reaction time split by order position. EB= 96% CI

Due to the short presentation time of the gabor displaying the orientation memorandum it was also important to ensure the participants were paying attention. Therefore, the participants fixation was examined. Because the participant would only need to fixate the edge of the gabor to encode the orientation and in consideration that the eye trackers used lacked precision the fixation boundary was set to 150 pixels surrounding the gabor edge. Therefore, giving a circular boundary of 15.19^o visual angle. See Appendix E.5 (p.358) for an example of the fixation boundary.

After filtering there was an average of 207.80 trials (SD=31.11). There was a maximum of 247 trials and a minimum of 123. Participants were retained seeing that they had 20 of more trials in each condition. The average for all conditions was ∼42 trials retained with a standard deviation of ∼6/7.

Results

Cognitive Load Manipulation

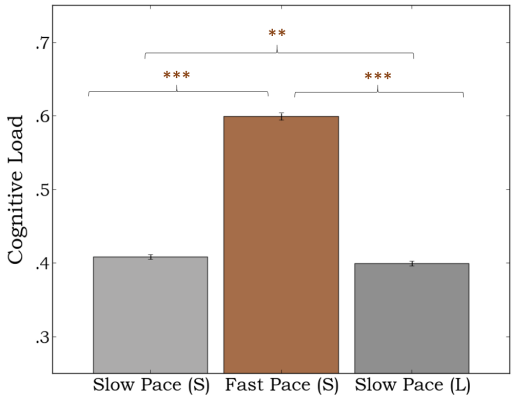


Figure 6.13: Cognitive Load by Condition

As can be seen in Figure 6.13, there was a significant main effect of condition for cognitive load [$F(2,78)=2274$, $p<.001$]. Tukey contrasts demonstrated that the fast pace condition had a significantly higher cognitive load as compared to the slow pace short ($Z=$ -57.06, $p<.001$) and slow pace long ($Z=$ -59.68, $p<.001$) conditions. The slow pace short condition also had a higher cognitive load as compared to slow pace long condition ($Z=$ -2.62, $p=.009$), this difference could be influenced by the participants becoming faster over the course of the interference task (Figure 6.12 B).

The average time spent on processing the interference task was 2107.84 (SD=130.98) for the slow pace short condition, 3091.72 ms (SD=181.35) for the fast pace condition and 3093.96 ms (SD=192.27) for the slow pace long condition. The average time available for refreshing the working memory trace of the orientation during the interference task was 3052.16 (SD= 130.98) for the slow pace short condition, 2068.28ms (SD= 181.35) for the fast pace condition and 4646.04ms (SD=192.27) in the short pace long condition. Therefore the participants had on average 983.88 ms less time to refresh the working memory trace on the fast pace condition as compared to the slow pace condition.

Shape Match Performance

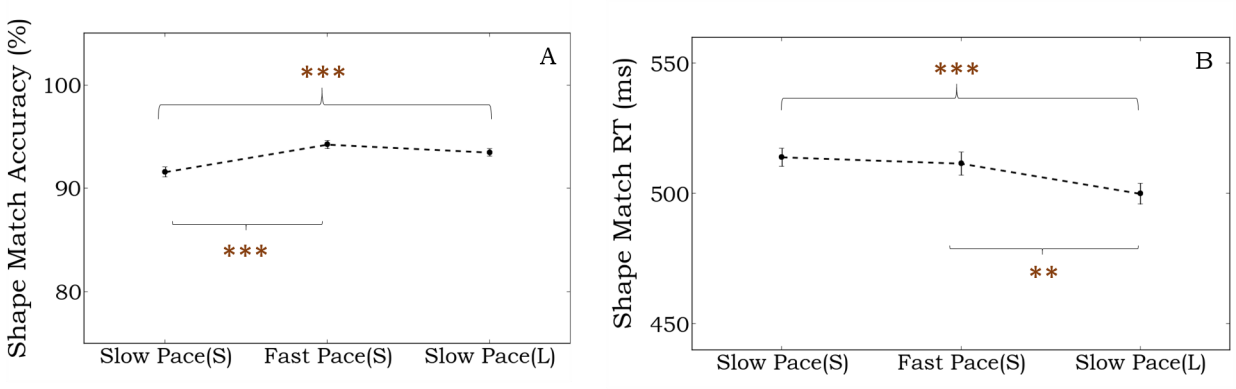


Figure 6.14: Interference task performance. A) Shape match accuracy. B) Shape match RT.

There is a significant main effect of shape match accuracy [$F(2,78)=28.14$, p <.001]. Contrasts demonstrated that the slow pace condition had a lower accuracy on average as compared to the fast paced condition (Z= -7.29, p <.001) and the slow pace long condition (Z= 5.18, p <.001). There was a significant effect of condition on shape match average RT [$F(2,78)=9.17$, p <.001]. Follow up contrasts found that average RT was quicker on the slow pace long condition as compared to the slow pace short (Z= -3.31, p=.001) and fast pace (Z= -4.01, p <.001) conditions.

Orientation Recall Performance by Condition

As seen in Figure 6.15 A, there was a significant main effect of condition [$F(4,156)=4.87$, p <.001] on angular error. Contrasts demonstrated: **1)** No difference in angular error between the two baseline conditions. **2)** In comparison to the baseline short condition, there was significantly more error on the short slow pace condition (Z=3.59, p=.003) and the fast pace condition (Z=2.60, p=.03). In comparison to the baseline long conditions, there was a trend for more error on the slow pace long condition (Z=2.07, p=.06) and the fast pace condition (Z=2.35, p=.04). **3)** There was no significant difference between the fast pace condition and either of the slow paced conditions. **4)** There was no difference observed between the two slow paced conditions.

As seen in Figure 6.15 B, there was a significant main effect of condition [$F(4,156)=21.56$, $p<.001$] on reaction time. Contrasts demonstrated: **1)** The baseline long condition had a significantly faster reaction time compared to the baseline short condition ($Z=$ -4.13, $p<.001$). **2)** The baseline short condition was significantly faster than the slow pace short condition ($Z=5.05$, $p<.001$), but not the fast pace condition. The baseline long condition was also significantly faster than the slow pace long condition ($Z=$ -4.77, $p<.001$) and the fast paced condition ($Z=5.0$, $p<.001$). **3)** The fast paced condition was also significantly quicker as compared to the slow pace short condition ($Z=4.18$, $p<.001$), but not the slow pace long condition. **4)** The slow pace long condition was significantly faster than the slow pace short condition ($Z=$ -4.77, $p<.001$).

As seen in Figure 6.15 C, there was a significant main effect of condition [$F(4,140)=7.31$, $p<.001$] on response time. Contrasts demonstrated: **1)** No significant difference between the two baseline conditions. **2)** Participants were significantly slower making a response on the baseline short condition as compared to the slow pace ($Z=$ -2.60, $p=.02$) and the fast pace condition ($Z=$ -4.22, $p<.001$). The baseline long condition had a significantly slower response time as compared to the fast paced condition ($Z=$ -4.58, $p<.001$), but not the slow paced long condition. **3)** There was no significant difference observed between the slow and fast paced short conditions. However, the fast paced condition was completed significantly quicker as compared to the slow pace long condition ($Z=3.45$, $p=.004$). **4)** There were no differences observed between the two slow paced conditions.

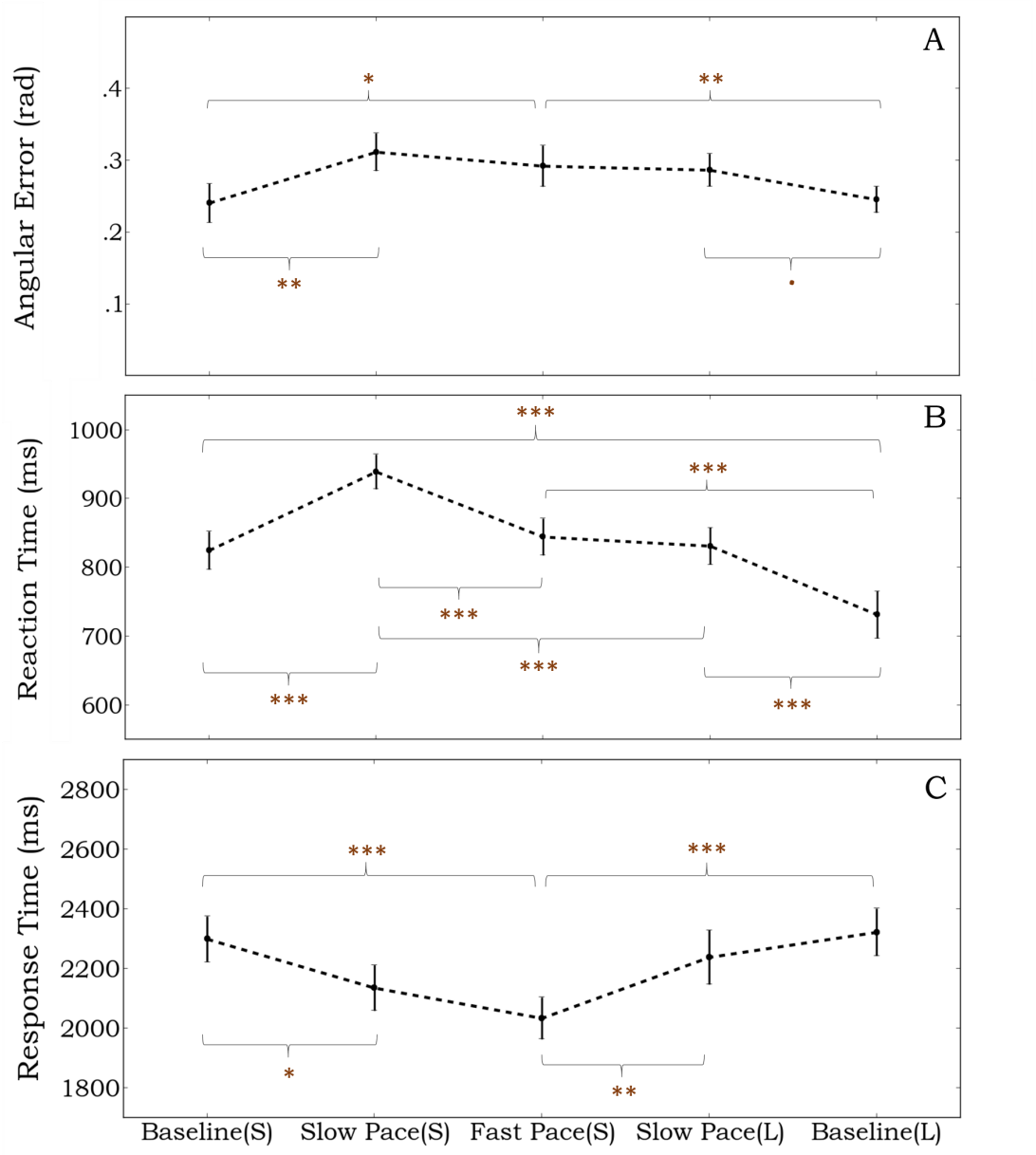


Figure 6.15: Orientation Recall Performance. A) Absolute angular error. B) Reaction time (screen onset - first dial press). C) Response time (first dial press - orientation submit).

Split by Digit Span

Previously individuals with high or low digit span performance were found to perform differently on the traditional TBRS complex span tasks (Barrouillet et al., 2008). The current sample was split using the median of the backwards digit span (Median= 4). There were three groups: below median (n=10), on the median (n=13) and above median (n=16). The backwards digit span was selected to split the sample, instead of the forward digit span because it is more related to executive function (it involves the manipulation of stored information) and has also previously been shown to be related with the precision of working memory recall (Zokaei et al., 2014). The sample characteristics split by group are given in Table 6.4. The group with a lower digit span tended to have slightly worse grades, reported higher levels of mood disturbance and had slightly higher reports of cognitive failures and mind wandering.

Table 6.4: Sample Characteristics Split by Digit Span

	Low	Mid	High
Backward DS	2.90(1.46)	4(0)	6.31(0.92)
Age	17.30(1.02)	17.00(0.97)	17.00(0.87)
GCSE Average	5.71(0.60)	5.92(0.82)	6.07(0.61)
Current Grade	4.1(D)	5.0(C)	5.2(C)
MWF	19.50(4.76)	17.00(3.67)	17.50(4.03)
CFQ	36.40(21.33)	45.50(12.61)	42.75(21.97)
BIS	64.80(7.54)	62.38(6.83)	64.69(9.73)
Depression	8.60(7.67)	8.17(8.79)	7.88(8.92)
Anxiety	9.50(8.11)	8.16(8.79)	7.50(7.53)
Stress	13.20(10.71)	14.83(10.37)	10.25(8.33)

MWF = Mind Wandering Frequency. CFQ = Cognitive Failures Questionnaire.
BIS = Barlett Impulsivity Scale. Mood reported on the DASS scale
DASS = Depression, Anxiety and Stress Scale
Grade coding: 3= E, 4 = D, 5 = C, 6 = B, 7 = A 8 = A*

Interference Task Performance Split by Digit Span

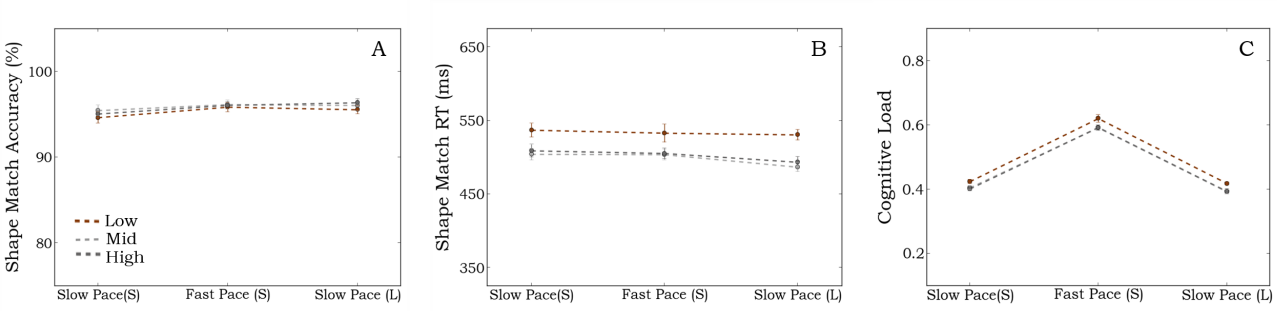


Figure 6.16: Interference Task Performance Split by Digit Span. A) Percentage of Correct Shape Matches. B) Average RT. C) Average Cognitive Load. (EB= 95% CI).

The performance on the shape match interference task was compared across the digit span groups. As can be seen in Figure 6.16 A, there was a main effect of condition on shape match accuracy [$F(2,78)=27.09$, $p<.001$]. However, there was no main effect or interaction with digit span group.

As seen in Figure 6.16 B, there was a main effect of condition on average shape match reaction time [$F(2,78)=7.93$, $p<.001$]. There was also a significant main effect of digit span group [$F(2,39)=6.59$, $p=.003$]. FDR corrected contrasts comparing the digit span groups found that the group of participants with the low digit span was significantly slower on the shape match judgements as compared to the middle group ($Z=$ -2.33, $p=.03$) and the high group ($Z=$ 2.58, $p=.03$).

As seen in Figure 6.16 C, there was a significant main effect of condition on cognitive load [$F(2,78)=2241.30$, $p<.001$]. There was also a significant main effect of digit span group [$F(2,39)=4.18$, $p=.02$]. FDR corrected contrasts found that the low digit span group had a significantly higher load as compared to the middle group ($Z=$ 2.52, $p=.02$) and the high span group ($Z=$ 2.71, $p=.02$). Overall it is suggested that lower span individuals take longer to complete the shape match judgements and therefore have less time available for refreshing activities during the concurrent task.

Orientation Recall Performance Split by Digit Span

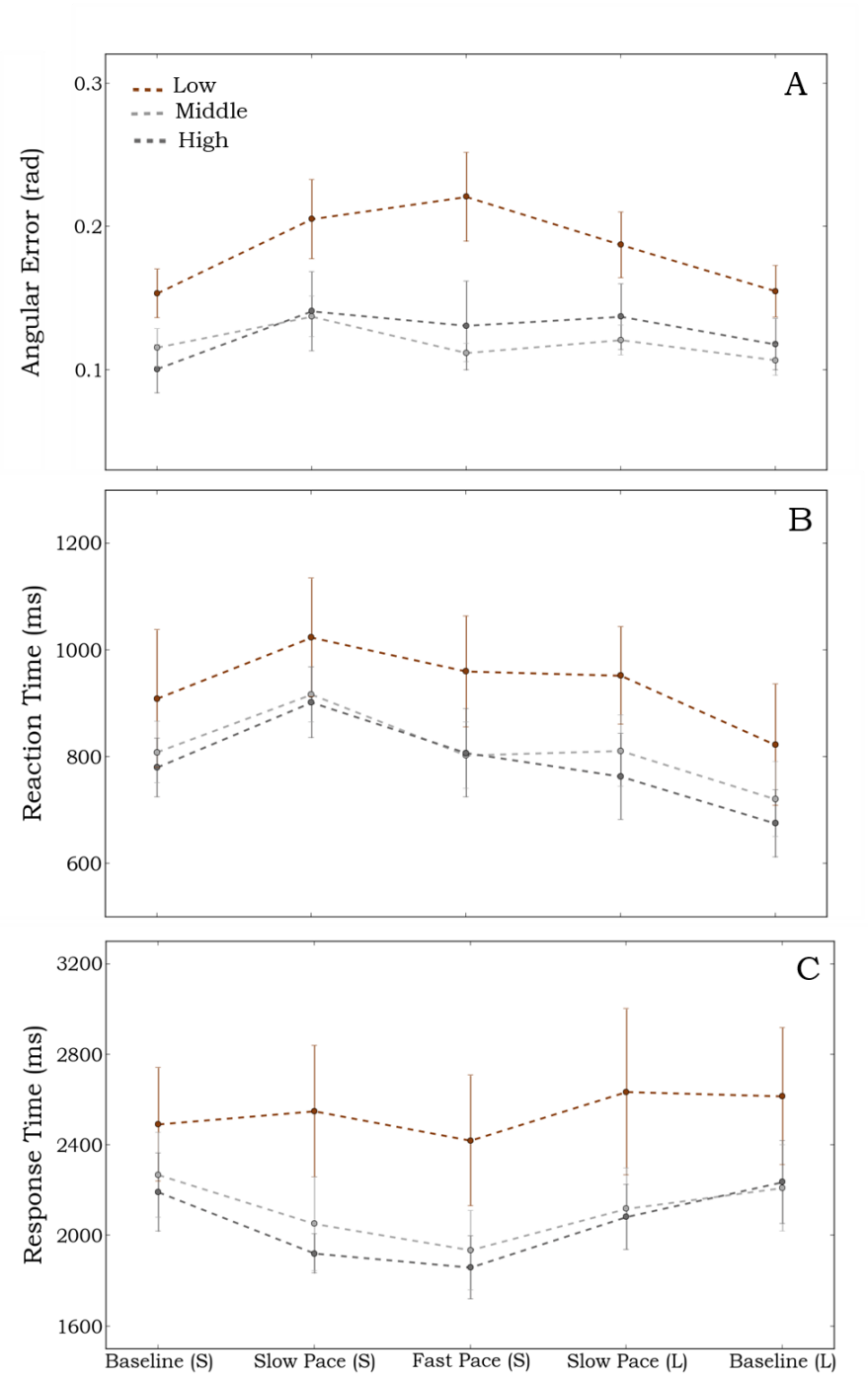


Figure 6.17: Orientation Recall Performance Split by Digit Span Group. A) Absolute Angular Error (distance from answer to target orientation). B) Average Reaction Time (screen onset-first dial turn). C) Average Response Time (first dial turn- answer submission). EB = 95% CI

A series of 3*5 mixed ANOVAs were run examining the effect of digit span group and its interaction with condition.

As can be seen in Figure 6.17 A, there was still a main effect of condition on angular error during orientation recall [$F(4,156)=6.09$, $p<.001$]. There was also a significant effect of digit span group [$F(2,39)=7.66$, $p=.002$], but no interaction between the terms. The low digit span group were more error prone. When compared to the other groups, the low digit span group was more error prone as compared to high digit span group on the slow pace condition ($p=.04$), the fast pace condition ($p<.001$) and the slow pace long ($p=.04$). The low digit span group was also significantly different on the baseline condition ($p=.04$) and the fast pace condition ($p=.008$) as compared to the median DS group.

As can be seen in Figure 6.17 B, there was a significant main effect of condition [$F(4,156)=21.07$, $p<.001$] on reaction time. However, there was no main effect of, or interaction with, digit span grouping. As can be seen in Figure 6.17 C, this pattern was also observed for response time, with a main effect of condition [$F(4,156)=6.78$, $p<.001$], but no main effect or interaction with digit span. Although the difference was not significant the low digit span group appeared to respond slightly slower and take longer to submit a response compared to the other two groups.

Experiment 3: Discussion

In experiment 3 the design from experiment 2 was retested in a larger sample, with the addition of also examining working memory capacity. Once again it was observed that the manipulation of cognitive load was successful, with the fast paced condition having a significantly higher load compared to the slow pace condition. This time there was also a small but significant difference between the slow paced conditions. This difference was considered to occur due to practice effects producing faster times on later shape match judgements.

In the combined results there was no difference in the amount of error during orientation recall between the two baseline conditions. Again this suggests that attentional refreshing was enough to protect from temporal decay and interference (Plancher & Barrouillet, 2013; Barrouillet & Camos, 2015). The angular error was also similar between the two slow pace conditions (despite the small difference in cognitive load). Although the interference task produced a decrement in the fidelity of orientation recall when compared to the baseline conditions, there were no differences seen from manipulating cognitive load. Therefore, the findings from experiment 2 were replicated.

However, there was a larger impact of the manipulation on reaction and response time as compared to experiment 2. It was observed that the conditions with a longer retention interval (slow pace long and baseline long) had a quicker reaction time on average. This may be explained due to having additional preparation time to make the switch back to recall. Overall the addition of an interference task slowed down the reaction time, but sped up the response time. The slowing of the reaction time was largest in the slow pace short condition. There are two factors that could have contributed. First, the slow pace condition could possibly have 4 or 6 shape matches. Therefore, in the slow pace short condition the participant would not have been able to prepare for the switch because there was the potential for the presentation of more shape matches. The slowing would

not have been as pronounced on the other conditions due to the predictability of when the interference task would end and the additional benefit of practice effects reducing the cognitive load of the later judgements.

Similarly to experiment 2 there was a lot of individual variability in how the participants were responding to the manipulation of cognitive load. Therefore, they were split by digit span to examine whether working memory capacity influenced the results. After splitting the sample by backward digit span it was observed that the low span individuals took longer on average to complete the shape matches and thus, had a higher cognitive load than the other two groups. Therefore, it was observed that the manipulation of cognitive load was stronger for participants with a lower working memory capacity. These findings corroborated previous work examining the relationship between working memory capacity and complex span performance (Barrouillet et al., 2008).

The groups were then compared on the orientation recall. Although no significant differences were seen for reaction time and response time, it was notable that lower span individuals were slightly slower than the other two groups on both measures. There was a significant main effect of digit span group for working memory error, with lower span individuals being more error prone overall than the other two groups. Although they significantly differed on multiple conditions, the difference was greatest in the fast pace condition. The mid span individuals seemed to have no effect of the cognitive load manipulation and the higher span individuals appeared to slightly improve in the fast paced condition. Perhaps indicative of them employing a strategy or simply having a memory trace which was stronger against interference. These results were in line with previous individual difference work done using complex span tasks (Barrouillet et al., 2008), but also extend these findings to include the precision with which a single item can be stored. The pattern of results suggests that this line of investigation warrants further investigation.

6.7 General Discussion

The current investigation aimed to examine the effect of cognitive load (as defined by the TBRS model) on the precision of feature recall. Previous work examining working memory span, has concluded that a higher cognitive load on a concurrent processing task resulted in shorter working memory spans (Barrouillet et al., 2004; Barrouillet & Camos, 2015). Over three experiments it was found that a concurrent processing task significantly impacted on the precision of feature recall. However, there were no significant differences between the conditions when manipulating cognitive load. There was also no significant decay seen between the two baseline conditions with differing retention intervals. The results will now be discussed in relation to the TBRS model and limited resource approach to working memory.

Firstly, the two baseline conditions were compared to examine whether there was temporal decay between the two time points. In all three experiments there was no significant difference seen between the two retention intervals (experiment 1: 4000ms, experiment 2 & 3: 2580ms). These findings fit with the TBRS model that suggests that although temporal decay exists, if attention is available for working memory maintenance (attentional refreshing), there should be little effect of the retention period (Barrouillet & Camos, 2015; Barrouillet et al., 2012). Studies using delayed adjustment tasks have found that the precision with which items are stored slowly degrades over time (Pertzov et al., 2013; Zhang & Luck, 2009). Although the TBRS complex span research has found that retention period has little effect on maintenance (although see their discussion on fatigue effects Barrouillet & Camos, 2015), it could be argued that the span tasks were ineffective at examining decay effects. The traces may have been decaying, but retained enough resolution to still be recalled.

Given previous research it could have been expected that the retention interval was more likely to have an effect when using a precision index (Pertzov et al., 2013; Zhang & Luck, 2009). The current investigation used a single item for recall. It has been found that an item within working memory can be held in the privileged state, modulated by attention allocation (Oberauer, 2009). Working memory items in the focus of attention (FoA) are said to be in a privileged state affording better recall as compared to items outside of the FoA (Lepsien & Nobre, 2007). Furthermore, these attended WM traces can be decoded from neural activity, whereas those outside the FoA cannot (Lewis-Peacock, Drysdale, Oberauer, & Postle, 2012). It is suggested that the item in the FoA is protected from decay, whereas the others are liable to temporal decay (Pertzov et al., 2013; Wang et al., 2017; Zokaei et al., 2014). Because in the experiments presented here there is one task relevant item to be remembered, it is likely that this item is held in this privileged state, without competition from distractors or other relevant WM traces (for a review of attention refreshing mechanisms see Camos et al., 2018). The low working memory load may account for the absence of temporal decay.

Another prediction of the TBRS model is that when cognitive load is held constant, increased retention period would have little impact on recall (Barrouillet & Camos, 2015). Although there was a significant difference between the two slow paced conditions in the first experiment, this effect was most likely due to a higher number of switches in the interference task. No differences were observed in the second two experiments after the number of switches had been equalised. The impact of switching is important to note for complex span designs, which have switching within the interference task (e.g. switching between types of operations). Although these finding are supportive of TBRS models assumptions regarding constant cognitive load, the absence of an increase of error for the higher cognitive load condition causes difficulties in interpretation. Our results suggest that cognitive load, number of items and the length of the retention period do not significantly impact the observed interference effect for single feature recall.

In all three of the experiments presented it was found that the interference task had a significantly negative impact on the precision of feature recall. This compliments previous research which has found that ignoring information given within the retention interval increases angular error when reporting orientation (Fallon, Mattiesing, Dolfen, Manohar, & Husain, 2018; Rademaker, Bloem, De Weerd, & Sack, 2015). However, it was expected that a higher cognitive load would result in a greater negative impact on the precision of recall. The reasoning behind this assumption was that in the lower cognitive load condition there would be more time available to refresh the working memory trace, resulting in less decay. However, this expectation was not met.

In the current investigation the type of memorandum given is distinctly different to those given in traditional TBRS complex span tasks (Barrouillet et al., 2004; Barrouillet & Camos, 2015). Particularly the use of one item feature has different demands when compared to the sequential recall of multiple items in span tasks. Firstly, the ability to remember one item feature does not rely on binding in time for correct sequential recall. The binding of information has been thought of as attentionally demanding (Humphreys, 2016; Wolfe, 2014). It could be that the attentional resource shared between processing and maintenance activities is also required for binding. It has indeed been suggested that the most important element of attentional refreshing is the strengthening of the binding of an item to its serial position or spatial location (Oberauer, 2002; Loaiza & McCabe, 2012). Moreover, Fallon et al (2018) found that ignoring irrelevant information whilst concurrently maintaining multiple items in working memory, led to increased instances of misbinding errors. Perhaps no difference was observed in the current investigation due to the low attentional demands associated with remembering one item feature.

It may be that the time available for refreshing affects span tasks because of the accumulating time debt which increases with each item added (e.g. time it takes for attention refresh * number of items to be refreshed) (Lemaire, Pageot, Plancher, &

Portrat, 2018; Camos et al., 2018). It has been suggested that each individual item can be refreshed in a time period of roughly 40-50ms (Vergauwe & Cowan, 2014; Jarrold et al., 2011; Vergauwe & Cowan, 2015). The length of the pause in which attention is available for refreshing would restrict the number of items that could be refreshed due to the accumulation of refresh time (Barrouillet & Camos, 2015; Camos et al., 2018).

When considering refresh time in relation to the recall of one single item feature the question arises to whether the memory trace would be refreshed multiple times if the pause time was long enough? Or would that item be briefly refreshed only once, before attention is returned to external processing? Furthermore, another question is how long attentional refreshing lasts in its protective effects before decay starts to reflect in the precision of recall. It could be that refreshing one item more than once within a pause period does not make a significant impact because of this time frame of decay. If there was little decay within that short difference, the additional refresh would not have a substantial impact on subsequent recall. In this instance the effect may be more notable when modulating the length of the processing rather than refresh time, because there would be more time for decay, rather than less time to refresh between the conditions. In the instance of one item recall, the cognitive load ratio may be secondary to the way in which the ratio was modulated. The refreshing mechanism is far more complex than first appeared (for a review see Camos et al., 2018) and more research is required to understand how it deals with the maintenance of one memory trace under dual task conditions.

Another way in which feature memory differs is in its familiarity. A letter or digit is a well-known rehearsed stimuli, which could interact with long term memory (Brady et al., 2016). Whereas, a specific orientation is more abstract and may not interact with long term memory in the same manner. The working memory trace of the orientation is likely to have recently been created as a new sensory/perceptual experience in which

the item did not already exist in the participants long term memory (Camos et al., 2018). However, it should be considered that some participants may have translated the abstract information into something easier to remember. For example, the participant could use a clock face to help them remember the orientation. This also allowed the visual information to be encoded into a connected phonological working memory trace (e.g. 10 o'clock), that could have been rehearsed differently than the visual working memory trace (e.g. sub-vocal rehearsal of time). Although the use of strategies was explicitly discouraged, it could explain some of the variability in the data. For example, high span individuals may be more practised in using alternative strategies to support memory performance and therefore can compensate for differing cognitive load. Considering that participants have previously reported using different strategies during maintenance in traditional complex span tasks (Dunlosky & Kane, 2007), further research is needed to specifically examine this contribution when examining recall precision.

It is also plausible that the minimal memory load of remembering one item was insufficient to prompt the participants to switch their attention to refreshing at all during the interference task, giving an interference effect that was similar between all cognitive load conditions. Further research could aim to increase memory load by including distractors or perhaps giving multiple features to remember (e.g. colour and orientation). Of particular interest would be using paradigms that require spatial or temporal binding to examine both the impact on precision and misbinding errors. It is likely that in the current design there was enough refresh time to successfully reactivate the working memory trace in all conditions. Further research that aims to examine a single item feature could employ a significantly more demanding interference task, with very little time remaining for refreshing. For now the current investigation suggests that cognitive load of the interference task does not modulate the fidelity of an item feature simultaneously maintained in working memory.

The comparison of participants with differing working memory span was illuminating and deserves further investigation in a larger sample size. The TBRS model predicts that the less time available for working memory refreshing the worse recall the person will have. Here these results are supported. The lower span individuals spent more time on the interference task, thus had a higher cognitive load and all round poorer performance on the orientation recall. These results corroborated Barroulliet et al 2008, who also found similar effects with complex span tasks. Tentatively the pattern of their results for low span participants suggests they may be more affected by the manipulation of cognitive load as compared to the other groups. This may suggest that the lower baseline capacity produced a greater trade off, which was not seen with the higher span individuals who would have found maintenance less challenging. This highlights how underlying working memory capacity may contribute to how attention is distributed during concurrent processing and maintenance demands.

Conclusions

In conclusion, the current investigation highlighted that concurrent processing demands disrupt the precision with which one feature can be concurrently maintained. However, in comparison to serial recall of complex span tasks, no evidence was found to suggest that varying cognitive load of this concurrent task impacted recall precision. There was a significant impact of baseline working memory capacity as measured by backward digit span, demonstrating that lower span individuals were more error prone and had a stronger manipulation of cognitive load.

Chapter 7

Discussion

The contents of this thesis have examined how attention is used in the pursuit of goal directed behaviour. Part one addressed the neural underpinnings and functional consequences of impaired attentional control following stroke. Part two examined dissociation of goal activation errors and addressed how attention is distributed during concurrent task demands. The results will be summarised, discussed and future avenues for investigation outlined.

7.1 Attentional Control in a Stroke Population

The first empirical chapter investigated the prevalence, persistence and functional consequences of impaired selective auditory attention following stroke. In line with previous research attentional impairment was prevalent in the subacute, (11% -52%) and chronic (12%- 31%) stages of stroke recovery (Fig 2.4, p.53, Hyndman et al., 2008; Barker-Collo et al., 2010). Worse auditory selective attention performance was observed in patients with left or bilateral hemispheric lesions (consistent with the conclusions of MacPherson et al., 2010). Although there was significant improvement between the acute and chronic phases on average for all attentional indices (Fig. 2.5, p.54), relatively few patients fully recovered as denoted by the 5th percentile cut-off score (8%-22%, Fig. 2.6, p.55). Thus, attentional impairment was observed as prevalent and persistent.

In the subacute stage of post-stroke recovery, all attentional indices were predictive of basic functional independence as measured by BIADL (Table 2.5, p.59). They explained unique variance (1%-3%) above that of a baseline model including stroke characteristics, demographics and additional cognitive scores. Although the explained variance was small, attentional indices explained a similar amount of variance as compared to other significant predictors such as lesion volume (1%), previous incidence of stroke (1%) and age (5%).

These results complement previous studies which have observed a relationship between auditory attention (the elevator counting task, Robertson et al., 1994) and functional status at discharge (Stapleton et al., 2001; Hyndman et al., 2008). The current analysis also extends these observations on attention to verbal information and demonstrates attentional impairment can explain unique variance above that of other influential factors. On the other hand, these results contradict past work which observed no relationship between an integrated visual-auditory continuous performance task (VA-CPT) and subacute BIADL scores (Barker-Collo et al., 2010). Although the VA-CPT task required monitoring and a selective response (press if you hear/see the number one), in comparison to the other tasks it did not require concurrent processing and working memory activities. This may be one factor that accounts for the difference in findings between different investigations.

In the chronic stage of recovery selective attention was a significant predictor of complex functional independence as measured by NEADL (Table 2.5, p.59), explaining 4% of the variance. In the prognostic analysis subacute sustained attention significantly predicted chronic NEADL, explaining 6% of the variance (similar to age, 5%). These observations are in line with previous work which has suggested that sustained and selective attention (elevator counting with and without distraction) are correlated with NEADL scores (Hyndman et al., 2008; Robertson et al., 1997). Moreover, the prognostic analysis supports research suggesting that discharge sustained attention correlates with NEADL one year (Hyndman et al., 2008) and at two years (Robertson et al., 1997) post stroke. In the current analysis sustained attention predicted chronic NEADL after controlling for stroke characteristics and demographics. However, previous investigations observed no link between attention and chronic outcome using a stepwise regression analysis (Hyndman et al., 2008). There are multiple reasons that could underlie this discrepancy and further research is required to fully understand the relationship between subacute sustained attention and long term outcome.

The rule finding and concept switching task (RFCS) (Humphreys et al., 2012) was also a significant predictor of subacute BIADL (3%) and chronic NEADL (5%)(Table 2.6, p.62). These results were similar to that observed on the selective attention score, whereas this was not the case for immediate story recall (Humphreys et al., 2012). This pattern of observations is suggestive that the link between the auditory attention task and functional status is driven by top-down attentional control rather than memory deficits. Although this question needs to be addressed more specifically, it is in line with work suggesting that more domain general executive impairments are most likely to account for functional impairment (Mole & Demeyere, 2018).

The observations in Chapter 2 suggest that impaired selective auditory attention has a small but significant impact on functional independence following stroke. It extended past work by demonstrating this relationship above that of other important factors (e.g. lesion volume and age) in a large sample. There are several important weaknesses to consider. Due to the retrospective nature of the analysis, daily activities could not be examined in detail. Impaired selective attention is likely to impact some activities more so than others and further investigation is required to fully understand the contribution of attention to independence following stroke. In line with this the current analysis did not include an objective measure of function (e.g. physiotherapy or occupational therapy assessment) and failed to include lifestyle factors that could have modulated how patients experienced impairment (e.g. returning to work). Another important consideration was that the current investigation did not include the same functional measurement at both time points, and thus is restricted in its observations regarding functional recovery. Future work should aim to incorporate more comprehensive measures to further clarify the relationship between attentional impairment and functional independence.

In Chapter 2 it was observed that left or bilateral lesions resulted in worse attentional impairment as compared to unilateral right lesions (Table 2.4, p.56). Moreover, the extent of damage to the frontal cortex appeared to have no observable relationship with the level of impairment. In order to examine the relationship between lesion location and attentional impairment in greater detail, chapter 3 utilised a VLSM approach in a sub-set of the previously reported patients.

It was observed that selective attention performance was associated with left hemispheric lesions to the IFGpo, PreCG, AI and posterior MTG. The extent of damage to the SLF III, the AF, frontal-insular tracts (1, 3 and 4), the frontal aslant tract and the posterior segment were also predictive of performance. When this score was split, isolated omission errors were associated with left hemispheric lesions to the SMA and the extent of damage to the CC, whereas there was no association observed for commission errors. The ability to sustain selectivity was associated with left hemispheric lesions to the IFGpo, MFG, frontal operculum, the insula, post/precentral gyrus, the supramarginal gyrus and the S/MTG. It was also associated with right hemispheric lesions to the MTG, the AG, the occipital fusiform gyrus, the precuneus and the parietal operculum. Performance on target word recall was associated with damage to the parietal operculum cortex, superior and inferior occipital fusiform gyrus, the frontal pole, cingulate, precuneus, the planum polar, insula and the MFG. The extent of damage to the SLF III, AF and the posterior segment was also predictive of recall performance. For an overview please see Table 3.3 (p.86) and 3.4. (p.88)

The results of the present investigation share similarities with previous VLSM work examining executive function (e.g. DLPFC, IFG, AI Gläscher et al., 2012; Robinson et al., 2014; Barbey et al., 2012; Varjai et al., 2017) and visual spatial attention (LPFC, S/MTG ,TPJ , SLF II/III, AF Karnath & Rorden, 2012; Mort et al., 2003; Corbetta et al., 2005; Chechlacz et al., 2010; He et al., 2007; Karnath, 2009; Thiebaut de Schotten,

Urbanski, Duffau, Volle, Lévy, et al., 2005). However, in contrast to investigations of visual spatial attention the results were predominantly left lateralised. This observation corresponds to previous work showing that the perisylvian network (LPFC, S/MTG and TPJ) is more important for language processing than spatial attention (Suchan & Karnath, 2011). These findings are also in line with a previous study which found that damage to the left lateral frontal regions were associated with worse performance on the elevator counting task (ECT, MacPherson et al., 2010). The observed importance of left hemispheric damage for the ECT and AAT could be influenced by their requirement for verbal working memory and perhaps sub-vocal rehearsal processes (Paulesu, Frith, & Frackowiak, 1993).

The relationship between target word recall and average performance on language tasks was examined (Fig. 3.4, p.91). Poor target word recall was associated with poorer performance on language tasks, especially for patients' with lesions in the left hemisphere. Moreover, target word recall had a significant negative relationship with performance on the attentional indices (Fig. 3.3, p.90). For commission errors the relationship was more complex, with worse performance associated with both perfect and a total inability to recall target information. It could be suggested that patients with a total inability to recall target information may stop responding. In order to better control for these confounds a control analysis was run in a sub-group of patients with perfect recall.

For patients with perfect target recall, selective attention was associated with left hemispheric lesions to the anterior insula and right hemispheric lesions to the IFGpo, MFG and the PreCG. The extent of damage to the uncinated fasciculus and frontal-insula tracts (1 and 2) was also predictive of performance. There were no associations with omission errors or the sustained attention index. However, isolated commission errors were associated with left hemispheric lesions to the IFGpt, the putamen, external capsule, the medial/posterior insula and the precuneus. Additional associations were

with right hemispheric lesions to the IFGpo and the MFG. The extent of damage to the inferior longitudinal, the AF, posterior segment and insular tract 1 was also predictive of performance. For an overview please see Table 3.6 (p.94) and 3.7 (p.100).

Complementary to the full analysis the regions implicated were similar to past studies that have investigated executive function (e.g. AI, IFG, MFG and PreCG Gläscher et al., 2012; Barbey et al., 2012; Varjai et al., 2017). However, in contrast to the analysis in the full sample most associations were now found with damage in the right hemisphere, perhaps due to removing the influence of verbal working memory. Commission errors were also associated with bilateral frontal lesions including cortical (IFG/MFG) and subcortical (putamen, external capsule) regions. These observations complement previous work that has suggested damage to the IFG is associated with increased commission errors (Molenberghs et al., 2009; Aron et al., 2003; Swick, Ashley, & Turken, 2008) and corroborates the association between basal ganglia infarction and executive dysfunction (e.g. Su, Chen, Kwan, Lin, & Guo, 2007).

The current investigation suggests that impaired auditory selective attention may result from damage to multiple demand regions (Duncan, 2013), sharing similarities with studies of executive dysfunction and impaired visual spatial attention. There are several important weaknesses. First, clinical CT scans lack resolution and can at times fail to clearly image lesions when acquired near to stroke onset. Second, the use of a mass univariate VLSM approach can be problematic because it fails to account for the correlation between voxels. If regions share vasculature they are commonly damaged together, resulting in erroneously attributing cognitive functions by association (Mah et al., 2014; Price et al., 2017). Moreover, diaschisis, by which a distal but connected brain regions loses function because of abnormal input from a damaged region, can also contribute to problems of localisation (Carrera & Tononi, 2014; Price et al., 2017). To circumvent these issues, research should aim to use a multivariate approach (Mah et al.,

2014) and include perfusion imaging (e.g. Saita et al., 2017).

In Chapter 3, selective attention was found to be associated with a wide range of brain regions that share similarities with past work examining executive dysfunction. Although executive dysfunction was originally considered a disorder of the frontal lobes, it has been reported after damage to posterior and subcortical regions (e.g. Godefroy, 2003; Collette et al., 2005; Hornberger et al., 2011; Manto & Mariën, 2015; Stoodley et al., 2016; Gläscher et al., 2012). In Chapter 4 it was aimed to examine whether executive dysfunction is experienced differently by posterior as compared to frontal patients. A BiFactor analysis was used to segregate executive functioning into superordinate and subordinate control processes.

The BiFactor analysis was run, segregating the common factor (taken to represent the shared requirement of using a task model to bias attention and action) and three independent factors: temporal attention/working memory, spatial attention and updating/shifting (Fig. 4.7, p.130). Individual factor scores were compared against a selection of age matched control participants. Although impairment on all factors was more common in the frontal-subcortical group, it was also present for some individuals with large distributed lesions or purely posterior lesions (Table 4.5, p.134). Group analysis was run comparing the patient groups to controls. On average both the frontal-subcortical and posterior groups were more impaired in comparison to the controls, whereas the frontal-posterior group were not (Fig. 4.8, p.136). It was demonstrated that both frontal subcortical and posterior patients were impaired on the common executive functioning factor. The only observed difference was that frontal-subcortical patients were more consistently impaired on temporal attention/working memory.

Lesion overlap maps were computed to examine whether there were regions of overlap for the impaired patients for each factor (Fig. 4.9, pg. 139). For the executive factor the regions of overlap were the bilateral basal ganglia, left occipital lobe and left cerebellum (crus I/II). All of the other factors had overlap in the basal ganglia, with temporal and spatial attention also demonstrating overlap in the bilateral precuneus and posterior occipital cortex (spatial attention also had overlap in the STG). This corroborated past work which linked the basal ganglia to attentional gating (Van Schouwenburg et al., 2015; Bednark et al., 2015) and past imaging research that has related subcortical regions to both superordinate and subordinate executive functions (Niendam et al., 2012). Moreover, these regions of overlap also share similarities with the findings reported in the previous chapter (e.g. puteman, precuneus and occipital lobe).

Executive dysfunction in the posterior group was examined in greater detail (Table 4.8, p. 142). Cerebellar damage was frequent in impaired posterior patients, particularly associated with damage to the crus I/II and to the cortico-ponto-cerebellum tract (normally due to posterior inferior artery damage). Crus I and II have both previously been linked with executive and attentional dysfunction (Ilg et al., 2013; Gottwald et al., 2004; Fiez et al., 1992) and crus II has connections with the frontal cortices via the thalamus (Middleton & Strick, 2000, 1994; Hallett & Grafman, 1997). Thus, these observations support past work suggesting that impaired communication between the cerebellum and the frontal lobe, can result in executive impairment (e.g. Stoodley et al., 2016; Schmahmann, 2004).

The current analysis also supports previous observations that executive impairment can result from posterior or subcortical brain damage (Rabinovici et al., 2015; Bettcher et al., 2016), in particular from damage to the basal ganglia (Camilleri et al., 2018; Cools et al., 2006) or cerebellum (Manto & Mariën, 2015; Stoodley et al., 2016). The current investigation extends those findings by demonstrating that subcortical and

cerebellar damage is associated with impairment on a global executive function factor (superordinate control).

The biggest weakness of this analysis is the relatively small sample size. Further studies are required to increase power to define overlapping lesions. Ideally, given that subcortical infarct has been linked to abnormal blood flow in the frontal lobe, further work should wherever possible include perfusion imaging (Beldarrain et al., 1997; Saita et al., 2017). Another important consideration is that this analysis was performed using a combination of MRI and CT scans and thus lesions were delineated from scans of differing resolutions. Poor resolution could be particularly problematic when investigating small subcortical regions and therefore further work should aim to use high resolution scans.

Future Directions for Part 1

One of the main problems highlighted in the current literature on executive function is that of task impurity. To address this problem, research has started to utilise BiFactor models which allow the dissociation between superordinate and subordinate control processes. In Chapter 4 it was observed that many patients presented with impairment on both the global executive and one or more of the subordinate factors. It might prove profitable to combine the BiFactor approach with VLSM methodology to better understand which types of damage lead to shared verses independent impairment. Moreover, it would also be interesting to investigate whether these processes differ in their contribution towards recovery and functional independence.

Previous work has demonstrated that executive dysfunction is predictive of performance on decision making tasks (Brand, Recknor, Grabenhorst, & Bechara, 2007). Moreover, damage to the VMPFC (Bechara, Damasio, Tranel, & Anderson, 1998; Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Tranel, & Damasio, 1997; Fellows & Farah, 2005; Gläscher et al., 2012), the amygdala (Bechara, Damasio, Damasio,

& Lee, 1999) and lateral PFC (Fellows & Farah, 2005; Clark, Manes, Antoun, Sahakian, & Robbins, 2003; MacPherson, Phillips, Della Sala, & Cantagallo, 2009; Ouerchefani, Ouerchefani, Allain, Rejeb, & Gall, 2017) have been associated with impairment. Post-stroke impairments in decision making are a substantially understudied area of research, particularly in regards to the potential impact they could have on functional independence. This area of research may be particularly pertinent to study due to the potential to have a direct impact on decisions related to medical care and recovery, in addition to capacity to manage finances and other daily requirements responsibly.

There are multiple reasons why the subjective experience of executive dysfunction may vary between individuals. It would be desirable to use a combination of self-report and more objective measures (e.g. physiotherapy or occupational therapy assessment) to assess functional independence. Given that stroke patients are sometimes unaware of their impairment, it would also be of benefit to take a measurement of awareness to control for during analysis. Recently, self-report measures have begun to segregate whether the participant has noticed impairment and whether it has a negative impact on their daily life (e.g. Patchick, Vail, Wood, & Bowen, 2015). This approach affords more clarity (both for the patient and researcher) and may prove to be enlightening in further investigations examining the relationship between cognitive difficulties and functional status. When undertaking this type of investigation it is also important to recognise that executive dysfunction is still poorly understood by the general population. If the patient has a poor understanding of what cognition is, they may be ineffective at noticing the impact it could be having on their daily lives.

Another important factor to consider when studying the influence of executive impairment on functional independence is lifestyle. Lifestyle factors can incorporate things such as environmental demand (e.g. returning to work, family commitments, and significant life events), level of support from family and friends and other factors that

might influence recovery (e.g. access to support, rehabilitation, physical activity). A large scale study examining the relationships between these factors (using structural equation modelling) would provide greater clarity regarding who is likely to be impacted negatively, and give some insight into factors that might help alleviate this impact. It is understood that older stroke patients score poorly on measures of executive function (MacPherson et al., 2017; Cipolotti et al., 2015). However, a younger stroke patient is more likely to take part in more demanding daily activities (e.g. returning to work, managing a household). These types of activities provide a greater likelihood of encountering novelty, multiple demands and problem solving. It is more likely that younger stroke patients may subjectively experience executive dysfunction and thus, a younger stroke sample might be more appropriate for the proposed analysis.

As mentioned before, executive dysfunction is still poorly understood by the general population. This lack of understanding can provide substantial difficulties when returning to work or applying for financial support. It would be of benefit to study the impact that cognitive dysfunction can have on these ecologically valid procedures. For example, many stroke patients apply for government financial support in the form of the Personal Independence Payment (PIP, https://www.gov.uk/pip). PIP is awarded based on how your disability functionally impacts daily life. Application is a multistep process, including a phone call, an extensive form and a face to face interview. The process is cognitively demanding, involving organisation, interpretation and ability to estimate the proportion of time. Anecdotally I have heard multiple stories from stroke survivors who have struggled with this process. Moreover, I personally supported someone at tribunal (to challenge the ineligibility decision). I observed the panel demand that she give an estimate regarding the proportion of time her disability impacted her over the course of a month. They asked her repeatedly (despite her saying she did not know each time), only quitting after she randomly guessed. Not only would this process provide an interesting ecologically valid outcome measure of the functional impact of executive dysfunction,

but it would also help to highlight the urgent need to address the lack of awareness and understanding regarding cognitive deficits in governmental processes.

Overall lesion volume and extent of overlap with the frontal cortex were found to have little impact in the current investigations. Further work might profitably examine whether extent of damage to particular networks may be more predictive. In this instance because the extent of damage to the MD network has been connected with fluid intelligence impairment (related to rule working memory) (Woolgar et al., 2010; Duncan et al., 2008), it would be interesting to examine whether the extent of damage to this network is predictive of outcome and whether it mediates the link between the attentional and functional measures.

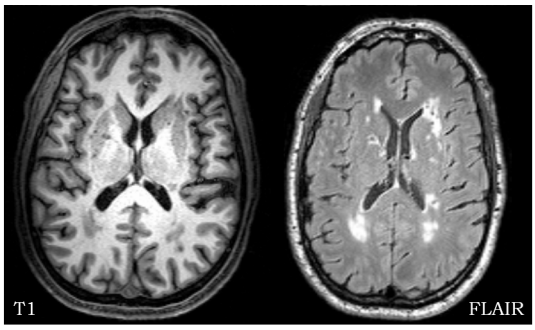


Figure 7.1: Example of subcortical cerebrovascular disease from chapter 4.

One important consideration for studies examining the link between brain damage and executive dysfunction is the frequency of subcortical cerebrovascular disease (SCD) (See Figure 7.1). The occurrence of SCD has previously been linked with executive dysfunction (Chui, 2007; Graham, Emery, & Hodges, 2004; Reed et al., 2007). The longitudinal increase in the volume of lucunes and white matter lesions has been found to correlate with declining executive dysfunction (Mungas et al., 2001, 2005). Moreover, this executive and memory dysfunction in patients with SCD has also been linked to poorer functional status (Bennett et al., 2002). It has also been observed that subcortical infarction can lead to abnormal blood metabolism in the frontal cortices (e.g. Kwan,

Reed, Eberling, & et al, 1999). It is suggested that future studies take care in evaluating stroke patients for existing signs of SCD, examining them explicitly or if the sample size affords it using signs of SCD in the exclusion criteria.

On a final note, a general change in perspective could be productive. Work in the ageing literature has begun to look at "super-agers" (e.g. Nyberg, Lvdn, Riklund, Lindenberger, & Bckman, 2012; Gefen et al., 2015), shifting the focus away from what influences decline and towards factors that relate to superior ageing. This shift in paradigm could also be beneficial in the stroke literature. It would be interesting to examine in depth the patients that have made the best cognitive and functional recoveries. How do they differ to patients with similar damage that have not recovered? This change in focus may allow different insights and may help provide valuable information for stroke protocols.

7.2 Attentional Control in a Healthy Population

In the first part of the thesis, evidence was presented in support of the view that goal directed behaviour is controlled by a complex mechanism, involving the interaction of multiple brain regions. A total breakdown of this process results in "goal neglect", in which the task requirements are ignored, despite having the knowledge and intention to follow them. Task impurity makes measuring goal neglect particularly difficult. In the second part of the thesis, my aim was to design a paradigm that could better dissociate goal activation errors (failures in monitoring verses failures in action selection) and use it to revisit the impact of infrequent task switching and perceptual difficulty of the instructional cue. For an overview of the design and measures see Figure 5.1 (p.172) and Figure 5.2 (p.176).

The first analysis aimed to establish whether response rule switching and cue type manipulations were comparable to previous paradigms (Fig. 5.3, p.179). Significant switching costs were observed in both speed and accuracy on the concurrent working memory task. Furthermore, the accuracy costs were greater when using the perceptually more difficult instructional cue. These findings are consistent with previous conceptualisations of residual switch costs (Monsell, 2003; De Jong, 2000) and the analysis of repeat number (Fig. 5.4, p.181) was comparable with investigations of repetition priming (Dreisbach & Haider, 2006; Altmann, 2005). Importantly, these observations were made after removing trials in which participants made a goal activation error.

The influence of switching and cue type on the occurrence of the different types of goal activation error was examined (Fig. 5.5, p.182). Switch trials had a significantly higher proportion of incorrect rule recall, an effect that was enhanced when using the symbolic instructional cue. There was a large decrease in errors between switch and trials with one repetition when using the symbolic cue (Fig. 5.7, p.186). Although continued repetition did still improve performance, the large initial impact is indicative of failure to encode the change in cue. The higher proportion of errors when using the perceptually harder cue is suggestive that the manipulation of environmental support can influence the effectiveness of top-down influences on external monitoring. These results are in line with the observation in previous goal neglect paradigms that some participants simply missed the second instructional cue (Duncan et al., 1996). On trials with incorrect rule recall participants fail to follow task requirements because they lack knowledge of what is currently required. A failure of top-down biasing of perception, rather than action selection.

Interestingly, the proportion of delayed configuration or goal neglect errors did not differ between switch and cue types (Fig. 5.5, p.182). These observations were not consistent with previous suggestions that these conditions increase the likelihood of goal

neglect (e.g. Duncan et al., 1996; Bhandari & Duncan, 2014). In past paradigms it was difficult to dissociate errors of monitoring from action selection. The analysis was run again using a goal neglect classification without the additional control afforded by the current paradigm. Using this classification the results were in support of previous research, with a higher proportion of goal neglect errors on switch as compared to repeat trials, and while using a perceptually harder cue. This difference was primarily driven by the inclusion of monitoring errors in the goal neglect classification (Fig. 5.6, p.184). Overall, this suggests that goal activation errors can be dissociated and may be differentially impacted by types of experimental manipulation.

The pattern of results on the repetition analysis was also distinct from that observed for incorrect rule recall, with no significant difference between switch and one repeat trials for either error type (Fig. 5.7, p.186). A decrease in error proportions did become significant for higher repeat numbers. This perhaps suggests that through repetition the selection of the required action becomes more competitive, although it should be noted that the effect on proportion of goal neglect errors was minimal. An important consideration here is that previous letter monitoring paradigms have employed a predictable switch following multiple repeats (e.g. Duncan et al., 1996; Iveson et al., 2017). Therefore, the higher proportion of goal neglect errors on trials with multiple repeats may be more representative of previous observations.

The impact of incorrect recall, delayed configuration and goal neglect on concurrent orientation recall was compared to performance on errorless repeat (baseline) and errorless switch trials (Fig. 5.8, p.188). All error times were seen to be associated with a greater speed and accuracy cost as compared to residual switch costs. The impact on task performance was incremental: delayed configuration, then goal neglect and finally incorrect rule recall. This finding fits with goal activation accounts of behaviour (De Jong et al., 1999; De Jong, 2000), in which different errors influence the ability of the

participant to prepare for the upcoming trial. Overall, these results suggest that goal activation errors can be dissociated and have a differential impact on task performance.

The current study extends previous research by using a novel approach to measure goal neglect, which allows greater segregation and comparison of goal activation errors. It was suggested that common experimental manipulations (used to promote higher incidents of goal neglect) may differentially impact failures in monitoring as compared to failures in action selection. However, an important weakness of the current design is that there are multiple differences between the cue types. Compared to the colour cue, the symbolic cue is perceptually harder to dissociate, is more visually complex, is not supported by stored semantic knowledge and is less salient. Moreover, it also includes more direct stimulus-response mapping (slants in the direction of the response rule). Further investigation would preferably manipulate the perceptual difficulty and directness of stimulus-response mapping separately and continuously (e.g. using salience and orientation of an arrow) to include a direct comparison of their effects on different error types. Another weakness of note is the relatively small proportions of goal neglect errors for many participants. Further research should aim to produce higher proportions of errors to allow for a more reliable comparison. This could be achieved by targeted sampling from individuals with a lower fluid intelligence (Duncan et al., 1996) or manipulation of novelty by introducing new task requirements at the start of each block (e.g. Bhandari & Duncan, 2014).

In the final empirical chapter a more specific question was addressed concerning how attentional control is distributed between concurrent task demands. During the pursuit of goal directed behaviour there is often a concurrent requirement for both working memory maintenance and external processing. Previous work suggested that attentional resources were shared in time, with attention being rapidly switched between the two processes (Barrouillet et al., 2004; Barrouillet & Camos, 2015). It was suggested

that the ratio of time between attentional capture of the processing task and attentional availability for working memory refreshing (Cognitive Load, Fig 6.1, p.205) influenced the trade-off in performance. Previous investigations addressed this question using complex span tasks, requiring sequential recall of familiar information (e.g. digits). This chapter revisited these assumptions in a different memory context by looking at the fidelity of recall for a single item feature. For an overview of the experimental design see Fig 6.2 (p.208).

The experimental design was found to significantly manipulate cognitive load (e.g. Fig. 6.13, p.239) in a manner that was comparable to past TBRS experiments (Barrouillet et al., 2004). In all three experiments the concurrent processing task significantly increased the angular error when reporting the orientation (e.g. Fig. 6.15, p.239). However, there was no difference observed between the interference tasks with differing cognitive load. In experiment 3, there was some indication that individuals with high or low working memory span may respond to the cognitive load manipulation differentially (Fig 6.16, p.241 and Fig 6.17, p.242). These observations may suggest that a higher working memory load is required to see a trade off in performance. Overall these findings correspond to past work that has found that participants can concurrently remember a small number of items on complex span tasks (Barrouillet & Camos, 2015) and raises questions regarding how attention is used for maintenance activities during brief pauses from processing.

For example, if the item feature was kept in the focus of attention for the duration of pause, longer pauses (lower cognitive load) should have resulted in less decay. Attentional refreshing is said to take approximately 50ms (Camos et al., 2018), so both cognitive load conditions would have sufficient time to refresh the item at least once. If the time was refreshed once and returned to processing the feature would have been refreshed more often in the fast pace condition due to the increased number of pauses. It is

uncertain whether the item would have been refreshed multiple times or even if multiple successive refreshes would be of any observable benefit. Overall these results may simply suggest that cognitive load is primarily of importance under conditions requiring sequential recall. These conditions could require attention to independently refresh individual items, with each item requiring additional time.

The current paradigm extended past TBRS work by examining the model assumptions under a different working memory context. There are some important design features to consider. In the first experiment, cognitive load was manipulated by adjusting both processing and maintenance periods simultaneously. This method of manipulating cognitive load can be called into question because it could inadvertently be making the processing task harder due to stricter time constraints (see Oberauer & Lewvandowsky, 2013). In the subsequent experiments this was addressed by using a timing that allowed for only the adjustment of pause times between conditions. The current design allowed 750ms to complete each shape match judgement. Participants often finished within 500ms, so the additional time may have contributed to lower manipulations of cognitive load than expected. One important criticism is that the use of intermittent processing tasks, with predictable pauses, may provide the condition for rapid switching. Further work is needed to examine whether cognitive load is important above that of the processing task structure.

Future Direction for Part 2

Addressing larger questions such as the impact of a particular cognitive impairment on the ability to live independently can be difficult when the cognitive function itself is not well understood. In part two, experimental work was performed to allow the control required to address some more fundamental questions about how goal directed behaviour is structured. The first question related to how different environmental influences may

interact with the effectiveness of attentional control. It was observed that there are multiple ways in which goal directed behaviour can be ineffective, each considered as a failure in top-down attentional control, but manifested distinctly and influenced with diversity. Here it suggested that greater resolution in our understanding can be achieved by adding additional control. However, whether these errors should be treated as a unified construct or unique entities in themselves remains for theoretical discussion.

For all types of goal activation error observed in Chapter 5, the task requirements were essentially neglected, however the reason for and presentation of this neglect differed. Perhaps the term"goal neglect" should not be treated as a type of error in itself, but instead should be considered as descriptive of a behavioural symptom. A description of what is seen, rather than why or how it is happening (similar to the term executive dysfunction). These terms certainly have standalone utility, but should be considered as higher order categorisation and accompanied with further clarification.

Terms related to a higher level of categorisation can be ambiguous and thus, should be treated with caution. For example, conclusions and statements made using these terms without additional clarification can lead to seemingly contradictory results. However, when used correctly higher level categorisation has many benefits, aiding communication by providing clarity and concision. Moreover, these broader classifications help to illuminate patterns between different types of situations or disorders which may otherwise go unnoticed. When the level of classification is used carefully and stated explicitly these broad, descriptive terms can be extremely beneficial.

On a similar note, caution should be taken when breaking apart multisystem phenomenon. The fractionalisation of higher order functions, can be enlightening but may also be misguiding. To illustrate this point I draw upon the metaphor of an orchestra. One approach to studying orchestral music would be to study each individual musician.

This approach would be insightful and could teach you a lot about the quality and effectiveness of each piece. However, this approach is unlikely to give a full explanation of the music. In the case of an orchestra, the music is much more than the sum of the individual parts. The music is defined by how the notes combine across instruments and influenced by group dynamics between musicians.

The same is true of attentional control. The effectiveness of each function is not independent, but dependent on the effectiveness of the other functions in temporal proximity. An example of these types of dynamics was given in Chapter 5, with an increase in processing time needed for cue identification delaying the selection of the appropriate action. Another example would be the number of repetitions effecting the likelihood of error. In the same manner as the orchestra, goal directed behaviour is much more than the sum of the fractionated parts. Executive function is not unitary or completely separable, but both simultaneously. It needs to be studied both as independent parts and as a system to be fully understood.

Experimental tasks by nature do not tend to study cognitive functions in isolation (despite the intention to do so). An example of this is how task performance can be influenced by tonic fluctuations in attentional resources. This interaction is particularly pertinent because of the use of long experimental procedures. The impact of these fluctuations on performance was examined in the piloting phase for the goal activation paradigm presented in Chapter 5. An analysis was run splitting participants performance into epochs within and outside of their individual median reaction time range (for further details on this type of analysis see Esterman et al., 2013). In compliment of the results on the authors CPT task, the analysis also demonstrated higher instances of incorrect rule recall in epochs of sub-optimal functioning (Esterman et al., 2013). The interaction between sustained and selective processes raises some fundamental questions. Is the increase in error due to a decaying task model which needs re-activation (Dockree

et al., 2007) or is it something more fundamentally associated with the structure and/or resource requirement of the proposed executive loop?

Examining these types of interaction has certainly advanced our understanding of the structure of cognitive control. The observed competition for attentional resources between tasks during concurrent processing has led to many developments in our understanding (Pashler, 1984; Baddeley & Hitch, 1974; Towse & Hitch, 1995; Case, 1985; Barrouillet et al., 2004). One of the current conceptualisations of attentional resource sharing is rapid and sequential switching proposed in the TBRS model examined in Chapter 6 (Barrouillet et al., 2004). The authors suggested that the trade-off in performance seen during concurrent processing and maintenance was governed by the time of attentional capture. This led to a new conceptualisation of cognitive load, which accounted for the additional time requirements of completing a more complex concurrent task. Although this view afforded greater clarity and control it has also raised further questions regarding the nature of attentional resource sharing.

Barrouillet and Camos (2015) suggest that the reason that cognitive load is important for concurrent processing and maintenance is because the executive loop can only refresh one item in working memory at a given time. It is therefore, suggested that attention is shifted between working memory items refreshing them sequentially. The estimated time for the running of one production rule (e.g. refresh or update) is suggested to be approximately 50ms (Anderson et al., 2004; Barrouillet & Camos, 2015; Camos et al., 2018). The more items to be remembered the longer it will take to sequentially refresh them. Therefore, resulting in time constraints to the number of items that can be successfully refreshed in a given time period. Further work is required to examine how these time constraints impact on the fidelity of multiple item recall. Seeing that complex span tasks require temporal binding, it is also important to address whether the impact of concurrent processing is due to the increase in bindings errors or simply due

to increased random guessing. This is a question that could be easily addressed using mixture modelling (see Bays et al., 2009).

TBRS complex span tasks are organised to have multiple brief pauses during the concurrent processing task. If the length of these pauses is what governs how many items can be refreshed, it could suggest that task structure is more important than the proposed cognitive load. Further work might profitably examine the impact of how the concurrent processing task is structured, when cognitive load remains constant. This could be achieved by utilising a continuous interference task (e.g. fast visual tracking with a maximum error boundary monitored with eye tracking). This design would allow a fluid manipulation of cognitive load affording the comparison of different structures with similar cognitive loads (manipulating the length and location of where the pauses occur during the maintenance period).

Another important consideration is that by structuring the interference task to have chunks segregated by brief pauses the researcher may be engineering a situation which produces the theorised rapid switching. It is imagined that when there are predictable brief pauses the optimum strategy would be to rapidly switch between the task elements. However, in a setup which is unpredictable or during continuous attentional capture, rapid switching may not be optimum. The design proposed above would also allow the flexible manipulation of the predictability of refresh pauses whilst maintaining cognitive load. Moreover, the new design proposal could also offer the manipulation of difficulty independent of time. This could be achieved by manipulating the error boundary during tracking. This manipulation could potentially allow new discussion on the original question regarding whether task complexity impacts on resource sharing above that of simply requiring additional time for completion (Barrouillet & Camos, 2001).

Above it was suggested that effort should be made to explicitly examine the interaction between cognitive functions. However, it is also important to simply acknowledge when there are sources of variability that cannot be controlled. For example, in the current design (and in past complex span tasks) we are simply unaware of how the participants are behaving in these brief pauses. Although errors in the interference task are visible and can be accounted for, errors in the brief pauses cannot. In the goal activation paradigm presented above it was highlighted that sometimes despite knowledge and intention participants neglect to follow task requirements. It has to be considered that even if participants intend to refresh working memory during the pauses, they may simply fail to do so (some or all of the time). There could be variability in how participants build this requirement into their task structure and the weight they give it in comparison to performing well on the interference task.

There are two other sources of variability of particular importance. The first is the use of strategy. Some examples of strategies reported by participants during piloting for the current design were: verbal rehearsal of the time the orientation would indicate if it were on a clock face, verbal rehearsal of which quadrant the orientation was in and one extreme example fixating on the location of the target orientation throughout the interference task. These strategies lead to enhanced performance and lesser impact of cognitive load. Strategy use is hard to control for because there is a risk of biasing the participant if explicit instructions are given. In further work is advisable to record strategy use subsequent to the experiment and check how it modulates performance.

7.3 Summary and Conclusions

Overall this thesis has highlighted the complexity of how attention contributes to the success of goal directed behaviour. It has demonstrated that diverse lesions within a complex network of brain regions can contribute to impaired attentional configuration and how this impairment can influence functional independence following stroke. Furthermore, it has tried to address the difficulties in dissociating errors arising from top-down control of behaviour and raised questions regarding how attentional resources are shared during concurrent processing. It is hoped that gaining greater understanding of how behaviour becomes goal directed will improve awareness, assessment and potential treatment for patients with executive dysfunction such as SB.

References

Adamson, J., Beswick, A., & Ebrahim, S. (2004). Is stroke the most common cause of disability ? *Journal of Stroke and Cerebrovascular Diseases*, *13*(4), 171-177. doi: 10.1016/j.jstrokecerebrovasdis.2004.06.003

Alexander, G. E., DeLong, M. R., & Strick, P. L. (1986). Parallel organization of functionally segregated circuits linking basal ganglia and cortex. *Annual Review of Neuroscience*, *9*, 357-381.

Alexander, M., Gillingham, S., Schweizer, T., & Stuss, D. T. (2012). Cognitive impairments due to focal cerebellar injuries in adults. *Cortex*, *48*, 980-990.

Allen, G., Buxton, R. B., Wong, E. C., & Courchesne, E. (1997). Attentional activation of the cerebellum independent of motor involvement. *Science*, *275*(5308), 1940-1943. doi: 10.1126/science.275.5308.1940

Allport, D. A., Styles, E. A., & Hsieh, S. (1994). Shifting intentional set. exploring the dynamic control of tasks. In C. Umilta & M. Moscovitch (Eds.), *Attention and performance xv: Conscious and nonconscious information processing.* (p. 421452). Cambridge, M.A.: MIT Press, Bradford Books.

Allport, D. A., & Wylie, G. (2000). Task switching, stimulus-response bindings, and negative priming. In *Control of cognitive processes: Attention and performance xviii* (p. 3570). Cambridge, MA: MIT Press.

Altmann, E. M. (2005). Repetition priming in task switching: Do the benefits dissipate? *Psychonomic Bulletin & Review*, *12*(3), 535–540. doi: 10.3758/BF03193801

Alvarez, G. A., & Cavanagh, P. (2004). The capacity of visual short-term memory is set both by visual information load and by number of objects. *Psychological Science*, *15*, 106111.

Anderson, J. R. (1983). *The architecture of cognition.* Cambridge, MA: Harvard University Press.

Anderson, J. R. (1993). *Rules of the mind.* Hillsdale, NJ: Lawrence Erlbaum Assoiciates.

Anderson, J. R., Bothell, D., Byrne, M. D., & Lebiere, C. (2004). An integrated theory of mind. *Psychological Review*, *111*(4), 103660. doi: 10.1037/0033-295X.111.4.1036

Anderson, J. R., Reder, L. M., & Lebiere, C. (1996). Working memory: Activation limitations on retrieval. *Cognitive Psychology*, *30*(3), 221 - 256. doi: 10.1006/cogp.1996.0007

Andrés, P., & Van der Linden, M. (2002). Are central executive functions working in patients with focal frontal lesions? *Neuropsychologia*, *40*(7), 835 - 845. doi: 10.1016/S0028-3932(01)00182-8

Anticevic, A., Repovs, G. L., Shulman, G., & Barch, D. (2010, 11). When less is more: Tpj and default network deactivation during encoding predicts working memory performance. *NeuroImage*, *49*, 2638-48. doi: 10.1016/j.neuroimage.2009.11.008

Aron, A. R., Durston, S., Eagle, D. M., Logan, G. D., Stinear, C. M., & Stuphorn, V. (2007). Converging evidence for a fronto-basal-ganglia network for inhibitory control of action and cognition. *Journal of Neuroscience*, *27*(44), 11860–11864. doi: 10.1523/JNEUROSCI.3644-07.2007

Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian1, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience*, *6*(2), 115-116. doi: 10.1038/nn1003

Aron, A. R., & Poldrack, R. A. (2006). Cortical and subcortical contributions to stop signal response inhibition: Role of the subthalamic nucleus. *Journal of Neuroscience*, *26*(9), 2424–2433. doi: 10.1523/JNEUROSCI.4682-05.2006

Asaad, W. F., Rainer, G., & Miller, E. K. (1998). Neural activity in the primate prefrontal cortex during associative learning. *Neuron*, *21*, 1399-1407.

Asaad, W. F., Rainer, G., & Miller, E. K. (2000). Task-specific neural activity in the primate prefrontal cortex. *Journal of Neurophysiology*, *84*(1), 451-459. doi: 10.1016/s0896-6273(00)80658-3

Ashburner, J., & Friston, K. J. (2005). Unified segmentation. *NeuroImage*, *26*(3), 839 - 851. doi: 10.1016/j.neuroimage.2005.02.018

Ayerbe, L., Ayis, Salma, A., Crichton, S., Rudd, Anthony, G., & Wolfe, Charles, D. A. (2015). Explanatory factors for the association between depression and long-term physical disability after stroke explanatory factors for the association between depression and long-term physical disability after stroke. *Age and Ageing*, *44*, 1054-1058. doi: 10.1093/ageing/afv132

Baddeley, A. D. (1986). *Working memory*. London: Oxford University Press.

Baddeley, A. D. (2000). The episodic buffer: a new componentof working memory? *Trends in Cognitive Sciences*, *4*, 417-423. doi: 10.1016/S1364-6613(00)01538-2

Baddeley, A. D., Della Sala, S., Papagno, C., & Spinnler, H. (1997). Dual-task performance in dysexecutive and nondysexecutive patients with a frontal lesion. *Neu-*

ropsychology, *11*(2), 187-94.

Baddeley, A. D., & Hitch, G. J. (1974). Working memory. In G. A. Bower (Ed.), *The psychology of learning and motivation* (Vol. 8, p. 647-667). New York: Academic Press.

Badre, D., & D′Esposito, M. (2009). Is the rostro-caudal axis of the frontal lobe hierarchical? *Nature Reviews Neuroscience*, *10*(9), 659669.

Baier, B., Dieterich, M., Stoeter, P., Birklein, F., & Müller, N. G. (2010). Anatomical correlate of impaired covert visual attentional processes in patients with cerebellar lesions. *Journal of Neuroscience*, *30*(10), 3770–3776. doi: 10.1523/JNEUROSCI.0487-09.2010

Barbey, A. K., Koenigs, M., & Grafman, J. (2012). Dorsolateral prefrontal contributions to human working memory. *Cortex*, *49*(5), 1195-205.

Barker-Collo, S. L., & Feigin, V. (2006). The Impact of Neuropsychological Deficits on Functional Stroke Outcomes. *Neuropsychological Review*, *16*, 53–64. doi: 10.1007/s11065-006-9007-5

Barker-Collo, S. L., Feigin, V. L., Lawes, C. M. M., Parag, V., & Senior, H. (2010). Attention deficits after incident stroke in the acute period: Frequency across types of attention and relationships to patient characteristics and functional outcomes. *Topics in Stroke Rehabilitation*, *17*(6), 463-476. doi: 10.1310/tsr1706-463

Barrouillet, P., Bernardin, S., & Camos, V. (2004). Time constraints and resource sharing in adults' working memory spans. *Journal of Experimental Psychology: General*, *133*(1), 83-100. doi: 10.1037/0096-3445.133.1.83

Barrouillet, P., Bernardin, S., Portrat, S., Vergauwe, E., & Camos, V. (2007). Time and cognitive load in working memory. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *33*(3), 570-585. doi: 10.1037/0278-7393.33.3.570

Barrouillet, P., & Camos, V. (2001). Developmental increase in working memory span: Resource sharing or temporal decay? *Journal of Memory and Language*, *45*, 1-20. doi: 10.1006/jmla.2001.2767

Barrouillet, P., & Camos, V. (2015). *Working memory: Loss and reconstruction.* Hove, UK: Psychology Press.

Barrouillet, P., De Paepe, A., & Langerock, N. (2012). Time causes forgetting from working memory. *Psychonomic Bulletin & Review*, *19*(1), 87-92. doi: 10.3758/s13423-011-0192-8

Barrouillet, P., Gavens, N., Vergauwe, E., Gaillard, V., & Camos, V. (2009). Working memory span development: a time-based resource-sharing account. *Developmental Psychology*, *45*, 477-490.

Barrouillet, P., Lepine, R., & Camos, V. (2008). Is the influence of working memory capacity on high-level cognition mediated by complexity or resource-dependent elementary processes? *Psychonomic Bulletin and Review*, *15*(3), 528-534. doi: 10.3758/PBR.15.3.52

Barrouillet, P., Portrait, S., Vergauwe, E., Diependaele, K., & Camos, V. (2011). Further evidence for temporal decay in working memory. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *37*, 1302-1317.

Barrouillet, P., Portrat, S., & Camos, V. (2011). On the law relating processing to storage in working memory. *Psychological Review*, *118*(2), 175-192.

Bartolomeo, P., Thiebaut de Schotten, M., & Chica, A. B. (2012). Brain networks of visuospatial attention and their disruption in visual neglect. *Frontiers in Human Neuroscience*, *6*, 110. doi: 10.3389/fnhum.2012.00110

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*, *67*(1), 1-48. doi: 10.18637/jss.v067.i01

Bates, E., Wilson, S. M., Saygin, A. P., Dick, F., Sereno, M. I., Knight, R. T., & Dronkers, N. F. (2003). Voxel-based lesionsymptom mapping. *Nature Neuroscience*, *6*(5), 448-450. doi: 10.1038/nn1050

Bauer, M., Kennett, S., & Driver, J. (2012). Attentional selection of location and modality in vision and touch modulates low-frequency activity in associated sensory cortices. *Journal of Neurophysiology*, *107*(9), 23422351. doi: 10.1152/jn.00973.2011

Bays, P. M., Catalao, R. F., & Husain, M. (2009). The precision of visual working memory is set by allocation of a shared resource. *Journal of Vision*, *9*(10), 7-11. doi: doi:10.1167/9.10.7

Bays, P. M., Gorgoraptis, N., Wee, N., Marshall, L., & Husain, M. (2011). Temporal dynamics of encoding, storage, and reallocation of visual working memory. *Journal of Vision*, *11*(10), 6. doi: 10.1167/11.10.6

Bays, P. M., & Husain, M. (2008). Dynamic shifts of limited working memory resources in human vision. *Science*, *321*(5890), 851-4.

Bays, P. M., Singh-Curry, V., Gorgoraptis, N., Driver, J., & Husain, M. (2010). Integration of goal- and stimulus-related visual signals revealed by damage to human parietal cortex. *The Journal of Neuroscience*, *30*(17), 5968 5978. doi: 10.1523/JNEUROSCI.0997-10.2010

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*,

50(1), 7 - 15. doi: https://doi.org/10.1016/0010-0277(94)90018-3

Bechara, A., Damasio, H., Damasio, A. R., & Lee, G. P. (1999). Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. *Journal of Neuroscience*, *19*(13), 5473–5481. doi: 10.1523/JNEUROSCI.19-13-05473 .1999

Bechara, A., Damasio, H., Tranel, D., & Anderson, S. W. (1998). Dissociation of working memory from decision making within the human prefrontal cortex. *Journal of Neuroscience*, *18*(1), 428-437. doi: 10.1523/JNEUROSCI.18-01-00428.1998

Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1997). Deciding advantageously before knowing the advantageous strategy. *Science*, *275*(5304), 1293-5.

Bednark, J. G., Campbell, M. E. J., & Cunnington, R. (2015). Basal ganglia and cortical networks for sequential ordering and rhythm of complex movements. *Frontiers in human neuroscience*, *9*, 421. doi: 10.3389/fnhum.2015.00421

Beldarrain, M. G., Garca-Monc, J. C., Quintana, J. M., Llorens, V., & Rodeo, E. (1997). Diaschisis and neuropsychological performance after cerebellar stroke. *Eur Neurol*, *37*, 82-89.

Bellebaum, C., & Daum, I. (2007). Cerebellar involvement in executive control. *The Cerebellum*, *6*(3), 184-192. doi: 10.1080/14734220601169707

Benajmini, Y., & Hochberg. (1995). Controlling the False Discovery Rate : A Practical and Powerful Approach to Multiple Testing. *Journal of the Royal Statistical Society*, *57*(1), 289-300.

Bennett, H. P., Corbett, A. J., Gaden, S., Grayson, D. A., Kril, J. J., & Broe, A. G. (2002). Subcortical Vascular Disease and Functional Decline: A 6Year Predictor Study. *Journal of the American Geriatrics Society*, *50*(2), 1969-1977. doi: 10.1046/ j.1532-5415.2002.50608.x

Bernal, B., & Ardila, A. (2009). The role of the arcuate fasciculus in conduction aphasia. *Brain*, *132*(9), 2309-2316. doi: 10.1093/brain/awp206

Berry, A. S., Zanto, T. P., Rutman, A. M., Clapp, W. C., & Gazzaley, A. (2009). Practice-related improvement in working memory is modulated by changes in processing external interference. *Journal of neurophysiology*, *102*(3), 1779-89.

Bettcher, B. M., Mungas, D., Patel, N., Elofson, J., Dutt, S., Wynn, M., ... Kramer, J. H. (2016). Neuroanatomical substrates of executive functions: Beyond prefrontal structures. *Neuropsychologia*, *85*, 100 - 109. doi: 10.1016/j.neuropsychologia.2016 .03.001

Bhandari, A., & Duncan, J. (2014). Goal neglect and knowledge chunking in the construction of novel behaviour. *Cognition*, *130*, 1130.

Bianchi, L. (1922). *The mechanism of the brain and the function of the frontal lobes*. Edinburgh: Livingstone.

Bichot, N. P., & Schall, J. (1999, 07). Effects of similarity and history on neural mechanisms of visual selection. nat. neurosci. 2, 549-554. *Nature neuroscience*, *2*, 549-54. doi: 10.1038/9205

Bichot, N. P., Schall, J. D., & Thompson, K. G. (1996). Visual feature selectivity in frontal eye fields induced by experience in mature macaques. *Nature*, *381*, 697-699.

Bidet-Caulet, A., Buchanan, K. G., Viswanath, H., Black, J., Scabini, D., Bonnet-Brilhault, F., & Knight, R. T. (2015). Impaired facilitatory mechanisms of auditory attention after damage of the lateral prefrontal cortex. *Cerebral Cortex*, *25*(11), 4126-4134. doi: 10.1093/cercor/bhu131

Bidet-Caulet, A., Fischer, C., Besle, J., Aguera, P.-E., Giard, M.-H., & Bertrand, O. (2007). Effects of Selective Attention on the Electrophysiological Representation of Concurrent Sounds in the Human Auditory Cortex. *Journal of Neuroscience*, *27*(35), 9252-9261.

Bisley, J. W., & Goldberg, M. E. (2003). Neuronal activity in the lateral intraparietal area and spatial attention. *Science*, *299*, 816.

Bisley, J. W., & Goldberg, M. E. (2010). Attention, Intention, and Priority in the Parietal Lobe. *Annual Review of Neuroscience*, *33*(1), 1–21. doi: 10.1146/annurev-neuro-060909-152823

Bode, S., & Haynes, J. D. (2009). Decoding sequential stages of task preparation in the human brain. *Neuroimage*, *45*, 606613.

Boets, B., Op de Beeck, H. P., Vandermosten, M., Scott, S. K., Gillebert, C. R., Mantini, D., ... Ghesquire, P. (2013). Intact but less accessible phonetic representations in adults with dyslexia. *Science*, *342*, 12511254.

Bosman, C., & Womelsdorf, T. (2009). *Neuronal signatures of selective attention synchronization and gain modulation as mechanisms for selective sensory information processing*. Verlag Berlin Heidelberg: Springer.

Bostan, A. C., & Strick, P. L. (2010). The cerebellum and basal ganglia are interconnected. *Neuropsychology Review*, *20*(3), 261-270. doi: 10.1007/s11065-010-9143-9

Boynton, G. (2005). Imaging orientation selectivity: Decoding conscious perception in v1. *Nature neuroscience*, *8*, 541-542. doi: 10.1038/nn0505-541

Brady, T., Stormer, V., & Alvarez, G. (2016). Working memory is not fixed capacity: more active storage capacity for real-world objects than for simple stimuli. *PNAS*, *113*, 7459-7464.

Brand, M., Recknor, E. C., Grabenhorst, F., & Bechara, A. (2007). Decisions un-

der ambiguity and decisions under risk: Correlations with executive functions and comparisons of two different gambling tasks with implicit and explicit rules. *Journal of Clinical and Experimental Neuropsychology*, *29*(1), 86-99. doi: 10.1080/13803390500507196

Brass, M., Derrfuss, J., Forstmann, B., & von Cramon, D. Y. (2005). The role of the inferior frontal junction area in cognitive control. *Trends in Cognitive Sciences*, *9*(7), 314 - 316. doi: https://doi.org/10.1016/j.tics.2005.05.001

Braver, T. S., & Cohen, J. D. (2000). On the control of control: the role of dopamine in regulating prefrontal function and working memory. In S. Monsell & J. Driver (Eds.), *In attention and performance* (Vol. XVIII, p. 713738). Cambridge, MA: MIT Press.

Brett, M., Hanke, M., Cipollini, B., Côté, M.-A., Markiewicz, C., Gerhard, S., ... Garyfallidis, E. (2016). *nibabel: 2.1.0.* doi: 10.5281/zenodo.60808

Brett, M., Leff, A. P., Rorden, C., & Ashburner, J. (2001). Spatial normalization of brain images with focal lesions using cost function masking. *NeuroImage*, *14*(2), 486 - 500. doi: 10.1006/nimg.2001.0845

Brissenden, J. A., Levin, E. J., Osher, D. E., Halko, M. A., & Somers, D. C. (2016). Functional evidence for a cerebellar node of the dorsal attention network. *Journal of Neuroscience*, *36*(22), 6083–6096. doi: 10.1523/JNEUROSCI.0344-16.2016

Broadbent, D. E., Cooper, P. F., FitzGerald, P., & Parkes, K. R. (1982). the cognitive failures questionnaire(cfq) and its correlates. *British Journal of Clinical Psychology*, *21*, 1-16.

Buckner, R. L. (2013). The cerebellum and cognitive function:25 years of insight from anatomy and neuroimaging. *Neuron*, *80*, 807 - 815. doi: 10.1016/j.neuron.2013.10.044

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain′s default network. *Annals of the New York Academy of Sciences*, *1124*(1), 1-38. doi: 10.1196/annals.1440.011

Bundesen, C. (1990). A Theory of Visual Attention. *Psychological Review*, *97*(4), 523–547.

Burgess, P. W. (2000). Strategy application disorder: the role of the frontal lobes in human multitasking. *Psychological Research*, *63*(3), 279–288. doi: 10.1007/s004269900006

Burgess, P. W., & Shallice, T. (1996). Bizarre responses, rule detection and frontal lobe lesions. *Cortex*, *32*(2), 241 - 259. doi: 10.1016/S0010-9452(96)80049-9

Buschman, T. J., Denovellis, E. L., Diogo, C., Bullock, D., & Miller, E. K. (2012). Syn-

chronous Oscillatory Neural Ensembles for Rules in the Prefrontal Cortex. *Neuron*, *76*(4), 838–846. doi: 10.1016/j.ajo.2009.07.014.Aqueous

Cabeza, R., & Nyberg, L. (2000). Imaging cognition ii: An empirical review of 275 pet and fmri studies. *Journal of Cognitive Neuroscience*, *12*(1), 1-47.

Caligiore, D., Pezzulo, G., Baldassarre, G., Bostan, A. C., Strick, P. L., Doya, K., ... Herreros, I. (2017). Consensus paper: Towards a systems-level view of cerebellar function: the interplay between cerebellum, basal ganglia, and cortex. *The Cerebellum*, *16*(1), 203–229. doi: 10.1007/s12311-016-0763-3

Camilleri, J., Mller, V., Fox, P., Laird, A., Hoffstaedter, F., Kalenscher, T., & Eickhoff, S. (2018). Definition and characterization of an extended multiple-demand network. *NeuroImage*, *15*, 138-147. doi: 10.1016/j.neuroimage.2017.10.020

Camos, V., Johnson, M., Loaiza, V., Portrat, S., Souza, A., & Vergauwe, E. (2018). What is attentional refreshing in working memory?: What is attentional refreshing? *Annals of the New York Academy of Sciences*, *1424*(1), 19-32. doi: 10.1111/nyas .13616

Caplan, L. R., Schmahmann, J. D., Kase, C. S., Feldmann, E., Baquis, G., Greenberg, J. P., ... Hier, D. B. (1990). Caudate infarcts. *Archives of Neurology*, *47*(2), 133-143. doi: 10.1001/archneur.1990.00530020029011

Cardoso, C. d. O., Branco, L. D., Cotrena, C., Kristensen, C. H., Schneider Bakos, D. D. G., & Fonseca, R. P. (2014). The impact of frontal and cerebellar lesions on decision making: evidence from the iowa gambling task. *Frontiers in Neuroscience*, *8*, 61. doi: 10.3389/fnins.2014.00061

Carp, J., Park, J., Hebrank, A., Park, D. C., & Polk, T. A. (2011). Age-related neural differentiation in the motor system. *PLoS One*, *6*, 16.

Carrera, E., & Tononi, G. (2014). Diaschisis: past, present, future. *Brain*, *137*(9), 2408-2422. doi: 10.1093/brain/awu101

Carter, A., Astafiev, S., Lang, C., Connor, L., Rengachary, J., Strube, M., ... Corbetta, M. (2010). Resting interhemispheric functional magnetic resonance imaging connectivity predicts performance after stroke. *Annals of Neurology*, *67*(3), 365-375. doi: 10.1002/ana.21905

Case, R. (1985). *Intellectual development: Birth to adulthood.* New York: Academic Press.

Case, R. (1992). *The mind's staircase: Exploring the conceptual underpinnings of children's thought and knowledge.* Hillsdale, NJ: Lawrence Erlbaum Associates.

Case, R., Kurland, M., & Goldberg, J. (1982). Operational efficiency and the growth of short-term memory. *Journal of Experimental Child Psychology*, *33*, 386-404.

Catani, M., DellAcqua, F., Vergani, F., Malik, F., Hodge, H., Roy, P., ... Thiebaut de Schotten, M. (2012). Short frontal lobe connections of the human brain. *Cortex*, *48*, 273-291. doi: 10.1016/j.cortex.2011.12.001

Catani, M., Jones, D. K., & ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology*, *57*, 8 - 16. doi: 10.1002/ana.20319

Catania, M., & Thiebaut de Schotten, M. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex*, *44*, 1105 - 1132. doi: 10.1016/j.cortex .2008.05.004

Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: A review of its functional anatomy and behavioural correlates. *Brain*, *129*(3), 564–583. doi: 10.1093/brain/ awl004

Chafee, M. V., & Goldman-Rakic, P. S. (2000). Inactivation of parietal and prefrontal cortex reveals interdependence of neural activity during memory-guided saccades. *Journal of neurophysiology*, *83*, 1550-1566.

Chait, M., de Cheveigne, A., Poeppel, D., & Simon, J. Z. (2010). Neural dynamics of attending and ignoring in human auditory cortex. *Neuropsychologia*, *48*, 3262-3271.

Charlton, R. A., & Morris, R. G. (2015). Associations between working memory and white matter integrity in normal ageing. In R. H. Logie & R. Morris (Eds.), *Working memory and ageing* (p. 97128). Hove, UK: Psychology Press.

Chechlacz, M., Rotshtein, P., Bickerton, W.-L., Hansen, P. C., Deb, S., & Humphreys, G. W. (2010). Separating neural correlates of allocentric and egocentric neglect: Distinct cortical sites and common white matter disconnections. *Cognitive Neuropsychology*, *27*(3), 277-303. doi: 10.1080/02643294.2010.519699

Chechlacz, M., Rotshtein, P., & Humphreys, G. W. (2012). Neuroanatomical dissections of unilateral visual neglect symptoms: Ale meta-analysis of lesion-symptom mapping. *Frontiers in human neuroscience*, *6*, 230.

Chen, S. A., & Desmond, J. E. (2005a). Cerebrocerebellar networks during articulatory rehearsal and verbal working memory tasks. *NeuroImage*, *24*(2), 332 - 338. doi: 10.1016/j.neuroimage.2004.08.032

Chen, S. A., & Desmond, J. E. (2005b). Temporal dynamics of cerebro-cerebellar network recruitment during a cognitive task. *Neuropsychologia*, *43*(9), 1227 - 1237. doi: 10.1016/j.neuropsychologia.2004.12.015

Chui, H. C. (2007). Subcortical ischemic vascular dementia. *Neurologic clinics*, *25*(3), 717-40.

Cipolotti, L., Healy, C., Chan, E., MacPherson, S., White, M., Woollett, K. K., ...

Shallice, T. (2015, 08). The effect of age on cognitive performance of frontal patients. *Neuropsychologia*, *75*, 233-241. doi: 10.1016/j.neuropsychologia.2015.06.011

Cipolotti, L., MacPherson, S. E., Gharooni, S., van Harskamp, N., Shallice, T., Chan, E., & Nachev, P. (2017). Cognitive estimation: Performance of patients with focal frontal and posterior lesions. *Neuropsychologia*. doi: 10.1016/j.neuropsychologia.2017.08.017

Cirstea, C. M., Ptito, A., & Levin, M. F. (2006). Feedback and cognition in arm motor skill reacquisition after stroke. *Stroke*, *37*, 1237–1242. doi: 10.1161/01.STR.0000217417.89347.63

Clark, L., Manes, F., Antoun, N., Sahakian, B., & Robbins, T. (2003, 02). Clark l, manes f, antoun n, sahakian bj, robbins tw. the contributions of lesion laterality and lesion volume to decision-making deficits following frontal lobe damage. neuropsychologia 41: 1474-1483. *Neuropsychologia*, *41*, 1474-83. doi: 10.1016/S0028-3932(03)00081-2

Clarke, A., & Tyler, L. K. (2014). Object-specific semantic coding in human perirhinal cortex. *Journal of Neuroscience*, *34*, 47664775.

Clower, D. M., Dum, R. P., & Strick, P. L. (2005). Basal ganglia and cerebellar inputs to aip. *Cerebral Cortex*, *15*(7), 913-920. doi: 10.1093/cercor/bhh190

Cole, M. W., & Schneider, W. (2007). The cognitive control network: Integrated cortical regions with dissociable functions. *NeuroImage*, *37*(1), 343-360. doi: 10.1016/j.neuroimage.2007.03.071

Collette, F., Van der Linden, M., Laureys, S., Delfiore, G., Degueldre, C., Luxen, A., & Salmon, E. (2005). Exploring the unity and diversity of the neural substrates of executive functioning. *Human Brain Mapping*, *25*(4), 409-423. doi: 10.1002/hbm.20118

Committeri, G., Pitzalis, S., Galati, G., Patria, F., Pelle, G., Sabatini, U., ... Pizzamiglio, L. (2007). Neural bases of personal and extrapersonal neglect in humans. *Brain*, *130*(2), 431-441. doi: 10.1093/brain/awl265

Cools, R., Ivry, R. B., & D′Esposito, M. (2006). The human striatum is necessary for responding to changes in stimulus relevance. *Journal of Cognitive Neuroscience*, *18*(12), 1973-1983. doi: 10.1162/jocn.2006.18.12.1973

Corbetta, M., Kincade, M. J., Lewis, C., Snyder, A. Z., & Sapir, A. (2005). Neural basis and recovery of spatial attention deficits in spatial neglect. *Nature Neuroscience*, *8*(11), 1603-1610. doi: 10.1038/nn1574

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven

attention in the brain. *Nature Reviews Neuroscience*, *3*, 201 - 215. doi: 10.1038/nrn755

Corbetta, M., & Shulman, G. L. (2011). Spatial neglect and attention networks. *Annual Review of Neuroscience*, *34*(1), 569-599. doi: 10.1146/annurev-neuro-061010-113731

Correani, A., & Humphreys, G. W. (2011). An impaired attentional dwell time after parietal and frontal lesions related to impaired selective attention not unilateral neglect. *Cognitive Neuropsychology*, *28*(5), 363-385. doi: 10.1080/02643294.2012.656587

Costello, A. B., & Osborne, J. W. (2005). Best practices in exploratory factor analysis: Four recommendations for getting the most from your analysis. *Practical Assessment, Research and Evaluation*, *10*(7), 1-9.

Cowan, N. (1995). *Attention and memory: An integrated framework*. New York: Oxford University Press.

Cowan, N. (1999). An emdedded-process model of working memory. In M. A & S. P (Eds.), *Model of working memory: Mechanisms of active maintenance and executive control* (p. 62-101). Cambridge: Cambridge University Press.

Cowan, N. (2005). *Working memory capacity.* Hove, East Sussex:Psychological Press.

Cowan, N. (2010). The magical mystery four: How is working memory capacity limited, and why? *Current Directions in Psychological Science*, *19*(1), 51-57.

Cowan, N., Saults, J. S., & Elliott, E. M. (2002). The search for what is fundamental int he development of working memory. *Advances in Child Development and Behaviour*, *29*, 1-49.

Crawford, J. R., Garthwaite, P. H., & Howell, D. C. (2009). On comparing a single case with a control sample: An alternative perspective. *Neuropsychologia*, *47*(13), 2690–2695. doi: 10.1016/j.neuropsychologia.2009.04.011

Crawford, J. R., & Howell, D. C. (1998). Comparing an individual's test score against norms derived from small samples. *The Clinical Neuropsychologist*, *12*(4), 482-486. doi: 10.1076/clin.12.4.482.7241

Critchley, M. (1953). *The parietal lobes*. Oxford, England: Williams and Wilkins.

Crittenden, B. M., Mitchell, D. J., & Duncan, J. (2016). Task encoding across the multiple demand cortex is consistent with a frontoparietal and cingulo-opercular dual networks distinction. *Journal of Neuroscience*, *36*(23), 6147–6155. doi: 10.1523/JNEUROSCI.4590-15.2016

Cronbach, L. J. (1951). Coefficient alpha and the internal structure of tests. *Psychometrika*, *16*(3), 297-334. doi: 10.1007/BF02310555

Dalmaijer, E. S., Mathôt, S., & Van der Stigchel, S. (2014). PyGaze: an open-source, cross-platform toolbox for minimal-effort programming of eyetracking experiments. *Behavior Research Methods*, *46*(4), 913–921. doi: 10.3758/s13428-013-0422-2

Damasio, A. R., Damasio, H., & Chui, H. C. (1980). Neglect following damage to frontal lobe or basal ganglia. *Neuropsychologia*, *18*(2), 123 - 132. doi: 10.1016/0028-3932(80)90058-5

Daneman, M., & Carpenter, P. A. (1980). Individual differences in working memory and reading. *Journal of Verbal Learning and Verbal Behavior*, *19*(4), 450 - 466. doi: 10.1016/S0022-5371(80)90312-6

Daum, I., & Ackermann, H. (1997). Neuropsychological abnormalities in cerebellar syndromes-fact or fiction? In R. J. Bradley, R. A. Harris, P. Jenner, & J. D. Schmahmann (Eds.), *The cerebellum and cognition* (Vol. 41, p. 455 - 471). Academic Press. doi: 10.1016/S0074-7742(08)60365-7

De Jong, R. (2000). An intention-activation account of residual switch cost. In S. Monsell & J. Driver (Eds.), *Control of cognitive processes: attention and performance xviii* (p. 331-357). Cambridge, MA: MIT Press.

De Jong, R. (2001). Adult age differences in goal activation and goal maintenance. *European Journal of Cognitive Psychology*, *13*(1-2), 71-89. doi: 10.1080/09541440042000223

De Jong, R., Berendsen, E., & Cools, R. (1999). Goal neglect and inhibitory limitations: dissociable causes of interference effects in conflict situations. *Acta Psychologica*, *101*(2-3), 379–394. doi: 10.1016/S0001-6918(99)00012-8

de Haan, B., & Karnath, H.-O. (2018). A hitchhiker's guide to lesion-behaviour mapping. *Neuropsychologia*, *115*, 5 - 16. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0028393217303962` (Special Issue: Lesions and Brain Mapping) doi: https://doi.org/10.1016/j.neuropsychologia.2017.10.021

Delis, D. C., Squire, L. R., Bihrle, A., & Massman, P. (1992). Componential analysis of problem-solving ability: Performance of patients with frontal lobe damage and amnesic patients on a new sorting test. *Neuropsychologia*, *30*(8), 683 - 697. doi: 10.1016/0028-3932(92)90039-O

Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annual Review of Neuroscience*, *18*(1), 193-222. doi: 10.1146/annurev.ne.18.030195.001205

Diamond, A. (2012). Executive functions. *Annual review of psychology*, *64*, 135-68.

Diamond, A., Carlson, S. M., & Beck, D. M. (2005). Preschool children's performance in task switching on the dimensional change card sort task: Separating the dimensions

aids the ability to switch. *Developmental Neuropsychology*, *28*(2), 689-729. doi: 10.1207/s15326942dn2802_7

Diedrichsen, J., Balsters, J. H., Flavell, J., Cussans, E., & Ramnani, N. (2009). A probabilistic mr atlas of the human cerebellum. *NeuroImage*, *46*(1), 39 - 46. doi: 10.1016/j.neuroimage.2009.01.045

Diedrichsen, J., Maderwald, S., Kper, M., Thrling, M., Rabe, K., Gizewski, E., ... Timmann, D. (2011). Imaging the deep cerebellar nuclei: A probabilistic atlas and normalization procedure. *NeuroImage*, *54*(3), 1786 - 1794. doi: 10.1016/j.neuroimage.2010.10.035

Dockree, P. M., Kelly, S. P., Foxe, J. J., Reilly, R. B., & Robertson, I. H. (2007). Optimal sustained attention is linked to the spectral content of background eeg activity: greater ongoing tonic alpha (10hz) power supports successful phasic goal activation. *European Journal of Neuroscience*, *25*(3), 900-907. doi: 10.1111/j.1460-9568.2007.05324.x

Dosenbach, N. U. F., Fair, D., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. T., ... Petersen, S. E. (2007). Distinct brain networks for adaptive and stable task control in humans. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(26). doi: 10.1073/pnas.0704320104

Dosenbach, N. U. F., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences*, *12*(3), 99 - 105. doi: 10.1016/j.tics.2008.01.001

Dosenbach, N. U. F., Visscher, K. M., Palmer, E. D., Miezin, F. M., Wenger, K. K., Kang, H. C., ... Petersen, S. E. (2006). A core system for the implementation of task sets. *Neuron*, *50*(5), 799 - 812. doi: 10.1016/j.neuron.2006.04.031

Douiri, A., Rudd, A. G., & Wolfe, C. D. (2013). Prevalence of poststroke cognitive impairment. *Stroke*, *44*(1), 138-145. doi: 10.1161/STROKEAHA.112.670844

Doya, K. (1999). What are the computations of the cerebellum, the basal ganglia and the cerebral cortex? *Neural Networks*, *12*(7), 961 - 974. doi: 10.1016/S0893-6080(99)00046-5

Doya, K. (2000). Complementary roles of basal ganglia and cerebellum in learning and motor control. *Current Opinion in Neurobiology 2000*, *10*, 732–739. doi: 10.1016/S0959-4388(00)00153-7

Dreisbach, G., & Haider, H. (2006). Preparatory adjustment of cognitive control in the task switching paradigm. *Psychonomic Bulletin & Review*, *13*(2), 334–338. doi: 10.3758/BF03193853

Driver, J. (2001). A selective review of selective attentionresearch from the past century.

British Journal of Psychology, *92*, 53-79. doi: 10.1348/000712601162103

Driver, J., & Husain, M. (2002). The role of spatial working memory deficits in pathological search by neglect patients. In H. O. Karnath, D. Milner, & G. Vallar (Eds.), *The cognitive and neural basis of spatial neglect* (p. 351-362). Oxford University Press, Oxford.

Dronkers, N. F., Wilkins, D. P., Van Valin, R. D., Redfern, B. B., & Jaeger, J. J. (2004). Lesion analysis of the brain areas involved in language comprehension. *Cognition*, *92*(1-2), 145-177. doi: 10.1016/j.cognition.2003.11.002

Duff, S. C., & Logie, R. H. (2001). Processing and storage in working memory span. *The Quarterly Journal of Experimental Psychology Section A*, *54*(1), 31-48. doi: 10.1080/02724980042000011

Duffau, H. (2012a). The frontal syndrome revisited: lessons from electrostimulation mapping studies. *Cortex*, *48*(1), 120-131.

Duffau, H. (2012b). The frontal syndrome revisited: Lessons from electrostimulation mapping studies. *Cortex*, *48*(1), 120 - 131. doi: 10.1016/j.cortex.2011.04.029

Dum, R. P., & Strick, P. L. (2003). An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. *Journal of Neurophysiology*, *89*(1), 634-639. doi: 10.1152/jn.00626.2002

Dumontheil, I., Thompson, R., & Duncan, J. (2011). Assembly and use of new task rules in fronto-parietal cortex. *Journal of Cognitive Neuroscience*, *23*, 168182.

Duncan, J. (1986). Disorganisation of behaviour after frontal lobe damage. *Cognitive Neuropsychology*, *3*(3), 271–290. doi: 10.1080/02643298608253360

Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. *Nature Reviews: Neuroscience*, *2*(11), 820-829. doi: 10.1038/35097575

Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends in Cognitive Sciences*, *14*(4), 172-179. doi: 10.1016/j.tics.2010.01.004

Duncan, J. (2013). The structure of cognition: Attentional episodes in mind and brain. *Neuron*, *80*(1), 35-50. doi: 10.1016/j.neuron.2013.09.015

Duncan, J., Burgess, P., & Emslie, H. (1995). Fluid intelligence after frontal lobe lesions. *Neuropsychologia*, *33*(3), 261-8. doi: 0028-3932(94)00124-3

Duncan, J., Emslie, H., & Williams, P. (1996). Intelligence and the Frontal Lobe : The Organization of Goal-Directed Behavior. *Cognitive Psychology*, *30*(3), 257-303. doi: 0010-0285/96

Duncan, J., & Miller, E. K. (2002). Cognitive focus through adaptive neural coding in the primate prefrontal cortex. In D. T. Stuss & R. T. Knight (Eds.), *Principles of*

frontal lobe function (p. 278-291). Oxford: Oxford University Press.

Duncan, J., Parr, A., Woolgar, A., Thompson, R., Bright, P., Cox, S., ... Nimmo-Smith, I. (2008). Goal Neglect and Spearman's g: Competing Parts of a Complex Task. *Journal of Experimental Psychology: General*, *137*(1), 131–148. doi: 10.1037/0096-3445.137.1.131

Duncan, J., Schramm, M., Thompson, R., & Dumontheil, I. (2012). Task rules, working memory, and fluid intelligence. *Psychonomic Bulletin & Review*, *19*(5), 864-870. doi: 10.3758/s13423-012-0225-y

Dunlosky, J., & Kane, M. J. (2007). The contributions of strategy use to working memory span: A comparison of strategy assessment methods. *Quarterly Journal of Experimental Psychology*, *60*(9), 1227-1245. doi: 10.1080/17470210600926075

Durstewitz, D., Vittoz, N. M., Floresco, S. B., & Seamans, J. K. (2010). Abrupt transitions between prefrontal neural ensemble states accompany behavioral transitions during rule learning. *Neuron*, *66*(3), 438 - 448. doi: https://doi.org/10.1016/j.neuron.2010.03.029

Engle, R. W. (2002). Working memory capacity as executive attention. *Current Directions in Psychological Science*, *11*(1), 19-23. doi: 10.1111/1467-8721.00160

Engle, R. W., & Kane, J., M. (2004). Executive attention, working memory capacity, and a two-facotr thereof cognitive control. In R. B (Ed.), *The psychology of learning and motivation* (Vol. 44, p. 145-199). NY: Elsevier.

Eslinger, P., & Grattan, L. (1993). Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. *Neuropsychologia*, *31*(1), 17-28. doi: 10.1016/0028-3932(93)90077-D

Esterman, M., Noonan, S. K., Rosenberg, M., & DeGutis, J. (2013). In the zone or zoning out? tracking behavioral and neural fluctuations during sustained attention. *Cerebral Cortex*, *23*(11), 2712-2723. doi: 10.1093/cercor/bhs261

Everling, S., Tinsley, C. J., Gaffan, D., & Duncan, J. (2002). Filtering of neural signals by focused attention in the monkey prefrontal cortex. *Nature Neuroscience*, *5*(7), 671-676. doi: 10.1038/nn874

Fallon, S. J., Mattiesing, R. M., Dolfen, N., Manohar, S. G., & Husain, M. (2018). Ignoring versus updating in working memory reveal differential roles of attention and feature binding. *Cortex*, *107*, 50 - 63. doi: 10.1016/j.cortex.2017.12.016

Fedorenko, E., Duncan, J., & Kanwisher, N. (2013). Broad domain generality in focal regions of frontal and parietal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(41), 16616-21. doi: 10.1073/pnas.1315235110

Fellows, L. K., & Farah, M. J. (2005). Different underlying impairments in decision-making following ventromedial and dorsolateral frontal lobe damage in humans. *Cerebral Cortex*, *15*(1), 58-63. doi: 10.1093/cercor/bhh108

Fernandez, E. S. (2014). Johnson: Johnson transformation [Computer software manual]. Retrieved from `https://cran.r-project.org/web/packages/Johnson/Johnson.pdf`

Field, A., Miles, J., & Field, Z. (2012). *Discovering statistics using r*. London: Sage.

Fiez, J. a., Petersen, S. e., Cheney, M. k., & Raichle, M. e. (1992). Impaired non-motor learning and error detection associated with cerebellar damage: a single case study. *Brain*, *115*(1), 155-178. doi: 10.1093/brain/115.1.155

Fisher, N. I. (1993). *Statistical analysis of circular data*. Cambridge UK: Cambridge University Press.

Foulon, C., Cerliani, L., Kinkingnhun, S., Levy, R., Rosso, C., Urbanski, M., ... Thiebaut de Schotten, M. (2018). Advanced lesion symptom mapping analyses and implementation as bcbtoolkit. *GigaScience*, *7*(3), 1-17. doi: 10.1093/gigascience/giy004

Fox, M. D., Corbetta, M., Snyder, A. Z., Vincent, J., & Raichle, M. (2006). Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. *Proceedings of the National Academy of Sciences of the United States of America*, *103*, 10046-10051.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences*, *102*(27), 9673-9678. doi: 10.1073/pnas.0504136102

Frank, M. J., Loughry, B., & OReilly, R. C. (2001). Interactions between the frontal cortex and basal ganglia in working memory: A computational model. *Cognitive, Affective, and Behavioral Neuroscience*, *1*, 137160.

Freedman, D., Riesenhuber, M., Poggio, T., & Miller, E. (2001). Categorical Representations of Visual Stimuli in the Primate Prefrontal Cortex. *Science*, *291*(5502), 312-316.

Friedman, N. P., & Miyake, A. (2017). Unity and diversity of executive functions: Individual differences as a window on cognitive structure. *Cortex*, *86*, 186-204. doi: 10.1016/j.cortex.2016.04.023

Friedman, N. P., Miyake, A., Young, S. E., DeFries, J. C., Corley, R. P., & Hewitt, J. K. (2008). Individual differences in executive functions are almost entirely genetic in origin. *Journal of Experimental Psychology*, *137*(2), 201-225. doi: 10.1037/

0096-3445.137.2.201

Friedrich, F. J., Egly, R., Rafal, R. D., & Beck, D. (1998). Spatial attention deficits in humans: A comparison of superior parietal and temporal-parietal junction lesions. *Neuropsychology*, *12*(2), 193-207. doi: 10.1037/0894-4105.12.2.193

Fuster, J. M. (2002). Physiology of executive function: The perception-action cycle. In D. T. Studd & R. T. Knight (Eds.), *Principles of frontal lobe function* (p. 96-109). Oxford, NY: Oxford University Press.

Fuster, J. M., Bodner, M., & Kroger, J. (2000). Cross-model and cros-temporal associations in neurons of the frontal cortex. *Nature*, *405*, 347-351.

Galantucci, S., Tartaglia, M. C., Wilson, S. M., Henry, M. L., Filippi, M., Agosta, F., ... Gorno-Tempini, M. L. (2011). White matter damage in primary progressive aphasias: a diffusion tensor tractography study. *Brain*, *134*(10), 3011-3029. doi: 10.1093/brain/awr099

Gallivan, J. P., & Culham, J. C. (2015). Neural coding within human brain areas involved in actions. *Current Opinion in Neurobiology*, *33*, 141 - 149. (Motor circuits and action) doi: 10.1016/j.conb.2015.03.012

Gavens, N., & Barrouillet, P. (2004). Delays of retention, processing efficiency, and attentional resources in working memory span development. *Journal of Memory and Language*, *51*.

Gazzaley, A. (2011). Influence of early attentional modulation on working memory. *Neuropsychologia*, *49*(6), 1410-1424. doi: 10.1016/j.neuropsychologia.2010.12.022

Gazzaley, A., Cooney, J. W., Rissman, J., & D′Esposito, M. (2005). Top-down suppression deficit underlies working memory impairment in normal aging. *Nature Neuroscience*, *8*(10), 1298-1300.

Gazzaley, A., & Nobra, A. C. (2012). Top-down modulation: bridging selective attention and working memory. *Trends of Cognitive Science*, *16*(2), 129-135.

Gefen, T., Peterson, M., Papastefan, S. T., Martersteck, A., Whitney, K., Rademaker, A., ... Geula, C. (2015). Morphometric and histologic substrates of cingulate integrity in elders with exceptional memory capacity. *Journal of Neuroscience*, *35*(4), 1781–1791. doi: 10.1523/JNEUROSCI.2998-14.2015

Giard, M. H., Fort, A., Mouchetant-Rostaling, Y., & Pernier, J. (2000). Neurophysiological mechanisms of auditory selective attention in humans. *Frontiers of Bioscience*, *5*, 84-94.

Gillebert, C. R., Humphreys, G. W., & Mantini, D. (2014). Automated delineation of stroke lesions using brain CT images. *NeuroImage: Clinical*, *4*, 540–548. doi: 10.1016/j.nicl.2014.03.009

Gillebert, C. R., Mantini, D., Thijs, V., Sunaert, S., Dupont, P., & Vandenberghe, R. (2011). Lesion evidence for the critical role of the intraparietal sulcus in spatial attention. *Brain*, *134*, 1694-709.

Giordano, B. L., McAdams, S., Zatorre, R. J., Kriegeskorte, N., & Belin, P. (2013). Abstract encoding of auditory objects in cortical activity patterns. *Cerebral Cortex*, *23*, 20252037.

Gitelman, D. R. (2003). Attention and its disordersimaging in clinical neuroscience. *British Medical Bulletin*, *65*(1), 21-34. doi: 10.1093/bmb/65.1.21

Gläscher, J., Adolphs, R., Damasio, H., Bechara, A., Rudrauf, D., Calamia, M., ... Tranel, D. (2012). Lesion mapping of cognitive control and value-based decision making in the prefrontal cortex. *Proceedings of the National Academy of Sciences*, *109*(36), 14681–14686. doi: 10.1073/pnas.1206608109

Godefroy, O. (2003). Frontal syndrome and disorders of executive functions. *Journal of Neurology*, *250*, 1-6.

Godefroy, O., Cabaret, M., Petit-Chenal, V., Pruvo, J.-P., & Rousseaux, M. (1999). Control functions of the frontal lobes. modularity of the central-supervisory system? *Cortex*, *35*(1), 1-20. doi: 10.1016/S0010-9452(08)70782-2

Godefroy, O., Rousseaux, M., Leys, D., Deste, A., Scheltens, P., & Pruvo, J. (1992). Frontal lobe dysfunction in unilateral lenticulostriate infarcts. prominent role of cortical lesions. *Archives of neurology*, *49*(12), 12851289. doi: 10.1001/archneur .1992.00530360087023

Godefroy, O., Rousseaux, M., Pruvo, J. P., Cabaret, M., & Leys, D. (1994). Neuropsychological changes related to unilateral lenticulostriate infarcts. *Journal of neurology, neurosurgery, and psychiatry*, *57*(4), 480-5.

Gorgoraptis, N., Catalao, R. F. G., Bays, P. M., & Husain, M. (2011). Dynamic updating of working memory resources for visual objects. *Journal of Neuroscience*, *31*(23), 8502–8511. doi: 10.1523/JNEUROSCI.0208-11.2011

Gottlieb, J., Kusunoki, M., & Goldberg, M. E. (1998). The representation of visual salience in monkey parietal cortex. *Nature*, *391*, 4814.

Gottwald, B., Mihajlovic, Z., Wilde, B., & Mehdorn, H. M. (2003). Does the cerebellum contribute to specific aspects of attention? *Neuropsychologia*, *41*, 14521460.

Gottwald, B., Wilde, B., Mihajlovic, Z., & Mehdorn, H. M. (2004). Evidence for distinct cognitive deficits after focal cerebellar lesions. *Journal of Neurology, Neurosurgery & Psychiatry*, *75*(11), 1524–1531. doi: 10.1136/jnnp.2003.018093

Graham, N. L., Emery, T., & Hodges, J. R. (2004). Distinctive cognitive profiles in alzheimer's disease and subcortical vascular dementia. *Journal of Neurology, Neu-*

rosurgery & Psychiatry, *75*(1), 61–71.

Halford, G. S., Cowan, N., & Andrews, G. (2007). Separating cognitive capacity from knowledge: a new hypothesis. *Trends in Cognitive Sciences*, *11*(6), 236 - 242. doi: https://doi.org/10.1016/j.tics.2007.04.001

Hallett, M., & Grafman, J. (1997). Executive function and motor skill learning. In R. J. Bradley, R. A. Harris, P. Jenner, & J. D. Schmahmann (Eds.), *The cerebellum and cognition* (Vol. 41, p. 297 - 323). Academic Press. doi: 10.1016/S0074-7742(08)60357-8

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: inhibition and attentional control. *NeuroImage*, *50*(3), 1313-1319. doi: 10.1016/j.neuroimage.2009.12.109

Hansen, J. C., & Hillyard, S. A. (1980). Endogeneous brain potentials associated with selective auditory attention. *Electroencephalography and Clinical Neurophysiology*, *49*(3), 277 - 290. doi: 10.1016/0013-4694(80)90222-9

Hartstra, E., Kühn, S., Verguts, T., & Brass, M. (2011). The implementation of verbal instructions: An fMRI study. *Human Brain Mapping*, *32*(11), 1811–1824. doi: 10.1002/hbm.21152

Hautzel, H., Mottaghy, F. M., Specht, K., Mller, H.-W., & Krause, B. J. (2009). Evidence of a modality-dependent role of the cerebellum in working memory? an fmri study comparing verbal and abstract n-back tasks. *NeuroImage*, *47*(4), 2073 - 2082. doi: 10.1016/j.neuroimage.2009.06.005

Hayes, S., Donnellan, C., & Stokes, E. (2013). Associations between executive function and physical function poststroke: a pilot study. *Physiotherapy*, *99*(2), 165 - 171. doi: https://doi.org/10.1016/j.physio.2012.05.002

Hayes, S., Donnellan, C., & Stokes, E. (2016). Executive dysfunction and balance function post-stroke: A cross-sectional study. *Physiotherapy*, *102*(1), 64 - 70. Retrieved from `http://www.sciencedirect.com/science/article/pii/S0031940615037529` doi: https://doi.org/10.1016/j.physio.2015.03.3719

Haynes, J. D., Sakai, K., Rees, G., Gilbert, S., Frith, C., & Passingham, R. E. (2007). Reading Hidden Intentions in the Human Brain. *Current Biology*, *17*(4), 323-328. doi: 10.1016/j.cub.2006.11.072

Hazy, T. E., Frank, M. J., & O'Reilly, R. C. (2007). Towards an executive without a homunculus: computational models of the prefrontal cortex/basal ganglia system. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *362*(1485), 1601-1613. doi: 10.1098/rstb.2007.2055

He, B. J., Snyder, A. Z., Vincent, J. L., Epstein, A., Shulman, G. L., & Corbetta, M.

(2007). Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. *Neuron*, *53*(6), 905918. doi: 10.1016/j.neuron .2007.02.013

Hertanu, J. S., Demoposalos, J. T., Yang, W. C., Calhoun, W. F., & Fenigstein, H. A. (1984). Stroke rehabilitation correlation and prognostic value of computerized tomography and sequential functional assessments. *Archives of Physical Medicine and Rehabilitation*, *65*, 505-508.

Heruti, R. J., Lusky, A., Dankner, R., Ring, H., Dolgopiat, M., Barell, V., ... Adunsky, A. (2002). Rehabilitation outcome of elderly patients after a first stroke : Effect of cognitive status at admission on the functional outcome. *Archives of Physical Medicine and Rehabilitation*, *83*, 742-749. doi: 10.1053/apmr.2002.32739

Heyder, K., Suchan, B., & Daum, I. (2004). Cortico-subcortical contributions to executive control. *Acta Psychologica*, *115*(2), 271 - 289. (Executive Control of Human Action) doi: https://doi.org/10.1016/j.actpsy.2003.12.010

Higo, T., Mars, R. B., Boorman, E. D., Buch, E. R., & Rushworth, M. F. (2011). Distributed and causal influence of frontal operculum in task control. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(10), 4230-5.

Hillis, A. E., Wityk, R. J., Barker, P. B., Beauchamp, N. J., Gailloud, P., Murphy, K., ... Metter, E. J. (2002). Subcortical aphasia and neglect in acute stroke: the role of cortical hypoperfusion. *Brain*, *125*, 1094-1104.

Hillstrom, A. P., Husain, M., Shapiro, K. L., & Rorden, C. (2004). Spatiotemporal dynamics of attention in visual neglect: A case study. *Cortex*, *40*(3), 433440. doi: 10.1016/S0010-9452(08)70137-0

Hillyard, S. A., Vogel, E. K., & Luck, S. J. (1998). Sensory gain control (amplification) as a mechanism of selective attention: Electrophysiological and neuroimaging evidence. *Philosophical Transactions of the Royal Society: Biological Sciences*, *353*, 12571270.

Hjaltason, H., Tegner, R., Tham, K., Levander, M., & Ericson, K. (1996). Sustained attention and awareness of disability in chronic neglect. *Neuropsychologia*, *34*, 122933.

Hornberger, M., Geng, J., & Hodges, J. R. (2011). Convergent grey and white matter evidence of orbitofrontal cortex changes related to disinhibition in behavioural variant frontotemporal dementia. *Brain*, *134*(9), 2502-2512. doi: 10.1093/brain/awr173

Houghton, G., Pritchard, R., & Grange, J. A. (2009). The role of cue-target translation in backward inhibition of attentional set. *Journal of Experimental Psychology:*

Learning, Memory, and Cognition, *35*(2), 466476.

Hubrich-Ungureanu, P., Kaemmerer, N., Henn, F. A., & Braus, D. F. (2002). Lateralized organization of the cerebellum in a silent verbal fluency task: a functional magnetic resonance imaging study in healthy volunteers. *Neuroscience Letters*, *319*(2), 91 - 94. doi: 10.1016/S0304-3940(01)02566-6

Humphreys, G. W. (2016). Feature confirmation in object perception: Feature integration theory 26 years on from the treisman bartlett lecture. *Quarterly Journal of Experimental Psychology*, *69*(10), 1910-1940. doi: 10.1080/17470218.2014.988736

Humphreys, G. W., Bickerton, W.-L., Samson, D., & Riddoch, J. M. (2012). *Birmingham Cognitive Screen (BCoS): A Screen for Individual Cognitive Profiling and Classification*. Hove, East Sussex.: Psychology Press.

Husain, M., & Kennard, C. (1996). Visual neglect associated with frontal lobe infarction. *Journal of Neurology*, *243*(3), 652 657. doi: 10.1007/BF00878662

Husain, M., & Kennard, C. (1997). Distractor-dependent frontal neglect. *Neuropsychologia*, *35*, 829841.

Husain, M., Mannan, S., Hodgson, T., Wojciulik, E., Driver, J., & C, K. (2001). Impaired spatial working memory across saccades contributes to abnormal search in parietal neglect. *Brain*, *124*, 941-952.

Husain, M., & Nachev, P. (2007). Space and the parietal cortex. *Trends in cognitive sciences*, *11*, 30-6. doi: 10.1016/j.tics.2006.10.011

Husain, M., & Rorden, C. (2003). Non-spatially lateralized mechanisms in hemispatial neglect. *Nature Reviews Neuroscience*, *4*, 26-36. doi: 10.1038/nrn1005

Hutchinson, A. D., Mathias, J. L., & Banich, M. T. (2008). Corpus callosum morphology in children and adolescents with attention deficit hyperactivity disorder: A meta-analytic review. *Neuropsychology*, *22*(3), 341-349. doi: 10.1037/0894-4105.22.3 .341

Hyndman, D., & Ashburn, A. (2003a). People with stroke living in the community: Attention deficits, balance, adl ability and falls. *Disabil Rehabil*, *25*, 81722.

Hyndman, D., & Ashburn, A. (2003b). People with stroke living in the community. Attention deficits, balance, ADL ability and falls. *Disability and Rehabilitation*, *25*(15), 817-822. doi: 10.1080/0963828031000122221

Hyndman, D., Pickering, R. M., & Ashburn, A. (2008). The influence of attention deficits on functional recovery post stroke during the first 12 months after discharge from hospital. *Journal of Neurology, Neurosurgery & Psychiatry*, *79*(6), 656–663. doi: 10.1136/jnnp.2007.125609

Ilg, W., Christensen, A., Mueller, O. M., Goericke, S. L., Giese, M. A., & Timmann,

D. (2013). Effects of cerebellar lesions on working memory interacting with motor tasks of different complexities. *Journal of Neurophysiology*, *110*(10), 2337-2349. doi: 10.1152/jn.00062.2013

Ilg, W., Giese, M. A., Gizewski, E. R., Schoch, B., & Timmann, D. (2008). The influence of focal cerebellar lesions on the control and adaptation of gait. *Brain*, *131*, 29132927.

Ito, M. (2008). Control of mental activities by internal models in the cerebellum. *Nature Reviews Neuroscience*, *9*, 304-313.

Iveson, M. H., Della Sala, S., Anderson, M., & MacPherson, S. E. (2017). Goal neglect, fluid intelligence and processing speed: Manipulating instruction load and inter-stimulus interval. *Acta Psychologica*, *176*, 1–10. doi: 10.1016/j.actpsy.2017.03.003

Jackson, J., Rich, A. N., Williams, M. A., & Woolgar, A. (2016). Feature-selective attention in frontoparietal cortex:multivoxel codes adjust to prioritize task-relevant information. *Journal of Cognitive Neuroscience*, *29*(2), 310-321.

Janssen, P., Srivastava, S., Ombelet, S., & Orban, G. A. (2008). Coding of shape and position in macaque lateral intraparietal area. *Journal of Neuroscience*, *28*(26), 6679–6690. doi: 10.1523/JNEUROSCI.0499-08.2008

Jarrold, C., Tam, H., Baddeley, A. D., & Harvey, C. E. (2011). How does processing affect storage in working memory tasks? evidence for both domain-general and domain-specific effects. *Journal of Experimental Psychology: Learning Memory and Cognition*, *37*(3), 688-705. doi: 10.1037/a0022527

Jehkonen, M., Ahonen, J.-P., Dastidar, P., Koivisto, A.-M., Laippala, P., Vilkki, J., & Molnr, G. (2000). Visual neglect as a predictor of functional outcome one year after stroke. *Acta Neurologica Scandinavica*, *101*(3), 195-201. doi: 10.1034/j.1600-0404.2000.101003195.x

Jongbloed, L. (1986). Prediction of function after stroke: a critical review. *Stroke*, *17*(4), 765-776. doi: 10.1161/01.STR.17.4.765

Kahneman, D. (1973). *Attention and effort*. Inglewood Cliffs, NJ: Prentice-Hall.

Kahnt, T., Grueschow, M., Speck, O., & Haynes, J. D. (2011). Perceptual learning and decision-making in human medial frontal cortex. *Neuron*, *70*, 549559.

Kaiser, H. F., & Rice, J. (1974). Little jiffy, mark iv. *Educational and Psychological Measurement*, *34*(1), 111-117. doi: 10.1177/001316447403400115

Kalaria, R. N., Akinyemi, R., & Ihara, M. (2016). Stroke injury, cognitive impairment and vascular dementia. *Biochimica et biophysica acta*, *1862*(5), 915-25.

Kane, M. J., & Engle, R. W. (2002). The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: An individual-

differences perspective. *Psychonomic Bulletin & Review*, *9*(4), 637–671. doi: 10.3758/BF03196323

Karlsson, M. P., Tervo, D. G. R., & Karpova, A. Y. (2012). Network resets in medial prefrontal cortex mark the onset of behavioral uncertainty. *Science*, *338*(6103), 135–139. doi: 10.1126/science.1226518

Karnath, H.-O. (2009). A right perisylvian neural network for human spatial orienting. In M. S. Gazzaniga (Ed.), *The cognitive neurosciences iv* (p. 259-268).

Karnath, H.-O., Fruhmann Berger, M., Kker, W., & Rorden, C. (2004). The anatomy of spatial neglect based on voxelwise statistical analysis: A study of 140 patients. *Cerebral Cortex*, *14*, 1164-72.

Karnath, H.-O., Himmelbach, M., & Rorden, C. (2002). The subcortical anatomy of human spatial neglect: putamen,caudate nucleus and pulvinar. *Brain*, *125*, 350360.

Karnath, H.-O., Rennig, J., Johannsen, L., & Rorden, C. (2011). The anatomy underlying acute versus chronic spatial neglect: a longitudinal study. *Brain*, *134*(3), 903-912. doi: 10.1093/brain/awq355

Karnath, H.-O., & Rorden, C. (2012). The anatomy of spatial neglect. *Neuropsychologia*, *50*(6), 1010-1017.

Karnath, H.-O., Zopf, R., Johannsen, L., Berger, M. F., Ngele, T., & Klose, U. (2005). Normalized perfusion mri to identify common areas of dysfunction: patients with basal ganglia neglect. *Brain*, *128*(10), 2462-2469. doi: 10.1093/brain/awh629

Kass, R. E., & Raftery, A. E. (1995). Bayes factors. *Journal of the American Statistical Association*, *90*, 773795. doi: 10.1080/01621459.1995.10476572

Kelly, R. M., & Strick, P. L. (2003). Cerebellar loops with motor cortex and prefrontal cortex of a nonhuman primate. *Journal of Neuroscience*, *23*(23), 8432–8444. doi: 10.1523/JNEUROSCI.23-23-08432.2003

Kennedy, K. M., & Raz, N. (2009). Aging White Matter and Cognition: Differential Effects of Regional Variations in Diffusion Properties on Memory, Executive Functions, and Speed. *Neuropsychologia*, *47*(3), 916927. doi: 10.1016/j.neuropsychologia.2009.01.001

Keren-Happuch, E., Chen, S.-H. A., Ho, M.-H. R., & Desmond, J. E. (2014). A meta-analysis of cerebellar contributions to higher cognition from pet and fmri studies. *Human Brain Mapping*, *35*(2), 593615. doi: 10.1002/hbm.22194

Kirschen, M. P., Chen, S. A., Schraedley-Desmond, P., & Desmond, J. E. (2005). Load- and practice-dependent increases in cerebro-cerebellar activation in verbal working memory: an fmri study. *NeuroImage*, *24*(2), 462 - 472. doi: 10.1016/j.neuroimage.2004.08.036

Klink, P. C., Jentgens, P., & Lorteije, J. A. M. (2014). Priority Maps Explain the Roles of Value, Attention, and Salience in Goal-Oriented Behavior. *Journal of Neuroscience*, *34*(42), 13867–13869. doi: 10.1523/JNEUROSCI.3249-14.2014

Kneebone, I. I., & Lincoln, N. B. (2012). Psychological problems after stroke and their management : State of knowledge. *Neuroscience and Medicine*, *3*, 83-89.

Knight, R. T., Hillyard, S. A., Woods, D. L., & Neville, H. J. (1980). The effects of frontal and temporal-parietal lesions on the auditory evoked potential in man. *Electroencephalography and Clinical Neurophysiology*, *50*(1), 112 - 124. doi: 10 .1016/0013-4694(80)90328-4

Knight, R. T., Hillyard, S. A., Woods, D. L., & Neville, H. J. (1981). The effects of frontal cortex lesions on event-related potentials during auditory selective attention. *Electroencephalography and Clinical Neurophysiology*, *52*, 571582.

Knoflach, M., Matosevic, B., Rücker, M., Furtner, M., Mair, A., Wille, G., ... Willeit, J. (2012). Functional recovery after ischemic stroke—a matter of age. *Neurology*, *78*(4), 279-285. doi: 10.1212/WNL.0b013e31824367ab

Koch, C., & Ullman, S. (1985). Shifts in selective visual attention: towards the underlying neural circuitry. *Hum Neurobiol*, *4*(4), 219-27.

Koenigs, M., Barbey, A., Postle, B., & Grafman, J. (2009). Superior parietal cortex is critical for the manipulation of information in working memory. *Journal of Neuroscience*, *29*(47), 14980–14986. doi: 10.1523/JNEUROSCI.3706-09.2009

Konow, A., & Pribram, K. H. (1970). Error recognition and utilization produced by injury to the frontal cortex in man. *Neuropsychologia*, *8*(4), 489–491. doi: 10.1016/ 0028-3932(70)90044-8

Kramer, J. H., Quitania, L., Dean, D., Neuhaus, J., Rosen, H. J., Halabi, C., ... Miller., B. L. (2007). Magnetic resonance imaging correlates of set shifting. *Journal of the International Neurology*, *13*(3). doi: 10.1017/S1355617707070567

Kramer, J. H., Reed, B. R., Mungas, D., Weiner, M. W., & Chui, H. C. (2002). Executive dysfunction in subcortical ischaemic vascular disease. *Journal of neurology, neurosurgery, and psychiatry*, *72*(2), 217-20.

Krause, M., Mahant, N., Kotschet, K., Fung, V. S., Vagg, D., Wong, C. H., & Morris, J. G. (2012). Dysexecutive behaviour following deep brain lesions a different type of disconnection syndrome? *Cortex*, *48*(1), 97 - 119. doi: 10.1016/j.cortex.2011.03 .014

Kronfeld-Duenias, V., Amir, O., Ezrati-Vinacour, R., Civier, O., & Ben-Shachar, M. (2014). The frontal aslant tract underlies speech fluency in persistent developmental stuttering. *Brain Structure and Function*, *221*(1), 365-381. doi: 10.1007/s00429

-014-0912-8

Kumral, E., Evyapan, D., & Balkir, K. (1999). Acute caudate vascular lesions. *Stroke*, *30*, 100108.

Kuznetsova, A., Bruun Brockhoff, P., & Haubo Bojesen Christensen, R. (2014). lmertest: Tests in linear mixed effects models [Computer software manual]. Retrieved from `http://CRAN.R-project.org/package=lmerTest` (R package version 2.0-20)

Kwakkel, G., Wagenaar, R. C., Kollen, B. J., & Lankhorst, G. J. (1996). Predicting disability in strokea critical review of the literature. *Age and Ageing*, *25*(6), 479-489. doi: 10.1093/ageing/25.6.479

Kwan, L. T., Reed, B. R., Eberling, J. L., & et al. (1999). Effects of subcortical cerebral infarction on cortical glucose metabolism and cognitive function. *Archives of Neurology*, *56*(7), 809-814. doi: 10.1001/archneur.56.7.809

Langerock, N., Vergauwe, E., & Barouillet, P. (2014). The maintenance of cross-domain associations in the episodic buffer. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *40*(4), 1096-1109.

Lemaire, B., Pageot, A., Plancher, G., & Portrat, S. (2018). What is the time course of working memory attentional refreshing? *Psychonomic Bulletin & Review*, *25*(1), 370-385. doi: 10.3758/s13423-017-1282-z

Lepsien, J., & Nobre, A. C. (2007). Attentional modulation of object representations in working memory. *Cerebral Cortex*, *17*(9), 2072-2083. doi: 10.1093/cercor/bhl116

Leskel, M., Hietanen, M., Kalska, H., Ylikoski, R., Pohjasvaara, T., Mntyl, R., & Erkinjuntti, T. (1999). Executive functions and speed of mental processing in elderly patients with frontal or nonfrontal ischemic stroke. *European Journal of Neurology*, *6*, 653-661. doi: 10.1046/j.1468-1331.1999.660653.x

Leśniak, M., Thomas, B., Seniów, J., Wojciech, C., & Członkowska, A. (2008). Frequency and prognostic value of cognitive disorders in stroke patients. *Dementia and Geriatric Cognitive Disorders*, *26*, 356-363. doi: 10.1159/000162262

Lewis-Peacock, J. A., Drysdale, A. T., Oberauer, K., & Postle, B. R. (2012). Neural evidence for a distinction between short-term memory and the focus of attention. *Journal of Cognitive Neuroscience*, *24*(1), 61-79. doi: 10.1162/jocn_a_00140

Leys, C., Ley, C., Klein, O., Bernard, P., & Licata, L. (2013). Detecting outliers: Do not use standard deviation around the mean, use absolute deviation around the median. *Journal of Experimental Social Psychology*, *49*(4), 764 - 766. doi: 10.1016/j.jesp.2013.03.013

Li, S., Ostwald, D., Giese, M., & Kourtzi, Z. (2007). Flexible coding for categorical decisions in the human brain. *The Journal of neuroscience : the official journal of*

the Society for Neuroscience, *27*(45), 12321–30. doi: 10.1523/JNEUROSCI.3795-07.2007

Liefooghe, B., Barrouillet, P., Vandierendonck, A., & Camos, V. (2008). Working memory costs of task switching. *Journal of Experimental Psychology: Learning, Memory and Cognition*, *34*, 478-494.

Linden, D. E., Oosterhof, N. N., Klein, C., & Downing, P. E. (2012). Mapping brain activation and information during category-specific visual working memory. *Journal of Neurophysiology*, *107*, 628639.

Liu-Ambrose, T., & Pang, J. J., M Y C and Eng. (2007). Executive function is independently associated with performances of balance and mobility in community-dwelling older adults after mild stroke: Implications for falls prevention. *Cerebrovascular Diseases*, *23*, 203210. doi: 10.1159/000097642

Loaiza, A., & McCabe, D. P. (2012). Temporalcontextual processing in working memory: Evidence from delayed cued recall and delayed free recall tests. *Memory & Cognition*, *40*(2), 191-203. doi: 10.3758/s13421-011-0148-2

Logan, G. D., & Gordon, R. D. (2001). Executive control of visual attention in dual-task situations. *Psychological Review*, *108*(2), 393-434. doi: 10.1037/0033-295X.108.2.393

Logie, R. H. (1986). Visual-spatial processing in working memory. *Quarterly Journal of Experimental Psychology*, *38*, 229-247.

Logie, R. H. (2016). Retiring the central executive. *Quarterly Journal of Experimental Psychology*, *69*(10), 2093-2109. doi: 10.1080/17470218.2015.1136657

Lovett, M. C., Reder, L. M., & Lebiere, C. (1999). Modeling working memory in a unified architecture: an act-r perspective. In M. A & S. P (Eds.), *Models of working memory: Mechanisms of active maintenance and executive control* (p. 135-182). Cambridge: Cambridge University Press.

Lovibond, S. H., & Lovibond, P. F. (1995). *Manual for depression, anxiety and stress scales* (2nd ed.). Psychology Foundation.

Low, E., Laycock, R., & Crewther, S. (2017). Neural markers associated with the temporal deployment of attention: A systematic review of non-motor psychophysical measures post-stroke. *Frontiers in Human Neuroscience*, *11*, 31. doi: 10.3389/fnhum.2017.00031

Luck, S. J., & Vogel, E. K. (1997). The capacity of visual working memory for features and conjunctions. *Nature*, *390*, 279-281.

Luria, A. (1966). *Higher cortical function man.* London: Tavistock Publications.

Ma, W. J., Husain, M., & Bays, P. M. (2014). The capacity of visual working memory

for features and conjunctions. *Nature Neuroscience*, *17*, 347-356.

MacPherson, S. E., Healy, C., Allerhand, M., Span, B., Tudor-Sfetea, C., White, M., ... Cipolotti, L. (2017). Cognitive reserve and cognitive performance of patients with focal frontal lesions. *Neuropsychologia*, *96*, 19 - 28. doi: https://doi.org/10.1016/j.neuropsychologia.2016.12.028

MacPherson, S. E., Phillips, L. H., Della Sala, S., & Cantagallo, A. (2009). Iowa gambling task impairment is not specific to ventromedial prefrontal lesions. *The Clinical Neuropsychologist*, *23*(3), 510-522. doi: 10.1080/13854040802396586

MacPherson, S. E., Sergio, D., Simon, R. C., Alessandra, G., & Matthew, H. I. (2015). *Handbook of frontal lobe assessment*. New York, NY: Oxford University Press.

MacPherson, S. E., Turner, M. S., Bozzali, M., Cipolotti, L., & Shallice, T. (2010). Frontal subregions mediating elevator counting task performance. *Neuropsychologia*, *48*(12), 3679 - 3682. doi: https://doi.org/10.1016/j.neuropsychologia.2010.07.033

Maechler, M., Rousseeuw, P., Croux, C., Todorov, V., Ruckstuhl, A., Salibian-Barrera, M., ... Anna di Palma, M. (2016). *Robustbase: Basic Robust Statistics R Package version 0.92-7.* Retrieved from `http://cran.r-project.org/package=robustbase`

Maguire, A. M., & Ogden, J. A. (2002). Mri brain scan analyses and neuropsychological profiles of nine patients with persisting unilateral neglect. *Neuropsychologia*, *40*(7), 879 - 887. doi: https://doi.org/10.1016/S0028-3932(01)00169-5

Mah, Y.-H., Husain, M., Rees, G., & Nachev, P. (2014). Human brain lesion-deficit inference remapped. *Brain*, *137*(9), 2522-2531. doi: 10.1093/brain/awu164

Mahoney, F. I., & Barthel, D. W. (1965). Functional evaluation: The barthel index. *Maryland State Medical Journal*, *14*, 61-65.

Majerus, S., Attout, L., D′Argembeau, A., Degueldre, C., Fias, W., Maquet, P., ... Balteau, E. (2012). Attention supports verbal short-term memory via competition between dorsal and ventral attention networks. *Cerebral Cortex*, *22*(5), 1086-1097. doi: 10.1093/cercor/bhr174

Mandonnet, E., Cerliani, L., Siuda-Krzywicka, K., Poisson, I., Zhi, N., Volle, E., & Thiebaut de Schotten, M. (2017). A network-level approach of cognitive flexibility impairment after surgery of a right temporo-parietal glioma. *Neurochirurgie*, *63*(4), 308-313. doi: 10.1016/j.neuchi.2017.03.003

Manohar, S. G., Pertzov, Y., & Husain, M. (2017). Short-term memory for spatial, sequential and duration information. *Current Opinion in Behavioral Sciences*, *17*, 20-26. (Memory in time and space) doi: 10.1016/j.cobeha.2017.05.023

Manto, M., & Mariën, P. (2015). Schmahmann's syndrome - identification of the third cornerstone of clinical ataxiology. *Cerebellum & Ataxias*, *2*(1), 2. doi: 10.1186/s40673-015-0023-1

Marek, S., Siegel, J. S., Gordon, E. M., Raut, R. V., Gratton, C., Newbold, D. J., ... Dosenbach, N. U. F. (2018). Spatial and temporal organization of the individual human cerebellum. *Neuron*, *100*(4), 977-993.

Marvel, C. L., & Desmond, J. E. (2010). The contributions of cerebro-cerebellar circuitry to executive verbal working memory. *Cortex*, *46*(7), 880895. doi: 10.1016/j.cortex.2009.08.017

Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: The default network and stimulus-independent thought. *Science*, *315*(5810), 393–395. doi: 10.1126/science.1131295

McDonald, R. P. (1999). *Test theory: A unified treatment.* Mahwah, NJ: Lawrence Erlbaum Associates.

Meiran, N. (1996). Reconfiguration of processing mode prior to task performance. *Journal of Experimental Psychology: Learning, Memory and Cognition*(22), 1-20.

Meiran, N., & Marciano, H. (2002). Limitations in advance task preparation: switching the relevant stimulus dimension in speeded same-different comparisons. *Mem Cognit*, *30*(4), 540-50.

Mendez, M., Adams, N., & Lewandowski, K. (1989). Neurobehavioral changes associated with caudate lesions. *Neurology*, *39*(3), 349354. doi: 10.1212/wnl.39.3.349

Menon, V., Adleman, N. E., White, C. D., Glover, G. H., & Reiss, a. L. (2001). Error-Related Brain Activation during a Go / NoGo Response Inhibition Task. *Human Brain Mapping*, *12*(April 2000), 131–143. doi: 10.1002/1097-0193(200103)12:3⟨131::AID-HBM1010⟩3.0.CO

Mian, M. K., Sheth, S. A., Patel, S. R., Spiliopoulos, K., Eskandar, E. N., & Williams, Z. M. (2012). Encoding of rules by neurons in the human dorsolateral prefrontal cortex. *Cerebral cortex*, *24*(3), 807-16.

Middleton, F. A., & Strick, P. L. (1994). Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science*, *266*(5184), 458-461. doi: 10.1126/science.7939688

Middleton, F. A., & Strick, P. L. (2000). Basal ganglia and cerebellar loops: motor and cognitive circuits. *Brain Research Reviews*, *31*(2), 236 - 250. doi: 10.1016/S0165-0173(99)00040-5

Middleton, F. A., & Strick, P. L. (2001). Cerebellar projections to the prefrontal cortex of the primate. *Journal of Neuroscience*, *21*(2), 700-712. doi: 10.1523/JNEUROSCI

.21-02-00700.2001

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, *24*, 167–202.

Miller, G. A. (1956). The magical number seven, plus or minus two: some limits on our capacity for processing information. *Psychological Review*, *63*(2), 81-97. doi: 10.1037/h0043158

Milner, B. A. (1963). Effects of different brain lesions on card sorting: The role of the frontal lobes. *Archives of Neurology*, *9*(1), 90-100. doi: 10.1001/archneur.1963.00460070100010

Milner, B. A., Broadbent, D. E., & Weiskrantz, L. (1982). Some cognitive effects of frontal-lobe lesions in man. *Philosophical Transactions of the Royal Society of London*, *298*(1089), 211-226. doi: 10.1098/rstb.1982.0083

Mink, J. W. (1996). The basal ganglia: focused selection and inhibition of competing motor programs. *Progress in Neurobiology*, *50*, 381425. doi: 10.1016/S0301-0082(96)00042-1

Mirza, S. S., Portegies, M. L. P., Wolters, F. J., Hofman, P. J., Aand Koudstaal, Tiemeier, H., & Ikram, M. A. (2016). Higher education is associated with a lower risk of dementia after a stroke or tia. the rotterdam study. *Neuroepidemiology*, *46*, 120-127. doi: 10.1159/000443649

Miyake, A., & Friedman, N. P. (2012). The nature and organization of individual differences in executive functions: Four general conclusions. *Current Directions in Psychological Science*, *21*(1), 8-14. doi: 10.1177/0963721411429458

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex frontal lobe tasks: A latent variable analysis. *Cognitive Psychology*, *41*(1), 49 - 100. doi: 10.1006/cogp.1999.0734

Mole, J. A., & Demeyere, N. (2018). The relationship between early post-stroke cognition and longer term activities and participation: A systematic review. *Neuropsychological Rehabilitation*, *0*(0), 1-25. doi: 10.1080/09602011.2018.1464934

Molenberghs, P., Gillebert, C. R., Schoofs, H., Dupont, P., Peeters, R., & Vandenberghe, R. (2009). Lesion neuroanatomy of the Sustained Attention to Response task. *Neuropsychologia*, *47*(13), 2866–2875. doi: 10.1016/j.neuropsychologia.2009.06.012

Monsell, S. (2003). Task switching. *Trends in Cognitive Sciences*, *7*(3), 134 - 140. doi: 10.1016/S1364-6613(03)00028-7

Morey, R. D., & Rouder, J. N. (2015). Bayesfactor: Computation of bayes factors for common designs [Computer software manual]. Retrieved from `http://CRAN.R`

-project.org/package=BayesFactor (R package version 0.9.11-1)

Mort, D. J., Malhotra, P., Mannan, S. K., Rorden, C., Pambakian, A., Kennard, C., & Husain, M. (2003). The anatomy of visual neglect. *Brain*, *126*, 1986 1997.

Mrazek, M. D., Phillips, D. T., Franklin, M. S., Broadway, J. M., & Schooler, J. W. (2013). Young and restless: validation of the mind wandering questionnaire(mwq) reveals disruptive impact of mind-wandering for youth. *Frontiers in Psychology*, *4*, 560. doi: 10.3389/fpsyg.2013.00560

Müller, V. I., Langner, R., Cieslik, E. C., Rottschy, C., & Eickhoff, S. B. (2015). Interindividual differences in cognitive flexibility: influence of gray matter volume, functional connectivity and trait impulsivity. *Brain Structure and Function*, *220*(4), 2401–2414. doi: 10.1007/s00429-014-0797-6

Munakata, Y., Morton, J. B., & Yerys, B. E. (2003). Children's perseveration: Attentional inertia and alternative accounts. *Developmental Science*, *6*(5), 471-473. doi: 10.1111/1467-7687.00302

Mungas, D., Harvey, D., Reed, B., Jagust, W., DeCarli, C., Beckett, L., ... Chui, H. (2005, 09). Longitudinal volumetric mri change and rate of cognitive decline. *Neurology*, *65*, 565-71. doi: 10.1212/01.wnl.0000172913.88973.0d

Mungas, D., Jagust, W. J., Reed, B. R., Kramer, J. H., Weiner, M. W., Schuff, N., ... Chui, H. C. (2001). Mri predictors of cognition in subcortical ischemic vascular disease and alzheimer's disease. *Neurology*, *57*(12), 2229–2235. doi: 10.1212/WNL.57.12.2229

Mushiake, H., Inase, M., & Tanji, J. (1990). Selective coding of motor sequence in the supplementary motor area of the monkey cerebral cortex. *Experimental Brain Research*, *82*(1), 208–210. doi: 10.1007/BF00230853

Mysiw, J. W., Beegan, J. G., & Gatens, P. F. (1989). Prospective cognitive assessment of stroke patients before inpatient rehabilitation. The relationship of the neurobehavioural cognitive status examination to functional improvement. *American Journal of Physical Medicine and Rehabilitation*, *68*(4), 168–171.

Nachev, P., Kennard, C., & Husain, M. (2008). Functional role of the supplementary and pre-supplementary motor areas. *Nature Reviews Neuroscience*, *9*(11), 856-869. doi: 10.1038/nrn2478

Neau, J.-P., Anllo, E. A., Bonnaud, V., Ingrand, P., & Gil, R. (2000). Neuropsychological disturbances in cerebellar infarcts. *Acta Neurologica Scandinavica*, *102*(6), 363-370. doi: 10.1034/j.1600-0404.2000.102006363.x

Nee, D. E., & Brown, J. W. (2012). Rostral-caudal gradients of abstraction revealed by multi-variate pattern analysis of working memory. *Neuroimage*, *63*, 12851294.

Nee, D. E., & Brown, J. W. (2013). Dissociable frontalstriatal and frontalparietal networks involved in updating hierarchical contexts in working memory. *Cerebral Cortex*, *23*(9), 2146-2158. doi: 10.1093/cercor/bhs194

Niendam, T., Laird, A., Ray, K., Dean, Y., Glahn, D., & Carter, C. (2012). Metaanalytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive, Affective, & Behavioral Neuroscience*, *12*, 241268.

Norman, D. (1981). Categorization of action slips. *Psychological Review*, *88*(1), 1-15. doi: 10.1037/0033-295X.88.1.1

Norman, D., & Shallice, T. (1986). Attention to action. Willed and Automatic Control of Behavior. In R. J. Davidson, G. E. Schwartz, & D. Shapiro (Eds.), *Consciousness and self-regulation.* Boston: Springer. doi: 10.1007/978-1-4757-0629-1_1

Nouri, F. M., & Lincoln, N. B. (1987). An extended activities of daily living scale for stroke patients. *Clinical Rehabilitation*, *1*, 301-305.

Novak, S., Johnson, J., & Greenwood, R. (1996). Barthel revisited: making guidelines work. *Clinical Rehabilitation*, *10*, 128–134.

Nuijten, M. B., Wetzels, R., Matzke, D., Dolan, C. V., & Wagenmakers, E.-J. (2015). A default bayesian hypothesis test for mediation. *Behavior Research Methods*, *47*(1), 85-97. doi: 10.3758/s13428-014-0470-2

Nyberg, L., Lvdn, M., Riklund, K., Lindenberger, U., & Bckman, L. (2012). Memory aging and brain maintenance. *Trends in Cognitive Sciences*, *16*(5), 292 - 305. doi: https://doi.org/10.1016/j.tics.2012.04.005

Nys, G. M. S., van Zandvoort, M. J. E., de Kort, P. L. M., Jansen, B. P. W., de Haan, E. H. F., & Kappelle, L. J. (2007). Cognitive Disorders in Acute Stroke. *Neurology*, *185*, 408–416. doi: 10.1159/000101464

Nys, G. M. S., van Zandvoort, M. J. E., de Kort, P. L. M., van der Worp, H. B., Jansen, B. P. W., Algra, A., ... Kappelle, L. J. (2005). The prognostic value of domain-specific cognitive abilities in acute first-ever stroke. *Neurology*, *64*, 821–827.

Oberauer, K. (2002). Access to information in working memory: Exploring the focus of attention. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *28*(3), 411-421. doi: 10.1037/0278-7393.28.3.411

Oberauer, K. (2009). Chapter 2 design for a working memory. In *The psychology of learning and motivation* (Vol. 51, p. 45 - 100). Academic Press. doi: 10.1016/S0079-7421(09)51002-X

Oberauer, K. (2010). Declarative and procedural working memory: Common principles, common capacity limits? *Psychologica Belgica*, *50*(3-4), 277308. doi: 10.5334/pb-50-3-4-277

Oberauer, K., & Lewvandowsky, S. (2013). Evidence against decay in verbal working memory. *Journal of Experimental Psychology*, *142*(1), 380-411.

Oberauer, K., Süß, H.-M., Wilhelm, O., & Wittmann, W. W. (2008). Which working memory functions predict intelligence? *Intelligence*, *36*(6), 641 - 652. doi: https://doi.org/10.1016/j.intell.2008.01.007

OReilly, R. C., & Frank, M. J. (2006). Making working memory work: A computational model of learning in the prefrontal cortex and basal ganglia. *Neural Computation*, *18*, 283-328.

Oros, R. I., Popescu, C. A., Iova, C. A., Mihancea, P., & Iova, S. O. (2016). The impact of cognitive impairment after stroke on activities of daily living. *International Journal of the Bioflux Society*, *8*(1), 2014–2017.

Osborne, J. W. (2014). *Best practices in exploratory factor analysis*. Charleston: CreateSpace Independent Publishing Platform.

Ouerchefani, R., Ouerchefani, N., Allain, P., Rejeb, M. R. B., & Gall, D. L. (2017). Contribution of different regions of the prefrontal cortex and lesion laterality to deficit of decision-making on the iowa gambling task. *Brain and Cognition*, *111*, 73 - 85. doi: https://doi.org/10.1016/j.bandc.2016.06.010

Owen, A. M., Downes, J. J., Sahakian, B. J., Polkey, C. E., & Robbins, T. W. (1990). Planning and spatial working memory following frontal lobe lesions in man. *Neuropsychologia*, *28*(10), 1021 - 1034. doi: 10.1016/0028-3932(90)90137-D

Özdemir, F., Birtane, M., Tabatabaei, R., Ekuklu, G., & Kokino, S. (2001). Cognitive Evaluation and Functional Outcome After Stroke. *American Journal of Physical Medicine and Rehabilitation*, *80*(6), 410–415. doi: 0894-9115/01/8006-0410/0

Páhlman, U., Gutiérrez-prez, C., Svborg, M., Knopp, E., & Tarkowski, E. (2011). Cognitive function and improvement of balance after stroke in elderly people: the gothenburg cognitive stroke study in the elderly. *Disability and Rehabilitation*, *33*(21-22), 1952-1962. doi: 10.3109/09638288.2011.553703

Páhlman, U., Marianne, S., & Elisabeth, T. (2012). Cognitive dysfunction and physical activity after stroke: The gothenburg cognitive stroke study in the elderly. *Journal of Stroke and Cerebrovascular Diseases*, *21*(8), 652 - 658. doi: 10.1016/j.jstrokecerebrovasdis.2011.02.012

Paker, N., Bugdayc, D., Tekdos, D., & Dere, C. (2010). Impact of cognitive impairment on functional outcome in stroke. *Stroke Research and Treatment*, 1-5. doi: 10.4061/2010/652612

Paolucci, S., Antonucci, G., Grasso, M. G., & Pizzamiglio, L. (2001). The role of unilateral spatial neglect in rehabilitation of right braindamaged ischemic stroke

patients: A matched comparison. *Archives of Physical Medicine and Rehabilitation*, *82*(6), 743 - 749. doi: https://doi.org/10.1053/apmr.2001.23191

Park, Y. H., Jang, J.-W., Park, S. Y., Wang, M. J., Lim, J.-S., Baek, M. J., ... Kim, S. (2015). Executive function as a strong predictor of recovery from disability in patients with acute stroke: A preliminary study. *Journal of Stroke and Cerebrovascular Diseases*, *24*(3), 554 - 561. doi: 10.1016/j.jstrokecerebrovasdis.2014.09.033

Pashler, H. (1984). Processing stages in overlapping tasks: Evidence for a central bottleneck. *Journal of Experimental Psychology: Human Perception and Performance*, *10*(3), 358-377. doi: 10.1037/0096-1523.10.3.358

Pashler, H., & Baylis, G. C. (1991). Procedural learning: 2. intertrial repetition effects in speeded-choice tasks. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *17*, 33-48.

Pashler, H. E. (1998). *The psychology of attention.* Cambridge, MA: MIT Press.

Patchick, E., Vail, A., Wood, A., & Bowen, A. (2015, 12). Precis (patient reported evaluation of cognitive state): Psychometric evaluation of a new patient reported outcome measure of the impact of stroke. *Clinical Rehabilitation*, *30*. doi: 10.1177/0269215515624480

Patel, M. D., Coshall, C., Rudd, A. G., & Wolfe, C. D. A. (2002). Cognitive Impairment after Stroke : Clinical Determinants and Its Associations with Long-Term Stroke Outcomes. *Journal of American Geriatric Society*, *50*, 700-706. doi: 0002-8614/02

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the barratt impulsiveness scale. *Journal of Clinical Psychology*, *6*, 768774.

Paulesu, E., Frith, C. D., & Frackowiak, R. S. J. (1993). The neural correlates of the verbal component of working memory. *Nature*, *362*, 342-345.

Peers, P. V., Ludwig, C. J., Rorden, C., Cusack, R., Bonfiglioli, C., Bundesen, C., ... Duncan, J. (2005). Attentional functions of parietal and frontal cortex. *Cerebral Cortex*, *15*(10), 1469-1484. doi: 10.1093/cercor/bhi029

Perani, D., Vallar, G., Cappa, S., Messa, C., & Fazio, F. (1987). Aphasia and neglect after subcortical stroke: a clinical/ cerebral perfusion correlation study). *Brain*, *110*, 121129.

Pertzov, Y., Bays, P. M., Joseph, S., & Husain, M. (2013). Rapid forgetting prevented by retrospective attention cues. *Journal of Experimental Psychology: Human Perception and Performance*, *39*(5), 1224-31.

Petersen, S. E., & Posner, M. T. (2012). The attention system of the human brain: 20 years after. *Annual Review of Neuroscience*, *35*, 7389. doi: 10.1146/annurev-neuro-062111-150525

Picton, T. W., Stuss, D. T., Alexander, P., Michael, Shallice, T., Binns, M. A., & Gillingham, S. (2007). Effects of focal frontal lesions on response inhibition. *Cerebral Cortex*, *17*(4), 826-838. doi: 10.1093/cercor/bhk031

Plancher, G., & Barrouillet, P. (2013). Forgetting from working memory: does novelty encoding matter? *Journal of Experimental Psychology: Learning, Memory and Cognition*, *39*, 110-125.

Pohjasvaara, T., Leskel, M., Vataja, R., Kalska, H., Ylikoski, R., Hietanen, M., ... Erkinjuntti, T. (2002). Post-stroke depression, executive dysfunction and functional outcome. *European Journal of Neurology*, *9*(3), 269-275. doi: 10.1046/j.1468-1331 .2002.00396.x

Power, J. D., & Petersen, S. E. (2013). Control-related systems in the human brain. *Current Opinion in Neurobiology*, *23*, 223228.

Price, C. J., Hope, T. M., & Seghier, M. L. (2017). Ten problems and solutions when predicting individual outcome from lesion site after stroke. *NeuroImage*, *145*, 200-208. doi: 10.1016/j.neuroimage.2016.08.006

Ptak, R. (2012). The frontoparietal attention network of the human brain: Action, saliency, and a priority map of the environment. *The Neuroscientist*, *18*(5), 502-515. doi: 10.1177/1073858411409051

Ptak, R., Schnider, A., & Fellrath, J. (2017). The dorsal frontoparietal network: A core system for emulated action. *Trends in Cognitive Sciences*, *21*(8), 589 - 599. doi: 10.1016/j.tics.2017.05.002

Quinn, J. G., & McConnell, J. (1996). Irrelevant pictures in visual working memory. *Quarterly Journal of Experimental Psychology*, *49*, 200-215.

Quinn, T. J., Langhorne, P., & Stott, D. J. (2011). Barthel index for stroke trials development , properties , and application. *Stroke*, *42*, 1146-1151. doi: 10.1161/ STROKEAHA.110.598540

Quintana, J., & Fuster, J. M. (1999). From perception to action: temporal integration functions of prefrontal and parietal neurons. *Cerebral Cortex*, *9*, 213-221.

R Core Team. (2014a). *R: A language and enviroment for statistical computing.* Vienna, Austria: R Foundation for Statistical Computing. Retrieved from `http://www.r-project.org/`.

R Core Team. (2014b). R: A language and environment for statistical computing [Computer software manual]. Vienna, Austria. Retrieved from `http://www.R-project.org/` (ISBN 3-900051-07-0)

Rabinovici, G. D., Stephens, M. L., & Possin, K. L. (2015). Executive dysfunction. continuum: Lifelong learning in neurology. *Behavioral Neurology and Neuropsychiatry*,

21(3), 646659. doi: 10.1212/01.CON.0000466658.05156.54

Rademaker, R. L., Bloem, I. M., De Weerd, P., & Sack, A. T. (2015). The impact of interference on short-term memory for visual orientation. *Journal of Experimental Psychology: Human Perception and Performance*, *41*(6), 1650-1665.

Rainer, G., & Miller, E. K. (2000). Effects of visual experience on the representation of objects in the prefrontal cortex. *neuron*, *27*, 179-189.

Raju, R. S., Sarma, P. S., & Pandian, J. D. (2010). Psychosocial problems, quality of life, and functional independence among indian stroke survivors. *Stroke*, *41*, 2932–2937. doi: 10.1161/STROKEAHA.110.596817

Rao, S. C., Rainer, G., & Miller, E. K. (1997). Integration of what and where in the primate prefrontal cortex. *Science*, *276*(5313), 821–824. doi: 10.1126/science.276.5313.821

Rao, S. M., Leo, G. J., Haughton, V. M., St. Aubin-Faubert, P., & Bernardin, L. (1989). Correlation of magnetic resonance imaging with neuropsychological testing in multiple sclerosis. *Neurology*, *39*(April 1988), 161-166.

Ratcliff, R. (1993). Methods for dealing with reaction time outliers. *Psychological Bulletin*, *114*(3), 510-532. doi: 10.1037/0033-2909.114.3.510

Ravizza, S. M., & Carter, C. S. (2008). Shifting set about task switching: behavioral and neural evidence for distinct forms of cognitive flexibility. *Neuropsychologia*, *46*(12), 2924-2935.

Ravizza, S. M., & Ciranni, M. A. (2002). Set shifting impairments as a function of working memory demands in older adults, prefrontal, and parkinson's disease patients. *Journal of Cognitive Neuroscience*, *14*(3), 472-483.

Ravizza, S. M., & Hazeltine, E. (2013). The benefits of stimulus-driven attention for working memory encoding. *Journal of Memory and Language*, *69*(3), 384 - 396. doi: https://doi.org/10.1016/j.jml.2013.05.007

Ravizza, S. M., McCormick, C. A., Schlerf, J. E., Justus, T., Ivry, R. B., & Fiez, J. A. (2006). Cerebellar damage produces selective deficits in verbal working memory. *Brain*, *129*(2), 306-320. doi: 10.1093/brain/awh685

Raye, C. L., Johnson, M. K., Mitchell, K. J., Greene, E. J., & Johnson, M. R. (2007). Refreshing: a minimal executive function. *Cortex*, *43*, 135-145.

Reason, J. (1990). *Human error*. Cambridge University Press. doi: 10.1017/CBO9781139062367

Reed, B. R., Mungas, D. M., Kramer, J. H., Ellis, W., Vinters, H. V., Zarow, C., ... Chui, H. C. (2007). Profiles of neuropsychological impairment in autopsy-defined alzheimer's disease and cerebrovascular disease. *Brain*, *130*(3), 731-739. doi: 10

.1093/brain/awl385

Reise, S. P., Moore, T. M., & Haviland, M. G. (2010). Bifactor models and rotations: exploring the extent to which multidimensional data yield univocal scale scores. *Journal of Personality Assessment*, *92*(6), 544559. doi: 10.1080/00223891.2010.496477

Rengachary, J., He, B. J., Shulman, G. L., & Corbetta, M. (2011). A behavioral analysis of spatial neglect and its recovery after stroke. *Frontiers in human neuroscience*, *5*. doi: 10.3389/fnhum.2011.00029

Repov, G., & Baddeley, A. D. (2006). The muti-model of working memory: explorations in experimental cognitive psychology. *Neuroscience*, *139*, 5-21.

Revelle, W. (2015). psych: Procedures for psychological, psychometric, and personality research [Computer software manual]. Evanston, Illinois. Retrieved from `http://CRAN.R-project.org/package=psych` (R package version 1.5.1)

Reverberi, C., Gorgen, K., & Haynes, J. D. (2012). Compositionality of rule representations in human prefrontal cortex. *Cerebral Cortex*, *22*, 12371246.

Reynolds, J. H., Chelazzi, L., & Desimone, R. (1999). Competitive mechanisms subserve attention in macaque areas v2 and v4. *Journal of Neuroscience*, *19*(5), 1736–1753. doi: 10.1523/JNEUROSCI.19-05-01736.1999

Reynolds, J. R., & OReilly, R. C. (2009). Developing pfc representations using reinforcement learning. *Cognition*, *113*(3), 281 - 292. (Reinforcement learning and higher cognition) doi: 10.1016/j.cognition.2009.05.015

Richter, S., Gerwig, M., Aslan, B., Wilhelm, H., Schoch, B., Dimitrova, A., ... Timmann, D. (2007). Cognitive functions in patients with mr-defined chronic focal cerebellar lesions. *Journal of Neurology*, *254*, 11931203.

Rieger, M., Gauggel, S., & Burmeister, K. (2003, 05). Inhibition of ongoing responses following frontal, nonfrontal, and basal ganglia lesions. *Neuropsychology*, *17*, 272-82. doi: 10.1037/0894-4105.17.2.272

Rilling, J. K., Glasser, M. F., Preuss, T. M., Ma, X., Zhao, T., Hu, X., & Behrens, T. E. J. (2008). The evolution of the arcuate fasciculus revealed with comparative DTI. *Nature Neuroscience*, *11*(4), 426-428. doi: 10.1038/nn2072

Ringman, J. M., Saver, J. L., Woolson, R. F., Clarke, W. R., & Adams, H. P. (2004). Frequency, risk factors, anatomy, and course of unilateral neglect in an acute stroke cohort. *Neurology*, *63*(3), 468–474. doi: 10.1212/01.WNL.0000133011.10689.CE

Rinne, P., Hassan, M., Goniotakis, D., Chohan, K., Sharma, P., Langdon, D., ... Bentley, P. (2013). Triple dissociation of attention networks in stroke according to lesion location. *Neurology*, *81*(9), 812-820. doi: 10.1212/WNL.0b013e3182a2ca34

Rishel, C. A., Huang, G., & Freedman, D. J. (2013). Independent category and spatial encoding in parietal cortex. *Neuron*, *77*(5), 969-979. doi: 10.1016/j.neuron.2013.01.007

Roberts, G., & Anderson, M. (2014). Task structure complexity and goal neglect in typically developing children. *Journal of Experimental Child Psychology*, *120*, 5972.

Robertson, I. H., Manly, T., Beschin, N., Daini, R., Haeske-Dewick, H., Hmberg, V., ... Weber, E. (1998). Auditory sustained attention is a marker of unilateral neglect. *Neuropsychologia*, *35*, 1527-32.

Robertson, I. H., Nimmo-Smith, I., Ward, T., & Ridgeway, V. (1994). *Test of everyday attention (tea).* Thames Valley Test Company.

Robertson, I. H., Ridgeway, V., Greenfield, E., & Parr, A. (1997). Motor recovery after stroke depends on intact sustained attention : A 2-year follow-up study. *Neuropsychology*, *11*(2), 290–295.

Robinson, H., Calamia, M., Gläscher, J., Bruss, J., & Tranel, D. (2014). Neuroanatomical correlates of executive functions: A neuropsychological approach using the examiner battery. *Journal of the International Neuropsychological Society: JINS*, *20*(1), 5263. doi: 10.1017/S135561771300060X

Roca, M., Garca, M., Ardila, M. J. T., Gadea, M. L. G., Torralva, T., Ferrari, J., ... Duncan, J. (2018). Rule reactivation and capture errors in goal directed behaviour. *Cortex*, *107*, 180 - 187. doi: 10.1016/j.cortex.2017.08.027

Rogers, R., & Monsell, S. (1995). Costs of a predictable switch between simple cognitive tasks. *Journal of Experimental Psychology: General*, *124*(2), 207-231. doi: 10.1037/0096-3445.124.2.207

Rorden, C., Bonilha, L., Fridriksson, J., Bender, B., & Karnath, H.-O. (2012). Age-specific ct and mri templates for spatial normalization. *NeuroImage*, *61*(4), 957 - 965. doi: 10.1016/j.neuroimage.2012.03.020

Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesion. *Behavioural Neurology*, *12*, 191-200.

Rorden, C., & Karnath, H.-O. (2004). Using human brain lesions to infer function: A relic from a past era in the fmri age? *Nature Reviews Neuroscience*, *5*, 813-9.

Rouder, J. N., Morey, R. D., Speckman, P. L., & Province, J. M. (2012). Default bayes factors for anova designs. *Journal of Mathematical Psychology*, *56*(5), 356 - 374. doi: 10.1016/j.jmp.2012.08.001

Roy, J. E., Riesenhuber, M., Poggio, T., & Miller, E. K. (2010). Prefrontal cortex activity during flexible categorization. *Journal of Neuroscience*, *30*(25), 8519–8528. doi: 10.1523/JNEUROSCI.4837-09.2010

Rueckert, L., & Grafman, J. (1996). Sustained attention deficits in pat ients with right frontal lesions. *Neuropsychologia*, *34*(10), 953 - 963. doi: h10.1016/0028-3932(96)00016-4

Rutman, A. M., Clapp, W. C., Chadick, J. Z., & Gazzaley, A. (2010). Early top-down control of visual processing predicts working memory performance. *Journal of Cognitive Neuroscience*, *22*(6), 1224-34.

Sacerdoti, E. D. (1974). Planning in a hierarchy of abstraction spaces. *Artificial Intelligence*, *5*(2), 115 - 135. doi: https://doi.org/10.1016/0004-3702(74)90026-5

Saita, K., Ogata, T., Watanabe, J., Tsuboi, Y., Takahara, M., Inoue, T., & Morishita, T. (2017). Contralateral cerebral hypometabolism after cerebellar stroke: A functional near-infrared spectroscopy study. *Journal of Stroke and Cerebrovascular Diseases*, *26*(4), 69 - 71. doi: 10.1016/j.jstrokecerebrovasdis.2017.01.014

Saka, O., McGuire, A., & Wolfe, C. D. A. (2009). Cost of stroke in the united kingdom. *Age and Ageing*, *38*(1), 27-32.

Sakagami, M., & Niki, H. (1994). Encoding of behavioral significance of visual stimuli by primate prefrontal neurons: relation to relevant task conditions. *Experimental Brain Research*, *97*(3), 423–436. doi: 10.1007/BF00241536

Salazar, R. F., Dotson, N. M., Bressler, S. L., & Gray, C. M. (2012). Content Specific Fronto-Parietal Synchronization during Visual Working Memory. *Science*, *338*(6110), 1097–1100. doi: 10.1126/science.1224000.Content

Salmi, J., Pallesen, K. J., Neuvonen, T., Brattico, E., Korvenoja, A., Salonen, O., & Carlson, S. (2010). Cognitive and motor loops of the human cerebro-cerebellar system. *Journal of Cognitive Neuroscience*, *22*(11), 2663-2676. doi: 10.1162/jocn.2009.21382

Sarker, S.-J., Rudd, A. G., Douiri, A., & Wolfe, C. D. A. (2012). Comparison of 2 Extended Activities of Daily Living Scales With the Barthel Index and Predictors of Their Outcomes Cohort Study Within the South London Stroke Register (SLSR). *Stroke*, *43*, 1362-1369. doi: 10.1161/STROKEAHA.111.645234

Sasson, E., Doniger, G., Pasternak, O., Tarrasch, R., & Assaf, Y. (2013). White matter correlates of cognitive domains in normal aging with diffusion tensor imaging. *Frontiers in Neuroscience*, *7*, 32. doi: 10.3389/fnins.2013.00032

Schiemanck, S. K., Kwakkel, G., Post, M. W. M., & Prevo, A. J. H. (2006). Predictive value of ischemic lesion volume assessed with magnetic resonance imaging for neurological deficits and functional outcome poststroke: A critical review of the literature. *Neurorehabilitation and Neural Repair*, *20*(4), 492-502. doi: 10.1177/1545968306289298

Schmahmann, J. D. (1996). Dysmetria of thought: Correlations and conundrums in the relationship between the cerebellum, learning, and cognitive processing. *Behavioral and Brain Sciences*, *19*(3), 472-473. doi: 10.1017/S0140525X00081851

Schmahmann, J. D. (1998). Dysmetria of thought: clinical consequences of cerebellar dysfunction on cognition and affect. *Trends in Cognitive Sciences*, *2*(9), 362 - 371. doi: 10.1016/S1364-6613(98)01218-2

Schmahmann, J. D. (2004). Disorders of the cerebellum: Ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *16*(3), 367-378. doi: 10.1176/jnp.16.3.367

Schmahmann, J. D., & Pandyat, D. N. (1997). The cerebrocerebellar system. In R. J. Bradley, R. A. Harris, P. Jenner, & J. D. Schmahmann (Eds.), *The cerebellum and cognition* (Vol. 41, p. 31 - 60). doi: 10.1016/S0074-7742(08)60346-3

Schmahmann, J. D., & Sherman, J. C. (1998). The cerebellar cognitive affective syndrome. *Brain*, *121*(4), 561-579. doi: 10.1093/brain/121.4.561

Schmid, J., & Leiman, J. M. (1957). The development of hierarchical factor solutions. *Psychometrika*, *22*(1), 53–61. doi: 10.1007/BF02289209

Schoenfeld, M. A., Hopf, J.-M., Martinez, A., Mai, H., Sattler, C., Gasde, A., ... Hillyard, S. (2007). Spatio-temporal analysis of feature-based attention. *Cerebral Cortex*, *17*(10), 2468-2477. doi: 10.1093/cercor/bhl154

Schoenfeld, M. A., Tempelmann, C., Martinez, A., Hopf, J. M., Sattler, C., Heinze, H. J., & Hillyard, S. A. (2003). Dynamics of feature binding during object-selective attention. *Proceedings of the National Academy of Sciences of the United States of America*, *100*(20), 11806-11.

Scolari, M., Seidl-Rathkopf, K. N., & Kastner, S. (2015). Functions of the human frontoparietal attention network: Evidence from neuroimaging. *Current Opinion in Behavioral Sciences*, *1*, 32 - 39. (Cognitive control) doi: 10.1016/j.cobeha.2014.08.003

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., & Kenna, H. e. a. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of Neuroscience*, *27*, 23492356.

Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *298*(1089), 199–209. doi: 10.1098/rstb.1982.0082

Shallice, T., & Burgess, P. (1991). High-order cognitive impairments and frontal lobe lesions in man. In H. S. Levin, H. M. Eisenberg, & A. L. Benton (Eds.), *Frontal lobe function and dysfunction* (p. 125-138). New York: Oxford University Press.

Shallice, T., Stuss, D. T., Alexander, M. P., Picton, T. W., & Derkzen, D. (2008). The multiple dimensions of sustained attention. *Cortex*, *44*(7), 794 - 805. doi: 10.1016/j.cortex.2007.04.002

Shapiro, K., Hillstrom, A., & Husain, M. (2002). Control of visuotemporal attention by inferior parietal and superior temporal cortex. *Current Biology*, *12*(15), 13201325.

Shinoura, N., Suzuki, Y., Yamada, R., Tabei, Y., Saito, K., & Yagi, K. (2009). Damage to the right superior longitudinal fasciculus in the inferior parietal lobe plays a role in spatial neglect. *Neuropsychologia*, *47*, 26002603.

Shomstein, S., & Yantis, S. (2004). Control of attention shifts between vision and audition in human cortex. *Journal of Neuroscience*, *24*(47), 10702–10706. doi: 10.1523/JNEUROSCI.2939-04.2004

Shomstein, S., & Yantis, S. (2006). Parietal cortex mediates voluntary control of spatial and nonspatial auditory attention. *Journal of Neuroscience*, *26*(2), 435–439. doi: 10.1523/JNEUROSCI.4408-05.2006

Sigala, N., Kusunoki, M., Nimmo-Smith, I., Gaffan, D., & Duncan, J. (2008). Hierarchical coding for sequential task events in the monkey prefrontal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *105*(33), 11969–11974. doi: 10.1073/pnas.0802569105

Simanova, I., Hagoort, P., Oostenveld, R., & van Gerven, M. A. (2014). Modality-independent decoding of semantic information from the human brain. *Cerebral Cortex*, *24*, 426434.

Skidmore, E. R., Whyte, E. M., Holm, M. B., Becker, J. T., Butters, M. A., Dew, M. A., ... Lenze, E. J. (2010). Cognitive and affective predictors of rehabilitation participation after stroke. *Archives of Physical Medicine and Rehabilitation*, *91*(2), 203-207. doi: 10.1016/j.apmr.2009.10.026

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science*, *283*(5408), 1657-1661. doi: 10.1126/science.283.5408.1657

Sokolov, A. A., Miall, R. C., & Ivry, R. B. (2017). The cerebellum: Adaptive prediction for movement and cognition. *Trends in Cognitive Sciences*, *21*(5), 313 - 332. doi: 10.1016/j.tics.2017.02.005

Sörös, P., Harnadek, M., Blake, T., Hachinski, V., & Chan, R. (2015). Executive dysfunction in patients with transient ischemic attack and minor stroke. *Journal of the Neurological Sciences*, *354*(1), 17 - 20. doi: https://doi.org/10.1016/j.jns.2015.04.022

Sperber, C., & Karnath, H.-O. (2016, 12). Impact of correction factors in human brain lesion-behavior inference. *Human Brain Mapping*, *38*, 16921701. doi: 10.1002/

hbm.23490

Spreng, R. N. (2012). The fallacy of a "task-negative" network. *Frontiers in Psychology*, *3*(145). doi: 10.3389/fpsyg.2012.00145

Spreng, R. N., Mar, R. A., & Kim, A. S. N. (2009). The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: A quantitative meta-analysis. *Journal of Cognitive Neuroscience*, *21*(3), 489-510. doi: 10.1162/jocn.2008.21029

Stanislaw, H., & Todorov, N. (1999). Calculation of signal detection theory measures. *Behavior Research Methods, Instruments, & Computers*, *31*(1), 137-149. doi: 10 .3758/BF03207704

Stapleton, T., Ashburn, A., & Stack, E. (2001). A pilot studyof attention deficits, balance control and falls in the subacute stage following stroke. *Clinical Rehabilitation*, *15*(4), 437-444. doi: 10.1191/026921501678310243

Stephens, S., Kenny, R. A., Rowan, E., Kalaria, R. N., Bradbury, M., Pearce, R., ... Ballard, C. G. (2005). Association between mild vascular cognitive impairment and impaired activities of daily living in older stroke survivors without dementia. *American Geriatrics Society*, *53*(1), 103-107. doi: 10.1111/j.1532-5415.2005.53019

Stewart, K. J., Gale, S. D., & Diamond, P. T. (2002). Utility of the wasi and hvlt-r during early assessment of post-stroke patients entering acute inpatient rehabilitation. american journal of physical medicine and rehabilitation. *American Journal of Physical Medicine and Rehabilitation*, *31*(3), 223-228.

Stokes, M. G., Kusunoki, M., Sigala, N., Nili, H., Gaffan, D., & Duncan, J. (2013). Dynamic coding for cognitive control in prefrontal cortex. *Neuron*, *78*(2), 364–375. doi: 10.1016/j.neuron.2013.01.039

Stoodley, C. J. (2012). The cerebellum and cognition: Evidence from functional imaging studies. *The Cerebellum*, *11*(2), 352-365. doi: 10.1007/s12311-011-0260-7

Stoodley, C. J., MacMore, J. P., Makris, N., Sherman, J. C., & Schmahmann, J. D. (2016). Location of lesion determines motor vs. cognitive consequences in patients with cerebellar stroke. *NeuroImage: Clinical*, *12*, 765775. doi: 10.1016/j.nicl.2016 .10.013

Stoodley, C. J., & Schmahmann, J. D. (2009). Functional topography in the human cerebellum: A meta-analysis of neuroimaging studies. *NeuroImage*, *44*(2), 489 - 501. doi: 10.1016/j.neuroimage.2008.08.039

Stoodley, C. J., & Schmahmann, J. D. (2010). Evidence for topographic organization in the cerebellum of motor control versus cognitive and affective processing. *Cortex*, *46*(7), 831 - 844. (Language, Cognition and the Cerebellum: Grappling with an

Enigma) doi: 10.1016/j.cortex.2009.11.008

Strick, P. L., Dum, R. P., & Fiez, J. A. (2009). Cerebellum and nonmotor function. *Annual Review of Neuroscience*, *32*(1), 413-434. doi: 10.1146/annurev.neuro.31.060407.125606

Striemer, C., Cantelmi, D., Cusimano, M., Danckert, J., & Schweizer, T. (2015). Deficits in reflexive covert attention following cerebellar injury. *Frontiers in Human Neuroscience*, *9*, 428. doi: 10.3389/fnhum.2015.00428

Stroke Association. (2017). *State of the Nation: Stroke Statistics.* Retrieved from `https://www.stroke.org.uk/sites/default/files/state_of_the_nation_2017_final_1.pdf`.

Sturm, W., Simone, A., Krause, B., Specht, K., Hesselmann, V., Radermacher, I., ... Willmes, K. (1999). Functional anatomy of intrinsic alertness: evidencefor a fronto-parietal-thalamic-brainstem network in theright hemisphere. *Neuropsychologia*, *37*(7), 797 - 805. doi: 10.1016/S0028-3932(98)00141-9

Stuss, D. T. (2011). Functions of the frontal lobes: Relation to executive functions. *Journal of the International Neuropsychological Society*, *17*(5). doi: 10.1017/S1355617711000695

Stuss, D. T., & Alexander, M. P. (2007). Is there a dysexecutive syndrome? *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *362*(1481), 901–915. doi: 10.1098/rstb.2007.2096

Stuss, D. T., & Knight, K. (2002). *Principles of frontal lobe function*. New York: Oxford University Press.

Stuss, D. T., Levine, B., Alexander, M. P., Hong, J., Palumbo, C., Hamer, L., ... Izukawa, D. (2000). Wisconsin card sorting test performance in patients with focal frontal and posterior brain damage: effects of lesion location and test structure on separable cognitive processes. *Neuropsychologia*, *38*(4), 388 - 402. doi: https://doi.org/10.1016/S0028-3932(99)00093-7

Su, C.-Y., Chen, H.-M., Kwan, A.-L., Lin, Y.-H., & Guo, N.-W. (2007). Neuropsychological impairment after hemorrhagic stroke in basal ganglia. *Archives of Clinical Neuropsychology*, *22*(4), 465 - 474. doi: https://doi.org/10.1016/j.acn.2007.01.025

Suchan, J., & Karnath, H. O. (2011). Spatial orienting by left hemisphere language areas: a relict from the past. *Brain*, *134*(10), 3059-70. doi: 10.1093/brain/awr120

Sudevan, P., & Taylor, D. A. (1987). The cuing and priming of cognitive operations. *Journal of Experimental Psychology: Human Perception and Performance*, *13*(1), 89-103.

Swaminathan, S. K., & Freedman, D. J. (2012). Preferential encoding of visual categories

in parietal cortex compared with prefrontal cortex. *Nature Neuroscience*, *15*, 315-320. doi: 10.1038/nn.3016

Swick, D., Ashley, V., & Turken, U. (2008). Left inferior frontal gyrus is critical for response inhibition. *BMC Neuroscience*, *9*. doi: 10.1186/1471-2202-9-102

Szczepanski, S. M., Konen, C. S., & Kastner, S. (2010). Mechanisms of spatial attention control in frontal and parietal cortex. *J Neurosci*, *30*(1), 148-60. doi: 10.1523/JNEUROSCI.3862-09.2010

Tatemichi, T. K., Desmond, D. W., Stem, Y., & Paik, M. (1994). Cognitive impairment after stroke : frequency , patterns , and relationship to functional abilities. *Journal of Neurology, Neurosurgery, and Psychiatry*, *57*, 202-207.

Tedesco, A. M., Chiricozzi, F. R., Clausi, S., Lupo, M., Molinari, M., & Leggio, M. G. (2011). The cerebellar cognitive profile. *Brain*, *134*, 36723686.

Teskey, M. L., & Masson, M. E. J. (2017). Components of competitor priming in task switching. *Memory and Cognition*, *45*, 1384-1397. doi: 10.3758/s13421-017-0734-z

Teuber, H. L. (1972). Unity and diversity of frontal lobe functions. *Acta Neurobiologiae Experimentalis*, *32*(2), 615-656.

Thiebaut De Schotten, M., ffytche, D. H., Bizzi, A., Dell′Acqua, F., Allin, M., Walshe, M., ... Catani, M. (2011). Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with mr diffusion tractography. *NeuroImage*, *54*(1), 49-59. doi: 10.1016/j.neuroimage.2010.07.055

Thiebaut de Schotten, M., & Foulon, C. (2017). The rise of a new associationist school for lesion-symptom mapping. *Brain*, *141*(1), 2-4. doi: 10.1093/brain/awx332

Thiebaut de Schotten, M., Urbanski, M., Duffau, H., Volle, E., Lévy, R., Dubois, B., & Bartolomeo, P. (2005). Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans. *Science*, *309*(5744), 2226–2228. doi: 10.1126/science.1116251

Thiebaut de Schotten, M., Urbanski, M., Duffau, H., Volle, E., Lvy, R., Dubois, B., & Bartolomeo, P. (2005). Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans. *Science*, *309*, 22262228.

Thoma, P., Koch, B., Heyder, K., Schwarz, M., & Daum, I. (2008). Subcortical contributions to multitasking and response inhibition. *Behavioural Brain Research*, *194*(2), 214 - 222. doi: 10.1016/j.bbr.2008.07.016

Thompson, K. G., Biscoe, K. L., & Sato, T. R. (2005). Neuronal basis of covert spatial attention in the frontal eye field. *The Journal of neuroscience*, *25*(41), 9479-9487.

Toth, L. J., & Assad, J. A. (2002). Dynamic coding of behaviourally relevant stimuli in parietal cortex. *Nature*, *415*(6868), 165168.

Townsend, J., Courchesne, E., Covington, J., Westerfield, M., Harris, N. S., Lyden, P., ... Press, G. A. (1999). Spatial attention deficits in patients with acquired or developmental cerebellar abnormality. *Journal of Neuroscience*, *19*(13), 5632–5643. doi: 10.1523/JNEUROSCI.19-13-05632.1999

Towse, J. N., & Hitch, G. J. (1995). Is there a relationship between task demand and storage space in tests of working memory capacity? *The Quarterly Journal of Experimental Psychology Section A*, *48*(1), 108-124. doi: 10.1080/14640749508401379

Towse, J. N., Hitch, G. J., & Hutton, U. (1998). A reevaluation of working memory capacity in children. *Journal of Memory and Language*, *39*, 195-217.

Towse, J. N., Lewis, C., & Knowles, M. (2007). When knowledge is not enough: the phenomenon of goal neglect in preschool children. *Journal of experimental child psychology*, *96*(4), 320–32. doi: 10.1016/j.jecp.2006.12.007

Treisman, A. (1998). Feature binding, attention and object perception. *Philosophical Transactions of the Royal Society*, *353*(1373), 1295-306. doi: 10.1098/rstb.1998.0284

Tsuchida, A., & Fellows, L. K. (2013). Are core component processes of executive function dissociable within the frontal lobes? evidence from humans with focal prefrontal damage. *Cortex*, *49*(7), 1790 - 1800. doi: 10.1016/j.cortex.2012.10.014

Turner, M. L., & Engle, R. W. (1989). Is working memory capacity task dependent? *Journal of Memory and Language*, *28*(2), 127 - 154. doi: 10.1016/0749-596X(89)90040-5

Urbanski, M., Thiebaut de Schotten, M., Rodrigo, S., Catani, M., Oppenheim, C., Touzé, E., ... Bartolomeo, P. (2008). Brain networks of spatial awareness: evidence from diffusion tensor imaging tractography. *Journal of Neurology, Neurosurgery and Psychiatry*, *79*, 98601.

Urbanski, M., Thiebaut de Schotten, M., Rodrigo, S., Oppenheim, C., Touzé, E., Méder, J. F., ... Bartolomeo, P. (2011). Dti-mr tractography of white matter damage in stroke patients with neglect. *Experimental Brain Research*, *208*(4), 491505. doi: 10.1007/s00221-010-2496-8

Vallar, G. (2001). Extrapersonal visual unilateral spatial neglect and its neuroanatomy. *NeuroImage*, *14*, S52-S58.

Vallar, G., & Perani, D. (1986). The anatomy of unilateral neglect after right hemisphere stroke lesions. a clinical/ ct-scan correlation study in man. *Neuropsychologia*, *24*, 609622.

van den Berg, R., Shin, H., Chou, W. C., George, R., & Ma, W. J. (2012). Variability in encoding precision accounts for visual short-term memory limitations. *Proc Natl*

Acad Sci USA, *109*, 87808785.

Vandenberghe, R., Molenberghs, P., & Gillebert, C. (2012). Spatial attention deficits in humans: The critical role of superior compared to inferior parietal lesions. *Neuropsychologia*, *50*, 1092-103.

Vandierendonck, A. (2012). Role of working memory in task switching. *Psychologica Belgica*, *52*(2-3), 229-253. doi: 10.5334/pb-52-2-3-229

van Schouwenburg, M. R., den Ouden, H. E. M., & Cools, R. (2010). The human basal ganglia modulate frontal-posterior connectivity during attention shifting. *Journal of Neuroscience*, *30*(29), 9910–9918. doi: 10.1523/JNEUROSCI.1111-10.2010

Van Schouwenburg, M. R., Den Ouden, H. E. M., & Cools, R. (2015). Selective attentional enhancement and inhibition of fronto-posterior connectivity by the basal ganglia during attention switching. *Cerebral Cortex*, *25*(6), 1527-1534. doi: 10.1093/cercor/bht345

van't Wout, F., Lavric, A., & Monsell, S. (2013). Are stimulusresponse rules represented phonologically for task-set preparation and maintenance? *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *39*(5), 1538-1551. doi: 10.1037/a0031672

van Zandvoort, M. J. E., Kessels, R. P. C., Nys, G. M. S., de Haan, E. H. F., & Kappelle, L. J. (2005). Early neuropsychological evaluation in patients with ischaemic stroke provides valid information. *Clinical Neurology and Neurosurgery*, *107*, 385–392. doi: 10.1016/j.clineuro.2004.10.012

Varjai, A., Mantini, D., Levenstein, J., Slavkova, E. D., Demeyere, N., & Gillebert, C. R. (2017). The role of left insula in executive set-switching: Lesion evidence from an acute stroke cohort. *Cortex*. doi: 10.1016/j.cortex.2017.11.009

Verdon, V., Schwartz, S., Lovblad, K.-O., Hauert, C.-A., & Vuilleumier, P. (2010). Neuroanatomy of hemispatial neglect and its functional components: a study using voxel-based lesion-symptom mapping. *Brain*, *133*(3), 880-894. doi: 10.1093/brain/awp305

Vergauwe, E., Barrouillet, P., & Camos, V. (2009). Visual and spatial working memory are not that dissociated after all: a time-based resource-sharing account. *Journal of Experimental Psychology: Learning, Memory and cognition*, *35*, 1012-1028.

Vergauwe, E., Barrouillet, P., & Camos, V. (2010). Do mental processes share a domain-general resource? *Psychological Science*, *21*, 384390.

Vergauwe, E., & Cowan, N. (2014). A common short-term memory retrieval rate may describe many cognitive procedures. *Frontiers in Human Neuroscience*, *8*, 126. doi: 10.3389/fnhum.2014.00126

Vergauwe, E., & Cowan, N. (2015). Attending to items in working memory: evidence that refreshing and memory search are closely related. *Psychon Bull Rev*, *22*(4), 10011006. doi: 10.3389/fnhum.2014.00126

Vilkki, J., Levnen, S., & Servo, A. (2002). Interference in dual-fluency tasks after anterior and posterior cerebral lesions. *Neuropsychologia*, *40*(3), 340 - 348. doi: 10.1016/S0028-3932(01)00090-2

Vincent, J. L., Kahn, I., Snyder, A. Z., Raichle, M. E., & Buckner, R. L. (2011). Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *Journal of Neurophysiology*, *105*(3), 1427-1427. doi: 10.1152/jn.z9k-0231 -corr.2010

Von Der Heide, R. J., Skipper, L. M., Klobusicky, E., & Olson, I. R. (2013). Dissecting the uncinate fasciculus: Disorders, controversies and a hypothesis. *Brain*, *136*(6), 1692–1707. doi: 10.1093/brain/awt094

Vorobyev, V. A., Alho, K., Medvedev, S. V., Pakhomov, S. V., Roudas, M. S., Rutkovskaya, J. M., ... Näätänen, R. (2004). Linguistic processing in visual and modality-nonspecific brain areas: PET recordings during selective attention. *Cognitive Brain Research*, *20*(2). doi: 10.1016/j.cogbrainres.2004.03.011

Voytek, B., & Knight, R. T. (2010). Prefrontal cortex and basal ganglia contributions to visual working memory. *Proceedings of the National Academy of Sciences*, *107*(42), 18167–18172. doi: 10.1073/pnas.1007277107

Wagenmakers, E., Wetzels, R., Borsboom, D., & van der Maas, H. L. J. (2011). Why psychologists must change the way they analyze their data: The case of psi: Comment on bem 2011. *Journal of Personality and Social Psychology*, *100*(3), 426-432.

Wagner, A., Par-Blagoev, E., Clark, J., & Poldrack, R. (2001). Recovering meaning: Left prefrontal cortex guides controlled semantic retrieval. *Neuron*, *31*, 329-38.

Wall, K. J., Cumming, T. B., & Copland, D. A. (2017). Determining the association between language and cognitive tests in poststroke aphasia. *Frontiers in Neurology*, *8*, 149. doi: 10.3389/fneur.2017.00149

Wallis, J. D., Anderson, K. C., & Miller, E. K. (2001). Single neurons in prefrontal cortex encode abstract rules. *Nature*, *411*, 953. doi: 10.1038/35082081

Wang, B., Yan, C., Wang, Z., Olivers, C. N. L., & Theeuwes, J. (2017). Adverse orienting effects on visual working memory encoding and maintenance. *Psychonomic Bulletin and Review*, *24*, 1261-1267. doi: 10.3758/s13423-016-1205-4

Wang, D., Buckner, R., & Liu, H. (2012). Cerebellar asymmetry and its relation to cerebral asymmetry estimated by intrinsic functional connectivity. *Journal of neurophysiology*, *109*, 46-57. doi: 10.1152/jn.00598.2012

Wang, X., Pathak, S., Stefaneanu, L., Yeh, F. C., Li, S., & Fernandez-Miranda, J. C. (2016). Subcomponents and connectivity of the superior longitudinal fasciculus in the human brain. *Brain Structure and Function*, *221*(4), 2075-2092. doi: 10.1007/s00429-015-1028-5

Watanabe, M. (1990). Prefrontal unit activity during associative learning in the monkey. *Experimental Brain Research*, *80*(2), 296–309. doi: 10.1007/BF00228157

Watanabe, M. (1992). Frontal units of the monkey coding the associative significance of visual and auditory stimuli. *Experimental Brain Research*, *89*(2), 233–247. doi: 10.1007/BF00228241

White, I. M., & Wise, S. P. (1999). Rule-dependent neuronal activity in the prefrontal cortex. *Experimental Brain Research*, *126*(3), 315–335. doi: 10.1007/s002210050740

Whyte, E., Skidmore, E., Aizenstein, H., Ricker, J., & Butters, M. (2011). Cognitive impairment in acquired brain injury: A predictor of rehabilitation outcomes and an opportunity for novel interventions. *The Journal of Injury, Function and Rehabilitation*, *3*, 45–51. doi: 10.1016/j.pmrj.2011.05.007.Cognitive

Wojciulik, E., Husain, M., Clarke, K., & Driver, J. (2001). Spatial working memory deficit in unilateral neglect. *Neuropsychologia*, *39*, 390396.

Wolfe, J. (2014). Approaches to visual search: Feature integration theory and guided search. *The Oxford Handbook of Attention*, *11*, 35-44.

Woods, D. L., Knight, R. T., & Scabini, D. (1993). Anatomical substrates of auditory selective attention: behavioral and electrophysiological effects of posterior association cortex lesions. *Cognitive Brain Research*, *1*(4), 227 - 240. doi: 10.1016/0926-6410(93)90007-R

Woolgar, A., Hampshire, A., Thompson, R., & Duncan, J. (2011). Adaptive Coding of Task-Relevant Information in Human Frontoparietal Cortex. *Journal of Neuroscience*, *31*(41), 14592–14599. doi: 10.1523/JNEUROSCI.2616-11.2011

Woolgar, A., Jackson, J., & Duncan, J. (2016). Coding of Visual, Auditory, Rule, and Response Information in the Brain: 10 Years of Multivoxel Pattern Analysis. *Journal of Cognitive Neuroscience*, *28*(10), 1433-1454. doi: 10.1162/jocn_a_00981

Woolgar, A., Parr, A., Cusack, R., Thompson, R., Nimmo-Smith, I., Torralva, T., ... Duncan, J. (2010). Fluid intelligence loss linked to restricted regions of damage within frontal and parietal cortex. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(33), 14899–14902. doi: 10.1073/pnas.1007928107

Woolgar, A., Williams, M., & Rich, A. (2015). Attention enhances multi-voxel representation of novel objects in frontal, parietal and visual cortices. *NeuroImage*, *109*,

429-437.

Yin, H. H. (2014). Action, time and the basal ganglia. *Philosophical Transactions of the Royal Society of London*, *369*(1637), 20120473. doi: 10.1098/rstb.2012.0473

Yochim, B., Baldo, J., Nelson, A., & Delis, D. C. (2007, 08). D-kefs trail making test performance in patients with lateral prefrontal cortex lesions. *Journal of the International Neuropsychological Society : JINS*, *13*, 704-9. doi: 10.1017/S1355617707070907

Zanto, T. P., & Gazzaley, A. (2009). Neural suppression of irrelevant information underlies optimal working memory performance. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *29*(10), 3059-66.

Zelinsky, G. J., & Bisley, J. W. (2015). The what, where, and why of priority maps and their interactions with visual working memory. *Annals of the New York Academy of Sciences*, *1339*(1), 154-64.

Zhang, J., Kriegeskorte, N., Carlin, J. D., & Rowe, J. B. (2013). Choosing the rules: Distinct and overlapping frontoparietal representations of task rules for perceptual decisions. *Journal of Neuroscience*, *33*, 1185211862.

Zhang, W., & Luck, S. J. (2009). Sudden death and gradual decay in visual working memory. *Psychological Science*, *20*(4), 423-428. doi: 10.1111/j.1467-9280.2009.02322.x

Ziemus, B., Baumann, O., Luerding, R., Schlosser, R., Schuierer, G., Bogdahn, U., & Greenlee, M. (2007). Impaired working-memory after cerebellar infarcts paralleled by changes in bold signal of a cortico-cerebellar circuit. *Neuropsychologia*, *45*(9), 2016 - 2024. doi: 10.1016/j.neuropsychologia.2007.02.012

Zinn, S., Bosworth, H. B., Hoenig, H. M., & Swartzwelder, S. H. (2007). Executive function deficits in acute stroke. *Archives of Physical Medicine and Rehabilitation*, *88*(2), 173-180. doi: 10.1016/j.apmr.2006.11.015

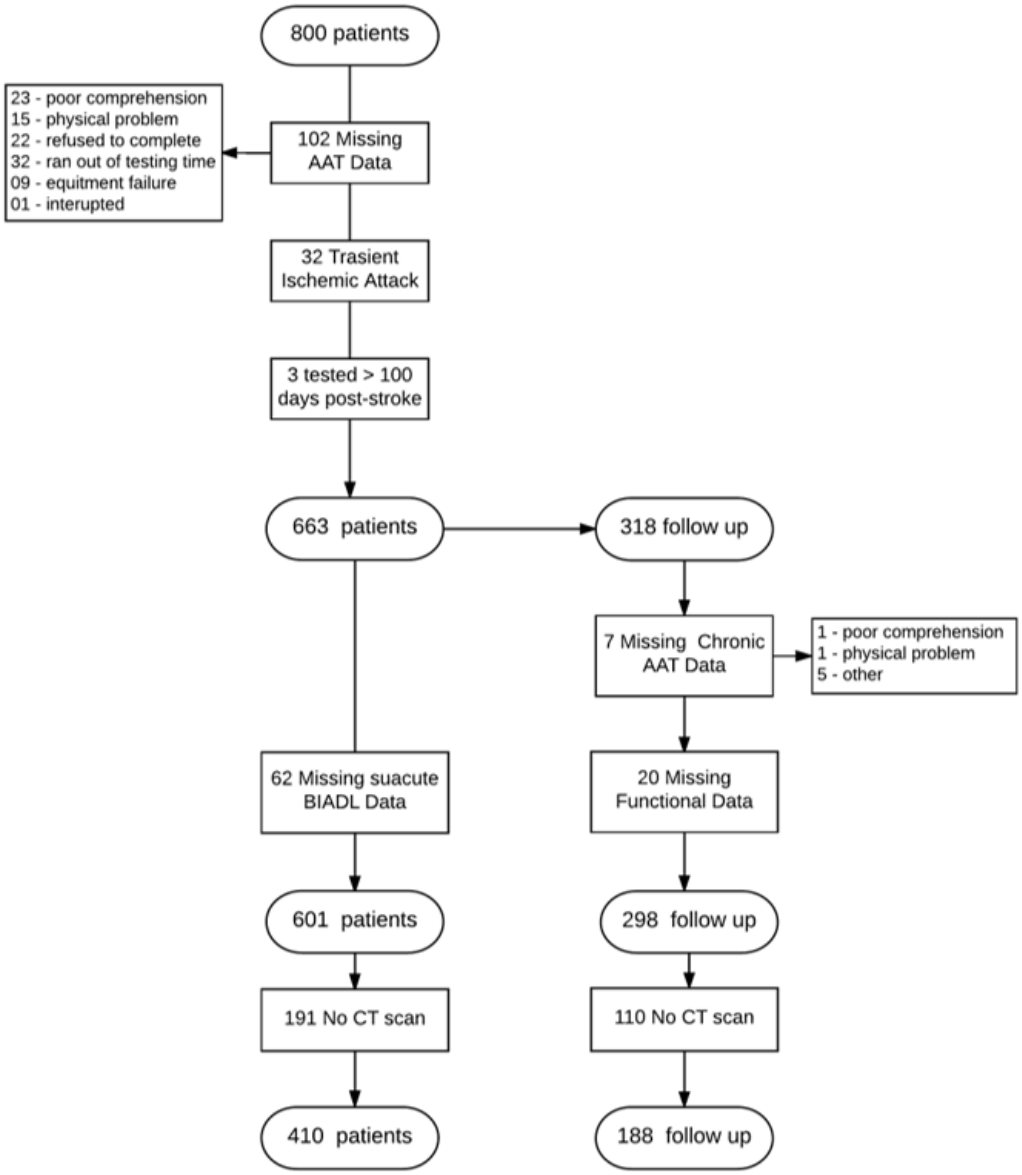
Zokaei, N., Burnett Heyes, S., Gorgoraptis, N., Budhdeo, S., & Husain, M. (2014). Working memory recall precision is a more sensitive index than span. *Journal of Neuropsychology*, *9*(2), 319-329. doi: 10.1111/jnp.12052

Appendices

Appendix A

The Functional Impact of Impaired Selective Auditory Attention.

A.1 Data Filtering Flow Chart



A.2 Missing Data Breakdown

In the subacute sample, years in education was missing for 12 patients (2%). Of these patients, level of education was available for 7 (1.16%) patients and the average number of years for that level bracket was imputed. For the remaining 5 patients (0.83%) the grand average was imputed. The worst score was imputed for the sustained attention index if patients were unable to complete the task. In the subacute sample 69 replacements were made (17%). In the follow up sample there were 24 chronic replacements (13%) and 13 subacute replacements (7%).

A.3 Supplementary Results

A.3.1 Relationship Between Cognitive Variables

To explore the relationship between the dependent variables Pearson's correlations were run (see the Table A.1). The variance Inflation factors were examined (using the VIF package 1.0 for R; Lin, 2015) to check whether there was multicollinearity. In some instances VIF values reached above 2. Therefore, 3 separate models were adopted, one included only the total score for selective attention, one including both error types (omissions & commissions) and one including solely the sustained attention score. The VIF factors indicated multicollinearity was not problematic with regards to target recall and it was utilised as a covariate in all models.

Table A.1: Relationship Between Variables of Interest

	Selective	Commissions	Omissions	Sustained
Commissions	-.44*			
Omissions	-.46*	-.01		
Sustained	-.85*	.33*	.35*	
Target Recall	.57*	-.34*	-.46*	-.51*

Pearson correlation. Results considered significant at * <0.05 uncorrected

A.3.2 Analysis in the Full Sample of 601 Patients.

The analysis run in the main text was also run in a larger sample of patients, including those that were removed due to not have access to a CT scan to calculate lesion volume from (N=601). As in the previous analysis robust linear regression including age, education, sentence comprehension and target word recall as covariates. Please see Table A.2 for an overview of the results.

Table A.2: Relationship between attention and functional status in the full sample.

		β	CI 2.5%:95%	T	P	$R2$	Model Deviation $X2$ P $R2$ change
Subacute	Target Recall	0.98	.46:1.51	3.65	.00*	.08	14.04(1) .00* .02
	Selective	1.21	0.52:1.89	3.48	.00*	.11	14.30(1) .00* .03
	Commission	-0.48	.-1.01:0.05	-1.77	.13	.10	01.75(1) .26 .00
	Omission	-0.77	-1.34:-0.20	-2.64	.03*		06.11(1) .03* .01
	Sustained	-0.99	-1.61:-0.36	-3.11	.00*	.10	11.26(1) .00* .02
Chronic	Target Recall	0.51	-.19:1.21	1.44	.23	.12	01.79(1) .26 .01
	Selective	1.42	0.55:2.29	3.21	.00*	.16	09.40(1) .00* .04
	Commission	-0.67	-1.13:0.02	-1.90	.11	.13	02.72(1) .18 .00
	Omission	-0.23	-1.13:0.66	-0.51	.68		00.23(1) .67 .01
	Sustained	-0.13	-1.05:0.79	-0.27	.79	.12	00.07(1) .79 .00
Prognostic	Target Recall	0.35	0.35: 1.33	0.70	.60	.12	00.68(1) .49 .00
	Selective	0.73	-0.34:1.80	1.34	.25	.16	02.39(1) .20 .00
	Commission	-0.28	-1.43:0.86	-0.49	.68	.15	00.33(1) .64 .00
	Omission	-0.86	-1.72:-.00	-1.97	.10		04.10(1) .09 .02
	Sustained	-1.30	-2.18:-0.42	-2.89	.00*	.15	09.99(1) .00* .03

Subacute refers to the time point within a 100 days post stroke. This analysis is looking at the relationship between BIADL and Attentional indices. Chronic refers to the follow up time point approximately 9 months post stroke. This analysis is looking at the relationship between NEADL and attentional indices. Prognostic refers to the analysis in which attentional indices at the subacute phase are being used to predict performance on the chronic NEADL.

A.4 Assessment Examiner Sheets

A.4.1 The Auditory Attention Task (BCoS)

11. AUDITORY ATTENTION

CD, Test Book pp. 69–72 (for aphasic examinees. (Audio stimuli also available from www.cognitionmatters.org.uk)

"You will hear a recording with a man saying different words. When the man says 'hello', 'please' or 'no' you have to tap on the table. When the man says something else, just ignore him. So the three words you have to respond to are: hello, please and no. Can you repeat these words?" (if the examinee does not recall the three words, repeat the words). **"We will start with an example."**

- *Where indicated on the protocol below, ask the examinee to recall the three target words.*
- *Practice should be repeated until the examinee makes no errors in a practice block OR can correctly recall the three target words after the practice block. If after the third practice block these conditions are not met, continue the test ONLY if the examinee tapped (correctly or incorrectly) to at least one of the spoken items.*
- *STOP if MORE THAN 8 ERRORS have occurred at the end of ANY BLOCK (block 1 OR block 2) but DO NOT FORGET to ASK for the three correct words at the end.*
- *When asking for the target words, present a multiple choice.*

PRACTICE 1

"Can you tell me the three words you have to respond to?" _____

1. Please	☐ **Taps** ☐ Does not tap
2. Thanks	☐ Taps ☐ **Does not tap**
3. Goodbye	☐ Taps ☐ **Does not tap**
4. Hello	☐ **Taps** ☐ Does not tap
5. Yes	☐ Taps ☐ **Does not tap**
6. No	☐ **Taps** ☐ Does not tap

"Can you tell me the three words you have to respond to?" _____

PRACTICE 2 (if necessary)

"Can you tell me the three words you have to respond to?" _____

1. Please	☐ **Taps** ☐ Does not tap
2. Thanks	☐ Taps ☐ **Does not tap**
3. Goodbye	☐ Taps ☐ **Does not tap**
4. Hello	☐ **Taps** ☐ Does not tap
5. Yes	☐ Taps ☐ **Does not tap**
6. No	☐ **Taps** ☐ Does not tap

"Can you tell me the three words you have to respond to?" _____

PRACTICE 3 (if necessary)

"Can you tell me the three words you have to respond to?" _____

1. Please	☐ **Taps** ☐ Does not tap
2. Thanks	☐ Taps ☐ **Does not tap**
3. Goodbye	☐ Taps ☐ **Does not tap**
4. Hello	☐ **Taps** ☐ Does not tap
5. Yes	☐ Taps ☐ **Does not tap**
6. No	☐ **Taps** ☐ Does not tap

"Can you tell me the three words you have to respond to?" _____

TEST

Block 1

Hello	☐ **Taps** ☐ Does not tap
Thanks	☐ Taps ☐ **Does not tap**
Goodbye	☐ Taps ☐ **Does not tap**
Yes	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap
No	☐ **Taps** ☐ Does not tap
Yes	☐ Taps ☐ **Does not tap**
Thanks	☐ Taps ☐ **Does not tap**
No	☐ **Taps** ☐ Does not tap
Hello	☐ **Taps** ☐ Does not tap
Goodbye	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap
Yes	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap
Thanks	☐ Taps ☐ **Does not tap**
Goodbye	☐ Taps ☐ **Does not tap**
Hello	☐ **Taps** ☐ Does not tap
No	☐ **Taps** ☐ Does not tap

11

Block 2

Hello	☐ **Taps** ☐ Does not tap
No	☐ **Taps** ☐ Does not tap
Yes	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap
Goodbye	☐ Taps ☐ **Does not tap**
No	☐ **Taps** ☐ Does not tap
Goodbye	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap
Yes	☐ Taps ☐ **Does not tap**
Hello	☐ **Taps** ☐ Does not tap
Thanks	☐ Taps ☐ **Does not tap**
Goodbye	☐ Taps ☐ **Does not tap**
No	☐ **Taps** ☐ Does not tap
Hello	☐ **Taps** ☐ Does not tap
Thanks	☐ Taps ☐ **Does not tap**
Yes	☐ Taps ☐ **Does not tap**
Thanks	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap

Block 3

Yes	☐ Taps ☐ **Does not tap**
Please	☐ **Taps** ☐ Does not tap
Yes	☐ Taps ☐ **Does not tap**
No	☐ **Taps** ☐ Does not tap
Please	☐ **Taps** ☐ Does not tap
Goodbye	☐ Taps ☐ **Does not tap**
Thanks	☐ Taps ☐ **Does not tap**
Goodbye	☐ Taps ☐ **Does not tap**
No	☐ **Taps** ☐ Does not tap
Thanks	☐ Taps ☐ **Does not tap**
Hello	☐ **Taps** ☐ Does not tap
Please	☐ **Taps** ☐ Does not tap
Thanks	☐ Taps ☐ **Does not tap**
No	☐ **Taps** ☐ Does not tap
Hello	☐ **Taps** ☐ Does not tap
Yes	☐ Taps ☐ **Does not tap**
Goodbye	☐ Taps ☐ **Does not tap**
Hello	☐ **Taps** ☐ Does not tap

Can you tell me the three words you had to respond to? _____

	Block 1	Block 2	Block 3
Number of correct responses:	/18	/18	/18
Number of false positives:	/9	/9	/9
Number of omissions:	/9	/9	/9

Condition of testing ____

(1=normal; NT or stopped due to 2=aphasia; 3=visual/spatial; 4=confusion; 5=fatigue; 6=motor; 7=other....)

Total number of correct responses ____/54

NOTE: If you stopped after block 1 or 2, score=total number of correct responses until you stopped. /54

Total number of false positives ____/27

NOTE: If you stopped after block 1 or 2, score= total number of false positives until you stopped.

Total number of omissions ____/27

NOTE: If you stopped after block 1 or 2, score= total number of omissions until you stopped.

Sustained attention index ____

(number of correct responses in block 1 minus number of correct responses in block 3)

NOTE: If you stopped after block 1 or 2, score=NA.

Response mode for recalling the target words ☐ free response ☐ multiple choice

Number of practices required ____/3

Number of words recalled at the end of the test ____/3

How well did the examinee understand the instructions?

(1=poor understanding even after the instructions were repeated, 2=relatively good understanding but the instructions had to be repeated, 3=good understanding, no need to repeat the instructions)

NOTE: This assessment should be based on the performance on the practice trials and the examinee's verbal or nonverbal request(s) for repetition.

12

Examinee's ID: ..... Date: .....

6. STORY RECALL AND RECOGNITION – IMMEDIATE RECALL

Test Book pp. 30–44, stopwatch.

"I will read you a story. Listen carefully because I will ask you to recall as many details of the story as possible afterwards." *Make sure the examinee is listening to you before starting to read the story.*
- *Read the story only ONCE. Then ask for free recall of the story.*
- *At the END of the free recall, present the corresponding multiple choice trials for any items that were either not reported, reported incompletely or reported incorrectly.*
- *Give FEEDBACK on the multiple choice questions.*

- *Allow a MAXIMUM of 2 min. for the FREE recall.*
- *If no response after 30 sec., give non-specific prompts (e.g., "how did the story start?") every 30 sec.*
- *Allow a MAXIMUM of 15 sec. for each set of MULTIPLE choices.*
- *If ERRORS and/or NO-RESPONSES occur on ALL 5 first questions, GIVE the responses for questions 6 to 12 IMMEDIATELY, and ask again for a response to question 13.*

- *If no reliable verbal response can be produced, give the multiple choice possibilities.*

Mrs Davis / from Manchester / met her neighbour / in the supermarket /. She told her that she had been robbed / the day before / while coming out of the post office /, just after having drawn her pension /. The two thieves /, who were teenage boys /, managed to get twenty-five pounds / from her handbag /. A passer-by who was a trainee police officer /, caught the thieves / just round the corner /.

Segments	Free recall 1		Recognition 1 (for error or omissions only)	
1) Mrs Davis	(1) ❑ *Mrs Davis*	(0.5) ❑ *Lady or Mr Davis*	1) What is the name of the person in the story? 1 **2** 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
2) Manchester	(1) ❑ *Manchester*		2) Where is she from? 1 2 **3** 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
3) Neighbour	(1) ❑ *Neighbour*		3) Who did she meet? 1 **2** 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
4) Supermarket	(1) ❑ *Supermarket*	(0.5) ❑ *Shop*	4) Where did she meet her? 1 2 3 **4**	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
5) Had been robbed	(1) ❑ *Robbed*	(0.5) ❑ *Attacked*	5) What did she tell her? 1 **2** 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
6) The day before	(1) ❑ *Day before*		6) When was she robbed? **1** 2 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
7) Post office	(1) ❑ *Coming out of post office*	(0.5) ❑ *(in) Post office*	7) Where was she robbed? 1 2 3 **4**	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
8) Pension	(1) ❑ *Drew her pension*	(0.5) ❑ *(was going to draw) Pension*	8) What was she doing at the post office? 1 2 **3** 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
9) Two	(1) ❑ *Two*		9) How many thieves were there? 1 2 3 **4**	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
10) Teenage boys	(1) ❑ *Teenage boys*	(0.5) ❑ *Boys*	10) Who were the thieves? 1 2 3 **4**	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
11) 25 pounds	(1) ❑ *25 pounds*		11) How much did they steal? 1 2 **3** 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
12) Handbag	(1) ❑ *Handbag*	(0.5) ❑ *Bag*	12) Where did they steal the money from? 1 2 **3** 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
13) Caught	(1) ❑ *Were caught*		13) What happened to the thieves at the end? **1** 2 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
14) Trainee police officer	(1) ❑ *Trainee police officer*	(0.5) ❑ *Police*	14) Who caught the thieves? 1 **2** 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*
15) Round the corner	(1) ❑ *Round the corner*		15) Where were the thieves caught? **1** 2 3 4	(1) ❑ *correct in free recall* (1) ❑ *correct in MC*

FREE recall ONLY – condition of testing (1=normal; NT or stopped due to 2=aphasia; 3=visual/spatial; 4=confusion; 5=fatigue; 6=motor; 7=other.....)	_____
FREE recall ONLY – total score (summing the "1" and "0.5" points columns)	_____/15
RECOGNITION ONLY – condition of testing (1=normal; NT or stopped due to 2=aphasia; 3=visual/spatial; 4=confusion; 5=fatigue; 6=motor; 7=other.....)	_____
FREE recall + RECOGNITION total score (summing the "1" points column BUT NOT the "0.5" points column) NOTE: If you skipped trials 6 to 12 in the multiple choice, give 0 points for trials 6 to 12. NOTE: Synonyms can be scored as "1"; information that is partially complete should be scored as "0.5".	_____/15

Comments (confabulations, perseverations etc.):

Examinee's ID: ..... Date: .....

10. RULE FINDING AND CONCEPT SWITCHING TEST

Test Book pp. 45–68.

"You will see a grid with a black dot. Can you please point to the black dot?" *Show where the black dot is (if the examinee cannot point to it. Then ask the examinee again to point to the black dot (this is just to ensure that they can give a reliable pointing response). Stop the task if the examinee cannot point reliably on the second attempt.*
"Ok. This dot will now move from page to page to a specific location. It can move to any of the grey or the coloured squares. The dot does not move randomly but follows a pattern. However, the rule governing the pattern can change. Look carefully at how the dot moves on each trial. You have to anticipate and show me where the dot will move next. Please remain attentive so that you can keep track of the changes."
- *Present the practice trials saying:*
"So for instance, if the dot is first here, then moves here *(show the second practice trial),* ***where is the dot most likely to move next?*** *(show the third practice trial)"*
- *Correct the examinee's response on the third practice item if necessary.*
- *When showing the trials, ALWAYS keep the previous trial directly above for the examinee to see.*
- *When showing the trials, point to the black dot.*
- *If the examinee does not know the location of the dot, ask him/her to guess.*

- *Allow a MAXIMUM of 15 sec. per trial.*
- *STOP if FEWER THAN 2 CORRECT responses are given up to TRIAL 11.*

	Rule	Stimulus	Expected response	Actual response	Accuracy 0/1	
1	To the right	B3	any			
2	To the right	C3	D3			
3	To the right	D3	E3			
4	To the right	E3	F3			Cross dimension switch
5	To red	B5	E3			
6	To red	E3	B5			
7	To red	B5	E3			
8	To red	E3	B5			
9	To red	B5	E3			
10	To red	E3	B5			
11	To red	B5	E3			Within dimension switch
12	To red	E6	B5			
13	To green	B5	E6			
14	To red	E6	B5			
15	To green	B5	E6			
16	To red	E6	B5			
17	To green	B5	E6			
18	To red	E6	B5			
19	To green	B5	E6			

Condition of testing (1=normal; NT or stopped due to 2=aphasia; 3=visual/spatial; 4=confusion; 5=fatigue; 6=motor; 7=other.....)	_____
Pointing PRETEST score (2=points correctly on the first attempt; 1=points correctly on the second attempt; 0=cannot point reliably)	_____
Number of correct responses NOTE: If stopped because no-response has been made up to trial 11, score=number correct until trial 11 /18.	_____/18
Number of correct rules detected (number of rules that are applied correctly on at least 2 consecutive trials) NOTE: If stopped because no-response has been made up to trial 11, score=number correct rules until trial 11 /3.	_____/3
How well did the examinee understand the instructions? (1=poor understanding even after the instructions were repeated, 2=relatively good understanding but the instructions had to be repeated, 3=good understanding, no need to repeat the instructions) NOTE: This assessment should be based on the performance on the practice trials and the examinee's verbal or nonverbal request(s) for repetition.	

A.4.3 Functional Measures

Nottingham Extended ADL Scale

The following questions are about everyday activities. Please answer by ticking ONE box for each question. Please record what you have ACTUALLY done in the last few weeks.

DID YOU.....	Not at all	with help	on your own with difficulty	on your own
1. Walk around outside?				
2. Climb stairs?				
3. Get in and out of a car?				
4. Walk over uneven ground?				
5. Cross roads?				
6. Travel on public transport?				
7. Manage to feed yourself?				
8. Manage to make yourself a hot drink?				
9. Take hot drinks from one room to another?				
10. Do the washing up?				
11. Make yourself a hot snack?				

	No	With help	On your own with difficulty	On your own
12. Manage your own money when out?				
13. Wash small items of clothing?				
14. Do your own housework?				
15. Do your own shopping?				
16. Do a full clothes wash?				
17. Read newspapers or books?				
18. Use the telephone?				
19. Write letters?				
20. Go out socially?				
21. Manage your own garden?				
22. Drive a car?				

Barthel ADL Index

Bowels
0 = incontinent (or needs to be given enema)
1 = occasional accident (once a week)
2 = continent

Bladder
0 = incontinent, or catheterized and unable to manage alone
1 = occasional accident (maximum once per 24 hours)
2 = continent

Grooming
0 = needs help with personal care
1 = independent face/hair/teeth/shaving

Toilet use
0 = dependent
1 = needs some help, but can do something alone
2 = independent (on and off, dressing, wiping)

Feeding
0 = unable
1 = needs help cutting, spreading butter etc.
2 = independent

Transfer (bed to chair and back)
0 = unable, no sitting balance
1 = major help (one or two people, physical), can sit
2 = minor help (physical or verbal)
3 = independent

Mobility
0 = immobile
1 = wheelchair independent, including corners
2 = walks with help of one person (verbal or physical)
3 = independent (but may use aid; for example, stick)

Dressing
0 = dependent
1 = needs help but can do about half unaided
2 = independent (including buttons, zips, laces etc.)

Stairs
0 = unable
1 = needs help (verbal, physical carrying aid)
2 = independent

Bathing
0 = dependent
1 = independent (or in shower)

SCORE /20

A.5 Cut-Off Scores

Table A.3: Cut-Off Scores 5th/95th Percentile

Measure	<64	65-74	>75
Selective Attention	51	50	46
Omission Errors	2	2	3
Commission Errors	2	2	6
Sustained Attention	1	1	2
Target Word Recall	3	3	2
Immediate Story Recall	6	6	3
Rule Finding	6	5	4

BCoS manual (Humphreys et al., 2012)

Appendix B

Lesion Anatomy of Auditory Selective Attention

B.1 Full Cognitive Assessment Overview

Table B.1: Results from full cognitive assessment (N=334)

Domain	Test	Mean	SD	Range
Comprehension	Time & space	05.44	00.98	0-06
	Personal information	07.42	01.29	0-08
	Nosognosia	02.86	00.42	0-03
Language	Picture naming	10.34	03.48	0-14
	Sentence construction	06.66	02.14	0-08
	Sentence reading	36.21	11.14	0-42
	Word writing	02.89	01.78	0-05
	Non word reading	04.19	02.10	0-06
Number	Number writing	03.66	01.72	0-05
	Number reading	07.45	02.65	0-09
	Calculations	02.15	01.50	0-04
Attention	Hearts total	38.74	13.99	0-50
	Hearts right neglect	-02.92	02.86	-1- -25
	Hearts left neglect	-04.61	05.03	-1- -25
	Auditory attention task	41.00	14.84	0-54
	Rule finding and switching	05.96	05.38	0-18
Praxis	Multistep object use	09.89	03.52	0-12
	Gesture production	10.41	02.46	0-12
	Gesture recognition	04.96	01.12	0-06
	Imitation	09.15	02.78	0-12
	Figure copy	33.65	11.75	0-47
Memory	Immediate story recall	05.99	03.05	0-15
	Immediate story recognition	11.66	03.29	0-15
	Delayed story recall	06.41	04.04	0-15
	Delayed story recognition	12.29	04.04	0-15
	Episodic recall	08.29	02.02	0-10

BCoS Assessment (Humphreys, 2012).

Appendix C

Executive Dysfunction: Beyond the Frontal Lobes

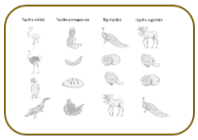
C.1 OCS+ Overview



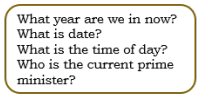
The practice is given to allow the participant time to get a feel for using the stylus and tablet. The practice includes joining two dots with the stylus, selecting a picture (pepper) on the screen and using a tapping response to select the blue pad (slight expansion of the pad gives feedback the tap is registered). As much time as is needed is given until the participant is comfortable using the equipment.



The picture naming task allows the assessment of expressive aphasia. The instructions are read out loud *"We will start with a series of pictures shown on the screen. Your task is to tell me what each one is"*. The participant is shown 4 pictures in succession and asked to name each of them out loud. The score range is **0 to 4**, with a high score indicating optimal performance.



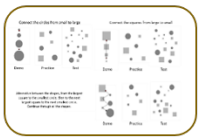
The semantics task continues the assessment of aphasia. The instructions are read out loud *"I will show a series of pictures on the screen and I will ask you some questions. Your task is to use this pen to tap the screen to give your answer"*. Four pictures are displayed on screen, with a question printed at the top. The examiner reads the question and the participant required to tap on the picture. The score ranges from **0 to 4,** with a high score indicating optimal performance
.



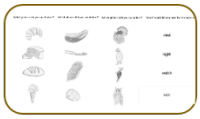
The participant is asked four questions, which are read aloud by the examiner. The score ranges from **0 to 4**, with a high score indicating optimal performance.



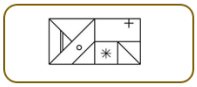
The word memory task allows the assessment of short term memory for verbal information. The instructions are read out loud *"I will read you some words. Please try and remember them"*. Five words displayed vertically stacked centrally on screen. The examiner points to each in succession while reading them aloud. The participant immediately tries to recall the words. The next set of instructions are then given *"Here are the words again. Try and remember them for later"*. The five words are displayed and once again the examiner points to each in succession while reading them aloud. The participant is then asked to recall them. The score ranges from **0 to 5** for each recall, with a high score indicating optimal performance.



The trail making task allows the assessment of executive function. The instructions are given *"I will ask you to use the pen to draw lines on the screen to connect some shapes. I will demonstrate how to do it as we go along"*. The trials is made up of three parts, first is the circle rule. In this part the participant joins the circles from small to large, whilst ignoring the squares. The second part is the square rule; in this part the participant joins squares from large to small, whilst ignoring the circles. The final part requires the participants to mix the circle and square rules by alternating from the largest square to the smallest circle. The first two rules have a score range of **0-7** and the mixed part has a score range of **0-14**. In each case high scores indicate better performance. The executive score is calculated as **Mixed/(Circles + Squares)*100**.



The recall and recognition test examines short term memory for verbal information and the previous tasks performed. The first instructions are given *"Can you tell me the words you had to remember?"*. If the participant cannot remember all the words, multiple choice options are given for them to select from. The score range is 0 to 5 for each free recall and the free recall plus recognition. High scores indicate better performance. The second set of instructions are given *"I will show you some pictures. Your task is to use the pen to tap the pictures you have seen earlier in the session"*. The participant is then shown a series of four screens, each with four pictures or four words for them to select from. The question was printed on the top of the screen and read aloud by the examiner. The score range is **0 to 5**, with higher scores indicating better performance.



The figure copy test examines praxis and short term memory for visual information. The first instructions are given *"I will show you a drawing. Your task is to use the pen to copy it in the space underneath it"*. The figure is a composite of geometric shapes, which remains on screen until the participant has copied it. The second set of instructions are given *"I will show you the same drawing again. This time the drawing will disappear after a short while. Your task is the remember it. After the drawing disappears, use your pen to draw it in the space provided"*. The figure stays on screen for two seconds, after which the participant draws as much as they can remember. Each figure element is scored for presence, accuracy and location, with a maximum score of **60**, which indicates optimal performance.



The rule finding and switching test examines executive function. The instructions are given *"In the next task you will see a pattern of squares and triangles. A red dot will appear on one of the shapes. The dot will move around the shapes following certain rules. Its previous position will be highlighted to help you remember. Your task is to predict where the dot goes next based on previous moves. Sometimes the rules will change without notice. When this happens, please try to pick up on the new rule. Because the rules change without notice, it is impossible for you to correctly predict the moves every time. Just try and do your best"*. The participant is presented with three columns of alternating geometric shapes (squares-triangles-squares), each of which contains 8 rows. There are 16 light shaded shapes and 8 pseudo randomly placed dark shaded shapes. A red dot moves around the grid of shapes according to certain rules (patterns). The participant needs to predict where the dot will move to next, based on the previous moves. They make the response by taping on the shape they predict the dot will move to. The previous position is highlighted to aid with memory. Every now and again the rule may change (5 rules in total). This happens without notice and the participant must try and adapt to the new rule. The score range is **0 to 46**, with a high score indicating optimal performance.



The auditory attention task examines selective and sustained attention to verbal information. The instructions are given *"You will now hear a recording with a series of words. Your task is to tap the screen with the pen after each word. There are three target words which you have to remember: GOODBYE DOWN NO. When you hear any of these words, tap the top blue button. When you hear any other words, tap the bottom yellow button. We will start with some practice}*. The task requires the participant to selective tap the right coloured pad, when responding to the target words and keep tapping the alternative pad for all other words. The participant is given up to three practice trials, in which each of the words are presented once. This is followed by a target word recall. The test itself is comprised of three continuous blocks of 27 word presentations (81 overall). Each block contains 3 presentations of each of the possible words, in a pseudo randomised order. Accuracy scores are devised separately for target words, related distractors and unrelated distractors. Each measure has a range of **0 to 27**, with high scores indicating optimal performance. This also allows indication of the number of false positives or false negatives, in which the wrong pad was selected. Furthermore, a sustained attention index is created by subtracting the total correct trials from the last block from those in the first block. The maximum score is **8**, with higher values reflecting poorer performance. Finally participants recall the target words, which ranges from **0-3** with high scores indicating better performance.



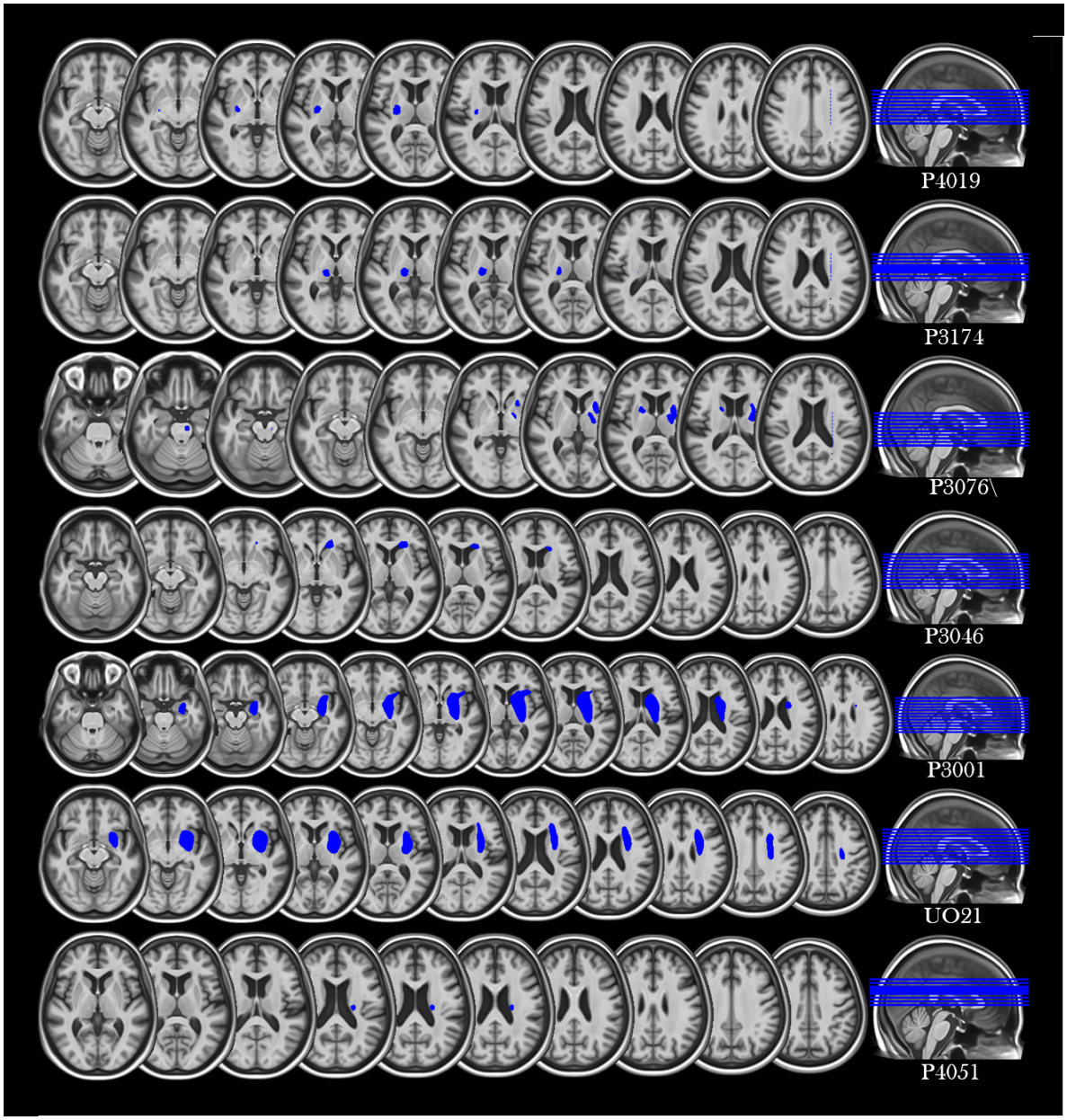
The visual selection task measures visual-spatial attention. The instructions are given *"You will see a set of drawings on the screen. Your task is to use your pen to select the fruits. There will be a practice first."* A practice is given with just one of each stimuli type in a line to ensure comprehension. The participant must then tap on all the fruits as quickly as possible. The score range is **0-30**, with higher scores indicating better performance. Furthermore, the number of false positives **(0-30)** can be measured, along with the asymmetry score (left bias **-12:12** right bias). The second task is identical apart from the visual feedback to indicate which fruits have already been selected is removed. Thus this task also relies on working memory for which locations have already been searched. The second instructions are given: *"You will see a similar set of drawings. The task again is to use your pen to select the fruits, but this time you'll have to remember the ones you have already selected and try not to select them more than once"*. The task is then performed as before. The same scores are devised as with the original test, along with the total number of revisits.



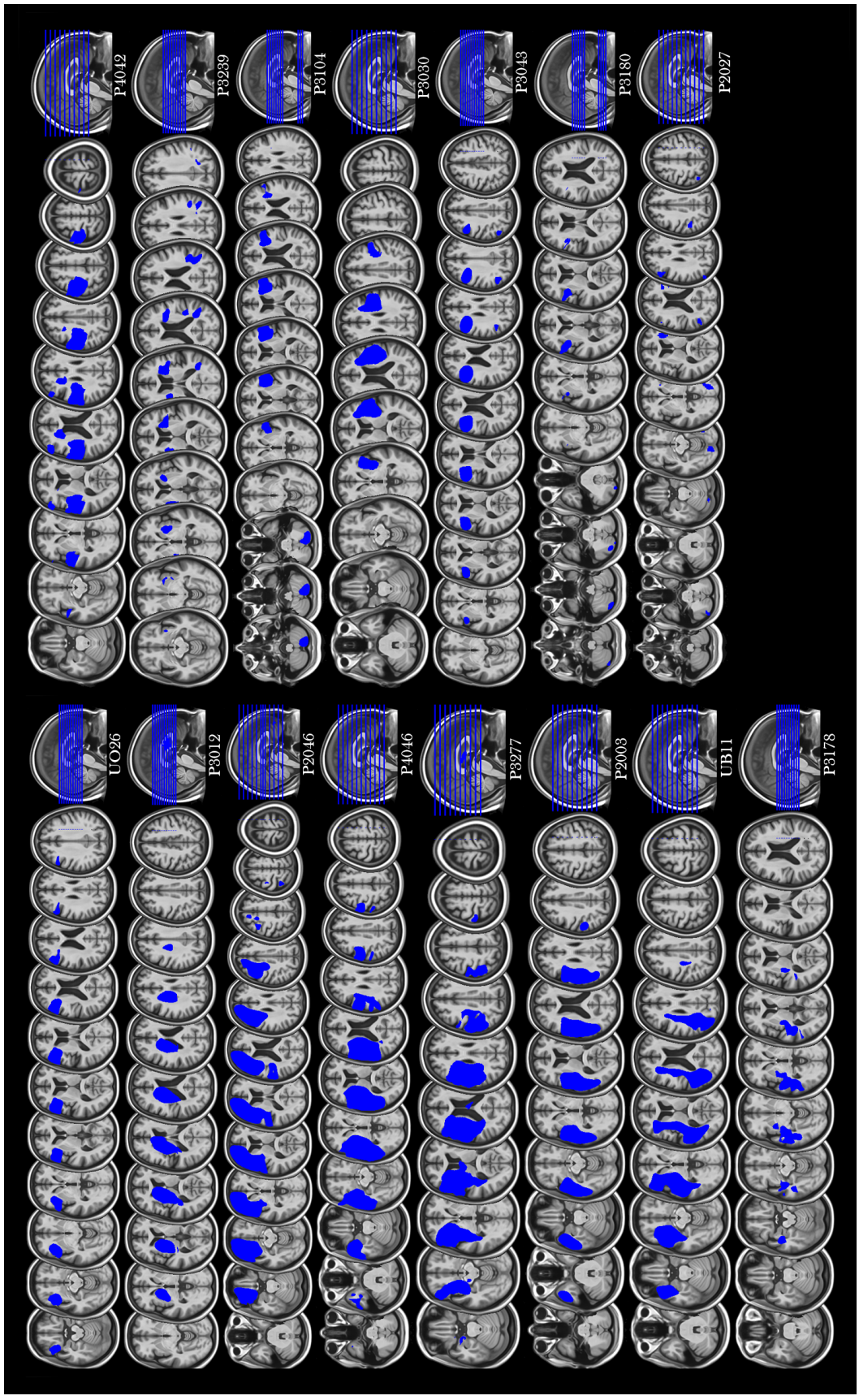
The overlapping figures test object recognition. The instructions are given *"You will see some outlines of objects. There will be a yellow dot somewhere on the outlines. Your task is to use the pen to trace the outline of the object that has the dot on its outline. The dot is the starting point"*. The participant is then draws around each item in turn and the participant is then asked to name the three objects. There are two measures devised, a goodness of fit between the traced items and the recall of the items (**0-3**).

C.2 Lesion Visualisation

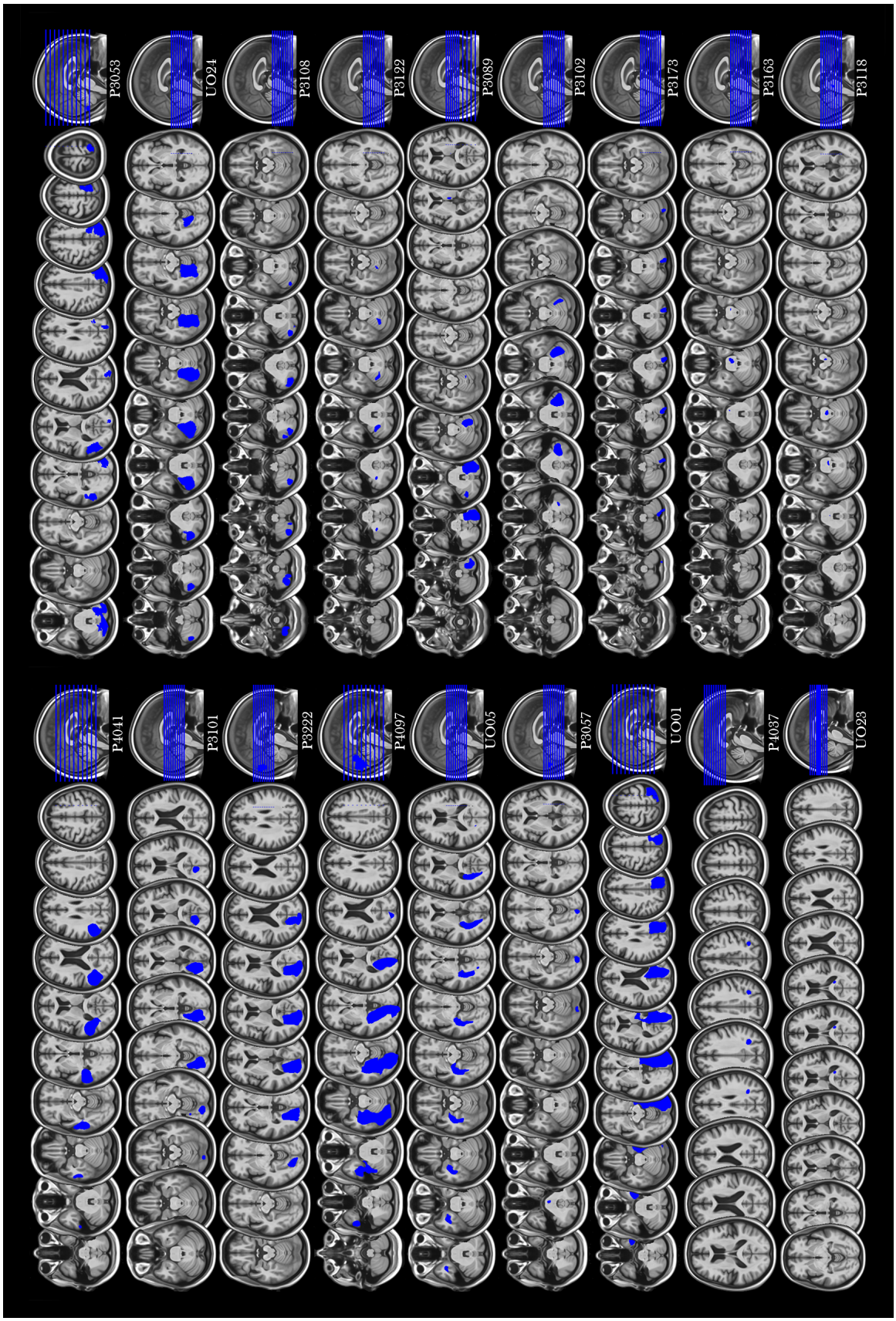
Frontal Group



Frontal and Posterior Group



Posterior Group



C.3 Lesion Overview

Table C.1: Patient Lesion Overview

Group	PID	Side	Volume	Largest Extent	Frontal	Motor	Limbic	Somato	Parietal	Temporal	Occipital	Cerebellum
Frontal	P3046	R	2.02	FL	0.52		0.01					
	P3001	R	27.76	FL	2.42		1.58			0.75		
	UO21	R	21.50	FL	3.74		0.25			0.46		
	P3076	R	4.15	BS	0.06							
	P4051	R	0.31	FL								
	P4019	L	1.47	FL								
	P3174	L	0.96	FL								
Frontal & Posterior	P3030	R	70.22	FL	27.94	3.55	0.04	0.09	0.36	16.19		
	P3104	R	33.57	FL	14.81	0.06				2.97		8.11
	UO26	L	31.24	FL	24.40					4.11		
	P3012	L	65.07	LL	7.79		10.18			5.52		
	P4042	L	91.58	FL	18.25	12.62		13.20	5.62	20.76		
	P2046	L	184.13	FL	94.90	3.91	9.19		1.22	17.90		
	P4046	L	172.04	TL	28.80	8.65	0.88	4.95	8.12	76.96	0.10	
	P3277	L	168.28	FL	56.51	5.30	3.32	8.09	17.18	20.12	0.01	
	P2003	L	121.11	TL	20.52	4.12	0.07	1.03	11.04	69.23	1.81	
	UB11	L	131.29	TL	28.35		1.23		5.88	42.17	9.39	
	P3178	L	20.50	TL	0.22		0.19			11.91		
	P3043	L	30.11	FL	20.66	1.67			1.61	1.14	0.18	
	P3180	L	6.78	FL	3.61				2.36	1.35	0.93	0.46
	P3239	B	19.09	FL	3.61				2.36	1.35	0.93	
	P2027	B	15.38	OL	4.20				1.47	0.58	4.80	3.94
Posterior	UO1	R	146.99	OL			8.01		15.78	23.01	57.86	50.94
	P4037	R	1.48	OL					0.14		0.18	
	UO23	R	0.47	LL				0.26			0.01	
	P3102	R	9.48	CB								8.23
	P3173	R	4.55	CB								3.02
	P3163	R	0.76	BS								
	P4041	L	39.22	TL			0.06		5.62	20.07	5.84	
	P3101	L	17.28	OL			0.01			0.82	14.94	11.74
	P3222	L	25.36	OL					0.10	0.45	23.68	6.21
	P4097	L	88.92	CB			3.68		0.04	18.15	30.79	53.64
	UO5	L	18.67	TL			2.54			10.11	4.89	
	UO24	L	32.54	CB						0.41	1.33	29.03
	P3108	L	8.93	CB								4.25
	P3122	L	2.46	CB								1.85
	P3057	B	1.77	CB							0.96	1.57
	P3053	B	64.55	OL		0.51	0.17	2.10	8.84	6.94	21.23	16.44
	P3089	B	28.97	CB							0.01	25.26
	P3118	B	0.62	BS								

Lobe Abbreviations: FL = Frontal Lobe, LL = Limbic Lobe, TL = Temporal Lobe, OL = Occipital Lobe, CB = Cerebellum, BS = Brain Stem

C.4 OCS+ Cut-Off Scores

Table C.2: OCS+ Overview for 150 Control Participants

		Age <50 (N=24)					Age 50-69 (N=61)					Age > 70 (N=65)				
	Measure	Mean	SD	Range	N	Cut-Off	Mean	SD	Range	N	Cut-Off	Mean	SD	Range	N	Cut-off
RF	Overall Accuracy	32.68	7.31	15-42	22	**20**	28.25	8.68	5-43	61	**11**	24.65	8.40	9-41	65	**12**
TMT	Executive Index	91.76	18.26	29-100	23	**53**	84.55	21.24	25-100	58	**41**	81.22	26.33	07-100	65	**29**
AAT	d-prime	3.87	0.65	1.71-4.46	24	**2.90**	3.66	0.87	1.05-4.46	58	**1.70**	3.69	0.72	1.40-4.46	58	**1.41**
	Sustained Index	1.11	0.07	1-1.25	24	**1.25**	1.11	0.20	.75-2	58	**1.53**	1.11	0.17	.75-2.75	58	**1.75**
	Target Recall	3.00	0	3-3	24	**3**	2.91	0.43	0-3	58	**2**	2.97	0.18	2-3	58	**2**
VST	d-prime	4.16	0.26	3.32-4.28	24	**3.80**	4.11	0.28	3.06-4.28	60	**3.80**	4.02	0.36	3.06-4.28	64	**3.25**
	Asymmetry	0.04	0.20	0-1	24	**0**	0.06	0.41	⁻1-1	60	**0-1**	⁻0.13	0.63	⁻2-1	64	**⁻1-1**
	WM Revisits	0.92	1.10	0-3	24	**3**	1.63	2.40	0-11	60	**6**	1.45	1.82	1-7	65	**6**
Memory	WM Im Recall 1	4.67	0.76	2-5	24	**3**	4.42	0.79	2-5	59	**3**	4.03	0.99	2-5	64	**2**
	WM Im Recall 2	5	0	5-5	24	**5**	4.93	0.31	3-5	59	**5**	4.75	0.56	3-5	64	**3**
	WM Del Recall/Recog	4.92	0.28	4-5	24	**4**	4.97	0.18	4-5	61	**5**	4.88	0.38	3-5	65	**4**
	Episodic Recall	3.63	0.58	2-4	24	**3**	3.63	0.52	2-4	60	**3**	3.60	0.52	2-4	65	**3**
	Orientation	3.79	0.41	3-4	24	**3**	3.90	0.30	3-4	61	**3**	3.86	0.35	3-4	65	**3**
Lang	Picture Naming	3.91	0.29	3-4	23	**3**	3.97	0.18	3-4	61	**4**	3.91	0.34	2-4	65	**3**
	Semantic	3.96	0.20	3-4	24	**4**	3.87	0.34	3-4	61	**3**	3.88	0.38	2-4	65	**3**

Overview of varying sample size. Auditory Attention (2-insufficient capacity on the practice trials, 2-auditory difficulties, 2-technical, 1-ran out of time). Visual Selection (2-technical). Visual Selection No Fee Back (1-technical). Trail Making Task (2-Interruption, 2-comprehension). Rule finding (1-comprehension, 1 examiner error).

C.5 Impairment on OCS+ Measures

Table C.3: Patient Task Impairment Overview

Group	PID	Side	Volume	Lobe[1]	Ori	Epi	Verbal Memory Im1	Verbal Memory Im2	Verbal Memory Del	Language PicName	Language Semantic	Other ObjRecog
Frontal	P3046	R	2.02	FL								
	P3001	R	27.76	FL			⊛**				⊛***	
	UO21	R	21.50	FL								
	P3076	R	4.15	BS								
	P4051	R	0.3	FL								
	P4019	L	1.5	FL					⊛***			
	P3174	L	0.96	FL		⊛**						
Frontal & Posterior	P3030	R	70.22	FL								
	P3104	R	33.57	FL		⊛**			⊛***			
	UO26	L	31.24	FL				⊛***	⊛***			
	P3012	L	65.07	LL			⊛**	⊛***				
	P4042	L	91.58	FL			⊛**	⊛***	⊛***			
	P2046	L	184.13	FL		⊛**	⊛**	⊛***	⊛***			
	P4046	L	172.04	TL				⊛***				
	P3277	L	168.28	FL	⊛***		⊛***	⊛***				⊛***
	P2003	L	121.11	TL				⊛***				
	UB11	L	131.29	TL				⊛***				
	P3178	L	20.50	TL								
	P3043	L	30.11	FL			⊛***	⊛***				
	P3180	L	6.78	FL								
	P3239	B	19.09	FL								
	P2027	B	15.38	OL	⊛***	⊛**	⊛**		⊛***	⊛***		
Posterior	UO01	R	146.99	OL								⊛***
	P4037	R	1.48	OL			⊛**	⊛***	⊛***			
	UO23	R	0.47	LL								
	P3102	R	9.48	CB				⊛**		⊛***		
	P3173	R	4.55	CB							⊛***	
	P3163	R	0.76	BS				⊛**				
	P4041	L	39.22	TL	⊛***		⊛**	⊛***	⊛***			
	P3101	L	17.28	OL								
	P3222	L	25.36	OL		⊛**				⊛***		⊛***
	P4097	L	88.92	CB	⊛***		⊛**			⊛***		
	UO05	L	18.67	TL			⊛**	⊛**	⊛***			
	UO24	L	32.54	CB								
	P3108	L	8.93	CB								
	P3122	L	2.46	CB	⊛***				⊛***			
	P3057	B	1.77	CB								
	P3053	B	64.55	OL	⊛***				⊛***	⊛***		
	P3089	B	28.97	CB							⊛***	
	P3118	B	0.62	BS				⊛***				
	Impairment Total				6	5	11	15	10	5	3	3

Lobe with greatest lesion extent: FL = Frontal Lobe, LL = Limbic Lobe, TL = Temporal Lobe
OL = Occipital Lobe, CB = Cerebellum, BS = Brain Stem
* P=<.05 **P=<.01 *** P=<.001 Crawford-Howell case control t-test
⊛ = 5^{th} percentile or below.

C.6 Frontal Subcortical Patient Overview

Table C.4: Patient Overview for Frontal Subcortical Group

Case	Age	Gen.	Ex.	Temp.	Spac.	Shif.	Lat.	Vol.	GM	SC	Other
P4051	68	F	⊛**	⊛***	⊛**	⊛**	R	0.31		Caud.	
P4019	86	M	⊛***	⊛*	⊛***	⊛**	L	1.47		Gp Put.	DelRC
P3046	84	F	⊛**	⊛***	⊛*	⊛*	R	2.02	F	Caud.	
P3076	65	M					B	4.15	F	L:Gpe R:Put. Gpe	
P3001	70	F	⊛***	⊛**	⊛***	⊛**	R	27.76	F/I	Caud. Thal. Gp Put.	Sm ImRC

Lat = Lateralisation, Vol = Volume, GM = Grey Matter, SC = Subcortical, Other = other OCS+ tests
F = Frontal, I = Insula, Caud. = Caudate, Gp = Globus Pallidus, Put = Putamen, Thal. = Thalamus
ImRC = Immediate word recall, DelRC = Delayed word recall, Sm = Semantics.
⊛ $< 5^{th}$ percentile * $p <.05$ **$p <.01$ *** $p <.001$

As seen in Figure C.4, patients in the frontal-subcortical group had lesions overlapping with multiple structures in the basal ganglia, in addition to damage to the striatal white matter. All patients apart from P3076 were impaired on all factors. The only observed difference was that P3076 had bilateral lesions, which was more substantial than some of the impaired patients. Both UB11 and P3239 who were impaired in the frontal/posterior group also had lesions overlapping with similar subcortical regions. P3034, who was impaired only on spatial and temporal attention factors had very minimal damage to the putamen. Interestingly, P3180's frontal lesion spared the subcortical structures, which make makes the lesion overlap with the CB lesion from the only other patient to experience impairment solely on the general factor of note.

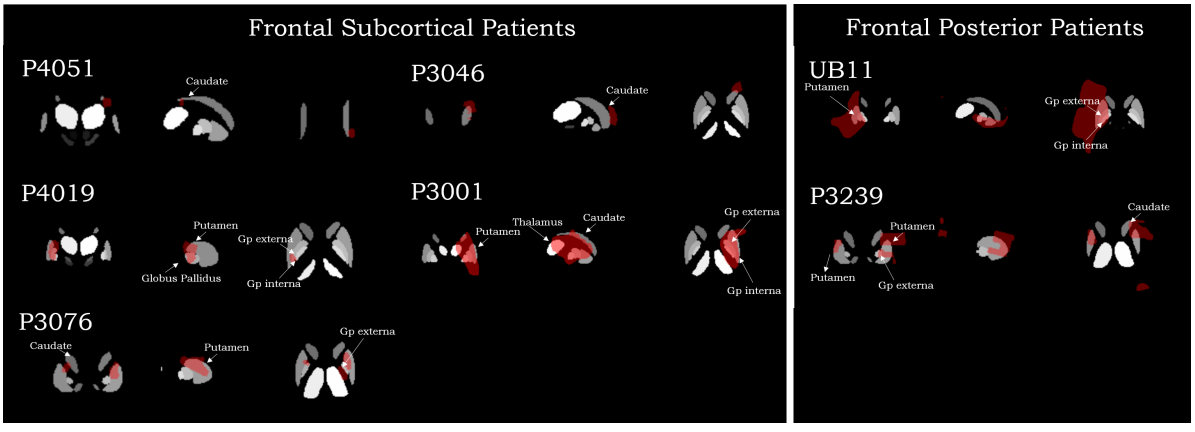


Figure C.3: Lesions displayed on Xiao & Collins (2015) Subcortical Atlas.

C.7 Additional Visualisations of Damage

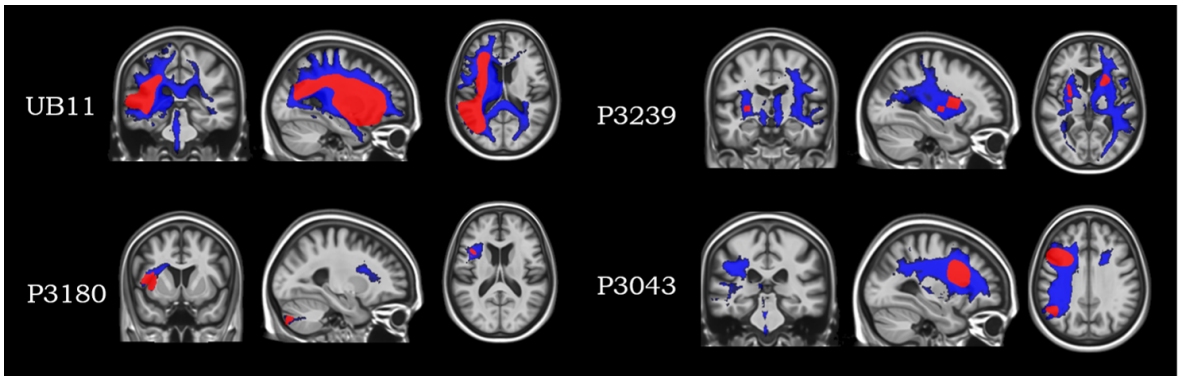


Figure C.4: White Matter Disconnection for Impaired Frontal/Posterior Patients.

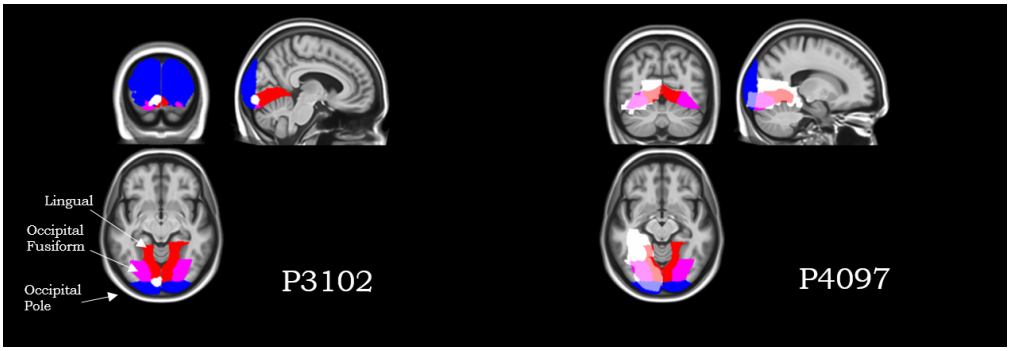


Figure C.5: Occipital Damage Overlap.

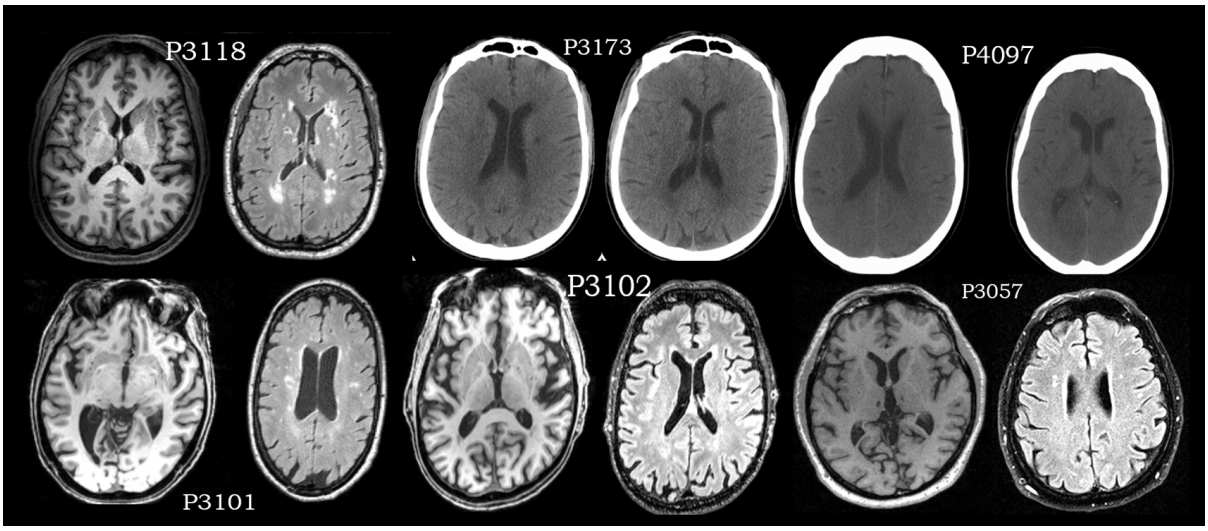


Figure C.6: Patient Scans Showing Signs of SCD.

Appendix D

Dissociating Goal Activation Errors

D.1 Task Instructions

The following task is designed to assess how well you can control your attention. We will ask you to perform a working memory task whilst following a set of rules. First let's learn the rules.
At the beginning of each trial we will show you a colour (symbol). The colour (symbol) tells you the direction you need to turn the dial.



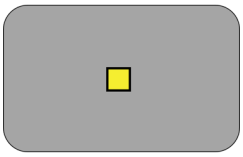
YELLOW (A bar slanted to the LEFT) means anticlockwise.



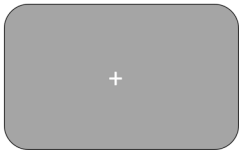
BLUE (A bar slanted to the RIGHT) means clockwise.



First you will see a white cross, please focus your attention on it.



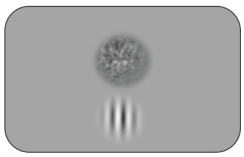
Next you will be shown the colour (symbol).
In this case it is yellow which means anticlockwise.



Another white cross will now appear before the next section of the task.

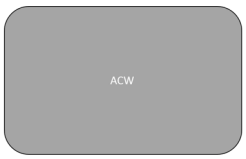


Next, you will see a set of lines. These lines will be presented slanted to a particular orientation (demonstrate different orientations with hand). The aim is to remember the orientation of the lines as precisely as possible.



The lines will disappear quickly. A second set of lines will appear at the bottom (point). You can move them using the dial. The aim is to move the lines to match the orientation you were shown before, whilst turning the dial in the direction indicated by the cue. Try to be as precise as possible.

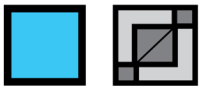
Now let's practice (Demonstrate how to use the dial and allow the participant to practice). After you are happy with the orientation you have entered press down on the top of the dial to continue.



On the next screen this sentence will appear: What cue did you see? Please indicate whether the cue at the beginning of the trial was anticlockwise (yellow), or clockwise (blue) by using the arrow keys (keys are labelled with CW and ACW). Your choice will appear on the screen.
When you are ready to start the next trial press down on the top of the dial.

Now before we begin the practice can you tell be which direction you turn the dial if the trial begins with this cue (point to cue)? and this cue (point to the other cue)?





D.2 Comparison of Response Rules

One potential source of variability in the goal activation paradigm could originate from bias between response rules, clock-wise verses anti-clockwise. In order to examine this, task performance was compared between the two response rules and compared across cue types. It was found that participants were significantly [$F(1,57)=17.96$, $p<.001$] faster to response on clockwise trials (M=578ms, SD=319) as compared to anti-clockwise trials (M=543ms, SD=307), however, there was no main effect of or interaction with cue type. This was corroborated by a Bayesian analysis in which favoured the model only containing the main effect of rule type ($BF_10 = 24.32, \pm 1.49\%$). This slightly slowed responding ($\sim$35ms) did not significantly impact the precision of recall. This was corroborated in a Bayesian top down analysis in which there was moderate evidence in favour of removing the main effect of rule type ($BF_01 = 3.71, \pm 25.26\%$), and weak evidence for removing cue type ($BF_01 = 1.81, \pm 29.17\%$) and the interaction ($BF_01 = 2.70, \pm 30.68\%$) from the model.

The impact of response rule on the proportion of delayed task configuration was examined. There was significant main effect of rule type for delayed configuration [$F(1,57)=4.67$, $p=.04$]. Although there was no main effect of cue type, there was a significant interaction between the terms [$F(1,57)=4.66$, $p=.04$]. Examination of the results demonstrated a negligent difference in the proportion of errors between the clockwise (M=4.8, SD=3.18) and anti-clockwise (M=5.03, SD=3.9) response rules for the symbolic cue group. However, this difference was larger for those using the colour cue with the anticlockwise rule producing a larger proportion of inhibitory errors (M=5.39, SD=5.31) as compared to the clockwise direction (M=3.61, SD=3.74). This was supported by a Bayesian analysis which favoured the model containing the main effect of rule type and the interaction ($BF_10 = 2.29, \pm 2.11\%$) and a top down analysis which gave evidence in favour of removing the main effect of cue type ($BF_01 = 2.26, \pm 4\%$). There was no effect of response

rule observed for incorrect rule recall, goal neglect or distance travelled before correction.

D.3 Distance from Probe to Target Orientation.

Another possible source of error in the current paradigm is the distance between the target orientation and the starting orientation of the onscreen gabor (probe) during orientation recall (the gabor start orientation was always 0^0). With the response rule direction taken into account, the distance between the start orientation and the target orientation was calculated. A mixed multilevel linear model to explore the impact of distance from start orientation to target orientation task performance.

First the effect on reaction time was tested. There was also a significant main effect off probe to target distance (β=-35.49, SE=8.41, t= -4.22, X^2=48.76, p <.001) and a significant interaction between switch type and probe to target distance (β=-36.99, SE=18.08, t = -2.05, X^2=7.46, p=.006). This demonstrated that the relationship between probe to target presentation and reaction time was steeper in the switch as compared to the repeat condition. In compliment with the main analysis, there was a significant switch cost (β=40.05, SE=33.15, t = 1.21, X^2=73.51, p <.001), but no main effect or interaction with of cue type.

The model was run again, this time with absolute angular error as the dependent variable. There was a significant main effect of probe to target distance, (β=-1.64, SE=0.35, t =-4.69, X^2=82.59, p <.001). Even after controlling for this influence the main analysis was replicated, with a cost in precision was observed when switching as compared to repeating the response rule (β=3.14, SE=1.38, t= -2.28, X^2=73.70, p <.001) and a marginally significant interaction between switch type and cue type (β=1.17, SE=1.94, t = 0.60, X^2=5.25, p=.02).

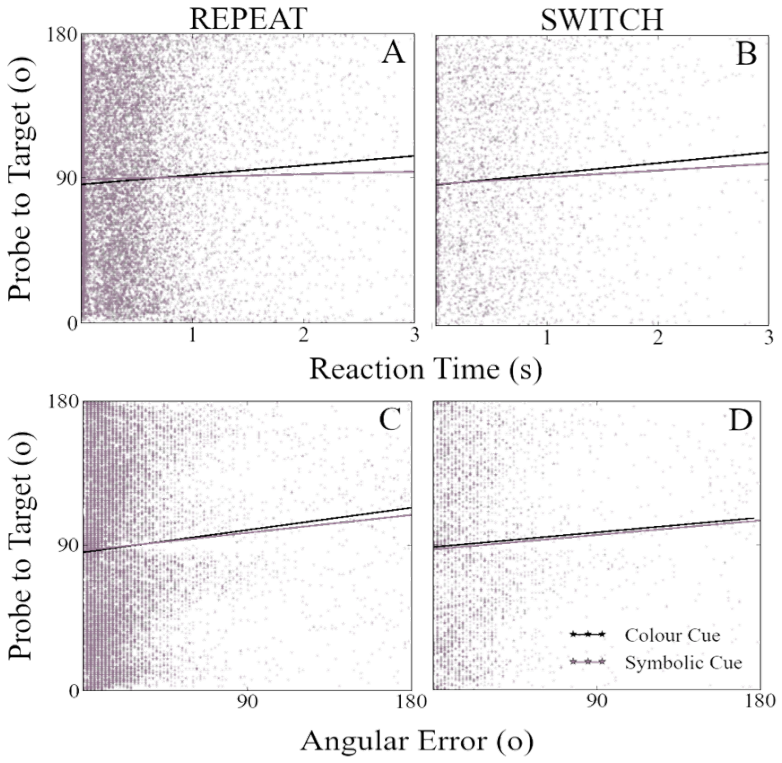


Figure D.1: The relationship between probe to target distance and task performance.

D.4 Target Overshoot

Another form of behaviour frequently observed on the task was characterised by completion of the trial in the correct direction, followed by an adjustment back. This type of behaviour has been termed overshoot and happened on an average of 11.07 trials (SD=36.46). Although this behaviour was discouraged if overtly observed in the practice session, it was not explicitly mentioned in the task instructions and therefore is not treated as a rule violation. Of the sample, 24 participants had occurrences of overshoot. If the median split is taken (11.5) it splits the group into 17 participants who have a few occurrences (M=2.5, SD=1.77, R=1-7) and 7 participants who had frequent occurrences (M=88.86, SD=71.12, R=16-204). Interestingly, for the participants making with few occurrences their performance is on average ∼8 degrees worse, whereas for those with consistent use of overshoot their performance is on average ∼3 degrees more accurate.

Although the participants from above the median split had a fairly consistent reaction time when comparing trials with and without instances of overshoot (without 549.28 ms compared to with 521.50 ms), participants with infrequent occurrences of overshoot demonstrated much slower reaction time on trials with overshoot (1054.11 ms as compared to 715.72 ms). For both groups overshoot slowed down the overall response time, however the group consistently using overshoot slowed down on average 185.43 ms more than the other group. Furthermore, those participants with higher instances of overshoot travelled on average 23 degrees before correction, whereas those inconsistently demonstrating overshoot travelled on average 45 degrees before correction. Taken together this is perhaps indicative of that the adjustment back is a strategy intended to report the orientation more precisely.

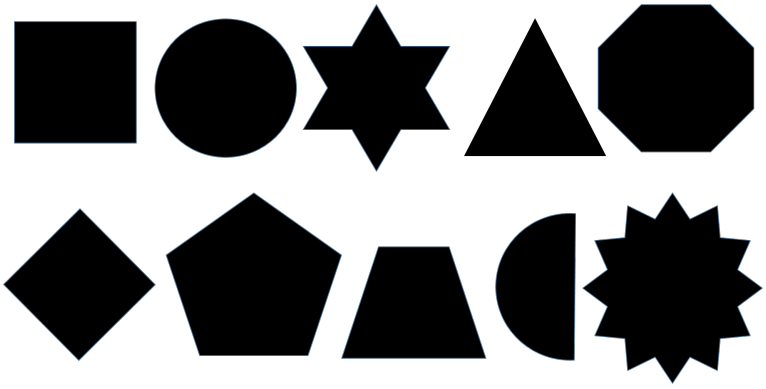
In order to check whether overshoot was influenced by the experimental manipulations a 2x2 model was run examining the main effect of cue and switch type on the proportion of overshoot. There was no main effect of cue or switch type and no interaction between them. This was echoed in a Bayesian analysis which gave evidence in favour of the removal of cue type ($BF_01 = 3.46, \pm 7.06\%$), switch type ($BF_01 = 5.26, \pm 9.83\%$) and the interaction term ($BF_01 = 3.87, \pm 13.62\%$). Therefore, is unlikely that overshoot was a cause of substantial bias in our main analysis.

Appendix E

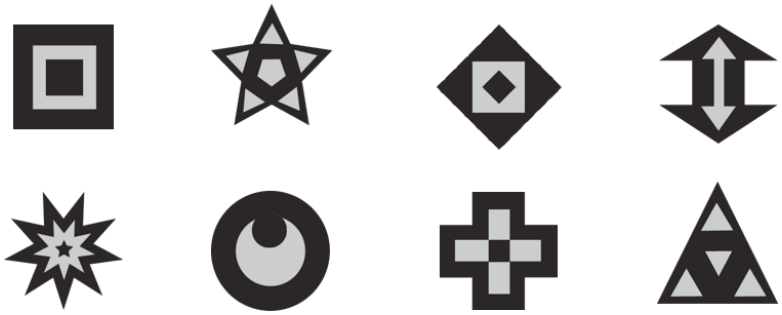
Attention in Processing and Maintenance

E.1 Experimental Stimuli

Experiment 1



Experiment 2 & 3



E.2 Experimental 3 Set-up for Multiple Participants



E.3 Experiment 2 & 3 Instructions

E.4 Experiment 2 & 3 Design Visualisation

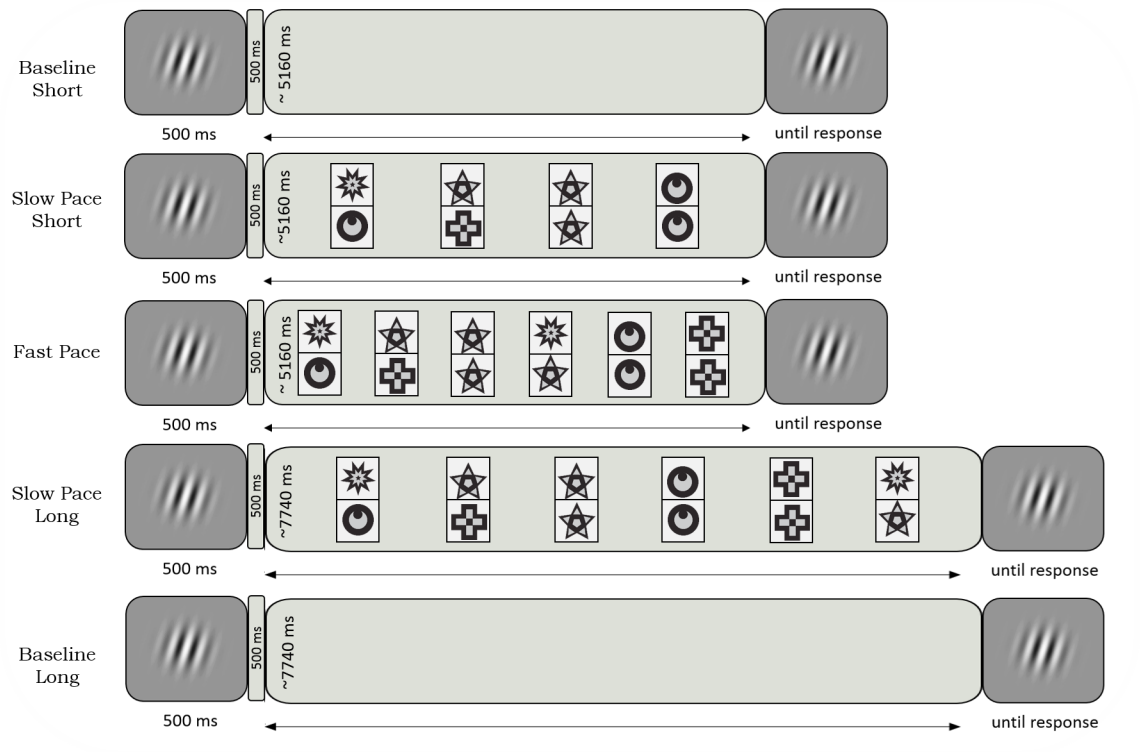


Figure E.1: Design visualisation for experiments 1 & 2.

E.5 Fixation Example

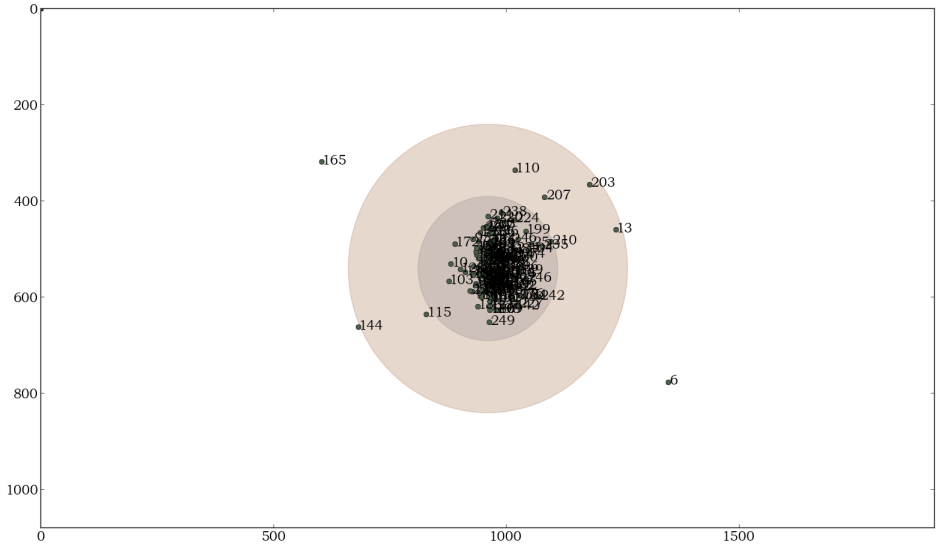


Figure E.2: Fixation cut-off example. Grey circle represents the gabor boundary and the orange the fixation cut off boundary.