Working memory training and transcranial electrical brain stimulation

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Dedicated to my Grandad Roy and Uncle Ant.

Declaration

This dissertation is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the Preface and specified in the text. It is not substantially the same as any that I have submitted, or, is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. I further state that no substantial part of my dissertation has already been submitted, or, is being concurrently submitted for any such degree, diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. It does not exceed the prescribed word limit set by the School of Clinical Medicine and the Board of Graduate Studies.

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Abstract

Working memory training improves performance on trained and untrained working memory tasks, but there is little consistent evidence that these gains benefit everyday tasks that rely on working memory. Evidence has shown that transcranial electrical stimulation (tES) may be an effective tool for enhancing cognitive training and promoting transfer. In the first study, participants completed Cogmed working memory training with either active or sham transcranial random noise stimulation (tRNS). Training was associated with substantial gains on the training activities and on transfer measures of working memory with common processing and storage demands to the training tasks. tRNS did not enhance gains on trained or untrained activities. The second study systematically investigated the boundary conditions to training transfer by testing whether gains following backward digit recall (BDR) training transferred within- and across-paradigm to untrained backward recall and *n*-back tasks with varying degrees of overlap with the training activity. A further aim was to test whether transcranial direct current stimulation (tDCS) enhanced training and transfer. Participants were allocated to one of three conditions: (i) BDR training with active tDCS, (ii) BDR training with sham tDCS, or (iii) visual search control training with sham tDCS. The results indicated that training transfer is constrained by paradigm, but not by stimulus domain or stimulus materials. There was no evidence that tDCS enhanced performance on the training or transfer tasks. The results of Study 1 and Study 2 provide no evidence that tES enhances the benefits of working memory training. The absence of transfer between backward recall training and *n*-back in Study 2 suggested the tasks might tap into distinct aspects of working memory. Consequently, the final study used a latent variable approach to explore the degree of overlap between different forms of backward recall and *n*-back tasks containing digits, letters, or spatial locations as stimuli. The best-fitting factor model included two distinct but related (r = .68) constructs corresponding to backward recall and *n*-back. Both categories of task were linked to a separate fluid reasoning construct, providing evidence that both are valid measures of higher-order complex cognition. Overall, the experiments in this thesis suggest that working memory tasks tap into separate processes and that training may be targeting and improving these distinct processes, explaining the absence of cross-paradigm transfer.

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Chapter 1 Literature review

1.1 Overview

This introductory chapter presents a comprehensive review of the literature that forms the theoretical basis for this thesis. It begins by introducing the concept of working memory in Section 1.2. This section provides a description of various influential models of working memory. In Section 1.3 different categories of behavioural tasks widely used to measure working memory capacity are discussed. Some of these paradigms are used in the experimental studies presented in this thesis. Working memory training is then introduced in Section 1.4, with a focus on the pattern of transfer effects typically observed following training. In Section 1.5 several types of non-invasive transcranial brain stimulation are described and the potential for these techniques to enhance cognitive training is reviewed. The final section of this chapter (Section 1.6) outlines the aims and structure of the thesis.

1.2 Working memory

Working memory is a limited capacity system responsible for the temporary maintenance of task-relevant information during the performance of a cognitive task (Baddeley & Hitch, 1974; Daneman & Carpenter, 1980; Miyake & Shah, 1999). It is an important mental faculty that plays a critical role in learning and is crucial for many complex cognitive abilities, such as reading comprehension (Daneman & Carpenter, 1980), following instructions (Gathercole, Durling, Evans, Jeffcock, & Stone, 2008; Jaroslawska, Gathercole, Allen, & Holmes, 2015), mental arithmetic (Adams & Hitch, 1997; Kyllonen & Christal, 1990) and reasoning (Kane et al., 2004; Kyllonen & Christal, 1990; Suß et al., 2002). Although working memory is a term often used synonymously with short-term memory, there is an important distinction between these two constructs. Working memory is a dynamic system that both stores and processes information (Salthouse, 1990), whereas short-term memory is the system responsible for the passive storage of information over brief periods of time. The term *processing* is used in a narrow sense when describing working memory. Maintenance mechanisms (i.e. rehearsal) are involved in simple span tasks (short-term memory tasks), but the processing involved in working memory tasks requires the manipulation or transformation of information (Oberauer, Süß, Schulze, Wilhelm, & Wittmann, 2000).

There are a number of different theoretical accounts of working memory. In 1974, Baddeley and Hitch introduced the multiple component model. In this framework working memory is compartmentalised into multiple specialised subcomponents (Baddeley & Hitch, 1974; Miyake & Shah, 1999). Alternative frameworks were subsequently proposed including, but not limited to, Cowan's embedded processes model (Cowan, 1988, 1995, 1999, 2005, 2008) and Engle and colleague's model of controlled attention (Engle, Kane, & Tuholski, 1999; Unsworth & Engle, 2007). The main distinction between these models is whether working memory is conceptualised as a distinct system (e.g. Baddeley, 2000; Baddeley & Hitch, 1974), or as a process of controlled attention that serves to maintain activated representations in long-term memory in a highly accessible state under conditions of interference or competition (e.g. Barrouillet, Bernardin, & Camos, 2004; Cowan, 2005; Engle, Tuholski, Laughlin, & Conway, 1999). Although these three competing accounts of working memory differ in terms of their emphasis and terminology (Baddeley, 2012b), there is some consensus among them. For instance, they all view working memory as a capacity limited system, meaning there is an upper limit to how much information can be retained and processed at a given time. They also emphasise a close relationship between working memory and attentional or executive control (Miyake & Shah, 1999). In the following sections these three influential models will be discussed in more detail: see Section 1.2.1 for the multiple component model, Section 1.2.2 for the embedded processes account, and section 1.2.3 for the attentional control framework.

The construct of working memory has been central to many theories of cognition (Miyake & Shah, 1999). It has also been influential in the field of individual differences research (Daneman & Carpenter, 1980; Engle, Kane, et al., 1999; Kyllonen & Christal, 1990; Oberauer et al., 2000). The limited capacity of working memory constrains performance on a number of cognitive tasks (Oberauer et al., 2000). Individual differences studies have revealed strong relationships between working memory capacity and other cognitive abilities, including reasoning ability, which is often used as a proxy of general fluid intelligence (Ackerman, Beier, & Boyle, 2002; Colom, Rebollo, Palacios, Juan-Espinosa, & Kyllonen, 2004; Conway, Cowan, Bunting, Therriault, & Minkoff, 2002; Engle, Laughlin, et al., 1999; Hambrick, 2003; Kane et al., 2004; Kyllonen & Christal, 1990; Mackintosh & Bennett, 2003; Suß et al., 2002). This research has been influential in validating working memory measures (i.e. determining whether tasks are measuring the same underlying theoretical construct; e.g. Kane, Conway, Miura, & Colflesh, 2007; Schmiedek, Hildebrandt, Lövdén, Lindenberger, & Wilhelm, 2009) and, more recently, in investigating the underlying structure of working memory using latent variable methods (e.g. Alloway, Gathercole, & Pickering, 2006). This will be discussed further in Chapter 4.

1.2.1 The multiple component model of working memory

The multiple component model, also known as the tripartite model, is arguably the most well-known and influential theoretical framework of working memory. It has inspired a wealth of research across experimental, cognitive, and developmental psychology. The original model proposed by Baddeley and Hitch in 1974 comprised three main components: an attentional control system called the central executive, and two modality-specific passive storage systems known as the phonological loop and visuo-spatial sketchpad. The phonological loop is responsible for the storage and manipulation of verbal information, whereas the visuo-spatial sketchpad maintains and processes visually- and spatially-coded information (Baddeley, 1986, 1992; Baddeley & Hitch, 1974).

The two systems serve only as temporary storage and rehearsal mechanisms, while the central executive is involved with allocation of attention or the simultaneous processing of information. Together, the three component subsystems provide a workspace for cognitive activity (Smith & Kosslyn, 2007). A fourth component, the episodic buffer, was subsequently added to the model in 2000. This additional component serves as an interface between the subsystems of working memory, long-term memory, and executive control (Baddeley, 2000; Baddeley, Allen, & Hitch, 2011). A widely cited version of the model, often used in empirical research, is presented in Figure 1.1 (Baddeley, 2000). Each subcomponent will be discussed in detail in the following sections: see Section 1.2.1.1 for the phonological loop, Section 1.2.1.1 for the visuo-spatial sketchpad, Section 1.2.1.3 for the central executive, and Section 1.2.1.4 for the episodic buffer.

Evidence for the structure of the model (see Figure 1.1.) has been provided by studies using the dual-task methodology. An assumption of the model is that if two tasks engage the same component of working memory (e.g. if two tasks both require visuo-spatial resources thereby taxing the visuo-spatial sketchpad subsystem), they cannot be performed as successfully together as they would if tasks were undertaken separately. Further, if two tasks make use of different components in working memory (e.g. if one tasks requires visuo-spatial resources thereby taxing the visuo-spatial sketchpad, while the other requires verbal resources taxing the phonological loop) then it should be possible to perform them equally well together as separately (Eysenck, 2001). The continuous repetition of a word (known as articulatory suppression) has been shown to impair verbal serial recall because it prevents articulatory rehearsal in the phonological loop (Alloway, Kerr, & Langheinrich, 2010; Baddeley, Lewis, & Vallar, 1984), but it does not interfere with memory for spatial locations (Alloway, Kerr, & Langheinrich, 2010; Smyth, Pearson, & Pendleton, 1988) suggesting that it does not require the resources of the visuo-spatial sketchpad. In contrast, spatial tapping of specific locations draws on visuo-spatial resources and disrupts spatial serial recall (Alloway et al., 2010; Smyth & Pendleton, 1989; Vandierendonck, Kemps, Fastame, & Szmalec, 2004), but leaves verbal recall unaffected (Alloway et al., 2010; Morris, 1989). These behavioural findings of double dissociations under dual-task conditions, along with evidence from neuropsychological patients (for an overview, see Meiser & Klauer, 1999) and developmental studies (e.g. Alloway, Gathercole, & Pickering, 2006), provide support for the separability of the verbal and visuo-spatial subcomponents of working memory. Studies have also shown that interference tasks that are attentionally demanding (e.g. random letter generation) cause the most substantial disruption to working memory tasks (e.g. Robbins et al., 1996). This is because attentionally demanding tasks block the operation of the central executive and therefore have the most profound effect on working memory performance.

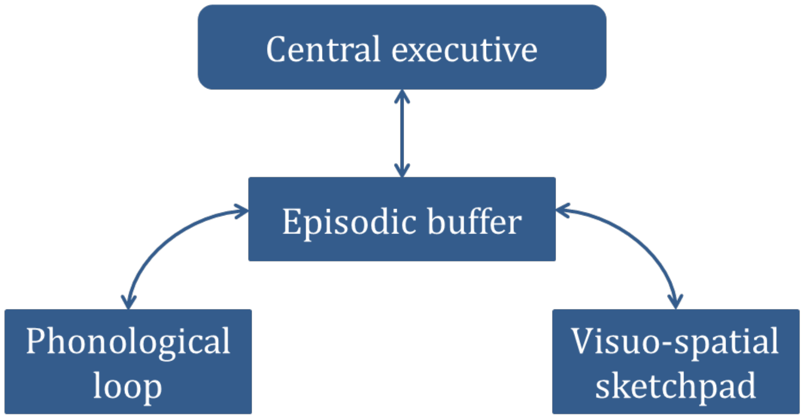


Figure 1.1 – A simplified representation of the multi-component model of working memory adapted from Baddeley (2000).

1.2.1.1 The phonological loop

The phonological loop is a specialised storage system for acoustic and speech-based information (Baddeley, 1986). This subsystem is thought to have evolved to support the acquisition of language (Baddeley, 2012a), as it preserves the order in which words are presented and allows the temporary representation of a phonological sequence to be retained so that new vocabulary can be encoded into long-term memory (Baddeley, Gathercole, & Papagno, 1998). The phonological loop comprises two further subcomponents: a short-term phonological store, which serves to hold verbal memory traces, and an articulatory rehearsal mechanism that can revive memory traces (Baddeley, 1986).

The phonological store acts as the mind's inner ear and holds information in a sound-based way as auditory-phonological code (e.g. spoken words). The store is passive, meaning information is held for approximately 2 s, after which time it is subject to rapid decay (Baddeley, 1986). In order to prevent information from being forgotten it must be attended to or refreshed via the active process of articulatory rehearsal, which occurs in the phonological loop. Rehearsal involves some kind of covert verbalisation (i.e. internal speech; Henry, 2012); it is linked to speech production and acts as the mind's inner voice. Rehearsal refreshes information held in the phonological store and prevents decay by reactivating fading phonological representations (Baddeley, 2012b). The phonological loop is named as such because information is transferred through the system in a loop; information enters the store for a brief period before the articulatory rehearsal mechanism is then used to recite the information so that it can enter the store again. The articulatory control mechanism also serves to convert visual material (i.e. written verbal information) into articulatory (sound-based) code so it can enter the phonological store. Auditory verbal information (e.g. spoken words) enters the store directly, but visually presented material (e.g. written words) must first be converted into phonological code via internal articulation before it can enter the store (Baddeley, 1986).

Early empirical evidence for the existence of a speech-like memory store was provided by the phonological similarity effect, whereby sequences of items that are acoustically similar (e.g. *man, mat, cap, can, cat*) are more difficult to recall than those that sound more distinct (e.g. *day, few, pen, hot, cow*; Baddeley, 1966; Conrad, 1964; Conrad & Hull, 1964). The effect arises through confusion in the activation of similar sound-based codes for different items in the phonological loop (Smith & Kosslyn, 2007), suggesting verbal information is phonologically or acoustically coded in working memory (Baddeley, 1966; Conrad & Hull, 1964). Another key finding is the word length effect, whereby participants find it easier to recall a sequence of short words (e.g. *sum, wit, twice, bond, harm*) versus long words (e.g. *university, physiology, individual, considerable, immediately*; Baddeley, Thomson, & Buchanan, 1975). This effect does not depend on the number of syllables of words *per se*, but on the length of time taken to articulate them (Baddeley, 1986). For example, performance is worse for two-syllable words with long vowel sounds compared to those with short vowel sounds (e.g. *harpoon* versus *wicket*; Baddeley, Thomson, & Buchanan, 1975). The multiple component model assumes that subvocal rehearsal occurs in real time. Thus, the word length effect arises because words that take longer to vocalise are rehearsed at a slow rate resulting in more time for the memory trace to deteriorate (Baddeley, 1986, 2012b). Evidence of the word length effect supports the existence of an articulatory subvocal rehearsal process (Baddeley, 1986, 2012b).

Articulatory suppression is a technique used to interfere with the rehearsal of phonological information. It requires participants to continuously repeat an irrelevant word, such as *the, the, the* (Baddeley, 2012b). The effect of suppression on both the word length and phonological similarity effects depends on the presentation modality of the materials. Both effects are abolished by suppression when the items for recall are presented visually, but remain when auditory items are presented (Baddeley et al., 1975). This is because visually presented items must be transformed into a phonological code via subvocalisation in the phonological loop to gain access to the store, whereas auditory material enters the phonological store automatically (Baddeley et al., 1984). Articulatory suppression is thought to prevent visual stimuli from being transformed into a phonological code because the loop is rendered unusable by interference from articulatory suppression (Baddeley, 1986; Baddeley et al., 1984, 1975).

1.2.1.2 The visuo-spatial sketchpad

The visuo-spatial sketchpad is responsible for the temporary storage and processing of visual and spatial information (Baddeley, 1986), and potentially kinaesthetic information (Smyth & Pendleton, 1990). This subsystem allows images to be manipulated in the mind's eye. It plays a role in navigation and following instructions (Garden, Cornoldi, & Logie, 2002; Jaroslawska et al., 2015) as it is responsible for keeping track of locations in relation to other objects in the environment (Baddeley, 1997). Early evidence demonstrating that visuo-spatial information required a specialised system comes from Baddeley, Grant, Wight and Thomson (1973). They found that performing a spatial tracking task, which involved keeping a stylus in contact with a moving spot of light, interfered with participants' ability to recall visuo-spatial (easily visualised) sequences, but not nonsense (difficult to visualise) sequences, of digits in a matrix.

This demonstrates there is a system for storing information using visual imagery and another that uses purely verbal encoding.

In 1995, Logie proposed that the visuo-spatial sketchpad could be further segmented into two components analogous to the phonological and articulatory rehearsal components of the phonological loop (Baddeley, 2012a). The first component, termed the visual cache, acts as a visual store and plays a role in retaining visual patterns (Baddeley & Logie, 1999; Logie, 1995). It is presumed to retain object information such as form and colour, and is closely linked with the visual perceptual system (Logie & Pearson, 1997). Information in this passive visual store is subject to time-based decay and interference (Logie, 1995), thus it must be actively rehearsed to be maintained. This is achieved by the second subcomponent, known as the inner scribe (Baddeley & Logie, 1999; Logie, 1995; Logie & Pearson, 1997). This is an active spatially-based system that is presumed to store information related to spatial sequences and is closely linked to planning and control of movement to targets in space (Logie & Pearson, 1997).

A number of studies have demonstrated a dissociation between visual and spatial working memory (for a review, see Klauer & Zhao, 2004). For example, they can be selectively disrupted by specific concurrent interference tasks. Exposure to tones played from different positions disrupts the retention of spatial locations but not the vividness of mental imagery (Smyth & Scholey, 1994), while exposure to dynamic visual noise interferes with the vividness of mental imagery (Baddeley & Andrade, 2000) but not memory for spatial locations (Pearson & Sahraie, 2003). Further evidence for the fractionation of the visual *what* and spatial *where* comes from double-dissociations of visual and spatial memory performance on tasks conducted in neuropsychological and clinical patients (Carlesimo, Perri, Turriziani, Tomaiuolo, & Caltagirone, 2001; Luzzatti, Vecchi, Agazzi, Cesa-Bianchi, & Vergani, 1998; Owen, Iddon, Hodges, Summers, & Robbins, 1997; Postle, Jonides, Smith, Corkin, & Growdon, 1997; Vicari, Bellucci, & Carlesimo, 2006). In addition, studies have shown that visual and spatial memory abilities follow different developmental trajectories during childhood. While visual working memory appears to develop moderately quickly from childhood to adulthood, the rate at which spatial working memory develops is relatively slower and steadier (Logie & Pearson, 1997; Pickering, Gathercole, Hall, & Lloyd, 2001). These converging findings provide evidence for distinct subcomponents for the retention of visual and spatial information.

1.2.1.3 The central executive

The central executive is the component that has overall control of the working memory system (Baddeley & Logie, 1999). The phonological loop and visuo-spatial sketchpad are often referred to as the slave systems as they are not *clever*; in other words they are not involved in the control of attention or in decision-making (Baddeley, 2012b). This job falls to the central executive, which is responsible for monitoring and coordinating the operation of the slave systems.

Initially, the central executive was described as a domain-general processor capable of attentional focus and it was also thought to have some capacity for storage and interfacing with long-term memory. In the original multiple component model, the central executive was lacking in detail (Baddeley & Hitch, 1974). Baddeley (1986) attempted to advance the concept by adapting the Norman and Shallice model of attentional control (Norman & Shallice, 1980) in which it was proposed attentional control is divided between two processes. The first relies on the automatic control of behaviour by habit patterns or schemas that are triggered by environmental cues. The second is an attentionally limited controller called the supervisory attentional system (SAS) that intervenes when routine control is insufficient (e.g. in tasks where planning or decision making is required).

In a further attempt to understand its functions, Baddeley (1996) endeavoured to fractionate the central executive into four areas, known under an umbrella term as *executive functions*. These included the capacity to: (1) coordinate performance of two concurrent tasks (focus attention), (2) switch between retrieval strategies (attentional control), (3) selectively attend to a stimulus and filter out irrelevant information, and (4) activate and hold information from long-term memory. The latter of these functions subsequently led to a revision of the central executive. The central executive did not have a mechanism for interacting with long-term memory, or for integrating information from different subsystems using different codes (i.e. verbal and visuo-spatial) without some sort of common storage system. Therefore, Baddeley (2000) introduced a new component to the working memory model called the episodic buffer (see Section 1.2.3.3). The addition of this component meant the central executive was no longer regarded as having capacity for storage, and it is now thought to only be responsible for the control and allocation of attention (Baddeley, 2000, 2012a).

1.2.1.4 The episodic buffer

In 2000, Baddeley added the episodic buffer to his model. The original tripartite model had no mechanism for allowing the phonological and visuo-spatial subsystems to interact, and offered no explanation for how working memory was associated with conscious awareness (Baddeley, 2003). The episodic buffer was developed to account for these issues and to also explain how working memory communicates with long-term memory (Baddeley, 2000). The buffer is assumed to be a limited-capacity store that uses multi-dimensional coding to bind together information and form integrated episodes or chunks (Baddeley, 2000, 2003, 2012b). It is a separate subsystem within working memory that is controlled by the central executive, although it can also be regarded as the storage component of the central executive (Baddeley, 2003). It acts as a global workspace and can be accessed by the central executive through conscious awareness (Baddeley, 2000, 2003). Generally, the system provides a temporary interface between the phonological loop, the visuo-spatial sketchpad, and long-term memory, and is responsible for integrating information from these different modalities (Baddeley, 2000).

1.2.2 The embedded processes model of working memory

Cowan's embedded processes model proposes that working memory is an activated portion of long-term memory, rather than a distinct short-term memory system (Cowan, 1988, 1995, 1999, 2005, 2008). According to this view, the idea of working memory is that task-relevant information must be made accessible for a temporary period of time (Cowan, 1999). This model assumes two embedded levels of activation. The first involves long-term memory representations, whereby an embedded subset of information in the long-term store takes on a temporarily heightened state of activation (Cowan, 1995). This level is not capacity-limited and so any information present in long-term memory can be activated. However, activation of long-term representations is time-limited and subject to decay and interference unless refreshed (Cowan, 1999, 2008). The second level, which is embedded within activated long-term memory, is called the focus of attention (Cowan, 1995). Information is made particularly salient when it falls under the focus of attention and it is thought to be limited in capacity to between three and five representational chunks (Cowan, 1995, 1999, 2001, 2010). These chunks can contain more than a single piece of information (Cowan, 2001, 2005). For example, an object encoded in working memory may contain multiple features such as location, colour, and shape that are combined to form an integrated chunk of information (Cowan, 2005). According to Cowan

(1995), the capacity-limited focus of attention is the primary limiting factor in the working memory system.

The embedded processes model also assumes a central attentional control component that plays a role in processing and reactivating items in memory (Cowan, 1988). Both voluntary and involuntary processes work together to control the focus of attention (Cowan, 1988, 1999). This attentional control system (akin to the central executive in Baddeley's model) uses volitional, effortful processes to control the focus of awareness and acts on recently activated sensory and categorical features from long-term memory (Cowan, 2005). Automatic, subconscious processes orient attention to stimuli that changes, or habituates to stimuli that do not change (Cowan, 1988). Individuals are consciously aware of items being processed by the central executive, whereas they are unaware of information being processed automatically (Cowan, 1988). For memory items to be maintained in the focus of attention they must be reactivated and the model proposes that the central executive may carry out an operation to keep items active in memory (Cowan, 1999). This could be achieved through mechanisms such as subvocal rehearsal or mental imagery. Alternatively, the model suggests that a different process of attentional refreshing is used to reactivate fading memory traces by recirculating them in the focus of attention (Cowan, 1992, 1995; see also Barrouillet et al., 2004; Johnson, 1992). During this process, sequential searching or scanning is used to reactivate items by moving the focus of attention to memory traces recurrently (Cowan, 1992, 1999).

1.2.3 The attentional control model of working memory

Engle and colleagues define working memory as the domain-general capacity for controlled and sustained attention in the face of interference or distraction (Engle, Kane, et al., 1999). The attentional control model has some similarities with Cowan's model and also views working memory as an activated subset of long-term memory traces (Engle & Kane, 2004; Engle, Kane, et al., 1999; Unsworth & Engle, 2007). However, there are some significant distinctions, namely the model's strong emphasis on the importance of inhibitory processes that are critical for protecting the contents working memory from potential disruption. Therefore, working memory reflects the ability for controlled attention, which is required to keep relevant information (e.g. task goals, stimulus, context) in a highly active and easily accessible state, especially when faced with interference or competition when it has to inhibit irrelevant information (Engle, Laughlin, et al., 1999; Engle & Kane, 2004; Engle, Kane, et al., 1999; Kane, Bleckley, Conway, & Engle, 2001).

According to the attentional control model, the working memory system consists of two qualitatively and functionally distinct subsystems, referred to as primary and secondary memory (e.g. Unsworth & Engle, 2007; Unsworth & Spillers, 2010). Primary memory serves to maintain distinct representations for ongoing processing by means of continued allocation of attention, and secondary memory is a probabilistic cue-dependent search component (Unsworth & Engle, 2007). Primary memory is an attentional process that has the ability to shield items from interference and is thought to have a capacity limit of approximately four items (e.g. Atkinson & Shiffrin, 1968; Cowan, 2001). Information is held in primary memory only as long as it is actively attended to; otherwise it is displaced and must be retrieved from secondary memory via a competitive cue-dependent search process (Unsworth & Engle, 2007). One key to successful retrieval is the ability to effectively restrict the search process to only relevant information by using different cues (e.g. categorical, temporal, or contextual). Once the search set has been delimited, representations can be sampled and retrieved more easily (Unsworth & Engle, 2007).

Engle and colleagues used a correlational approach to understand the structure of working memory. Accordingly, in their framework individual differences in working memory capacity are not determined by how many items can be stored *per se*, but reflect dissimilarities in the ability for controlled processing (Engle, 2002; Engle & Kane, 2004). Supporting evidence is provided by studies in which large numbers of individuals perform working memory capacity tests and are then grouped as high or low ability based on their memory span. Performance of these two groups can be compared across a number of measures to investigate what might underpin differences in their memory span (e.g. Engle, Laughlin, et al., 1999; Engle & Kane, 2004; Kane et al., 2001; Kane, Poole, Tuholski, & Engle, 2006; Kane & Engle, 2003; Rosen & Engle, 1997). Evidence has shown that individuals with low working memory spans perform more poorly than those with high spans on tasks that do not place a significant burden on memory capacity but do require attentional control. For example, Kane and Engle (2003) examined performance on the Stroop task, which is a classic interference task that requires active goal maintenance and inhibition of competing stimulus representations. Larger memory spans were found to predict better performance on the Stroop task, suggesting differences in working memory capacity reflect differences in executive attentional control.

1.3 Measuring working memory

The capacity of working memory can be measured using a variety of tasks. Firstly, it is important to make a distinction between tasks that measure short-term memory and those that engage working memory. Short-term memory simply involves the temporary storage of information and can therefore be measured using simple span tasks (i.e. assessments requiring the storage and immediate serial recall of phonological or visuo-spatial information such as digits or spatial locations). However, working memory tasks must also engage the central executive, and thus involve both storage and processing (Daneman & Carpenter, 1980). The most common categories of working memory task include: serial recall tasks, interpolated processing tasks, and updating tasks (see Figure 1.2; each category will be discussed in more detail in the following sections: see Section 1.3.1 for serial recall tasks, Section 1.3.2 for interpolated processing tasks, and Section 1.3.3 for updating tasks). As well as being measures of working memory capacity, these tasks are also used as training activities in cognitive training studies, as will be discussed in more detail in Chapter 3.

Working memory consists of multiple interacting systems. For example, separate components for different kinds of verbal and visuo-spatial information (Baddeley & Hitch, 1974). Working memory tasks can be can be operationalised in a number of ways to tap into these different components. Task content (memory items) can be manipulated to specifically target verbal or visuo-spatial working memory by using digits or spatial locations, respectively. Task stimuli can also be manipulated within domain (e.g. digits, letters, or words within the verbal domain). Verbal information can also be presented auditorily or visually. The working memory system also involves different types of processes, including memory and attention (Conway, Macnamara, & Engel de Abreu, 2013). These different processes might have different mechanisms for encoding, representing and maintaining stimuli, and for manipulation, recognition and retrieval (Conway et al., 2013). When measuring working memory capacity it is important to consider that tasks might recruit different processes differentially (Conway et al., 2013). The tasks might also vary in terms of their structural properties (e.g. interpolated storage items with irrelevant distractor activities versus recalling a sequence in reverse order, see Figure 1.2). Despite these differences, the general consensus is that a working memory task is defined by the requirement to store information while engaging in simultaneous effortful processing. This could take the form of processing the storage items, or other material, or it could be the requirement to control attention during storage (Baddeley & Hitch, 1974; Daneman & Carpenter, 1980; Engle, Kane, et al., 1999; Kane et al., 2001).

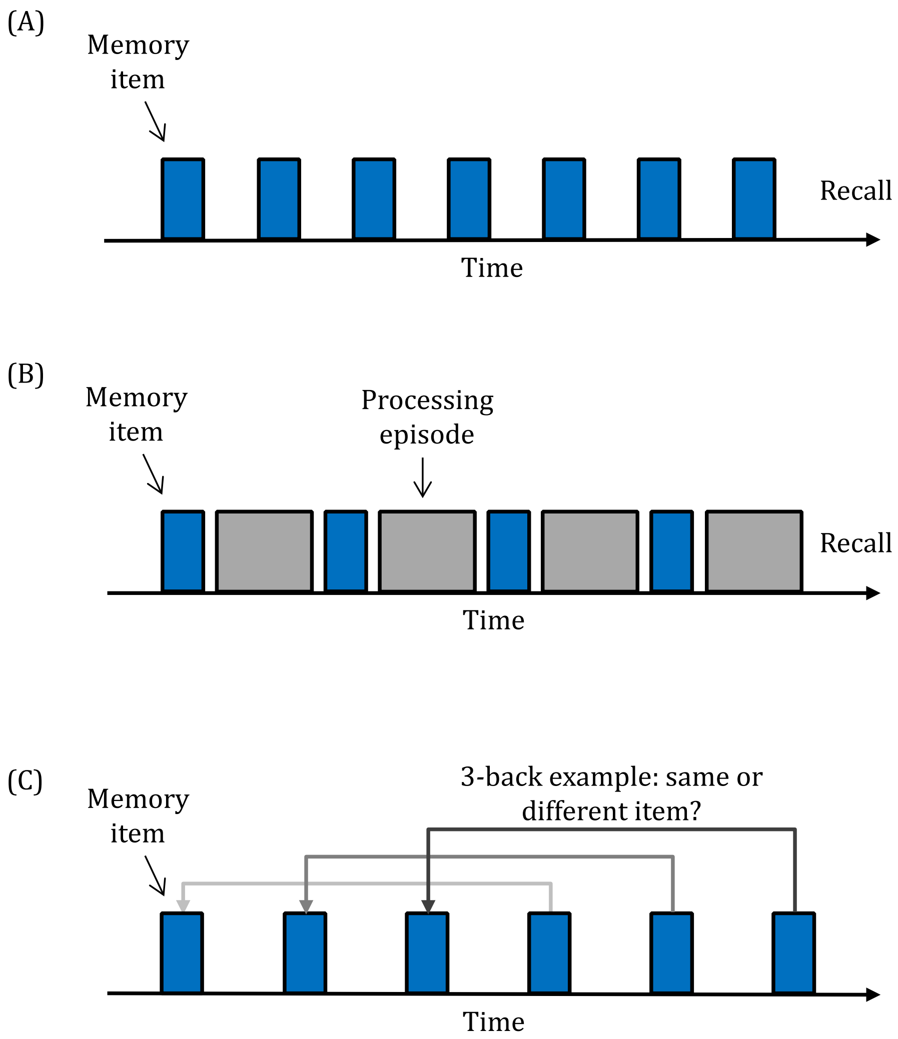


Figure 1.2 – A schematic representation of the structure of different working memory paradigms including: (A) serial recall tasks, (B) interpolated processing tasks, and (C) updating tasks (an example of *n*-back is shown).

1.3.1 Serial recall tasks

Serial recall tasks involve a list of stimuli presented one item at a time. See Figure 1.2 (A) for an illustration of the serial recall task structure. As discussed previously, there is a distinction between simple span measures of short-term memory, which involve the immediate serial recall of stored items (e.g. forward digit recall), and simple span tasks with intrinsic processing, which require participants to transform the storage material prior to recall (e.g. backward digit recall). Backward recall tasks are similar to simple span tasks except the participant must recall the stimuli in the reverse order. Therefore, the internal representation of the list must be transformed prior to recall (Conway et al., 2013). The difficulty of the task, or load on working memory, can be made greater by increasing list length.

Serial recall tests are simple to administer and can be found in a number of widely used standardised cognitive assessments, such as the Children's Memory Scale (CMS; Cohen, 2001), the Wechsler Memory Scale (WMS; Wechsler, 2009), the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 2008), the Wechsler Intelligence Scale for Children (WISC; Wechsler, 2003), and the Automated Working Memory Assessment (AWMA; Alloway, 2007). These tools are useful in developmental research as they enable researchers to track memory span from early childhood through to adulthood. Standardised assessments are also commonly used in educational and clinical practice to identify individuals with learning difficulties.

1.3.2 Interpolated processing tasks

Interpolated processing tasks, commonly known as complex span tasks, are well-established measures of working memory capacity (Daneman & Carpenter, 1980; Schmiedek et al., 2009). They were designed based on the principles of the multiple component model (Baddeley & Hitch, 1974; Conway et al., 2005), with the purpose of tapping into both the storage and processing functions of working memory (Daneman & Carpenter, 1980). During complex span, to-be-remembered items (e.g. digits) are presented between interleaved episodes of a processing task, such as solving maths problems (Conway et al., 2005, 2013). Typically, one item is presented between each processing episode. Participants then recall the sequence of memory items in forward serial order. See Figure 1.2 (B) for an illustration of the complex span task structure. Complex span tasks are essentially dual-tasks as they require the simultaneous performance of a primary simple span task and secondary disruptive processing activity (Conway et al., 2013; Schmiedek, Lövdén, & Lindenberger, 2014). The load on working memory can be manipulated by increasing or decreasing the number of to-be-remembered items and corresponding interleaving processing episodes.

Complex span tasks can be operationalised in different ways by manipulating the storage materials as well as the nature of the processing task. There are many examples of complex span in both the verbal and spatial domains, including reading span (Daneman & Carpenter, 1980; Engle, Laughlin, et al., 1999; Kane et al., 2004; Schmiedek et al., 2009), operation span (Engle, Laughlin, et al., 1999; Kane et al., 2004; Turner & Engle, 1989; Unsworth, Heitz, Schrock, & Engle, 2005), counting span (Case, Kurland, & Goldberg, 1982; Engle, Laughlin, et al., 1999; Kane et al., 2004; Schmiedek et al., 2009), navigation span (Kane et al., 2004), rotation span (Kane et al., 2004; Schmiedek et al., 2009; Shah & Miyake, 1996), and symmetry span (Kane et al., 2004; Redick et al., 2013). Generally, these different versions of complex span follow the same basic structure but vary in terms of the type of stimuli presented for the primary memory span task (e.g. digits, letters, words, spatial locations), and the type of secondary processing task (e.g. reading sentences aloud, solving simple arithmetic problems, judging the veracity of sentences, rhyme judgement of letters, counting the number of objects in an array, judging shape symmetry, pattern matching; Conway et al., 2013). The structure of complex span tasks can also differ slightly; sometimes the primary memory task is embedded in the secondary task. For example, in another version of complex span, participants complete reading comprehension as the processing task, whilst also encoding the final word of each sentence as the primary task (Daneman & Carpenter, 1980).

1.3.3 Updating tasks

Working memory can also be assessed by tasks involving the continuous updating of memory items. The process of updating is considered a fundamental characteristic of the working memory system (Ecker, Lewandowsky, Oberauer, & Chee, 2010; Miyake et al., 2000). During cognitive activities, task-relevant information must be readily accessible and so must be continuously updated in accordance with changes in the environment (Conway et al., 2013). There are different paradigms that tap into working memory updating including *n*-back, running span, alpha span, and memory-updating tasks.

n-back is arguably the most widely used updating paradigm. In this task a continuous stream of stimuli (e.g. digits) is presented. Items are shown one at a time, and participants must decide whether the current item being presented matches one that was presented *n* items back in the sequence. See Figure 1.2 (C) for an illustration of the *n*-back task structure. To successfully complete this task, representations of memory items must be successively updated as new information becomes available (Szmalec, Verbruggen, Vandierendonck, & Kemps, 2011). This paradigm is frequently used in neuroimaging experiments (Owen, McMillan, Laird, & Bullmore, 2005) due to the simple response requirements and the ability to tightly control the timing of stimulus presentation (Conway et al., 2013).

Another common updating task is running span (e.g. Harrison et al., 2013; Pollack, Johnson, & Knaff, 1959). In this task participants are again shown a continuous series of items presented one at a time. The sequence finishes at an unknown point, at which time the participant must recall the most recent *n* items (e.g. the last five digits). Crucially, the sequence length is unpredictable. Alpha span is also used to tap into updating. In the original version participants were presented with a list of words and required to recall the first letter of each word in the correct alphabetical order (Craik, 1986; Oberauer et al., 2000; Suß et al., 2002). In a recently adapted version of this task, a sequence of 10 letters is presented, each with a corresponding digit (Schmiedek et al., 2009). Participants must continuously put the letters in alphabetical order and respond to each letter-digit pair to indicate whether the digit corresponds to the current alphabetical position of the letter relative to the others.

An alternative updating paradigm is the memory-updating task, during which individuals must update memorised digits by arithmetic operations that are performed on them (Oberauer et al., 2000; Salthouse, Babcock, & Shaw, 1991; Schmiedek et al., 2009). For example, participants are required to remember a series of digits presented in individual boxes that are shown in a row at the beginning of a trial (Schmiedek et al., 2009). Each of the digits must then be independently updated according to a corresponding arithmetic operation appearing in an associated box below where a particular digit appeared. Participants must then recall the final values.

When using any variation of updating tasks the load on working memory can be increased or decreased, for example by varying the *n* level in the *n*-back task (e.g. increasing from one-back to two-back) or changing the number of items for recall in the running span task. Although distinct in terms of their structural properties and task demands, updating tasks share some common features. For example, they all require the building, maintenance, updating, and releasing of arbitrary temporary bindings between content (i.e. stimuli) and context (e.g. serial position; Oberauer, Süß, Wilhelm, & Sander, 2007; Schmiedek et al., 2009). Performance in updating tasks also depends on the ability to resist proactive interference (i.e. the disruptive effect of prior information/learning on remembering new information). For example, during the *n*-back task it can be difficult to distinguish between relevant and irrelevant items (Szmalec et al., 2011).

1.4 Working memory training

Working memory underpins practical abilities such as following instructions (Engle, Carullo, & Collins, 1991; Jaroslawska et al., 2015), mathematical calculation (Raghubar, Barnes, & Hecht, 2010), reading comprehension (Daneman & Carpenter, 1980), and maintaining focused attention (Gathercole, Durling, et al., 2008; Kane et al., 2001). It is considered one of the fundamental building blocks of learning, and low working memory is associated with poor academic progress in school (e.g. Gathercole, Alloway, et al., 2008). Impairments in working memory are also typical among individuals with developmental disorders such as attention-deficit hyperactivity disorder (ADHD; Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005), dyslexia (Jeffries & Everatt, 2004), dyscalculia (Mammarella, Hill, Devine, Caviola, & Szucs, 2015), and specific language impairment (SLI; Archibald & Gathercole, 2006), where they are linked to difficulties in paying attention and learning. Therefore, there is a need for remediation of working memory problems in clinical and educational practice.

Traditionally, working memory was thought to be a fixed trait that is unchangeable once adult levels of performance are reached (Johnson & De Haan, 2011). More recently, studies have claimed that working memory capacity may be flexible and can be enhanced through intensive computerised training on adaptive memory tasks (e.g. Klingberg, 2010; Morrison & Chein, 2011). A standard working memory training protocol typically involves practice on a number of activities designed to tax working memory for approximately 15 hr (Klingberg, 2010). The training regime is adaptive; the difficulty level of the tasks is adjusted on a trial by trial basis so that it is titrated to the current ability level of each participant (Klingberg, 2010). Individuals who receive active adaptive training are usually compared to a control group who either receive no training (no-intervention), a placebo/low dose of working memory training (i.e. non-adaptive training capped at a low memory load), or adaptive training of another cognitively demanding task with no memory load. Substantial and long-lasting improvements have been widely reported on untrained working memory measures following training (e.g. Dunning, Holmes, & Gathercole, 2013; Klingberg et al., 2005), although there are limits on the degree to which performance transfers to untrained memory tasks (Gathercole, Dunning, Holmes, & Norris, 2018). Transfer following training will be discussed further in the following section (see Section 1.4.1).

The type of paradigm used to train working memory varies across studies. Many studies use updating tasks (e.g. Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Minear et al., 2016; Redick et al., 2013) and complex span tasks (e.g. Chein & Morrison, 2010; Harrison et al., 2013; Minear et al., 2016). Other commercial programmes such as Cogmed (Cogmed, 2005) mainly involve training on serial recall tasks with intrinsic processing (e.g. Dunning et al., 2013; Holmes, Gathercole, & Dunning, 2009; Klingberg et al., 2005; Klingberg, Forssberg, & Westerberg, 2002).

1.4.1 Transfer following working memory training

The ultimate goal of working memory training is not to make people better at working memory tasks *per se*, but to enhance the underlying construct of working memory so that behavioural improvements can be attained across the wide range of abilities that depend on working memory. Therefore, to consider cognitive training an effective tool, it must promote the generalisation of training effects to untrained tasks. This is referred to as training transfer. A distinction can be made between near and far transfer. Near transfer refers to gains in a similar context to that which is trained (e.g. other working memory tasks), whereas far transfer refers to enhancements in a dissimilar context (e.g. novel tasks that do not share many common features with the trained tasks but which rely on working memory, such as tests of mathematical reasoning).

Numerous studies have reported strong evidence for near transfer, demonstrating that working memory training improves performance on trained and on untrained working memory tasks (e.g. Dunning, Holmes, & Gathercole, 2013; Holmes, Woolgar, Hampshire, & Gathercole, 2017; von Bastian & Oberauer, 2013). Enhancements in working memory performance are also associated with changes in neural activity and network connectivity in the brain areas supporting working memory (Astle, Barnes, Baker, Colclough, & Woolrich, 2015; Barnes, Woolrich, Baker, Colclough, & Astle, 2015; Buschkuehl, Hernandez-Garcia, Jaeggi, Bernard, & Jonides, 2014; E. Dahlin, Neely, Larsson, Bäckman, & Nyberg, 2008; Kundu, Sutterer, Emrich, & Postle, 2013; Langer, von Bastian, Wirz, Oberauer, & Jäncke, 2013; Olesen, Westerberg, & Klingberg, 2004; Takeuchi et al., 2010). For example, Astle and collegues (2015) found increases in the strength of neural connections between frontal regions and areas responsible for processing visual information following working memory training. These findings suggest that training could be producing fundamental and enduring changes in the cognitive and neural systems that underpin working memory.

Some researchers have likened cognitive training to physical exercise (e.g. Jaeggi et al., 2011), whereby training particular muscles through one physical activity is expected to benefit general physical fitness. It has been proposed that through enhancing a general cognitive ability such as working memory, improvements will be observed on a broad range of tasks involving that function. Some studies have reported far transfer to measures of fluid intelligence (Jaeggi et al., 2011, 2008; Jaeggi, Studer-Luethi, et al., 2010; Klingberg et al., 2002), reading (Chein & Morrison, 2010; K. Dahlin, 2011; Karbach, Strobach, & Schubert, 2015; Loosli, Buschkuehl, Perrig, & Jaeggi, 2012), inhibition (Chein & Morrison, 2010), selective attention (Klingberg et al., 2005), and mathematical ability (Holmes et al., 2009). These studies are supported by outcomes from systematic literature reviews and meta-analyses that reveal some positive evidence for far transfer following training (Au et al., 2014; Karbach & Verhaeghen, 2014; Klingberg, 2010; Morrison & Chein, 2011; Spencer-Smith & Klingberg, 2015; Titz & Karbach, 2014). Together these broad cognitive benefits support the theory that training is enhancing the underlying mechanism of working memory.

However, these positive results have been outnumbered by null results and the consensus from studies employing more rigorous testing methods (see Section 1.4.2) is that training benefits are apparent on other working memory tasks, but that this does not extend to other cognitive abilities closely associated with working memory such as non-verbal reasoning, verbal IQ, attentional control, or arithmetic (Melby-Lervåg & Hulme, 2012; Melby-Lervåg, Redick, & Hulme, 2016; Redick, 2015; Shipstead, Redick, & Engle, 2012; Simons et al., 2016; Soveri, Antfolk, Karlsson, Salo, & Laine, 2017). Moreover, recent studies have suggested that transfer within working memory following training may be constrained by the type of memory task trained.

If training is altering the fundamental capacity or efficiency of working memory, training-related improvements would be expected to transfer across different working memory tasks. For example, training on working memory tasks involving interpolated processing should result in improvements on updating and backward serial recall tasks. However, transfer typically only occurs when there is substantial overlap in the processes and structural properties between the training and transfer tasks (e.g. Dunning, Holmes, & Gathercole, 2013; Holmes, Woolgar, Hampshire, & Gathercole, 2017; von Bastian & Oberauer, 2013). For example, there is little evidence for transfer from *n*-back to untrained complex span measures (Holmes et al., 2018; Minear et al., 2016; Redick et al., 2013; Thompson et al., 2013), or vice versa (Holmes et al., 2018; Minear et al., 2016). These narrow patterns of generalisation suggest that transfer is process- or task-specific (Minear et al., 2016; Sprenger et al., 2013; von Bastian & Oberauer, 2013, 2014), and that training is not enhancing the underlying construct of working memory. The mechanisms that might be mediating transfer within working memory will be discussed further in Chapter 3.

1.4.2 Methodological issues in training studies

Many published intervention studies of near and far transfer effects have major shortcomings in terms of design or analysis, and the sometimes contradictory results across different studies might be explained by methodological issues prevalent in the cognitive training literature (Redick et al., 2013; for reviews, see Shipstead et al., 2012; Simons et al., 2016). A common problem is lack of an adequate control group. Some studies reporting positive far transfer effects have compared a treatment group to a no-contact control (e.g. Chein & Morrison, 2010; Jaeggi et al., 2008; Olesen et al., 2004). While this approach might rule out simple test-retest effects, it does not control for motivational or expectancy effects (Morrison & Chein, 2011; Shipstead et al., 2012). Consequently, participants may recognise they have been allocated to a control condition and that they are not expected to show pre- to post-test improvements (Shipstead et al., 2012). Comparison to a no-contact control condition can therefore lead to inflated estimates of training gains (Morrison & Chein, 2011).

An alternative approach is to include an active control working memory training group involving participants either training on a non-adaptive (placebo) version of the paradigm (e.g. Holmes et al., 2009; Klingberg et al., 2005), or receiving a lower dose of training (e.g. Klingberg et al., 2002). The active control group is not expected to benefit from training but is supposedly matched with the treatment group in terms of time engaging in an activity and effort invested (Morrison & Chein, 2011). However, participants in the control condition are unlikely to receive any feedback that their ability is changing, and still might be aware of group allocation (Shipstead et al., 2012). In order to truly control for participants' motivations, beliefs, and expectations, an active control condition must be as difficult and engaging as the working memory training but not involve activities that draw on working memory resources (Redick et al., 2013; Sternberg, 2008). Therefore, any generalisation effects can be directly attributed to the working memory training rather than to peripheral experiences in the lab (Shipstead et al., 2012). Researchers must also ensure participants are randomly assigned to groups to reduce bias (Simons et al., 2016), and make sure they are matched at baseline so that pre-existing differences between individuals do not mediate group differences at outcome (Melby-Lervåg & Hulme, 2012).

When studies apply rigorous methodological standards such as double-blind, randomised controlled trials (RCT) with a placebo-control training group, there is limited evidence for far transfer. For example, in a study not using an RCT design, Holmes, Gathercole and Dunning (2009) showed that ~20 days of Cogmed training had a positive impact on the mathematical skills of children. However, this finding was not replicated in a later study by the authors which used a double-blind RCT design (Dunning et al., 2013). Similarly, although Jaeggi, Buschkuehl, Jonides and Perrig (2008) found evidence of transfer to fluid intelligence following dual *n*-back training, this was only significant when compared to a no-intervention control group. This effect was not replicated in a similar study when dual *n*-back training was compared to an active control training group (Redick et al., 2013). In another study working memory training was shown to reduce parent-rated symptoms of ADHD including inattention and hyperactivity. However, recent meta-analytic studies found little evidence for this effect once raters were blinded to intervention condition (Cortese et al., 2015; Rapport, Orban, Kofler, & Friedman, 2013; Sonuga-Barke et al., 2013). Overall, these data stress the importance of using rigorous methodologies to evaluate the effectiveness of working memory training.

1.5 Transcranial electrical stimulation (tES)

Transcranial electrical stimulation (tES) is a non-invasive brain stimulation technique that delivers a weak electrical current through the scalp to affect processing in the underlying cortex (Brunoni et al., 2012). In the last decade there has been a growing body of evidence suggesting tES is a promising tool for neuro-enhancement (Elmasry, Loo, & Martin, 2015). There are numerous stimulation protocols, including transcranial direct current stimulation (tDCS), transcranial alternating current stimulation (tACS), and transcranial random noise stimulation (tRNS). During tDCS the stimulation current is held constant and can be used to deliver anodal (positive) or cathodal (negative) stimulation to increase or decrease neuronal excitability in the cortex (Paulus, 2011). During tACS the current is time dependent with a sinusoidal shape (i.e. alternating), and is used to interact or couple with ongoing oscillatory rhythms in the brain (Paulus, 2011). In tRNS the current is varied randomly, which appears to generate excitability increases in the cortex (Terney, Chaieb, Moliadze, Antal, & Paulus, 2008). See Figure 1.3 for a simplified illustration of the waveforms for each type of stimulation protocol. Each of these methods is described in more detail in the following sections (see Section 1.5.1 for tDCS, Section 1.5.2 for tACS, and Section 1.5.3 for tRNS). In this thesis tES is used as the collective term to refer to these stimulation protocols.

tES is usually delivered using two or more rubber electrodes placed inside saline soaked sponges that are positioned on the scalp (Nitsche & Paulus, 2000, 2001; Priori, Berardelli, Rona, Accornero, & Manfredi, 1998; Woods et al., 2016). The electrodes are connected to a battery-driven machine which enables the researcher to adjust current intensity and the duration of stimulation. Stimulation site on the scalp is typically determined using the standard international 10 - 20 electroencephalogram (EEG) placement system to locate regions of interest. However, tES has relatively poor focal resolution and the electrodes are likely to result in moderately wide-spread stimulation of brain regions (Woods et al., 2016). In the case of unilateral stimulation, an active electrode is placed over a region of interest and a reference (return) electrode is typically placed over the contralateral supraorbital region or at another extracephalic location (e.g. shoulder).

In general, tES is well-tolerated with only rare cases reporting mild adverse effects (Brunoni et al., 2012; Gandiga, Hummel, & Cohen, 2006). The most commonly reported side-effects include tingling, itching, fatigue, burning, and pain, but are usually reported as mild in severity (Kessler, Turkeltaub, Benson, & Hamilton, 2012; Poreisz, Boros, Antal, & Paulus, 2007). These sensations depend on stimulation intensity and are more likely to occur as a result of tDCS than tACS or tRNS (Paulus, Antal, & Nitsche, 2013). Briefly ramping the intensity of the electrical current up and down at the beginning and end of the stimulation period can be used to reduce the likelihood or severity of sensations associated with tES (DaSilva, Volz, Bikson, & Fregni, 2011).

An important methodological consideration in tES research is the inclusion of an appropriate control group. Due to the common sensations reported with active (real) stimulation, simply attaching electrodes to the scalp and not delivering any current is not sufficient to blind participants (and investigators) to group allocation. As is the case with cognitive training, knowledge of allocation to a control group may affect participants' motivation and expectancy effects. To determine whether active stimulation is having a significant effect over and above a placebo effect, a sham (fake stimulation) condition is often used. During the standard application of sham tES, stimulation intensity is slowly ramped up (over ~15 s) and faded out again after a short period (≤ 30 s) of real stimulation (Ambrus et al., 2012; Gandiga et al., 2006). This protocol mimics the sensory side-effects sometimes experienced when receiving electrical currents, which are usually greater at the beginning of stimulation (Paulus et al., 2013).

A tES machine can be programmed in advance allowing researchers to run double-blind sham-controlled trials. One investigator programmes the machine to deliver active or sham stimulation, while another simply turns it on and off during testing remaining blind to group allocation. It has been argued that this design should be standard procedure in the tES field (Nitsche et al., 2008). Even though sensory side-effects are still more common in active compared to placebo stimulation (Kessler et al., 2012), sham stimulation has proven to be a successful method for blinding both participants and investigators, who cannot reliably distinguish sham from 1 mA of active stimulation (Gandiga et al., 2006). There are also differences across the different stimulation protocols. Although active and sham tDCS appear to be indistinguishable at lower intensities, perceived differences in sensations between conditions are more likely to be reported with higher current strengths (e.g. 2 mA; Kessler et al., 2012; Palm et al., 2013; Russo, Wallace, Fitzgerald, & Cooper, 2013). Furthermore, tDCS has a 50% perception threshold at 400 µA (Ambrus, Paulus, & Antal, 2010) whereas this threshold is at 1200 µA in the case of tRNS, making it much easier to blind participants using the former technique (Ambrus et al., 2010).

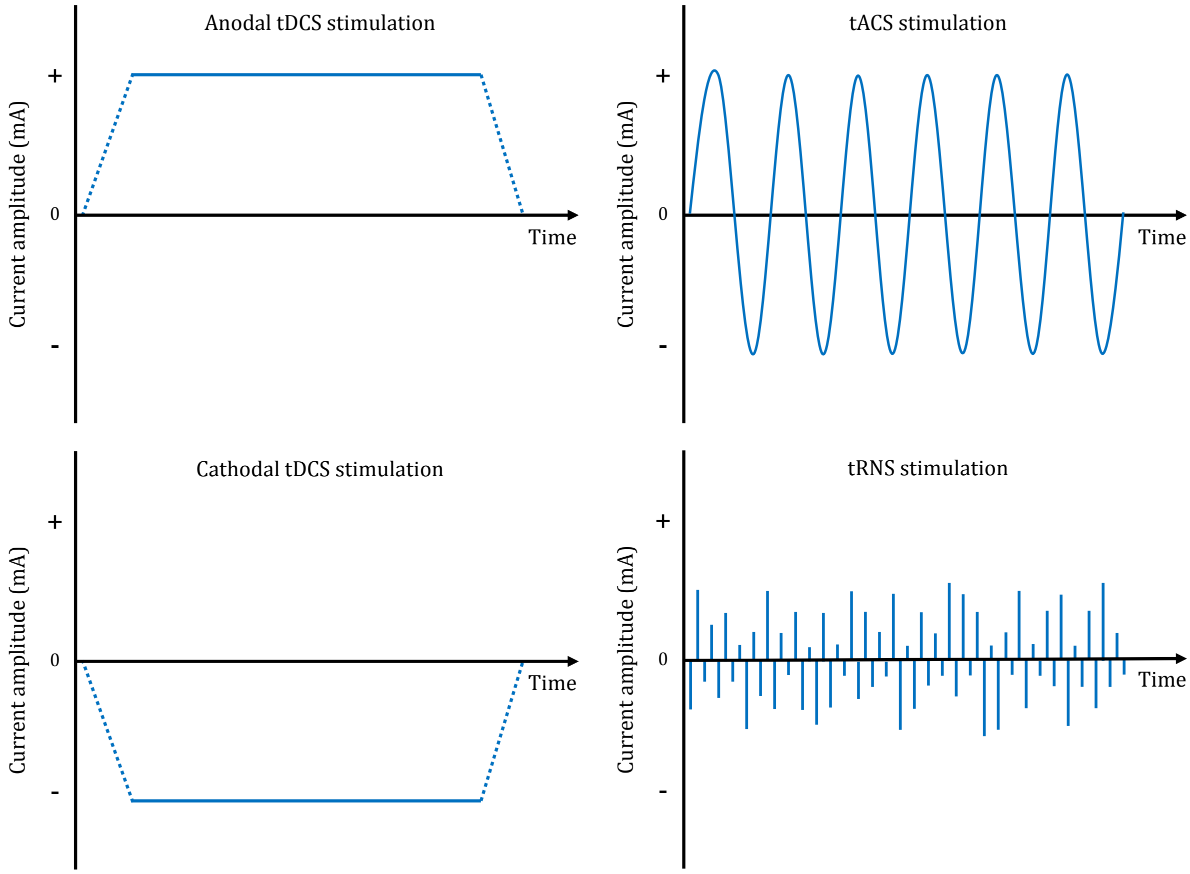


Figure 1.3 – A simplified illustration of the waveforms for each type of stimulation protocol: anodal transcranial direct current stimulation (tDCS), cathodal tDCS, transcranial alternating current stimulation (tACS), and transcranial random noise stimulation (tRNS).

1.5.1 Transcranial direct current stimulation (tDCS)

tDCS was first introduced as a non-invasive brain stimulation technique approximately 15 years ago (Nitsche & Paulus, 2000; Priori et al., 1998) and is used to modulate cortical excitability. During tDCS a low level of constant current is delivered to a cortical brain region (Flöel & Cohen, 2007). The physiological effects of tDCS have been examined mainly in terms of motor evoked potential (MEP) changes following stimulation to the motor cortex as measured by transcranial magnetic stimulation (TMS; Nitsche & Paulus, 2000; Priori, Berardelli, Rona, Accornero, & Manfredi, 1998). These studies have revealed that tDCS is capable of inducing cortical excitability and activity changes, and that the nature of these modulations depends of the polarity (i.e. direction) of the current flow (Liebetanz, Nitsche, Tergau, & Paulus, 2002; Nitsche et al., 2005). In general, anodal (positive) tDCS produces increased excitability, whereas cathodal (negative) stimulation results in decreased neuronal activity (see Figure 1.3; Boros, Poreisz, Münchau, Paulus, & Nitsche, 2008; Nitsche, Fricke, et al., 2003; Nitsche & Paulus, 2000; Paulus, 2004, 2011). The directional effects of stimulation on neuronal excitability have been mirrored in behavioural data. Increases in excitability are associated with enhanced cortical processing and therefore improved performance in a behavioural task (e.g. Cattaneo, Pisoni, & Papagno, 2011; Flöel et al., 2008), whereas decreases in excitability hinder performance (e.g. Vines, Schnider, & Schlaug, 2006).

During tDCS an anodal (positively charged) electrode and a cathodal (negatively charged) electrode are connected to a constant current direct current (DC) stimulator. To apply tDCS, a target electrode is placed over a location corresponding to an underlying brain region of interest, and a return electrode is placed at a reference location. During anodal stimulation the anode is used as the target electrode and the cathode as the reference, whereas during cathodal stimulation the cathode takes the place of the target electrode and the anode is used as the reference. During active stimulation a constant direct current is sent from the anode, through intervening brain tissue, to the cathode to allow effective modulation of neuronal excitability under the target electrode (Nitsche et al., 2008). The contralateral orbit (forehead) is the most common location for placement of the reference electrode in human studies using tDCS (for a review, see Nitsche et al., 2008). The term reference electrode does not necessarily mean that the electrode is functionally inactive, but that neuronal excitability changes under this electrode are beyond the scope of interest for a particular experiment (Nitsche et al., 2008). The position of the reference electrode does influence the pattern of overall current flow through the brain however, and so it may also influence brain modulation under the active electrode. It is therefore important to consider the location of both electrodes when deciding stimulation montage (DaSilva et al., 2011).

The aim of tDCS is to produce cortical changes lasting beyond the length of stimulation. The duration of physiological after-effects depends on the intensity and duration of the applied current (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013). When applied to the motor cortex, increasing the current intensity and/or stimulation duration, typically results in longer-lasting and stronger after-effects (Nitsche, Nitsche, et al., 2003; Nitsche & Paulus, 2000, 2001). In terms of intensity, there is a narrow window of current strength for inducing tDCS-related after-effects. In the literature, the intensity typically ranges from 0.5 to 2.0 mA (Nitsche & Paulus, 2011), with currents below 0.5 mA unlikely to produce noticeable effects. Nitsche and Paulus (2000) found that a stimulation intensity of at least 0.6 mA was required to produce after-effects (when applied for 5 min), as measured by MEPs. If current intensity is increased to 3 mA, tDCS starts to become painful (Furubayashi et al., 2008). In terms of duration, it appears that stimulation must be applied for at least 3 min (at 1 mA) to produce noticeable after-effects (Nitsche & Paulus, 2000), and tDCS can produce stable after-effects for up to an hour if applied for 9 – 13 min (Nitsche, Nitsche, et al., 2003; Nitsche & Paulus, 2000, 2001). Stimulation duration usually ranges from 10 to 20 min (Moreno-Duarte et al., 2014).

More recently, evidence has shown that intensity-dependent effects following tDCS to the motor cortex are non-linear and that increasing the current strength does not necessarily increase the efficacy of stimulation. For example, Batsikadze et al. (2013) found that when increasing the current intensity from 1 mA to 2 mA, the typical inhibitory effect of cathodal stimulation is shifted in the opposite direction. Similarly, data shows there may also be an upper limit for the duration of tDCS. The after-effects of stimulation cannot be extended indefinitely and prolonging stimulation does not always prolong after-effects but may also reverse them (Paulus et al., 2013). For example, doubling the stimulation duration of anodal tDCS from 13 to 26 min was found to convert an MEP increase in excitability to inhibition (Monte-Silva et al., 2013). Taken together, these findings suggest that although it is broadly true that polarity-dependent changes are directional, higher intensity currents and longer durations do not necessarily result in relative increases of sustained after-effects (Parkin, Ekhtiari, & Walsh, 2015). It appears there is an upper limit for sustaining excitatory or inhibitory after-effects, and therefore there are probably optimal stimulation parameters for maximising the duration of these effects (Paulus et al., 2013). For instance, some research has suggested that spaced intervals of tDCS may produce longer-lasting effects (e.g. Monte-Silva, Kuo, Liebetanz, Paulus, & Nitsche, 2010). Currently, it is not clear what the best stimulation montage is for maximising the duration of after-effects. It is important to note that most of the methodological concepts and rationale for a typical stimulation montage rely on MEP measurements from the motor cortex. However, different stimulation durations and intensities may result in different after-effects when applied to other cortical areas.

1.5.2 Transcranial alternating current stimulation (tACS)

tACS is a type of oscillatory stimulation that delivers a non-constant current to the brain (see Figure 1.3; Moreno-Duarte et al., 2014). Like tDCS, it has been shown to influence cortical excitability and activity (Antal et al., 2008; Chaieb, Antal, & Paulus, 2011; Moliadze, Antal, & Paulus, 2010; Wach et al., 2013) as well as facilitate performance in behavioural tasks such as implicit motor learning (Antal et al., 2008; Moliadze et al., 2010). The aim of tACS is to interfere with ongoing rhythms in the cortex (Paulus, 2011) and it can be used to entrain intrinsic brain oscillations to specific frequency bands (Antal et al., 2008; Paulus et al., 2013; Tavakoli & Yun, 2017), that is to say it can couple the oscillatory behaviour of the brain. A number of studies have established a close relationship between brain oscillations and cognitive functions (for reviews, see Engel, Fries, & Singer, 2001; Herrmann, Munk, & Engel, 2004). Therefore, tACS may be a useful tool for establishing causal links between rhythmic cortical activities and their cognitive functions (Herrmann, Rach, Neuling, & Strüber, 2013; Kanai, Chaieb, Antal, Walsh, & Paulus, 2008).

Application of tACS usually involves delivering sinusoidal stimulation (i.e. an alternating current), but other waveforms are possible (Antal & Paulus, 2013). The main parameters that determine the direction and duration of the tACS-induced effects are the frequency, intensity, and phase of the stimulation (Antal & Paulus, 2013). In general, during tACS a bidirectional, biphasic current is delivered in sinusoidal waves (Moreno-Duarte et al., 2014). The typical time for stimulation ranges from 2 – 5 min at intensities between 0.25 – 1 mA (Moreno-Duarte et al., 2014). Unlike tDCS, duration related effects of tACS on MEPs have not yet been systematically investigated (Antal & Paulus, 2013). tACS can be administered in a wide frequency range (Antal & Paulus, 2013). Typically it is applied at conventional EEG frequencies (0.1 – 80 Hz) and in the so called *ripple range* of 140 Hz, which may be able to interact with ongoing rhythms in the cortex (Antal & Paulus, 2013; Moliadze et al., 2010). Different frequencies can have different effects on the brain and behaviour. While some frequencies show a trend towards MEP inhibition, others yield excitability increases, and some result in behavioural improvements (for an overview, see Antal & Paulus, 2013). The after-effects of stimulation also appear to be dependent on intensity. For example, 1 mA of tACS at 140 Hz results in significant increases of cortical excitability as measured by MEPs (Moliadze et al., 2010). However, reducing the intensity of stimulation to 0.4 mA switched the excitatory effect to inhibition, and the intermediate intensity ranges of 0.6 and 0.8 mA had no effect at all (Moliadze, Atalay, Antal, & Paulus, 2012).

1.5.3 Transcranial random noise stimulation (tRNS)

tRNS is another form of non-invasive electrical brain stimulation used to induce cortical excitability and resulting plasticity (Chaieb, Paulus, & Antal, 2011; Terney et al., 2008). Like tACS, tRNS is a relatively new technique and consequently less is known about it compared to tDCS. It is essentially a special form of tACS with a white noise characteristic (Antal & Paulus, 2013; Terney et al., 2008). Unlike tDCS, tRNS is not polarity specific and can be applied unilaterally. During stimulation an alternating current is applied along with random amplitudes (see Figure 1.3). While tACS uses a fixed frequency, tRNS applies a current within a broad frequency spectrum between 0.1 Hz and 640 Hz with a random noise distribution (Antal & Paulus, 2013; Terney et al., 2008).

As with other forms of tES, there are numerous stimulation parameters that can be altered when using tRNS. A typical tRNS montage involves a randomly alternating level of current between -500 and +500 μA, with a sampling rate of 1280 samples per second and high range frequencies between 100 and 640 Hz, providing a current of 1 mA (Moreno-Duarte et al., 2014; Terney et al., 2008). These parameters have been shown to elicit increased cortical excitability in the motor cortex of healthy participants lasting up to 60 min following 10 min of stimulation (Terney et al., 2008). In terms of duration, a minimum of 5 min appears to be necessary to observe an effect (Chaieb et al., 2009). tRNS has also been shown to generate some behavioural improvements that are similar to those observed with anodal tDCS (e.g. Cappelletti et al., 2013; Romanska, Rezlescu, Susilo, Duchaine, & Banissy, 2015; Snowball et al., 2013). It also offers some potential methodological advantages over tDCS in terms of enhancing cognitive abilities, which will be reviewed further in Chapter 2.

1.5.4 Mechanism of action

Explorations into the mechanisms that underlie the behavioural improvements found with tES have mostly concentrated on tDCS, and literature on the physiological and cognitive effects of tRNS and tACS is still limited. Therefore, this section mainly discusses findings investigating the mechanism of action in terms of tDCS.

The principal physiological mechanism of tDCS is thought to be the subthreshold modulation of neuronal membrane potentials (Flöel & Cohen, 2007; Paulus, 2004; Woods et al., 2016). tDCS is not thought to cause resting neurons to fire or directly induce activity in cortical areas; rather it modulates the spontaneous neuronal activity at the level of membrane potential (Sparing & Mottaghy, 2008; Woods et al., 2016). Anodal stimulation causes a shift towards depolarization of cortical neurons, while cathodal tDCS is thought to shift neuronal membranes towards hyperpolarization (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013; Nitsche & Paulus, 2000; Paulus, 2004, 2011). Therefore tES may facilitate learning by enhancing plasticity via mechanisms similar to long-term potentiation (LTP) or long-term depression (LTD), which underlie learning and memory (Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Flöel & Cohen, 2007). However, this explanation has been criticised as being overly-simplistic (de Berker, Bikson, & Bestmann, 2013). Although there is evidence that tES has the capacity to change membrane excitability and membrane potentials, it remains unclear how this is related to observed behavioural changes elicited by stimulation (Bestmann, de Berker, & Bonaiuto, 2015).

There is an important distinction to make regarding the effects tDCS has on the brain. On the one hand, some methods have focused on examining immediate short-lasting effects of tDCS (i.e. the online effects of tDCS on neurons during stimulation), whereas others have investigated the formation of long-lasting after-effects (Sparing & Mottaghy, 2008). In terms of the online effects of tDCS, findings from pharmacological studies support the theory that short-lasting changes are dependent on polarity-specific shifts in the resting membrane potential of cells. These shifts in cortical excitability modulate the conductance of sodium and calcium channels, and blocking these channels using specific drugs can reduce or abolish the effects of anodal stimulation (Nitsche, Fricke, et al., 2003; Stagg & Nitsche, 2011). However, these effects are short-lasting and are not thought to have any significant effects on synaptic plasticity (Sparing & Mottaghy, 2008; Stagg & Nitsche, 2011).

The sustained after-effects elicited by prolonged tDCS are thought to be N-methyl-D-aspartate (NMDA) receptor dependent, as these receptors are involved in neuroplastic changes (Fritsch et al., 2010; Liebetanz et al., 2002; Nitsche, Fricke, et al., 2003). NMDA is a glutamate receptor and ion channel protein that is activated when glutamate and glycine bind to it. It plays a crucial role in controlling synaptic plasticity and is therefore an important cellular mechanism for learning and memory function (Bennett, 2000; Li & Tsien, 2013). Evidence for the involvement of this receptor is provided by pharmacological research demonstrating that drugs used to antagonise NMDA receptors eliminate both the prolonged excitability enhancement produced by anodal stimulation and the excitability decrease caused by cathodal tDCS (Liebetanz et al., 2002; Nitsche, Fricke, et al., 2003). These findings suggest that tDCS might lead to strengthening of synaptic connections (Fritsch et al., 2010) via a mechanism that is similar to LTP (Nitsche & Paulus, 2000; Stagg & Nitsche, 2011), a cellular correlate of learning and memory (Bliss & Collingridge, 1993; Martin, Grimwood, & Morris, 2000). Although antagonising NMDA receptors prevented the induction of long-lasting after-effects, it did not alter the excitability changes found during shorter-lasting stimulation that do not elicit after-effects (Nitsche, Fricke, et al., 2003). This is in line with the theory that short-lasting online effects are generated solely by modulating resting membrane potential, whereas after-effects are also dependent on modulations of NMDA receptor efficacy (Liebetanz et al., 2002; Sparing & Mottaghy, 2008).

tRNS can produce similar after-effects to tDCS and has been shown to induce persistent excitability increases in the motor cortex lasting for at least 60 min (Terney et al., 2008). However, the mechanism responsible for this cortical excitability alteration is not yet fully understood (Chaieb, Antal, & Paulus, 2015). Pharmacological studies have revealed that tDCS is NMDA receptor dependent (Liebetanz et al., 2002). However, NMDA receptor antagonist and agonist neuroactive drugs have no effect on excitability changes observed with tRNS (Chaieb et al., 2015), suggesting a different mechanism is operating. An alternative mechanism that has been proposed is the repeated potentiation, or opening, of sodium channels (Paulus, 2011). Evidence for this theory is provided by Chaieb et al. (2015) who found that a drug used to block sodium channels showed a tendency toward inhibiting MEPs following 10 min of tRNS with a current intensity of 1 mA.

In terms of tACS, when applied in the EEG range (0.1 – 80 Hz) it is thought to entrain or synchronise neuronal networks, therefore inducing changes in ongoing oscillatory brain activity (Antal & Paulus, 2013; Paulus et al., 2013). However, it may be having a different effect when applied outside of the conventional EEG frequency range (e.g. in the 140 Hz range and low kHz range of 1 – 5 kHz). tACS applied for 10 min with 1 mA intensity in the low kHz range has been shown to increase excitability in a similar way to anodal tDCS (Chaieb, Antal, et al., 2011). This type of stimulation is not thought to interfere with oscillatory activity, but may influence the membrane excitability of neurons (Moliadze et al., 2010). Therefore, tACS in this higher frequency range might modulate plasticity via a similar biochemical mechanism to tRNS (e.g. by influencing calcium ion concentration of post-synaptic neurons).

In general, the mechanisms of action that mediate the cortical and behavioural changes associated with tES are not well understood, especially in the case of tRNS and tACS. Although, they may involve different mechanisms, it is thought that tDCS, tRNS and tACS are all able to drive excitability changes, which in turn may facilitate learning.

1.5.5 tES for cognitive enhancement

Many studies have explored the cognitive-behavioural effects of non-invasive brain stimulation such as tES (for a review, see Nitsche & Paulus, 2011). Promising results suggest that tES can enhance a number of cognitive abilities such as language learning (e.g. Cattaneo et al., 2011; Flöel et al., 2008), attention (e.g. Gladwin, den Uyl, Fregni, & Wiers, 2012; Roy, Sparing, Fink, & Hesse, 2015), and mental arithmetic (e.g. Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013). Many studies have focused on the potential of tES for the enhancement of working memory (e.g. Jeon & Han, 2012).

An important consideration in tES studies is the location of stimulation, as the brain region that is targeted must be involved in task performance. Tasks that engage working memory typically recruit areas in the frontal and parietal cortex, and the dorsolateral prefrontal cortex (DLPFC) appears to play a particularly important role in executive functioning and working memory. The DLPFC is also proposed to support both storage and processing components of working memory. Evidence from patients with lesions to DLPFC supports the involvement of this region in working memory, for example, Barbey Koenigs and Grafman (2013) found that damage to the DLPFC is associated with deficits in working memory, and suggested that the left DLPFC is especially involved in the manipulation of information in working memory. Furthermore, TMS (which disrupts cortical activity) delivered over the left DLPFC has been shown to impair working memory performance (e.g. Mull & Seyal, 2001). Numerous functional neuroimaging studies have also demonstrated that activation within the DLPFC is associated with performance of working memory tasks (e.g. D'Esposito et al., 1998; D'Esposito, Postle, Ballard, & Lease, 1999; Hautzel et al., 2002; for reviews, see D'Esposito, Postle, & Rypma, 2000; Owen et al., 2005; Smith & Jonides, 1999; Wager & Smith, 2003). This converging evidence demonstrates the critical role it plays in working memory, and consequently the DLPFC has become a popular target region in non-invasive brain stimulation studies involving working memory (for reviews, see Brunoni & Vanderhasselt, 2014; Dedoncker, Brunoni, Baeken, & Vanderhasselt, 2016; Hill, Fitzgerald, & Hoy, 2016; Tremblay et al., 2014).

Many studies have shown that anodal tDCS over the left DLPFC enhances performance in working memory tasks in single sessions (Andrews, Hoy, Enticott, Daskalakis, & Fitzgerald, 2011; Boggio et al., 2006; Fregni et al., 2005; Hoy et al., 2013; Jeon & Han, 2012; Jo et al., 2009; Keeser et al., 2011; Mulquiney, Hoy, Daskalakis, & Fitzgerald, 2011; Ohn et al., 2008; Teo, Hoy, Daskalakis, & Fitzgerald, 2011; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011; for reviews, see Berryhill, 2014; Coffman, Clark, & Parasuraman, 2014; Hill, Fitzgerald, & Hoy, 2016; Kuo & Nitsche, 2012; Tremblay et al., 2014). However, findings are mixed and recent reviews of the literature suggest there is no reliable evidence that tDCS is capable of inducing cognitive or neurophysiological changes in the brain in single sessions (Horvath, Forte, & Carter, 2015). Additional studies have also found that tES can enhance the effects of cognitive training in a number of domains (for a review, see Elmasry, Loo, & Martin, 2015). Studies that have investigated the use of tDCS in multi-session working memory training protocols have produced mixed results. Some have shown that tDCS can boost both online training gains and transfer effects to untrained tasks, and that these effects are sustained for several months (Au et al., 2016; Ruf, Fallgatter, & Plewnia, 2017; Trumbo et al., 2016). However, other studies have failed to demonstrate such enhancements (Martin et al., 2013; Richmond, Wolk, Chein, & Olson, 2014), and a recent meta-analysis concluded that tDCS was not much more effective for boosting working memory training than sham stimulation (Nilsson, Lebedev, Rydström, & Lövdén, 2017). Studies combining tDCS and working memory training will be considered in more detail in Chapter 3 of this thesis. The promise of tRNS for boosting the effects of cognitive training has also been explored in other domains (e.g. arithmetic training; Snowball et al., 2013), but not yet for working memory. The potential of tRNS for enhancing working memory training will be explored further in Chapter 2.

1.6 Main aims of thesis

To date, studies of working memory training have demonstrated narrow patterns of transfer (see Section 1.4.1), and little is known about the precise cognitive mechanisms that mediate the generalisation of learning to untrained tasks. There is also little research investigating the consequences of combining working memory training with tES (see Section 1.5.5). Therefore, the overarching aims of the work presented in this thesis were to examine the effects of combining working memory training with tES, to investigate patterns of transfer to untrained tasks following working memory training, and also to elucidate the processes involved in tasks commonly used to measure and train working memory.

The first study (see Chapter 2), *Does transcranial random noise stimulation (tRNS) enhance the effects of working memory training?,* sought to determine whether stimulation applied during multi-session working memory training could: (i) enhance gains on the training activities, (ii) enhance gains on transfer tests of working memory with similar task structures to the training tasks, and (iii) promote far transfer in terms of improvements on both working memory tasks with distinct structures to the training tasks and to measures of other cognitive abilities that are related to working memory. The primary aim of this experiment was to test whether stimulation could enhance *any* gains following working memory training. For this reason, Cogmed was chosen as the training tool because it has been extensively researched and yields larger effect sizes for changes in working memory than other training packages (Cogmed, 2005; Schwaighofer, Fischer, & Bühner, 2015). Using a program that is known to produce training gains provided the ideal starting point for investigating whether stimulation could produce any additive benefits. A more nuanced aim of the experimental work was to track patterns of transfer across different working memory paradigms both following training alone and when training was combined with stimulation. However, the Cogmed program was not optimal in this regard as it included a variety of working memory tasks (e.g. verbal and non-verbal serial recall and serial recall with intrinsic processing paradigms). Using a training program that involves practice on a single paradigm may make it easier to track patterns of transfer more carefully.

With this in mind, the aims of the second study (see Chapter 3), *Backward digit training: Cross-paradigm transfer and the effects of transcranial direct current stimulation (tDCS)*, were to systematically investigate the extent to which the benefits of working memory training transfer within and across working memory paradigms following training on a single working memory task, and also to investigate whether tDCS could enhance these effects. Irrespective of the impact tDCS has on the generalisation of training effects, the inclusion of an active control training group and the systematic manipulation of outcome measures yielded important new data about the extent to which working memory training effects transfer within and across untrained working memory tasks.

The third experimental section of this thesis (see Chapter 4), *Backward recall and n-back measures of working memory: A large scale latent variable analysis,* was conducted to investigate the overlap in the processes involved in two tasks that are widely used to measure working memory. Backward recall tasks are commonly used in behavioural studies, while *n*-back tasks are frequently used in neuroimaging studies of working memory. Despite both types of task being labelled as working memory tests, they differ substantially in terms of their structural properties and the processes involved. Therefore, data was collected online from a large sample of adults (N ~700) using different backward recall and *n*-back tasks. This enabled the factor structure underpinning these tasks to be assessed using a latent variable analysis approach, thus providing novel data about whether these paradigms can be used interchangeably as measures of working memory.

Chapter 5 summarises the entire thesis. The main findings and conclusions of the empirical studies are discussed, along with various theoretical and methodological implications of the results. Finally, limitations and potential areas for future research are identified.

Chapter 2 Does transcranial random noise stimulation (tRNS) enhance the effects of working memory training?

The data reported in this chapter have been published in the *Journal of Cognitive Neuroscience* (see Appendix A).

2.1 Aims

Intensive adaptive training boosts performance on trained and untrained working memory tasks (e.g. Dunning, Holmes, & Gathercole, 2013). However, there is little evidence that gains generalise to working memory tasks that involve different processes to training activities (e.g. Minear et al., 2016). Transcranial random noise stimulation (tRNS) has been shown to enhance the efficacy and generalisability of cognitive training in other domains, such as mathematics training (e.g. Cappelletti et al., 2013; Snowball et al., 2013). The potential additive benefit of combining this technique with working memory training has not yet been explored. The aim of this experiment was to investigate, using the current best practice in training, stimulation, and intervention design, whether tRNS applied during multi-session working memory training: (1) enhances gains on training activities, (2) boosts gains on memory tasks that share features with the training activities, (3) promotes generalisation of gains to memory tasks with processing demands that were not trained, and (4) promotes far transfer to tests of cognitive processes associated with working memory.

2.2 Introduction

Evidence presented in the literature review has shown that intensive, adaptive training on working memory tasks boosts performance on trained and untrained working memory tasks, and that the benefits of training are greatest when the training activities and transfer tasks share common cognitive and neural components (E. Dahlin, Neely, et al., 2008; Sprenger et al., 2013; von Bastian & Oberauer, 2013; see Section 1.4.1). Some studies have shown transfer across different categories of working memory task (e.g. Harrison et al., 2013). However, most report selective benefits from training to tasks that are structurally similar (e.g. to the same type of task such as complex span), or to tasks with overlapping processing demands (e.g. updating; Dahlin et al., 2008; Redick et al., 2013; Thompson et al., 2013; von Bastian & Oberauer, 2013). There is little evidence for transfer to working memory tests with distinct processing demands and structural properties (Melby-Lervåg & Hulme, 2012; Shipstead, Redick, & Engle, 2010). Furthermore, when studies employ the most rigorous randomised controlled trial (RCT) designs there is no reliable evidence to substantiate the claim that training gains generalise to complex everyday activities that depend on working memory, such as academic attainment or focussed attention (e.g. Cortese et al., 2015; Dunning et al., 2013; Rapport, Orban, Kofler, & Friedman, 2013). For working memory training to be considered an effective tool for enhancing working memory performance in everyday tasks, research must first establish methods that promote the transfer of gains from highly specific memory tasks.

tRNS is a relatively new technique for non-invasive brain stimulation. It has not yet been extensively researched, but there is growing evidence that it can enhance the effects of intensive training in other cognitive domains such as mathematics. In a study conducted by Snowball and colleagues (2013), 20 min of tRNS was applied bilaterally to the dorsolateral prefrontal cortex (DLPFC) at a current strength of 1 mA during arithmetic training. Significantly greater improvements on untrained mathematical problems were reported immediately after training and at a 6 month follow-up for an active versus sham control group. In a similar study, numerosity discrimination training combined with 1 mA of tRNS applied bilaterally to the parietal cortex for 20 min resulted in steeper learning curves and long-lasting improvements in magnitude judgements lasting up to 4 months, when compared to training alone (with sham tRNS), active tRNS over a control cortical location (motor area), or active parietal tRNS alone (Cappelletti et al., 2013). tRNS has also been shown to improve the effects of cognitive training in developmental populations. Looi et al. (2017) investigated the effects of numerical training combined with tRNS in children with mathematical learning difficulties. Stimulation applied for 20 min, with current intensity of 0.75 mA over bilateral DLPFC, enhanced accuracy and was associated with a steeper rate of learning during training relative to a sham tRNS control group. tRNS also modulated generalisation to an untrained test of mathematical ability. Together, these findings demonstrate the potential of tRNS for enhancing cognitive training.

While numerous studies have examined working memory training combined with transcranial direct current stimulation (tDCS; Au et al., 2016; Martin et al., 2013; Richmond et al., 2014; Ruf et al., 2017), there are currently no studies that have investigated the effects of tRNS and working memory training. One study examined the effect of tRNS in a single session, and did not find any significant changes in performance on a working memory task when applied over left DLPFC (Mulquiney et al., 2011). tRNS offers some potential methodological advantage over tDCS. Firstly, while tDCS is a polarity dependent form of tES that generates opposing excitatory and inhibitory activity under the two stimulating electrodes, tRNS is polarity-independent and can therefore be applied bilaterally to the cortex (Paulus, 2011; Terney et al., 2008). Furthermore, tRNS has a higher cutaneous perception threshold than tDCS making it particularly suitable for blinding groups to stimulation condition (Ambrus et al., 2010).

The aim of this study was to investigate, for the first time, whether tRNS could modulate on-task training gains and enhance transfer to both trained and untrained working memory tasks and other cognitive abilities related to working memory when combined with working memory training. Following Snowball et al. (2013), high-frequency tRNS (101 – 640 Hz) at a current strength of 1 mA was applied bilaterally over DLPFC. The DLPFC was chosen as the stimulation site as it is a region of the brain associated with working memory function (Owen et al., 2005) and is influenced by working memory training (Takeuchi et al., 2010). Participants completed Cogmed working memory training (Cogmed, 2005), a program that has been extensively researched and yields larger effect sizes for changes in working memory compared to other training packages (Schwaighofer et al., 2015).

It was predicted that tRNS would modulate learning during working memory training leading to faster and greater gains on trained tasks, in line with findings reported for mathematics training by Snowball and colleagues. A wide battery of outcome measures with varying degrees of overlap with the trained activities was administered before and after training to map the extent to which gains transferred beyond the trained tasks. Working memory can be measured using a variety of tasks including: (i) simple span tasks, which involve the immediate serial recall of stored items (e.g. digit recall), (ii) simple span tasks with intrinsic processing, which require participants to transform the storage material prior to recall (e.g. backward digit recall), (iii) complex span tasks, in which processing episodes are interpolated between storage items, and (iv) *n*-back tasks, which require the continuous updating of a list of storage items (see Section 1.3 for more details). The training program used in this study included both simple span and simple span with intrinsic processing tasks. The primary outcome measures were working memory tasks with processing components that overlap with the training tasks (i.e. forward and backward recall tasks). Any advancement to training via tRNS should be evident in these measures as well as the trained tasks. Next, to determine whether any benefits of combining training with tRNS extend beyond specific trained processes, transfer to untrained working memory tests with different processing demands to the trained activities was also assessed. This involved measuring performance on tasks with non-overlapping processing demands that have a novel task structure (i.e. complex span and *n*-back). Secondary tests of cognitive processes that are associated with working memory, including measures of inhibition (Kane & Engle, 2003) and selective attention (de Fockert, Rees, Frith, & Lavie, 2001), were included alongside measures of information processing and standardised assessments of general cognitive abilities (e.g. language and non-verbal reasoning), to assess whether stimulation promotes transfer beyond working memory paradigms (i.e. far transfer). An emotional recognition task with no memory component was included as a non-memory control task.

2.3 Method

2.3.1 Participants

Thirty native-English speaking adults aged 18 - 35 years (11 male) were recruited via the MRC Cognition and Brain Sciences Unit research participation recruitment system and through advertisements within Cambridge University colleges, and were paid for their participation. All participants had normal or normal-to-corrected vision and were stimulation compatible, i.e. they had no history of neurological disease or psychiatric disorder, no history or family history of epilepsy or other seizures, no metallic object(s) in the body, no cardiac pacemaker, and no history of head, throat, or brain surgery, were not taking any drugs that affect the central nervous system (including medication and illicit drugs, excluding alcohol) such as antiepileptic drugs, antidepressants, benzodiazepines, and L-dopa. See Table 2.1 for participant characteristics.

2.3.2 Procedure

The study used a double-blind randomised controlled design. All participants completed two pre-training sessions, each lasting approximately 2 hrs. Following pre-assessment, participants were assigned to either an active (6 male, 9 female) or sham stimulation group (5 male, 10 female). Stratified randomisation was used to ensure groups were matched for age, sex, IQ, and baseline short-term and working memory ability (see Table 2.1 for a summary of participant characteristics by group). All participants completed 10 sessions of working memory training over approximately 19 days. Sessions were run individually with each participant. Pre-training assessments were re-administered at the end of training in two separate sessions. Written informed consent was obtained prior to testing. The study was approved by and conducted in accordance with the guidelines of the Cambridge University Psychology Research Ethics Committee and the MRC Cognition and Brain Sciences Unit (ethics code = PRE.2013.87; see Appendix B for a copy of the ethics approval letter).

Table 2.1 – Participant characteristics by group.

	Stimulation		*Sham*		*Group comparison*		
	M	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*
Age (years)	25.270	5.509	24.730	4.008	0.303	.764	0.113
IQ	120.667	8.524	119.333	10.834	0.375	.711	0.138
Verbal short-term memory	101.067	15.696	100.600	16.322	0.080	.937	0.029
VS short-term memory	103.733	23.313	106.667	22.064	-0.354	.726	-0.129
Verbal working memory	101.000	20.078	101.733	19.282	-0.102	.919	-0.037
VS working memory	103.133	22.427	107.867	15.287	-0.675	.505	-0.251
Time to complete training (days)	19.330	4.515	18.333	3.867	0.652	.520	0.238

Note. VS = visuo-spatial.

2.3.3 Materials

2.3.3.1 Transfer tasks

Process-specific memory tasks

Eight tasks with processing components that overlapped with the training tasks were administered. Participants completed four standardised subtests from the Automated Working Memory Assessment (AWMA; Alloway, 2007). These included a test of verbal short-term memory (digit recall), visuo-spatial short-term memory (dot matrix), verbal working memory (backward digit recall), and visuo-spatial working memory (Mr X). Digit recall involved the immediate serial recall of a list of spoken digits and dot matrix required the immediate serial recall of dots presented on a 4 x 4 matrix. Backward digit recall involved the reproduction of a sequence of spoken numbers in backward order. Mr. X required participants to judge whether two cartoon characters were holding a ball in same or different hands when positioned at different orientations, while recalling the location of the ball in serial order at the end of each trial. Standard scores (M = 100, SD = 15) were calculated for each task. Participants also completed four computerized experimental tests of verbal and visuo-spatial storage (i.e. short-term memory) and of verbal and visuo-spatial storage with intrinsic processing (i.e. working memory). Prior to each task participants were presented with audio instructions with example trials, and all responses were made using a computer mouse. The storage tasks required participants to recall items in serial order. Participants were presented with a list of auditory digits in the verbal storage task and a series of spatial locations (nine squares at random locations were presented on-screen and a single box would light up on each trial) for the visuo-spatial version. Participants began the tasks at a span of two items which then increased by one item in each subsequent block if participants scored three or more correct trials. The task was discontinued if participants scored incorrectly on three or more trials. The verbal and visuo-spatial working memory tasks were identical to the storage tasks, except participants were required to recall digits or spatial locations in backward order. Maximum span length reached was used to score all tasks.

Memory tasks with distinct processes

Two *n*-back and two complex span tasks were used as memory tasks involving different processes to the training activities. Separate verbal and visuo-spatial variants of each were administered. During the *n*-back tasks participants were required to continuously update a list of auditory digits (verbal) or on-screen abstract line drawings (visuo-spatial). During the *n*-back tasks participants had to judge whether or not a currently presented digit or image matched an item that was presented *n* items back in the sequence by pressing a keyboard button. During each block participants were presented with a continuous list of 20 + *n* items during which there were a total of six possible matches. Responding to a non-target (a false alarm) or failing to respond to a match (missing a target) were counted as errors. If five or more errors were made within a block then the task would end. If less than five errors were made then participants would progress to the next block at which the difficulty level increased by one (e.g. *n*-back increased from one-back to two-back). Maximum *n*-level reached was used to score these tasks. For both the complex span tasks, participants were presented with a series of verbal or visuo-spatial storage items interleaved with a same-domain processing task, which was presented for 6 s between each to-be-remembered item. In the verbal complex span task storage items were comprised of spoken numbers (digits 1 - 9, excluding two-syllable *seven*) and during the processing episodes participants performed a rhyme judgment task on spoken letter names (excluding polysyllabic *W*). Responses were made by clicking an on-screen *rhyme* or *non-rhyme* button. Half of the letter pairs rhymed and were constrained to avoid successive alphabetical letters, familiar acronyms, words, or names. In the visuo-spatial complex span task participants were presented with nine squares in random locations and a single box would light up for each storage item. During the interval task participants had to decide whether patterns of lines inside a pair of hexagons were the same by clicking an on-screen *match* or *mismatch* button accordingly. At the end of each trial participants were required to recall the storage items in serial order by clicking the sequence on an on-screen digit or spatial location keypad. For both complex span tasks storage span began at one and the number of items in the sequence increased by one unless a discontinue rule was met. Participants performed three trials at each span length. The task was discontinued if two out of three trials were incorrect, if no response was made for any of the processing judgments, or if accuracy for all attempted processing judgments across the span was less than 66%. Maximum span reached was used to score the complex span tasks.

Cognitive process associated with working memory

Parallel verbal and visuo-spatial tests of executive function were administered. Two flanker tests were used as measures of verbal and visuo-spatial selective attention. Both tasks consisted of 240 trials: 80 baseline, 80 congruent, and 80 incongruent (all trials presented in a random order). During the baseline condition participants were presented with a letter (verbal) or arrow (visuo-spatial) and instructed to click a corresponding button matching the target letter (A or B) or arrow (← or →). During the congruent trials participants were presented with an array of 5 identical letters (e.g. BBBBB) or arrows (e.g. →→→→→) and asked to click the button matching the middle letter or arrow. During the incongruent trials participants were presented with a target item in the centre of an array but flanked by different items (e.g. AABAA or ←←→←←). Participants were again required to click a corresponding button matching the centre target item. The average reaction time of the difference between congruent and incongruent trials was used to index the Flanker effect.

Measures of inhibitory control were provided by two Stroop tasks (verbal and visuo-spatial). Both tasks consisted of 144 trials: 48 baseline, 48 congruent, and 48 incongruent trials (presented in blocks by condition). On baseline trials in the verbal Stroop task, neutral words (e.g. *when*) were presented on screen printed in red, green, blue, or yellow. Participants were required to click the corresponding colour block from a choice of four below. On congruent trials, participants were presented with colour words printed in the same colour as the word (e.g. *red* appeared on-screen, printed in red ink), and again had to click on the block corresponding to the colour the word was printed in. On incongruent trials, colour words were presented in a different colour to the word itself (e.g. *green* appeared on-screen, printed in yellow). Participants were required to ignore the colour name and again click on the block matching the colour the word was printed in. In the visuo-spatial Stroop task participants were presented with an arrow and required to make a judgment on the direction it was pointing. In the baseline trials the arrow appeared in the centre of a box pointing up, down, left, or right. Participants were required to click an arrow from a choice of four below that pointed in the same direction. In congruent trials an arrow appeared with the arrowhead touching the same side of the box to which it was pointing (e.g. an arrow pointing up, with the arrowhead touching the top side of the box). Again, participants were instructed to click on an arrow from a choice of four below which was pointing the same way as the target item. On incongruent trials an arrow appeared in a position in the box incongruent to the way it was pointing (e.g. an arrow pointing up, could appear with part of the arrow touching the left-hand, right-hand, or bottom side of the box). Participants were required to ignore the position of the arrow and respond by selecting one arrow of a choice of four below which matched the direction the target arrow was pointing. The difference between the mean reaction time for correct trials in the incongruent condition and the mean reaction time for correct trials in the congruent condition was used to calculate the Stroop effect.

Information processing and general cognitive abilities

Two information processing tasks, one verbal and the other visuo-spatial, were also administered. During the verbal processing task, auditory pairs of monosyllabic letters were presented. Participants had to judge whether each pair of letters rhymed by clicking either a green *match* or red *non-match* on-screen button accordingly. Participants could make a response at the onset of the second letter. Pairs were constrained to avoid successive letters in alphabet (e.g. *L, M*), highly confusable fricative letter names (e.g. *F, S*), and familiar acronyms (e.g. *PC, IT, GB*) being presented. In total, there were 50 unique ordered pairs, half of which rhymed. During the visuo-spatial processing task participants were required to judge whether line patterns inside 50 pairs of hexagons were the same or different by clicking a *match* or *non-match* button. Reaction times for correct trials were used to score both processing tasks.

Two subtests of the Wechsler Abbreviated Scaled of Intelligence (WASI; Wechsler, 1999) were also administered. A test of verbal (Vocabulary) and of non-verbal (Matrix Reasoning) IQ were administered: *t* scores were derived for these two measures and used to calculate a composite score of IQ. This composite score was used for matching participants on baseline performance when assigning to group, but was not used as an outcome measure. The Numerical Operations task of the Wechsler Individual Achievement Test Second Edition (WIAT-II; Wechsler, 2005) was also used to measure mathematical ability. Forms A and B of the Peabody Picture Vocabulary Test, Fourth Edition (PPVT-4) were used for a measure of receptive vocabulary (Dunn & Dunn, 2007).

Cognitive task with no memory load

The Facial Expressions of Emotion Test (Young, Perrett, Calder, Sprengelmeyer, & Ekman, 2002) was used as a measure of emotion expression recognition. This task was included as it has no memory load, meaning it would be possible to test whether any potential gains in cognitive tasks after training or training with stimulation were specific to working memory-loaded activities. During this task participants were presented with 30 morphed faces on an emotional continuum ranging between happiness-surprise, surprise-fear, fear-sadness, sadness-disgust, disgust-anger, and anger-happiness over five blocks. Participants were required to judge which of six emotion labels (*happy, sad, anger, fear, disgust*, and *surprise*) best described each facial expression. Responses were made by clicking one of six boxes with each label presented at the bottom of the screen. There was no limit on response time. Only trials with morphed images of 70% or 90% bias towards a particular expression were used to assess performance. Performance was measured using accuracy scores (total correct out of 20 for each of the six expressions).

2.3.3.2 Training

All participants completed 10 sessions of adaptive Cogmed Working Memory Training (Cogmed, 2005). Each session lasted approximately 45 min (excluding set-up) and involved repeated practice on eight training exercises. Each exercise included 15 trials per session, yielding a total of 120 trials in each session across the tasks. The training tasks were completed according to one of two counterbalanced task orders, to ensure all tasks were completed under active stimulation for those in the stimulation group. A mixed-measures ANOVA with order (A or B) and task (gain for each of the eight training activities) revealed there were no order effects for either the active stimulation group, F (7, 91) = 1.462, p = .191, η_p^2 = .101, or sham stimulation group, F (7, 91) = .943, p = .478, η_p^2 = .068. During the first training session, all exercises were set at an initial low difficulty level of a span of two. The training program followed an algorithm that calibrated the difficulty of each task, by increasing or decreasing span, on a trial-by-trial basis according to the performance of each participant to ensure they were continuously working close to their personal memory limits. Motivational features were built into the training program including a display showing current performance and previous personal high scores. Participants also accumulated *energy* during each exercise which could be used to play a reward racing game at the end of each training session. All responses were made by clicking the items displayed on-screen.

Training involved three simple span tasks requiring immediate serial recall of verbal or visuo-spatial items; these included: Visual Data Link, Data Room, and Decoder (see Figure 2.1 for a screenshot of each of these tasks). During the Visual Data Link task, a sequence of lamps would light up on a 4 x 4 grid and participants were instructed to reproduce the order in which the lamps lit up. In Data Room, a series of lamps within a three-dimensional room would light up and participants were instructed to click on the lamps in the order which they lit up. During Decoder, participants were presented with a row of lamps and three empty boxes in a column underneath each lamp. A sequence of letters was spoken aloud and at the same time a lamp would light up for each letter (from left to right). Participants were instructed to recall the sequence of letters in serial order. For each letter to be recalled a choice of 3 was presented underneath the corresponding lamp and participants were required to click the correct series of letters.

Training also involved five storage tasks with intrinsic processing: Input Module, Input Module with Lid, Number Grid, Rotating Data Link, and Rotating Dots (see Figure 2.1 for a screenshot of each of these tasks). During Input Module, participants were presented with a number keypad (displaying digits 1 - 9). A series of numbers were spoken aloud at the same time as the corresponding numbers lit up on the keypad. Participants were required to recall the sequence in backward order by clicking the number buttons on the keypad. Input Module with Lid was identical, except the keypad was covered by a lid as the numbers were spoken aloud. The lid would then open up and participants had to recall the digits in backward order. During Numbered Grid, a display showing a 4 x 4 grid of covered boxes was presented. Certain numbers would be revealed in a random order at random locations on the grid. Participants had to recall the sequence of digits in ascending numerical order by clicking the correct location of the number. In the Rotating Data Link task, participants were presented with a sequence of lamps lighting up on a 4 x 4 grid. The display would then rotate clockwise by 90 degrees and participants were asked to recall the correct serial order in which the lamps lit up whilst in their new positions. During the Rotating Dots task, ten lamps were presented in a circular display which continuously rotated in a clockwise direction. Lamps would light up in a sequence and participants were required to recall the correct order by clicking the lamps as they continued to rotate.

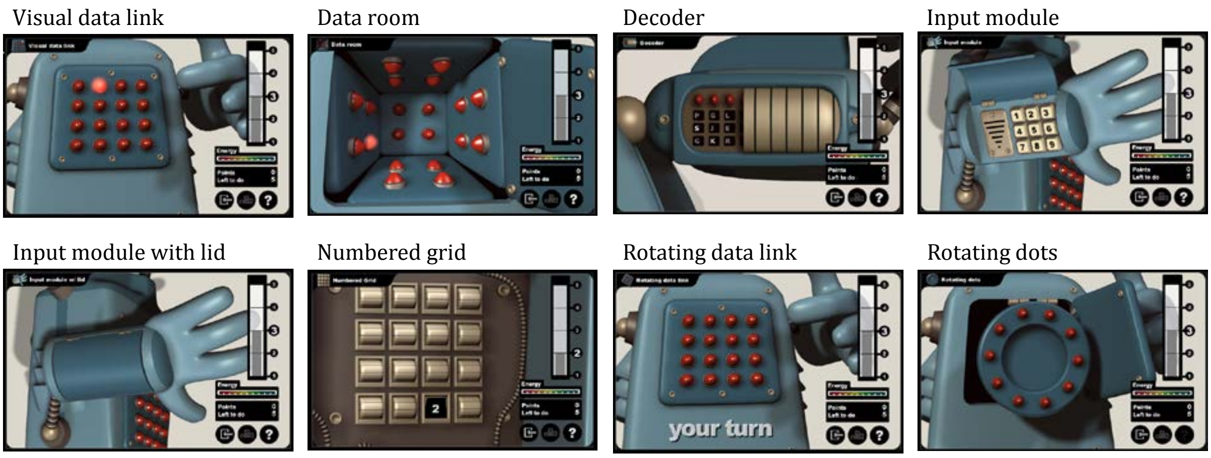


Figure 2.1 – A screenshot of each training activity.

The average span level reached by participants was calculated for each individual training activity for each of the 10 training sessions and was used to measure participants learning on the trained tasks. During session one, participants began at a storage item span level of two for every task. The maximum span participants could reach in this session was below the baseline ability of all participants. As no training took place during the first session it was excluded from all statistical analyses.

2.3.3.3 Stimulation

A pair of 5 x 5 cm rubber electrodes were placed inside saline-soaked synthetic sponges and secured to the head of each participant using a rubber headband. The electrodes were positioned over areas of scalp corresponding to the right and left DLPFC identified using the standard international 10 - 20 EEG procedure (locations F3 and F4). Stimulation was driven via a battery-driven electrical stimulator (Version DC-Stimulator-Plus; NeuroConn). Participants in the active stimulation group received 20 min of high frequency tRNS which began at the onset of training, with 15 s of increasing and decreasing ramps at the beginning and end of stimulation. As in the study by Snowball et al. (2013), high frequency tRNS (101 – 640 Hz) was used, at a current strength of 1 mA, with no DC offset (i.e. varying between -0.5 mA and +0.5 mA), at a sampling rate of 1280 sample/s. For the sham group the stimulator was set to fade in for 15 s and then out over 15 s at the beginning of each session. The display of the stimulator machine was identical for the stimulation and sham groups; hence the experimenter was also blind to the type of stimulation being applied.

2.4 Results

As well as conducting traditional analyses relying on null hypothesis significance testing (NHST), statistical tests using Bayes factors (BF) were also performed. Using Bayesian tests, the strength of evidence can be quantified for the null hypothesis (that stimulation does not enhance on-task training gains) compared to the alternative hypothesis (that stimulation enhances on-task training gains). All Bayesian analyses have been conducted using JASP (The JASP Team., 2017) with default prior scales. Inverse BF (BF_{10}) have been calculated to express the odds in favour of the alternative hypothesis (stimulation has an effect) compared with the null (no effect of stimulation). Therefore, in this study a BF_{10} of 1 to 3 implies weak/anecdotal positive support for the alternative hypothesis, a BF_{10} of 3 to 10 suggests substantial positive evidence for the alternative hypothesis, and a BF_{10} above 10 indicates strong positive evidence for the alternative hypothesis (Kass & Raftery, 1995).

2.4.1 Training data

Training data for both groups, averaged across all tasks are presented in Figure 2.2. A nine by two mixed measures ANOVA, with a between-subjects factor of session (2 to 10) and a within-subjects factor of group (stimulation and sham), was conducted on the average scores of all training activities combined. The analysis revealed a significant main effect of session, $F\,(8, 224) = 105.114$, $p < .001$, $\eta_p^2 = .790$. The main effect of Group, $F\,(1, 28) = .201$, $p = .658$, $\eta_p^2 = .007$, and the interaction between group and session, $F\,(8, 224) = .478$, $p = .871$, $\eta_p^2 = .017$, were non-significant (see Table 2.2). These results suggest that although participants improved in the training over time, stimulation had no additional effect on these gains. Bayesian ANOVAs revealed that a simple main effects model in which group and session were entered separately was preferred to a model that included a group by session interaction ($BF_{10} = 44.202$; see Table 2.2).

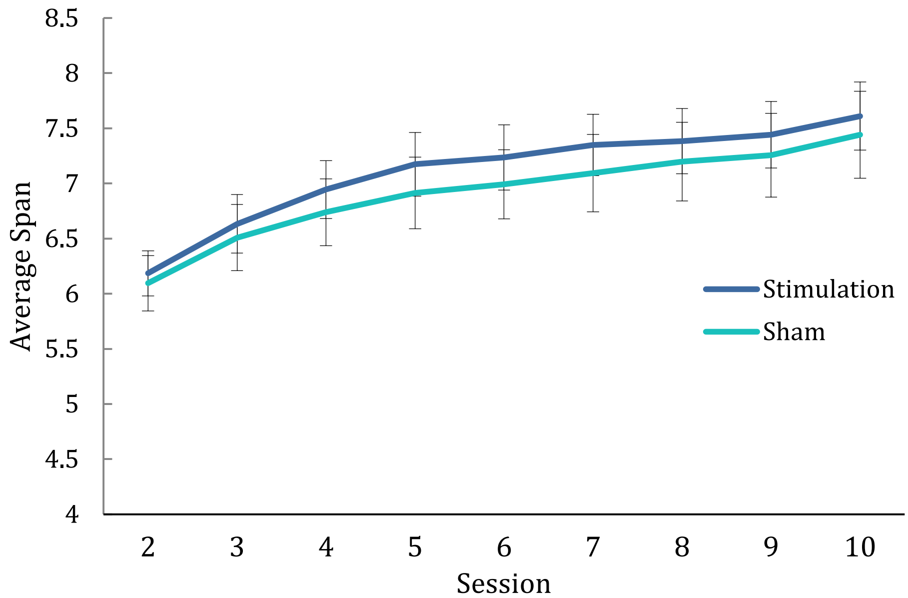


Figure 2.2 – Training data by group, averaged across all training tasks. Note that data from session 1 are not displayed as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants).

Mixed measures ANOVAs were also conducted on participants' training scores for each individual training activity. Performance across all eight tasks for both training groups is presented in Figure 2.3. Group (stimulation and sham) and session (2 to 10) were entered as the between- and within-subjects factors, respectively, for each of the eight tasks. Analyses revealed significant main effects for all tasks (all p values < .001), indicating that participants improved on each task over time. There were no significant main effects of group and no significant interactions between session and group for any of the activities (all *p*s > .05), suggesting no group differences in gains. Bayesian ANOVAs revealed that a simple main effects model in which group and session were entered separately was preferred to a model that included a group by time interaction for each of the tasks (BF_{10} ranging from 8.811 to 74.285 in favour of the main effects model; see Table 2.2), providing strong evidence for similar gains for all eight of the training tasks for both groups.

Next, general linear regression models were conducted for each training task to investigate whether there were any group differences in overall gains for each of the eight training tasks and for average performance across all tasks. For all models, group (active and sham stimulation) was entered as the independent variable and session 10 scores were entered as the dependent variable. Group did not significantly predict training gains (averaged across all tasks), or gains on any of the individual training tasks (see Table 2.2). Bayesian regression analyses were also performed with group (active and sham stimulation) entered as the independent variable, but did not provide any evidence that stimulation influenced gains on any of the training activities, or on average performance across all tasks (all BF_{10} scores < .5; see Table 2.2).

Table 2.2 – Changes in training task performance by group.

	Gains from sessions 2 to 10								Group by session			
	Stimulation		Sham		Group comparison			Bayesian ANOVA BF_{10}				Bayesian ANOVA BF_{10}
	M	*SD*	*M*	*SD*	*Beta*	*t*	*p*		*F*	*p*	*Partial eta*	
Average across all tasks	1.426	0.513	1.346	0.689	-0.064	-0.340	0.737	0.360	0.478	.871	0.017	44.202
Visual data link	1.165	0.631	1.167	0.673	0.029	0.156	0.877	0.348	0.232	.985	0.008	74.285
Data room	1.028	0.739	0.672	0.647	-0.107	-0.567	0.575	0.389	1.136	.340	0.039	8.913
Decoder	0.867	0.761	0.818	0.447	-0.069	-0.368	0.716	0.363	0.236	.984	0.008	60.758
Input module	2.737	2.078	2.719	2.112	-0.085	-0.451	0.655	0.372	0.952	.474	0.033	13.161
Input module with lid	2.611	1.345	2.051	1.511	-0.133	-0.712	0.482	0.417	1.123	.349	0.039	8.811
Number grid	1.025	0.804	1.071	0.837	0.059	0.311	0.758	0.357	0.430	.902	0.015	40.550
Rotating data link	0.959	0.636	0.955	0.748	-0.062	-0.331	0.743	0.359	0.216	.988	0.008	67.100
Rotating dots	1.000	0.686	1.269	0.497	0.008	0.042	0.967	0.345	0.740	.656	0.026	22.717

Note. Data from session 1 were not analysed as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants.

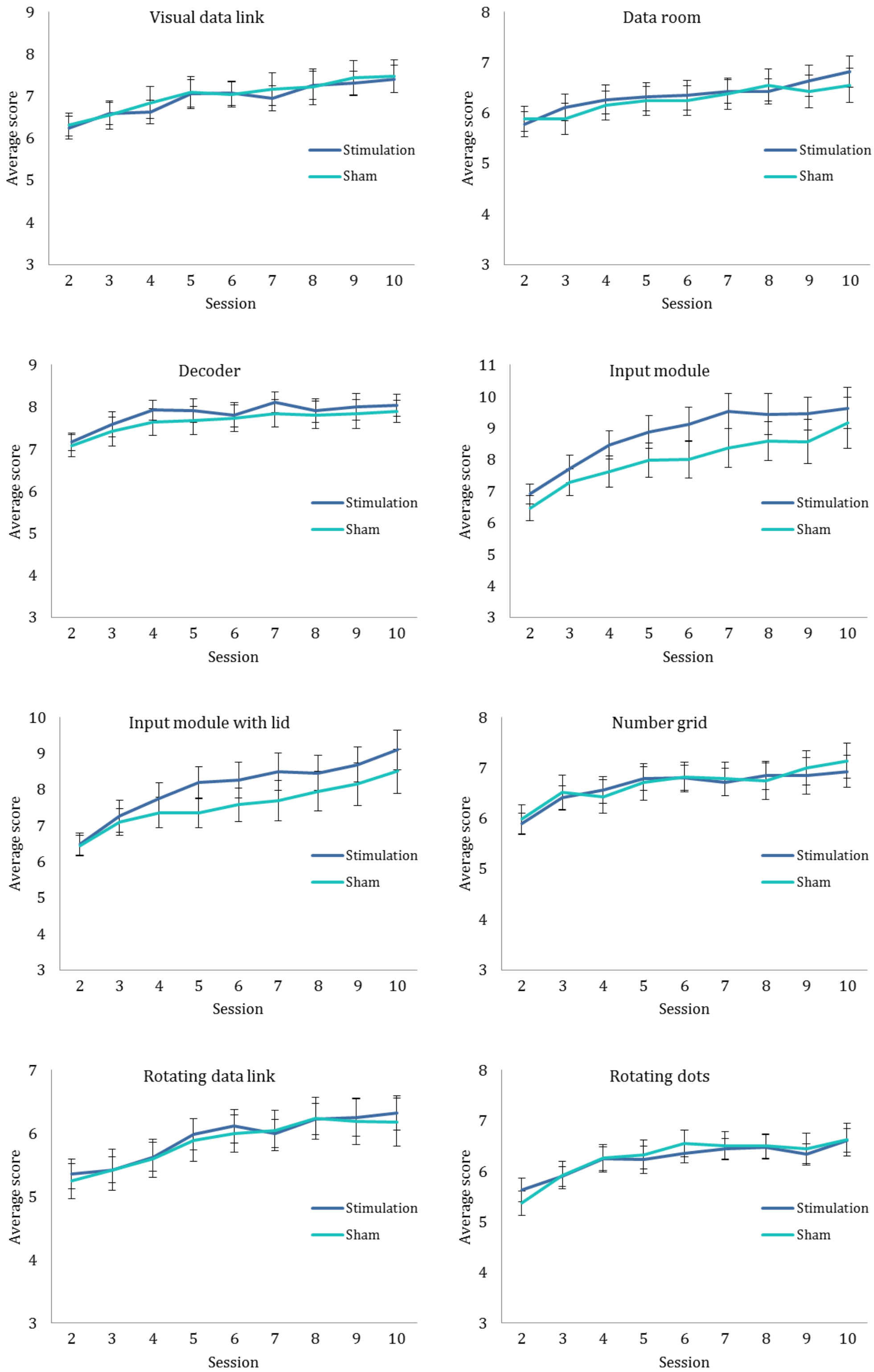


Figure 2.3 – Training data for individual training tasks by group. Data from session 1 are not displayed as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants).

Table 2.3 –Group comparisons of rate of change in performance by group.

	Stimulation			*Sham*			*Group comparison*			*Bayesian t test BF_{10}*
	N	*M*	*SD*	*N*	*M*	*SD*	*t*	*p*	*Cohen's d*	
Average across all tasks	11	0.194	0.087	8	0.138	0.070	1.480	.157	-0.713	0.345
Visual data link	10	0.059	0.286	8	0.171	0.149	-1.002	.331	0.515	0.380
Data room	10	0.067	0.134	8	0.157	0.187	-1.200	.248	0.561	0.347
Decoder	12	0.161	0.188	11	0.173	0.128	1.208	.870	0.076	1.352
Input module	12	0.465	0.302	6	0.257	0.081	1.629	.123	-1.086	1.332
Input module with lid	9	0.367	0.217	8	0.153	0.194	2.123	.051	-1.041	0.715
Number grid	12	0.051	0.456	11	0.210	0.226	-1.041	.310	0.466	0.379
Rotating data link	7	-0.047	0.523	9	0.145	0.139	0.088	.306	0.580	2.135
Rotating dots	12	0.261	0.488	10	0.277	0.075	-0.101	.920	0.057	0.634

Note. Data from session 1 were not analysed as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants).

To investigate whether stimulation enhanced the speed of learning on the training activities, Order 2 polynomial (quadratic) functions ($y = x^2 + x + c$) were computed for each individual training task, and for average performance across all tasks, for each participant separately. These functions allowed the approximate point at which maximum performance was reached (i.e. the asymptote) to be calculated. If stimulation enhanced learning, then the stimulation group should reach the asymptotic point faster than those in the sham group. The polynomial functions were also used to calculate the rate of change, in other words, how quickly participants reached asymptotic performance. The rate of change index was calculated by dividing the maximum score at asymptote by the number of sessions taken to reach asymptotic performance for each participant. Independent samples *t*-tests were then used to compare rate of change scores between groups (see Table 2.3). Only curves that showed an asymptote within the observable training session window were included in the analysis (i.e. if asymptote < session 2 or > session 10). There were no significant differences in rate of change scores between the stimulation and sham groups for the average across tasks, nor for each of the individual tasks. The rate of change score for the Input Module with Lid task approached significance (p = .051), but this result did not survive a correction for multiple comparisons (Bonferroni corrected p = .006). Bayesian independent samples *t*-tests on the rate of change scores for each training task, and for the average across all tasks, provided equivocal support for the null and alternative hypotheses (all BF_{10} scores ranged from 0.345 to 2.135; see Table 2.3). Together, these results suggest that stimulation does not enhance the speed at which participants learn on the training tasks.

2.4.2 Transfer tasks

To investigate the effect of training alone on transfer, a series of paired-samples *t*-tests were performed to compare pre- and post-training scores for each outcome measure on the sample as a whole (see Table 2.4). Family-wise Bonferroni corrections were made to correct for multiple testing. Accordingly, the thresholds for statistical significance were: for process-specific memory tests and for tests of cognitive processes associated with working memory, $p < .006$; for non-process-specific memory tasks and general cognitive abilities, $p < .0125$; for the cognitive task with no memory load, $p < .05$. Significant main effects of training were found for all of the process-specific working memory tasks (all ps $\leq .005$), which persisted after correction for multiple comparisons. Bayesian *t*-tests also provided strong evidence for these effects (BF_{10} ranging from 7.597 to 131219 in favour of the alternative hypothesis that training had an effect on these measures; see Table 2.4). Further *t*-tests demonstrated no evidence for transfer to memory tasks with distinct processes to the training activities following familywise correction for multiple comparisons (all ps $\geq .014$). Bayesian *t*-tests corroborated this pattern of effects for all tasks except for the visuo-spatial *n*-back measure, where a BF_{10} of 3.322 indicated that there was positive evidence for a training effect (all remaining BF_{10} scores ranged from 0.199 to 2.917). Transfer effects to verbal and visuo-spatial information processing tasks and the number operations measure reached significance (all ps $\leq .009$), with BF_{10} scores ranging from 4.726 to 1374 in favour of a training effect. Following familywise correction for multiple comparisons, there was no evidence for training gains on measures of selective attention, inhibitory control, language, and non-verbal reasoning, or on a cognitive task with no memory load (all ps ≥ 0.18). Bayesian *t*-tests confirmed this pattern of effects. BF_{10} scores ranged from 0.195 to 0.319 in support of the null hypothesis for no effect of training on a cognitive task with no memory load, or measures of selective attention and inhibitory control. BF_{10} scores for measures of language and non-verbal reasoning ranged from 0.510 to 2.766 demonstrating equivocal support for the null and alternative hypotheses.

Next, the influence of stimulation on transfer was examined. The pre- to post-training gains for the active and sham stimulation groups are presented in Figure 2.4 for the process-specific tasks and in Figure 2.5 for memory tasks that do not share common processes with the training activities. General linear regression analyses were conducted on all outcome measures. Pre-training scores and group (active or sham stimulation) were entered as the independent variables and post-training scores entered as the dependent variable. Results demonstrated that stimulation group was significant predictor of post-training scores on the verbal *n*-back measure, a memory task with distinct processing properties to the training activities. Training gains were significantly greater for the active versus sham stimulation group (p = .046), however this effect did not survive familywise correction for multiple comparisons (see Table 2.5). Training-related differences all on all other transfer measures were not significant (all ps ≤ .09). Bayesian regression analyses were also performed. A BF_{10} of 1.695 for the verbal *n*-back task provided equivocal support for the null and alternative hypothesis (see Table 2.5). Bayesian tests for all other transfer tasks favoured the null hypothesis (no effect of stimulation; BF_{10} scores ranging from 0.114 to 0.514). In summary, these results provide no compelling evidence that stimulation enhances performance beyond training alone on any outcome measure.

Table 2.4 – Training related changes in transfer tasks on the sample as a whole.

	Pre-training		*Post-training*		*Pre to post*			*Bayesian t test BF_{10}*
	M	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*	
Process-specific memory tasks								
Digit recall	100.833	15.735	108.567	15.850	-4.500	***<.001***	0.490	255.700
Dot matrix	105.200	22.352	120.100	21.865	-6.971	***<.001***	0.674	131219.000
Backward digit recall	101.367	19.345	115.200	15.338	-5.897	***<.001***	0.798	8818.000
Mr X	105.500	19.011	114.733	16.885	-5.541	***<.001***	0.514	3573.000
Verbal storage	7.967	1.351	8.967	1.732	-4.664	***<.001***	0.649	385.700
VS storage	7.267	1.311	8.033	1.752	-3.516	***.001***	0.500	23.720
Verbal backward	6.567	1.612	8.133	1.548	-4.683	***<.001***	0.991	405.000
VS backward	6.433	1.695	7.367	1.921	-3.006	***.005***	0.517	7.597
Memory tasks with distinct processes								
Verbal N-back	4.933	1.660	5.400	2.313	-1.304	.203	0.235	0.419
VS N-back	3.567	1.547	4.333	1.936	-2.605	**.014**	0.440	3.322
Verbal complex span	6.133	2.300	6.900	2.551	-2.538	**.017**	0.316	2.917
VS complex span	4.667	1.863	4.600	2.061	0.220	.827	-0.034	0.199
Processes associated with working memory								
Verbal Flanker effect	82.774	31.099	79.324	66.107	0.335	.740	-0.071	0.205
VS Flanker effect	75.165	76.888	74.031	66.553	0.064	.949	-0.016	0.195
Verbal Stroop effect	43.349	130.081	76.764	136.269	-1.004	.324	0.251	0.308
VS Stroop effect	124.442	68.500	145.107	114.984	-1.043	.306	0.225	0.319
Information processing and general cognitive abilities								
Verbal processing	2071.471	580.697	1916.782	328.809	2.780	***.009***	-0.340	4.726
VS processing	1221.261	435.736	1017.350	308.897	5.166	***<.001***	-0.548	1374.000
Matrix reasoning	60.667	4.950	62.600	4.223	-2.511	**.018**	0.421	2.766
Vocabulary	61.700	8.125	63.533	8.427	-2.483	**.019**	0.221	2.624
Number Operations	112.400	17.047	115.800	15.624	-3.111	***.004***	0.208	9.532
Peabody Picture Vocabulary Test	110.467	14.277	112.567	18.823	-1.467	.153	0.127	0.510
Cognitive task with no memory load								
Emotion hexagon	89.806	8.704	89.698	8.212	0.088	.930	-0.013	0.195

Note. **Bold** text denote significant effects at $p < .05$ level, ***bold italics*** indicate significant effects after family-wise correction for multiple comparison. VS = visuo-spatial.

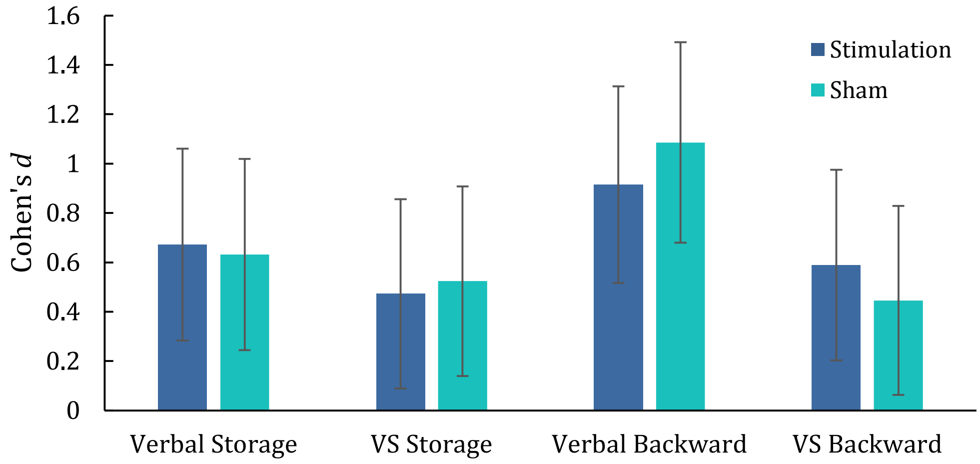


Figure 2.4 – Change in process-specific memory tasks by group. Mean effect sizes for pre- to post-training gains are displayed. VS = visuo-spatial.

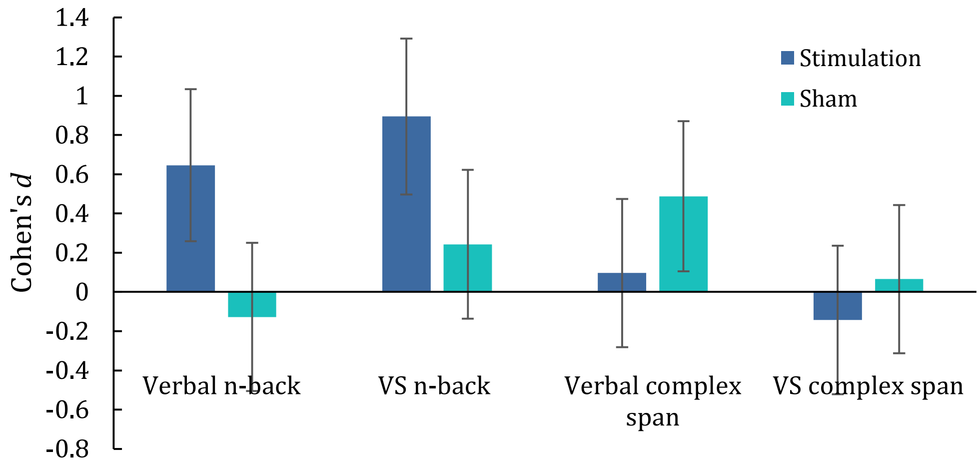


Figure 2.5 – Change in memory tasks with distinct processes by group. Mean effect sizes for pre- to post-training gains are displayed. VS = visuo-spatial.

Table 2.5 (continued on the next page) – Training and stimulation effects by group.

	Stimulation				*Sham*				*Baseline group comparisons*			*Group comparison in training gain*			
	Pre-training		*Post-training*		*Pre-training*		*Post-training*								
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*	*Beta*	*t*	*p*	*Bayesian regression BF_{10}*
Process-specific memory tasks															
Digit recall	101.067	15.696	110.467	15.264	100.600	16.322	106.667	16.723	0.080	.937	0.029	-0.110	-1.019	.317	0.270
Dot matrix	103.733	23.313	120.867	23.676	106.667	22.064	119.333	20.701	-0.354	.726	-0.129	-0.093	-0.966	.343	0.223
Backward digit recall	101.000	20.078	113.867	15.95	101.733	19.282	116.533	15.137	-0.102	.919	-0.037	0.074	0.584	.564	0.249
Mr X	103.133	22.247	110.667	19.667	107.867	15.287	118.800	12.974	-0.675	.505	-0.251	0.136	1.523	.139	0.381
Verbal storage	8.000	1.690	9.067	1.486	7.933	0.961	8.867	1.995	0.133	.895	0.051	-0.040	-0.310	.759	0.231
VS storage	7.533	1.125	8.200	1.699	7.000	1.464	7.867	1.846	1.119	.273	0.412	0.057	0.426	.673	0.243
Verbal backward	7.000	1.512	8.400	1.549	6.133	1.642	7.867	1.552	1.504	.144	0.550	-0.092	-0.491	.627	0.473
VS backward	6.200	1.699	7.200	1.699	6.667	1.718	7.533	2.167	-0.748	.461	-0.273	0.010	0.059	.953	0.323
Memory tasks with distinct processes															
Verbal *n*-back	4.800	1.612	6.000	2.104	5.067	1.751	4.800	2.426	-0.434	.668	-0.159	-0.311	-2.088	**.046**	1.695
VS *n*-back	3.200	0.862	4.200	1.373	3.933	1.981	4.467	2.416	-1.315	.199	-0.516	-0.077	-0.483	.633	0.337
Verbal complex span	6.600	1.595	6.800	2.541	5.667	2.820	7.000	2.646	1.116	.274	0.423	0.208	1.757	.090	0.286
VS complex span	4.733	1.335	4.467	2.386	4.600	2.324	4.733	1.751	0.193	.849	0.073	0.089	0.613	.545	0.322
Processes associated with working memory															
Verbal Flanker effect	79.551	16.718	74.196	30.288	85.998	41.250	84.452	89.882	-0.561	.579	-0.222	0.024	0.144	.886	0.345
VS Flanker effect	51.239	45.467	84.178	65.175	99.091	94.614	63.883	68.603	-1.766	.088	-0.683	-0.205	-1.033	.311	0.514
Verbal Stroop effect	8.534	45.324	81.750	184.192	78.164	174.354	71.778	66.971	-1.497	.146	-0.634	-0.059	-0.296	.770	0.381
VS Stroop effect	131.600	43.697	159.288	135.996	117.285	87.753	130.926	91.984	0.566	.576	0.218	-0.085	-0.479	.636	0.430

Note. **Bold** text denote significant effects at $p < .05$ level. VS = visuo-spatial.

Table 2.5 (continued) – Training and stimulation effects by group.

	Stimulation				*Sham*				*Baseline group comparisons*			*Group comparison in training gain*			
	Pre-training		*Post-training*		*Pre-training*		*Post-training*								
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*	*Beta*	*t*	*p*	*Bayesian regression BF_{10}*
Information processing and general cognitive abilities															
Verbal processing	1951.487	121.174	1822.971	107.384	2191.454	808.066	2010.594	439.959	-1.137	.265	-0.516	0.101	1.374	.181	.244
VS processing	1142.336	213.788	946.584	179.034	1300.186	578.135	1088.117	393.530	-0.992	.330	-0.399	0.072	0.805	.428	.174
Matrix reasoning	62.067	4.847	63.000	3.836	59.267	4.803	62.200	4.678	1.589	.123	0.580	0.079	0.489	.629	.341
Vocabulary	61.067	7.324	62.800	7.757	62.333	9.069	64.267	9.262	-0.421	.677	-0.154	0.019	0.206	.839	.135
Number Operations	111.867	18.712	116.867	14.764	112.933	15.850	114.733	16.888	-0.168	.867	-0.062	-0.099	-1.534	.137	.270
Peabody Picture Vocabulary Test	108.267	13.285	110.533	17.125	112.667	15.342	114.600	20.780	-0.840	.410	-0.307	-0.036	-0.483	.633	.114
Cognitive task with no memory load															
Emotion hexagon	88.833	9.193	90.135	8.732	90.778	8.389	89.262	7.940	-0.605	.550	-0.221	-0.134	-0.976	.338	.373

Note. **Bold** text denote significant effects at $p < .05$ level. VS = visuo-spatial.

2.5 Discussion

As predicted, adaptive working memory training was associated with gains on the training activities and enhanced performance on transfer measures with processing and storage demands in common with the training tasks. These data are consistent with previous research demonstrating that practice improves performance on the training tasks and that training improves performance on working memory tasks that share overlapping features with the training activities (E. Dahlin, Neely, et al., 2008; Melby-Lervåg & Hulme, 2012; von Bastian & Oberauer, 2013).

There was little evidence for the benefits of training alone on working memory measures that had minimal overlap with the training tasks. The Cogmed training involved practice on several serial recall activities that required the reproduction of a sequence of verbal or visuo-spatial memory items, or the mental manipulation of items prior to recall (e.g. reversing a sequence of digits or rotating a sequence of spatial locations). Training did not improve performance on complex span tasks, which have a novel structure that involves switching between the storage of memory items and an unrelated processing activity. There was a small training-related gain on the visuo-spatial *n*-back measure, which involves continuous updating and recognition of items. However, this effect did not survive correction for multiple comparisons, and the Bayesian analyses revealed positive but not strong evidence for this finding. Overall, this pattern of effects is consistent with previous literature demonstrating that training produces task-specific learning that does not generalise to other categories of working memory paradigm (Dunning & Holmes, 2014; Holmes et al., 2018; Minear et al., 2016; von Bastian & Oberauer, 2013).

There was also no evidence for more distant transfer of working memory training effects without stimulation to tests of non-verbal reasoning and language ability. Small increases in speed of responses on tests of verbal and visuo-spatial information processing were observed, along with small improvements on a test of mathematical ability (three standard score points). However, without a no-intervention test-retest, or placebo training control group, it cannot be determined whether these effects reflect genuine training benefits or repetition effects. The general pattern of far transfer is consistent with the working memory training literature, which provides no consistent evidence that training alone ameliorates the everyday difficulties associated with working memory, such as problems in attentional focus and learning (Dunning et al., 2013; Holmes et al., 2015; Shipstead et al., 2012; Simons et al., 2016).

tRNS did not modulate the speed of learning or magnitude of gains on the training tasks, and there was no evidence that it facilitated the generalization of gains to untrained working memory tasks that were similar in structure to training activities. There was no effect of stimulation on the majority of working memory transfer tasks with distinct processing demands, including visuo-spatial *n*-back, verbal complex span, and visuo-spatial complex span. tRNS was found to modulate gains on the verbal *n*-back task, a paradigm that does not share common processes with the trained activities. Training gains were significantly greater for participants who received active versus sham stimulation, however this effect did not survive correction for multiple comparisons and Bayesian analyses provided equivocal support for the null and alternative hypothesis. There was also no enhancement by stimulation to other measures of far transfer, including tests of mathematics, attention, and processing speed. Therefore, there is little evidence from the current study that random noise stimulation boosts transfer to either working memory measures or other cognitive tasks that have minimal overlap with the training activities. Crucially, the results of the current experiment demonstrate that tRNS does not overcome major limitations to enhance far transfer following training.

The results of this experiment are inconsistent with findings in another cognitive domain where tRNS was found to enhance learning when combined with mathematics training (e.g. Cappelletti et al., 2013; Snowball et al., 2013). This may reflect differences in the impact of tRNS on the different interventions, as working memory training and mathematical training could have different effects on the neural substrates they target. Furthermore, it is unclear how the complexity of the training programs and their doses interact with stimulation. In the current study, training involved practice on a variety of tasks, yet in the studies conducted by Cappelletti et al. (2013) and Snowball et al. (2013), participants trained on either a single task, or on two tasks, respectively. tES may be more effective when combined with intensive, concentrated training on a single paradigm; this will be investigated in a follow-up experiment (see Chapter 3). Further research also needs to be conducted to examine the impact of different stimulation protocols when applied to other cortical regions and combined with different training regimes. Candidate factors for further investigate include the type, duration, and intensity of stimulation (Batsikadze et al., 2013; Monte-Silva et al., 2010). For example tDCS, an alternative type of stimulation, has shown promise for enhancing working memory training (e.g. Au et al., 2014; Ruf et al., 2017). This will be discussed further in the following chapter (see Chapter 3).

To conclude, this experiment provides the first test of the potential additive benefits of combining tRNS with working memory training. Strong training gains were observed on trained activities and overlapping transfer tasks in participants irrespective of stimulation condition.

However, using the most rigorous intervention design, there was no reliable evidence that random noise stimulation enhances the rate of learning or magnitude in gains on the training tasks, or that it extends the limited transfer found with working memory training.

Although it did not survive the correction for multiple comparisons, the significant group difference found for the verbal *n*-back task, provides some indication that tRNS may have promoted the generalization of training gains to working memory tasks that involve a different structure. It is possible that this is a genuine effect that has been lost in this large-scale exploratory study or that it may simply be a spurious finding. To investigate this effect, a more focused follow-up study was conducted to examine whether stimulation enhances the transfer of training gains across two well-validated working memory paradigms (see Chapter 3).

Chapter 3 Backward digit training: Cross-paradigm transfer and the effects of transcranial direct current stimulation (tDCS)

3.1 Aims

Working memory training is associated with improvements on untrained memory tasks when features overlap between the trained activities and transfer tasks (E. Dahlin, Neely, et al., 2008; Soveri, Antfolk, et al., 2017; Soveri, Karlsson, Waris, Grönholm-Nyman, & Laine, 2017; von Bastian & Oberauer, 2014). To date, there has been little systematic investigation into the processes or features that must overlap between trained and untrained tasks for transfer to occur. They could include paradigm-specific skills such as updating (E. Dahlin, Neely, et al., 2008), or processes related to encoding or maintaining the memory items (Ericsson, Chase, & Faloon, 1980; Minear et al., 2016; von Bastian & Oberauer, 2014). Transcranial direct current stimulation (tDCS) has been shown to enhance on-task working memory training gains (Au et al., 2016; Richmond et al., 2014; Ruf et al., 2017) and promote transfer to untrained tasks (Au et al., 2016; Ruf et al., 2017), but there has been no systematic investigation into the limits of these potential enhancements across untrained tasks. The two key aims of this study were to: (1) understand the limits of transfer within working memory by examining the task characteristics that must overlap between training and transfer activities for transfer to occur, and (2) to examine whether tDCS can enhance training and/or promote the generalisation of training effects within and across working memory paradigms.

3.2 Introduction

3.2.1 Training transfer

Improvements on untrained working memory tasks following training typically only occur under circumstances where there is substantial overlap between the structural properties, features, and processes of training and transfer tasks (Melby-Lervåg & Hulme, 2012; Simons et al., 2016). There is little evidence that training benefits everyday functions that rely on working memory (e.g. Dunning, Holmes, & Gathercole, 2013), or that training-related gains generalise to other working memory tasks that involve distinct processes to the training activities (Simons et al., 2016). These findings suggest that training is not altering the fundamental capacity or efficiency of working memory, and instead support a task- or process-specific theory of transfer. According to these accounts, training is promoting the development of processes or strategies that are specific to the training activities and transfer occurs for untrained tests with shared processes and characteristics (E. Dahlin, Neely, et al., 2008; Dunning & Holmes, 2014; Gathercole et al., 2018; Minear et al., 2016; Sprenger et al., 2013; von Bastian & Oberauer, 2014). This idea is not new. In fact, over a hundred years ago Thorndike and Woodworth's (1901) principle of *identical elements* stated that the level of similarity between the training and test situation will determine the degree to which information is transferred. The more similar the training and test situations are, the more likely it is that information will transfer. Conversely, if the situations have nothing in common then transfer is unlikely.

The boundary conditions for transfer following working memory training are not well understood: it is not clear what the overlapping properties must be between the training and test tasks to generate transfer. So far, the field of working memory training has been hampered by a lack of theory driven accounts of transfer and a lack of hypothesis driven research (von Bastian & Oberauer, 2014). Many studies rely on post hoc explanations of observed patterns of transfer (e.g. Sprenger et al., 2013; von Bastian & Oberauer, 2013), or include a variety of training activities and/or outcome measures with varying degrees of overlapping task features, which makes it difficult to isolate the task properties that constrain transfer (e.g. Anguera et al., 2012; Redick et al., 2013; Sprenger et al., 2013; Thompson et al., 2013; von Bastian, Langer, Jäncke, & Oberauer, 2013). To understand the boundary conditions to transfer, studies are needed that systematically manipulate common characteristics across training and transfer tasks.

Task- and process-specific accounts of transfer predict the benefits of training will be minimal across different categories of working memory task (e.g. *n*-back to complex span) because the training and outcome activities share so few overlapping features. However, it remains unclear whether limits on cross-paradigm transfer are associated with processes or strategies tied specifically to the trained task (e.g. the requirement to update the contents of working memory as in an *n*-back task), or to other aspects of the task content including stimulus-specific features such as the domain of to-be-remembered items (i.e. verbal or visuo-spatial materials) and the type of memoranda (e.g. materials could be digits or letters). Therefore, there are a number of candidate task characteristics that might drive transfer including: paradigm, stimulus domain, and stimulus materials. Each of these will be considered in the following sections (see Section 3.2.1.1 for paradigm, Section 3.2.1.2 for stimulus domain, and Section 3.2.1.3 for stimulus materials).

3.2.1.1 Paradigm

Working memory can be measured and trained using a variety of different paradigms such as backward recall, complex span, and *n*-back. Although these tasks are considered valid indicators of working memory capacity, they differ in terms of their storage and processing demands (e.g. explicit serial recall, interpolated processing, or updating and recognition). For a full description of different categories of working memory task see Section 1.3. Transfer might be mediated by paradigm-specific cognitive processes. For example, repeated practice on a complex span task could be training coordinated processes to protect memory items from distraction, whereas practice on *n*-back could be training the ability to update the contents of working memory.

Investigations into cross-paradigm transfer have produced mixed results. Some studies do report cross-task transfer. Several studies have reported positive transfer following *n*-back training to complex span (Anguera et al., 2012; Schwarb, Nail, & Schumacher, 2016). Similarly, in an unpublished report conducted by Seidler and colleagues (2010), participants showed small improvements on operation span following *n*-back training. However, the majority of studies fail to demonstrate transfer across different categories of working task (e.g. Holmes, Woolgar, Hampshire, & Gathercole, 2018; Li et al., 2008; Minear et al., 2016; Redick et al., 2013; Thompson et al., 2013). For example, Redick et al. (2013) failed to show transfer to symmetry or running span tasks following dual *n*-back training containing visuo-spatial (location of squares) and auditory verbal (letters) materials. Similarly, Thompson et al. (2013) found that dual *n*-back training, also involving auditory letters and visual spatial locations, did not transfer to operation span or reading span tasks. Several other studies have also reported an absence of training effects from practice on *n*-back tasks to complex span tasks (Chooi & Thompson, 2012; Holmes et al., 2018; Lilienthal, Tamez, Shelton, Myerson, & Hale, 2013) and vice versa (Holmes et al., 2018; von Bastian et al., 2013). Similarly, Shavelson, Yuan, Alonzo, Klingberg, and Anderson, (2008) found that gains following training on a working memory program with a variety of tasks focusing on forward and backward serial recall (e.g. Cogmed) did not transfer to a complex span task (operation span), or an updating task (running span). Another study failed to show transfer from *n*-back training to backward digit span (Heinzel et al., 2014).

The lack of cross-paradigm transfer between different working memory tasks supports the theory that paradigm is a boundary condition to transfer. One explanation for this pattern of effects is that transfer is mediated by paradigm-specific cognitive processes. For example, Dahlin, Neely, Larsson, Bäckman, and Nyberg (2008) reported transfer to *n*-back following training on a running span task, but not to a Stroop task. They suggested this pattern of gains might reflect improvements in the ability to update the contents of working memory following training, which benefitted other tasks involving updating (i.e. running span) but not tasks with different processing requirements (i.e. Stroop). Functional imaging also revealed training-related activity in a striatal region that mirrored activity observed during the updating transfer task. Therefore, transfer may only occur if the training and transfer tasks engage overlapping brain regions and share processing demands.

If training is enhancing task-specific cognitive processes then the benefits of training would be predicted for untrained tasks that involve the same processes. For example, *n*-back tasks require regular updating of the contents of working memory, and so training benefits from *n*-back would be predicted to generalise to other tasks requiring updating such as running span. However, evidence supporting this idea is inconsistent. For example, while one study found that training on a dual *n*-back task was associated with significant gains on running span, but not complex span (Lilienthal et al., 2013), another failed to demonstrate such effects of transfer from *n*-back to running span (Redick et al., 2013). This explanation fails to explain why transfer effects are often absent across paradigms that involve the same cognitive processes. If training is enhancing paradigm-specific processes then within-paradigm transfer to tasks that use novel materials is also expected (e.g. complex span to untrained versions of complex span). These effects are also inconsistent. Training on verbal (operation) and visuo-spatial (symmetry) complex span tasks results in generalisation to untrained complex span tasks, despite them containing different distractor episodes and novel memory items to those used in the training activities (Harrison et al., 2013). This could be due to complex span training enhancing the ability to resist interpolated distraction. Similarly, gains are found on untrained versions of *n*-back with novel materials following *n*-back training (Holmes et al., 2018; Minear et al., 2016). However, some studies fail to show transfer within-paradigm to untrained versions of complex span with novel materials (Holmes et al., 2018; Minear et al., 2016). Note that for the Minear et al. (2016) study, a composite complex span score was used to measure transfer.

An alternative theory, which builds on the process-specific account, is that training promotes the development of novel cognitive routines for trained tasks and transfer will occur when these routines can be applied to untrained tasks (Gathercole et al., 2018). According to this framework, in order to perform a working memory task that has a complex and unfamiliar structure, a new routine must be constructed and refined. Cognitive routines co-ordinate existing component cognitive processes into a novel sequence to meet task demands and have a hierarchical structure composed of repeated sub-routines. With repeated practice over time they become more efficient and autonomous (Gathercole et al., 2018), mirroring the types of changes that are found during the course of acquiring other complex cognitive skills (Anderson, 1982; Tenison & Anderson, 2016). This framework differs to previous accounts of transfer. While a process-specific account might argue that training is enhancing a single underlying process (e.g. updating), this new theory refers to the sequencing and coordination of processes, and the extent to which this sequence of processes can be applied to untrained tasks.

Gathercole et al.'s (2018) framework also makes specific predictions about training and transfer. First, training will only occur for tasks that are highly unfamiliar: there will be minimal training gains for tasks that can be performed using routines or mechanisms that are already highly practiced (Gathercole et al., 2018). For example, the processes required to perform a verbal short-term memory task such as forward digit recall are well-established and commonly used in everyday life (Baddeley et al., 1984; Gathercole et al., 2018). There is therefore no need to establish a new routine to perform the task, and limited scope for training gains. Small gains on such tasks might reflect fine tuning of existing mechanisms. Second, transfer will only occur if the cognitive routines or strategies developed during training can be readily modified to meet the demands of an untrained working memory task. For example, training on an unfamiliar task such as backward recall with digits requires a new routine to be developed for the recall phase. In order to successfully perform this task, the routine must draw on established cognitive processes to make repeated covert cycles of forward recall through the sequence to enable the final digit to be reported. The novel aspect of the routine comes in peeling off the final digit successively with each cycle through the sequence (Anders & Lillyquist, 1971; Thomas, Milner, & Hanerlandt, 2003). Transfer is predicted for other tasks to which the same routine can be applied. For example to untrained backward span tasks with other types of verbal material, such as letters or words. However, the overall cognitive routines that are employed to perform other types of task such as complex span and *n*-back are distinct, and so this framework does not predict cross-paradigm transfer.

3.2.1.2 Stimulus domain

It is unclear whether cross-stimulus domain transfer occurs within a working memory paradigm (e.g. backward recall training with digits to backward spatial recall). Working memory training might be targeting processes or strategies that are specific to the verbal or visuo-spatial domain of task content. For instance, training on tasks with verbal stimuli might promote the development of chunking that can be used to remember verbal items such as letters and digits, but is unlikely to be used for visuo-spatial materials. Transfer might therefore be predicted across trained and untrained tasks with same-domain stimuli, but not across training and transfer tasks with different domain-stimuli. As described earlier (see Section 1.2.1), verbal and visuo-spatial recall are both served by specific processes for encoding and maintaining item and order information. Verbal information is stored and maintained in the phonological loop, while visuo-spatial information is held in the visuo-spatial sketchpad (Baddeley, 1986, 2012b; Baddeley & Logie, 1999; Logie, 1995; Logie & Pearson, 1997).

According to the theory proposed by Gathercole and colleagues (2018) that training involves creating a new routine to perform unfamiliar task, transfer is not predicted to an untrained task with materials from a different domain to the training task (i.e. training on backward recall with verbal materials such as digits will not transfer to backward spatial recall). This is for two reasons. Firstly, backward versus forward recall results in a greater impairment in span for verbal than for spatial stimuli (Isaacs & Vargha-Khadem, 1989), suggesting the processes required for reversing verbal and visuo-spatial materials are fundamentally different. Second, while verbal rehearsal is a well-practiced mechanism established in short-term memory, the efficiency of spatial rehearsal is less practiced and much more attentionally demanding (Gathercole et al., 2018; Pearson, Ball, & Smith, 2014). Therefore, it is anticipated that the routines required for backward span tasks with verbal and spatial stimuli will differ substantially.

Within-paradigm cross-stimulus domain transfer effects are inconsistent. Some studies demonstrate positive effects. For example, *n*-back training with spatial locations transfers to untrained *n*-back tasks with letters or digits (Buschkuehl et al., 2014; Li et al., 2008), and vice versa (Bürki, Ludwig, Chicherio, & de Ribaupierre, 2014). On the other hand, some fail to show this pattern. Blacker et al. (2017) found no benefits on verbal complex span containing letters and numerical operations following training on a visuo-spatial complex span task involving spatial locations and symmetry judgement of shapes. Therefore, it is unclear whether stimulus domain is a barrier to transfer, and so far, no studies have investigated cross-domain transfer within a backward serial recall paradigm.

3.2.1.3 Stimulus materials

The type of memoranda could also be a barrier to transfer. Training-related improvements could arise through the development or refinement of stimulus-specific mnemonic strategies (Gathercole et al., 2018; Minear et al., 2016), such as chunking to remember a series of letters as a word or familiar acronym, or mentally tracing a shape to remember spatial locations. Such strategies could be specific to the memory items (type of material), as found in a study showing that training for sequences of digits was tied to the use of mnemonic strategies (based on familiar units of long-distance running times) that could not be applied to novel letter materials (Ericsson, Chase, and Faloon, 1980). This account assumes that the development of such material-specific strategies should lead to training-related gains on other tasks with the same content. However, Minear et al. (2016) found that participants completing spatial *n*-back training reported using mental imagery (e.g. tracing shapes) to keep track of sequence locations, but found no evidence of transfer to visuo-spatial complex span tasks that also involved keeping track of spatial locations. Likewise, following verbal complex span training, most of the participants reported using a strategy specifically for remembering letters (i.e. chunking to remember sequences by associating the letters with words and forming sentences, or linking letters with acronyms or people's initials), but no improvements were found on other untrained memory tasks using letters.

Some studies have, however, found within-paradigm transfer to tasks with different categories of stimuli in the same domain. For example, training on an *n*-back task with letters transfers to *n*-back with digits (Küper & Karbach, 2016). Similarly, gains on *n*-back tasks containing visuo-spatial items such as shapes or objects have been found following training on *n*-back with spatial locations (Jaeggi, Studer-Luethi, et al., 2010). These results indicate that material specificity may not be a boundary condition to transfer.

3.2.2 Stimulation

Neuroimaging studies have shown that the dorsolateral prefrontal cortex (DLPFC) plays an important role in working memory (Curtis & D'Esposito, 2003; D'Esposito et al., 1998; Owen, 1997, 2000; see Section 1.5.5 for more details), and tDCS applied this region has been shown to boost working memory performance in single sessions in numerous studies (Andrews et al., 2011; Boggio et al., 2006; Fregni et al., 2005; Jeon & Han, 2012). Several studies have also investigated the use of tDCS in multi-session training protocols with young healthy adults and produced mixed results (Au et al., 2016; Martin et al., 2013; Richmond et al., 2014; Ruf et al., 2017). Au et al. (2014) found evidence for an enhanced rate of learning (i.e. a steeper rate of improvement) for participants completing visuo-spatial *n*-back working memory training with active tDCS over left or right DLPFC relative to those receiving sham tDCS. Stimulation also enhanced performance on untrained versions of *n*-back relative to sham stimulation in this study. Similarly, Ruf et al. (2017) found that active tDCS to left and right DLPFC enhanced the rate of learning for verbal and spatial versions of *n*-back working memory training and also led to greater improvements on an untrained version of *n*-back relative to sham stimulation.

Other studies have failed to demonstrate enhancements by tDCS. Richmond, Wolk, Chein and Olson (2014) found that active tDCS over left DLPFC resulted in enhanced on-task training gains on a verbal, but not spatial, complex span task relative to sham stimulation. Although they found evidence that tDCS shifted the learning curve of training upwards, it did not increase the rate of learning. The authors also claimed that stimulation enhanced transfer to untrained working memory tasks, however this was only found for the active stimulation with training group when they were compared to a no-intervention group. Critically, no significant differences were found between the training groups with active and sham tDCS. Consequently, this effect can be attributed to training alone. In another study by Martin et al. (2013), tDCS applied over the left DLPFC during dual *n*-back working memory training did not enhance on-task training gains. In terms of transfer, although the training group with real stimulation showed greater gains on an untrained working memory task at outcome compared to a tDCS only group (no training), again no significant differences were found between the training groups with active versus sham stimulation (Martin et al., 2013).

3.2.3 Aims

3.2.3.1 Training transfer

To increase our understanding of the constraints on transfer it is important to track the degree, or distance, to which training gains generalise within and across different categories of working memory paradigm. The novel aim of the current study was to do this by systematically manipulating the degree of overlap between training and transfer tasks to test whether paradigm, stimulus domain, or stimulus material constrain transfer. Table 3.1 summarises the training and transfer tasks. The generalisation of gains following training on backward digit recall (BDR) was tracked both to other variants of backward recall (with letters and spatial locations) and also to different variants of *n*-back tasks.

Within-paradigm transfer was explored to test whether stimulus type or domain restricted transfer. A number of backward recall measures were included at outcome to assess: (i) generalisation to the same paradigm with the same materials (BDR), (ii) transfer to the same paradigm with novel stimuli in the same domain (backward letter recall), and (iii) transfer to the same measure with novel materials in a different domain (backward recall with spatial locations). Post-training gains on backward letter recall would demonstrate that category of materials does not constrain transfer, and gains on backward spatial recall would suggest that neither does stimulus domain.

Table 3.1 – Trained and untrained tasks.

Task paradigm	*Stimulus domain*	*Stimulus category*
Training		
Backward recall	Verbal	Digits
Transfer		
Backward recall	Verbal	Digits
Backward recall	Verbal	Letters
Backward recall	Visuo-spatial	Spatial locations
n-back	Verbal	Digits
n-back	Verbal	Letters

Cross-paradigm effects were tested by including two *n*-back tasks at pre- and post-training: (i) an *n*-back task with the same materials as the training task (*n*-back with digits), and (ii) an *n*-back task with distinct materials from the training task, but from the same domain as the memory items in the training task (*n*-back with letters). If paradigm is a barrier to transfer, then transfer is not predicted from training on backward digit recall to any of the n-back tasks. This may be due to substantial differences in the structural properties and processing demands of the tasks. During *n*-back a full sequence of items must be refreshed as a new item is added to the list and the first item is dropped, meaning the serial position of storage items must be continuously updated as the list is presented. In contrast, in a backward recall task all storage items are presented prior to any manipulation of information, meaning the whole sequence must be held in mind and then transformed following encoding. *n*-back also requires recognition and familiarity-based responding during list presentation, while backward serial order tasks require explicit recall (Oberauer, 2005). Given the substantial differences in the structural properties of the tasks, there will be little overlap between the cognitive routines for the two paradigms, meaning cross-paradigm transfer is unlikely (Gathercole et al., 2018). Gains on *n*-back with digits would mean training transfers across paradigm and across stimuli, and improvements on *n*-back with letters would mean paradigm and stimulus materials do not constrain transfer. Lack of transfer to any *n*-back task would suggest that paradigm is barrier to transfer.

A common methodological limitation in the cognitive training field is the lack of an adequate active control training group (Redick et al., 2013). Typically, no-intervention or placebo (non-adaptive training) groups are used as controls. However these protocols are not sufficiently cognitively demanding and fail to control for motivation and expectancy effects (see Section 1.4.2, for further explanation). To overcome this problem the current study included an active control training group who completed an adaptive visual search task. Performance on visual search is unrelated to working memory ability (Kane et al., 2006), and adaptive training on this task does not result in gains on working memory transfer measures (Harrison et al., 2013; Redick et al., 2013). Note that the group completing visual search training also received sham stimulation to control for any potential placebo effects associated with giving sham stimulation to the sham BDR training control group.

3.2.3.2 Stimulation

A second aim was to investigate whether tDCS could enhance working memory training and transfer. For a detailed description of this technique and its potential in enhancing various cognitive abilities, see Section 1.5. The current study aimed to test whether active tDCS enhances training performance on a single BDR paradigm relative to a sham control group completing the same training regime. The inclusion of the various forms of backward recall and *n*-back paradigms at pre- and post-training enabled the effects of stimulation on transfer to untrained working memory tasks to be tested systematically. As with training effects, if tDCS enhances transfer within paradigm then gains are predicted for untrained backward recall tasks, and if it enhances cross-paradigm transfer then gains are expected for the *n*-back tasks.

3.2.3.3 Summary of aims and predictions

In summary, the key aims of this study are (1) to systematically investigate the boundary conditions to training transfer by testing whether the benefits of training on a BDR task transfer to untrained working memory tasks with varying degrees of overlap with the training task, and (2) to test whether tDCS can enhance on-task training gains and transfer. It was predicted that following training alone, paradigm would be a boundary condition to transfer (i.e. no significant transfer would be observed to any *n*-back task). Based on previous findings, category of materials within domain was not expected to be a barrier and so significant transfer to backward digit and backward letter recall was predicted. However, no specific predictions were made regarding transfer to backward spatial recall. In terms of the additional benefits of stimulation, it was predicted that the working memory training group with active stimulation would show greater on-task training gains relative to the working memory training group with sham stimulation, and therefore greater gains would also be observed for the BDR outcome measure as it is the same as the trained task. This finding would be consistent with previous reports by Au et al. (2016), Richmond et al. (2014), and Ruf et al. (2017). For transfer to novel tasks, no specific predictions are made regarding the effects of tDCS to backward recall (with letter or spatial locations), or to *n*-back (with letters or digits) due to the mixed and inconsistent findings of previous stimulation studies.

The protocol for this study was pre-registered with the Open Science Framework (www.osf.io/r4q3s; see Appendix C).

3.3 Method

3.3.1 Participants

Forty-eight right-handed, native English-speaking adults (31 female) aged 18-35 years (*M* = 23.229, *SD* = 3.680) with normal or corrected-to-normal vision completed this study. Participants were recruited via the MRC Cognition and Brain Sciences Unit, University of Cambridge research participation system or through advertisements within Cambridge University colleges. All participants were stimulation compatible, i.e. they had no history of neurological disease or psychiatric disorder, no history or family history of epilepsy or other seizures, no metallic object(s) in the body, no cardiac pacemaker and no history of head, throat, or brain surgery, were not taking any drugs that affect the central nervous system (including medication and illicit drugs, excluding alcohol) such as antiepileptic drugs, antidepressants, benzodiazepines, and L-dopa.

3.3.2 Procedure

This was a double-blind randomised controlled study. Participants completed the transfer tests in pre- and post-training sessions (average completion time, including short breaks and practice trials = 87.344 min). After completing the pre-training session, participants were assigned to one of three training groups: visual search training with sham stimulation (*n* = 16, 11 female), BDR training with sham stimulation (*n* = 16, 11 female), or BDR training with active stimulation (*n* = 16, 9 female). Stratified randomisation was used to ensure groups were matched for age, sex, and baseline scores on all the pre-training tasks. The investigator who performed the randomisation was independent of the experimenter who collected the data. Participants then completed three days of adaptive training with active or sham tDCS. Following training participants completed the post-training session. All test and training sessions were conducted individually with each participant. Written informed consent was obtained prior to testing. The study was approved by, and conducted in accordance with the guidelines of the University of Cambridge Psychology Research Ethics Committee and the MRC Cognition and Brain Sciences Unit (ethics code = PRE.2016.016; see Appendix D for a copy of the ethics approval letter).

3.3.3 Materials

All training and transfer tasks were computerised.

3.3.3.1 Transfer tasks

Backward recall

Participants completed three backward recall measures, each with a different set of stimuli; (i) digits (1 to 9), (ii) letters (B C D F G H J K L; i.e. the first 9 letters of the alphabet excluding vowels), or (iii) spatial locations (nine boxes at random but fixed locations on the computer screen). Trials were presented in blocks, each consisting of four trials. For each trial the to-be-remembered items or locations were presented visually on screen one at a time for 1000 ms, followed by a blank screen for 1000 ms. Participants were then prompted to recall the sequence in backward order via a touchscreen keypad of digits, letters, or spatial locations depending on the task administered (unlimited response time). All tasks started at a span of three items which increased by one item in each subsequent block if the participant scored three or more correct trials. The task was discontinued if two or more trials were incorrect in a block. Maximum span, as measured by the level the task discontinued on minus one, was recorded.

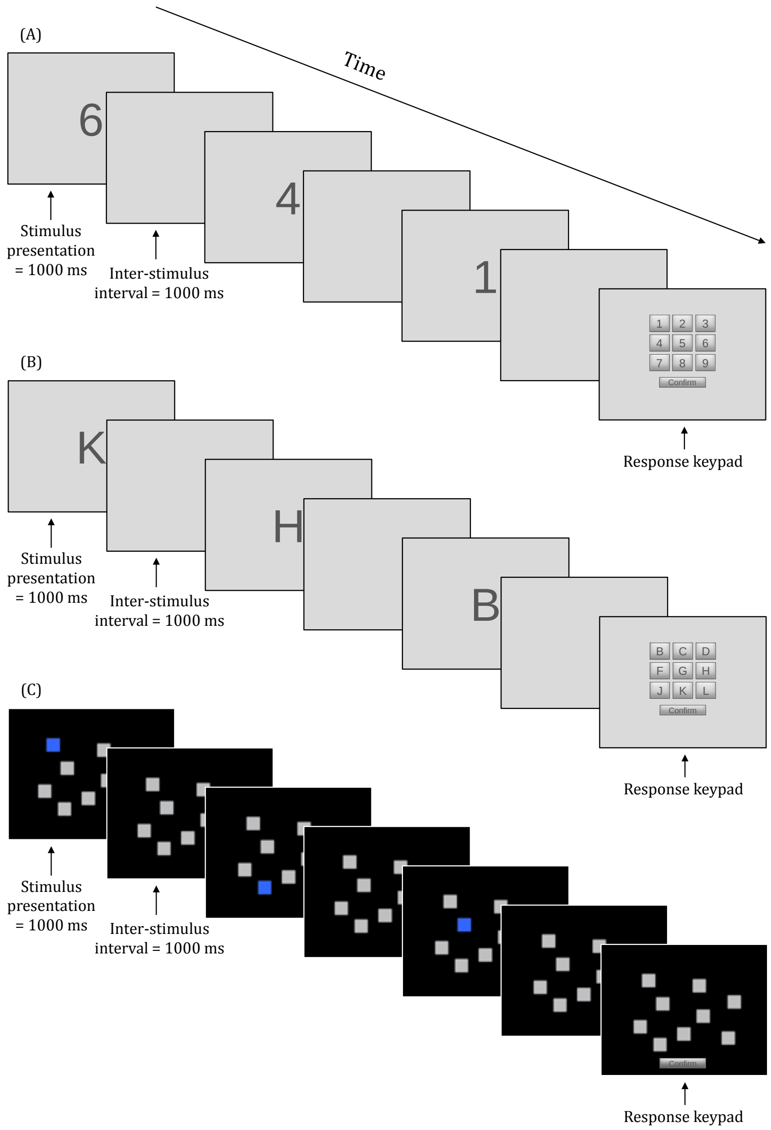


Figure 3.1 – Backward recall tasks (illustrated for a span of 3 items), including: (A) backward digit recall, (B) backward letter recall, and (C) backward spatial recall.

n-back

Two *n*-back transfer tasks were administered; one with digits (1 to 9) and one with letters (B C D F G H J K L). Stimuli were presented one at a time in continuous blocks of 20 + *n* items, where *n* corresponded to the number of items back to be matched. Each item was presented for 760 ms, followed by a blank screen for 2500 ms. Participants were required to indicate whether the current item on screen matched the one presented *n* items back in the sequence via a button press. For example, on two-back (*n* = 2) participants had to decide whether the number on screen matched the one presented two items previously in the sequence. In each block there were a total of six possible targets (matches), and 14 + *n* non-targets. Participants were only required to respond to matches, and could do so at any time during stimulus presentation or the fixation window for a given trial. An error was scored if participants pressed the button for a non-target (a false alarm), or if participants failed to press the button when a match was present (a miss). Total errors were scored as a combination of false alarms and misses. The first block began at one-back and the difficulty level increased by one in each subsequent block if less than five total errors were made (e.g. increase from one-back to two-back). If five or more total errors were made within a block then the task would end. Maximum *n*-level, as measured by final *n*-level minus one, was scored.

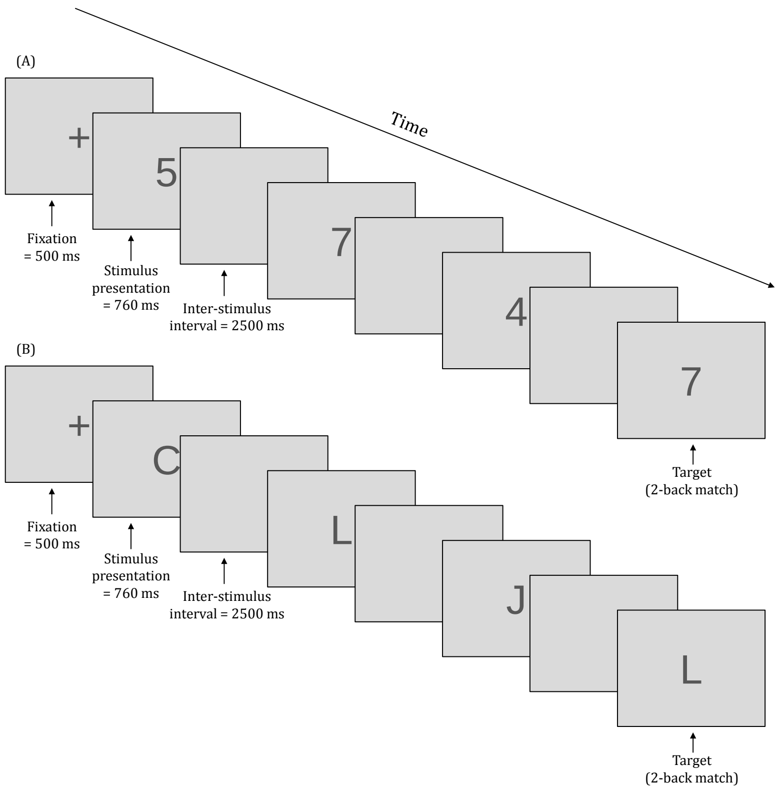


Figure 3.2 – *n*-back tasks (illustrated for a two-back level), including: (A) *n*-back with digits, and (B) *n*-back with letters.

3.3.3.2 Training tasks

Backward digit recall

BDR training involved reverse serial recall of sequences of digits. The stimuli, presentation rate, and response methods were identical to the BDR transfer task (see Figure 1.1). Trials were presented in blocks of four trials. This was an adaptive task, meaning the difficulty level was increased or decreased depending on performance. During the first training session the difficulty level was titrated to individual baseline performance (as measured at pre-test) minus one. During the second and third training sessions the task would begin at the highest level reached during the previous training session minus one. The rules for progression up and down the levels within each training tasks were: increase by one storage item if three consecutive correct responses were made, decrease by one item if two consecutive incorrect responses were made, otherwise the sequence length remained the same. Participants completed three training sessions, with 100 trials per training day, yielding 300 trials in total. Average performance, as measured as the average span level reached on correct trials, was scored for each training session.

Visual search

An adaptive visual search task was used as the active control training program (Harrison et al., 2013; Redick et al., 2013). On each trial participants were presented with a brief array of letters for 500 ms. This array contained a single left or right facing target *F* and multiple distractors made up of left and right facing *E*s, and left and right tilted *T*s (see Figure 3.3). Participants were then presented with a mask screen for 2500 ms during which time they had to indicate whether the target *F* was facing left or right via button presses. If participants did not respond during this window the trial was scored as incorrect. The difficulty of the task was manipulated by increasing or decreasing the size of the array. Each increase in difficulty alternated between adding another column and then another row to the array. For example; level one was a 2 x 2 array, level two was a 2 x 3 array, level three was a 3 x 3 array, and so on. The rules for progression up and down the levels within the visual search training tasks were: increase difficulty level by one if accuracy in the previous block was equal to or greater than 87.5%, decrease difficulty level by one if accuracy in the previous block was equal to or less than 75%, otherwise the difficulty level remained the same. Each training session began at level one. Participants completed three days of training. There were 30 blocks per session, with each block containing 24 trials, yielding 2160 trials over the three training sessions. Average performance, as measured by the average level of difficulty reached across all trials, was scored for each training session.

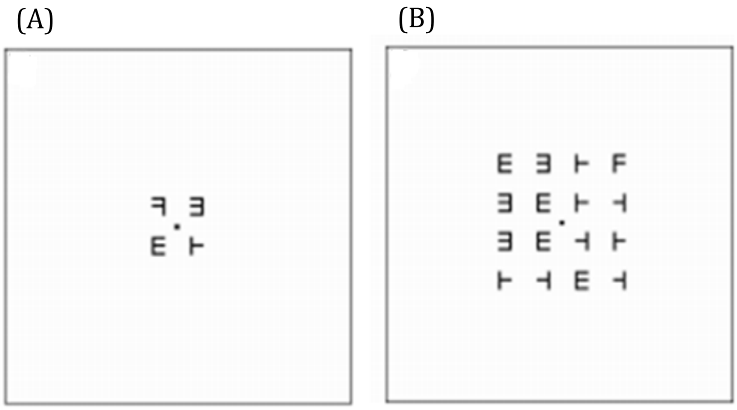


Figure 3.3 – Visual search training task, with illustrations of arrays for (A) level one and (B) level five.

3.3.3.3 Stimulation

tDCS was applied to the left DLPFC via two 5 x 5 cm rubber electrodes covered with saline-soaked sponges. An anodal electrode was positioned on the scalp over the area corresponding to region F3 according to standard international 10-20 EEG electrode placement procedure, and a reference cathodal electrode was position over the contralateral supraorbital area. Electrodes were secured with a rubber headband and stimulation was delivered using a battery-driven electrical stimulator (DC-STIMULATOR-PLUS; NeuroConn). Participants in the active stimulation group received 10 min of tDCS at 1 mA with 15 s of increasing and decreasing ramps at the beginning and end of stimulation. For those in a sham condition, stimulation faded in for 15 s and then was ramped down over 15 s to mimic the initial sensations associated with actual stimulation and blind participants to their stimulation condition. The display of the simulation machine was identical for active and sham conditions ensuring the participants were blind to the type of stimulation being delivered. The experimenter was blind to stimulation condition for participants in the two BDR training groups, but knew participants in the visual search group were receiving sham stimulation.

3.3.4 Analysis plan

This plan has been reproduced from the pre-registered report (www.osf.io/r4q3s; see Appendix C). The tense has been changed to fit with the context of the chapter.

On-task training gains

To investigate whether participants showed gains on the training tasks, paired-sample *t*-tests were performed separately for each of the three groups. In each case, average performance on training day one was compared to average performance on training day three. Average performance was measured as the average level of difficulty reached on correct trials. It was predicted that performance will be significantly higher on day three compared to day one for each training group.

Within- and cross-paradigm training effects following backward recall training

To test whether training on BDR benefited performance on other backward recall tasks (within-paradigm transfer) and on *n*-back tasks (cross-paradigm transfer); general linear regression analyses were performed separately for each of the five outcome measures. In each case, post-training scores were entered as the dependent variable with pre-training scores and group (backward recall training with sham stimulation or visual search training with sham stimulation) entered as the independent variables. A Bonferroni correction for multiple comparisons was used for each regression. As there are five outcome variables the alpha level was $p < .01$. It was predicted that there would be significantly greater gains on backward recall with digits and letters following BDR training with sham stimulation compared to visual search training with sham stimulation. No predictions were made regarding the extent to which BDR training alone (i.e. with sham stimulation) would lead to transfer to backward spatial recall. Gains were not predicted for either group on the two *n*-back tasks.

Modulation of on-task training gains by stimulation

A general linear regression was performed to test whether stimulation (active or sham) predicted differences between the pre- to post-training scores for BDR training. Performance on training day three was entered as the dependent variable, and group (active or sham) and training day one performance were entered as the independent variables. It was predicted that BDR training with active stimulation would result in significantly greater training gains than BDR with sham stimulation.

Enhancement of within- and cross-paradigm training effects with stimulation

To investigate whether stimulation enhanced the transfer of training effects both within and across working memory paradigms, general linear regressions were conducted separately for each outcome measure with stimulation group as the predictor. In all cases, post-training scores were entered as the dependent variable with pre-training scores and group (BDR with active stimulation and BDR with sham stimulation) entered as independent variables. Bonferroni corrections for multiple comparisons were applied for each set of analyses (i.e. a correction of five, setting the alpha level at $p < .01$). A significantly greater pre- to post-training score was predicted for the backward recall with active stimulation group compared to the backward recall with sham stimulation group on the BDR transfer measure. No predictions were made regarding the extent to which stimulation would impact transfer to the other backward recall outcome measures (letters or spatial). For cross-paradigm transfer, no predictions were made regarding the extent to which stimulation would impact transfer to *n*-back letters or *n*-back spatial.

3.3.5 Inference criteria

According to the analysis plan the standard $p < .05$ value was used for determining results of the paired sample *t*-tests used for on-task training gains. A Bonferroni corrected alpha level was used in all analyses investigating the transfer of training gains. As there were five outcome measures a $p < .01$ value was used. All confirmatory analyses (i.e. those reported in the analysis plan) rely on null hypothesis significance testing (NHST). In addition to traditional NHST, Bayesian methods were also employed. Bayes factors (BF) were computed to allow the strength of evidence favouring the alternative versus the null hypotheses to be quantified (Sprenger et al., 2013). These analyses are exploratory (i.e. they were not stated in the pre-registered report), and were computed in JASP (The JASP Team., 2017) with default prior scales. Inverse BF (BF_{10}) were used to express the odds in favour of the alternative hypothesis (BDR training and/or stimulation has an effect) compared to the null (no effect of BDR training and/or tDCS). A BF_{10} of 3-10 indicates positive/substantial support for the alternative hypothesis and a BF_{10} of > 10 corresponds to positive/strong evidence for the alternative hypothesis (Kass & Raftery, 1995).

3.4 Results

3.4.1 Training

As shown in Figure 3.4 all training groups improved over the three training sessions (improvements in the three training groups as a function of session relative to performance in session 1; i.e. session 2/session 1; session 3/session 1). Means and standard deviations of average performance in each training session by group are shown in Table 3.2. To examine on-task training gains, paired-sample *t*-tests were performed separately for each training group. Average performance on day three of training was significantly greater than on day one of training for all training groups; visual search with sham, t (15) = -3.901, p = .001, Cohen's d = 0.903; BDR with sham, t (15) = -5.166, p < .001, Cohen's d = 0.961; and BDR with active stimulation, t (15) = -5.486, p < .001, Cohen's d = 1.006. Bayesian t-tests provided strong evidence for these improvements (visual search sham, BF_{10} = 56.610; BDR sham, BF_{10} = 504.700; BDR active, BF_{10} = 862.100).

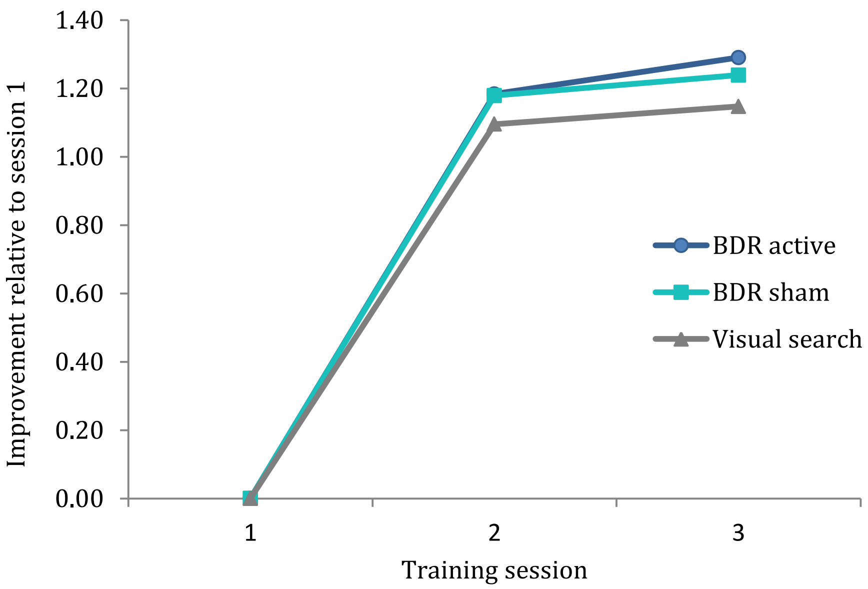


Figure 3.4 – Improvements in the three training groups are shown as a function of session relative to performance in session 1 (i.e. session 2/session 1; session 3/session 1). Note that averages in each session are calculated based on correct trials for the two BDR groups and all trials for the visual search group. BDR active = backward digit recall training with active stimulation, BDR sham = backward digit recall training with sham stimulation.

To test whether stimulation enhanced on-task training gains for BDR, a general linear regression was run with performance on day three entered as the dependent variable, and group (stimulation or sham) and training day one performance entered as the independent variables. Group did not significantly predict performance on day three showing that stimulation did not enhance training (p = .589). A Bayesian linear regression favoured the null hypothesis (no effect of stimulation on training; BF_{10} = .138).

Table 3.2 – Average training performance in each session by group.

	Session 1		*Session 2*		*Session 3*	
	M	*SD*	*M*	*SD*	*M*	*SD*
BDR active	7.764	1.490	9.187	2.293	10.015	2.793
BDR sham	7.418	1.159	8.744	1.996	9.189	2.336
Visual search	4.790	0.574	5.246	0.766	5.494	0.941

Note. BDR = backward digit recall.

Rate of learning on the training activities was compared between the two backward recall training groups. This analysis was exploratory (i.e. not stated in the pre-registered analysis plan). Order 2 polynomial (quadratic) functions ($y = x^2 + x + c$) were computed for each participant separately. These functions allowed the approximate point at the point at which each participant reached asymptotic performance during training to be identified (based on average performance on each training day). If stimulation enhanced learning, the stimulation group should reach this point faster than the sham group. The rate of change (i.e. how quickly participants reached asymptotic performance) was calculated as maximum score at asymptote/number of sessions to reach asymptote. Group differences in the rate of change were compared using an independent samples *t*-test. Data were excluded for curves in which the asymptote was outside the observable training window (i.e. if asymptote < 0 or > 3), and so a reduce sample size of 11 was used in this analysis. There was no significant group difference between the BDR with active stimulation (M = .775, SD = .792) and BDR with sham stimulation (M = 1.049, SD = .743) training groups, t (20) = -.838, p = .412 (Cohen's d = .357). A Bayesian *t*-test provided equivocal support for the null and alternative hypotheses, suggesting that stimulation does not enhance the rate of learning (BF_{10} = .412).

3.4.2 Transfer

Performance in each condition is summarised in Figure 3.5. To investigate the effects of training alone on transfer, the BDR sham group was compared to the visual search sham group. A general linear regression analysis was conducted on each of the five outcome measures (see Table 3.3 for a summary of these results). In each case, post-training scores were entered as the dependent variable with pre-training scores and group (BDR sham or visual search sham) entered as the independent variable. Greater gains were observed for BDR sham than for visual search sham on the BDR transfer task ($p < .001$; $BF_{10} = 3476.9$). Significantly greater gains were also observed for the backward letter ($p = .016$; $BF_{10} = 3.651$) and backward spatial ($p = .013$; $BF_{10} = 4.553$) recall tasks for the BDR sham group relative to the visual search group, but these effects did not survive a correction for multiple comparisons. There was no evidence for transfer to either *n*-back task (all *p*s ≥ .06; all BF_{10}s ≤ 1.416).

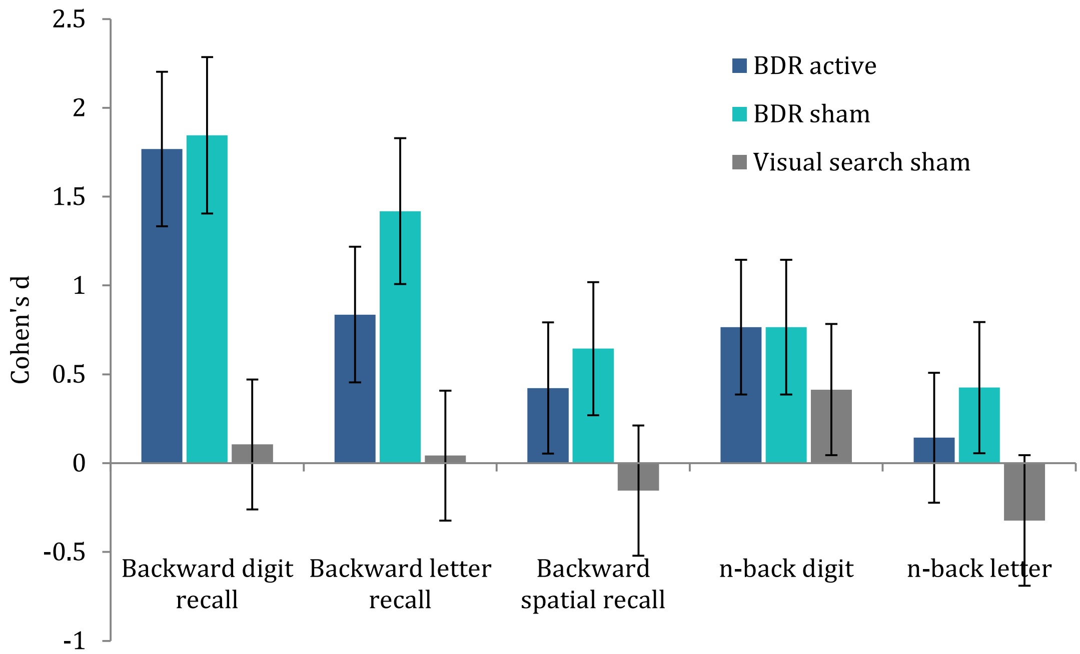


Figure 3.5 – Transfer to untrained tasks. Changes in within-paradigm transfer measures (backward recall tasks) and cross-paradigm transfer measures (*n*-back tasks). BDR active = backward digit recall training with active stimulation, BDR sham = backward digit recall training with sham stimulation.

To investigate the influence of stimulation on transfer within and across working memory paradigms, general linear regression analyses were used to compare the BDR training with active stimulation group to the BDR with sham stimulation group (see Table 3.3 for a summary of these results). In all cases, post-training scores were entered as the dependent variable with pre-training scores and group (BDR with active stimulation and BDR with sham stimulation) entered as independent variables. Group did not predict post-training scores for any of the backward recall or *n*-back outcome measures (all *p*s > .580). Bayesian regression analyses were also conducted, confirming these effects. BF_{10} scores for the backward recall tasks with digits (0.271) and spatial locations (0.316) favoured the null hypothesis that stimulation does not enhance transfer. All remaining BF_{10} scores ranged from 0.385 to 0.413, providing equivocal support for the null and alternative hypotheses (see Table 3.3). These results suggest that stimulation does not enhance transfer.

Table 3.3 – Group comparisons of training and stimulation.

	Group comparison of training effects: visual search sham versus BDR sham				*Group comparison of stimulation effects: BDR sham versus BDR active*			
	Beta	*t*	*p*	*Bayesian Regression BF_{10}*	*Beta*	*t*	*p*	*Bayesian Regression BF_{10}*
Backward digit	-0.650	-5.676	***<0.001***	3476.900	-0.004	-0.290	0.977	0.271
Backward letter	-0.423	-2.551	**0.016**	3.651	-0.610	-0.350	0.729	0.400
Backward spatial	-0.408	-2.632	**0.013**	4.553	0.031	0.201	0.842	0.316
n-back digit	-0.158	-0.983	0.334	0.512	0.032	0.179	0.859	0.385
n-back letter	-0.309	-1.958	0.060	1.416	0.098	0.559	0.580	0.413

Note. **Bold** text denote significant effects at $p < .05$ level, ***bold italics*** indicate significant effects after family-wise correction for multiple comparison. BDR = backward digit recall.

3.5 Discussion

The present study examined the boundary conditions to transfer by testing whether the benefits of training on a BDR task generalised to untrained working memory tasks with varying degrees of overlap with the training activity. It also tested the extent to which tDCS enhanced on-task training gains and transfer. As predicted, significant gains were observed on the training activities for all three training groups over the three training sessions. The magnitude of gains was similar across all three tasks, demonstrating that intense practice on cognitively challenging and adaptive tasks leads to improvements in performance on the tasks being trained. This is consistent with many previous studies that have shown on-task training gains for working memory (E. Dahlin, Nyberg, Bäckman, & Neely, 2008; Dunning et al., 2013; Holmes et al., 2009; Jaeggi et al., 2008; Karbach et al., 2015), visual search (Harrison et al., 2013; Redick et al., 2013), and other higher-level cognitive tasks such as inhibition (Thorell, Lindqvist, Nutley, Bohlin, & Klingberg, 2009), and arithmetic training (Fendrich, Healy, & Bourne, 1993; Park & Brannon, 2013). There was also strong evidence for improvements on the BDR outcome measure for the groups who trained on BDR with and without stimulation. This reflects the training effects on BDR and is consistent with the proposal that training provides the opportunity to develop novel cognitive routines for unfamiliar and demanding tasks (Gathercole et al., 2018).

There was no evidence for cross-paradigm transfer. Changes in performance on the *n*-back tasks following BDR training with sham stimulation were not significantly different to those observed for the visual search training with sham group, even when the *n*-back transfer task contained the same materials (digits) as the training activity. This suggests transfer is not mediated by specific expertise related to task content, for example in the basic skills or knowledge tied to the task materials (e.g. mnemonic strategies such as chunking letters into familiar words; von Bastian & Oberauer, 2014). The data are consistent with previous studies showing that working memory training effects do not generalise across working memory tasks (Dunning & Holmes, 2014; Holmes et al., 2018; Li et al., 2008; Minear et al., 2016; Sprenger et al., 2013; von Bastian & Oberauer, 2013), suggesting that paradigm constrains transfer even when other features such as the memory items are held constant across tasks.

The absence of transfer from training on BDR to *n*-back suggests training effects are driven by task-specific skills or processes rather than an increase in the efficiency of the working memory system as proposed by Klingberg (2010). If training enhanced the underlying capacity of working memory, transfer would be observed across paradigms. The data are consistent with the proposal that training promotes the development of novel cognitive routines that can be applied to untrained tasks with same task structure (Gathercole et al., 2018). Differences in the cognitive routines required for backward recall and *n*-back tasks may explain the absence of transfer across paradigms. For BDR, a routine must be developed that enables reverse serial order of verbal items. This could involve using established cognitive processes such as sub-vocal rehearsal to make repeated covert cycles of forward recall through the list to report the final digit, then peeling each of them off successively (Anders & Lillyquist, 1971; Thomas et al., 2003). In contrast, the greatest demand in *n*-back is the continuous updating of the contents of working memory. This might involve the temporary storage of a sequence of items and regular updating of item-order bindings with each successively presented item (Oberauer, 2005).

There was some evidence that task material (letters, digits, or spatial locations) and stimulus domain are not boundary conditions for transfer. Although improvements on backward letter and backward spatial recall tasks were not significantly greater following BDR training without stimulation relative to visual search training (without stimulation), Bayesian analyses provided positive evidence for within-paradigm transfer across materials within (backward letters) and across (backward spatial) domain. On balance these data suggest that stimuli characteristics, including the category of material and domain of the stimuli, do not constrain transfer when the trained and untrained tasks have the same higher-order task structure (e.g. they are the same working memory paradigm). This is consistent with previous reports of transfer across different materials within the same paradigm (Anguera et al., 2012; Holmes et al., 2018; Jaeggi, Studer-Luethi, et al., 2010; Küper & Karbach, 2016; Minear et al., 2016). The effect sizes for gains on the backward digit, letter, and spatial tasks diminished respectively with distance from the training tasks for those who trained on the BDR task without stimulation. Finding larger gains for backward digit than backward letter recall, and for backward letter than backward spatial recall is consistent with the idea that the greater the number of features in common between training and transfer tasks, the more likely it is that transfer will occur (Gathercole et al., 2018; Thorndike & Woodworth, 1901). Transfer from BDR to backward letters may reflect the application of common strategies for verbal rehearsal. The processes required for reversing verbal and visuo-spatial materials are thought to be fundamentally different (Isaacs & Vargha-Khadem, 1989). If training is promoting the development of a novel cognitive routine during BDR training that is coordinating the execution of existing verbal processes, then it could be more easily applied to other backward tasks with verbal stimuli (letters) compared to one with visuo-spatial materials (Gathercole et al., 2018).

tDCS applied to the left DLPFC did not enhance on-task training gains, nor did it enhance the benefits of training for any of the untrained activities. These absence of benefits during training are inconsistent with previous findings showing that tDCS enhances the rate of learning in working memory training using verbal and visuo-spatial *n*-back tasks (Au et al., 2016; Ruf et al., 2017). This may reflect differences in the impact of tDCS on different types of training activities, resulting from the malleability of the neural substrates targeted by BDR and *n*-back, and the complexity of the training programs and their doses. Differences could also be due to discrepancies in the stimulation parameters used. Au et al. (2016) applied 25 min of tDCS, at a current intensity of 2 mA, while the current study used 1 mA for 10 min. Similarly, although 1 mA of tDCS was applied in the study conducted by Ruf et al. (2017), this was for a longer duration of 20 min. Future research needs to develop a greater understanding of the neurophysiological mechanisms of stimulation and the impact of different tES parameters (e.g. current intensity and duration) when combined with different training regimes. The results of the current investigation are, however, consistent with the outcomes of a recent meta-analysis demonstrating that active tDCS is no more effective than sham tDCS for altering working memory performance (Nilsson et al., 2017). The results are also in line with data presented in Chapter 2 showing that transcranial random noise stimulation (tRNS), an alternative form of tES, has no effect when applied during working memory training (Holmes, Byrne, Gathercole, & Ewbank, 2016). Finding that tDCS did not enhance the generalisation of training gains to untrained tasks is consistent with previous studies reporting no differences in performance between active tDCS and sham stimulation groups on transfer tasks following working memory training (Martin et al., 2013; Richmond et al., 2014). Together these studies suggest that tES is not an effective tool for enhancing the effects of cognitive training, and their use for therapeutic purposes is likely to be limited.

In summary, the current study establishes that transfer following working memory training is tightly tied to the characteristics of the training regimes. Transfer does not extend across global changes in working memory paradigm, but it does occur within paradigm for backward recall tasks where it is unconstrained by both stimulus materials and stimulus domain. The absence of transfer between backward recall training and *n*-back outcome measures suggests both tasks may tap into distinct aspects of working memory. With this in mind, the final study presented in this thesis (Chapter 4) was designed to examine the degree of overlap between different forms of backward recall and *n*-back tasks using a latent variable approach. A final clear conclusion of the current data is that when using the most rigorous, randomised sham-controlled intervention design, there is no evidence that tDCS enhances the benefits of working memory training.

Chapter 4 Backward recall and *n*-back measures of working memory: A large-scale latent variable analysis

4.1 Aims

Working memory tasks are widely used as prospective indicators of academic attainment and have been used to train cognitive function (Alloway & Alloway, 2010; Bull, Espy, & Wiebe, 2008; Dunning et al., 2013; Harrison et al., 2013; Jaeggi et al., 2008). It is therefore important to establish what the various tasks designed to assess working memory are measuring so that the specific cognitive processes that might be important for learning or amenable to training can be better understood. The primary aim of this study was to investigate the overlap in the processes involved in two widely used measures of working memory – backward recall and *n*-back. Backward recall tasks are commonly used in behavioural studies, while *n*-back tasks are used more frequently in neuroimaging experiments (Owen et al., 2005). Both require information to be simultaneously stored and processed for short periods of time, a key requirement of a task tapping working memory, but there are differences in the overall task structures and the processes involved. A latent variable approach was employed to investigate the degree of overlap between different variants of *n*-back and backward recall tasks. Multiple versions of each of the two types of paradigm were used. The tasks contained different memoranda that varied within domain (e.g. two types of verbal material; digits or letters) and across domain (e.g. spatial locations or verbal material). Varying materials within and across tasks allowed the variance specific to task materials (content) and category of task to be assessed (e.g. Schmiedek, Hildebrandt, Lövdén, Lindenberger, & Wilhelm, 2009). Tasks might be related by memory items due to the use of material-specific strategies (e.g. chunking letters into familiar words), due to an overlap in task processing demands (e.g. maintaining items for serial recall via rehearsal), or due to overlap in the domain-specific systems that support the storage and rehearsal of verbal and visuo-spatial information. A second aim was to examine the relationship between the working memory tasks and fluid reasoning to test whether there is a single underlying general ability factor for all tasks or distinct but related constructs for working memory and reasoning.

4.2 Introduction

4.2.1 Background

There are a wide variety of working memory tasks including serial recall, interpolated processing, and updating tasks (see Section 1.3 for a full description). All involve the temporary maintenance and simultaneous manipulation of information. Despite these commonalities, the processes involved in different categories of task can differ substantially (e.g. reversing digit sequences for backward serial recall, rapidly switching between storing items and unrelated interpolated processing activities for complex span, or updating/refreshing sequences of storage items during *n*-back). Many studies have tested the construct validity of working memory tasks, that is, the degree to which a task is measuring what it claims to be measuring. An individual differences approach is useful in this regard (e.g. Jaeggi, Buschkuehl, Perrig, & Meier, 2010; Kane et al., 2007; Redick & Lindsey, 2013; Schmiedek et al., 2009). By investigating how well different working memory tasks are correlated with each other, and also with other measures of complex cognition, it is possible to determine whether tasks are tapping into the same underlying construct (Kane et al., 2007). There might be strong associations between tasks from the same paradigm (e.g. a group of *n*-back tasks), between those that contain the same stimulus materials (e.g. letters), or between those with same-domain stimuli (e.g. visuo-spatial materials). Identifying the associations between tasks provides information about the underlying processes they have in common. For example, if tasks group together at the paradigm level, this suggests that commonalities in the paradigm structures and processes may explain the shared variance between tasks, but if tasks with common stimuli are linked it suggests the strategies used for particular materials are important for task performance. The aim of the current study is to investigate the degree of overlap between backward recall and *n*-back measures of working memory.

Previous studies investigating the relationship between different working memory tasks have predominantly focussed on complex span and *n*-back tasks. Complex span tasks containing different storage items and distractor tasks correlate extremely well with each other and also with other measures of working memory, including updating tasks such as *n*-back, memory updating, and alpha span (e.g. Schmiedek, Hildebrandt, Lövdén, Lindenberger, & Wilhelm, 2009). Complex span scores also predict performance on a wide variety of other cognitive tasks that are linked with working memory such as tests of language comprehension (Daneman & Carpenter, 1980; Kane et al., 2004), attentional control (Kane, Conway, Hambrick, & Engle, 2008), and measures of general fluid intelligence (e.g. Schmiedek et al., 2009).

In contrast, weak associations have been reported between *n*-back and other tasks such as complex span (Jaeggi, Studer-Luethi, et al., 2010; Jaeggi, Buschkuehl, et al., 2010; Kane et al., 2007; Roberts & Gibson, 2002) and backward digit span (Dobbs & Rule, 1989; McAuley & White, 2011; Miller, Price, Okun, Montijo, & Bowers, 2009; Roberts, 1998; Roberts & Gibson, 2002). These findings suggest *n*-back tasks might be measuring distinct constructs or processes to other working memory tasks (Kane et al., 2007). The low correlations between these tasks could be attributed to methodological issues (Schmiedek et al., 2009; Wilhelm, Hildebrandt, & Oberauer, 2013). First, associations may be reduced due to a mismatch of content modality across *n*-back, and complex and backward span paradigms (e.g. visual versus auditory presentation, or differences in the type and domain of the stimuli). For example, in Kane et al. (2007) *n*-back and complex span tasks were only weakly related, but this could be explained by differences in paradigm (*n*-back or complex span) or stimuli (*n*-back contained letters, while complex span contained numerical operations and words). Using a single indicator for a paradigm can also be problematic. In Miller et al. (2009) only one *n*-back task with letters and one backward recall task with digits was used. Likewise in Kane et al. (2007) performance on both *n*-back and complex span was assessed using a single task. When performance is averaged across multiple versions of each type of task, stronger associations are found. For example, Shamosh et al. (2008) reported a much higher correlation than Kane et al. (2007) between composites of two *n*-back tasks and four complex span tasks.

However, aggregation of multiple tasks does not eliminate the influence of content- and task-specific variance and measurement error (Schmiedek et al., 2009). To overcome these issues, a latent variable approach can be used to establish a more accurate picture of construct overlap between two tasks measuring working memory (Schmiedek et al., 2014). Using this method Schmiedek et al. (2009) reported much higher correlations between two latent constructs for measures of complex span and updating. Modifying task demands across paradigms can also increase task overlap. Shelton and colleagues (2007) reported that an adjustment to the processing demands of *n*-back with free recall instead of speeded recognition resulted in stronger correlations with complex span than the standard paradigm.

Fewer studies have validated backward recall tasks against other tests of working memory, and those that have typically focus on backward digit recall (BDR) exclusively. This task requires reverse serial order recall of a sequence of digits. It likely relies on short-term memory serial order mechanisms to maintain the verbal sequence, but the added requirement to recall the items in reverse order imposes a substantial and attentionally demanding processing load that is often assumed to be similar to the executive loads of other working memory tasks such as complex span (Alloway et al., 2006; Bull et al., 2008). Evidence that backward span is significantly more strongly related to *n*-back than to forward span (Redick & Lindsey, 2013), and that backward digit span is related to reasoning ability (e.g. Suß et al., 2002), support the idea that backward recall tasks have an executive component. Indeed, Redick and Lindsey (2013) reported that the correlation between *n*-back and backward digit span was significantly greater than the correlation between *n*-back and complex span, suggesting not only that it shares variance with other widely used working memory tasks, but also that it may have more in common with some working memory paradigms than others.

Some studies have shown that backward digit span is weakly correlated with other working memory tasks such as complex span (e.g. Hilbert, Nakagawa, Puci, Zech, & Bühner, 2015). Linked to this, it has been suggested that backward and forward recall both tap into the same underlying short-term memory ability, and that the executive demands of backward recall tasks are minimal (Dobbs & Rule, 1989; Engle, Laughlin, et al., 1999; Rosen & Engle, 1997; St Clair-Thompson, 2010; St Clair-Thompson & Allen, 2013). Factor analytic studies showing that forward and backward recall tasks load onto the same factor (Colom, Abad, Rebollo, & Shih, 2005; Engle, Laughlin, et al., 1999) provide support for this. St Clair-Thompson and Allen (2013) argue that differences in forward and backward digit span reflect dissimilarities in the recruitment of visuo-spatial resources or strategies during the recall phase, rather than differences between the attentional or executive demands of the two tasks. They propose that forward recall is suited to a phonological code, whereas backward recall is supported by a visuo-spatial code, and that BDR reflects short-term memory and the strategic use of visual imagery rather than the executive component of working memory (St Clair-Thompson & Allen, 2013).

The aim of the current study was to elucidate the relationship between backward span and *n*-back tasks. Both tasks require participants to maintain memory items over brief periods of time and to update the list of items being held. These common features make them ideal candidates for assessing working memory and suggest they might tap into similar aspects of working memory function (maintenance and updating). However, there are studies showing the two paradigms are weakly associated (Dobbs & Rule, 1989; McAuley & White, 2011; Miller et al., 2009; Roberts, 1998; Roberts & Gibson, 2002; and for a meta-analysis, see Redick & Lindsey, 2013), and in training studies, practice on one category of task does not transfer to the other (Byrne, Ewbank, Redick, & Holmes, 2018; Heinzel et al., 2014). Practice on *n*-back tasks consistently improves performance on untrained *n*-back tasks (Buschkuehl et al., 2014; Holmes et al., 2018; Jaeggi, Studer-Luethi, et al., 2010; Li et al., 2008), but these effects do not transfer to backward recall tasks (Heinzel et al., 2014). Similarly, practice on backward digit span leads to substantial improvements on untrained variants of backward recall tasks, but does not benefit performance on *n*-back tasks even when they contain the same memory items (Byrne et al., 2018; see Chapter 3). The absence of transfer across backward recall and *n*-back tasks suggests the two paradigms tap into different processes because improving the processes in one does not result in improvements to the other.

Weak associations might be found between the two paradigms due to differences in the task properties. These include differences in the recall demands of the tasks; *n*-back requires familiarity-based recognition whereas backward serial order tasks require explicit recall (Oberauer, 2005). The updating demands of both tasks are also slightly different. For *n*-back, the full sequence has to be refreshed as a new item is added to the list and the first item dropped. In contrast, for backward recall the whole sequence has to be held in mind and transformed and updated at the point of recall. Finally, the task structures are different: for backward recall all storage items are presented prior to any updating, transformation, or recall of the material, whereas for *n*-back tasks participants have to update the to-be-remembered items and make responses while the list is being presented.

There are issues with previous studies exploring the relationship between these paradigms that make it difficult to draw strong conclusions (Dobbs & Rule, 1989; McAuley & White, 2011; Miller et al., 2009; Roberts, 1998; Roberts & Gibson, 2002). First, backward recall was measured exclusively with digits in all studies; none used stimuli from a different category (e.g. letters) or domain (spatial). Second, there was a mismatch of task content between the backward recall and *n*-back measures (e.g. digits and letters). Finally, the majority of studies used only single indicators for each task.

To investigate whether these two tasks share overlapping processes, and to overcome the limitations of previous studies, a latent variable approach was used with multiple indicators of each of the two types of working memory task. The tasks contained different memoranda that varied within domain (e.g. two types of verbal material; digits and letters) and across domain (e.g. spatial locations or verbal material). The set of backward recall tasks were: BDR, backward letter recall, and backward spatial recall. The *n*-back tasks included: *n*-back with digits, *n*-back with letters, and *n*-back with spatial locations. Varying materials within and across tasks allowed the variance specific to task materials (content) and category of task (e.g. Schmiedek et al., 2009, 2014) to be assessed. Including three tests of each paradigm allowed variance specific to paradigm to be tested. Unlike previous studies, web-based data collection methods were used to maximise the sample size. It is necessary to collect data from a very large sample to conduct latent variable modelling and detect meaningful differences between constructs. A sample size of *N* greater than 500 is recommended for looking for complex or subtle differences between factors (Wolf, Harrington, Clark, and Miller, 2013) and the number of participants needed multiplies up quickly as a factor of the relatedness between the measures.

Confirmatory factor analysis was used to test four competing models of the underlying structure of the backward recall and *n*-back tasks. These models are outlined in the following section (see Section 4.2.2). It was hypothesized that one of four alternative working memory models would best describe the data to explain the interrelationships between the backward recall and *n*-back tasks. Once the best-fitting model of working memory was determined, a secondary research question was to explore the relationship between the working memory tasks and fluid reasoning to test whether there is a single underlying general ability factor for all tasks (e.g. a '*g*' factor; Duncan et al., 2000), or distinct but related constructs for working memory and reasoning (e.g. Schmiedek et al., 2009, 2014).

Working memory and fluid intelligence represent dissociable but strongly related cognitive skills (e.g. Alloway & Alloway, 2010; Colom, Rebollo, Palacios, Juan-Espinosa, & Kyllonen, 2004). This has been demonstrated previously by Schmiedek and colleagues using latent factor approaches. In one study they identified two related constructs for updating and complex span tasks that predicted a separate reasoning factor equally well (Schmiedek et al., 2009). More recently, they reported a number of working memory measures were best captured by four latent working memory task factors corresponding to working memory paradigm (Schmiedek et al., 2014). These four paradigm factors loaded on to a single higher-order working memory construct factor, which was related to a separate reasoning factor. To address the secondary research question here, the best-fitting working memory model was expanded to include reasoning. This multi-factor model was then compared to one where all working memory and reasoning tasks loaded on to a single general intelligence factor (*g*).

In summary, the two key research questions were: (1) what accounts for individual differences in performance on backward recall and *n*-back tasks, and (2) how are the two classes of working memory paradigm (backward recall and *n*-back) related to fluid reasoning?

The protocol for this study was pre-registered with the Open Science Framework (www.osf.io/9qarp/; see Appendix E).

4.2.2 Models

Confirmatory factor analysis was used to test four competing models of the underlying structure of six *n*-back and backward recall tasks: (A) a single-factor model that assumed all tasks tap a single underlying working memory construct (e.g. Alloway et al., 2006; Kane et al., 2004), (B) a two-factor paradigm model that assumed a latent correlation between separate backward recall and *n*-back factors (e.g. similar to two distinct but related structures for complex span and updating tasks reported by Schmiedek et al., 2009), (C) a two-factor model that assumed separate domain-specific visuo-spatial and verbal latent constructs (Daneman & Tardif, 1987; Shah & Miyake, 1996), and (D) a three-factor materials model that assumed separate constructs based on the memory items - digits, letters, or spatial locations. Evidence supporting each of these models is described in detail below. The outline for the models has been reproduced from the pre-registration document: www.osf.io/9qarp/ (see Appendix E).

(A) Single-factor working memory model

This is consistent with domain-general theories of working memory that propose performance on working memory tasks is dependent on a domain-general central executive or attentional control system (Alloway et al., 2006; Baddeley, 1986; Engle & Kane, 2004; Engle, Kane, et al., 1999; Kane et al., 2004). Previous confirmatory factor analyses confirm this view. For example, in a study conducted by Kane et al. (2004) participants completed a number of working memory tasks. The verbal working memory tasks (operation span, word span, and counting span) required participants to remember sequences of verbal information such as words, letters, or digits while also completing an additional processing task (solving arithmetic problems, judging the veracity of sentences, or counting shapes). The spatial working memory tasks, which included rotation span, symmetry span, and navigation span, involved remembering sequences of visuo-spatial information such as arrows, matrix locations, or paths of moving balls, whilst simultaneously performing a processing task (letter rotation, symmetry judgement, or navigation around a letter shape). Confirmatory factor analyses revealed the verbal and visuo-spatial working memory tasks tapped into a unitary construct (Kane et al., 2004). Similar findings are provided by Alloway et al. (2006) who assessed performance on 12 tasks designed to measure verbal and visuo-spatial short-term and working memory. Short-term memory tasks such as digit span and dot matrix simply required the reproduction of a sequence of verbal or visuo-spatial items, while working memory tasks had additional processing demands such as reversing the sequence (e.g. BDR) or making decisions prior to recall. For example, a task called Mr X, required participants to judge whether two cartoon characters were holding a ball in same or different hands when positioned at different orientations, as well as recalling the location of the ball in serial order at the end of each trial. Alloway and colleagues (2006) found that although tasks measuring the temporary storage of information depended on separate domain-specific verbal and visuo-spatial factors, the processing of information within working memory was supported by a common domain-general component. Based on these results the single-factor model assumed that different versions of backward recall and *n*-back tasks would tap into a single underlying working memory construct.

(B) Two-factor domain model

Domain-specific accounts of working memory propose that separate pools of resources support the maintenance and processing of verbal and visuo-spatial information (Daneman & Tardif, 1987; Friedman & Miyake, 2000; Shah & Miyake, 1996). Individual differences studies using verbal and visuo-spatial working memory tasks support this account. For example, Shah and Miyake (1996) found only a weak correlation between measures of verbal and spatial working memory. In their study participants completed a verbal working memory reading span task, which involved reading sentences aloud whilst simultaneously remembering the final word of each sentence, and a spatial working memory span task, which involved mental rotation of letters whilst simultaneously remembering their orientation. The authors found that verbal working memory was highly correlated with other verbal ability measures (i.e. verbal scholastic aptitude test scores), but not with tests of spatial ability measures (i.e. spatial visualization and perceptual speed). They also found that spatial working memory strongly predicted spatial ability but not verbal ability. In an exploratory factor analysis spatial span and spatial ability measures loaded on one factor (i.e. a spatial factor) and tests of verbal span and verbal ability on another (i.e. a verbal factor), suggesting there are distinct cognitive resources supporting spatial and verbal working memory (Shah & Miyake, 1996).

The distinction between verbal and visuo-spatial working memory is also reflected in separable domain-specific short-term memory stores, and the ways in which verbal and spatial materials are represented and rehearsed internally/mentally. Verbal working memory is considered phonological in nature (Gathercole, Frankish, Pickering, & Peaker, 1999), and relies on an internal articulatory rehearsal process (Baddeley, 2000; Baddeley et al., 1975). Therefore, tasks using different categories of materials within the verbal domain (e.g. digits, letters) may be represented internally in the same system, and rely on the same maintenance processes. Subvocal rehearsal is one possible maintenance mechanism that enables phonological representations to be serially reactivated in short term memory to prevent decay over time (Baddeley et al., 1975; Gathercole, Adams, & Hitch, 1994). On the other hand, tasks involving visuo-spatial materials (e.g. recalling spatial locations in a matrix) may rely on a distinct system dedicated to the maintenance of visual and spatial information (e.g. forming and maintaining mental images). A rehearsal strategy for maintaining temporary visuo-spatial representations has been proposed, which is distinct to phonological maintenance mechanisms and involves the covert allocation of attention to a series of memorized locations (Pearson et al., 2014; Postle, Awh, Jonides, Smith, & D'Esposito, 2004). Based on these accounts of working memory, this two-factor model assumed separate domain-specific latent constructs for verbal and visuo-spatial information. The model predicted that that performance on verbal and visuo-spatial working memory tasks would be dissociable, but related, because the tasks rely on different representational and maintenance systems.

(C) Two-factor paradigm model

Backward recall and *n*-back tasks both require the temporary maintenance and processing of verbal or visuo-spatial information but they differ in terms of processing demands. For example, performing a backward recall task requires explicit serial recall, whereas an *n*-back task requires recognition and can be completed using familiarity-based responding (Oberauer, 2005). Paradigm-specific latent constructs have been found for other working memory tasks. For example, Schmiedek et al. (2009) reported a two-factor structure for complex span and updating tasks (e.g. *n*-back); both categories of task accounted for inter-individual differences in working memory equally well, and were best captured by distinct but related paradigm-specific factors. Patterns of transfer observed following working memory training also support the idea that working memory tasks might group together based on paradigm-specific processes. Transfer to untrained tasks is consistent and robust if there is substantial overlap between the processes involved in the trained and untrained activities (Sprenger et al., 2013). For example, Dahlin, Neely, Larsson, Bäckman, and Nyberg (2008) reported transfer to *n*-back, but not to a Stroop task, following training on a running span task. This pattern of transfer was speculated to reflect improvements in the ability to update the contents of working memory following training, which benefitted other memory task requiring updating but not tasks with different processing requirements like inhibition. Working memory paradigm has also been shown to be a boundary condition to transfer following training, while stimulus domain of the memory items (i.e. verbal or visuo-spatial) and category of materials within paradigm (e.g. letters or digits) is not (Byrne et al., 2018; Holmes et al., 2018; Minear et al., 2016). Together these data suggest that training-related changes are not associated with material-specific strategies, but are instead tied to the processes involved in the specific training task administered. It is therefore possible that different categories of working memory task will group together because they share variance common to the processes involved in the task (e.g. updating versus serial recall). This two-factor paradigm model assumed a correlation between two distinct backward recall and *n*-back latent constructs.

(D) Three-factor materials model

This model assumed that performance across the different working memory tasks would be best described by expertise related to the specific type of stimuli, for example in basic skills or knowledge tied to digits, letters or spatial materials. Within the training literature it has been suggested that transfer might be mediated by the acquisition of content-specific skills and knowledge (von Bastian & Oberauer, 2014). That is, training-related improvements could arise through the development or refinement of stimulus-specific mnemonic strategies (Gathercole et al., 2018; Minear et al., 2016). These strategies could be specific to content domain. For example chunking can be used to remember verbal items as familiar names or acronyms, but it is unlikely to be used for visuo-spatial materials. Strategies could be specific to materials within a domain. A striking example of this comes from a study showing that training for sequences of digits was tied to the use of mnemonic strategies that could not be applied to novel letter materials (Ericsson et al., 1980). Similarly, Minear et al. (2016) found that participants who completed verbal working memory training reported using strategies specific to letters. During training participants used chunking to remember sequences by associating the letters with words and forming sentences, or linking letters with acronyms or people's initials. This three-factor model assumed separate constructs for each category of memory item as follows: factor one, *n*-back with digits and BDR; factor two, *n*-back with letters and backward letter recall; and factor three, *n*-back with spatial locations and backward spatial recall.

4.3 Method

4.3.1 Participants

Seven-hundred and seven native-English speaking participants aged 18-35 completed this study. All had normal or corrected to normal vision, and no literacy difficulties. They were paid for taking part. Data from four participants were excluded because the participants did not follow the study instructions correctly. A total sample size of 703 participants (421 female) was used for the analyses. Participants were recruited through Prolific Academic (https://www.prolific.ac/), a widely used online crowdsourcing platform, and completed the tasks online. Participants signed up to this website are given a unique ID to ensure anonymity.

4.3.2 Procedure

Each participant completed six memory tasks and a reasoning task in a single session according to one of 12 possible task orders. The backward recall tasks were grouped together (i.e. completed consecutively), and the *n*-back tasks were also grouped together. The task order within these two groups was counterbalanced (i.e. all possible permutations for the three tasks were used), yielding six orders for each of the two groups of tasks. The two groups of backward recall and *n*-back tasks were then counterbalanced, resulting in six possible task orders in which the backward recall tasks were completed first, and six in which the *n*-back tasks were completed first. This yielded a total of 12 task orders. An additional reasoning task was completed in between the *n*-back and backward recall tasks in all conditions (i.e. it was always the fourth task completed).

Order effects were tested in a series of ANOVAs. First, differences in whether the three *n*-back or three backward recall tasks were completed in the first or second block were explored. A two by three mixed measures ANOVA with order (first or second) and backward recall task (backward recall with digits, letters, and spatial locations) was conducted. Mauchley's test indicated that the assumption of sphericity had been violated, χ^2 (2) = 66.171, $p < .001$, therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity ($\varepsilon = .919$). There were no order effects for the backward recall tasks, F (1.831, 1250.381) = 2.710, $p = .067$, $\eta_p^2 = .919$. The same ANOVA was conducted for the *n*-back tasks. There were also no order effects for completing the three *n*-back tasks in the first or second part of the experiment, F (2, 1366) = 2.078, $p = .126$, $\eta_p^2 = .003$. Next, order effects within each paradigm were assessed (i.e.

to test whether there was a difference in performance related to completing a task within a block in the first, second, or third position). One-way ANOVAs were conducted to compare the effects of position (first, second, or third) on task performance for each task separately (e.g. comparing whether performance for backward letter recall differed when it was completed first, second, or third in a block). No significant order effects were found for backward recall with letters or spatial locations, or for any of the *n*-back measures (all *p*s ≤ .005; see Appendix F for a summary of these tests). There was a significant effect of task position on backward recall with digits, F (2) = 3.977, p = .019, η_p^2 = .011. Post-hoc analyses revealed that participants who completed the task in the second position performed significantly better compared to those who completed it in the third position (p = .016).

Participants completed practice trials before beginning each task. Feedback for correct and incorrect responses was shown on screen for the practice trials, but was not provided during the proper tasks. Data were collected between 15th August and 16th October 2017. Informed consent was obtained online prior to testing. The study was approved by, and conducted in accordance with the guidelines of the University of Cambridge Psychology Research Ethics Committee and the MRC Cognition and Brain Sciences Unit, University of Cambridge (ethics code = PRE.2017.001; see Appendix G for a copy of the ethics approval letter).

4.3.3 Materials

The tasks were created using the software program Gorilla (https://gorilla.sc/) that has been developed by Cauldron (http://www.cauldron.sc/). The experiment was hosted on the online crowdsourcing platform Prolific Academic (https://www.prolific.ac/). Participants completed the study on a laptop or desktop computer, and all responses were made using a mouse or keyboard.

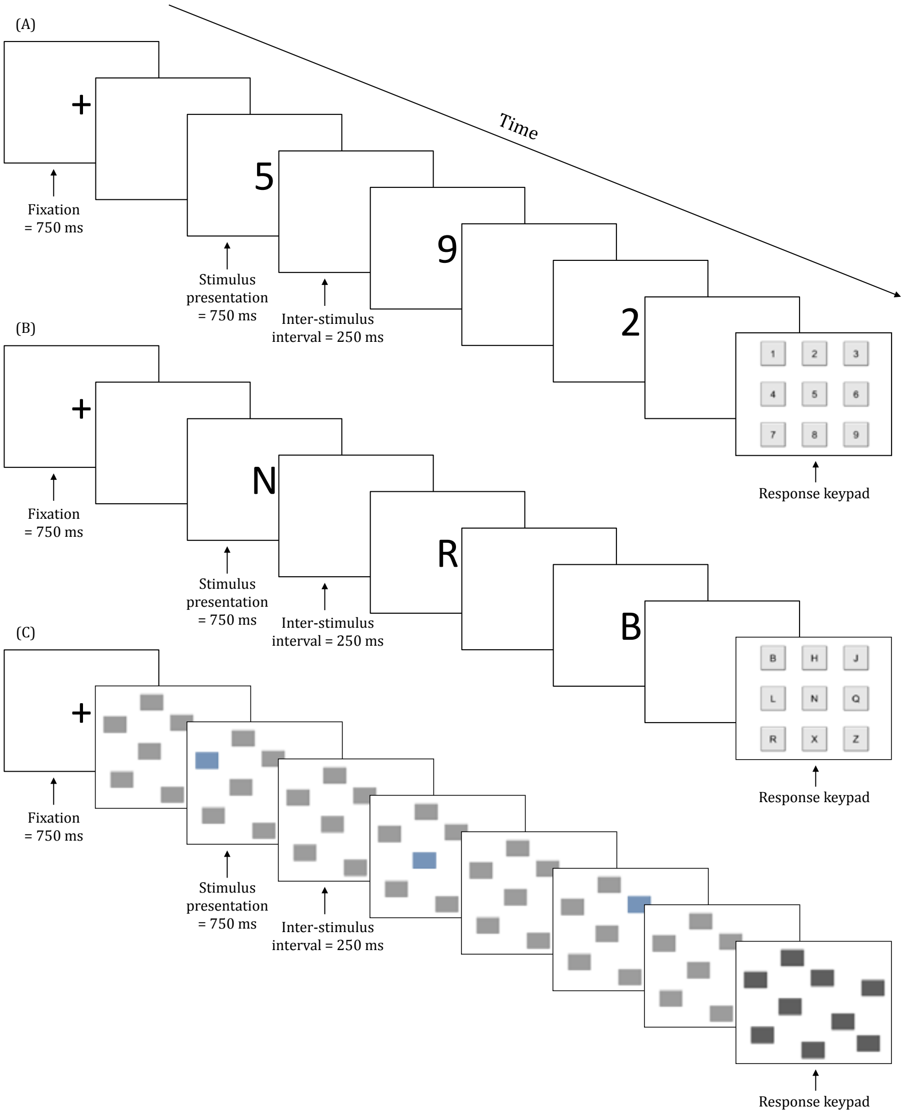


Figure 4.1 – Backward recall tasks (illustrated for a span of three items): including (A) backward digit recall, (B) backward letter recall, and (C) backward spatial recall.

Backward recall

Participants completed three backward recall tasks (see Figure 4.1), each containing different stimuli: (i) digits (1 to 9), (ii) phonologically distinct letters (B H J L N Q R X Z), or (iii) spatial locations (nine random but fixed locations on the computer screen). Trials were presented in blocks, each consisting of four trials. During each trial items were presented visually on screen one at a time (stimulus presentation = 750 ms, inter-stimulus interval = 250 ms). Participants were then prompted to recall the sequence in backward order via an onscreen keypad of digits, letters, or spatial locations. Participants began each task at a span of three items. Span length was increased by one item in each subsequent block if there were three or more correct trials.

The tasks were discontinued if two or more trials were incorrect within a block, or if the maximum span level was reached (span 13). Maximum span reached was scored for each of the backward recall tasks (i.e. the final span in which the participant met the criterion of at least three out of four correct trials).

n-back

Participants completed three *n*-back tasks (see Figure 4.2), each containing different stimuli: (i) digits (1 to 9), (ii) phonologically distinct letters (B H J L N Q R X Z), or (iii) spatial locations. For each task, stimuli were presented one at a time on screen in a random order (stimulus presentation = 760 ms, inter-stimulus interval = 2000 ms). Participants were required to indicate whether the current item on screen matched the one presented *n* items back in the sequence via a button press. In each block participants were presented with a continuous sequence of 20 + *n* items, during which there were a total of six possible targets (matches) and 14 + *n* non-targets. An error was scored if participants pressed the button for a non-target (false alarm), or if participants failed to press the button when a match was present (miss). Total errors were calculated as false alarms plus misses combined. The first block began at one-back and difficulty level was increased by one in each subsequent block if less than five errors were made (e.g. an increase from one-back to two-back). The task ended if five or more errors were made within a block, or if the maximum level was reached (12-back). The maximum *n*-level reached was scored for each of the *n*-back tasks (i.e. the final level in which the participant met the criterion of less than five errors in a block).

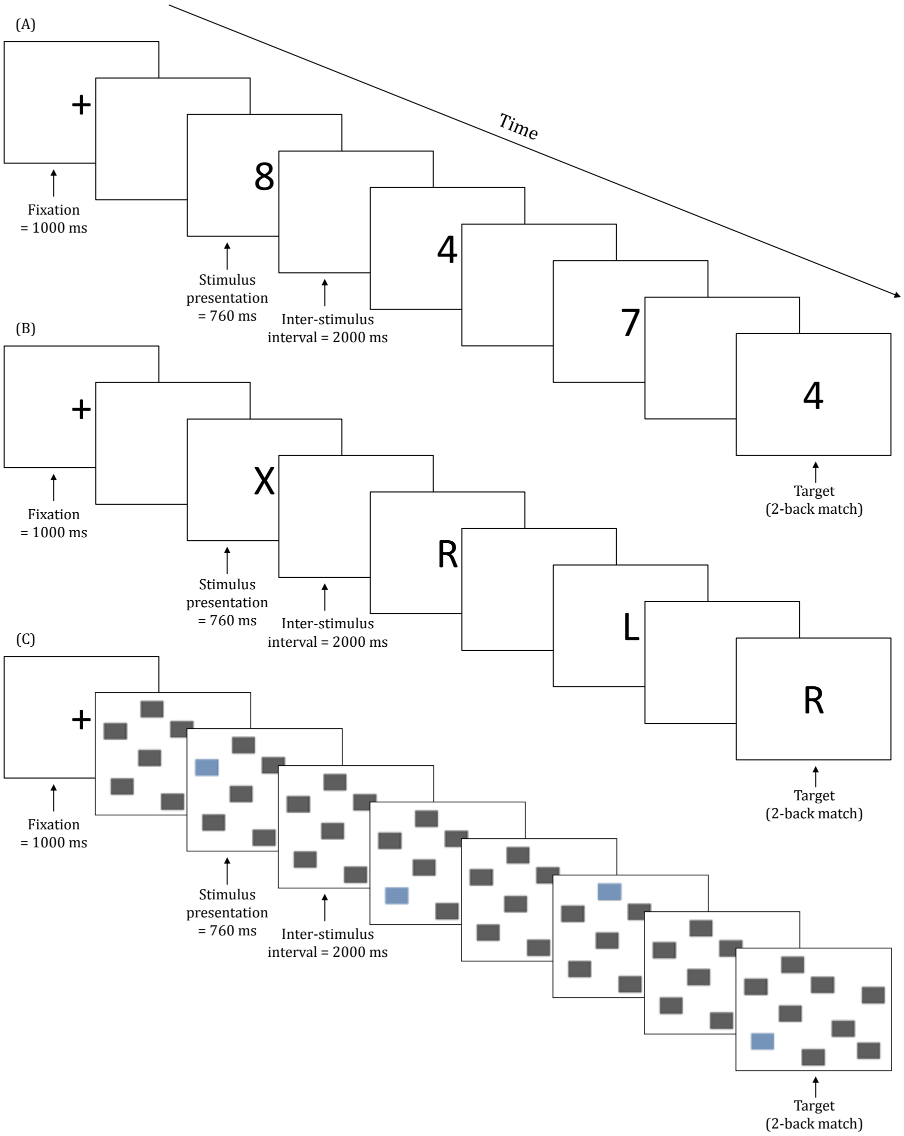


Figure 4.2 – *n*-back tasks (illustrated for a two-back level): including (A) *n*-back with digits, (B) *n*-back with letters, and (C) *n*-back with spatial locations.

Relational reasoning

During the relational reasoning task (Knoll et al., 2016), participants were presented with 80 puzzles one at a time on screen (see Figure 4.3 for a screenshot of this task). Each puzzle consisted of a 3 x 3 matrix (nine spaces in total). Eight of the spaces contained shapes, but the bottom right space was empty. Participants were also presented with four boxes at the bottom of the screen containing shapes, and were required to select the box with the correct answer – the box containing the piece that was missing from the empty space in the matrix. The shapes in the matrix varied by colour, size, shape, and position. Difficulty level also varied. Participants were given 30 s to complete each trial, and a prompt appeared on screen when only 5 s remained. Odd and even items were scored separately to give two relational reasoning scores. In each case the number of correct responses (out of 40) was used in the analyses as the measure of ability.

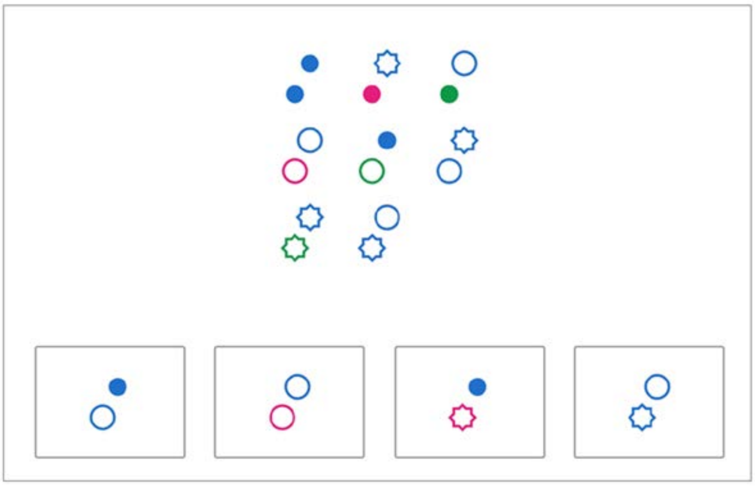


Figure 4.3 – Screenshot of a trial from the relational reasoning task.

4.3.4 Analysis plan

This plan has been reproduced from the pre-registered report (www.osf.io/9qarp/; see Appendix E). The tense has been changed to fit with the context of the chapter.

To address the primary research question, confirmatory factor analysis was conducted to find the best fitting model for the six working memory tasks. The following models were compared: (A) a single working memory factor model, (B) a two-factor domain-specific verbal and visuo-spatial construct model, (C) a two-factor backward recall and *n*-back paradigm model, and (D) a three-factor digit, letter, and spatial materials model. The best-fitting model(s) were identified using a number of widely used fit statistics (see Section 4.3.5 for a summary of these fit indices).

After establishing interrelationships among the working memory measures and determining the best fitting and most parsimonious working memory model for the variables, the secondary research question was addressed (i.e. how are the two classes of working memory paradigm, backward recall and *n*-back, related to fluid reasoning?). The parameters of the best-fitting working memory model were fixed and a reasoning factor was added to examine whether the working memory factor(s) and the reasoning tasks load on a single factor or on distinct but related constructs. If a single-factor working memory model was preferred, the plan was to examine whether the working memory factor is very strongly or perfectly correlated with a fluid reasoning factor. Alternatively, if a multi-factor model was preferred then the relationship between the working memory factors and fluid reasoning would be examined to see whether it was identical or stronger for certain sub-factors. This multi-factor model was then compared to a single-factor general ability model that included all working memory and reasoning tasks.

All R code for this analysis is available in Appendix H.

4.3.5 Model fit and comparison

Models were estimated in the lavaan software package (Version 0.5-20; Rosseel, 2012) in R version 3.1.3 (R Core Team, 2015) using maximum likelihood estimation and robust standard errors, for which the Yuan-Bentler (YB) scaled test statistic is reported. Missing observations were dealt with using the full maximum likelihood (FIML) parameter estimation technique. The overall fit of each model was assessed using the χ^2 test, the comparative fit index (CFI; range: 0-1.0; acceptable fit: .95-.97, good fit: ≥ .97; Schermelleh-Engel, Moosbrugger, & Müller, 2003), and the root mean square error of approximation (RMSEA; range: 0-1.0; acceptable fit: < .08, good fit: ≤ .05; Schermelleh-Engel et al., 2003) which is reported with 90% confidence intervals. The four models were also compared. When models were nested, they were compared via a likelihood ratio test (i.e. the scaled χ^2 difference test); otherwise non-nested models were directly compared via the Akaike information criteria (AIC).

4.4 Results

4.4.1 Preliminary analyses

The data were screened to identify outliers (i.e. scores deviating 3.5 SDs from the sample mean on that task). Twenty-nine observations were removed during data screening for outliers, and an additional 14 observations were missing due to technical problems during data collection (total missing observations = 37). Descriptive statistics are summarised in Table 4.1. A correlation matrix of all tasks is displayed in Table 4.2. There were no differences in maximum span reached across the three backward recall tasks, nor across the three *n*-back tasks. All tasks were positively correlated (all *p*s < .01). The strongest patterns of association were observed between backward digit and backward letter recall (r = .526), and between the three n-back tasks (all rs > .4). The two relational reasoning scores were very highly correlated, as expected given they were two halves of the same test.

Table 4.1 – Descriptive statistics for all variables.

Variable	*N*	*M*	*SD*	*Skewness*	*Kurtosis*
Backward digit recall	698	5.307	1.695	0.479	-0.187
Backward letter recall	690	4.470	1.247	0.844	0.704
Backward spatial recall	702	5.068	1.214	-0.405	-0.734
n-back with digits	694	3.307	1.723	0.977	1.047
n-back with letters	698	3.032	1.658	0.757	0.380
n-back with spatial locations	699	2.774	1.511	0.984	0.591
Relational reasoning even	700	24.921	7.604	-0.096	-0.879
Relational reasoning odd	700	23.787	7.431	0.037	-0.683

Table 4.2 – Correlation matrix for all tasks; simple coefficients are displayed (N = 703).

Variable	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
1. Backward digit recall	–							
2. Backward letter recall	.526*	–						
3. Backward spatial recall	.205*	.232*	–					
4. *n*-back with digits	.172*	.258*	.198*	–				
5. *n*-back with letters	.182*	.272*	.173*	.410*	–			
6. *n*-back with spatial locations	.114*	.183*	.217*	.421*	.407*	–		
7. Relational reasoning even	.315*	.322*	.362*	.353*	.369*	.356*	–	
8. Relational reasoning odd	.320*	.317*	.331*	.372*	.369*	.340*	.905*	–

Note. * p < .01.

4.4.2 Confirmatory factor analysis

Confirmatory factor analysis was used to identify the best-fitting factor model for the six memory tasks. The models tested are displayed in Figure 4.4. Fit indices for each model are provided in Table 4.3. The fit statistics revealed that the single-factor model (A), χ^2 (9) = 195.825, RMSEA = 0.172 (90% confidence interval [CI] = .151, .194), and CFI = .678, the two-factor domain model (B), χ^2 (8) = 204.926, RMSEA = .187 (90% CI = .164, .211), and CFI = .660, and the three-factor materials model (D), χ^2 (6) = 189.847, RMSEA = .209 (90% CI = .181, .237), and CFI = 683, were a poor fit to data. The two-factor paradigm model (C), χ^2 (8) = 29.108, RMSEA = .061 (90% CI = .038, .086), and CFI = .964, was an acceptable fit to the data demonstrating that separate but related latent constructs corresponding to backward recall and *n*-back best capture the data.

The fit of the single-factor working memory model (A) was compared with each of the other models using χ^2 difference tests because it was nested the other models. These analyses revealed that the fit of the single-factor model was not significantly different to the domain model (B), $\Delta\ \chi^2 = 0.150$, $\Delta\ df = 1$, $p = .700$, but it did provide a significantly better account of the data than the materials model (D), $\Delta\ \chi^2 = 22.367$, $\Delta\ df = 3$, p < .001. The two-factor paradigm model (C) outperformed the single-factor model (A), $\Delta\ \chi^2 = 272.820$, $\Delta\ df = 1$, $p < .001$. The AIC measurement was used to directly compare the other models to one another. The two-factor paradigm model (C) was the best fit with the lowest relative AIC value (see Table 4.3).

Table 4.3 – Fit statistics for each model in the primary confirmatory and exploratory factor analyses.

Model		χ^2	*df*	*YB*	*RMSEA*	*CFI*	*AIC*
Confirmatory factor analysis							
(A)	Single-factor working memory	195.825	9	.932	.172 [.151, .194]	.678	14739
(B)	Two-factor domain	204.926	8	.889	.187 [.164, .211]	.660	14741
(C)	Two-factor paradigm	29.108	8	.977	.061 [.038, .086]	.964	14587
(D)	Three-factor materials	189.847	6	.826	.209 [.181, .237]	.683	14720
Exploratory factor analysis							
(E)	Single-factor working memory with BDR & BLR link	24.154	8	.996	.054 [.030, .079]	.972	14583
(F)	Two-factor domain with BDR & BLR link	25.036	7	.953	.061 [.035, .088]	.969	14585
(G)	Two-factor paradigm with BDR & BLR link	10.658	7	.970	.027 [.000, .059]	.994	14571

Note. For root mean errors of approximation (RMSEAs), 90% confidence intervals are given. CFI = comparative fit index; AIC = Akaike information criterion. The χ^2 reported is the Yuan-Bentler scaled χ^2, with the scaling factor reported as YB. BDR = backward digit recall, BLR = backward letter recall.

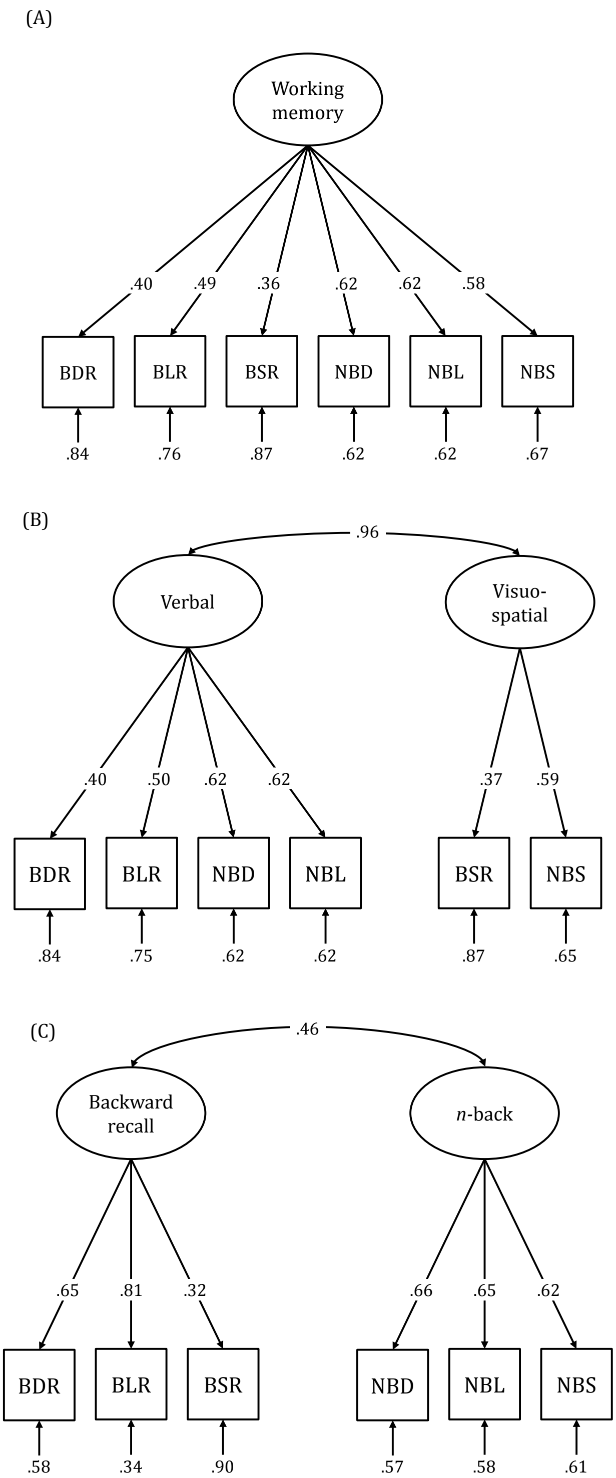


Figure 4.4 (continued on the next page) – Models A (single-factor working memory), B (two-factor domain), and C (two-factor paradigm), where ovals represent latent factors and observed variables are shown in squares. BDR = backward digit recall, BLR = backward letter recall, BSR = backward spatial recall, NBD = *n*-back with digits, NBL = *n*-back with letters, NBS = *n*-back with spatial locations.

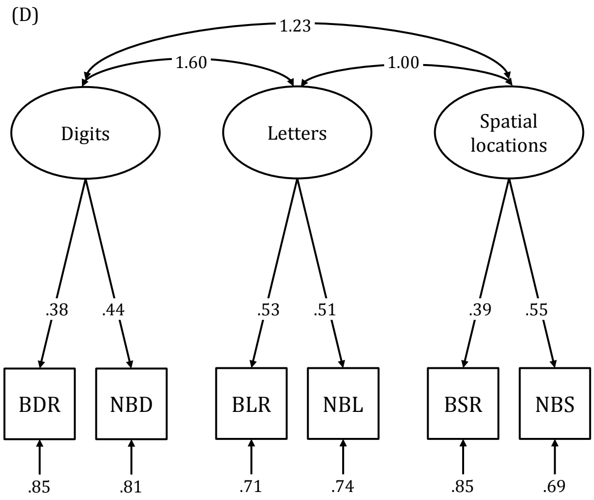


Figure 4.4 (continued) – Model D (three-factor materials), where ovals represent latent factors and observed variables are shown in squares. BDR = backward digit recall, BLR = backward letter recall, BSR = backward spatial recall, NBD = *n*-back with digits, NBL = *n*-back with letters, NBS = *n*-back with spatial locations.

4.4.3 Exploratory factor analysis

Modification indices (using the χ^2 statistic) were calculated for the single-factor model (A), two-factor domain model (B), and three-factor materials model (D), to explore why they were such a poor fit to the data. None of the modifications suggested for the materials model were appropriate, and so this model was not adjusted. The modification indices for the single-factor model revealed that adding a specific link between the BDR and backward letter recall (BLR) measures to allow them to co-vary would improve the model fit with an estimated change in χ^2 of 148.713. A single-factor model allowing these two indicators to co-vary was tested, and the model fit improved substantially (see Figure 4.5, Model E). The revised model was a good fit to the data, χ^2 (8) = 24.154, RMSEA = .054 (90% CI = .030, .079), and CFI = .972, and statistically superior to the single-factor model without the modification (Model A), $\Delta\ \chi^2 = 377.66$, $\Delta\ df = 1$, $p < .001$. The same fix between BDR and BLR was suggested for the domain model, with an estimated χ^2 change of 149.145. The revised domain model with the same fix (see Figure 4.5, Model F) also improved and was an acceptable fit to the data, χ^2 (7) = 25.036, RMSEA = .061 (90% CI = .035, .088), and CFI = .969, and was significantly better than the original domain model (B), $\Delta\ \chi^2 = 357.63$, $\Delta\ df = 1$, $p < .001$. A χ^2 difference test revealed the modified single-factor and domain models were not significantly different, $\Delta\ \chi^2 = 0.145$, $\Delta\ df = 1$, $p < .704$.

Next, to compare directly whether the modified single-factor model (E) was better than the best-fitting two-factor paradigm model (C) from the confirmatory analyses, the same modification was added to the two-factor paradigm model (see Figure 4.5, Model G). Fit indices revealed this model was a very good fit to the data, χ^2 (7) = 10.658, RMSEA = .027 (90% CI = .000, .059), and CFI = .994, and a statistically better fit than the same model without the modification (Model B), $\Delta\ \chi^2$ = 17.587, $\Delta\ df$ = 1, p < .001. The χ^2 statistic for Model G was non-significant (p = .145), a further indication this model was a good fit. A χ^2 difference test demonstrated that the two-factor paradigm model with the link between BDR and BLR (Model G) outperformed the single-factor model with the same link (Model E), $\Delta\ \chi^2$ = 11.668, $\Delta\ df$ = 1, p < .001. The revised paradigm model (G) could not be directly compared with the modified domain model (F) as these models were not nested. However, based on there being no significant difference between the adjusted single-factor model (E) and domain model (F), but the revised paradigm model (G) being statistically superior to the adjusted single-factor model (E) in conjunction with a comparison of fit indices, it could be assumed that the modified paradigm model (G) was better than the adjusted domain model (F). This was confirmed by the AIC values (see Table 4.3), revealing that the best-fitting model of the working memory tasks was a paradigm-based model with a specific link between the two verbal backward recall tasks.

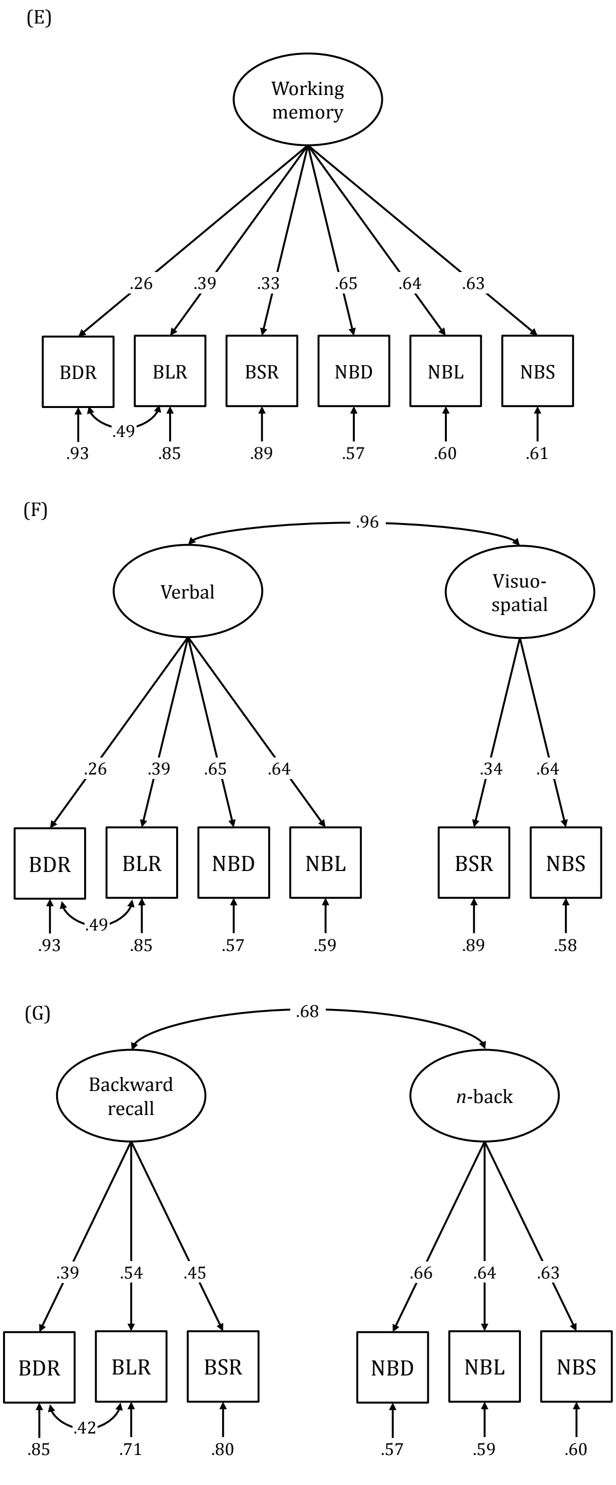


Figure 4.5 – Models E (single-factor working memory, with BDR and BLR link), F (two-factor domain, with BDR and BLR link), and G (two-factor paradigm, with BDR and BLR link), where ovals represent latent factors and observed variables are shown in squares. BDR = backward digit recall, BLR = backward letter recall, BSR = backward spatial recall, NBD = *n*-back with digits, NBL = *n*-back with letters, NBS = *n*-back with spatial locations.

4.4.4 Secondary analyses

A secondary aim of this study was to explore how the working memory tasks are related to relational reasoning. Specific aims were to test whether a model with all tasks loading on a single factor (working memory and relational reasoning) provides a better account of the data than a model with a separate relational reasoning factor that is linked to the two paradigm factors, which are defined in the best-fitting model from the previous confirmatory and exploratory analyses. Two sets of models were generated. Fit indices for each model are provided in Table 4.4. One comprised three correlated latent variables – one each for the backward recall, *n*-back, and reasoning tasks. A reasoning construct was added to the original two-factor paradigm model (C), and also to the modified paradigm model (G) with a link between BDR and BLR. These are illustrated in Figure 4.6 as Models H and I, respectively. Fit indices for both of these models were very good: Model H, χ^2 (17) = 63.574, RMSEA = .062 (90% CI = .046, .079), and CFI = .976, and Model I, χ^2 (16) = 23.576, RMSEA = .026 (90% CI = .000, .047), and CFI = .996. The χ^2 statistic for Model I was non-significant (p = .099), further indicating the good fit of this model. A comparison of the two models using the χ^2 difference test and the AIC showed a superior fit on both indices for Model I, $\Delta\,\chi^2$ = 67.627, $\Delta\,df$ = 1, p < .001 (AIC: Model H = 22789, Model I = 22752).

Table 4.4 – Fit statistics for each model included in the secondary analyses.

Model		χ^2	*df*	*YB*	*RMSEA*	*CFI*	*AIC*
(H)	Three-factor paradigm & reasoning	63.574	17	.980	.062 [.046, .079]	.976	22789
(I)	Three-factor paradigm & reasoning, with RR_E & RR_O link, and BDR & BLR link	23.576	16	1.006	.026 [.000, .047]	.996	22752
(J)	Single-factor general ability	364.420	20	1.074	.157 [.143, .170]	.819	23112
(K)	Single-factor general ability with BDR & BLR link	65.683	18	1.009	.061 [.046, .078]	.975	22791

Note. For root mean errors of approximation (RMSEAs), 90% confidence intervals are given. CFI = comparative fit index; AIC = Akaike information criterion. The χ^2 reported is the Yuan-Bentler scaled χ^2, with the scaling factor reported as YB. RR_E = relational reasoning even items, RR_O = relational reasoning odd items, BDR = backward digit recall, BLR = backward letter recall.

The second set of models assumed a single latent construct for all measures (three backward recall, three *n*-back, and two relational reasoning tasks). In the first model no constraints were added (see Figure 4.7, Model J) and it was a poor fit to the data: χ^2 (20) = 364.420, RMSEA = .157 (90% CI = .143, .170), and CFI = .819. Modification indices suggested fit could be improved by constraining the two reasoning tasks (estimated reduction in χ^2 = 238.094), and then again by adding a link between BDR and BLR (estimated χ^2 reduction = 124.770). These alterations were applied incrementally. The resulting model (K) is presented in Figure 4.7. It was an acceptable fit to the data, χ^2 (18) = 65.683, RMSEA = .061 (90% CI = .046, .078), and CFI = .975, and statistically superior to the same single-factor model without the modifications (Model J), $\Delta\ \chi^2$ = 196.310, $\Delta\ df$ = 2, p < .001 (AIC: Model J = 23112, Model K = 22791).

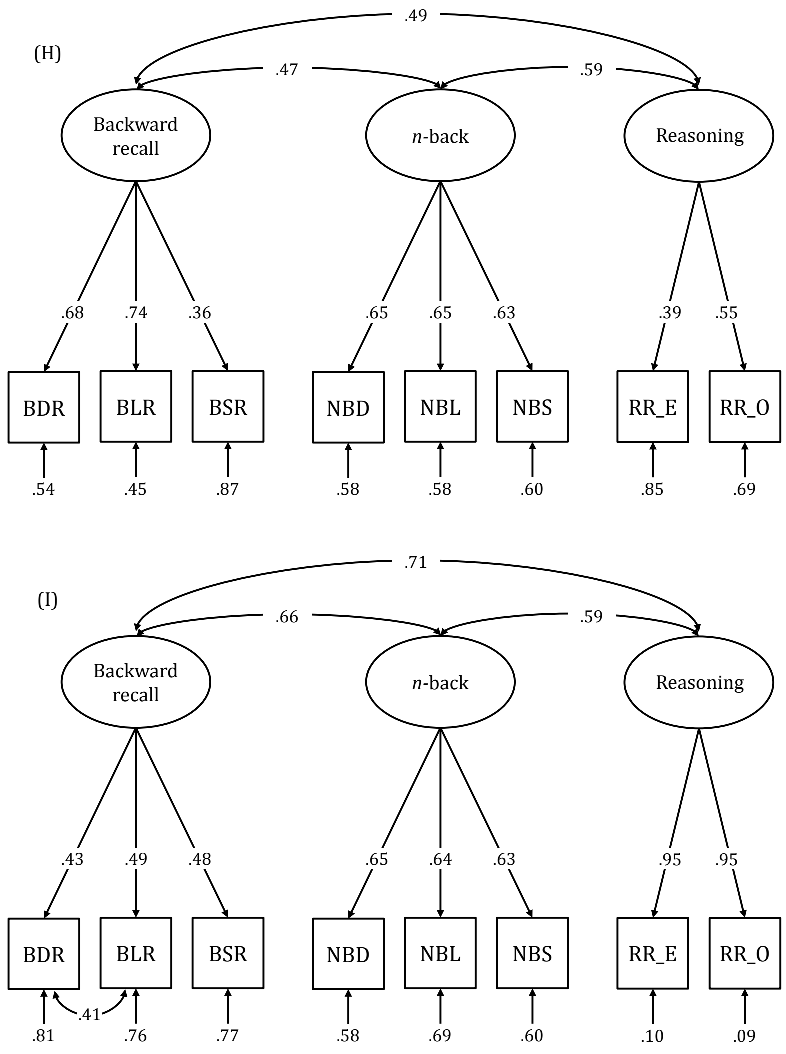
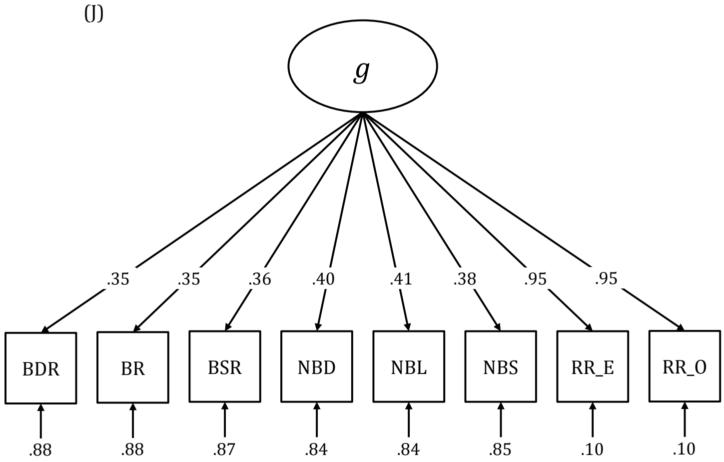


Figure 4.6 – Models H (three-factor paradigm and reasoning) and I (three-factor paradigm and reasoning, with BDR and BLR link). Latent factors are shown in ovals and squares represent observed variables. BDR = backward digit recall, BLR = backward letter recall, BSR = backward spatial recall, NBD = *n*-back with digits, NBL = *n*-back with letters, NBS = *n*-back with spatial locations, RR_E = relational reasoning even items, RR_O = relational reasoning odd items.

Finally, a χ^2 difference test demonstrated that Model I outperformed Model K, $\Delta\ \chi^2 = 41.136$, $\Delta\ df = 2$, $p < .001$. This was confirmed by the AIC values (see Table 4.4), revealing that the best fitting model of the working memory and relational reasoning tasks was a three-factor model with latent constructs corresponding to backward recall, *n*-back, and reasoning, that has a specific link between BDR and BLR. These distinct latent constructs were strongly related to each other, and the relationship between backward recall and reasoning, and between *n*-back and reasoning, was similar (see Figure 4.6, Model I).

(J)



(K)

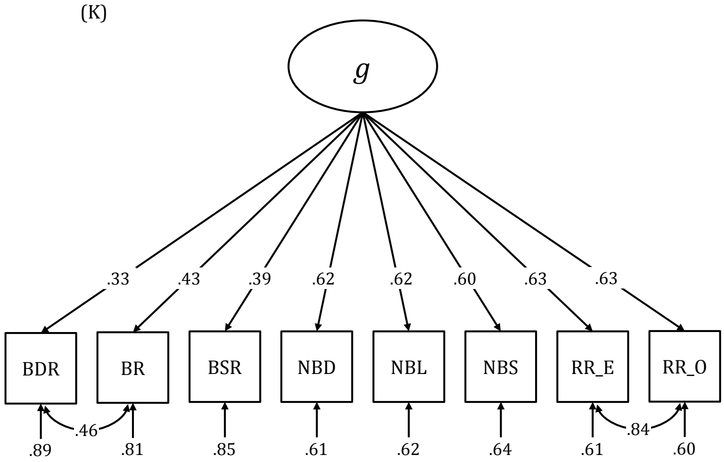


Figure 4.7 – Models J (single-factor general ability model) and K (single-factor general ability model with RR_E and RR_O link, and BDR and BLR link). Latent factors are shown in ovals and squares represent observed variables. *g* = general ability factor, BDR = backward digit recall, BLR = backward letter recall, BSR = backward spatial recall, NBD = *n*-back with digits, NBL = *n*-back with letters, NBS = *n*-back with spatial locations, RR_E = relational reasoning even items, RR_O = relational reasoning odd items.

4.5 Discussion

The goal of this study was to examine the relationship between variations of backward recall and *n*-back measures of working memory by means of a latent variable approach. Confirmatory factor analysis revealed that the best-fitting model was one that split the working memory tasks by paradigm. The data were best-captured by two distinct backward recall and *n*-back latent constructs that were related to one another (r = .68). This suggests the tasks have something in common, but that they also tap into distinct processes too. The underlying structure of these paradigms is similar to that found for measures of complex span and updating. Schmiedek et al. (2014) reported that these tasks also loaded on two distinct but correlated paradigm factors (r = .69). The findings are also consistent with the training literature showing that transfer effects are constrained by paradigm: improving performance on one type of working memory task, does not lead to improved performance on another category of working memory task (Byrne et al., 2018; Holmes et al., 2018; Li et al., 2008; Minear et al., 2016; Redick et al., 2013; Sprenger et al., 2013; Thompson et al., 2013).

The data are, however, inconsistent with the outcomes of previous studies reporting much lower correlations (Dobbs & Rule, 1989; McAuley & White, 2011; Miller et al., 2009; Roberts, 1998; Roberts & Gibson, 2002), and the results of a meta-analysis where BDR and *n*-back tasks were weakly related (r = .31; Redick & Lindsey, 2013). Differences in the strength of the relationship between these paradigms may be due to methodological differences. A latent variable approach was used here, which included multiple indicators of each paradigm. The previous studies, however, focussed exclusively on a single BDR task, and although some included multiple *n*-back tasks with verbal (letters, words) and spatial materials (locations, shapes; McAuley & White, 2011; Redick & Lindsey, 2013), many used only a single indicator of *n*-back with either letters or words (Dobbs & Rule, 1989; Miller et al., 2009; Roberts, 1998; Roberts & Gibson, 2002). Using a latent variable approach overcomes the problem that correlations between single tasks are attenuated by paradigm-specific and content-specific sources of individual variation as well as measurement error (Schmiedek et al., 2009, 2014).

Working memory is a multifaceted system that relies on a range of processes including encoding, maintenance, recall, recognition, familiarity, updating, temporal ordering, binding, attention, and inhibition (Oberauer et al., 2007; Redick & Lindsey, 2013; Unsworth & Spillers, 2010). The substantial correlation between the backward recall and *n*-back constructs suggests they share a common source of variance, which might be the variance attributed to processes linked with working memory such as the mechanisms used for building, maintaining, and updating arbitrary bindings between memory items and their serial position (Oberauer et al., 2007; Schmiedek et al., 2009). During backward recall, participants must reorder information following encoding (at the point of recall), meaning relative serial positions of the memory items must be updated (e.g. the sequence 5 2 7 3 must be reordered with 3 in the first serial position, 7 in the second serial positon, etc.). Similarly, in *n*-back the serial positon of items that have been previously encoded must be updated as new items are continuously presented (e.g. an item going from being in position *n*, to position $n - 1$, to position $n - 2$, etc.; Redick & Lindsey, 2013). The similarity of this reordering process and the role of binding items to the appropriate temporal context may account for the construct overlap between these two tasks (Oberauer, 2005; Redick & Lindsey, 2013; Szmalec et al., 2011).

The two paradigm-specific factors were not perfectly correlated suggesting they are measuring distinct sub-processes of the working memory system, or processes specific to the paradigms, in addition to the variance they have in common. These might correspond to differences in the retrieval demands of the two tasks, which differ considerably. Backward recall involves explicit serial recall and participants must retrieve items using only self-generated cues (Kane et al., 2007). In contrast, *n*-back requires recognition and can be completed using familiarity-based responding (Oberauer, 2005). The tasks also have different updating requirements. For *n*-back, the full sequence must be refreshed as new items are added and old ones are dropped, while for backward recall the whole sequence has to be held in mind and transformed and updated at the point of recall. Data presented in the previous chapter of this thesis revealed that BDR training gains transferred to untrained variants of backward recall tasks but not to untrained *n*-back tasks (Byrne et al., 2018; see Chapter 3). The current data are consistent with this pattern of transfer and suggest training may be enhancing the paradigm-specific mechanisms required in backward recall, but not improving other processes that are specifically involved in *n*-back performance or shared between *n*-back and backward recall.

The best-fitting model of the working memory tasks included a specific link between the two verbal backward recall tasks (BDR and BLR). This suggests that as well as there being a split at the paradigm level between backward recall and *n*-back, there appears to be a distinction within the backward recall construct between verbal and visuo-spatial tasks. This likely reflects the use of common cognitive processes or strategies for reverse serial recall tasks of verbal items. For example, individuals might engage in repeated covert cycles of forward serial recall through the list of encoded memory items, each time recalling the last item and then peeling them off sequentially (Anders & Lillyquist, 1971; Thomas et al., 2003). This involves drawing on verbal rehearsal processes that are established in the phonological short-term memory system to support the maintenance of verbal material (Page & Norris, 1998), as well as a cognitive routine for recalling the last item in the sequence (Gathercole et al., 2018). The use of a common maintenance mechanism for the digit and letter stimuli in the backward recall tasks, combined with a common cognitive routine (Gathercole et al., 2018) for reversing the sequence explains why these two tasks are strongly related. In contrast, spatial rehearsal is not a well-established or highly-practiced component of the visuo-spatial short-term memory system. It relies more heavily on general attentional resources to guide the execution of covert oculomotor planning processes (Pearson et al., 2014), and the maintenance of visuo-spatial items is supported by a distinct system within working memory (Allen, Baddeley, & Hitch, 2006; Baddeley et al., 2011; Logie, 1995).

No such additional link between the verbal tasks was suggested for the *n*-back construct. This is in line with a previous study showing that *n*-back performance is independent of stimulus material (Jaeggi, Buschkuehl, et al., 2010) and suggests the mechanisms supporting performance on *n*-back tasks may be more domain-general than those supporting backward recall. The requirement for explicit recall in backward recall may encourage participants to engage in rehearsal processes more readily than *n*-back tasks that rely on recognition-based responses. Speculatively, the greater tendency for domain-specific rehearsal processes for backward recall may explain why domain-specificity was observed for these tasks and not *n*-back.

A model that included separate working memory paradigm and reasoning constructs was preferred to one where all working memory and reasoning measures loaded on a single factor. This supports the idea that working memory and *Gf* are highly related but dissociable constructs (Kovacs & Conway, 2016), if reasoning is used as a proxy of non-verbal IQ. Both categories of working memory task were linked to the separate fluid reasoning construct. This is consistent with many previous individual differences studies showing strong associations between working memory capacity and general fluid intelligence (Engle, Laughlin, et al., 1999; Engle & Kane, 2004; Kane et al., 2004; Schmiedek et al., 2009, 2014). It also provides evidence that both paradigms are valid measures of higher-order complex cognition. There is a debate concerning whether BDR is a measure of working memory because it requires items to be stored and item order to be manipulated (Alloway et al., 2006) or a measure of short-term memory that also draws on the strategic use of visual imagery (Rosen & Engle, 1997; St Clair-Thompson, 2010; St Clair-Thompson & Allen, 2013). Although short-term memory tasks were not included in the current study, the shared variance between the backward recall tasks and both the *n*-back and fluid reasoning constructs suggests it shares common variance with other measures of higher-order complex cognition, meaning it potentially taps into more than just short-term memory.

In summary, these results show that two categories of task used widely to measure working memory, *n*-back and backward recall, tap into distinct processes but that they also share common variance with one another and non-verbal reasoning. Building, maintaining, and updating arbitrary bindings may constitute the cognitive mechanisms shared between the three constructs (Oberauer et al., 2007; Schmiedek et al., 2009). Distinctions at the paradigm level might reflect differences in retrieval demands (i.e. active recall versus recognition based responding) or updating requirements (i.e. continuous updating during stimulus presentation versus transformation and updating at the point of recall after a list is presented). These findings suggest that backward recall and *n*-back tasks can be used interchangeably as measures of working memory, but with the caveat that although they measure the temporary processing and storage of information they are doing so in ways that tap into distinct processes. Working memory training may be training these processes that are specific to each paradigm and not those that contribute to the shared variance between tasks, explaining why many studies fail to produce cross-paradigm training transfer.

Chapter 5 General discussion

The overarching aim of the research presented in this thesis was to investigate the effects of combining working memory training and transcranial electrical stimulation (tES). The first two experiments attempted to enhance working memory training with different forms of tES. In the first study, transcranial random noise stimulation (tRNS) was used but did not have any effect on performance. Evidence suggests that transcranial direct current stimulation (tDCS) could be more effective for enhancing working memory performance compared to tRNS (Mulquiney et al., 2011), therefore tDCS was used in the second experiment. The second study also examined transfer effects following training. This is the first experiment to systematically investigate the boundary conditions to transfer following training on backward recall. The three constraints tested were: task paradigm (i.e. backward recall and *n*-back), domain of materials (i.e. verbal or visuo-spatial), and type of memoranda (e.g. digit or letter materials). The results of this study led to the third experiment, in which the overlap between different types of working memory tasks was examined. In this final experiment, novel web-based methods were used to gather data for a large-scale latent variable analysis. Using an individual differences approach this study examined the shared variance between a series of backward recall and *n*-back tasks. The main findings and conclusions of these experiments are presented in Section 5.1. These are followed by a discussion of the theoretical and methodological implications of this research in Section 5.2. Limitations and possible future lines of enquiry are discussed in Section 5.3 and Section 5.4, respectively. Finally, the conclusion gives a brief summary of the key outcomes in Section 5.5.

5.1 Summary of results

The results of the first experiment showed that adaptive working memory training was associated with substantial gains on the training activities and enhanced performance on transfer measures with processing and storage demands in common with the training tasks. However, there was no reliable evidence that tRNS over bilateral dorsolateral prefrontal cortex

(DLPFC) enhanced gains on the training activities or facilitated the transfer of gains to untrained working memory tasks. Similarly, the second experiment showed that tDCS to left DLPFC did not boost gains on trained or untrained working memory tasks when combined with backward digit recall (BDR) training. These findings contrast earlier studies demonstrating that stimulation is an effective tool for boosting the rate of learning and magnitude of on-task training gains, and promoting generalisation to untrained tasks (Au et al., 2016; Ruf et al., 2017; Snowball et al., 2013). However, the current data is in accordance with studies that show, when using the most rigorous randomised-controlled study designs, there is little evidence that tES enhances the effects of cognitive training or transfer (Martin et al., 2013; Nilsson et al., 2017; Richmond et al., 2014). The clear conclusion of the first two experiments is that, when using the current best standards in intervention design and combining training and stimulation protocols that have been shown to be effective in other domains, there is no evidence that tES targeting DLPFC enhances the benefits of working memory training.

The inclusion of an active control training group in the second experiment also allowed the transfer effects of training alone to be explored. Overall the findings showed that transfer following training is limited, and is constrained by paradigm. Post-training gains were found on backward recall with digits, letters, and spatial locations following BDR training. However, there was no evidence of transfer to any *n*-back task, even when the task contained the same type of materials as the training activity (i.e. digits). These results indicate that paradigm is a boundary condition for training transfer, but that type and domain of stimuli are not. These results are consistent with previous studies showing that working memory training does not transfer to other categories of working memory paradigm (e.g. Dunning & Holmes, 2014; Holmes et al., 2017; Li et al., 2008; Minear et al., 2016; Sprenger et al., 2013; von Bastian & Oberauer, 2013). The effects sizes for gains on the backward recall tasks with digits, letters, and spatial locations diminished respectively with distance from the training task, suggesting that the greater the number of features in common between training and transfer tasks, the more likely it is that transfer will be observed (Gathercole et al., 2018; Thorndike & Woodworth, 1901).

Finally, the third study examined the overlap between two widely used working memory paradigms, backward recall and *n*-back, using a latent variable approach. Confirmatory factor analysis revealed that three backward recall tasks loaded on a latent backward recall construct and three *n*-back tasks loaded on a distinct *n*-back factor, and that these two factors were substantially related to each other (r = .68). Distinctions at a paradigm level might reflect differences in retrieval demands (i.e. explicit recall versus recognition) or updating requirements (i.e. updating at recall versus continuous updating). Both categories of working memory task were also linked to a separate fluid reasoning construct, providing evidence that both tasks are valid measures of higher-order complex cognition. The underlying structure of the tasks is similar to that reported by Schmiedek and colleagues (2009), who found distinct but related latent factors for complex span and updating measures that both predicted reasoning ability equally well. Overall, the findings of the study suggest that backward recall and *n*-back tasks are valid indicators of working memory ability, but although they both measure the temporary storage and processing of information they are tapping into different sub-processes.

5.2 Implications

The outcomes of this thesis have significant implications for the potential use of tES as a tool for enhancing working memory, for establishing the boundary conditions to transfer following training, and for understanding the processes involved in different tasks commonly used to measure and train working memory function. The experiments presented in this thesis also have important methodological implications for intervention studies involving stimulation and training that promise cognitive enhancement.

5.2.1 Theoretical implications

Using the current best standards in intervention design, and testing two different stimulation montages, the results presented in this thesis provide no evidence that tES enhances the effects of working memory training, and do not support the use of these stimulation methods as therapeutic tools to remediate working memory problems. The data presented also enhance our understanding of the boundary conditions for training transfer. The limited generalisation of gains observed across the two training studies supports process-specific theories of training transfer. That is, training is promoting the development of processes or strategies that are specific to the training activities (E. Dahlin, Neely, et al., 2008; Dunning & Holmes, 2014; Gathercole et al., 2018; Minear et al., 2016; Sprenger et al., 2013; von Bastian & Oberauer, 2014). More specifically, the pattern of results may provide support for a recent proposal by Gathercole and colleagues (2018) that expands on the process-specific account and suggests that working memory training is promoting the creation of novel cognitive routines. This framework argues that when individuals encounter a complex and unfamiliar working memory task, a novel routine must be constructed and refined that co-ordinates and executes existing component cognitive processes in a new sequence (Gathercole et al., 2018). Over time, with repeated practice of sub-routines during training, the routine becomes more efficient and automatic and can then be readily applied to unfamiliar transfer tasks share the same higher-order structure. The BDR task used as the training activity in Study 2 required a new routine to be developed for the recall phase. To perform the task properly, the routine must coordinate established cognitive processes to make repeated covert cycles of forward recall through the list of items so the final digit can be reported. The novel aspect of the routine involves peeling off the final digit repeatedly with each successive cycle through the list (Anders & Lillyquist, 1971; Thomas et al., 2003). As predicted by the framework, transfer to untrained backward recall tasks with novel materials was observed; this is because the routine can be applied to a new task that has the same higher-order structure (forward covert cycles, reporting the final item, and then peeling back repeatedly). Furthermore, no transfer was found to *n*-back, another unusual and demanding working memory task. According to Gathercole et al's (2018) theory, *n*-back requires a different routine. The cognitive challenge of this task is to update the positional information of memoranda and at the same time compare each new item with the one *n*-back in the list. A possible routine for this task could involve the repeated updating of item-order bindings as each new item is presented (Oberauer, 2005). The routine for BDR cannot be readily adapted to fit the higher-order structure of *n*-back, and so the framework does not predict transfer from BDR training to *n*-back, in accordance with results of Study 2.

The work presented in Chapter 4 provides insight into the relationship between backward recall and *n*-back tasks. By examining the construct overlap between different working memory tasks, the processes that might be amenable to training can be better understood. The results of Study 3 suggest that the two types of paradigm are tapping into distinct processes. It could be that working memory training is targeting the processes that are specific to each paradigm and not those that contribute to the shared variance between tasks, explaining why cross-paradigm transfer was not observed in Study 2. Furthermore, the best-fitting model in Study 3 included a specific link between the two verbal backward recall tasks (backward digit and letter recall), suggesting there is a distinction between verbal and visuo-spatial backward recall tasks. This may reflect common mechanisms used for reverse serial recall of verbal items that draw on verbal rehearsal mechanisms established in the phonological short-term memory system (Page & Norris, 1998). Serial recall for spatial materials is supported by a distinct system within working memory (Allen et al., 2006; Baddeley et al., 2011; Logie, 1995). Therefore, the transfer observed from BDR to the backward letter task in Study 2, may have been greater than transfer to backward spatial recall because of the application of common strategies for verbal rehearsal. No specific was link was required between the verbal *n*-back tasks in Study 3, suggesting the mechanisms involved in the performance of this task may be more domain-general. Based on this finding, it could be predicted that *n*-back training might result in more domain-general transfer effects compared to backward recall training. The spatial and verbal mechanisms used during *n*-back may be more similar than those used for reverse serial recall of verbal and visuo-spatial information. Therefore it might be predicted that the effect sizes for gains following *n*-back training with digits may be relatively similar for *n*-back with letters and spatial locations. This idea is supported by findings from previous studies showing that *n*-back training transfers across stimulus domain (Bürki et al., 2014; Buschkuehl et al., 2014; Li et al., 2008).

5.2.2 Methodological implications

In both the cognitive training and stimulation research fields, there is a need for standard methodological practices. Firstly, appropriate control groups are required to ensure that participants are matched on motivation and expectancy effects (Morrison & Chein, 2011; Parkin et al., 2015; Shipstead et al., 2012). For studies investigating the effects of working memory training, in order to truly control for participants' motivations, beliefs, and expectations, the active control condition must be as difficult and engaging as the working memory training but not involve activities that draw on working memory resources (Redick et al., 2013; Sternberg, 2008), therefore any generalisation effects can be directly attributed to the working memory training rather than to peripheral experiences in the lab (Shipstead et al., 2012).

In the case of stimulation research, ideally a sham control group completing the same activities as the active group should be used (e.g. Au et al., 2016). In the wider literature, although claiming a positive effect of stimulation, some studies fail to make the critical comparison between active and sham stimulation groups, meaning differences cannot be attributed to stimulation *per se* and might simply reflect the benefits of training (Martin et al., 2013; Richmond et al., 2014). It has been argued that stimulation studies must include an active control site of stimulation (Parkin et al., 2015). There were no anatomical controls included in either of the current stimulation experiments, but this was not an issue given no significant stimulation effects were observed. However, in the case of a positive effect of stimulation, a further confirmatory study with an anatomical control site would be needed in order to claim anatomically specific effects. This is an important consideration that should be taken into account in future stimulation studies.

In terms of experimental design, participant and investigator blinding is recommended where possible. For stimulation, double-blinding is simple as the tES machine can be programed in advance to deliver active or sham stimulation. Therefore, one investigator programs the machine prior to testing while another simply turns it on and off during the experiment, remaining blind to group allocation. For research involving cognitive training this is more difficult. Using appropriate control groups, participants should be naïve to their condition. However, unless separate investigators are used to deliver the training and transfer sessions, they will be aware of group allocation. Researchers must also ensure participants are randomly assigned to groups to reduce bias (Simons et al., 2016), and make sure they are matched at baseline so that pre-existing differences between individuals do not mediate group differences at outcome (Melby-Lervåg & Hulme, 2012).

The two intervention studies presented in this thesis involved tightly controlled rigorous designs. Both were randomised-controlled trials with appropriate control conditions to ensure participants were matched on motivation and expectancy effects. For stimulation this was a sham condition, and for training this was a visual search training regime that was as cognitively demanding as active working memory training but had no memory load. Participants were blind to both stimulation and training conditions. The experimenter was blind to all stimulation groups (expect for the visual search sham stimulation group), but was not naïve to training group allocation.

New interventions that promise cognitive enhancement such as working memory training and brain stimulation are appealing to the scientific community, practitioners, and the general public. They generate high levels of intense research activity and are characterised by high levels of early positive results that are typically not sustained over longer periods, possibly due to publication bias. There is evidence that intervention studies that report positive or significant results are more likely to be published, and of selectively reporting outcome measures based on their direction of results (i.e. outcome reporting bias; Dwan et al., 2010; Dwan, Gamble, Williamson, & Kirkham, 2013). Regardless of outcome (i.e. the direction of results), the persuasiveness of results should be based on the strength of evidence combined with experimental rigour. Going forward, pre-registration appears to be a promising practice that may overcome some of the methodological issues in intervention research. Pre-registration is an open science research practice whereby researchers outline their study protocol, which includes the rationale, hypotheses, study design, and (statistical) analysis plan, before starting an experiment (i.e. prior to any data collection). This ensures that researchers develop their study design and analysis plan to directly address the specific research questions of the study in advance. Using this approach, researchers must clearly distinguish between confirmatory (hypothesis testing) and exploratory analyses. The protocols for Study 2 and 3 of this thesis were both registered online via the Open Science Framework before any data collection was started.

A novel approach was used in this thesis to systematically test the boundary conditions to transfer. By carefully manipulating the degree of overlap in features between the training and transfer tasks, the distance to which training on a single working memory task transfers within and across paradigm could be tracked. Previous training studies often rely on post hoc explanations for observed patterns of transfer (e.g. Sprenger et al., 2013; von Bastian & Oberauer, 2013), and many include a variety of training and transfer tasks with varying degrees of overlap, making it difficult to map patterns of transfer and establish what constrains the generalisation of training gains (e.g. Anguera et al., 2012; Redick et al., 2013; Sprenger et al., 2013; Thompson et al., 2013; von Bastian, Langer, Jäncke, & Oberauer, 2013). Going forward, future studies investigating transfer should be hypothesis driven. For example, by including only outcome measures that directly address specific research questions.

In Study 3, data from a large sample size (~700) was collected via online methods. Although there were challenges developing web-based activities and monitoring participants' performance of cognitive tasks remotely, this method had a number of methodological advantages. A large amount of data could be collected in a relatively short amount of time, which provides more statistical power than previous studies investigating individual differences in working memory performance. As well as web-based methods being advantageous for individual differences studies, whereby large samples allow sufficient power to detect subtle inter-individual differences in performance, they also show promise for the cognitive training research field. Currently, near and far transfer effects across working memory training studies are inconsistent. One reason for this is they are typically underpowered due to inadequate sample sizes. Data collection in training studies is time consuming, as it usually involves practice on working memory activities for ~15 hours over multiple sessions (Klingberg, 2010). In future, larger samples could be established via web-based testing methods, producing results with greater statistical power.

5.3 Limitations

The data conclusively showed no evidence that tES enhances the effects of working memory training, despite testing two different stimulation techniques (tRNS and tDCS), and when combined with two different training regimes (i.e. multiple Cogmed tasks and a single BDR task). However, a limitation of the current research was the lack of different stimulation parameters tested. The tES research field is relatively new and further research is needed to understand the impact of different stimulation protocols when applied to different cortical regions and combined with different training regimes. There are numerous different ways the stimulation machine can be configured. Candidate factors for further investigation include type, duration, and intensity of stimulation (Batsikadze et al., 2013; Monte-Silva et al., 2010), as well as the timing of stimulation relative to the task (Pirulli, Fertonani, & Miniussi, 2013), and individual differences in brain anatomy (Opitz, Paulus, Will, Antunes, & Thielscher, 2015).

As discussed in the Literature Review (see Section 1.5.1), the non-linear after-effects of increasing intensity and duration of stimulation on motor evoked potentials (MEPs) suggest that tES is not operating mechanistically in a push and pull way between excitation and inhibition (Parkin et al., 2015). Another potential moderator of tES is the state of the participant during stimulation. Antal, Terney, Poreisz, and Paulus (2007) measured MEPs before and after a number of conditions which combined tDCS and different activities. They showed that the same type of tDCS induced different MEP responses depending on whether participants were sitting passively, engaged in a cognitive task, or performing a simple motor task. Excitability in the motor cortex was lower following anodal tDCS and higher after cathodal stimulation when performing the cognitive task compared to the passive condition. Whereas performing the motor exercise reduced excitability after both anodal and cathodal tDCS compared to the passive condition. These results suggest that the physiological effects of tDCS on the cortex are highly dependent on the state of the participant during stimulation.

Currently, there are no guidelines for tES settings. Typically, the standard duration and intensity parameters used have been determined by the after-effects measured from the motor cortex; however these parameters are only valid if MEPs are taken as a marker. Caution must be taken when making assumptions about the mechanistic effects stimulation is having when applied to different cortical regions, as it may not respond in the same way as the motor cortex to changes in intensity or duration. In this thesis, the configurations used in the two stimulation studies were determined by the parameters used in previous tES studies that have shown positive effects (e.g. Hoy et al., 2013; Snowball et al., 2013). However, due to the many moderators and mediators that could be influencing the effects of stimulation, it is unclear whether 20 minutes of tRNS for 1 mA applied to bilateral DLPFC, or 10 minutes of tDCS for 1 mA applied to the left DLPFC, had the intended excitatory effects on cortical activity under the electrodes.

Another potential limitation of the current research was the lack of a control training group in the first experiment. Although small gains were made on some of the far transfer measures in the first experiment, without the inclusion of a test-retest control group or control training group, it is impossible to determine whether these reflected genuine training benefits or repetition effects. However, these additional control groups were not required to test the key research question in this study; specifically, whether stimulation modulates the effects of working memory training. The critical conditions needed to address the main aim were included (i.e. active stimulation with training versus sham stimulation with training).

A disadvantage of the current work, and a general limitation in the wider research field of both cognitive training and tES, is the time-consuming nature of data collection. The relatively small sample size of Study 1 (N = 30) and Study 2 (N = 48) could mean these experiments were underpowered. In order to apply stimulation, each session must be completed individually with each participant. For example, in Study 1, a single participant took ~18 hours (over 14 sessions) to complete the whole experiment. Following correction for multiple comparisons, the transfer effects observed to backward letter and spatial recall in Study 2 were non-significant. The relatively small sample size may have resulted in limited power to detect significant effects. For this reason, Bayesian analyses were also employed. As the Bayesian tests were exploratory, a confirmatory follow-on experiment is proposed to examine whether the pattern of transfer effects observed in this experiment can be replicated. A larger sample size would provide sufficient power to detect significant effects with confidence. The final experiment demonstrated the advantages of web-based methods for collecting large amounts of data in a relatively short period of time, and this may be a promising avenue for the future of working memory training research.

5.4 Future directions

In the future, it would be beneficial to replicate and extend the current investigations into the transfer effects following working memory training. A follow-on experiment based on the results of this thesis is recommended. This proposed study will investigate within- and cross-paradigm transfer effects following online working memory training. Participants will be allocated to one of three training conditions: including (i) BDR, (ii) *n*-back with digits, or (iii) no-memory load control training. Participants will complete a number of pre- and post-training assessments that will be designed to systematically track the degree to which training gains on backward recall and *n*-back transfer, to test whether paradigm, stimulus domain, and stimulus category are barriers to transfer. The outcome measures will include three backward recall tests (with digits, letters, and spatial locations), and three *n*-back tasks (also with digits, letters, and spatial locations). Web-based methods could be used to maximise the sample size. First, it is predicted that the transfer effects observed in Study 2 following training alone (without tES) will be replicated. Participants who complete the BDR training will show significant gains on all backward recall tasks, and the increase in performance will be significantly greater for backward letter recall relative to backward spatial recall. It is anticipated that the larger sample size will provide sufficient power to detect significant effects with confidence. Transfer effects following *n*-back training are expected to be more domain-general. It is predicted that *n*-back training will result in significant gains to untrained *n*-back tasks with novel materials, but the effect sizes for these gains will be comparable for *n*-back with letters and spatial locations. This prediction is based on the finding in Study 3 that there is less domain-specificity for *n*-back than backward recall tasks. Finally, it is expected that paradigm will be a barrier to transfer for BDR and *n*-back training, and so no cross-paradigm transfer is predicted for any condition.

Another line of further investigation could be to explore individual differences across different categories of working memory task. The final study in this thesis used different versions of backward recall and *n*-back to investigate construct overlap between these two tasks. In future it would be interesting to explore their relationship with other types of working memory tasks such as complex span and running span. Furthermore, in Study 3, a number of different models were examined using confirmatory factor analysis to explore what drives performance on different working memory tasks. The model that assumed the tasks would be split by domain (verbal and visuo-spatial tasks), and the model that split the tasks by materials (digits, letters, and spatial locations), were both a poor fit to the data. However, the tasks used as indicators for the constructs were not optimised for finding a domain or materials split in the data, as some of these constructs had fewer indicators than others. In a future study, the indicators should include an equal number of tasks that involve particular paradigms, domains, and materials.

5.5 Conclusions

At this relatively early point in the brain stimulation research field, the clear conclusion from this thesis is that, when combining training stimulation protocols that have been shown to be effective in other studies, there is no evidence that tES enhances the benefits of working memory training. In addition, when using rigorous intervention design, training transfer does not extend across global changes in working memory paradigm, but does occur within paradigm and is not constrained by stimulus domain or stimulus materials. Working memory training may be targeting processes that are specific to each paradigm and not those that contribute to the shared variance between tasks, explaining why many studies fail to produce cross-paradigm transfer effects.

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Appendix A Study I journal publication

Transcranial Random Noise Stimulation Does Not Enhance the Effects of Working Memory Training

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Abstract

■ Transcranial random noise stimulation (tRNS), a noninvasive brain stimulation technique, enhances the generalization and sustainability of gains following mathematical training. Here it is combined for the first time with working memory training in a double-blind randomized controlled trial. Adults completed 10 sessions of Cogmed Working Memory Training with either active tRNS or sham stimulation applied bilaterally to dorsolateral pFC. Training was associated with gains on both the training tasks and on untrained tests of working memory that shared overlapping processes with the training tasks, but not with improvements on working memory tasks with distinct processing demands or tests of other cognitive abilities (e.g., IQ, maths). There was no evidence that tRNS increased the magnitude or transfer of these gains. Thus, combining tRNS with Cogmed Working Memory Training provides no additional therapeutic value. ■

INTRODUCTION

Intensive training of working memory, the ability to retain information for short periods of time for ongoing mental activities, generates robust gains on untrained tests of working memory (von Bastian & Oberauer, 2013; Dahlin, Neely, Larsson, Bäckman, & Nyberg, 2008). In other cognitive domains, the efficacy and generalization of training benefits has been enhanced by transcranial electrical stimulation (Cappelletti et al., 2013; Snowball et al., 2013; Ditye, Jacobson, Walsh, & Lavidor, 2012). In this study, we combined the two approaches to investigate whether stimulation could increase the rate and magnitude of training gains and extend the benefits of training beyond highly similar untrained tests of working memory. To provide a rigorous test of the potential added value of stimulation we used a double-blind randomized controlled design, with sham stimulation as the control, and tested performance on multiple outcome measures. To maximize opportunities for modulating behavior, a multisession training program that consistently produces large gains in working memory was used (Schwaighofer, Fischer, & Bühner, 2015) in conjunction with stimulation parameters that have been shown to enhance the effects of maths training (Snowball et al., 2013).

Working memory training involves practice on working memory tasks that continually adapt to an individual's ability. The benefits of training are greatest for untrained tests of working memory that draw on the same underlying cognitive and neural processes as the training activities (Sprenger et al., 2013; von Bastian & Oberauer, 2013; Dahlin et al., 2008). This has been termed process-specific transfer, and it is associated with changes in the neural structures and networks linked with working memory (Astle, Barnes, Baker, Colclough, & Woolrich, 2015; Kundu, Sutterer, Emrich, & Postle, 2013; Takeuchi et al., 2010; Dahlin et al., 2008; Olesen, Westerberg, & Klingberg, 2004). Evidence for the transfer of training gains to tests of working memory with distinct processing demands to the training tasks is less clear. Some studies report positive transfer across different categories of working memory tasks. For example, training on complex span tasks, which involve rapidly switching between the storage of memory items and an interpolated unrelated processing activity, generates gains on running span tasks that require the continuous monitoring and updating of a sequence of items (Harrison et al., 2013). However, other studies report selective benefits only for transfer tests of working memory that are the same as the training activities, with no transfer across working memory paradigms (e.g., Redick et al., 2013; Thompson et al., 2013; von Bastian & Oberauer, 2013). When the most rigorous randomized controlled study designs are used, there is little to no evidence for the generalization of training-related effects to complex everyday activities that depend on working memory, such as academic attainment and focussed attention (e.g., Cortese et al., 2015; Dunning, Holmes, & Gathercole, 2013; Rapport, Orban, Kofler, & Friedman, 2013).

Transcranial electrical stimulation is a noninvasive neuromodulatory tool in which a weak electric current is delivered to the brain through a pair of electrodes attached to the scalp. Transcranial electrical stimulation is associated with changes in cortical excitability (Nitsche &

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Paulus, 2000) and has been proposed to enhance learning by inducing long-term potentiation (Stagg & Nitsche, 2011). The potential of noninvasive brain stimulation to modulate and enhance human cognition means that, when combined with a learning task, it has the potential not only to increase the efficacy of cognitive training but also to enhance the generalization of training gains.

Previous studies combining stimulation with working memory training have used transcranial direct current stimulation (tDCS; Richmond, Wolk, Chein, & Olson, 2014; Martin et al., 2013), a polarity-dependent technique that generates opposing excitatory and inhibitory activity under the two electrodes: Anodal stimulation pulls neurons toward depolarization and is associated with an increase in cortical excitability, whereas cathodal hyperpolarizes neurons and is associated with decreased excitability, or inhibition (Nitsche & Paulus, 2000). In one study, tDCS shifted the learning curve of the training tasks upward relative to sham stimulation, but it did not enhance the rate of learning on these activities (Richmond et al., 2014). In the other, stimulation did not increase on-task training gains (Martin et al., 2013). Active stimulation combined with working memory training was associated with greater gains on untrained tests than either no intervention (no stimulation and no training; Richmond et al., 2014) or stimulation alone (no training; Martin et al., 2013). Both studies concluded that active tDCS enhanced the transfer of training outcomes. There is a problem with this conclusion, as critically there were no significant differences between groups who received training with active stimulation and groups who received training with sham (placebo) stimulation on the transfer tests. As such, these gains can be attributed to training alone. In both studies, tDCS anodal stimulation was applied to left dorsolateral pFC (DLPFC), meaning right DLPFC was either not stimulated (Martin et al., 2013) or was under cathodal stimulation (Richmond et al., 2014). Working memory task performance is associated with bilateral activation of DLPFC (Rottschy et al., 2012). Failure to stimulate DLPFC bilaterally may therefore explain why crucial differences between the active and sham stimulation groups were not significant.

In other cognitive domains, transcranial random noise stimulation (tRNS), an alternative method of brain stimulation, has shown more promise. Snowball et al. (2013) found tRNS applied bilaterally to the DLPFC to be effective in enhancing the efficacy and generalizability of gains following arithmetic training. Changes in neural activity and improvements on untrained mathematical problems persisted 6 months after training for the tRNS group relative to the sham group (Snowball et al., 2013). Similarly, Cappelletti et al. (2013) reported significantly steeper learning curves and long-lasting improvements in magnitude judgments following numerosity training combined with tRNS applied bilaterally to parietal regions compared with sham stimulation, training combined with tRNS over motor cortex, or tRNS alone.

In the current study, we investigated, for the first time, whether tRNS could modulate on-task training gains and enhance transfer to both untrained working memory tasks and other cognitive abilities related to working memory when combined with working memory training. tRNS offers potential advantages over tDCS, the stimulation technique combined with working memory training in previous studies (Richmond et al., 2014; Martin et al., 2013). Most importantly, it is polarity-independent allowing for bilateral stimulation of DLPFC, a region of the brain associated with working memory function (Owen, McMillan, Laird, & Bullmore, 2005) and influenced by working memory training (Takeuchi et al., 2010). It also has a higher cutaneous perception threshold, making it particularly suitable for blinding groups to stimulation condition (Ambrus, Paulus, & Antal, 2010).

Following Snowball et al. (2013), high-frequency (101–640 Hz) tRNS at a current strength of 1 mA was applied bilaterally over DLPFC. Cogmed Working Memory Training (Cogmed, 2005), a program that has been extensively researched and yields larger effect sizes for process-specific changes than other training packages (Schwaighofer et al., 2015; Sprenger et al., 2013), was used. Unlike many studies that have investigated the impact of training on working memory in a single session (e.g., Fregni et al., 2005), this package provided multisession training, allowing us to investigate the effects of stimulation on learning. A double-blind randomized controlled trial design was employed. Multiple outcome measures varied the degrees of overlap with the trained activities, allowing us to map out the extent to which gains generalized beyond the trained tasks. The primary outcome measures were working memory tests with processing components that overlapped with the training tasks. Any enhancement to training via stimulation should be evident in these measures as well as the trained tasks. To determine whether any benefits of combining training with stimulation extend beyond specific trained processes, participants also completed untrained working memory tasks with different processing demands to those in the training tasks. Secondary measures of cognitive processes linked with working memory, including tests of inhibition (Kane & Engle, 2003) and measures of selective attention (de Fockert, Rees, Frith, & Lavie, 2001), were included alongside tests of information processing and standardized tests of general cognitive abilities (e.g., language and nonverbal reasoning) to test whether stimulation enhanced transfer beyond working memory paradigms. An emotional recognition task with no memory component was included as a nonmemory control task. Previous studies claiming that cognitive training or brain stimulation are effective have relied on null hypothesis significance testing (NHST) to imply that the alternative hypothesis is true; they have rarely quantified the degree to which the evidence supports the null or alternative hypotheses (Sprenger et al., 2013). For this reason, Bayesian methods were employed to evaluate the strength of the evidence for and against the null hypothesis in addition to traditional NHST.

METHODS

Participants

Thirty native English-speaking adults aged between 18 and 35 years (11 men) provided written informed consent to participate in this study, which was approved by the University of Cambridge's psychology research ethics committee. All participants were recruited through the MRC Cognition and Brain Sciences Unit's research participation system. All participants were stimulation compatible (i.e., no metal implants or pacemakers, no previous history of epilepsy, head injury or neurological disorders, not currently taking medication affecting the CNS), had normal or corrected-to-normal hearing and vision, and were right-handed.

Materials

Process-specific Memory Tasks

Eight tests with processing components that overlapped with the training tasks were administered. These included four standardized tests from the Automated Working Memory Assessment (Alloway, 2007): a test of verbal STM (digit recall), visuospatial (VS) STM (dot matrix), verbal working memory (WM) (backward digit recall) and VS WM (Mr X). Standard scores (M = 100, SD = 15) were calculated for each task. Participants also completed four computerized experimental tests of verbal and VS storage (STM) and of verbal and VS storage with intrinsic processing (working memory). The storage tasks required participants to recall either a list of digits (verbal) or spatial locations (VS) in serial order. The working memory tasks were identical to the storage tasks, except participants were required to recall the digits (verbal) or spatial locations (VS) in reverse order. Trials were presented in blocks of four trials. Sequences in the first block started at a span of two items and increased in length by one item in each subsequent block if participants scored three or more trials correct. The tasks discontinued if two or more errors were made in any block. The maximum span length reached at this point was scored.

Memory Tasks with Distinct Processes

Participants completed four working memory tasks involving distinct processes to the training activities, two n-back tasks and two complex span tasks. For both n-back tasks, participants were presented with a sequence of stimuli one at a time (auditory digits for verbal n-back and abstract line drawings for VS n-back) and had to indicate by a key press when the current stimulus matched one presented n items back in the sequence. Sequences were presented in blocks containing $20 + n$ items. There were six target items (matches) in each block. The first block started at 1-back and increased in difficulty by 1 in each subsequent block if less than five errors were made (e.g., increased from 1-back to 2-back). The tasks discontinued when five or more errors were made within a block. False alarms (responding to a nontarget) and misses (failing to respond when a match was present) were counted as errors (missing a target). The maximum n-back level reached to this point was scored. For both complex span tasks, participants were presented with a series of storage items (digits for the verbal task and spatial locations for the VS task) interpolated with a same-domain processing task, which was presented for 6 sec in-between the presentation of each storage item. The processing tasks required participants to judge whether two letters rhymed (verbal task) or to decide whether patterns of lines presented inside a pair of hexagons matched (VS task). Participants were required to recall the storage items in serial order at the end of the trial. Trials were presented in blocks of 3. The first block started at a span of 1 (one storage item and one processing episode) and increased by a span of 1 (additional storage item and an additional processing episode) if two or more trials were correct in any block. Trials were scored as correct if all storage items were recalled in the correct serial order and >66% of the processing items were correct. The tasks discontinued if two of the three trials in a block were incorrect. A trial was incorrect if the storage items were recalled incorrectly, accuracy for the processing tasks was <66%, or if there were no responses for the processing tasks. The maximum span reached was scored.

Cognitive Processes Associated with Working Memory

Participants completed a set of tasks that included parallel verbal and VS tests of executive function. Two flanker tasks were administered to provide measures of verbal and VS selective attention. Both tasks consisted of 240 trials: 80 baseline, 80 congruent, and 80 incongruent. Trials were presented in a random order. In the baseline condition, participants were required to click on a button on a computer screen showing a letter (verbal) or arrow (VS) matching the one presented in a box on screen. In the congruent condition, participants were presented with a row of five identical letters (verbal) or a row of five arrows pointing in the same direction (VS). They were required to click on the letter or arrow corresponding to the middle letter/arrow shown below. In the incongruent condition, the central arrow or letter was flanked by incongruent stimuli (e.g., AABAA). Again, participants were asked to respond to the middle stimulus by selecting the appropriate response button shown on screen. RTs for correct trials were recorded for all conditions. The average RT difference between correct congruent and incongruent trials was used to index the Flanker effect.

Indices of inhibitory control were provided by two Stroop tasks. Both tasks consisted of 48 baseline, 48 congruent, and 48 incongruent trials. These were presented in blocks by condition. On baseline trials in the verbal Stroop task, neutral words (e.g., "when") were presented on screen printed in yellow, blue, green, or red. Participants were required to click on a color block matching the color the word was printed in. On congruent trials, participants were presented with color words printed in the same color as the word (e.g., "yellow" appeared on screen, printed in yellow ink) and were again asked to click on the color the word was printed in. On incongruent trials, color words were presented in different colors to the word itself (e.g., "yellow" was printed in red ink). Participants were required to inhibit the overlearned verbal response of reading the color word and instead click on the ink color. On neutral trials in the VS Stroop task, an arrow appeared in the center of a box, pointing either up, down, left, or right. Participants were required to click on the arrow pointing in the same direction from a choice of four presented in a box below. On congruent trials, an arrow appeared touching the edge of the box at a position congruent with the direction it was pointing (e.g., an arrow pointing right appeared on screen with the arrowhead touching the right hand side of the box). Participants were asked to select the arrow pointing the same way as the one in the box from a choice of four below. On incongruent trials, participants were presented with an arrow in a position in a box that was incongruent to the direction it was pointing (e.g., an arrow pointing right could appear at the left, top, or bottom of the box). Participants were required to inhibit the prepotent response associated with the position of the arrow and instead respond to the direction of the arrowhead by selecting one of four arrows below. For both tasks, RTs for correct trials were recorded for each condition. The Stroop effect was calculated as the difference between the mean RT for correct trials in the incongruent condition and the mean RT for correct trials in the congruent condition.

Information Processing and General Cognitive Abilities

Participants completed two information processing tasks. The verbal processing task required participants to judge whether pairs of letters rhymed. Fifty auditory letter pairs were presented, consisting of monosyllabic English alphabet letter names. Pairs were constrained to avoid successive letters in the alphabet (e.g., J, K), highly confusable fricative letter names (e.g., F, S), and familiar acronyms (e.g., PC, IT, US). A parallel VS processing task required participants to judge whether the line patterns shown on two hexagons presented simultaneously were the same or different. Fifty pairs of hexagons were shown. RTs for correct trials were scored for both tasks.

Two subtests of the Wechsler Abbreviated Scaled of Intelligence (Wechsler, 1999), tests of verbal (Vocabulary) and of nonverbal (Matrix Reasoning) IQ, were also administered. t Scores were derived for each subtest and used to calculate a composite standard score for IQ. The Numerical Operations task of the Wechsler Individual Achievement Test Second Edition (Wechsler, 2005) was used to measure math ability. The Peabody Picture Vocabulary Test Fourth Edition, a measure of receptive vocabulary (Dunn & Dunn, 2007), was also given.

Cognitive Task with No Memory Load

The Facial Expressions of Emotion test (Young, Perrett, Calder, Sprengelmeyer, & Ekman, 2002) is a measure of emotion expression recognition. Participants were presented with 30 morphed faces on an emotional continuum ranging between happiness–surprise, surprise–fear, fear–sadness, sadness–disgust, disgust–anger, and anger–happiness over five blocks. Participants were required to judge which of six emotion labels (happy, sad, anger, fear, disgust, and surprise) best described each facial expression. Only trials with morphed images of 70% or 90% bias toward a particular expression were used to assess performance. Proportion correct across all blocks was scored.

Training

Participants completed 10 sessions of Cogmed Working Memory Training (Cogmed, 2005). Each session lasted approximately 45 min and involved repeated practice on eight training exercises (15 trials on each task totaling 120 trials). Participants completed the same eight tasks in each training session, in one of two counterbalanced task orders. Task order was counterbalanced to ensure all tasks were completed under active stimulation for those in the stimulation group. A mixed ANOVA with order (A or B) and task (gain for each of the eight training tasks) revealed that there were no order effects for either the active stimulation, $F(7, 91) = 1.462, p = .191, \eta_p^2 = .101$, or sham stimulation, $F(7, 91) = .943, p = .478, \eta_p^2 = .068$, groups. Three training tasks required the immediate serial recall of verbal or VS items (Visual Data, Data Room, and Decoder). Five further tasks required mental manipulation (e.g., mental rotation or reversing the sequence) prior to recall (Input Module, Input Module with Lid, Number Grid, Rotating Data Link, and Rotating Dots). Full details about the training program are provided at www.cogmed.com/rm. All training exercises started at a span of two in the first session. An adaptive algorithm was used to calibrate the difficulty of each task to current performance on a trial-by-trial basis. Task difficulty increased by a span of one following three consecutive correct responses and decreased by a span of one following two consecutive incorrect answers. The average span was recorded for each task in each session. Data from Session 1 was not included in the analyses as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants).

Stimulation

tRNS was applied bilaterally over the DLPFC. Standard 5 × 5 cm rubber electrodes, covered with saline-soaked sponges, were placed on the scalp on areas corresponding to regions F3 and F4 identified using the standard international 10–20 EEG electrode placement procedure. They were fixed by a rubber headband. Stimulation was delivered via a battery-driven electrical stimulator (DC-STIMULATOR-PLUS; NeuroConn). Following Snowball et al. (2013), high-frequency tRNS (101–640 Hz) at a current strength of 1 mA with no DC offset (i.e., varying between −0.5 and +0.5 mA) at a sampling rate of 1280 sample/sec was used. Participants in the active stimulation group received 20 min of tRNS with 15 sec of increasing and decreasing ramps at the beginning and end of stimulation. To maximize opportunities for modulating behavior, stimulation began at the onset of training (Pirulli, Fertonani, & Miniussi, 2013). Stimulation faded in for 15 sec and out over 15 sec at the beginning of each session for the sham group to blind participants to their stimulation condition (Priori, Hallett, & Rothwell, 2009). The stimulation machine display was identical for both groups ensuring both the experimenter and participants were blind to the type of stimulation being applied. Participants were asked to rate the extent to which they experienced any physical sensations from the stimulation on a scale of 1–10 (1 being *not at all*). The ratings were similar (stimulation $M = 1.000$, $SD = 1.363$, sham $M = .9333$, $SD = 1.580$) and did not differ significantly between groups, $t(28) = 1.24$, $p = .902$, Cohen's $d = .046$, indicating that group blinding was effective.

Procedure

This was a double-blind randomized controlled study. Participants completed two pretraining sessions, each lasting approximately 2 hr. They were assigned to either an active (9 women) or sham (10 women) stimulation condition ($n = 15$ per group) after preassessment. Stratified randomization was used to ensure the groups were matched at baseline in terms of age, sex, IQ, and standardized short-term and working memory scores (Table 1). The demand characteristics of the study were identical between the active and sham groups; both completed the same training, were unaware whether they were receiving active or sham stimulation, and were paid for their time. A no-contact control group was not included as they would have been poorly matched in terms of motivation and other demand characteristics (e.g., Shipstead, Redick, & Engle, 2012). Participants then completed 10 sessions of adaptive working memory training with either active or sham stimulation across ~19 days. Training sessions were run individually with each participant. The time taken to complete training did not differ between groups (Table 1). All pretraining tasks were readministered at the end of training.

RESULTS

Training Data

General linear regression models were conducted for each training task to investigate whether there were any group differences in overall gains. For all models, Session 10 scores were entered as the dependent variable, with group (active stimulation or sham) entered as the independent variable. Group did not significantly predict training gains on any task, nor did it predict average gains across the training tasks (Table 2).

Previous studies claiming that cognitive training or brain stimulation are effective have relied on NHST to imply the alternative hypothesis is true; they have rarely quantified the degree to which the evidence supports the null or alternative hypotheses (Sprenger et al., 2013). For this reason, Bayesian methods were employed to quantify the strength of the evidence for the null hypothesis (stimulation does not enhance on-task gains) versus the alternative (stimulation boosts training gains). Bayesian regression analyses conducted in JASP (Love et al., 2015) with default prior scales were conducted for each training task, with group (active stimulation or

Table 1. Group Characteristics

	Stimulation		*Sham*		*Group Comparison*		
	M	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*
Age (years)	25.270	5.509	24.730	4.008	0.303	.764	0.113
IQ	120.667	8.524	119.333	10.834	0.375	.711	0.138
Verbal STM	101.067	15.696	100.600	16.322	0.080	.937	0.029
VS STM	103.733	23.313	106.667	22.064	−0.354	.726	−0.129
Verbal WM	101.000	20.078	101.733	19.282	−0.102	.919	−0.037
VS WM	103.133	22.427	107.867	15.287	−0.675	.505	−0.251
Time to complete training (days)	19.330	4.515	18.333	3.867	0.652	.520	0.238

Table 2. Changes in Training Task Performance by Group

	Gains from Sessions 2 to 10								*Group by Session*				*Rate of Change*											
	Stimulation		*Sham*		*Group Comparison*			*Bayesian Regression*				*Bayesian ANOVA*	*Stimulation*			*Sham*			*Group Comparison*			*Bayesian t Test*
	M	*SD*	*M*	*SD*	*Beta*	*t*	*p*	BF_{10}	*F*	*p*	*Partial Eta*	BF_{10}	*N*	*M*	*SD*	*N*	*M*	*SD*	*t*	*p*	*Cohen's d*	BF_{10}
Average across all tasks	1.426	0.513	1.346	0.689	−0.068	−0.361	.721	0.36	0.478	.871	0.017	44.202	11	0.194	0.087	8	0.138	0.07	1.48	.157	−0.713	0.345
Visual data link	1.165	0.631	1.167	0.673	0.029	0.156	.877	0.348	0.232	.985	0.008	74.285	10	0.059	0.286	8	0.171	0.149	−1.002	.331	0.515	0.38
Data room	1.028	0.739	0.672	0.647	−0.107	−0.567	.575	0.389	1.136	.34	0.039	8.913	10	0.067	0.134	8	0.157	0.187	−1.2	.248	0.561	0.347
Decoder	0.867	0.761	0.818	0.447	−0.069	−0.368	.716	0.363	0.236	.984	0.008	60.758	12	0.161	0.188	11	0.173	0.128	1.208	.87	0.076	1.352
Input module	2.737	2.078	2.719	2.112	−0.085	−0.451	.655	0.372	0.952	.474	0.033	13.161	12	0.465	0.302	6	0.257	0.081	1.629	.123	−1.086	1.332
Input module with lid	2.611	1.345	2.051	1.511	−0.133	−0.712	.482	0.417	1.123	.349	0.039	8.811	9	0.367	0.217	8	0.153	0.194	2.123	.051	−1.041	0.715
Number grid	1.025	0.804	1.071	0.837	0.059	0.311	.758	0.357	0.43	.902	0.015	40.550	12	0.051	0.456	11	0.21	0.226	−1.041	.31	0.466	0.379
Rotating data link	0.959	0.636	0.955	0.748	−0.062	−0.331	.743	0.359	0.216	.988	0.008	67.100	7	−0.047	0.523	9	0.145	0.139	0.088	.306	0.58	2.135
Rotating dots	1.000	0.686	1.269	0.497	0.008	0.042	.967	0.345	0.74	.656	0.026	22.717	12	0.261	0.488	10	0.277	0.075	−0.101	.92	0.057	0.634

Data from Session 1 were not analyzed as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants).

sham) entered as an independent variable. Inverse BF (BF_{10}) were used to express the odds in favor of the alternative hypothesis (group has an effect) compared with the null (no effect of tRNS). As a point of reference: BF_{10} of 1–3 indicates weak/anecdotal evidence for the alternative hypothesis; BF_{10} of 3–10 corresponds to positive/substantial support for the alternative hypothesis and $BF_{10} > 10$ indicates positive/strong evidence for the alternative hypothesis (Kass & Raftery, 1995). Bayesian regression analyses, conducted for all training tasks with group entered as the independent variable, yielded no evidence that stimulation influenced gains on the training activities, $BF_{10} < .5$ for all tasks (Table 2).

Mixed effects ANOVAs with Session (2–10) as a within-subject factor and Group (stimulation or sham) as a between-subject factor were conducted to investigate whether there were any group differences in training performance across sessions. These analyses revealed a significant main effect of Session for memory span in both groups on each of the training tasks (all ps $< .01$) and also on span scores averaged across tasks (Figure 1). Neither the main effects of Group or the Group × Session interactions were significant (see Figure 1 for scores averaged across tasks and Table 2 for the Group × Session interaction terms for each task). Bayesian ANOVAs revealed that a simple main effects model in which Group and Session were entered separately was preferred to a model that included a Group × Time interaction for all tasks and for scores averaged across tasks (BF_{10} ranging from 8.913 to 74.285 in favor of the main effects model; Table 2). There was therefore strong evidence for similar training performance across sessions for both groups.

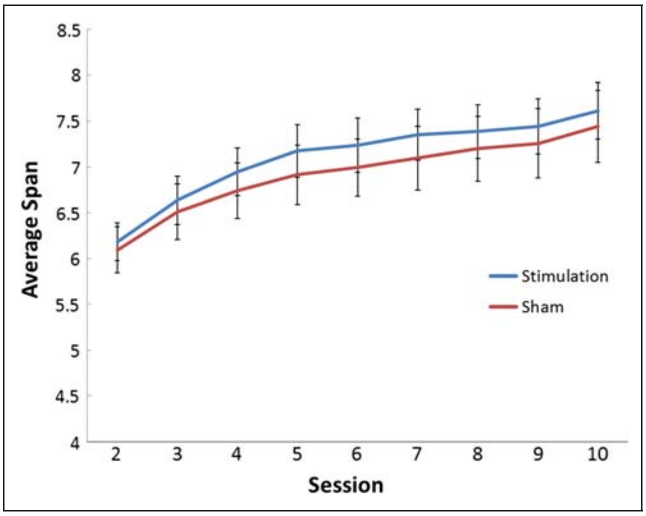

Figure 1. Training data by group, averaged across all eight training tasks. A main effect of Session, $F(8, 224) = 105.114$, $p < .001$, $\eta_p^2 = .790$, revealed significant training gains. The absence of a main effect of Group, $F(1, 28) = .201$, $p = .658$, $\eta_p^2 = .007$, or Group × Session interaction, $F(8, 224) = .478$, $p = .871$, $\eta_p^2 = .017$, indicates that gains were not modulated by stimulation. Data from Session 1 are not displayed as there was no training in this session (the maximum span participants could reach was below the baseline ability of all participants).

Rate of learning on the training activities was estimated by computing a polynomial function that identified the point at which each participant reached asymptotic performance on each task. If stimulation enhances learning, the stimulation group should reach this point faster than the sham group. The functions of the polynomials provided the rate of change to asymptote for each participant on each task. These were computed for each individual training task and for average performance across tasks by approximating each participant's performance with a function that allowed for two turning points; the second corresponded to the point at which they reached asymptote. The functions of the polynomials were then used to calculate how quickly each participant reached their asymptote for each task. This ROC index was calculated as maximum score at asymptote/number of sessions to reach asymptote. Group differences in rate of change values were then compared in a series of independent samples t tests (see Table 2). Data were excluded for curves in which the asymptote was outside the observable training window (i.e., if asymptote <2 or >10). There were no significant group differences in rate of change for any task or for rate of change in scores averaged across tasks. Bayesian independent samples t tests revealed no evidence for group differences in rates of change (all $BF_{10} < 3$), indicating that stimulation did not increase the speed of learning on the training activities (Table 2).

Transfer Tasks

The influences of training and stimulation on transfer were first assessed on the sample as a whole (Table 3). Significant main effects of Training were observed on all working memory tests sharing processes with the training tasks (all ps $< .001$). Bayesian analyses indicated that there was strong evidence for these effects. After familywise correction for multiple comparisons, there were no significant main effects of Training on memory tasks involving distinct processes to the training activities. The outcomes of Bayesian t tests concurred with this pattern of effects for all measures except VS n-back, where a BF_{10} of 3.322 suggested that there was positive evidence for a training effect. Training gains on verbal and VS information processing tasks and the number operations measure reached significance, with $BF_{10} > 3$ in all cases. There was no evidence for training effects on measures of selective attention, inhibitory control, language, or nonverbal reasoning.

To examine the effect of stimulation on transfer, general linear regression analyses were performed with posttraining scores as dependent variables and pretraining scores and group (active or sham stimulation) as independent variables. Stimulation group was a significant predictor of posttraining scores on a verbal n-back task, a memory test that did not share common processes with the trained activities. Training gains were significantly greater for the

Table 3. Training-related Changes in Transfer Tasks

	Pretraining		*Posttraining*		*Pre to Post*			
	M	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*	*Bayesian t Test BF_{10}*
Process-specific Memory Tasks								
Digit recall	100.833	15.735	108.567	15.85	−4.500	***<.001***	0.490	255.700
Dot matrix	105.2	22.352	120.1	21.865	−6.971	***<.001***	0.674	131219.000
Backward digit recall	101.367	19.345	115.2	15.338	−5.897	***<.001***	0.798	8818.000
Mr X	105.5	19.011	114.733	16.885	−5.541	***<.001***	0.514	3573.000
Verbal storage	7.967	1.351	8.967	1.732	−4.664	***<.001***	0.649	385.700
VS storage	7.267	1.311	8.033	1.752	−3.516	***<.001***	0.500	23.720
Verbal backward	6.567	1.612	8.133	1.548	−4.683	***<.001***	0.991	405.000
VS backward	6.433	1.695	7.367	1.921	−3.006	***.005***	0.517	7.597
Non Process-specific Memory Tasks								
Verbal *n*-back	4.933	1.66	5.4	2.313	−1.304	.203	0.235	0.419
VS *n*-back	3.567	1.547	4.333	1.936	−2.605	**.014**	0.440	3.322
Verbal complex span	6.133	2.3	6.9	2.551	−2.538	**.017**	0.316	2.917
VS complex span	4.667	1.863	4.6	2.061	0.220	.827	−0.034	0.199
Processes Associated with WM								
Verbal Flanker effect	82.774	31.099	79.324	66.107	0.335	.740	−0.071	0.205
VS Flanker effect	75.165	76.888	74.031	66.553	0.064	.949	−0.016	0.195
Verbal Stroop effect	43.349	130.08	76.764	136.27	−1.004	.324	0.251	0.308
VS Stroop effect	124.442	68.5	145.107	114.98	−1.043	.306	0.225	0.319
General Cognitive Abilities								
Verbal processing	2071.47	580.7	1916.78	328.81	2.780	***.009***	−0.340	4.726
VS processing	1221.26	435.74	1017.35	308.9	5.166	***<.001***	−0.548	1374.000
Matrix reasoning	60.667	4.95	62.6	4.223	−2.511	**.018**	0.421	2.766
Vocabulary	61.7	8.125	63.533	8.427	−2.483	**.019**	0.221	2.624
Number operations	112.4	17.047	115.8	15.624	−3.111	***.004***	0.208	9.532
Peabody Picture Vocabulary Test	110.467	14.277	112.567	18.823	−1.467	.153	0.127	0.510
Cognitive Task with No Memory Load								
Emotion hexagon	89.806	8.704	89.698	8.212	0.088	.930	−0.013	0.195

Bold text indicates significant effect at $p < .05$ level; ***bold italics*** denote significant effects after family-wise correction for multiple comparison.

active stimulation group ($p = .046$), but this effect did not withstand correction for multiple comparisons (Table 4). Training-related differences between groups on all other measures were nonsignificant (see Figure 2). Bayesian regression analyses favored the null hypothesis with $BF_{10} < 1$ for all outcome measures, except verbal *n*-back. For this task $BF_{10} = 1.695$, providing equivocal support for the null and alternative hypotheses (Table 4). In summary, these analyses provide no strong evidence that stimulation enhances performance beyond training alone on any outcome measure.

Table 4. Training and Stimulation Effects by Group

	Stimulation Group				*Sham Group*				*Baseline Group Comparisons*			*Group Comparison in Training Gains*			
	Pretraining		*Posttraining*		*Pretraining*		*Posttraining*								*Bayesian Regression*
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*	*Beta*	*t*	*p*	BF_{10}
Process-specific Memory Tasks															
Digit recall	101.067	15.696	110.467	15.264	100.600	16.322	106.667	16.723	0.080	.937	0.029	−0.110	−1.019	.317	0.27
Dot matrix	103.733	23.313	120.867	23.676	106.667	22.064	119.333	20.701	−0.354	.726	−0.129	−0.093	−0.966	.343	0.223
Backward digit recall	101.000	20.078	113.867	15.95	101.733	19.282	116.533	15.137	−0.102	.919	−0.037	0.074	0.584	.564	0.249
Mr X	103.133	22.247	110.667	19.667	107.867	15.287	118.800	12.974	−0.675	.505	−0.251	0.136	1.523	.139	0.381
Verbal storage	8.000	1.690	9.067	1.486	7.933	0.961	8.867	1.995	0.133	.895	0.051	−0.040	−0.310	.759	0.231
VS storage	7.533	1.125	8.200	1.699	7.000	1.464	7.867	1.846	1.119	.273	0.412	0.057	0.426	.673	0.243
Verbal backward	7.000	1.512	8.400	1.549	6.133	1.642	7.867	1.552	1.504	.144	0.550	−0.092	−0.491	.627	0.473
VS backward	6.200	1.699	7.200	1.699	6.667	1.718	7.533	2.167	−0.748	.461	−0.273	0.010	0.059	.953	0.323
Non–process-specific Memory Tasks															
Verbal *n*-back	4.800	1.612	6.000	2.104	5.067	1.751	4.800	2.426	−0.434	.668	−0.159	−0.311	−2.088	**.046**	1.695
VS *n*-back	3.200	0.862	4.200	1.373	3.933	1.981	4.467	2.416	−1.315	.199	−0.516	−0.077	−0.483	.633	0.337
Verbal complex span	6.600	1.595	6.800	2.541	5.667	2.820	7.000	2.646	1.116	.274	0.423	0.208	1.757	.090	0.286
VS complex span	4.733	1.335	4.467	2.386	4.600	2.324	4.733	1.751	0.193	.849	0.073	0.089	0.613	.545	0.322
Processes Associated with WM															
Verbal Flanker effect	79.551	16.718	74.196	30.288	85.998	41.250	84.452	89.882	−0.561	.579	−0.222	0.024	0.144	.886	0.345
VS Flanker effect	51.239	45.467	84.178	65.175	99.091	94.614	63.883	68.603	−1.766	.088	−0.683	−0.205	−1.033	.311	0.514
Verbal Stroop effect	8.534	45.324	81.750	184.192	78.164	174.354	71.778	66.971	−1.497	.146	−0.634	−0.059	−0.296	.770	0.381
VS Stroop effect	131.600	43.697	159.288	135.996	117.285	87.753	130.926	91.984	0.566	.576	0.218	−0.085	−0.479	.636	0.43

Table 4. (*continued*)

	Stimulation Group				*Sham Group*				*Baseline Group Comparisons*			*Group Comparison in Training Gains*			
	Pretraining		*Posttraining*		*Pretraining*		*Posttraining*								*Bayesian Regression*
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*t*	*p*	*Cohen's d*	*Beta*	*t*	*p*	BF_{10}
General Cognitive Ability															
Verbal processing	1951.487	121.174	1822.971	107.384	2191.454	808.066	2010.594	439.959	−1.137	.265	−0.516	0.101	1.374	.181	0.244
VS processing	1142.336	213.788	946.584	179.034	1300.186	578.135	1088.117	393.530	−0.992	.330	−0.399	0.072	0.805	.428	0.174
Matrix reasoning	62.067	4.847	63.000	3.836	59.267	4.803	62.200	4.678	1.589	.123	0.580	0.079	0.489	.629	0.341
Vocabulary	61.067	7.324	62.800	7.757	62.333	9.069	64.267	9.262	−0.421	.677	−0.154	0.019	0.206	.839	0.135
Number Operations	111.867	18.712	116.867	14.764	112.933	15.85	114.733	16.888	−0.168	.867	−0.062	−0.099	−1.534	.137	0.27
Peabody Picture Vocabulary Test	108.267	13.285	110.533	17.125	112.667	15.342	114.600	20.780	−0.84	.41	−0.307	−0.036	−0.483	.633	0.114
Cognitive Task with No Memory Load															
Emotion hexagon	88.833	9.193	90.135	8.732	90.778	8.389	89.262	7.940	−0.605	.550	−0.221	−0.134	−0.976	.338	0.373

Bold text indicates significant effect at $p < .05$ level.

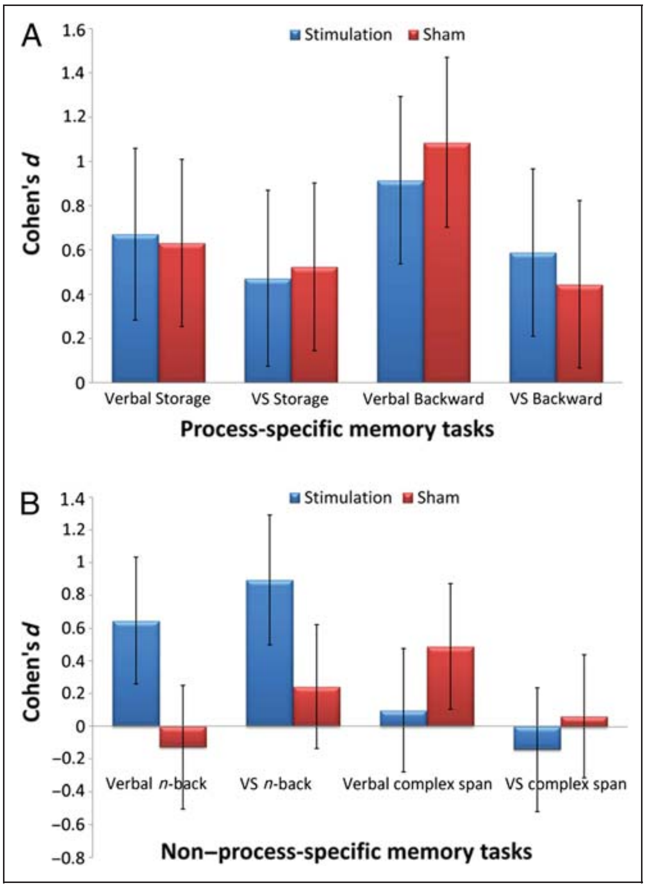

Figure 2. Changes in process-specific (A) and non–process-specific (B) memory tasks by group. Mean effect sizes are displayed. General linear regression models revealed no significant differences in how the groups responded to training (all *p*s > .6; Table 3), demonstrating that stimulation did not enhance transfer to untrained tests of memory.

DISCUSSION

This randomized controlled trial provides the first test of the potential additive benefits of combining tRNS with working memory training. An effective training program (Schwaighofer et al., 2015) was employed in conjunction with stimulation parameters that have been used to enhance training gains in another cognitive domain (Snowball et al., 2013). tRNS did not enhance the rate, magnitude, or degree of transfer of working memory training in an active stimulation group relative to a sham group. Strong training gains were found on trained activities in participants irrespective of stimulation condition, and as in previous research, these effects extended to transfer tests with processing and storage demands in common with the training activities (Melby-Lervåg & Hulme, 2013; von Bastian & Oberauer, 2013; Dahlin et al., 2008).

By contrast, on memory tests with minimal overlap with the training activities there was little evidence for the benefits of training alone. The training tasks involved practice on serial memory paradigms that required either the reproduction of a sequence of verbal or VS items, or mental manipulation of the items prior to recall (e.g., reversing a sequence of digits or rotating a sequence of spatial items 90°). No training-related enhancements were found on transfer tests of working memory that involved switching between the storage of memory items and an unrelated processing activity (complex span). There was a small training gain on a VS *n*-back task involving the continuous updating and recognition of a set of items. Although this did not survive a correction for multiple comparisons, Bayesian analyses suggested that there was positive but not strong evidence for this effect. There was no evidence for transfer to a verbal *n*-back task. On balance, this pattern of effects is consistent with previous reports that training induces the learning of task-specific strategies that do not generalize to other categories of working memory task (Dunning & Holmes, 2014; von Bastian & Oberauer, 2013).

There was also no evidence for more distant transfer of working memory training without stimulation to tests of nonverbal reasoning and language ability. Small gains were observed on a test of mathematical ability (three standard score points) and short increases in speed of responses on tests of verbal and VS information processing were also found, but in the absence of a no-intervention test–retest control group, it is impossible to determine whether these reflect genuine training benefits or repetition effects. This pattern of far transfer effects is largely consistent with the working memory training literature, which provides no consistent evidence that training alone ameliorates the everyday difficulties associated with working memory such as problems in attentional focus and learning (Holmes et al., 2015; Dunning et al., 2013; Shipstead et al., 2012; see Simons et al., in press, for a review).

Crucially, the results of the current experiment demonstrate that tRNS does not extend the limited transfer found with working memory training. In line with previous studies that have combined working memory training with a different stimulation technique, tDCS, there were no differences in performance between the active tRNS and sham stimulation groups on any of the transfer tests (Richmond et al., 2014; Martin et al., 2013). Together the results of these studies provide no evidence to support the use of combining training with stimulation as a therapeutic tool to improve working memory function.

There was also no evidence that stimulation modulated the speed of learning or magnitude of gains on the training tasks. These results provide a challenge to the hypothesis that tRNS provides a global facilitation in brain plasticity when combined with a learning task (e.g., Cohen Kadosh, Levy, O'Shea, Shea, & Savulescu, 2012). They are also inconsistent with findings in another cognitive domain, suggesting that tRNS enhances learning when coupled with mathematics training (Cappelletti et al., 2013; Snowball et al., 2013). This may reflect differences in the impact of tRNS on the different interventions, resulting from the malleability of the neural substrates targeted by the working memory and mathematical training programs, and the complexity of the training programs and their doses. Future research needs to develop a greater understanding of the neurophysiological underpinnings of stimulation and the impact of different stimulation protocols when applied to different scalp regions and combined with different training regimes. Candidate factors for further investigation include the type, duration and intensity of stimulation (Batsikadze, Moliadze, Paulus, Kuo, & Nitsche, 2013; Monte-Silva, Kuo, Liebetanz, Paulus, & Nitsche, 2010), the timing of stimulation relative to the task (Pirulli et al., 2013), individual differences in brain anatomy (Opitz, Paulus, Will, Antunes, & Thielscher, 2015), and the functional state of the brain during stimulation (Antal, Terney, Poreisz, & Paulus, 2007).

New interventions that promise cognitive enhancement such as working memory training and brain stimulation are appealing to the scientific community, practitioners, and the general public alike, generating high levels of interest and intense research activity. Their history also shows that they are marked by high levels of early positive results that are typically not sustained over longer periods, probably because of publication bias (Dwan, Gamble, Williamson, & Kirkham, 2013; Scherer, Langenberg, & von Elm, 2007). At this relatively early point in the brain stimulation research field, the clear conclusion from this study is that, when using the most rigorous intervention design and combining training and stimulation protocols that have been shown to be effective in other domains, there is no evidence that tRNS targeting bilateral DLPFC enhances the benefits of Cogmed Working Memory Training.

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Appendix B Study I ethics approval letter

Karen Douglas
Secretary

Dr J Holmes
MRC Cognition and Brain Sciences Unit
15 Chaucer Road
Cambridge
CB2 2EF

UNIVERSITY OF CAMBRIDGE

CAMBRIDGE PSYCHOLOGY RESEARCH ETHICS COMMITTEE

16 September 2013

Application No: Pre.2013.87

Dear Dr Holmes

Using Transcranial Electrical Stimulation to enhance the effects of cognitive training

The Cambridge Psychology Research Ethics Committee has given ethical approval to your research project: Using Transcranial Electrical Stimulation to enhance the effects of cognitive training, as set out in your application dated 13 August 2013.

The Committee attaches certain standard conditions to all ethical approvals. These are:

(a) that if the staff conducting the research should change, any new staff should read the application submitted to the Committee for ethical approval and this letter (and any subsequent letter concerning this application for ethical approval);

(b) that if the procedures used in the research project should change or the project itself should be changed you should consider whether it is necessary to submit a further application for any modified or additional procedures to be approved;

(c) that if the employment or departmental affiliation of the staff should change you should notify us of that fact.

Members of the Committee also ask that you inform them should you encounter any unexpected ethical issues.

If you would let us know that you that you are able to accept these conditions, I will record that you have been given ethical approval.

Yours sincerely

K S Douglas

K S Douglas

cc: Dr M Ewbank

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Appendix C Study II pre-registration

Open Science Framework Pre-registration

Study Information

Title:

Does transcranial electrical stimulation during working memory training enhance cross-paradigm transfer effects?

Contributors:

Elizabeth Mary Byrne, Michael Ewbank, Joni Holmes

Date registered:

2016-03-04

Research questions:

This study addresses seven questions:

1) Do participants show gains on an adaptive backward digit recall training task that is designed to improve verbal working memory performance?

2) Do participants show gains on an adaptive visual search training program that has no memory load?

3) Do gains following backward digit recall (working memory) training transfer to backward recall tasks with the same stimuli (digits), with novel same-domain materials (letters), and with novel cross-domain stimuli (spatial locations; i.e. within-paradigm transfer)?

4) Do gains following backward digit recall training transfer to a different category of working memory task (i.e. N-back tasks that are different to the training activity) that has the same materials (digits), and that has novel same-domain materials (letters; i.e. cross-paradigm transfer)?

5) Does transcranial direct current stimulation (tDCS) enhance performance on backward digit recall (working memory) training?

6) Does tDCS enhance the transfer of backward digit recall training gains within the same working memory paradigm with the same materials (backward digit recall), with novel same-domain materials (backward letter recall), and with novel cross-domain materials (backward spatial recall)?

7) Does tDCS enhance transfer of backward digit recall training gains across different categories of working memory paradigms with the same materials (N-back with digits), and with novel same-domain novel materials (N-back with letters)?

Hypotheses:

A randomized controlled study will be run to compare three training groups: (1) backward digit recall training (i.e. working memory training) with active transcranial direct current stimulation (tDCS), (2) backward digit recall training with sham stimulation, and (3) visual search training (cognitive training with no memory load) with sham stimulation.

To map the extent to which gains following backward digit recall training transfer within-paradigm, three backward recall measures will be included at outcome; (1) a backward recall task with the same stimuli as the training task (digits), (2) a backward recall task with novel materials in the same domain as the training task (letters), and (3) a backward recall task with different-domain stimuli (spatial locations). To investigate whether gains following backward recall training transfer across working memory paradigms, two N-back tasks will be included; (1) an N-back task with the same stimuli as the training task (digits), and (2) an N-back task with novel materials in the same domain as the training task (letters).

To investigate whether backward digit recall training effects transfer within and across working memory paradigms, group comparisons will be made between the sham backward recall training group and the sham visual search training group. Neither group will receive active stimulation. They will be matched in terms of baseline performance, training duration and expectancy effects (participants will be not made aware as to whether they are receiving active or sham stimulation). The only group difference is the type of training received.

To investigate whether tDCS enhances training gains and/or transfer effects, the two backward recall training groups (active stimulation and sham stimulation) will be compared. Both groups will be matched at baseline and will complete identical training regimes. Participants will be not made aware as to whether they are receiving active or sham stimulation. The only difference between groups is the type of stimulation applied.

Research question 1
Do participants show gains on an adaptive backward digit recall training task that is designed to improve verbal working memory performance?

Hypothesis
Participants will show on-task training gains on an adaptive backward digit recall training task.

Prediction
Several studies have shown that intensive, adaptive training on computerized working memory tasks boosts performance on trained working memory tasks (e.g. Dunning *et al.*, 2013). Therefore, it is predicted that performance will improve over 3 training sessions (one-tailed).

Research question 2
Do participants show gains on an adaptive visual search training program that has no memory load?

Hypothesis
Participants will show on-task training gains on an adaptive visual search training task.

Prediction
Evidence demonstrates that subjects show learning during intensive and adaptive training on a visual search paradigm (Harrison *et al*., 2013; Redick *et al*., 2013), therefore significant improvements are predicted on a visual search training task over three training sessions (one-tailed).

Research question 3
Do gains following backward digit recall (working memory) training transfer to backward recall tasks with the same stimuli (digits), with novel same-domain materials (letters), and with novel cross-domain stimuli (spatial locations; i.e. within-paradigm transfer)?
Hypothesis
Transfer following backward digit recall training will be observed within the same paradigm to the same stimuli (backward digit recall task) and to different stimuli within the same domain (backward letter recall task).

Predictions
Recent evidence demonstrates that working memory training boosts performance on outcome measures of trained and untrained working memory measures, but only under conditions where there is substantial overlap between the processes involved in the training and transfer tasks (Dahlin *et al*., 2008; Sprenger *et al.,* 2013). Performance on visual search tasks is unrelated to working memory ability (Kane *et al.,* 2006), and visual search training does not result in gains on working memory transfer measures (Harrison *et al*., 2013; Redick *et al*., 2013). Therefore, significantly greater gains are predicted on the backward digit recall transfer task following training on backward digit recall with sham stimulation compared to training on visual search with sham stimulation (one-tailed).

Evidence suggests that working memory training leads to gains on the same working memory task with different materials (Harrison *et al.,* 2013); however it is unclear whether this transfer is domain specific. When maintaining (and reversing) verbal information in working memory, individuals typically rehearse via the process of subvocal (internal) repetition (Pisoni & Cleary, 2003). If verbal working memory training is targeting this verbal rehearsal process then transfer to other verbal materials should be observed. Therefore, significantly greater gains are predicted at outcome on backward letter recall following backward digit recall training with sham stimulation versus visual search training with sham stimulation (one-tailed).

On the other hand, there is also evidence to support the idea that individuals have a domain-general serial order mechanism that supports serial rehearsal of verbal and visuo-spatial information (Hurlstone, Hitch & Baddeley, 2014). If verbal working memory training is targeting a domain-specific subvocal rehearsal process then transfer should only be observed for same-domain (letters) and not cross-domain (spatial) materials. However, if backward digit recall training is targeting a domain-general serial order rehearsal process then transfer to materials within- (letters) and across-domain (spatial) may be observed. Therefore, no predictions are made regarding the extent to which backward digit recall training alone (i.e. with sham stimulation) will result in transfer to backward spatial recall (two-tailed).

Research question 4
Do gains following backward digit recall training transfer to a different category of working memory task (i.e. N-back tasks that are different to the training activity) that has the same materials (digits), or novel same-domain materials (letters; i.e. cross-paradigm transfer)?

Hypothesis
Working memory training alone (with sham stimulation) will not yield cross-paradigm benefits, irrespective of the stimuli.

Prediction
Evidence suggests that working memory training gains transfer to untrained working memory measures only when there is substantial overlap between the processes involved in the training and transfer tasks (Dahlin *et al*., 2008; Sprenger *et al*., 2015). Backward digit recall and N-back are both widely used measures of working memory that require items to be held in working memory and updated. There are, however, important differences in the processing demands of the two tasks. N-back tasks require recognition whereas backward serial order tasks require explicit recall. The updating demands of both tasks are also subtly different; during N-back the full sequence must be refreshed as a new item is added to the list and the first item is dropped, however during backward digit recall the whole sequence must be held in mind and then transformed at the point of recall. Evidence suggests that working memory training promotes the use of task-specific strategies which do not transfer across different categories of working memory tasks (Dunning & Holmes, 2014; von Bastian & Oberauer, 2013). Based on previous findings no significant differences are predicted between the backward recall training with sham stimulation group and the visual search training with sham stimulation group on either N-back measure (one-tailed).

Research question 5
Does transcranial direct current stimulation (tDCS) enhance performance on backward digit recall (working memory) training?

Hypothesis
tDCS will enhance on-task training gains.

Prediction
tDCS is a non-invasive neuromodulation technique that delivers a weak electrical current through the scalp to affect processing in the underlying cortex (Brunoni *et al*., 2012). It is thought to work through shifting neurons towards depolarization, increasing neuronal excitability and leading to more spontaneous neuronal firing (Paulus *et al.,* 2013). tDCS may therefore facilitate learning by enhancing plasticity via the mechanism of long-term potentiation (Andrews *et al*., 2011). Previous research has shown that tDCS can significantly enhance performance when applied during verbal working memory training (Richmond *et al.,* 2014). Therefore, significantly greater gains are predicted for backward digit recall training combined with active versus sham stimulation (one-tailed).

Research question 6
Does tDCS enhance the transfer of backward digit recall training gains within the same working memory paradigm with the same materials (backward digit recall), with novel same-domain materials (backward letter recall), and with novel cross-domain materials (backward spatial recall)?

Hypothesis
tDCS will enhance the transfer of working memory training gains within the same working memory paradigm with the same materials.

Predictions
tDCS has been shown to boost performance on trained working memory tasks (Richmond *et al.,* 2014). It is predicted these benefits will transfer to untrained tests that are the same as the training tasks, and therefore that participants who receive backward digit recall training with active stimulation will show significantly greater gains on the backward digit recall transfer task than those who receive sham stimulation (one-tailed). There is no clear evidence that tDCS promotes the transfer of working memory training gains beyond the trained tasks (Martin *et al.*, 2013; Richmond *et al.,* 2014), therefore no predictions are made regarding the extent to which tDCS will impact on transfer to backward recall with letters or spatial locations (two-tailed).

Research question 7
Does tDCS enhance transfer of backward digit recall training gains across different categories of working memory paradigms with the same materials (N-back with digits), and with novel same-domain novel materials (N-back with letters)?

Hypothesis
No directional hypothesis are made regarding the extent to which tDCS will enhance the transfer of working memory training gains across working memory paradigms with the same or different stimuli.
Predictions
Previous studies that have investigated the potential benefits of transcranial electrical stimulation for enhancing cross-paradigm transfer demonstrate mixed findings. In a previous study, active transcranial random noise stimulation (a different stimulation technique) combined with working memory training was associated with significantly greater gains on a working memory transfer task with different processing demands to the trained tasks (i.e. cross-paradigm transfer) compared to sham stimulation. This effect did not withstand correction for multiple comparisons and Bayesian statistics revealed equivocal evidence for both an enhancement by stimulation and no effect of stimulation (Holmes *et al.,* submitted). Other studies have shown no evidence for cross-paradigm transfer, for example, Martin *et al.* (2013) found no difference between active and sham tDCS groups on any transfer tasks following working memory training. As previous studies have produced mixed results no predictions are made regarding to extent to which tDCS will promote transfer to N-back with digits or N-back with letters (two-tailed).

Sampling Plan

Existing data:

Registration prior to creation of data.

Explanation of existing data:

N/A

Data collection procedures:

Participants
48 right-handed, healthy adult volunteers, male and female, who are native English speakers with normal or corrected to normal vision, between the ages of 18- 35 years will be recruited via the Medical Research Council Cognition and Brain Sciences Unit (MRC CBSU) volunteer panel.

Eligibility requirements
Standard exclusion criteria for transcranial electrical stimulation studies will apply. Participants must have no prior or existing history of neurological disease, psychiatric disorder, epilepsy or other seizures, no family history of epilepsy or other seizures, no metallic object in body, no cardiac pacemaker and no history of head, throat or brain surgery. They will not be eligible to take part if they are taking any drugs that affect the central nervous system (including medication and illicit drugs, excluding alcohol) such as antiepileptic drugs, antidepressants, benzodiazepines and L-dopa.

Recruitment
The study will be advertised on an online recruitment database that is visible to people who have volunteered to take part in psychological research at the MRC CBSU. Information about the purpose of the study, the brain stimulation technique used and the eligibility criteria will be stated in the advert. Potential participants will be contacted by telephone or email, given a volunteer information sheet providing full details about the research, and if they are deemed suitable (i.e. they meet the eligibility criteria) they will be invited to participate. Participants will be paid standard MRC CBU rates for testing: £10 per hour for tDCS sessions, and £6 per hour for behavioural testing. A contribution will also be paid towards travel expenses.

Study procedure
Each participant will be required to attend five sessions over a period of seven days. Each session will last approximately 1 hour 15 mins. In session one, participants will complete a set of pre-training baseline measures, including: (1) backward digit recall, (2) backward letter recall, (3) backward spatial recall, (4) N-back with digits, and (5) N-back with letters (see details below). Participants will then be assigned to one of three groups (backward digit recall training with active stimulation, backward digit recall training with sham stimulation, or visual search training with sham stimulation) by a researcher who has not been involved in pre-training and who is not administering either the training or post-training assessments. Stratified randomization will be used to ensure groups are matched for baseline performance on the five tasks, age and gender. In sessions two, three and four participants will complete approximately 1 hour (including a short break) of adaptive training (see details below) with 10 minutes of either active or sham transcranial direct current stimulation (tDCS). In session five participants will complete a set of post-training assessments, which will include all five tasks administered before training.

Training and transfer tasks
All tasks and outcome measures will be completed on a computer.

Backward digit recall training task
Participants will complete an adaptive, computerized backward digit recall task which will increase or decrease in difficulty depending on performance. Trials will be presented in blocks, each consisting of four trials. During each trial, digits (1 to 9) will be presented visually on screen one at a time. Participants will then be prompted to recall the sequence in backward order via a touchscreen keypad of digits. During the first training session the difficulty level will be titrated to individual baseline performance (as measured at pre-test) minus one. During the second and third training session the task will start at the last level worked at during the previous training session minus one. The rules for progression up and down the levels within

each training tasks are: increase by one storage item if three consecutive correct responses are made, decrease by one item if two consecutive incorrect responses are made, otherwise the sequence length remains the same. Participants will complete 100 trials per training session, yielding 300 trials in total over the three training sessions.

Visual search training task
On each trial participants will be presented with a left or right facing target F within an array of distractors made up of left and right facing *E*s, and left and right tilted *T*s, on screen. Participants will then be presented with a mask screen during which they must indicate whether the target *F* was facing left or right via button presses. The difficulty of the task will be manipulated by increasing the size of the array. Each increase in difficulty will alternate between adding another column and then another row to the array. For example; level one is a 2x2 array, level 2 is a 2x3 array, level 3 is a 3x3 array, and so on. The rules for progression up and down the levels within the visual search training tasks will be: increase difficulty level by one if accuracy of previous block is equal to or greater than 87.5%, decrease difficulty level by one if accuracy of previous block is equal to or less than 75%, otherwise the difficulty level will remain the same. Each visual search training session will begin at difficulty level one. Participants will complete 30 blocks per training session. Each block will contain 24 trials, yielding 2160 trials over the three training sessions.

Backward recall outcome measures
Participants will complete three backward recall transfer tasks, each with a different set of stimuli; (1) digits (1 to 9), (2) letters (A B C D F G H J K), or (3) spatial locations (nine boxes at random but fixed locations on the computer screen). Trials will be presented in blocks, each consisting of four trials. During each trial items will be presented visually on screen one at a time. Participants will then be prompted to recall the sequence in backward order via a touchscreen keypad of digits, letters or spatial locations. Participants will begin the tasks at a span of three items which will increase by one item in each subsequent block if they score three or more correct trials. The task will be discontinued if participants were scored incorrectly on two or more trials.

N-back transfer task
Participants will be presented with a random sequence of single digits (1 to 9) one at a time on screen and will have to indicate whether the current item on screen matches one presented n items back in the sequence via a button press. During each block participants will be presented with a continuous sequence of 20 +N items during which there will be a total of 6 possible targets (matches). An error will be scored if participants press the button for a non-target (false alarm), or if participants fail to press the button when a match is present (miss). Total errors will be made up of false alarms and misses combined. The first block will begin at 1-back and the difficulty level will increase by one in each subsequent block if less than five total errors are made (e.g. increase from 1-back to 2-back). If five or more total errors were made within a block the task would end.

Study timeline
Data collection will be completed by the end of February 2017.

Sample size:

48 participants will be recruited for this study (n=16 per training condition). If a participant does not complete all five sessions of the study, all of their data will be excluded and a new participant will be recruited.
Sample size rationale:

Based on the time available to complete data collection, 16 participants per condition (total n=48) is the maximum achievable sample size. This is representative of the typical sample size used of the majority of experimental studies investigating the effects of working memory training and transcranial electrical brain stimulation.

Stopping rule:

Data collection will terminate once the total sample size of 48 is reached.

Variables

Manipulated variables:

Two variables will be manipulated in this study and combined to create 3 conditions.

Training variable (2 levels)
(1) Backward digit recall training
(2) Visual search training

tDCS variable (2 levels)
(1) Active stimulation
(2) Sham (placebo) stimulation

Study conditions
(1) Backward digit recall training with active stimulation
(2) Backward digit recall training with sham stimulation
(3) Visual search training with sham stimulation

Measured variables:

On-task training variables
(1) Backward digit recall with active stimulation, session one average span
(2) Backward digit recall with active stimulation, session three average span
(3) Backward digit recall with sham stimulation, session one average span
(4) Backward digit recall with sham stimulation, session three average span
(5) Visual search training with sham stimulation, session one average score
(6) Visual search training with sham stimulation, session three average score

Pre- to post-training outcome measure variables
(1) Backward digit recall, pre-training maximum span
(2) Backward digit recall, post-training maximum span
(3) Backward letter recall, pre-training maximum span
(4) Backward letter recall, post-training maximum span
(5) Backward spatial recall, pre-training maximum span
(6) Backward spatial recall, post-training maximum span
(7) N-back digits, pre-training maximum N-level
(8) N-back digits, post-training maximum N-level
(9) N-back letters, pre-training maximum N-level
(10) N-back letters, post-training maximum N-level

Indices:

The means and standard deviations will be calculated for each of the measured variables.

Indices for on-task training gains
For the two backward digit recall training conditions, the means and standard deviations of the average span reached on day one and day three (calculated from correct trials only) will be compared. For visual search training the means and standard deviations of the average score achieved on day one and day three will be compared.

Indices for pre- to post-training outcome measures
For the three backward digit recall transfer measures, the mean and standard deviations of the maximum span reached before and after training will be used. For the two N-back measures, the means and deviations of the maximum N-level reached before and after training will be used.

Design Plan

Study type:

Experiment - A researcher randomly assigns treatments to study subjects, this includes field or lab experiments. This is also known as an intervention experiment and includes randomized controlled trials.

Blinding:

For studies that involve human subjects, they will not know the treatment group to which they have been assigned.

Research personnel who interact directly with the study subjects (either human or non-human subjects) will not be aware of the assigned treatments.

Study design:

A mixed-measures design will be used. There will be one between-subjects factor of group, with 3 levels: (1) backward digit recall training with active stimulation, (2) backward digit recall training with sham stimulation, and (3) visual search training with sham stimulation. Within-subject variables include on-task training gains for each of the 3 groups, as well as changes on each of the five transfer tasks: (1) backward digit recall, (2) backward letter recall, (3) backward spatial recall, (4) N-back digits, and (5) N-back letters.

Randomization:

Participants will be assigned to one of the three training groups using stratified randomization, matched for age, gender and baseline scores on all the outcome measures.

Training groups
(1) Backward digit recall training with active stimulation
(2) Backward digit recall training with sham stimulation
(3) Visual search training with sham stimulation

Outcome measures

(1) Backward digit recall
(2) Backward letter recall
(3) Backward spatial recall
(4) N-back digits
(5) N-back letters

Analysis Plan

Statistical models:

On-task training gains
To investigate whether participants show gains on the training tasks, paired-sample t-tests will be performed separately for each of the three groups. In each case, average performance on training day one will be compared to average performance on training day three. Average performance will be measured as the average level of difficulty reached on correct trials. It is predicted that performance will be significantly higher on day three compared to day one for each training group.

Within- and cross-paradigm training effects following backward recall training
To test whether training on backward digit recall benefits performance on other backward recall tasks (within-paradigm transfer) and on N-back tasks (cross-paradigm transfer), general linear regression analyses will be performed separately for each of the five outcome measures. In each case, post-training scores will be entered as the dependent variable with pre-training scores and group (backward recall training with sham stimulation or visual search training with sham stimulation) entered as the independent variables. A Bonferroni correction for multiple comparisons will be made for each regression. As there are five outcome variables the alpha level will be $p<.01$.

It is predicted that there will be significantly greater gains on backward recall with digits and letters following backward digit recall training with sham stimulation group compared to visual search training with sham stimulation. No predictions are made regarding the extent to which backward digit recall training alone (i.e. with sham stimulation) will lead to transfer to backward spatial recall. Gains are not predicted for either group on the two N-back tasks.

Modulation of on-task training gains by stimulation
A general linear regression will be performed to test whether stimulation (active or sham) predicts differences between the pre- to post-training scores for backward digit recall training. Performance on training day three will be entered as the dependent variable, and group (active or sham) and training day one performance will be entered as the independent variables. It is predicted that backward digit recall training with active stimulation will result in significantly greater training gains than backward digit recall with sham stimulation.

Enhancement of within- and cross-paradigm training effects with stimulation
To investigate whether stimulation enhances the transfer of training effects both within and across working memory paradigms, general linear regressions will be conducted separately for each outcome measure with stimulation group as the predictor. In all cases, post-training scores will be entered as the dependent variable with pre-training scores and group (backward digit recall with active stimulation and backward digit recall with sham stimulation) entered as independent variables. Bonferroni corrections for multiple comparisons will be applied for each set analysis (i.e. a correction of five, setting the alpha level at $p<.01$). Significantly greater pre- to post-training scores are predicted for the backward recall with active stimulation group compared to the backward recall with sham stimulation group on the backward digit recall

transfer measure. No predictions are made regarding the extent to which stimulation will impact transfer to the other backward recall outcome measures (letters or spatial). For cross-paradigm transfer, no predictions are made regarding the extent to which stimulation will impact transfer to N-back letters or N-back spatial.

Transformations:

N/A

Follow-up analyses:

Further follow-up analyses are not required for this study.

Inference criteria:

The standard $p<.05$ value will be used for determining results of the paired sample t-tests that will be used to investigate on-task training gains. A Bonferroni corrected alpha level will be used in all analyses investigating the transfer of training gains. There are five outcome measures, so a $p<.01$ value will be used.

Data Exclusion:

Data will not be excluded based on participants' scores. If a participant does not complete all five sessions of the study, all of their data will be excluded and a new participant will be recruited.

Missing data:
Data from participants who do not complete all five sessions, or do not complete all five sessions within a seven day period, will be excluded from the analysis.

Exploratory analysis:

N/A

Scripts

N/A

Other

Blinding: All participants will be blind to whether they are receiving the real and placebo sham stimulation. The experimenter will be blind to the stimulation condition for participants in the two backward digit recall training groups; however they will be aware that participants in the visual search group are receiving sham stimulation.

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Appendix D Study II ethics approval letter

Karen Douglas
Secretary

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UNIVERSITY OF CAMBRIDGE

CAMBRIDGE PSYCHOLOGY RESEARCH ETHICS COMMITTEE

4 March 2016

Application No: PRE.2016.016

Dear Dr Holmes

Does transcranial electrical stimulation promote cross-paradigm transfer effects

The Cambridge Psychology Research Ethics Committee has given ethical approval to your research project: Does transcranial electrical stimulation promote cross-paradigm transfer effects, as set out in your application dated 20 January 2016.

The Committee attaches certain standard conditions to all ethical approvals. These are:

(a) that if the staff conducting the research should change, any new staff should read the application submitted to the Committee for ethical approval and this letter (and any subsequent letter concerning this application for ethical approval);
(b) that if the procedures used in the research project should change or the project itself should be changed, you should consider whether it is necessary to submit a further application for any modified or additional procedures to be approved;
(c) that if the employment or departmental affiliation of the staff should change, you should notify us of that fact.

Members of the Committee also ask that you inform them should you encounter any unexpected ethical issues.

If you would let us know that you are able to accept these conditions, we will record that you have been given ethical approval.

Please note that there have been changes to the procedures regarding amendments. Full details are given on the REC website.

Yours sincerely

K S Douglas

cc Elizabeth Byrne

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Appendix E Study III pre-registration

Open Science Framework Pre-registration

Study Information

Title:

Backward recall and *n*-back measures of working memory: a large-scale latent variable analysis

Contributors:

Elizabeth Byrne, Rebecca Gilbert, Rogier Kievit and Joni Holmes

Registered:

2017-08-15

Research questions:

The primary aim of this study is to investigate the processes involved in two widely used measures of working memory – backward recall and *n*-back. A secondary aim is to understand the relationship between these measures and nonverbal reasoning.

Backward recall tasks are commonly used in behavioural studies, while *n*-back tasks are frequently used in neuroimaging experiments (Owen, McMillan, Laird, and Bullmore, 2005). Although both tasks measure the ability to simultaneously store and process information there are substantial differences in the structural properties of the tasks and the processes involved. For example, performing a backward recall task requires explicit serial recall, whereas an *n*-back task requires recognition and can be completed using familiarity-based responding. The main aim of this study is to investigate whether these two tasks share overlapping processes using a latent variable approach. Multiple versions of each of the two types of working memory task will be used. They will contain different memoranda that will vary within domain (e.g. two types of verbal material, digits and letters) and across domain (e.g. spatial locations or verbal material). Varying materials within and across tasks allows us to assess the variance specific to task materials (content) and category of task (e.g. Schmiedek, Hildebrandt, Lövdén, Lindenberger, and Wilhelm, 2009). For example, tasks might be related due to the use of material-specific strategies (e.g. chunking letters into familiar words) or to an overlap in task processing demands (e.g. maintaining items for serial recall via rehearsal).

A latent variable approach will be used to test competing models of the underlying structure of six *n*-back and backward recall tasks. Four models will be compared: (1) a single-factor model that assumes all tasks tap a single underlying working memory construct (e.g. Alloway, Gathercole, and Pickering, 2006; Kane et al., 2004), (2) a two-factor model that assumes separate domain-specific visuo-spatial and verbal latent constructs (Daneman and Tardif, 1987; Shah and Miyake, 1996), (3) a two-factor paradigm model that assumes a latent correlation between separate backward recall and *n*-back factors (e.g. similar to two distinct but related structures for complex span and updating tasks reported by Schmiedek et al., 2009), and (4) a three-factor materials model that assumes separate constructs based on the memory items - digits, letters or spatial locations.

Once the best-fitting model of working memory has been determined, the relationship between the two categories of working memory task and fluid reasoning will be examined to test whether there is a single underlying general ability factor for all tasks (e.g. a *'g'* factor; Duncan et al., 2000), or two distinct but related constructs for working memory and reasoning (e.g. Schmiedek et al., 2009; Schmiedek, Lövdén, and Lindenberger, 2014).

In summary, the two key research questions are:

(1) What accounts for individual differences in performance on backward recall and *n*-back tasks?

(2) How are the two classes of working memory paradigm (backward recall and *n*-back) related to fluid reasoning?

Hypotheses:

Primary research question: What accounts for individual differences in performance on backward recall and *n*-back tasks?

It is hypothesized that one of four alternative working memory models will best describe the data, and explain the interrelationships between the backward recall and *n*-back tasks. These models are described below (see the PDF attachment 'Working memory models' in the analysis section, for an illustration of how these models will be constructed).

Model 1
A single factor model that assumes different versions of backward recall and *n*-back tasks tap into a single underlying working memory construct. This is consistent with domain-general theories of working memory that propose performance on working memory tasks is dependent on a domain-general central executive or attentional control system (Alloway et al., 2006; Baddeley, 1986; Engle and Kane, 2004; Engle, Kane, and Tuholski, 1999; Kane et al., 2004). Previous confirmatory factor analyses (CFA) support this view. For example, in a study conducted by Kane et al. (2004) participants completed a number of working memory tasks. The verbal working memory tasks (operation, word and counting span) required participants to remember sequences of verbal information such as words, letters or digits while also completing an additional processing task (solving arithmetic problems, judging the veracity of sentences, or counting shapes). The spatial working memory tasks (rotation span, symmetry span and navigation span) involved remembering sequences of visuo-spatial information such as arrows, matrix locations or paths of moving balls, whilst simultaneously performing a processing task (letter rotation, symmetry judgement or navigation around a letter shape). Following CFA the authors found that the verbal and visuo-spatial working memory tasks tapped into a unitary construct (Kane et al., 2004). Similarly, Alloway et al. (2006) found that although tasks

measuring the temporary storage of information (e.g. digit span, dot matrix) depended on separate domain-specific verbal and visuo-spatial stores, the processing of information within working memory was supported by a common domain-general component.

Model 2

A two-factor structure that assumes separate domain-specific latent constructs for verbal and visuo-spatial information. This is consistent with a domain-specific view of working memory in which separate pools of resources support verbal and visuo-spatial working memory (Daneman and Tardif, 1987; Friedman and Miyake, 2000; Shah and Miyake, 1996). Evidence for the domain-specific account comes from individual differences studies using verbal and visuo-spatial working memory tasks. For example, Shah and Miyake (1996) found only a weak correlation between measures of verbal and spatial working memory. In their study participants completed a verbal working memory reading span task, which involved reading sentences aloud whilst simultaneously remembering the final word of each sentence, and a spatial working memory span task, which involved mental rotation of letters whilst simultaneously remembering their orientation. The authors found that verbal working memory was highly correlated with verbal ability measures (i.e. verbal scholastic aptitude test scores), but not with spatial ability measures (i.e. tests of spatial visualization and perceptual speed), and that spatial working memory strongly predicted spatial ability but not verbal ability. The authors also conducted an exploratory factor analysis and found that spatial span and spatial ability measures loaded on one factor (i.e. a spatial factor), whereas tests of verbal span and verbal ability loaded on another (i.e. a verbal factor), suggesting there are distinct cognitive resources for spatial and verbal working memory (Shah and Miyake, 1996). The distinction between verbal and visuo-spatial working memory is also reflected in separable domain-specific short term memory stores, and the ways in which verbal and spatial materials are represented and rehearsed internally/mentally. Verbal working memory is considered phonological in nature (Gathercole, Frankish, Pickering, and Peaker, 1999), and relies on an internal articulatory rehearsal process (Baddeley, 2000; Baddeley, Thomson, and Buchanan, 1975). Therefore, tasks using different categories of materials within the verbal domain (e.g. digits, letters) may be represented internally in the same system, and rely on the same maintenance processes. Subvocal rehearsal is one possible maintenance mechanism that enables phonological representations to be serially reactivated in short term memory to prevent decay over time (Baddeley et al., 1975; Gathercole, Adams, and Hitch, 1994). On the other hand, tasks involving visuo-spatial materials (e.g. recalling spatial locations in a matrix) may rely on a distinct system dedicated to the maintenance of visual and spatial information (e.g. for forming and maintaining mental images). A rehearsal strategy for maintaining temporary visuo-spatial representations has been proposed, which is distinct to phonological maintenance mechanisms and involves the covert allocation of attention to a series of memorized locations (Pearson, Ball, and Smith, 2014; Postle, Awh, Jonides, Smith, and D'Esposito, 2004). Therefore, according to these theories and studies, model 2 predicts that performance on verbal and visuo-spatial working memory tasks will be dissociable because the tasks rely on different representational and maintenance systems. The two constructs are predicted to be linked.

Model 3

A two-factor paradigm model that assumes a correlation between distinct backward recall and *n*-back latent constructs. Although backward recall and *n*-back tasks both involve storage and processing, they differ in terms of their processing demands. For example, backward recall involves explicit serial recall whereas *n*-back relies on familiarity and recognition based responding. Schmiedek et al. (2009) reported a paradigm-based latent structure for complex span and updating tasks (e.g. *n*-back); both categories of task could account for inter-individual differences in working memory equally well and were best captured by distinct but related paradigm-specific factors. Data from the working memory training literature supports the idea that working memory tasks might group together based on the overlap in cognitive processes involved in the tasks. Transfer to untrained tasks is consistent and robust if there is substantial overlap between the processes involved in the trained and untrained activities (Sprenger et al., 2013). For example, Dahlin, Neely, Larsson, Bäckman, and Nyberg (2008) reported transfer to *n*-back following training on a running span task, but not to a Stroop task. This pattern of gains was speculated to reflect improvements in the ability to update the contents of working memory following training, which benefitted other tasks involving updating, and not tasks with different processing requirements. Other training studies have also demonstrated that working memory paradigm is a boundary condition to transfer, but that the stimulus domain of the memory items (verbal or visuo-spatial) and category of materials within paradigm (e.g. letters or digits) is not (Byrne, Ewbank, Redick, and Holmes, 2017; Holmes, Woolgar, Hampshire, and Gathercole, 2017; Minear et al., 2016). These findings suggest that training related changes are not associated with material-specific strategies, but are tied to the processes involved in the specific training task administered. It is therefore possible that different categories of working memory task will group together because they share variance common to the processes involved in the task (e.g. updating vs serial recall).

Model 4

A three factor model with separate constructs for each category of memory item as follows: factor one, digit *n*-back and backward digit recall; factor two, backward letter recall and *n*-back letters; and factor three, *n*-back with spatial locations and backward spatial recall. This model assumes that performance across the different working memory tasks will be best described by expertise related to the specific type of stimuli, for example in basic skills or knowledge tied to digits, letters or spatial materials. Within the working memory training literature it has been suggested that transfer might be mediated by the acquisition of content-specific skills and knowledge (von Bastian and Oberauer, 2014). That is, training-related improvements could arise through the development or refinement of stimuli-specific mnemonic strategies (Gathercole, Dunning, Holmes, and Norris, 2017; Minear et al., 2016). These strategies could be specific to content domain, for example chunking can be used to remember verbal items, but it is unlikely to be used for visuo-spatial materials. Such strategies could be specific to materials even within domain. A striking example of this comes from a study showing that training for sequences of digits was tied to the use of mnemonic strategies that could not be applied to novel letter materials (Ericsson, Chase, and Faloon, 1980). Similarly, Minear et al. (2016) found that participants who completed verbal working memory training reported using strategies specific to letters. During training participants used chunking to remember sequences by associating the letters with words and forming sentences, or linking letters with acronyms or people's initials (Minear et al., 2016).

Secondary research question: How are the two classes of working memory paradigm (backward recall and *n*-back) related to fluid reasoning?

Working memory and fluid intelligence represent dissociable but strongly related cognitive skills (e.g. Alloway and Alloway, 2010; Colom, Rebollo, Palacios, Juan-Espinosa, and Kyllonen, 2004). This has been demonstrated previously by Schmiedek and colleagues using latent factor approaches. In one study they identified two related constructs for updating and complex span tasks that predicted a separate reasoning factor equally well (Schmiedek et al., 2009). More recently, they reported a number of working memory measures were best captured by four latent working memory task factors corresponding to working memory paradigm (Schmiedek et al., 2014). These four paradigm factors loaded on to a single higher-order working memory construct factor, which was related to a separate reasoning factor. To address the secondary research question the best-fitting working memory model will be expanded to include reasoning. If a single factor working memory model is preferred, we will examine whether this working memory factor is very strongly or perfectly correlated with a fluid reasoning factor (cf. Kyllonen and Christal, 1990). If a multi-factor working memory model is preferred then the relationship between the working memory factors and fluid reasoning will be examined to investigate whether it is stronger for particular working memory sub-factors.

Sampling plan

Existing data:

Registration prior to creation of data.

Explanation of existing data:

N/A

Data collection procedures:

Participants
700 Native-English speaking participants aged 18-35 with normal or corrected to normal vision and no literacy difficulties will be recruited.

Recruitment
This study will be hosted on the online crowdsourcing platform Prolific Academic. Participants will be paid approximately £9 for completing the experiment.

Study procedure
Each participant will be required to complete seven cognitive tasks in a single session. The tasks are (1) backward digit recall, (2) backward letter recall, (3) backward spatial location recall, (4) *n*-back with digits, (5) *n*-back with letters, (6) *n*-back with spatial locations, and (7) relational reasoning. Participants will complete the tasks according to one of 12 possible task orders. The backward recall tasks will be grouped together (i.e. completed consecutively), and the *n*-back tasks will also be grouped together. The task order within these two groups will be counterbalanced (i.e. all possible permutations for the 3 tasks will be used), yielding 6 orders for each of the two groups of tasks. The two groups of backward recall and *n*-back tasks will be counterbalanced. This will result in 6 possible task orders in which the backward recall tasks are completed first, and 6 in which the *n*-back tasks will be completed first (yielding a total of 12 task orders). The reasoning task will be completed in between the *n*-back and backward recall tasks in all conditions (i.e. it will always be the fourth task completed). Participants will complete practice trials before beginning each task. Feedback for correct and incorrect responses will be shown on screen for the practice trials, but will not be provided during the proper tasks.

Materials
The tasks have been created by the research team using Gorilla (https://www.research.sc/#intro), software developed by Cauldron (http://www.cauldron.sc/welcome). The experiment will be hosted on the online crowdsourcing platform Prolific Academic (https://www.prolific.ac/). Participants will use a laptop or desktop computer, and responses will be made using a mouse or keyboard.

Backward recall
Participants will complete 3 backward recall tasks, each containing different stimuli: (i) digits (1 to 9), (ii) letters (B H J L N Q R X Z), or (iii) spatial locations (nine random but fixed locations on the computer screen). Trials will be presented in blocks, each consisting of four trials. During each trial items will be presented visually on screen one at a time. Participants will then be prompted to recall the sequence in backward order via an onscreen keypad of digits, letters or spatial locations. Participants will begin the tasks at a span of three items. Span length will increase by one item in each subsequent block if there are three or more correct trials. The task will be discontinued if participants get two or more incorrect trials within a block, or if the maximum level is reached (span 13). The measure of ability used in analyses will be the maximum span reached for each of the backward recall tasks (i.e. the final span in which the participant met the criterion of at least three out of four correct trials). Reaction times, as well as number of correct and incorrect trials, and of individual items within trials, will also be recorded.

n-back
Participants will complete 3 *n*-back tasks, each containing different stimuli: (i) digits (1 to 9), (ii) letters (B H J L N Q R X Z), or (iii) spatial locations. For each task, stimuli will be presented one at a time on screen in a random order. Participants will be required to indicate whether the current item on screen matches one presented *n* items back in the sequence via a button press. During each block participants will be presented with a continuous sequence of 20 +N items during which there will be a total of 6 possible targets (matches). An error will be scored if participants press the button for a non-target (false alarm), or if participants fail to press the button when a match is present (miss). Total errors will be calculated as false alarms plus misses combined. The first block will begin at 1-back and the difficulty level will increase by one in each subsequent block if less than five errors are made (e.g. increase from 1-back to 2-back). The task will end if five or more errors are made within a block, or if the maximum level is reached (12-back). The measure of ability used in analyses will be the maximum *n*-level reached for each of the *n*-back tasks (i.e. the final level in which the participant met the criterion of less than five errors in a block). Reaction times, as well as number of hits, misses, false alarms and correct rejections will also be recorded.

Relational reasoning
Participants will be presented with 80 puzzles one at a time on screen. Each puzzle will consist of a 3x3 matrix (nine spaces in total). Eight of the spaces will contain shapes, but the bottom right space will be empty. Participants will be presented with four boxes at the bottom of the screen containing shapes, and will be required to select the box with the correct answer – the box containing the piece that is missing from the empty space in the matrix. The shapes in the matrix will vary by colour, size, shape and position and will vary in levels of difficulty. Participants will have 30s to complete each trial, and a prompt will appear on screen when 5s remains. Odd and even items will be scored separately to give two relational reasoning scores. In each case the number of correct responses (out of 40) will be used in the analyses as the measure of ability. Reaction times, as well as errors due to incorrect response and errors due to timeout will also be recorded.

Study timeline
Data collection will be completed by January 2018.

Sample size:

The target sample size is 700.

Sample size rationale:

It is necessary to collect data from a very large sample to conduct latent variable modelling. A sample size of n greater than 500 is recommended for looking for complex/subtle differences between factors (Wolf, Harrington, Clark, and Miller, 2013) and the number of participants needed multiplies up very quickly as a factor of the relatedness between the measures. 700 participants will be recruited to provide sufficient high quality data to detect meaningful differences between latent construct (e.g. data from at least n=500, but ideally 650 to 700). Based on a sample size of n=700, this study will yield statistical power of .997 to detect covariances between the tasks.

Stopping rule:

Data collection will stop when the target *n* (700) is reached. The sample size accounts for attrition and so additional data will not be collected if any is excluded.

Manipulated variables:

N/A

Measured variables:

Backward digit recall maximum span
Backward letter recall maximum span
Backward spatial recall maximum span
n-back digit maximum *n*-level
n-back letter maximum *n*-level
n-back spatial maximum *n*-level
Relational reasoning odd items total items correct
Relational reasoning even items total items correct

Indices:

Factor analytic techniques will be used to understand the underlying latent constructs in the data. The factor models will be based on performance and covariance of performance across the different tasks. Raw scores (maximum span for backward recall tasks, maximum level for *n*-back tasks and total items correct for relational reasoning) will be used in the factor models.

Design Plan

Study type:

Observational Study - Data is collected from study subjects that are not randomly assigned to a treatment. This includes surveys, "natural experiments," and regression discontinuity designs.

Blinding:

No blinding is involved in this study.

Study design:

This is a cohort study looking at individual differences.

Randomization:

N/A

Analysis Plan

Statistical models:

Statistical model: Confirmatory factor analysis (CFA)

To address the primary research question, CFA will be conducted to find the best fitting model for the six working memory tasks. The following models will be compared: (1) a single working memory factor model, (2) a two-factor domain-specific verbal and visuo-spatial construct model (3) a two-factor backward recall and *n*-back paradigm model, and (4) a three-factor digit, letter and spatial materials model. See attached file ('Working memory models') for illustrations of how these models will be constructed. If necessary to aid convergence, equality constraints will be imposed on the factor loadings (within factor) or residual variances (across task). The best-fitting model(s) will be identified using a number of widely used fit statistics. These will include chi-square, the root mean square error of approximation (RMSEA) and the comparative fit index (CFI). The likelihood ratio test (LRT) and the Akaike information criterion (AIC) will also be used to directly compare models.

After establishing interrelationships among the working memory measures and determining the best fitting and most parsimonious working memory model for the variables, the secondary research question will be addressed (i.e. how are the two classes of working memory paradigm, backward recall and *n*-back, related to fluid reasoning?). The parameters of the best-fitting working memory model will be fixed and a reasoning factor will be added to examine whether the working memory factor(s) and the reasoning tasks load on a single factor or on distinct but related constructs. If a single factor working model is preferred, we will examine whether the working memory factor is very strongly or perfectly correlated with a fluid reasoning factor. Alternatively, if a multi-factor model is preferred then the relationship between the working memory factors and fluid reasoning will be examined to see whether it is identical or stronger for certain sub-factors.

Transformations:

N/A

Follow-up analyses:

N/A

Inference criteria:

The estimation method used to fit the models will be the maximum likelihood estimation (MLE). A number of fit indices will be used to determine how well the competing models fit the data.

Chi-square test statistic
The chi-square test statistic will be used to evaluate the goodness-of-fit for the competing models. It will be reported with degrees of freedom and p values. With CFA a significant result indicates that the specified model is significantly different from the data (i.e. it does not fit the data). The goodness-of-fit is therefore determined by small and non-significant chi-square values. Chi-square test statistic values close to zero indicate better fit and p values less than .05 will be used to establish significance, however a significant chi square is anticipated for all of the models due to the large sample size, so additional fit indices will be used.

RMSEA
The RMSEA (reported with 90% confidence intervals) ranges from 0 to 1, with smaller values indicative of better model fit (values less than .08 indicate acceptable fit, values equal to or less than .05 suggest a good fit, values between .08 and .10 suggest mediocre fit and those greater than .10 are considered not acceptable).

CFI
The CFI ranges from zero to one with higher values indicative of better fit (values equal to or greater than .90 indicate good model fit and those close to 1.0 are considered a very good fit).

AIC
The AIC measures the relative quality of a collection of models to each other and can be used to compare all models (i.e. this measure can be used to compare non-nested models). This value cannot be interpreted in isolation. Models with a relatively lower AIC have a better fit.

LRT
The LRT will be used to directly compare models. This test is only appropriate for nested models (i.e. model 1).

Data exclusion:

Exclusion of poor quality data
During data collection incoming data will be screened for quality. Participants who have particularly high or low scores will be flagged and checked to make sure they completed the tasks correctly. Extremely high or low scores will be identified by comparison with existing data on the tasks that was collected as part of a previous study (Byrne et al., 2017). To check whether participants are completing the tasks properly, error rates and reaction times will be checked. For backward recall a very low error rate may indicate cheating (e.g. writing down memory items), and a high error rate in conjunction with very fast response times may indicate participants are not trying to remember any items for a particular trial (i.e. just 'clicking through' the task). For the *n*-back tasks hits, misses, false alarms and correction rejections can be used to check participants' accuracy. Again, high or low error rates may indicate cheating or 'clicking through' the task. For the relational reasoning task errors made during the easiest trials (spread throughout the task) and very fast reaction times might indicate that participants are not trying to solve the puzzles (i.e. just 'clicking through' the task). Data may be excluded for participants who produce poor quality data. Participants who are not following the instructions properly (e.g. cheating, 'clicking through' the tasks), will not be paid for their participation (in line with Prolific Academic guidelines). It can be difficult to judge 'proper' performance for online data collection, so decisions to exclude participants will be made by agreement between the primary experimenter (EB) and one other member of the research team (JH, BG or RK). Participants will have the option to leave feedback at the end of the experiment to indicate whether anything might have interfered with their performance on any of the tasks (e.g. did they get distracted or encounter any technical difficulties during a trial or task). Poor quality data may be identified

this way. Data for particular tasks where this has happened will be excluded. Remaining data for other tasks completed by the same participants will still be included in the analysis.

Outliers
Data will be screened for outliers. Scores which deviate by more than 3.5 SDs from the mean of the sample will be excluded.

Missing data:

Data from all completed tasks will be analysed. If a participant has not completed all tasks, or if data from a single task is excluded, the remaining completed tasks will still be included in the analysis. Missing cases will be dealt with using the full information maximum likelihood (FIML) parameter estimation technique. Participants who are excluded (for example, on the grounds of not completing the study properly) will not be replaced as the sample size of 700 accounts for some attrition.

Exploratory analysis:

Exploratory analysis for the primary and/or secondary research questions

Once the best fitting model has been determined we may also explore higher-order factor models for working memory (e.g. for model 4 there may be a higher-order verbal factor for the digit and letter tasks that use verbal materials, which may be related to the spatial factor).

Other

For the primary research question max span reached on the backward recall tasks, and max *n*-level reached on the *n*-back tasks, will be used as the measure of ability in the main statistical analysis. Although additional variables are available (e.g. trials/items correct for backward recall and number of hits for *n*-back) maximum span in the backward recall tasks and maximum level in the *n*-back tasks will be used as indices of memory capacity (i.e. the number of items a participant can hold in mind). The additional measures that will also be scored for backward recall are the number of trials correct and the number of individual items correct. For *n*-back the number of hits, misses, false alarms and correct rejections will be scored. Reaction times will be recorded for all tasks. These additional indices provide more sensitive measures of performance (i.e. more data points and potentially more variance in scores) and may be used in exploratory analyses if greater sensitivity is required.

Scripts

N/A

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Appendix F Study III order effect ANOVAs

One-way ANOVAs were conducted to compare the effects of position (first, second, or third) on task performance for each task separately (e.g. comparing whether performance for backward letter recall differed when it was completed first, second or third in block). The results are shown below for each task.

Backward digit recall, F (2) = 3.977, p = .019, η_p^2 = .011
Backward letter recall, F (2) = .105, p = .900, η_p^2 = .000
Backward spatial recall, F (2) = .290, p = .749, η_p^2 = .001
n-back with digits, F (2) = 1.628, p = .197, η_p^2 = .005
n-back with letters, F (2) = .354, p = .702, η_p^2 = .001
n-back with spatial locations, F (2) = .238, p = .788, η_p^2 = .001

Appendix G Study III ethics approval letter

Karen Douglas
Secretary

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UNIVERSITY OF CAMBRIDGE

CAMBRIDGE PSYCHOLOGY RESEARCH ETHICS COMMITTEE

26 January 2017

Application No: PRE.2017.001

Dear Dr Holmes

Indiviual differences in working memory tasks: backward recall and N-back

The Cambridge Psychology Research Ethics Committee has given ethical approval to your research project: "Indiviual differences in working memory tasks: backward recall and N-back", as set out in your application dated 9 January 2017.

The Committee attaches certain standard conditions to all ethical approvals. These are:

(a) that if the staff conducting the research should change, any new staff should read the application submitted to the Committee for ethical approval and this letter (and any subsequent letter concerning this application for ethical approval);
(b) that if the procedures used in the research project should change or the project itself should be changed, you should consider whether it is necessary to submit a further application for any modified or additional procedures to be approved;
(c) that if the employment or departmental affiliation of the staff should change, you should notify us of that fact.

Members of the Committee also ask that you inform them should you encounter any unexpected ethical issues.

If you would let us know that you are able to accept these conditions, we will record that you have been given ethical approval.

Please note that there have been changes to the procedures regarding amendments. Full details are given on the REC website.

Yours sincerely

K S Douglas

K S Douglas

cc Elizabeth Byrne

Appendix H Study III R analysis script

```
# R Script for Chapter 4 (Study 3): Backward recall and n-back measures of working memory: A large-scale latent
variable analysis
# Elizabeth M. Byrne

library(lavaan)
library(foreign)
library(haven)
library(semPlot)

#read in data
wm_data = read.spss ("wm_data.sav", to.data.frame=TRUE)

# Primary analysis
# Define models (Confirmatory factor analysis)
single_wm <- ' # Model A - latent variable definition
                 working_memory =~ BDR + BLR + BSR + NBD + NBL +NBS
'

twofactor_paradigm <- ' # Model B - latent variable definition
                          backward_recall =~ BDR + BLR + BSR
                          n_back          =~ NBD + NBL + NBS
'

twofactor_domain <- ' # Model C - Latent variable definition
                        verbal        =~ BDR + BLR + NBD + NBL
                        visuo_spatial =~ BSR + NBS
'

threefactor_material<-' # Model D - Latent variable definition
                        digits  =~ BDR + NBD
                        letters =~ BLR + NBL
                        spatial =~ BSR + NBS
'

# Fit models: CFA
fit_single_wm <- sem(single_wm, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_single_wm, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_single_wm,what='std',cut=.1)

fit_twofactor_domain <- sem(twofactor_domain, data=wm_data, estimator='mlr', missing='fiml')
summary(fit_twofactor_domain, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_twofactor_domain,what='std',cut=.1)


fit_twofactor_paradigm <- sem(twofactor_paradigm, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_twofactor_paradigm, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_twofactor_paradigm,what='std',cut=.1)

anova(fit_single_wm_original,fit_twofactor_paradigm)

fit_threefactor_material <- sem(threefactor_material, estimator='mlr',data=wm_data, missing='fiml')
summary(fit_threefactor_material, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_threefactor_material,what='std',cut=.1)

# Chi sqaure difference tests for CFA
anova(fit_single_wm_original,fit_twofactor_paradigm)
anova(fit_single_wm_original,fit_twofactor_domain)
anova(fit_single_wm,fit_threefactor_material)

# Modification indices for the orignial four models
modificationindices(fit_single_wm)
modificationindices(fit_twofactor_paradigm)
modificationindices(fit_twofactor_domain)
modificationindices(fit_threefactor_material)

# Define models (Exploratory factor analysis)
single_wm_fix <- ' # Model E - Latent variable definition
                     working_memory =~ BDR + BLR + BSR + NBD + NBL +NBS
                     BDR ~~ BLR
'

twofactor_paradigm_fix <- ' # Model F - Latent variable definition
                              backward_recall =~ BDR + BLR + BSR
                              n_back          =~ NBD + NBL + NBS
                              BDR ~~ BLR
'

twofactor_domain_fix <- '   # Model G - Latent variable definition
                              verbal        =~ BDR + BLR + NBD + NBL
                              visuo_spatial =~ BSR + NBS
                              BDR ~~ BLR
'

# Fit models: EFA
fit_single_wm_fix <- sem(single_wm_fix, data=wm_data,estimator='mlr', missing='fiml')
```

```
summary(fit_single_wm_fix, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_single_wm_fix,what='std',cut=.1)

fit_twofactor_domain_fix <- sem(twofactor_domain_fix, data=wm_data, estimator='mlr', missing='fiml')
summary(fit_twofactor_domain_fix, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_twofactor_domain_fix,what='std',cut=.1)

fit_twofactor_paradigm_fix <- sem(twofactor_paradigm_fix, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_twofactor_paradigm_fix, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_twofactor_paradigm_fix,what='std',cut=.1)

# Chi sqaure difference tests for EFA
anova(fit_single_wm,fit_single_wm_fix)
anova(fit_twofactor_domain, fit_twofactor_domain_fix)
anova(fit_twofactor_paradigm, fit_twofactor_paradigm_fix)
anova(fit_twofactor_domain_fix,fit_single_wm_fix)
anova(fit_twofactor_paradigm_fix,fit_single_wm_fix)

# Secondary analysis
# Define GF models
threefactor_paradigm_gf <- ' # Model H - Latent variable definition
                               backward_recall =~ BDR + BLR + BSR
                               n_back   =~ NBD + NBL + NBS
                               gf  =~ RR_even + RR_odd

'

threefactor_paradigm_gf_fix <- ' # Model I - Latent variable definition
                                   backward_recall =~ BDR + BLR + BSR
                                   n_back          =~ NBD + NBL + NBS
                                   gf              =~ RR_even + RR_odd
                                   BDR ~~ BLR
'

single_gf <- ' # Model J - Latent variable definition
                 gf =~ BDR + BLR + BSR + NBD + NBL + NBS + RR_even + RR_odd
'

single_gf_fix <- ' # Model K - Latent variable definition
                     gf =~ BDR + BLR + BSR + NBD + NBL + NBS + RR_even + RR_odd
                     RR_even ~~ RR_odd
                     BDR~~BLR
'

# Fit GF models: Secondary analysis
fit_threefactor_paradigm_gf <- sem(threefactor_paradigm_gf, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_threefactor_paradigm_gf, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_threefactor_paradigm_gf,what='std',cut=.1)

fit_threefactor_paradigm_gf_fix <- sem(threefactor_paradigm_gf_fix, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_threefactor_paradigm_gf_fix, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_threefactor_paradigm_gf_fix,what='std',cut=.1)

fit_single_gf <- sem(single_gf, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_single_gf, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_single_gf,what='std',cut=.1)

# Modification indices for single factor GF model:
modificationindices(fit_single_gf)

fit_single_gf_fix <- sem(single_gf_fix, data=wm_data,estimator='mlr', missing='fiml')
summary(fit_single_gf_fix, fit.measures=TRUE, standardized=TRUE, rsquare=TRUE,ci=T)
semPaths(fit_single_gf_fix,what='std',cut=.1)

# Chi sqaure difference tests for secondary analyses
anova(fit_threefactor_paradigm_gf,fit_threefactor_paradigm_gf_fix)
anova(fit_single_gf,fit_single_gf_fix)
anova(fit_single_gf_fix, fit_threefactor_paradigm_gf_fix)
```