

**PUBLISHED AS:**

Henson, R.N.A. (2001). Neural working memory: applications of the Working Memory model to neuropsychology and neuroimaging. In Andrade, J. (Ed.), *Working Memory: a work in progress* (pp. 151-173). London: Routledge.

**Neural Working Memory**

The Working Memory (WM) model of Baddeley and Hitch (1974) has proved hugely influential in neuropsychological and, more recently, neuroimaging investigations of working memory. In the present chapter, I aim to illustrate this influence via three distinctions made by the WM model: the distinction between 1) verbal and visuospatial information, 2) storage and rehearsal, and 3) maintenance and manipulation.

The WM model postulates separate memory systems for maintaining verbal and visuospatial information: the Phonological Loop (PL) and the Visuospatial Sketchpad (VSSP) respectively. Temporary storage of a phonological representation of an unfamiliar telephone number, for example, would engage the PL, whereas maintenance of an image of its visual appearance would engage the VSSP.

Maintenance of information in the WM model comprises two components: passive *storage* of information, subject to loss by decay or interference over time, and active *rehearsal*, which preempts such loss. Within in the PL for example, storage is subserved by the Phonological Store and rehearsal is subserved by the Articulatory Control Process. For a telephone number, storage might correspond to some representations of the digits and their order, and rehearsal would correspond to the common strategy of (subvocally) repeating the sequence of digits to oneself.

The third component of the WM model, the Central Executive (CE), is engaged when information must be manipulated. Whereas maintenance simply entails keeping information in mind in the absence of an external stimulus, manipulation refers to the further transformation or “re-representation” of the information being maintained<sup>1</sup>. An example of manipulation would be the process of reordering the digits in the telephone number (e.g., in descending numerical order).

The main argument in the present chapter is that these distinctions are respected at the functional anatomical level. In other words, the proposal is that the components of the WM model are realised by distinct brain regions. The main evidence for this claim derives from studies of acquired deficits following localised brain damage (data from developmental disorders or diffuse brain diseases are not discussed here). Converging evidence comes from recent neuroimaging studies of healthy individuals performing working memory tasks. Whether or not this functional segregation is ultimately valid is less relevant however: The purpose of the argument is to illustrate how any brain-behaviour mapping must begin with a successful theory of the behavioural phenomena, in this case, the Working Memory model.

Finally, additional results from neuropsychological and neuroimaging studies will be mentioned that are not well captured by Working Memory model. These include, for example, the distinction between visual object and visual spatial information and between

---

<sup>1</sup> Manipulation is rarely strictly defined; rather it is often used to refer to any working memory process that involves more than simple maintenance.

different types of manipulation, such as monitoring, generating strategies, selecting competing information and planning. These distinctions are used to address the remaining aims of this book, regarding the weaknesses and future of the WM model.

### **Maintenance of Verbal versus Visuospatial Material**

The verbal-visuospatial distinction appears to correspond to a hemispheric lateralisation, with regions of the left hemisphere subserving maintenance of verbalisable material and regions of the right hemisphere subserving maintenance of nonverbalisable, visuospatial material. This left-right lateralisation of verbal-spatial working memory originates from neuropsychological studies. De Renzi and Nichelli (1975), for example, found that a group of patients with left-hemisphere lesions was impaired on several verbal working memory tasks relative to both a group of healthy controls and a group with right-hemisphere lesions. Conversely, the right-hemisphere group was impaired on several spatial working memory tasks relative to the left-hemisphere group (though the difference was not reliable in this case).

Group studies like these are bolstered by single-case studies, such as Patient P.V. (Vallar & Baddeley, 1984), who was severely impaired on verbal working memory tasks but performed normally on spatial working memory tasks, and Patient E.L.D. (Hanley, Young, & Pearson, 1991), who was impaired on spatial working memory tasks but performed normally on verbal working memory tasks. P.V. suffered from a large stroke-induced lesion of the left-hemisphere, whereas E.L.D. suffered from an aneurysm-induced haematoma in the right Sylvian Fissure (the sulcus joining A to F in the lower panel of Figure 1). Importantly, neither patient was impaired on verbal or spatial non-working memory tasks, such as tests of perception, or tests of long-term memory for previously learned verbal or spatial information. Data from these patients thus comprise a double dissociation between brain regions subserving verbal and spatial working memory.

This lateralisation of working memory has been bolstered by recent neuroimaging studies. A common test of maintenance in working memory is the Sternberg task (Sternberg, 1969). Participants in this task are presented with a *memory set* of typically 3-9 stimuli, which are then removed for several seconds before the appearance of a single probe stimulus. Their goal is to decide whether or not the probe stimulus was one of the stimuli in the memory set. To isolate brain areas involved in maintenance from those involved in perceptual or motor components of the task, functional images obtained during the Sternberg task are contrasted with those obtained in a control task in which the memory set and probe item are presented simultaneously, alleviating any memory requirement (Figure 2).

Using a verbal Sternberg task, Awh et al. (1996) reported significant activations in several left hemisphere regions, including inferior and superior parietal cortex (BA 7/40), inferior frontal cortex (BA 44; Broca's area) and premotor cortex (BA 6)<sup>2</sup> – see Figure 1. Similar regions were implicated by Paulesu, Frith, & Frackowiak (1993b), who compared two Sternberg tasks: one using letters and one using nonverbalisable symbols.

---

<sup>2</sup> Brodmann Areas (BA) are brain regions distinguished by their cytoarchitecture, i.e. the nature and distribution of different cell types (Brodmann, 1909).

This left hemisphere network of inferior frontal, parietal and motor areas (plus right cerebellum) is a consistent finding in studies of maintenance in verbal working memory (Smith & Jonides, 1997). Note however that, though the activations in these studies are generally stronger on the left than right, they are often bilateral. The functional significance of activation in homologous areas of the right hemisphere is unknown: it might be task-relevant (even if not necessary, given the neuropsychological evidence), or it might simply reflect spill-over of activity from the left hemisphere via cortico-callosal connections.

Activations in visuospatial maintenance tasks are often seen in homologous regions of the right hemisphere. Jonides et al. (1993), for example, reported activations in right inferior parietal cortex (BA 40), right premotor cortex (BA 6) and right inferior frontal cortex (BA 47) when comparing a spatial Sternberg task with its perceptual-motor control. The only additional activation was in anterior extrastriate occipital cortex (BA 19), an area often associated with visual imagery (Kosslyn et al., 1993). Comparable findings were reported by Smith, Jonides and Koeppel (1996) and Paulesu et al. (1993a) in direct comparisons of visuospatial versus verbal Sternberg tasks. Unlike the Jonides et al. comparison however, the Paulesu et al. task required maintenance of abstract, visual form, with little or no requirement for spatial information. This raises an important question as to whether the visual aspects of working memory can be dissociated from spatial aspects.

### **Maintenance of Visual Object versus Visual Spatial Information**

Though a distinction between visual and spatial information is not made explicit in the WM model (given that behavioural dissociations between visual and spatial maintenance are rarely clear cut (Baddeley, 1986; Pearson, q.v.), it has been an important distinction within the neuroscientific community.

The dissociation in the visual processing of object and spatial information is clearest in electrophysiological research on nonhuman primates. A ventral stream from occipital cortex to inferior temporal cortex appears specialised for object information and a dorsal stream from occipital cortex to inferior parietal cortex appears specialised for spatial information (Mishkin, Ungerleider, & Macko, 1983; though see Milner & Goodale, 1993). These “what versus where” streams may continue into prefrontal cortex, where cells have been found that fire only when information must be retained during a delay following stimulus offset. Specifically, it has been argued that prefrontal cells ventrolateral to the principal sulcus code for object information during a delay, whereas prefrontal cells within and dorsolateral to the principal sulcus code for spatial information during a delay (Wilson, Scalaidhe, & Goldman-Rakic, 1993).

Similar dissociations might be expected in the functional anatomy of human working memory. Levine, Wallach and Farah (1985) for example reported a double dissociation between two patients, one of whom had problems imagining visual features such as the shape of a Spaniel’s ears, but had no problem describing routes or locating towns on maps, and the other of whom had the opposite pattern of deficit. The first patient had bilateral temporo-occipital damage, whereas the second had bilateral parieto-occipital damage. Consistent with a dorsal spatial route, lesions to right parietal cortex are associated with the neglect syndrome (Bisiach, 1993), an apparent loss of visual

information from one side of space (usually the left). Though these deficits concern long-term memory and perception, rather than working memory per se, they support a ventral-dorsal visual-spatial distinction in humans. Selective impairment of short-term visual maintenance was reported by Warrington and Rabin (1971). They described patients with left posterior damage who had deficits in a visual span task using random strings of letters, digits, lines or curves. The patients were less impaired when the strings of letters approximated words, and unimpaired on auditory digit span tests. Patients with right posterior damage did not show the same pattern of impairment. These data suggest the existence of a (sublexical) visual store in posterior left cortex.

Neuroimaging evidence supports such a spatial-object distinction, though the distinction also tends to be lateralised to the left for object information and to the right for spatial information. Smith and Jonides (1994) for example compared the spatial version of Sternberg task used by Jonides et al. (1993) with an object version that used abstract shapes (and for which spatial location was irrelevant; Figure 2). When contrasted with the spatial version, the object version revealed activations that were predominantly left-lateralised, including premotor cortex (BA 6), inferior parietal cortex (BA 40) and inferior temporal cortex (BA 37). The former two regions were close to those associated with verbal working memory tasks (see above), suggesting that participants were verbally recoding the abstract shapes. The inferior temporal region is consistent with the nonhuman primate data suggesting a specific role for this area in processing object information (e.g., Desimone & Gross, 1979) and the deficits following left posterior lesions in humans (Warrington & Rabin, 1971). A more direct comparison of object and spatial information was made by Smith et al. (1995). Participants were presented with two abstract shapes and, following a 3 second delay, a single probe shape prompting a yes-no response. In the test of object working memory, the task was to decide whether the probe matched one of the memory set in shape (regardless of its location on the screen). In the test of spatial working memory, the task was to decide whether the probe matched one of the memory set in its location (regardless of its shape). Thus identical stimuli were presented in both cases; the only difference was the task instruction. The areas more active in the object task than spatial task were left posterior parietal cortex and left inferior temporal cortex, a subset of the areas implicated in the Smith and Jonides (1994) study. The areas more active in the spatial task were again right inferior frontal, right posterior parietal, right anterior occipital and right premotor cortices. Similar studies dissociating ventral from dorsal posterior regions for visual object versus visual spatial working memory respectively have been reported by McCarthy et al. (1996) and Belger et al. (1998).

Courtney, Ungerleider, Kell and Haxby (1997) used rapid fMRI scanning of a delayed-matching-to-sample task, in order to identify areas whose activity was sustained during the delay between the sample and test stimuli (i.e., reflected mnemonic rather than perceptual or motor components of the task). These areas included right inferior occipital cortex (BA 18/19), and bilateral ventral (BA 45/47) and dorsal (BA 46) lateral frontal cortex. The inferior occipital activation is consistent with the Smith et al. studies of object maintenance, though the opposite lateralisation may reflect the fact that Courtney et al.'s objects were faces rather than abstract pictures.

The above dissociations are suggestive of separate neural systems for object and spatial working memory, with an inferior temporo-occipital specialisation for

maintenance of visual object information, and a right parietal specialisation for maintenance of visual spatial information. Neuroimaging studies are yet to find evidence for the ventral-dorsal object-spatial dissociation of prefrontal cortex suggested by some nonhuman primate research however (see Owen, 1997, and Petrides, 1994). The dorsolateral prefrontal activations associated with manipulation in human working memory tasks are, if anything, dissociated (lateralised) for verbal versus spatial information, rather than spatial versus object information, and the evidence for an object-spatial distinction is not as clear as that for a verbal-visuospatial distinction. Indeed, the results from human imaging experiments are often difficult to interpret because participants are able to label abstract objects, allowing use of a verbal working memory system. One possible solution, adopted in a long-term memory study by Owen, Milner, Petrides and Evans (1996b), is to require discrimination of two very similar pictures of a familiar, nameable object: Because the same verbal label is likely to be applied, successful discrimination requires use of more detailed visual object memory. Furthermore, little research has attempted to distinguish spatial from visual maintenance by examining spatial working memory tasks using auditory stimuli.

### **Yet Other Material-Specific Stores?**

It is possible that yet more material-specific stores will be associated with distinct brain areas. For example, there is both psychological (Crowder & Morton, 1969) and neuropsychological (Samson & Zatorre, 1992) evidence for temporary storage of precategory, auditory information, which may be localised in right superior temporal cortex (Zatorre, Evans, & Meyer, 1994). There is also evidence for a short-lived iconic visual store (Phillips, 1974), which may reflect sustained activity in primary visual cortex, and even a short-lived motoric store in nonhuman primate motor cortex (Smyrnis, Taira, Ashe, & Georgopoulos, 1992). However, it is not clear whether these stores qualify as working memories, in the sense that information can be actively maintained or manipulated. Rather, these stores would seem to correspond to passive stores that lack a rehearsal process, as discussed below.

### **Storage versus Rehearsal**

Maintenance consists of two components: passive storage and active rehearsal. The rehearsal-storage dissociation appears to reflect an anterior-posterior anatomical segregation, with storage involving posterior areas of parietal, temporal and occipital cortices and rehearsal involving posterior areas of frontal cortex.

### **Verbal Storage and Rehearsal**

For verbal material, this posterior-anterior storage-rehearsal dissociation is suggested by findings that patients with lesions in left inferior parietal cortex show dramatic verbal working memory deficits, whereas patients with lesions in inferior frontal cortex (e.g., Broca's area) show less dramatic deficits, despite considerable articulatory problems (Vallar & Shallice, 1990). This pattern can be explained if damage to inferior parietal cortex prevents verbal storage, whereas damage to inferior frontal

cortex prevents rehearsal but leaves storage intact. Because patients with anterior brain damage may still be able to store verbal information for short periods of time, they would be less impaired on immediate tests of verbal working memory.

This group difference is again supported by single-case studies. Vallar, DiBetta and Silveri (1997) report a patient L.A., who had lesions in inferior parietal and superior/middle temporal areas of the left hemisphere. L.A. showed an impaired verbal memory span and no evidence of a phonological similarity effect, suggesting impaired storage. L.A. did however show an effect of articulatory suppression, suggesting that she retained the ability to rehearse. This pattern of deficit was contrasted with that of a patient T.O., who had lesions in premotor, frontal paraventricular and anterior insula areas of the left hemisphere. T.O. showed a phonological similarity effect with auditory presentation of stimuli, but no effect of articulatory suppression, suggesting intact storage but impaired rehearsal.

Many single-case studies have now been reported with a selective impairment of verbal short-term storage when material is presented auditorily (the “auditory-verbal short-term memory syndrome”, Vallar & Shallice, 1990). These patients show memory spans for auditory-verbal material of only 2-3 items, combined with normal speech perception and production, normal long-term memory, normal short-term memory for nonverbal auditory material and relatively unimpaired short-term memory for visual-verbal material. The less severe impairment in these patients when verbal material is presented visually is often attributed to use of an alternative, visuospatial store (see above). Despite a range of different aetiologies, the most common lesion site in these patients is left inferior parietal cortex (posterior to Wernicke’s area), in a region called the supramarginal gyrus (Figure 1).

To distinguish storage and rehearsal in their neuroimaging experiment, Awh et al. (1996) compared a two-back verbal working memory task (see Figure 2) with a control task of continuous subvocal repetition of a single item. Subtraction of the control task the memory task revealed significant activation in left inferior parietal cortex (BA 40), bilateral superior parietal cortex (BA 7), bilateral supplementary motor area (BA 6), right thalamus and right cerebellum. Any difference in inferior frontal cortex (e.g., Broca’s area) failed to reach significance. Using a different control of letter rhyme judgement, which is believed to require articulatory rehearsal (Besner, 1987), Paulesu et al. (1993b) reported greater relative activity in left inferior parietal cortex (BA 40) for their Sternberg task, but little difference in inferior frontal cortex (BA 44). Both studies therefore implicate left inferior parietal cortex (BA 40) in storage, which was more active the memory tasks, and left inferior frontal cortex (BA 44) in rehearsal, which was common to both memory and articulatory control tasks. Indeed, storage of verbal information is associated with left parietal activation in almost every verbal working memory study (with the possible exception of Fiez et al., 1996, though see Jonides et al., 1998), in good agreement with the neuropsychological evidence.

A common suggestion (Jonides et al., 1996) is that the other areas activated during maintenance of verbal material, including left premotor cortex, supplementary motor cortex and right cerebellum, together with left inferior frontal cortex, comprise a network involved in speech production, consistent with the articulatory nature of rehearsal proposed by Baddeley (1986; though see Bishop & Robson, 1989). (The activation in supplementary motor cortex and right cerebellum when Awh et al., 1996,

contrasted their memory task with their repetition task may reflect additional speech processes, such as seriation, that were required in the more demanding two-back memory task.) More recent imaging studies have sought to dissociate not only brain regions involved in storage and rehearsal, but also those involved in the recoding of visual items into a phonological form, and the temporal grouping of items during rehearsal. Using the Burgess and Hitch (in press) computational model of the Phonological Loop for example, Henson, Burgess and Frith (in press) suggested that left inferior frontal activations are associated with the retrieval of output phonology (used in recoding), whereas left premotor activations are associated with the processes of seriation and timing of rehearsal (used in grouping). Further functional decomposition of the network of brain areas associated with maintenance of verbal information is likely to benefit from the use of such explicit models.

### **Visuospatial Storage and Rehearsal**

Developments of the Visuospatial Sketchpad component of the WM model distinguish between storage of visual material in a Visual Cache and its rehearsal via an Inner Scribe (Logie, 1994; Pearson, q.v.), analogous to the Phonological Loop. The neuropsychological and neuroimaging evidence reviewed above suggests that the Visual Cache might exist in left temporo-occipital cortex. The localisation of the Inner Scribe is less clear however. Right parietal cortex may subserve spatial rehearsal processes, or it may subserve a spatial store that is independent of any visual object store. Moreover the precise nature of visuospatial rehearsal processes is far from clear. The hypothesis that visuospatial rehearsal corresponds to planned eye-movements has little supportive evidence (Baddeley, 1986), and activations of areas associated with eye movements, such as frontal eye fields (BA 8), pulvinar nucleus, or superior colliculus, are yet to be observed in neuroimaging studies of visuospatial working memory. An alternative hypothesis that rehearsal of visuospatial information involves an internal attentional mechanism is consistent with neuroimaging studies of spatial attention, which activate similar areas of right superior parietal cortex (BA 7), independent of eye movement (Corbetta, Miezin, Shulman, & Petersen, 93; Coull & Nobre, 1998). A tentative hypothesis is that visuospatial information is stored over abstract or object visual representations in occipital cortex and inferior temporal cortex respectively, which are spatially organised via associations with right parietal cortex. These representations may be refreshed by a process of sequential, selective attention via each visual-spatial association; a process that engages right superior parietal cortex (BA 7), right premotor cortex (BA 6) and right inferior frontal cortex (BA 47).

### **Manipulation**

The functional anatomy of manipulation in working memory is less well defined than maintenance. Executive processes are generally associated with frontal cortex, on the basis that patients with frontal damage usually present with a general impairment in complex behavioural tasks, but not routine or automatic tasks (Shallice, 1988). Lesions to anterior and midlateral regions of prefrontal cortex for example do not normally impair maintenance: A review by D'Esposito and Postle (in press) found no evidence that

patients with dorsolateral prefrontal lesions were impaired on span tasks. This suggests that manipulation is subserved by frontal regions distinct from those subserving maintenance.

However, many different types of manipulation have been proposed (e.g., monitoring, updating, selecting, inhibiting) and a huge range of different tasks have been examined that involve at least one type of manipulation. Without attempting a precise definition of different types of manipulation, I concentrate below on four types of task that have been used extensively in neuropsychology and/or neuroimaging.

### Monitoring Tasks

Two simple tasks that combine maintenance and manipulation, and which have proved useful in neuroimaging studies, are the Continuous Performance Test (CPT) and the N-back task (Figure 2). Both tasks require monitoring of a continuous sequence of stimuli for the occurrence of a target that is contingent on preceding stimuli. Participants in a verbal CPT respond positively whenever a target letter (e.g., X) follows a specified context letter (e.g., A), and negatively otherwise. This task has a small maintenance component, in that the correct response to a stimulus requires memory for the prior stimulus, and a small manipulation component in order to update working memory whenever the context letter is not followed by the target letter. Participants in the N-back task respond positively whenever the current stimulus matches the stimulus  $N$  positions back in the sequence. For  $N > 0$ , this task requires both maintenance of the last  $N$  stimuli (in order) and updating of these stimuli each time a new stimulus occurs (for  $N = 0$ , the task is simply to respond whenever a prespecified target occurs, which requires no updating).  $N$  is often viewed as proportional to the *working memory load* -- the demands placed on maintenance and/or manipulation processes.

Barch et al. (1997) used the CPT to distinguish the concept of *working memory load* from less interesting concepts like task difficulty, mental effort, or arousal. This dissociation is important given that working memory tasks typically involve greater error rates and/or longer reaction times than their control tasks. To increase the working memory load, Barch et al. lengthened the time interval between the context letter and target letter. To vary the level of task difficulty, they compared conditions in which the stimuli were visually degraded with conditions in which the stimuli were intact. Consistent with their expectations, variations in maintenance duration had no significant effect on error rates or reaction times, unlike variations in visual degradation, which increased both error rates and reaction times. Moreover, a double dissociation was observed between areas such as left dorsolateral prefrontal cortex (BA 9/46), left inferior frontal cortex (BA 6/44) and left posterior parietal cortex (BA 7/40), which showed effects of maintenance duration but no significant effect of visual degradation, and areas such as the anterior cingulate (BA 8/32) and right inferior frontal cortex (BA 44/45/47), which showed effects of visual degradation but no significant effect of maintenance duration. These results suggest that the left frontal and left parietal activations seen in verbal working memory studies are not simply an artifact of greater task difficulty.

Braver et al. (1997) varied verbal working memory load by increasing  $N$  from  $N = 0$  to  $N = 3$  in a letter-version of the N-back task. Areas in which activity was a linear increasing function of load included dorsolateral prefrontal cortex (BA 9/46), inferior



frontal cortex (BA 6/44) and parietal cortex (BA 7/40), bilaterally in each case, as well as a number of left motor, premotor and supplementary motor areas (BA 4/6). Similar results were reported by Jonides et al. (1997). On the basis of the studies reviewed above, the inferior frontal, posterior parietal and motor activations are likely to reflect the network of areas involved in maintenance of verbal information (e.g., the storage and rehearsal of the most recent  $N$  letters). This would implicate the additional bilateral activation of dorsolateral prefrontal cortex in manipulation (e.g., updating of the particular letters being maintained). It would be valuable to examine the effects of increasing working memory load in the  $N$ -back task in patients with frontal damage.

Smith et al. (1996) reported activation in similar dorsolateral regions when a 3-back task was compared with a control task in which participants monitored stimuli for the occurrence of one of three target stimuli ('equating' the maintenance component). Activations of these regions were lateralised with respect to whether the 3-back task involved verbal or spatial stimuli, with greater left dorsolateral activation in the former and greater right dorsolateral activation in the latter. In a similar study, Owen et al. (1998) compared spatial and object  $N$ -back tasks with a single target control task. Although differences between the spatial and object memory-related activations were observed in posterior regions, such as posterior parietal cortex (BA 7/40) for the spatial task, and middle and anterior temporal cortex (BA 21/22/38) for the object task, the coordinates of the peaks of the bilateral dorsolateral prefrontal activations for the two tasks were within 2mm of each other. This suggests that manipulation processes are common to spatial and object working memory, unlike the apparent lateralisation of verbal and spatial manipulation processes.

An alternative method of dissociating maintenance and manipulation was reported by Cohen et al. (1997), who measured activity at four different peristimulus times during an  $N$ -back task. Areas involved in transient processes, such as perceiving stimuli and producing responses, would be expected to show an effect of time but no effect of load ( $N$ ), whereas areas involved in sustained processes such as maintenance would be expected to show an effect of load but no effect of time. Furthermore, areas involved in manipulation processes might be expected to show an interaction between load and time (updating the target item being a transient process that becomes more demanding as  $N$  increases). As expected, areas associated with stimulus perception, such as visual cortex, showed effects of time, but no effect of load. Contrary to expectations however, areas showing an effect of load but not time included dorsolateral prefrontal cortex (BA 9/46), which, unlike the Braver et al study, showed a nonlinear effect of load, such that activity was considerably greater for the 2- and 3-back tasks than for the 0- and 1-back tasks. The reason for this discrepancy between the two studies is not clear. It may reflect a difference in the strategies used by the two groups of participants: The jump in dorsolateral prefrontal activity between the 1- and 2-back tasks in the Cohen et al. study may reflect a strategic change between updating a single item in working memory and updating a sequence of two or more items in serial order. Nonetheless, this approach to distinguishing transient and sustained effects in working memory tasks is clearly an important methodological advance, and one that may prove valuable in teasing apart the processes of manipulation and maintenance in future studies.

## Generation Tasks

A task that has been used in neuropsychological, electrophysiological and neuroimaging studies is the self-ordered generation task (Milner, 1982). Participants in this task select one stimulus from a finite set such that, over trials, every stimulus has been selected once (without repetition). This task involves not only maintaining and updating information about which stimuli have already been selected, but also comparison of this information with the set of possible stimuli in order to select each new stimulus. Patients with frontal lesions are impaired at self-ordering tasks (Petrides & Milner, 1982) and analogous deficits are seen in primates with dorsolateral prefrontal lesions (Petrides, 1994).

Petrides, Alivisatos, Evans, & Meyer (1993a; Petrides, Alivisatos, Meyer, & Evans, 1993b) compared brain activity during performance of a self-ordering task with a control task in participants responded to one of a set of stimuli that was indicated each trial. When the stimuli were abstract designs, the ordering task produced greater activation in right dorsolateral prefrontal cortex, as predicted (Petrides et al., 1993a) and supporting a right lateralisation of visuospatial working memory. When the stimuli were verbal (digits), the dorsolateral prefrontal activation was bilateral (Petrides et al., 1993b). This prefrontal activation did not owe simply to the self-generated nature of the ordering task: When an externally-ordered condition was tested in which participants monitored a random sequence of heard digits in order to detect which digit 1-10 was omitted, the same bilateral dorsolateral prefrontal activation was observed (Petrides et al., 1993b).

Another generation task is random number generation (Baddeley, 1966), in which numbers must be generated without conforming to any rule or pattern (meaning that repetition is of course possible). Tasks like these involve not only internal monitoring of previous responses (rather than the external monitoring of the CPT and N-back tasks), but inhibition of prepotent responses and well-learned schemata. Frith, Friston, Liddle and Frackowiak (1991) reported bilateral dorsal frontal activations when generative, random key pressing was compared with reactive, stimulus-driven key pressing. Jahanshahi, Dirnberger, Fuller and Frith (submitted) observed left dorsolateral activation when random number generation was compared with counting, and this activity was negatively related to indices of randomness and higher generation rates. Interestingly, right ventrolateral activation was also seen when random number generation was compared with counting, but did not correlate with randomness indices or generation rate, suggesting that this region is involved in maintenance processes unrelated to the difficulty of random generation. Surprisingly, though Alzheimer and Parkinson patients have been shown to be impaired at random generation, there have been few studies of the effects of localised frontal lesions on random generation in humans.

Other generation tasks like verbal fluency, a common clinical test of frontal lobe damage, involve selection of stimuli from much larger sets. The verbal fluency task requires generation without repetition of, for example, as many animal names (category fluency), or words beginning with a specified letter (letter fluency), as possible in a short period of time. This task involves not only monitoring but also development of new strategies to aid generation (e.g., first thinking of pets, then safari animals, etc. Baddeley and Wilson (1988) reported that patient RJ, who suffered bilateral frontal damage, was

only able to give four animal names in 60 seconds (cf. a dozen or more in controls). The PET study of Frith et al. (1991) found left dorsolateral prefrontal activation when letter fluency was compared with word repetition. Considerable evidence thus exists for a role of dorsolateral prefrontal cortex, on the left for verbal information and right for visuospatial evidence, in the manipulation processes required by generation tasks.

### **Dual Tasks**

Combining two tasks simultaneously often makes demands on working memory (Baddeley, 1986), typically requiring the switching between information appropriate for one or other task. Patients with frontal lesions tend to be disproportionately impaired at dual versus single task performance (McDowell, Whyte, & D'Esposito, 1997), again suggesting a frontal role in these aspects of working memory.

D'Esposito et al. (1995) compared brain activity when participants performed two tasks concurrently with activity when each task was performed alone. Neither of the two tasks, a spatial rotation task and a semantic judgement task, produced significant activation of dorsolateral prefrontal cortex when performed alone; only when combined was significant activation of this area observed. Importantly, this activation was unlikely to owe simply to the impaired performance of both tasks when combined, because a second experiment in which performance of the rotation task was impaired by decreasing the interval between stimuli did not reveal any significant increase in dorsolateral prefrontal activity. However, a dual-task PET study by Klingberg (1998), using a visual and an auditory task in which participants indicated when a stimulus was of lower luminance or pitch respectively than the previous stimulus, found no cortical area that was activated specifically in the dual-task condition. Moreover, Goldberg et al. (1998) found that the dorsolateral activation associated with a Wisconsin card-sorting task was actually diminished when combined with an auditory verbal shadowing task, and Fletcher et al. (1995) found that the dorsolateral activation associated with elaborative verbal encoding was diminished when combined with a visuo-motor secondary task. One possible explanation for these results is that one or both of the tasks of Klingberg (1998), Goldberg et al. (1998) and Fletcher et al. (1995) required manipulation even when performed alone, consistent with the dorsolateral prefrontal activations observed in each case. This might leave less scope for additional dorsolateral activation when the tasks are combined, or even a decrement in dorsolateral activation when performance of both tasks suffers under dual-task conditions, as observed by Goldberg et al. (1998) and Fletcher et al. (1995).

### **Complex Planning Tasks**

Shallice (1982) introduced the Tower of London task in order to test planning deficits in patients with frontal lesions. Participants in this task must rearrange a set of balls on pegs in order to match a specified goal state. Because of the constraints on legal movements of the balls, this task requires planning of a number of separate moves in order to attain the goal state, often via various subgoals, in the minimum number of moves. Shallice found that patients with left frontal lesions were more impaired on this task than patients with right frontal lesions. Owen, Downes, Sahakian, Polkey and

Robbins (1990) however found that patients with both left and right frontal lesions were impaired on this task relative to controls. Importantly, their deficit remained even when movement execution times were subtracted, and neither type of patient was significantly impaired on the Corsi blocks test of visuospatial maintenance, suggesting that the deficit was confined to manipulation processes (i.e., planning). However, the site and extent of the frontal lesions in both studies were highly variable, preventing any further localisation within prefrontal cortex.

Owen, Doyon, Petrides and Evans (1996a) compared brain activity in healthy individuals performing a computerised version of the Tower of London task (indicating moves on a touch-sensitive screen) with activity when they simply touched highlighted balls (yoked to their number and speed of moves in the Tower of London condition). Activation of left dorsolateral prefrontal cortex was observed, as well as several activations in right premotor and parietal cortices that may be associated with visuospatial maintenance. When Baker et al. (1996) used a version of the Tower of London task in which no movement was required (participants were shown an initial and a goal state, and simply indicated the minimum number of moves from the initial to the goal state), subtraction of easy (2-3 move solutions) from difficult (4-5 move solutions) conditions revealed activation in right dorsolateral prefrontal, bilateral premotor and medial parietal cortices (though the same activations were not seen in a similar comparison by Owen et al., 1996a). These studies are at least suggestive of a dorsolateral (perhaps bilateral) prefrontal role in manipulation, even if manipulation has not yet been completely dissociated from maintenance in this task.

## Conclusions

### *What are the successes of the WM model?*

I hope that the above review, albeit brief, illustrates how successful the WM model has been in interpreting neuropsychological evidence and guiding the design of neuroimaging experiments. Much progress has been made in the functional anatomy of human working memory, profiting from WM distinctions between verbal versus visuospatial information, storage versus rehearsal, and maintenance versus manipulation. Indeed, one can already attempt a preliminary mapping of WM model components onto the brain: the CE maps to midlateral prefrontal regions, particularly left and right dorsal lateral prefrontal cortex; the Phonological Store maps to left inferior parietal cortex; the Articulatory Control Process maps to left premotor regions (including Broca's area), left supplementary motor regions and perhaps right cerebellum; the Visual Cache maps to bilateral anterior occipital and/or inferior temporal regions; and the Inner Scribe maps to right premotor and right superior parietal regions.

### *What are the competing models?*

There are few, if any, competing models of human working memory, at least that conform to a structural perspective (see Ward, q.v.). Indeed, it is difficult not to assume a structural model if one believes in functional segregation of the brain (the onus is on procedural models to interpret, for example, selective neuropsychological deficits).

*What are the weaknesses of the WM model?*

The main weakness of the WM model from the present perspective is its simplicity (i.e. lack of further components). For example, other researchers have argued for additional material-specific stores, particularly for visual object and visual spatial material. The CE may also be fractionated by the type of material being manipulated, particularly for verbal versus visuospatial material. Moreover, the type of processes subserved by the CE are not clearly defined in the WM model. The detailed task-analysis that is often required for neuroimaging studies for example is not supplied by the WM model. Though few other models fare any better (at least at a consensual level), neuroscientists clearly need a common theoretical framework with which to describe and dissociate executive (manipulation) processes.

*What is the future of the WM model?*

Many researchers believe that the WM model can be tested and developed without ever mapping it onto anatomy. This may or may not be the case. I believe nonetheless that future research should aim for a WM model that is mapped onto distinct brain regions, in order to make contact with the wealth of recent neuropsychological and neuroimaging data. This will be aided by a more detailed specification of the WM components, preferably through computational models that make explicit assumptions about the processes involved in the various working memory tasks (see Page & Henson, q.v.). A particularly important area of development is the functional decomposition of the concept of manipulation. This will address the question of whether frontal cortex is equipotential in its capacity for manipulation, or whether subregions exist with distinct functionality. Preliminary evidence exists for at least two levels of executive processes, with ventrolateral prefrontal cortex involved for comparison or selection of information in working memory, and dorsolateral prefrontal cortex involved only when additional processing is required (Owen, 1997; Petrides, 1994). In the more distant future, a successful WM model will need not only to map out functionally specialised brain regions, but also address the important question of how precisely these regions interact during performance of working memory tasks.

## References

- Awh, E., Jonides, J., Smith, E. E., Schumacher, E. H., Koeppel, R. A., & Katz, S. (1996). Dissociation of storage and rehearsal in verbal working memory. *Psychological Science*, 7, 25-31.
- Baddeley, A., & Wilson, B. (1988). Frontal amnesia and the dysexecutive syndrome. *Brain Cogn*, 7(2), 212-30.
- Baddeley, A. D. (1966). The capacity for generating information by randomization. *Quarterly Journal of Experimental Psychology*, 18, 119-129.
- Baddeley, A. D. (1986). *Working Memory*. Oxford : Oxford University Press.
- Baddeley, A. D., & Hitch, G. J. (1974). Working Memory. In G. Bower (Ed.), *Recent advances in learning and motivation* (8 ed., pp. 47-90). New York: Academic Press.
- Baker, S. C., Rogers, R. D., Owen, A. M., Frith, C. D., Dolan, R. J., Frackowiak, R. S., & Robbins, T. W. (1996). Neural systems engaged by planning: a PET study of the Tower of London task. *Neuropsychologia*, 34(6), 515-26.
- Barch, D. M., Braver, T. S., Nystrom, L. E., Forman, S. D., Noll, D. C., & Cohen, J. D. (1997). Dissociating working memory from task difficulty in human prefrontal cortex. *Neuropsychologia*, 35, 1373-1380.
- Belger, A., Puce, A., Krystal, J. H., Gore, J. C., Goldman-Rakic, P., & McCarthy, G. (1998). Dissociation of mnemonic and perceptual processes during spatial and nonspatial working memory using fMRI. *Hum Brain Mapp*, 6(1), 14-32.
- Besner, D. (1987). Phonology, lexical access in reading and articulatory suppression: a critical review. *The Quarterly Journal of Experimental Psychology*, 39A, 467-478.
- Bishop, D.V.M., & Robson, J. (1989). Unimpaired short-term memory and rhyme judgement in congenitally speechless individuals: implications for the notion of "articulatory coding". *The Quarterly Journal of Experimental Psychology*, 41A, 123-140.
- Bisiach, E. (1993). Mental representation in unilateral neglect and related disorders: the twentieth Bartlett Memorial Lecture. *Q J Exp Psychol [A]*, 46(3), 435-61.
- Braver, T. S., Cohen, J. D., Nystrom, L. E., Jonides, J., Smith, E. E., & Noll, D. C. (1997). A parametric study of prefrontal cortex involvement in human working memory. *Neuroimage*, 5, 49-62.
- Brodmann, K. (1909). *Vergleichende Lokalisationslehre der Grosshirnrinde in ihren Prinzipien dargestellt auf Grund des Zellenbaues*. Leipzig: Barth.
- Burgess, N., & Hitch, G. J. (in press). Memory for serial order: a network model of the phonological loop and its timing. *Psychological Review*.
- Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., & Smith, E. E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature*, 386, 604-608.
- Corbetta, M., Miezin, F. M., Shulman, G. L., & Petersen, S. (1993). A PET study of visuospatial attention. *The Journal of Neuroscience*, 13(3), 1202-1226.
- Coull, J. T., & Nobre, A. C. (1998). Where and when to pay attention: the neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. *Journal of Neuroscience*, 18, 7426-7435.

- Courtney, S. M., Ungerleider, L. G., Kell, K., & Haxby, J. V. (1997). Transient and sustained activity in a distributed neural system for human working memory. *Nature*, *386*, 608-611.
- Crowder, R. G., & Morton, J. (1969). Precategorical acoustic storage. *Perception and Psychophysics*, *5*, 365-373.
- De Renzi, E., & Nichelli, P. (1975). Verbal and non-verbal short-term memory impairment following hemispheric damage. *Cortex*, *11*, 341-353.
- Desimone, R., & Gross, C. G. (1979). Visual areas in the temporal cortex of the Macaque. *Brain Research*, *178*, 363-380.
- D'Esposito, M., Detre, J. A., Alsop, D. C., Shin, R. K., Atlas, S., & Grossman, M. (1995). The neural basis of the central executive system of working memory. *Nature*, *16*, 279-281.
- Fiez, J. A., Raife, E. A., Balota, D. A., Schwarz, J. P., Raichle, M. E., & Peterson, S. E. (1996). A positron emission tomography study of the short-term maintenance of verbal information. *The Journal of Neuroscience*, *16*, 808-822.
- Fletcher, P. C., Frith, C. D., Grasby, P. M., Shallice, T., Frackowiak, R. S. J., & Dolan, R. J. (1995). Brain systems for encoding and retrieval of auditory-verbal memory: an in vivo study in humans. *Brain*, *118*, 401-416.
- Frith, C. D., Friston, K. J., Liddle, P. F., & Frackowiak, R. S. J. (1991). Willed action and the prefrontal cortex in man: a study with PET. *Proceedings of the Royal Society of London B*, *244*, 241-246.
- Goldberg, T. E., Berman, K. F., Fleming, K., Ostrem, J., Van Horn, J. D., Esposito, G., Mattay, V. S., Gold, J. M., & Weinberger, D. R. (1998). Uncoupling Cognitive Workload and Prefrontal Cortical Physiology: A PET rCBF Study. *Neuroimage*, *7*(4), 296-303.
- Hanley, R. J., Young, A. W., & Pearson, N. A. (1991). Impairment of the visuo-spatial sketchpad. *The Quarterly Journal of Experimental Psychology*, *43A*, 101-125.
- Henson, R. N. A., Burgess, N., & Frith, C. D. (in press). Recoding, storage, rehearsal and grouping in verbal short-term memory: an fMRI study. *Neuropsychologia*.
- Jahanshahi, M., Dirnberger, G., Fuller, R., & Frith, C. D. (submitted). The role of dorsolateral prefrontal cortex in random number generation: a study with positron emission tomography. .
- Jonides, J., Reuter-Lorentz, P. A., Smith, E. E., Awh, E., Barnes, L. L., Drain, M., Glass, J., Lauber, E., Patalano, A. L., & Schumacher, E. (1996). Verbal and spatial working memory in humans. In D. Medin (Ed.), *The Psychology of Learning and Motivation* (pp. 43-88). London: Academic Press.
- Jonides, J., Schumacher, E. H., Smith, E. E., Koeppe, R. A., Awh, E., Reuter-Lorenz, P. A., Marshuetz, C., & Willis, C. R. (1998). The role of parietal cortex in verbal working memory. *The Journal of Neuroscience*, *18*, 5026-5034.
- Jonides, J., Schumacher, E. H., Smith, E. E., Lauber, E. J., Awh, E., Minoshima, S., & Koeppe, R. A. (1997). Verbal working memory load affects regional brain activation as measured by PET. *Journal of Cognitive Neuroscience*, *9*, 462-475.

- Jonides, J., Smith, E. E., Koeppe, R. A., Awh, E., Minoshima, S., & Mintum, M. (1993). Spatial working memory in humans as revealed by PET. *Nature*, *363*, 623-625.
- Klingberg, T. (1998). Concurrent performance of two working memory tasks: potential mechanisms of interference. *Cereb Cortex*, *8*(7), 593-601.
- Kosslyn, S. M., Alpert, N. M., Thompson, W. L., Maljkovic, V., Weise, S. B., Chabris, C. F., Hamilton, S. E., Rauch, S. L., & Buonanno, F. S. (1993). Visual mental imagery activates topographically organized visual cortex: PET investigations. *Journal of Cognitive Neuroscience*, *5*, 263-287.
- Levine, D. N., Wallach, J., & Farah, M. (1985). Two visual systems in mental imagery: dissociation of "what" and "where" in imagery disorders due to bilateral posterior cerebral lesions. *Neurology*, *35*, 1010-1018.
- Logie, R. H. (1994). *Visuo-spatial working memory*. London: Psychology Press.
- McCarthy, G., Puce, A., Constable, R. T., Krystal, J. H., Gore, J. C., & Goldman-Rakic, P. (1996). Activation of human prefrontal cortex during spatial and nonspatial working memory tasks measured by functional MRI. *Cerebral Cortex*, *6*, 600-611.
- McDowell, S., Whyte, J., & D'Esposito, M. (1997). Working memory impairments in traumatic brain injury: evidence from a dual-task paradigm. *Neuropsychologia*, *35*(10), 1341-53.
- Milner, A. D., & Goodale, M. A. (1993). Visual pathways to perception and action. In T. P. Hicks, S. Molotchnikoff, & T. Ono (Eds.), *Progress in brain research*. Amsterdam: Elsevier.
- Milner, B. (1982). Some cognitive effects of frontal-lobe lesions in man. *Philosophical Transactions of the Royal Society of London*, *298*, 211-226.
- Mishkin, M., Ungerleider, L. G., & Macko, K. A. (1983). Object vision and spatial vision: two cortical pathways. *Trends in Neuroscience*, *6*, 414-417.
- Owen, A. M. (1997). The functional organization of working memory processes within the human lateral frontal cortex: the contribution of functional neuroimaging. *European Journal of Neuroscience*, *9*, 1329-1339.
- Owen, A. M., Downes, J. J., Sahakian, B. J., Polkey, C. E., & Robbins, T. W. (1990). Planning and spatial working memory following frontal lobe lesions. *Neuropsychologia*, *28*, 1021-1034.
- Owen, A. M., Doyon, J., Petrides, M., & Evans, A. C. (1996a). Planning and spatial working memory: a positron emission tomography study in humans. *Eur J Neurosci*, *8*(2), 353-64.
- Owen, A. M., Milner, B., Petrides, M., & Evans, A. C. (1996b). Memory for object features versus memory for object location: A positron emission tomography study of encoding and retrieval processes. *P.N.A.S.*, *93*, 9212-9217.
- Owen, A. M., Stern, C. E., Look, R. B., Tracey, I., Rosen, B. R., & Petrides, M. (1998). Functional organization of spatial and nonspatial working memory processing within the human lateral frontal cortex. *Proc Natl Acad Sci U S A*, *95*(13), 7721-6.
- Paulesu, E., Frith, C. D., Bench, C. J., Bottini, P. M., Grasby, P. M., & Frackowiak, R. S. J. (1993a). Functional anatomy of working memory: the visuospatial "sketchpad". *Journal of Cerebral Blood Flow and Metabolism*, *13*, 551.

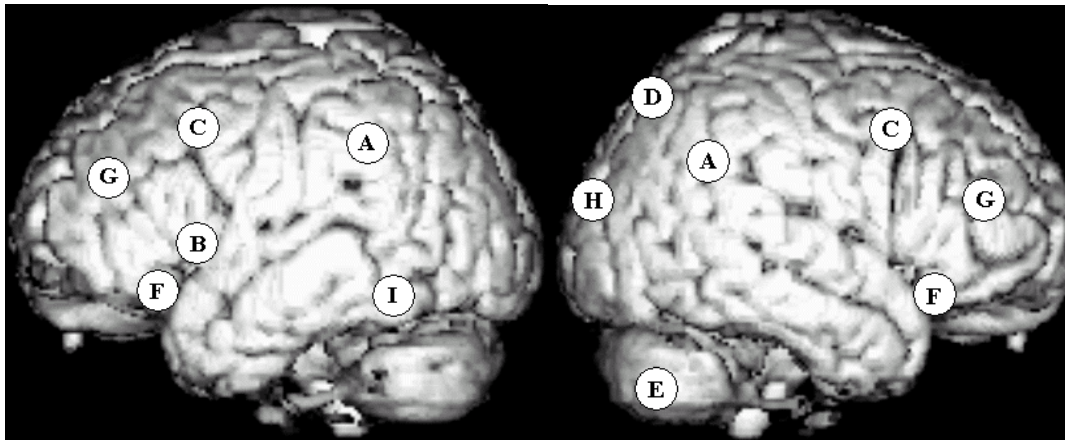


- Paulesu, E., Frith, C. D., & Frackowiak, R. S. J. (1993b). The neural correlates of the verbal component of working memory. *Nature*, *362*, 342-344.
- Petrides, M. (1994). Frontal lobes and working memory: evidence from investigations of the effects of cortical excisions in non-human primates. In F. Boller & J. Grafman (Eds.), *Handbook of Neuropsychology (Volume 9)* (pp. 59-82). Amsterdam: Elsevier Science.
- Petrides, M., Alivisatos, B., Evans, A., & Meyer, E. (1993a). Dissociation of human mid-dorsolateral from posterior dorsolateral frontal cortex in memory processing. *Proceedings of the National Academy of Science, USA*, *90*, 873-877.
- Petrides, M., Alivisatos, B., Meyer, E., & Evans, A. C. (1993b). Functional activation of the human frontal cortex during the performance of verbal working memory tasks. *Proceedings of the National Academy of Sciences, USA*, *90*, 878-882.
- Petrides, M., & Milner, B. (1982). Deficits in subject-ordered tasks after frontal- and temporal-lobe lesions in man. *Neuropsychologia*, *20*, 249-262.
- Samson, S., & Zatorre, R. J. (1992). Learning and retention of melodic and verbal information after unilateral temporal lobectomy. *Neuropsychologia*, *30*(9), 815-26.
- Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London*, *298*, 199-209.
- Shallice, T. (1988). *From neuropsychology to mental structure*. (Vol. 14). Cambridge: Cambridge University Press.
- Smith, E. E., & Jonides, J. (1997). Working memory: a view from neuroimaging. *Cognitive Psychology*, *33*, 5-42.
- Smith, E. E., Jonides, J., & Koeppel, R. A. (1996). Dissociating verbal and spatial working memory using PET. *Cerebral Cortex*, *6*, 11-20.
- Smith, E. E., & Jonides, J. J. (1994). Working memory in humans: Neuropsychological evidence. In M. Gazzaniga (Ed.), *The cognitive neurosciences*. Cambridge, MA: MIT Press.
- Smith, E. E., Jonides, J. J., Koeppel, R. A., Awh, E., Schumacher, E. H., & Minoshima, S. (1995). Spatial versus object working memory: PET investigations. *Journal of Cognitive Neuroscience*, *7*, 337-356.
- Smyrnis, N., Taira, M., Ashe, J., & Georgopoulos, A. P. (1992). Motor cortical activity in a memorized delay task. *Exp Brain Res*, *92*(1), 139-51.
- Sternberg, S. (1969). Memory scanning: mental processes revealed by reaction time experiments. *American Scientist*, *57*, 421-457.
- Vallar, G., & Baddeley, A. D. (1984). Fractionation of working memory: neuropsychological evidence for a phonological short-term store. *Journal of Verbal Learning and Verbal Behaviour*, *23*, 151-161.
- Vallar, G., DiBetta, A. M., & Silveri, M. C. (1997). The phonological short-term store-rehearsal system: patterns of impairment and neural correlates. *Neuropsychologia*, *35*, 795-812.
- Vallar, G., & Shallice, T. (1990). *Neuropsychological impairments of short-term memory*. Cambridge: Cambridge University Press.

- Warrington, E. K., & Rabin, P. (1971). Visual span and apprehension in patients with unilateral cerebral lesions. *Quarterly Journal of Experimental Psychology*, *23*, 423-431.
- Wilson, F. A. W., Scaldie, S. P., & Goldman-Rakic, P. S. (1993). Dissociation of object and spatial processing domains in primate prefrontal cortex. *Science*, *260*, 1955-1958.
- Zatorre, R. J., Evans, A. C., & Meyer, E. (1994). Neural mechanisms underlying melodic perception and memory for pitch. *J Neurosci*, *14*(4), 1908-19.

Figure 1: Approximate location of brain regions in left (top panel) and right (bottom panel) hemispheres typically associated with working memory. A=Inferior parietal, B=Broca's (inferior premotor), C=Premotor, D=Superior parietal, E=Cerebellum, F=Ventrolateral prefrontal, G=Dorsolateral prefrontal, H=anterior occipital, I=Inferior Temporal.

Figure 2: Examples of typical maintenance and manipulation tasks used in neuroimaging.



Typical Verbal Maintenance Task



Typical Spatial Maintenance Task



Typical Object Maintenance Task



Continuous Performance Task



N-back Task

