The Building Blocks of Cognition in the Brain:
A review of neuroimaging studies on working memory[*]

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Maintenance and manipulation of representations in working memory (WM) is the foundation for all cognitive processing. This paper will review neuroimaging studies focusing on the maintenance process of WM. In the first section, brain regions that increase activity during maintenance in WM are examined separately for each domain of information. Next, the controversy on the principle of functional organization of the prefrontal cortex, namely the hypotheses of domain-specificity vs. process-specificity. In the second section, the cognitive nature of the sustained prefrontal activity associated with WM will be examined. The differential functions of the dorsolateral and ventrolateral prefrontal cortex will be discussed in relation to mnemonic and extra-mnemonic processes. In the third section, the overlap between the mechanism of long-term and WM will be reviewed along with the introduction of the component process approach to cognitive neuroscience.

Key words : working memory, maintenance, long-term memory, fMRI

During the 1950-60s, burgeoning interest in computer science and information theory also influenced memory research resulting in attempts to develop models of information processing based on a computer analogy. The concept of short-term memory (STM) dissociable from long -term memory (LTM) stimulated research in cognitive psychology. The two most influential models of memory were developed by Waugh & Norman (1965) and Atkinson & Shiffrin (1968). These models postulated a short-term store for temporary, immediately accessible representations, separate from a long-term store for permanent memories, along with a rehearsal mechanism which enabled short-term representations to be transferred into the long-term store. STM was incorporated into a more complex framework of working memory (WM); a multi-component system capable of storage and processing (Baddeley & Hitch, 1974). With the development of neuroimaging techniques, the neural mechanism of WM became the focus of research during the 1990s.

The initial studies on the neural bases of WM were conducted with single-cell recordings in awake monkeys. Neurons in the vicinity of the principal sulcus showed sustained neural firing throughout the delay period of an oculomotor delayed-response task (Funahashi et al., 1989). Ensuing human neuroimaging studies during the early 1990s also found sustained prefrontal activations when information had to be held in WM in the absence of external stimulation. Based on these data, it was believed that the neurons in the prefrontal cortex (PFC) enabled short-term maintenance of mental representations. However, it has taken more than a decade to understand what the sustained prefrontal activations truly reflect. Without much contemplation, one might think that the prefrontal neural correlates reflect short-term storage of information during a delay. Only recently has it been demonstrated that prefrontal correlates of maintenance in WM reflect top-down executive control to keep goal-relevant representations active while the short term storage is supported by posterior neural systems involved in LTM and higher order sensory processing. The finding that the short-term storage of information is enabled by the contribution of posterior LTM systems led to an important realization in memory research that there are striking parallels between components of LTM and WM (Buckner & Koutsta al, 1998; Wagner, 1999). Neural substrates of encoding and retrieval were observed to be equivalent for both LTM and WM. More generally, the functional organization of memory in the brain does not seem to reflect the coarse distinction at the cognitive systems level (LTM vs. WM) but rather to the nature of component processes (e.g., encoding, retrieval) that constitute memory.

By no means is this view stating that there are no distinctions between LTM and WM. Of course, as is already well known, there also exists separable representations and processes that pertain only to WM or LTM, which may well be represented by distinct neural mechanisms, but what is being emphasized here is that there are interactions between these two memory systems both at the cognitive and neural levels.

WM is the basic foundation for all cognitive processing. Therefore, it is important to understand the mechanism of WM first in order to understand more complex information processing. This paper will review the early neuroimaging literature on the neural bases of WM focusing on simple maintenance.

The Neural Bases of WM Maintenance

Which brain regions work to keep information online in WM ?

Early studies of human WM focused on the locus of neural activity corresponding to online maintenance of information based on the widely accepted model of WM (Baddeley & Hitch, 1974). In this section, the neural bases of each sub-component of the WM system will be reviewed.

Verbal domain. Based on Baddeley & Hitch's model of WM (1974), verbal WM consists of the short-term phonological store and the subvocal rehearsal process. In support of this model, many studies found evidence of separate neural correlates for each sub-component of verbal WM. A positron emission tomography (PET) study by Paulesu et al. (1993) used a delayed letter recognition task and three control tasks; rhyme judgment, no delay letter recognition and similarity judgment of visual shapes. Neural activation related to phonological in contrast to visual processing were found mainly in the inferior frontal gyrus (IFG) near Broca's area, the supplementary motor area (SMA), the primary motor area, and the supramarginal gyrus (SMG). When the activation from the rhyming task was subtracted from the phonological recognition task, only the SMG remained significantly active. This result suggests that subvocal rehearsal is supported by frontal regions related to speech production while the short-term phonological store relates to the left inferior parietal cortex. This finding was replicated by another PET study by Awh and colleagues (1996). In their first experiment, when the activity from a delayed letter recognition task was contrasted with a no delay letter recognition task, Broca's area, the premotor area, the SMA and the left SMG was significantly activated. In their second experiment, a 2-back letter WM task was used along with two

control conditions; a search control and a rehearsal control. During the search control condition, subjects saw a sequence of letters as in the memory condition, but had to decide whether or not each letter matched a single target letter specified at the beginning of the experiment. The rehearsal control task required subjects to silently rehearse each letter presented. When the activation from the search control task was subtracted from that of the memory condition, left hemisphere speech regions and the posterior parietal cortex (PPC) along with the right posterior and superior parietal cortex (SPC) and the SMA was activated. When the activation from the rehearsal control was subtracted from the memory condition, activation in the PPC remained active, but the frontal regions did not. This finding can be interpreted as indicating that the phonological storage component corresponds to activations in the PPC, whereas the subvocal rehearsal process is associated with speech related areas of the IFG. The results from early studies of verbal WM converged on the same conclusion on the neural correlates of verbal WM and its component systems. More recent studies which provide information on what these neural activations reflect will be discussed in later sections of the paper.

Visuospatial domain. Baddeley's original model of WM does not describe a rehearsal mechanism for visuospatial information. In revision of Baddeley's model, Logie (1995) decomposed the visuospatial sketchpad into the 'visual cache' for non-spatial visual storage and 'visual scribe' for spatial rehearsal. Note that the rehearsal mechanism of the visual scribe applies only to visuospatial information but not to non-spatial visual information. Baddeley and colleagues (1986) proposed that rehearsal in spatial WM might rely on implicit programs for eye movements. Although eye movements have been shown to disrupt maintenance of spatial information, it has also been found that spatially directed arm movements can also interfere with spatial WM, implicating that a more general attentional mechanism underlies spatial rehearsal. On the other hand, non-spatial, visual information such as features, abstract shapes or patterns lacks a rehearsal mechanism (Washburn & Astur, 1998). Human behavioral studies show that subjects resort to verbalization or semantic strategies for maintenance of these non-spatial visual information (even though they are hard to verbalize or semantically label) owing to the lack of rehearsal mechanism (Golby et al., 2001; Postle et al., 2005).

Jonides and colleagues (1993) reported that spatial WM was associated with activations in the right prefrontal, occipital, parietal, and premotor cortex. The same group conducted another study contrasting delayed-recognition of

objects and spatial locations (Smith et al., 1995). The spatial task primarily activated right hemisphere regions (occipital, parietal and prefrontal areas) whereas the object task revealed activations mainly in the left inferior temporal and parietal regions. From these observations, they concluded that there may be different WM buffers for object and spatial information.

Courtney et al. (1996; 1997; 1998) reported dissociable neural correlates of object (face) and spatial WM in the PFC. In their reports, delayed-recognition of faces resulted in sustained activation in the PFC, and fusiform gyrus (FG) whereas the spatial WM task was associated with activations in the parietal lobe and the superior frontal sulcus (SFS). Based on these results, the authors claimed that the neural mechanisms of visual object and spatial WM are dissociable. Awh and colleagues reported a series of studies (1998; 1999; 2000; 2001) on the cognitive and neural mechanism of spatial WM. These researchers argue that active maintenance of spatial information is accomplished by means of focal shifts of spatial attention to memorized locations. Making use of the fact that orienting of spatial attention causes improvements in visual processing at attended locations in space, Awh et al hypothesized that if spatial attention is involved in spatial rehearsal, maintaining a spatial location in WM will cause similar facilitation of visual

processing at the location being rehearsed. Consistent with their hypothesis, Awh et al. (1999, 2000) showed that the visual areas in the occipital lobe showed modulation of activity similar to the effect of spatial attention during a spatial WM task. Furthermore, using an interference paradigm, Awh et al. (1998) showed that when subjects were forced to direct attention away from the locations held in WM, their spatial WM was impaired. This interference effect indicates that spatial orienting is a necessary part of spatial WM rather than being just a correlate of spatial WM.

On the other hand, maintenance of familiar visual objects activates category-selective regions of the inferior temporal (IT) cortex along with the lateral PFC (Jha & McCarthy, 2000; Druzgal & D'Esposito, 2003; Ranganath et al., 2004). The fusiform face area (FFA) and the parahippocampal place area (PPA) have been consistently found to activate along with the lateral PFC during online maintenance of faces and houses, respectively (Jha & McCarthy, 2000; Druzgal & D'Esposito, 2003; Ranganath et al., 2004). In these studies, the delay period activations were stronger and more sustained in the lateral PFC compared to IT regions suggesting a possible distinction between the function of these activations. Several lines of evidence show that the nature of the delay period activation of the PFC differs qualitatively

from that of posterior cortices in that the PFC activity reflects executive control over representations held in WM. Miller and Cohen's theory suggests that the PFC plays an executive role in protecting WM representations against distraction (Miller & Cohen, 2001) while representations are processed in WM. As an inquiry of the mechanism of protection against distraction, Sakai and colleagues (2002) proposed that the dorsolateral PFC (DLPFC) may enable the transformation of memory traces into representations that are more resistant to distraction by interacting with posterior neural regions. This study showed that sustained activation of the DLPFC during the delay period of a WM task predicts successful maintenance of memory traces in the face of distraction. Furthermore, when the magnitude of the DLPFC activity was high, the magnitudes of activation in other regions showing sustained delay-period activity were more tightly correlated. The authors interpreted this result as indicating that optimal engagement of the DLPFC provides top-down input to other areas of the brain thereby protecting memory traces against distraction. In line with this model, Kessler and Kiefer (2005) proposed that the PFC maintains links (or addresses) to the posterior locations where memory representations are stored, to reactivate goal-relevant representations when distractors cause interference. A follow up study

by the same authors (Sakai and Passingham, 2004) demonstrated a modulation of prefrontal retrieval phase activity depending on the degree of interference; a stronger activation of the PFC was observed during conditions requiring more intense interference resolution. Therefore, in addition to their initial hypothesis of active maintenance during delay, an interference resolution mechanism during the retrieval phase was included in their hypothesis of prefrontal function during WM.

In short, these theories and experimental evidence support the idea that the delay period activity of the PFC reflect an executive control signal to prevent information from decay or interference while these representations may be stored in posterior regions of the brain.

Principles of functional organization of WM in the PFC

So far we have reviewed the findings from earlier neuroimaging studies of WM. A shrewd reader may already have noticed that there must have been a heated debate on how WM is organized in the PFC. Two divergent positions have been established which fundamentally differ in terms of the precise functions ascribed to the lateral PFC. Domain-specificity and process-specificity are the two competing hypotheses on the functional organization of the PFC.

Domain-specificity versus process-specificity.
Single cell recordings of the monkey brain during WM tasks showed that different neurons fired for different types of stimuli. The neurons that were active during spatial WM tasks tended to be located in more dorsal regions of the frontal lobe whereas neurons that were related to object WM were located more ventrally (Goldman- Rakic, 1987). From these results came the hypothesis of 'domain-specificity' of WM organization in the PFC. Domain-specificity states that PFC regions can be functionally organized by the type (or domain) of information maintained in WM. Numerous studies have been conducted to test the validity of the domain-specific model of WM in the human PFC. Based on initial findings from monkeys, the domain-specificity hypothesis predicted that spatial WM involves the DLPFC and non-spatial/visual WM involves the VLPFC. This model has theoretical appeal because it preserves the topographical dorsal-ventral organization of 'what' and 'where' (or how) visual pathways and extends it to the PFC.

An alternative framework for understanding the functional organization of WM in the PFC is 'process-specificity' (Petrides, 1994). According to this model, basic memory functions of storage and immediate processing of perceived or retrieved information are carried out in the sensory cortex and the posterior association areas.

The frontal lobes receive and act upon this information either via (1) bi-directional connections between the posterior association areas and the VLPFC (which in turn projects to the DLPFC) or via (2) direct connections between DLPFC and the medial temporal lobes (MTL). In other words, the VLPFC constitutes the first-level of interaction between posterior cortical regions and the entire lateral PFC. In this respect, the VLPFC is assumed to be critical for second order memory processes such as, judgments about the occurrence or non-occurrence of remembered stimuli. In contrast, the DLPFC is assumed to provide a third level of processing, such as monitoring and manipulation of remembered information. Therefore, this process-specific model states that WM processes within the PFC are hierarchically organized according to the nature of cognitive processing.

Many studies have been conducted to investigate this issue. In D'Esposito and colleagues' (1998) meta-analysis, there was no evidence supporting a dorsal/ventral segregation of the PFC depending on the type of material. However, they found a tendency of hemispheric lateralization by stimulus type in the VLPFC. The VLPFC showed right lateralization for spatial material and left lateralization for non-spatial material, whereas the DLPFC tended to show bilateral or right lateralized activation

regardless of stimulus type. Another meta-analysis by Wager and Smith (2003) reported that simple maintenance of verbal material induced consistent left lateralized activation in the VLPFC. However, segregation of spatial and non-spatial representations was not found in the PFC but mainly in the SPC and IT cortex, respectively.

From a series of within-subject experiments, Nystrom et al. (2000) tested whether there are distinct neural activity between: (1) letters vs. abstract shapes, (2) letters vs. spatial locations, and (3) shapes vs. spatial locations. Although regions of activation are not distinguished clearly along either the left/right or dorsal/ventral dimensions, there was one region in the posterior part SFS showing selective activation for spatial information. However, its activity also increased as WM loads for letters and shapes increased, thus this region cannot be solely active for maintenance of spatial information.

Additional evidence that go against domain-specificity comes from electrophysiological experiments. In contrast to earlier single-cell recording studies, follow-up studies found that 1) many neurons show selectivity for both object and spatial stimuli (Rainer et al., 1998), 2) neurons that were tuned only to spatial or non-spatial aspects of the stimulus were found to be intermixed in the lateral PFC (Postle & D 'Esposito, 1999), 3) stimulus selectivity of the neurons change adaptively according to task demand and context (Rao et al., 1997; Assad et al., 2000). Altogether, these findings pose a challenge to the hypothesis of domain-specificity.

On the contrary, the process-specificity hypothesis accumulated a large body of supporting evidence. Owen and colleagues (1996; 1998; 1999) provided empirical support for a dorsal-ventral organization by process in human PFC initially with blocked fMRI experiments. Follow-up studies based on event-related fMRI experiments enabled the identification of neural activations related to the processes that occur during specific phases of a given trial, resolving issues remaining from previous studies and providing further support for the process-specific model. For example, in D 'Esposito, Postle et al. (1999) contrasted two types of delayed response tasks, during which subjects either retained a sequence of letters (maintenance) or reordered them in alphabetical order (manipulation) across a delay period. Consistent with the process-specific model, activity during the delay period was found in both DLPFC and VLPFC during both types of trials, but only DLPFC showed greater activity for manipulation compared to maintenance. Altogether, a large body of evidence seems to favor process-specificity more than domain-specificity. However, two major deviations from Petrides ' original model should be noted. First, not only the VLPFC but also

the DLPFC was involved in simple maintenance. (D'Esposito, Postle, Ballard et al. 1999; Courtney et al., 1997; Zarahn et al., 1999). Secondly, the role of the VLPFC in maintenance of spatial information also deviates from the proposal of the Petrides original model. Spatial maintenance more commonly recruited the SFS rather than the VLPFC (Courtney et al., 1996; Rowe et al., 2000; Zarahn et al., 1999). With ongoing revision and development, the process-oriented model of the organization of the PFC became a dominant framework expanding in scope to include more complex functions of WM and cognitive control functions of the anterior portions of the PFC.

What does sustained delay period PFC activity truly reflect?

We have seen that WM maintenance is associated with sustained activity in the PFC. The next critical question in the cognitive neuroscience of WM relates to the interpretation of sustained delay-period PFC activity. Is this activity purely mnemonic in nature? Does it reflect temporary storage? How does the functions of the DLPFC and VLPFC differ?

In relation to this issue, Petrides (1994) and colleagues initially posited an extra-mnemonic (i.e., executive) role of the DLPFC and a mnemonic role of the VLPFC; i.e., DLPFC was thought to monitor and manipulate (or process) representations in WM while not being directly involved in maintaining or storing information. More recent studies demonstrated that the DLPFC also supports mnemonic processes such as simple maintenance of information in WM. One approach researchers adopted to investigate this issue was to determine whether activations in the DLPFC were modulated by memory load. The basic assumption underlying this approach is that a mnemonic signal related to maintenance will increase with increasing memory load whereas an extra-mnemonic signal will be less sensitive to variation in memory load.

Brain activity reflecting mnemonic vs. extra-mnemonic WM processes

Verbal domain. In order to determine whether or not the delay-period activation of the DLPFC reflects a mnemonic process, Postle, Berger and colleagues (1999) examined neural activations observed during 'maintenance' and 'maintenance plus manipulation' conditions. In the 'maintenance' condition, the subject's task was to maintain a sequence of letters in the order in which they were presented. In the 'maintenance plus manipulation' condition, the subject had to rearrange the letters in alphabetical order while holding them in WM. The activity in the DLPFC was sustained during

sustained maintenance but the effect of memory load did not span the entire delay interval, whereas the sustained activity in the perisylvian cortex showed an effect of memory load throughout the delay. Only the DLPFC showed differential activity between conditions. Based on these observations, the authors concluded that the role of the DLPFC is extra-mnenomic, i.e., not to maintain stimuli, but to manipulate and process representations held in WM. However, the authors' conclusion that the DLPFC is not involved in maintenance is questionable. First, given that the capacity for verbal information is likely to be larger than 5 letters, the memory load tested (5 vs. 2 letters) may not have been large enough to yield a significant effect. Secondly, the authors disregarded the effect of memory load during the early phases of the delay in the DLPFC. The effect of memory load in the DLPFC was present during the delay but just didn't span the entire delay interval. In this circumstance, one cannot reject the possibility that the DLPFC is involved in simple maintenance. Using a delayed letter recognition task (memory load: 1-8 letters), Rypma and colleagues (2002) examined effects of memory load during different phases of a single trial. A linear increase in DLPFC activation as a function of memory load was found during the delay (especially during the early phase) and response phases of the trial. (VLPFC showed a linear

decrease as a function of memory load during the encoding phase and a linear increase during the delay and response phases.) This study therefore demonstrates that the DLPFC *is* involved in simple maintenance along with the VLPFC. Similar results were found in Habeck et al. (2005). Further, lesion studies demonstrated the causal link between the PFC and rehearsal and between posterior regions and short-term storage (D'Esposito & Postle, 1999; Gruber & von Cramon, 2003). D'Esposito & Postle (1999) tested patients on delayed-response and short- term span tasks. Delayed response tasks using a prolonged delay require the process of rehearsal more than short-term storage. On the other hand, short-term span tasks (immediate recall paradigms) mainly measure the capacity of storage while minimizing the need to rehearse. The authors found a double dissociation between prefrontal and posterior lesions for performance of these tasks. Patients with PFC lesions were impaired in maintenance over a temporal delay (especially when the delay was filled with distractors) but not in the span of immediate recall. On the contrary, posterior lesions impaired WM span but not rehearsal. Considered together with the evidence that the capacity limit of WM is reflected in activation patterns of the posterior parietal lobes (Todd and Marois, 2004), the storage component of WM seems to depend more on the posterior regions of the brain. More

recently, Gruber & von Cramon (2003) used a domain-specific interference paradigm and demonstrated the necessity of the DLPFC (and the inferior parietal cortex) for non-articulatory maintenance of phonological information. In contrast, the functioning of the left premotor area was necessary for subvocal rehearsal. These studies clearly demonstrate the importance and causal contribution of the DLPFC for simple maintenance.

Visuospatial domain. Using delayed-recognition task of faces (load 1-3), Jha and McCarthy (2000) investigated the sensitivity of delay-period brain activity to variation in memory load. They used long delay intervals (15, 24 seconds) in order to exclude confounding effects from sensorimotor processes that occur before and after the delay. Many regions, including the lateral PFC, the cingulate cortex, the intraparietal sulcus (IPS), and FFA showed load sensitive activations during delay. However, none of these memory load effects was significant during the later portions of the delay. The middle frontal gyrus (MFG) showed the largest increase in activation along with a latency shift with increasing memory load. These results are similar to the results from Postle, Berger et al. (1999)'s in that the memory load was prominent only in the early period of the delay. In another study using a delayed face

recognition paradigm (memory load 1-4), Druzgal and D'Esposito (2003) investigated the relative contributions of the lateral PFC and FFA. The PFC regions of interest (MFG and IFG) showed a memory load effect during all phases of the task. The memory load effect on PFC activation showed a step function, showing the largest increase when the load changed from 2 faces to 3 faces. The FFA also showed a memory load effect during the encoding and delay phases of the task. The analysis of time-to-peak activity revealed that the peak activity of the FFA preceded that of the PFC during encoding, whereas the peak activity of the PFC preceded that of the FFA during the retrieval phase. These results were interpreted as indicating that the encoding process occurs in a bottom-up fashion from sensory systems towards the PFC, whereas the retrieval and decision process follows a top-down direction from the PFC to lower level systems. The authors proposed a model of face WM in which the PFC biases activity in the posterior uni-modal association cortex in favor of behaviorally relevant representations.

Leung et al. (2002, 2004) used event-related fMRI to examine the effect of memory load and the duration of delay on the activity of the spatial WM circuit. The neural activations reflecting spatial maintenance were found in the precentral sulcus, the premotor area, the MFG

and IFG, the parietal-occipital junction, and the lateral occipital regions. Among these areas, the MFG showed the most sustained activity throughout the delay interval tested up to 24 seconds. The effect of memory load in the PFC resulted in an inverted U shaped function, consisting of a positive slope from load 1 to 3 and a negative slope from load 3 to 4. The authors interpreted this pattern as reflecting a processing limitation in spatial maintenance as memory load reaches the limit of capacity.

Putting pieces together

The second generation of WM studies aimed to understand the nature of sustained brain activity correlated with maintenance in WM. The mechanism of maintaining information online can be thought to be composed of both mnemonic and extra-mnemonic processes. Sustained delay-period activity of the PFC was found to reflect rehearsal and top-down control signals to keep representations active in WM (i.e., active maintenance) while not being the locus of temporary storage, per se. In addition, studies aimed to examine whether sustained DLPFC activity during WM delay was purely extra-mnemonic by examining the effect of memory load on delay period activity of the DLPFC. The pattern of memory load effects was not consistent across studies. Some studies found

a step function (Smith et al., 1998; Cohen et al, 1997; Druzgal and D'Esposito, 2003; Jha & McCarthy, 2000) while others reported a linear function (Rypma et al., 2002; Nystrom et al., 2000) or an inverted U (Leung et al., 2004) pattern. There may be several reasons for the inconsistency. The first is the range of memory load tested with respect to the capacity limit. The effect of memory load can differ depending on whether or not the range of memory load is within, approaching or exceeding capacity. Secondly, the effect of memory load can differ depending on the type of stimulus, since the capacity limit differs for different types of stimuli. For example, the capacity of verbal stimuli is about 7 ± 2 whereas the limit of visual stimuli is about 4 (Leung et al., 2004). Thirdly, the length of delay can be an important factor influencing memory load effects. If the delay interval is too short, processes related to encoding and response preparation can confound maintenance related activations, whereas if the delay interval is too long, the nature of the maintenance process may change towards the end of delay. For example, as the delay period is lengthened, representations may gradually change from being visual, holistic and icon-like to being more analytical, symbolic, verbalizable and more resistant to decay (Haxby et al., 1995; Barch et al., 1997). Moreover, after a certain amount of rehearsal, temporary

representations may be incidentally encoded into LTM, deviating from the maintenance process in WM.

Rethinking the structure and representations of WM. Having examined the neural mechanism of WM maintenance, several findings point to a need to revise Baddeley's widely-accepted, multi-modal WM model. First, it seems unnecessary to combine visual and spatial WM into one visuospatial sketchpad. Although Logie's revised model divides the visuospatial sketchpad into subcomponents of the visual cache and visual scribe, this revision still does not fully capture the distinctions between visual and spatial WM. Spatial WM should be a separate system with an attention-based rehearsal mechanism in which storage and rehearsal processes are intertwined. Non-spatial/visual WM should be a separate system having a storage mechanism dependent on LTM systems while lacking a rehearsal mechanism of its own. Secondly, the possibility of a stimulus being encoded into multiple representations in different modalities should be accommodated in the WM system. There are ubiquitous examples of this possibility, a prominent one being the dual coding of visual information; i.e., visual information are coded into two representations, one visual and the other verbal (Paivio, 1971). Third, it should be emphasized that the modality in which the stimulus is presented may or may not correspond to the modality in which it will be processed in WM. In general, stimuli will be coded into WM in a way that maximizes processing efficiency and reduce cognitive load. For example, a sequence of famous people's faces is more likely to be maintained as verbal representations (by rehearsing their names) rather than as visual representations. Lastly, it should also be noted that the modality of representations may not be a discrete categorical dimension as commonly assumed but rather a continuous dimension of 'relative verbalizability'. This issue was raised by several studies demonstrating that even abstract, unfamiliar stimuli is verbally rehearsed and that the ease of verbalizability determines the degree of hemispheric lateralization of neural activations (Golby et al., 2001; Wagner et al., 1998; Postle et al, 2005).

Overlapping mechanisms of WM and LTM

When Waugh and Norman published their influential paper in 1965, the distinction between memory functions for temporary and permanent representations became a major issue in cognitive psychology. The difference between WM and LTM was emphasized and the two cognitive systems were studied independently from each other. However, after several decades

of neuroimaging research, parallels between neural mechanisms of LTM and WM are becoming apparent. Not only are the neural substrates of encoding and retrieval similar for LTM and WM (Ranganath et al., 2003), the effect of stimulus modality on the pattern of brain activity is also similar between memory systems. During encoding, activation of the VLPFC and the MTL is lateralized depending on the modality of the representation being encoded into both WM and LTM (Kelley et al., 1998; Campo et al., 2005). Maintenance of perceived and recalled information depends on the same mechanism as that of WM which implies that memory recalled from LTM practically becomes a representation held in WM (Ranganath et al., 2003; 2004). During retrieval of representations from both LTM and WM, the dorsal and anterior lateral PFC regions are activated without showing lateralization of activation by material-specificity (Braver et al., 2001). Based on these findings, several researchers propose that prefrontal activation during episodic memory formation may reflect the recruitment of WM processes in the service of episodic encoding and retrieval (Wagner, 1999; Buckner & Koutstaal, 1998). In a review of neuroimaging studies of memory, Wagner highlighted the relationship between LTM and WM in encoding and retrieval (Wagner, 1999). Wagner stated that (1) activation of the VLPFC during episodic

encoding may reflect the contribution of material-specific maintenance mechanisms of WM (2) activations of the DLPFC and anterior PFC during episodic retrieval may reflect the involvement of material-independent manipulation processes of WM. Indeed, episodic encoding and maintenance in WM both recruit the VLPFC in a lateralized pattern depending on stimulus modality (left lateralization for verbal and right lateralization for visuospatial material). Also, the overlap between the mechanism of episodic retrieval and executive processes of WM makes sense since attempts to remember the detailed context of a past event are likely to involve monitoring and evaluating the products of retrieval. Taken together, focusing on the component processes of cognition (e.g., encoding verbalizable information), rather than looking for global distinctions between high level cognitive concepts (e.g., LTM and WM) leads to more parsimonious models of the functional organization of the brain.

The component process approach. The importance of working with simple cognitive processes has been emphasized by Johnson and colleagues (2003). The authors suggest a component process approach of functional localization in which a simple component cognitive operation is mapped onto its neural correlate. Indeed the lack of clarity about the functional organization of the

PFC is partly due to the complex nature of the tasks that have been used in the literature. Johnson and colleagues' 'Multiple-entry Modular Memory' (MEM) model exemplifies a process-oriented approach to memory subsystems in which the primary descriptive units are simple cognitive actions, such as refreshing, rehearsing, reactivating, retrieving, discovering, initiating, noting, and shifting. These component processes are the building blocks for WM, LTM and other higher-order cognitive functions. Based on this approach, Johnson et al. (2003) tested existing models of the functional organization of the PFC. The authors found dissociable neural activations for component process of 'refreshing' versus 'noting' which was further modulated by stimulus type leading to a conclusion that the PFC is organized by a specific combination of component process and material type.

Another example that nicely demonstrates the benefits of the component process approach comes from neuroimaging studies of episodic retrieval. Several researchers found differential activation patterns for 'free recall' versus 'cued recall' (or 'recognition'). Greater DLPFC and anterior PFC activation was found for free recall whereas greater VLPFC activation was observed for cued recall (or recognition). Considering that the free recall requires more monitoring and evaluation of one's own mnemonic activity compared to cued recall or recognition, the

differential pattern for different types of retrieval stresses how analyzing the nature of component processes can be useful in examining the function al organization of the brain.

Future application of the component process approach may reveal that the common regions of the frontal lobe recruited by diverse cognitive demands can be further specified by dissociable networks correlated with distinct component processes of cognition.

Conclusions

This paper examined the literature on the neural mechanisms of maintenance in WM. A critical distinction was made between active maintenance and temporary storage. Online maintenance of representations in WM is accomplished by coordination between posterior neural systems responsible for temporary storage and prefrontal regions providing top-down control to keep posterior representations active.

The flip side of this observation reveals the contribution of LTM to short-term storage demonstrating that the mechanism of WM and LTM are not independent. WM also contributes to LTM formation, for example, neural systems activated during the encoding process of WM are also involved in episodic encoding processes of LTM. Also, neural correlates of manipulation and monitoring in WM also overlap with

monitoring and evaluating information retrieved from LTM. In other words, neural mechanisms of component processes of mnemonic and extra-mnemonic functions are engaged flexibly regardless of the distinction between WM and LTM at the cognitive systems level.

What is apparent from these observations is that efficiency and flexibility governs the functional architecture of the brain. The brain works in a way that maximizes efficiency by taking advantage of the remarkable flexibility of our neural systems. For example, when encountered with information to be held in mind, the brain looks for familiarity or any meaningful pattern to form an efficient mental representation in order to reduce the dimension of the information to be coded. Another example comes from the ubiquitous use of verbalization. The brain tries to maximize the use of language which provides a powerful means to identify and label bits of information even when the stimulus is presented in a hard to verbalize format. Also, each neural system seems to have a specialized role in certain aspects of processing while having the flexibility to acquire new processing capacities and help out when needed. The evidence considered in this paper altogether leads to a conclusion that there are separable neural mechanisms for component processes of cognition which are flexibly recruited to maximize efficiency in meeting the demands of diverse cognitive contexts. This paper serves as the first in a series of reviews that will be published on the cognitive neuroscience of WM and executive processing. The next paper will review neuroimaging studies of executive WM and cognitive control.

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인지 과정의 기초적 신경 기제:
작업 기억에 대한 뇌 영상 연구 개관

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작업 기억의 정보 유지 및 조작 기능은 모든 인지적 정보 처리의 기반이다. 이 논문은 작업 기억의 정보 유지 기능과 관련한 뇌 영상 연구들에 대한 개관이다. 본 논문의 첫 번째 주제는 정보의 종류(언어적, 시각적, 공간적 정보)에 따라 작업 기억의 가장 기초적인 과제인 '정보 유지(maintenance)' 기능과 관련하여 활동이 증가하는 뇌 영역에 대한 고찰이다. 또한, 전두엽의 기능적 조직화(functional organization)의 원리에 대한 논쟁(domain-specificity vs. process-specificity)과 각 논지를 지지하는 실험적 증거들이 함께 소개된다. 두 번째 주제는 작업 기억에 정보가 유지되는 동안 지속적으로 활동하는 전두엽의 뇌 신호의 특성을 살펴보는 것이다. 기억(mnemonic) 및 기억-외적(extra-mnemonic) 정보 처리와 관련하여 상측 외전두엽과 하측 외전두엽 간의 서로 구별되는 특성에 대한 논의를 정리해 볼 것이다. 세 번째 주제는 장기 기억과 작업 기억 의 기제 간의 공통점과 공유되는 신경학적 기제들에 대한 논의이다. 이와 함께 인지 과정의 신경적 기반에 대한 연구에서 복잡한 인지 과정의 세부적 구성 요소(micro component process)를 단위로 실험하는 인지 신경과학의 접근 방법이 소개된다.

주제어 : 작업 기억, 유지 기능, 장기 기억, 기능성 자기 공명 영상