

Pessoa, L. & Ungerleider, L.G. (2004). Top-down mechanisms for working memory and attentional processes. In M. S. Gazzaniga (Ed.), *The New Cognitive Neurosciences, 3rd Edition*, pp. 919-930, MIT Press.

Top-down Mechanisms for Working Memory and Attentional Processes

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Acknowledgements

We wish to thank David Sturman for assistance in the preparation of the manuscript. The authors' research was supported by the National Institute of Mental Health Intramural Research Program.

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Introduction

Maintaining information in working memory (WM), such as when we rehearse the route to a restaurant, as well as directing attention, such as when we search for a familiar face in the crowd, constitute fundamental cognitive capabilities of the primate brain. Both activities are considered “top-down”, as they depend on goal-directed processes that rely on previous knowledge, and not incoming sensory stimulation. Top-down processes should be contrasted to “bottom-up” ones, such as the deployment of attention in reaction to a sudden movement in the periphery of the visual field, which is a sensory-driven, reflexive process. Understanding the neural bases of top-down control involved in WM and visual attention, is among the most challenging goals of cognitive neuroscience. In this chapter, we will review neuroimaging studies that have investigated this question in the past decade or so. The picture emerging from this line of research points to considerable overlap between the neural substrates that control WM and those that control attention. At the same time, there is growing evidence that the control structures for attention differ according to the type of attentive process, in that goal-directed and reflexive attention appear to be mediated by separable networks of frontal and parietal regions.

The Control of Working Memory

Working memory refers to the process of actively maintaining relevant information in mind for brief periods of time. In a typical WM paradigm, on each trial, a sample stimulus is presented, followed by a delay of several seconds, and then a test stimulus is shown. The subject’s task is to indicate whether or not the test stimulus matches the sample. This type of WM task requires primarily maintenance operations, in which the short-term memory store is emptied after each trial.

WM has been extensively investigated in monkeys, where the importance of prefrontal regions has been established. Lesions of the dorsolateral prefrontal cortex, especially within and surrounding the principal sulcus (Brodmann area [BA] 46), greatly impair WM performance (Goldman and Rosvold, 1970; Bauer and Fuster, 1976; Funahashi et al., 1993). At the same time, results from single-cell studies have demonstrated that prefrontal neurons show stimulus-specific sustained discharge during the delay period (Fuster and Alexander, 1971; Kubota and Niki, 1971); for reviews, see (Goldman-Rakic, 1995; Fuster, 1997). This sustained activity has been interpreted to be the neural correlate of maintenance processes that take place during the delay, and thus has been taken to be the neural signature of WM (Fuster, 2001). Sustained activity during the delay interval is not confined, however, to the prefrontal cortex. Depending on the type of stimulus, cells with sustained responses have been found in the inferior temporal cortex (for visual patterns or color stimuli; Fuster and Jervey, 1982; Chelazzi et al., 1998), the parietal cortex (for visuospatial stimuli; Chafee and Goldman-Rakic, 1998, 2000), and the premotor cortex (for particular motor responses; Bruce and Goldberg, 1985).

In tasks similar to those used in monkeys, functional brain imaging studies in humans have also provided evidence supporting the role of prefrontal regions in WM by demonstrating sustained signals during delay intervals (Cohen et al., 1997; Courtney et al., 1997); for review, see (D’Esposito, 2001). The prefrontal regions that show this activity include the middle frontal gyrus (BA 9/46), thought to be the human homologue of the principal sulcus region of dorsolateral prefrontal cortex (DLPFC) in monkeys, as well as more ventral regions in the inferior frontal gyrus (BA 44, 45, 47). As in monkeys, several studies in humans have shown that regions outside of prefrontal cortex also exhibit sustained delay activity, including the inferior temporal cortex (Courtney et al., 1998), the parietal cortex (D’Esposito et al., 1998; Jonides et al., 1998; Rowe et al., 2000), and the premotor cortex (Courtney et al., 1998; Petit et al., 1998).

What determines successful performance in a WM task? Results from single-cell studies help clarify how neural activity may contribute to behavioral performance. It has been reported

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that, on trials in which monkeys make errors, activity during the delay interval fails to be sustained (Fuster, 1973; Rosenkilde et al., 1981; Watanabe, 1986a, b; Funahashi et al., 1989), suggesting that activity during the delay bridges the gap between the sample and test stimuli to enable monkeys to correctly match them. However, the interpretation of the precise relationship between delay activity and performance as investigated in single-cell studies is often problematic. For example, the analysis of error trials has been typically assessed on a very limited number of such trials. Monkeys are generally trained to perform at very high levels of performance (90% correct or higher), such that only very few error trials are available for a given cell, largely precluding a quantitative assessment of the relationship between neuronal firing during WM delays and behavioral performance. Additionally, in single-cell studies, it is possible that for incorrect trials the monkey never encoded the sample stimulus effectively, which in turn would lead to reduced neural activity during the delay.

In a recent functional magnetic resonance imaging (fMRI) study, we investigated how the moment-to-moment activity within cortical regions, as indexed by fMRI, contributes to success or failure on individual trials of a WM task (Pessoa et al., 2002b). Specifically, we examined how the entire network of regions engaged in visual WM was differentially activated during trials that led to correct and incorrect outcomes. We hypothesized that different components of the task, namely, encoding, delay, and test, would engage different nodes of the WM network to a greater extent on correct trials compared to incorrect trials and provide the neural correlates of WM performance. In particular, we hypothesized that fMRI activity during the delay interval would be stronger and more sustained on correct than on incorrect trials, and would thus predict task performance.

Figure 1

The task we employed to investigate this question is shown in Figure 1. In WM trials, after a 1-s fixation, a sample visual display was presented for 0.5 s, followed by a 6-s fixation, and a test display for 0.5 s. Subjects were then prompted by a display with the letter “m” (for memory) to indicate “same” or “different” by using two hand-held buttons. “Same” meant the test matched the sample, and “different” meant it did not match. Subjects also indicated the confidence level of their response by indicating “high” or “low” (via button presses) when “c” appeared on the display. Each of the two response periods lasted 2 s. Finally, a blank screen terminated the trial, which lasted 2 s (inter-trial interval). Subjects were instructed to maintain fixation for those displays with a fixation spot. Subjects also performed control trials that did not have any maintenance demands, for which they were instructed to maintain fixation and press both buttons in both response periods.

To explore the neural substrates of WM performance on a trial-by-trial basis, we first isolated the entire network of regions involved in WM independent of performance by comparing fMRI signals for WM and control trials. The main regions revealed by this contrast included dorsal occipital, inferior temporal, parietal, as well as premotor and prefrontal cortex, as illustrated on a surface rendering of the left and right hemispheres in Figure 2. Having isolated the WM network, we then probed how it was differentially activated according to task performance. This was accomplished by comparing correct and incorrect trials during each task phase, namely, encoding, maintenance, and test. Our results demonstrated that different nodes were activated to a greater extent for correct compared to incorrect trials during the distinct components of the task. Additionally, as we anticipated, signals during the delay interval were both stronger and more sustained for correct compared to incorrect trials. For the purpose of this section, we will confine our discussion to the results pertaining only to the delay interval.

Figure 2

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Regions exhibiting differential signals during the delay, namely, stronger activity during correct relative to incorrect trials, were almost exclusively in frontal and parietal cortex, and included the DLPFC, frontal eye field (FEF), and supplementary eye field (SEF) in frontal cortex, and superior parietal lobule (SPL) and intraparietal sulcus (IPS) in parietal cortex. As illustrated in Figure 3A and B, for the right IPS and right FEF, respectively, activity in these regions on correct trials rose during encoding, was sustained through the delay interval and at test, and declined thereafter. No such sustained activity during the delay was observed on incorrect trials. But, could it be the case that stronger delay activity during correct trials relative to incorrect trials simply reflected ineffective encoding during incorrect trials? In other words, for incorrect trials, subjects might have failed to encode the stimulus, thereby preventing them from any attempt to maintain the encoded item. To address this possibility, we performed additional analyses confined to only those trials with stronger than average encoding-related activation. The results obtained in this manner were virtually identical to the ones shown in Figure 3, arguing that strongly encoded items do not predict good performance in the absence of sustained signals in frontal and parietal cortex during the delay.

In order to quantify the relationship between fMRI signal amplitude and performance, we used a logistic regression analysis. This analysis revealed that the strength of the fMRI signal during the delay interval reliably predicted task performance: For example, a 1% increase in signal in the right IPS or right FEF increased the likelihood of success to close to 70% (Figure 3C and D, respectively), and in the left DLPFC to close to 65%. A significant logistic regression fit was also obtained for the SPL, but not the SEF. Our results thus provide direct evidence linking sustained activity during the delay interval with behavioral success on a trial-by-trial basis.

Figure 3

Both single-cell and lesion studies in monkeys have demonstrated that the DLPFC (BA 9/46) is centrally involved in WM (Goldman-Rakic, 1995; Fuster, 1997), and in humans the corresponding region is commonly activated in WM tasks (for reviews, see (Cabeza and Nyberg, 2000; D'Esposito, 2001)). Our study showed that the DLPFC is not only involved in WM but also that its contribution to correct performance is significant; see also (Sakai et al., 2002).

Another region that showed a significant contribution of sustained delay signals for WM performance included the FEF in the precentral sulcus extending forward into the superior frontal sulcus (BA 6/8). Several imaging studies have revealed WM-related activity in the vicinity of the precentral sulcus and the superior frontal sulcus. Although such activity has often been attributed to hand or eye movements within premotor cortex, WM studies that have explicitly controlled all motor responses have also observed activations in this region (Jonides et al., 1993; Smith et al., 1995; Courtney et al., 1996). Critically, sustained activity has been demonstrated in the superior frontal sulcus during the delay interval of WM tasks (Courtney et al., 1998; Postle et al., 2000) and this activity appears to be greater for spatial than for object WM (Courtney et al., 1998).

Within parietal cortex, bilateral SPL (BA 7) and IPS (BA 40) also exhibited differential delay signals. This finding is consistent with previous imaging work demonstrating SPL activation associated with both spatial and verbal WM tasks and IPS activation with object WM tasks as well (for reviews, see (Cabeza and Nyberg, 2000; D'Esposito, 2001)). Recently, Rowe et al. (2000) have suggested that the posterior IPS may be especially important for maintenance processes, as it exhibited sustained activity over long WM delays (close to 20 s).

Taken together, neuroimaging studies reveal a fronto-parietal network of brain regions that is critical for WM. This network includes the IPS and SPL in parietal cortex and the FEF and DLPFC in frontal cortex, which were shown in our study to reliably predict task performance on trial-by-trial basis.

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The Control of Attention

Attention and WM are closely related cognitive processes, which has led to the idea that they may share common neural mechanisms (Desimone and Duncan, 1995; Kastner and Ungerleider, 2000; Awh and Jonides, 2001). For instance, when we attempt to find a famous painting in a museum gallery, presumably, we maintain in mind some mental representation of the painting and attentively compare the paintings around the gallery to the one we are looking for. In this section, we will review the neural substrates of the control of visuospatial attention, and compare them to those associated with WM. As the close link between these two types of mechanisms suggests, their neural substrates show a large degree of overlap.

What we perceive depends critically on where we direct our attention. Attention to a location dramatically improves the accuracy and speed of detecting a target at that location. Attention has been shown not only to increase perceptual sensitivity for target discrimination but also to reduce the interference caused by nearby distracters. Moreover, attention is highly flexible and can be deployed in a manner that best serves the organism's momentary behavioral goals: either to locations, to visual features, or to objects. Attention can also be based on internal goals (e.g., finding a familiar face in the crowd) or depend on the external environment (e.g., as when a loud alarm sounds).

Visual attention has been studied extensively in single-cell recording experiments in monkeys and neuroimaging studies in humans. These experiments have shown that attention affects activity in areas of the brain that process stimulus features, such as color, motion, texture, and shape. The paradigmatic finding in monkeys is that when attention is directed to a single stimulus, there is an increase in the firing rate of neurons that respond to the attended stimulus (Motter, 1993; Motter, 1994). In a similar fashion, in humans, increases in fMRI signals have been reported for attended relative to unattended items. Such attentional effects have been observed in many visual cortical areas, including V1, V2, V4, TEO, and MT.

If attention modulates activity in visual processing areas, what is the source of these attentional effects? In humans, studies of patients suffering from attentional deficits due to brain damage (such as in the neglect syndrome; (Mesulam, 1981; Rafal, 1998), as well as functional brain imaging studies of healthy individuals performing attentionally demanding tasks, have revealed a distributed network of higher-order areas in frontal and parietal cortex that appears to be involved in the generation and control of attentional top-down feedback signals. Further, there exists an anatomical substrate for such top-down influences, inasmuch as tract-tracing studies in monkeys have demonstrated direct feedback projections to extrastriate visual areas V4 and TEO from parietal cortex (in particular, area LIP) and to inferior temporal cortex (area TE) from prefrontal cortex, as well as indirect feedback projections to areas V4 and TEO from prefrontal cortex via parietal cortex (Cavada and Goldman-Rakic, 1989; Ungerleider et al., 1989; Webster et al., 1994).

Our WM study described above (see Figure 1) provided the opportunity to compare circuits involved in WM with those involved in goal-directed attention. For this purpose, we investigated the activations revealed by the contrast of the encoding phase of the trial relative to a similar period during control trials in which subjects simply viewed a blank screen, and compared those activations to WM-related ones. We reasoned that the contrast involving encoding would reveal regions involved in goal-directed attention because, behaviorally, a key component of successfully performing the task involved directing attention to the to-be-encoded stimulus array. The most robust activations revealed by this contrast involved a fronto-parietal network of regions (Figure 4A) consisting of the SPL (BA 7), the anterior IPS (BA 40), the FEF (BA 6), and the SEF (BA 6/32). Also consistently activated were the precuneus (BA 18/19), the precentral gyrus (BA 6), the dorsolateral portion of the MFG (DLPFC, BA 46), and the IFG/anterior insula (BA 44); these latter regions are not shown in Figure 4.

Figure 4

At the same time, as described earlier, WM delay-related activations (revealed by the contrast of WM and control trials during the delay period) were observed in several brain regions (Figure 4B), including the SPL (BA 7), anterior IPS (BA 40), FEF (BA 6), SEF (BA 6), and DLPFC of the middle frontal gyrus (MFG, BA 9/46), with the strongest activations observed in the SPL, FEF, and SEF at a relatively dorsal plane ($z = +47$ in Talairach space). The remarkable overlap between the regions engaged by goal-directed attention and WM maintenance (compare Figures 4A and 4B) lends further credence to the idea that the two functions share key mechanisms and neural structures, consistent with several proposals (Mesulam, 1981, 1990; Desimone and Duncan, 1995; Awh and Jonides, 2001).

Recently, we have performed a meta-analysis of foci of activation from ten studies across several independent laboratories (Kastner and Ungerleider, 2000; Pessoa et al., 2002a). The results of this analysis, shown in Figure 4C, reveal that a fronto-parietal network of regions consisting of areas in the SPL, IPS, FEF, and SEF is consistently activated in a variety of tasks involving visuospatial attention (Corbetta et al., 1993; Fink et al., 1997; Nobre et al., 1997; Vandenberghe et al., 1997; Corbetta et al., 1998; Culham et al., 1998; Gitelman et al., 1999; Kim et al., 1999; Rosen et al., 1999). In addition, but less consistently, activations in the lateral prefrontal cortex in the region of the MFG, and the anterior cingulate cortex (ACC) have also reported. A common feature among the visuospatial tasks in these experiments is that subjects were asked to maintain fixation at a central spot and to direct attention covertly to peripheral target locations in order to detect a stimulus (Corbetta et al., 1993; Nobre et al., 1997; Corbetta et al., 1998; Gitelman et al., 1999; Kim et al., 1999; Rosen et al., 1999), to discriminate it (Fink et al., 1997; Vandenberghe et al., 1997; Kastner et al., 1999) or to track its movement (Culham et al., 1998). Thus, there appears to be a general spatial attention network that operates independently of the specific requirements of the visuospatial task.

The results of the meta-analysis provide further support for the idea that the activation sites revealed by the contrast of the encoding phase of the WM task relative to rest were indeed involved in goal-directed attention. As can be observed by inspecting Figure 4, there was a large degree of concordance between encoding-related activations (Fig. 4A) and sites involved in spatial attention (Fig. 4C).

Although activations outside of visual cortex in attention tasks have been indicative of regions involved in attentional control, in many of these studies, it was not possible to separate signals associated with visual cues that prime the subject to expect potential subsequent visual targets from signals associated with the attended targets themselves. This was because cues and targets typically follow each other in rapid succession. More recent neuroimaging studies, however, have attempted to explicitly investigate top-down modulation in attentional paradigms by disentangling cue- and target-related activity by, for instance, introducing a longer interval between the two (Kastner et al., 1999; Hopfinger et al., 2000). In this way, the effects of attention in the presence and in the absence of visual stimulation can be assessed. The reasoning is that purely target-related activity should be observed in visual processing areas that respond to the specific stimulus (e.g., area MT to moving stimuli). By contrast, expectation- or cue-related activity that is uncontaminated by ensuing target-related activity should reflect mainly “top-down” signals and be observed in regions of the brain that control attention.

Attention-related signals in the human visual cortex in the absence of visual stimulation were investigated by Kastner et al. (1999) by including an *expectation period* preceding the presentation of visual stimuli. The expectation period was initiated by a cue presented briefly next to the fixation point 11 seconds before the onset of the stimuli. At the appearance of the cue, subjects covertly shifted attention to the peripheral target location in anticipation of a target stimulus that would appear there. In this way, the effects of attention in the absence and presence

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of visual stimulation could be identified. Directed attention in the absence of visual stimulation activated the *same* distributed network of areas as directed attention in the presence of visual stimulation and included the FEF, the SEF, and the SPL. The increase in activity in these frontal and parietal areas during the expectation period (in the absence of visual input) was sustained throughout the expectation period and the attended visual presentations. These results suggest that the activity reflected the attentional operations of the task *per se* and not the effects of attention on visual processing.

Converging evidence for a fronto-parietal network of regions involved in attentional control comes from additional imaging studies. For example, by using a spatial attention Posner-type task, Corbetta et al. (2000) showed that the IPS was uniquely active when attention was directed toward and maintained at a relevant location (preceding target presentation), suggesting that the IPS is a top-down source of biasing signals observed in visual cortex. The same investigators (Shulman et al., 1999) found, when studying attention to motion, cue-related activity in FEF, as well as in several sites in the IPS. Finally, Hopfinger et al. (2000) obtained evidence for a wider attentional control network, including the superior frontal gyrus, MFG, SPL, IPS, as well as superior temporal gyrus. This latter region has been identified in lesion studies as a key site responsible for neglect (Karnath et al., 2001). Interestingly, a recent fMRI study indicates that the top-down control of attention to visual features draws on a network of areas that largely overlaps with the one revealed by spatial attention tasks (Giesbrecht and Mangun, in press; Giesbrecht et al., submitted). This raises the possibility that the control of attention may rely on a common network of brain regions, irrespective of the attribute attended; see also (Vandenberghe et al., 2001).

Taken together, the above studies provide evidence that a distributed fronto-parietal attentional network may be the source of feedback that generates the top-down biasing signals modulating activity in visual cortex. This would explain the finding that functional brain imaging studies using different visuospatial attention tasks have described very similar attentional networks.

Top-down vs. Bottom-up Attentional Control

Thus far, we have considered top-down mechanisms needed for the control of WM and goal-directed attention. Further, we have shown how similar fronto-parietal networks are likely engaged by both processes. Goal-directed attention is often referred to as *endogenous* attention. Goal-directed attention provides a fundamental mechanism by which behaviorally relevant information is favored relative to less important items. However, another type of attention, often referred to as *exogenous* attention, also plays an important role in guiding the allocation of processing resources and, thereby, in shaping behavior. For example, consider a person trekking in the desert when a sudden movement is observed in the periphery of his or her visual field. In such a case, attention is involuntarily directed to that location, allowing the person to ascertain the nature of the moving object, for instance, whether it is just a squirrel or whether it is a threatening snake. Thus, endogenous attention is under top-down control, while exogenous attention is largely stimulus driven.

The distinction between endogenous and exogenous attention can be explored in the context of change detection. Detecting changes in an ever-changing environment is highly advantageous, and may be critical for survival. In the real world, changes are often accompanied by transients of some sort, such as motion signals that attract attention to their location (Yantis and Johnson, 1990; Remington et al., 1992). In general, the attention-catching effect of a sudden or distinctive stimulus can be shown by flashing a light at a certain location in space and comparing the time it takes for subjects to react to a subsequent stimulus at that location to the time when no initial flashing takes place (Posner and Cohen, 1984). Moreover, evidence indicates

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that when an item is seen to change (e.g., from a vertical to a horizontal bar), attention is drawn to the location of that item to facilitate visual processing. For example, Thornton and Fernandez-Duque (2000) showed that subjects are faster to discriminate a subsequent target at the location of a change than at a distant location (see also (Smilek et al., 2000; Rensink, 2002)), indicating that a change can function as an orienting cue.

Interestingly, changes may occur in the absence of accompanying transients, such as those occurring during saccades, blinks, or flicker. Under these circumstances, changes can be quite difficult to detect, and even large changes may go unnoticed in the absence of focused attention (Rensink et al., 1997; Rensink, 2002). In such situations, *goal-directed attention* (endogenous attention) appears necessarily to be focused on the region of space in which a change occurs at the time the change takes place. When this is not the case because of, say, saccades or flicker, “change blindness” will ensue (e.g., an engine repeatedly appearing and disappearing from the photograph of an airplane may go unnoticed). In most instances, however, changes in the environment are in fact accompanied by transients. Thus, change detection is associated with two related, but distinct, events, namely, a reflexive deployment of attention that can have an orienting function, akin to exogenous attention, and a goal-directed allocation of attention that may be instrumental in allowing changes to be perceived in demanding situations.

To investigate the neural correlates of attentional mechanisms involved in change detection that are more closely tied to exogenous attention, we compared activations on correct change vs. correct no-change trials during the test phase of our WM task (Figure 1). To minimize the contributions of varying attentional states that might have occurred during the long experimental fMRI session, we analyzed *only* high-confidence, correct trials. Contrasting detected vs. undetected changes, as Beck et al. (2001) did in their study of change detection, would have involved correct (detected) and incorrect (undetected) trials, which likely would have included contributions due to variations in the subject’s attentional state. Indeed, Ress et al. (2000) attributed fluctuations in activity in V1 to trial-to-trial fluctuations in attention, which, they suggested, accounted for the variability in behavioral performance on a target detection task. We have also proposed that such fluctuations in attention have a similar role on behavioral performance in the context of our WM task (Pessoa et al., 2002b). Thus, we reasoned that by analyzing correct trials only we would minimize the potentially large contributions of varying attentional states.

The contrast of correct change vs. correct no-change trials during the test phase revealed activations in fronto-parietal sites (Figure 5A) that included the anterior IPS (BA 40), the precuneus (BA 19), the superior frontal gyrus (SFG; BA 6/8), the MFG (BA 9), the ACC (BA 32), and the inferior frontal gyrus (IFG)/anterior insula (BA 44). We also observed change-related responses to the stimulus array in cortical visual areas, most notably in the inferior temporal gyrus (ITG). Subcortically, the right putamen, the cerebellum and pulvinar, both mainly on the right, showed greater activation on correct trials for the change compared to no-change contrast. Our interpretation of these results is that change detection activates frontal and parietal regions via bottom-up mechanisms, thereby triggering attentional mechanisms located in these regions, which then function via top-down feedback to deploy attention to the location of a change, enabling further, more elaborate processing of the stimulus. Moreover, subcortical sites, such as the pulvinar, may also participate in the deployment of attention and thereby contribute to the processing of the stimulus.

Figure 5

In a task involving a decision, such as determining whether a change occurred or not, do brain activations follow the physical stimulus or the subject’s report? To investigate this question, we asked whether the same areas activated by correctly detecting a change were also more active when the subjects reported a change but none had actually occurred? If this were true, then the

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pattern of activation for false alarms (on incorrect match trials) compared to misses (on incorrect non-match trials) should be similar to the one observed for rejects (on correct non-match trials) compared to hits (on correct match trials). Note that for false alarm trials, no physical change occurred, but subjects reported perceiving a change with high confidence; for miss trials, a physical change occurred, but subjects reported that no change occurred, again with high confidence. Although the number of high-confidence, incorrect trials was small and the associated activations were generally weaker, this contrast revealed a network of activations with a striking degree of overlap with the network observed when subjects correctly detected a change (compare Figures 5A and 5B). Thus, we suggest that reporting a change, whether or not it actually occurred, generates virtually the same pattern of activation.

A related dissociation between physical parameters and perceptual reports has been observed in the visual cortex of monkeys observing threshold or ambiguous stimuli. For example, Bradley et al. (1998) showed that the responses of MT neurons to bi-stable, rotating cylinders defined by structure-from-motion cues were linked to the perception of which surface was perceived in front. This was also true for error trials in which the monkey's behavioral response reflected neuronal responses (the cell's preferred depth) rather than the physical cues of the stimulus. In another single-cell study, Thompson and Schall (1999, 2000) probed the neural substrates of target detection and showed that neural responses in the FEF to a target stimulus were greater when the target was detected than when it was missed. Moreover, neural responses were greater on false alarm trials than on trials in which the target was absent.

What is the relationship between change-related activations on the one hand and those associated with goal-directed attention, on the other hand? Although there was overlap between the locations of activations found during change detection at test and those for goal-directed attention, such as the anterior IPS, a notable feature of the comparison was the *lack* of overlap at more dorsal brain sites. In particular, the SPL, FEF, and SEF were strongly driven by goal-directed attention but not by the detection of a change. Conversely, regions strongly recruited during the detection of a change that were not recruited by goal-directed attention included the pulvinar and the cerebellum.

Thus, the most conspicuous feature of the networks activated by change detection and goal-directed attention was that they were *largely non-overlapping*, with the notable exception of the anterior IPS, which was shared by both networks. Moreover, it appears that attentional processes associated with goal-directed attention recruit more *dorsal* cortical territories in both frontal and parietal cortex than those associated with change detection. Regions triggered by change detection were generally situated more *ventrally* (compare Figures 4A and 5A), and included the MFG, the ACC, and the IFG/anterior insula. Importantly, processes engaged by WM maintenance recruited the same dorsal fronto-parietal regions associated with goal-directed attention (compare Figures 4A and 4C).

Discussion

We reviewed evidence from fMRI studies that a fronto-parietal network is critically involved in the top-down control of spatial attention. This is a similar network as the one proposed by Mesulam (1980), based on studies of patients with brain lesions. This fronto-parietal network shows a remarkable degree of overlap with the one involved in maintaining information during the delay period of a WM task. Both networks rely heavily on dorsal areas of the brain. Such congruence of activated sites agrees well with the idea that goal-directed attention and WM share common mechanisms. Indeed, it has been proposed that they should not be viewed as separate processes, but instead as inter-dependent ones. For instance, Desimone (1998) proposed that attention is derived, at least in part, from the impact of short term memory mechanisms (i.e., working memory) on cortical sensory representations.

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We also reviewed evidence from our WM study that change-detection activations involve a different network of regions that is situated more ventrally. We interpreted change-related activations as associated with a more reflexive deployment of attention toward the location of the change, akin to exogenous attention. Behavioral studies demonstrate that endogenous and exogenous attention involve different mechanisms. For example, the facilitation due to a sensory cue in exogenous attention (e.g., a bright flash) appears more rapidly (~ 50 ms) than that observed in goal-directed attention. Moreover, unlike what is observed in endogenous attention, sensory cues produce a prolonged inhibition of processing (called “inhibition of return”) after the initial facilitation. Thus, it is generally believed that endogenous and exogenous attention comprise distinct systems (Jonides, 1981). Our findings of overlapping but separable dorsal and ventral neural systems subserving processes more closely tied to top-down and stimulus-driven attention, respectively, is thus consistent with the separation between these two types of attentional processes, as suggested by behavioral experiments.

Our proposal shares its key elements with the one advanced by Corbetta and Shulman (2002). Based on their own studies, as well as both neuroimaging and patient reports, they postulated the existence of two anatomically segregated, but interacting, networks for spatial attention. According to their scheme, a dorsal fronto-parietal system is involved in the generation of attentional sets associated with goal-directed stimulus-response selection (endogenous attention). Key nodes within this largely bilateral network would include the SPL, IPS, and the FEF. A second, more ventral system, which is strongly lateralized to the right hemisphere, is proposed to detect behaviorally relevant stimuli and to work as an alerting mechanism for the first system when these stimuli are detected outside the focus of processing (exogenous attention). In our WM study, we did not find evidence for a right lateralization of the ventral network engaged by change detection. One reason could be that change detection behaves slightly differently from more direct exogenous mechanisms recruited, for instance, by a loud sound or a flashing stimulus. Interestingly, in our study, the dorsal and ventral networks intersected at the anterior IPS, which may constitute a common processing node that links the two networks. In general, endogenous and exogenous attention strongly interact in the generation of behavior (see (Corbetta and Shulman, 2002) and, in neural terms, such interactions may be mediated by anatomical connections known to exist between the dorsal and ventral networks (Distler et al., 1993; Webster et al., 1993), as well as common anatomical regions, such as the IPS.

We also found evidence in our WM study for the involvement of subcortical structures in exogenous attention, including the pulvinar and the cerebellum. Single-cell studies in monkeys reveal that the pulvinar nucleus of the thalamus has an important role in selective attention processes (Chalupa, 1977; Petersen et al., 1985). As summarized by Robinson and Petersen (1992), pulvinar cells generate signals related to the salience of visual objects and are involved in the selection of salient targets and the filtering of non-salient distracters. In monkeys, pulvinar lesions lead to impairments in active visual scanning (Ungerleider and Christensen, 1979), and inactivation of the pulvinar produces a slowing down of attention shifts (Petersen et al., 1987). In humans, the right pulvinar is the principal site in the thalamus associated with spatial neglect (Karnath et al., 2002). Imaging studies with humans also have obtained evidence of pulvinar involvement in attentional processes (LaBerge and Buchsbaum, 1990; Corbetta et al., 1991), although not consistently. In our WM study, we found robust and consistent pulvinar activation, which we suggest was involved in the deployment of spatial attention to the location of the change.

Like the pulvinar, the cerebellar cortex was strongly activated when subjects detected a change. There is now evidence that the cerebellum has functions beyond those of motor processing (Middleton and Strick, 1994; Fiez et al., 1996; Schmahmann, 1996; Thach, 1996). In particular, based on studies of patients with cerebellar lesions, it has been proposed that the cerebellum mediates rapid shifts in attention (Akshoomoff and Courchesne, 1992, 1994). In an

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fMRI study to test cerebellar involvement in attentional processes, Le et al. (1998) compared a condition of shifting attention to a condition of sustained attention, which revealed lateral cerebellar activation; see also (Allen et al., 1997). Thus, our findings are consistent with the idea that the cerebellum is involved in attentional processes in general, and in the detection of change in particular.

Conclusion

In this chapter, we have reviewed studies that show that frontal and parietal brain regions are centrally involved in the control of WM and attention. Results from imaging studies, including our own, suggest that sites important for WM are strongly involved in goal-directed (endogenous) attention, and involve a dorsal fronto-parietal network, including the SPL, IPS, FEF, and SEF. At the same time, reflexive (exogenous) attention relies on an overlapping but distinct network that also involves fronto-parietal sites, but is located more ventrally to encompass the MFG, ACC, and IFG. Moreover, this network includes subcortical sites such as the pulvinar and the cerebellum. A key site of overlap between the two networks is the anterior IPS. Distinguishing the precise functional contributions of the different nodes subserving the top-down control of attention and WM, as well as those involved in reflexive attention, is a task for future investigations.

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Figure Captions

Figure 1. Experimental design. In working memory trials, subjects indicated whether the sample and test displays were the same or different (note that the bar orientation on the upper right changed in the present case). They also indicated the confidence of their response (high vs. low).

Figure 2. Working memory network. The regions within this network were revealed by the contrast of working memory vs. fixation control trials. The statistical group maps of functional activations are shown overlaid onto a three-dimensional rendering of the brain of a representative individual. The color bar indicates p values (uncorrected). Abbreviations: DLPFC: dorsolateral prefrontal cortex; DO: dorsal occipital; FEF: frontal eye field; IPS: intraparietal sulcus; ITG: inferior temporal gyrus; P. MFG: posterior middle frontal gyrus; SPL: superior parietal lobule. Reprinted with permission from Cell Press.

Figure 3. (A,B) Performance-related activity in the intraparietal sulcus (IPS, A) and the frontal eye field (FEF, B) during the three phases of the working memory (WM) task: encoding, delay, and test. Performance-related activity was obtained by comparing activity for correct and incorrect trials at each task phase. Functional group maps are shown overlaid onto structural scans from a representative individual. Arrow indicates the region from which the fitted hemodynamic responses were obtained. The level of the coronal section is indicated on the small whole-brain inset. The bar below the x axis codes the periods when the sample stimulus (light gray), the delay (intermediate gray), and the test stimulus (dark gray) occurred during the task. The vertical gray bar indicates the delay interval. (C,D) The contingency between signal amplitude and the subjects' performance was assessed with a logistic regression analysis for every time point within WM trials. Activity at 8 and 10 s for the FEF, and 8, 10, and 12 s for the IPS, significantly predicted performance ($p < 0.05$), such that for a 1% increase in fMRI signal, the probability of being correct for that trial increased from chance to close to 70% (y-axis).

Figure 4. Regions involved in visual spatial attention and visual working memory. (A) Encoding vs. rest on the WM task. (B) Working memory network revealed by the contrast of working memory delay vs. rest. (C) Regions in the spatial attention network as determined by a meta-analysis of imaging data. The statistical group map is shown overlaid on a structural scan of a representative individual. The level of the axial section is indicated on the small whole-brain inset: (1) Corbetta et al. (1993); (2) Fink et al. (1997); (3) Nobre et al. (1997); (4) Vandenberg et al. (1997); (5) Corbetta et al. (1998); (6) Kastner et al. (1999); (7) Rosen et al. (1999); (8) Corbetta et al. (2000); (9) Hopfinger et al. (2000).

Figure 5. Similar brain activations occur on correct change and false alarm trials. (A) Functional group maps showing regions activated at test on correct change (non-match) compared to no-change (match) trials. (B) Functional group maps showing regions activated at test on incorrect no-change (false alarms) compared to incorrect change (miss) trials, at the same slice levels. Although the number of high-confidence, incorrect trials was small and the associated activations weaker, comparing the two patterns of activation revealed a great deal of overlap. Statistical group maps are shown overlaid on structural scans from a representative individual. The level of the axial and coronal sections is indicated on the small whole-brain insets. The color bar indicates p values (uncorrected). Reprinted with permission from Oxford University Press.

Pessoa, L. & Ungerleider, L.G. (2004). Top-down mechanisms for working memory and attentional processes. In M. S. Gazzaniga (Ed.), *The New Cognitive Neurosciences, 3rd Edition*, pp. 919-930, MIT Press.

References

- Akshoomoff NA, Courchesne E (1992) A new role for the cerebellum in cognitive operations. *Behavioral Neuroscience* 106:731-738.
- Akshoomoff NA, Courchesne E (1994) ERP evidence for a shifting attention deficit in patients with damage to the cerebellum. *Journal of Cognitive Neuroscience* 6:388-399.
- Allen G, Buxton RB, Wong EC, Courchesne E (1997) Attentional activation of the cerebellum independent of motor movement. *Science* 275:1940-1943.
- Awh E, Jonides J (2001) Overlapping mechanisms of attention and spatial working memory. *Trends in Cognitive Sciences* 5:119-126.
- Bauer RH, Fuster JM (1976) Delayed-matching and delayed-response deficit from cooling dorsolateral prefrontal cortex in monkeys. *Journal of Comparative and Physiological Psychology* 90:293-302.
- Bruce CJ, Goldberg ME (1985) Primate frontal eye fields. I. Single neurons discharging before saccades. *Journal of Neurophysiology* 53:603-635.
- Cabeza R, Nyberg L (2000) Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience* 12:1-47.
- Cavada C, Goldman-Rakic PS (1989) Posterior parietal cortex in rhesus monkey: II. Evidence for segregated cortico-cortical networks linking sensory and limbic areas with the frontal lobe. *Journal of Comparative Neurology* 287:422-445.
- Chafee MV, Goldman-Rakic PS (1998) Matching patterns of activity in primate prefrontal area 8a and parietal area 7ip neurons during a spatial working memory task. *Journal of Neurophysiology* 79:2919-2940.
- Chafee MV, Goldman-Rakic PS (2000) Inactivation of parietal and prefrontal cortex reveals interdependence of neural activity during memory-guided saccades. *Journal of Neurophysiology* 83:1550-1566.
- Chalupa LM (1977) A review of cat and monkey studies implicating the pulvinar in visual function. *Behavioral Biology* 20:149-167.
- Chelazzi L, Duncan J, Miller EK, Desimone R (1998) Responses of neurons in inferior temporal cortex during memory-guided visual search. *Journal of Neurophysiology* 80:2918-2940.
- Cohen JD, Perlstein WM, Braver TS, Nystrom LE, Noll DC, Jonides J, Smith EE (1997) Temporal dynamics of brain activation during a working memory task. *Nature* 386: 604-608.
- Corbetta M, Shulman GL (2002) Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews Neuroscience* 3:201-215.
- Corbetta M, Miezin FM, Shulman GL, Petersen SE (1993) A PET study of visuospatial attention. *Journal of Neuroscience* 13:1202-1226.
- Corbetta M, Miezin FM, Dornmeyer S, Shulman GL, Petersen SE (1991) Selective and divided attention during visual discriminations of shape, color, and speed: functional anatomy by positron emission tomography. *Journal of Neuroscience* 11:2382-2402.
- Corbetta M, Akbudak E, Conturo TE, Snyder AZ, Ollinger JM, Drury HA, Linenweber MR, Petersen SE, Raichle ME, Van Essen DC, Shulman GL (1998) A common network of functional areas for attention and eye movements. *Neuron* 21:761-773.
- Courtney SM, Ungerleider LG, Keil K, Haxby JV (1996) Object and spatial visual working memory activate separate neural systems in human cortex. *Cerebral Cortex* 6:39-49.

Pessoa, L. & Ungerleider, L.G. (2004). Top-down mechanisms for working memory and attentional processes. In M. S. Gazzaniga (Ed.), *The New Cognitive Neurosciences, 3rd Edition*, pp. 919-930, MIT Press.

Courtney SM, Ungerleider LG, Keil K, Haxby JV (1997) Transient and sustained activity in a distributed neural system for human working memory. *Nature* 386:608-611.

Courtney SM, Petit L, Maisog JM, Ungerleider LG, Haxby JV (1998) An area specialized for spatial working memory in human frontal cortex. *Science* 279:1347-1351.

Culham JC, Brandt SA, Cavanagh P, Kanwisher NG, Dale AM, Tootell RB (1998) Cortical fMRI activation produced by attentive tracking of moving targets. *Journal of Neurophysiology* 80:2657-2670.

Desimone R, Duncan J (1995) Neural mechanisms of selective attention. *Annual Review of Neuroscience* 18:193-222.

D'Esposito M (2001) Functional neuroimaging of working memory. In: *Handbook of functional neuroimaging of cognition* (Cabeza R, Kingstone A, eds), pp 293-327. Cambridge, MA: The MIT Press.

D'Esposito M, Aguirre GK, Zarahn E, Ballard D, Shin RK, Lease J (1998) Functional MRI studies of spatial and nonspatial working memory. *Cognitive Brain Research* 7:1-13.

Distler C, Boussaoud D, Desimone R, Ungerleider LG (1993) Cortical connections of inferior temporal area TEO in macaques. *Journal of Comparative Neurology* 334:125-150.

Fiez JA, Raife EA, Balota DA, Schwarz JP, Raichle ME, Petersen SE (1996) A positron emission tomography study of the short-term maintenance of verbal information. *Journal of Neuroscience* 16:808-822.

Fink GR, Dolan RJ, Halligan PW, Marshall JC, Frith CD (1997) Space-based and object-based visual attention: shared and specific neural domains. *Brain* 120:2013-2028.

Funahashi S, Bruce SJ, Goldman-Rakic PS (1989) Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *Journal of Neurophysiology* 61:1-19.

Funahashi S, Bruce CJ, Goldman-Rakic PS (1993) Dorsolateral prefrontal lesions and oculomotor delayed response performance: evidence for mnemonic "scotomas". *Journal of Neuroscience* 13:1479-1497.

Fuster JM (1973) Unit activity in prefrontal cortex during delayed-response performance: Neuronal correlates of transient memory. *Journal of Neurophysiology* 36:61-78.

Fuster JM (1997) *The prefrontal cortex: Anatomy, physiology, and neuropsychology of the frontal lobes*. New York: Raven.

Fuster JM (2001) The prefrontal cortex: An update: Time is of the essence. *Neuron* 30:319-333.

Fuster JM, Alexander GE (1971) Neuron activity related to short-term memory. *Science* 173:652-654.

Fuster JM, Jervey JP (1982) Neuronal firing in the inferotemporal cortex of the monkey in a visual memory task. *Journal of Neuroscience* 2:361-375.

Giesbrecht B, Mangun GR (in press) The neural mechanisms of top-down control. In: *The cognitive and neural bases of spatial neglect* (Karnath HO, Milner D, Vallar G, eds). Oxford: Oxford University Press.

Giesbrecht B, Woldorff MG, Song AW, Mangun GR (submitted) Neural mechanisms of top-down control during spatial and feature attention.

Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Kim YH, Meyer JR, Mesulam M (1999) A large-scale distributed network for covert spatial attention: Further anatomical delineation based on stringent behavioural and cognitive controls. *Brain* 122:1093-1106.

Goldman PS, Rosvold HE (1970) Localization of function within the dorsolateral prefrontal cortex of the rhesus monkey. *Experimental Neurology* 27:291-304.

Pessoa, L. & Ungerleider, L.G. (2004). Top-down mechanisms for working memory and attentional processes. In M. S. Gazzaniga (Ed.), *The New Cognitive Neurosciences, 3rd Edition*, pp. 919-930, MIT Press.

Goldman-Rakic PS (1995) Cellular basis of working memory. *Neuron* 14:477-485.

Hopfinger JB, Buonocore MH, Mangun GR (2000) The neural mechanisms of top-down attentional control. *Nature Neuroscience* 3:284-291.

Jonides J (1981) In: *Attention and Performance XI* (Posner MI, Marin O, eds), pp 187-205. Hillsdale, NJ: Erlbaum.

Jonides J, Smith EE, Koeppe RA, Awh E, Minoshima S, Mintun MA (1993) Spatial working memory in humans as revealed by PET. *Nature* 363:623-625.

Jonides J, Schumacher EH, Smith EE, Koeppe RA, Awh E, Reuter-Lorenz PA, C. Marshuetz C, Willis CR (1998) The role of parietal cortex in verbal working memory. *Journal of Neuroscience* 18:5026-5034.

Karnath HO, Ferber S, Himmelbach M (2001) Spatial awareness is a function of the temporal not the posterior parietal lobe. *Nature* 411:950-953.

Karnath HO, Himmelbach M, Rorden C (2002) The subcortical anatomy of human spatial neglect: putamen, caudate nucleus and pulvinar. *Brain* 125:350-360.

Kastner S, Ungerleider LG (2000) Mechanisms of visual attention in the human cortex. *Annual Review of Neuroscience* 23:315-341.

Kastner S, Pinsk MA, De Weerd P, Desimone R, Ungerleider LG (1999) Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron* 22:751-761.

Kim YH, Gitelman DR, Nobre AC, Parrish TB, LaBar KS, Mesulam MM (1999) The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. *NeuroImage* 9:269-277.

Kubota K, Niki H (1971) Prefrontal cortical unit activity and delayed alternation performance in monkeys. *Journal of Neurophysiology* 34:337-347.

LaBerge D, Buchsbaum MS (1990) Positron emission tomographic measurements of pulvinar activity during an attention task. *Journal of Neuroscience* 10:613-619.

Mesulam MM (1981) A cortical network for directed attention and unilateral neglect. *Annals of Neurology* 10:309-325.

Mesulam MM (1990) Large-scale neurocognitive networks and distributed processing for attention, language, and memory. *Annals of Neurology* 28:597-613.

Middleton FA, Strick PL (1994) Anatomical evidence for cerebellar and basal ganglia involvement in higher cognitive function. *Science* 266:458-461.

Motter BC (1993) Focal attention produces spatially selective processing in visual cortical areas V1, V2, and V4 in the presence of competing stimuli. *Journal of Neurophysiology* 70:909-919.

Motter BC (1994) Neuronal correlates of attentive selection for color or luminance in extrastriate area V4. *Journal of Neuroscience* 14:2178-2189.

Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RSJ, Frith CD (1997) Functional localization of the system for visuospatial attention using positron emission tomography. *Brain* 120:515-533.

Pessoa L, Kastner S, Ungerleider LG (2002a) Attentional control of the processing of neural and emotional stimuli. *Cognitive Brain Research* 15:31-45.

Pessoa L, Gutierrez E, Bandettini PB, Ungerleider LG (2002b) Neural correlates of visual working memory: fMRI amplitude predicts task performance. *Neuron* 35:975-987.

- Pessoa, L. & Ungerleider, L.G. (2004).** Top-down mechanisms for working memory and attentional processes. In M. S. Gazzaniga (Ed.), *The New Cognitive Neurosciences, 3rd Edition*, pp. 919-930, MIT Press.
- Petersen SE, Robinson DL, Keys W (1985) Pulvinar nuclei of the behaving rhesus monkey: visual responses and their modulation. *Journal of Neurophysiology* 54:867-886.
- Petersen SE, Robinson DL, Morris JD (1987) Contributions of the pulvinar to visual spatial attention. *Neuropsychologia* 25:97-105.
- Petit L, Courtney SM, Ungerleider LG, Haxby JV (1998) Sustained activity in the medial wall during working memory delays. *Journal of Neuroscience* 18:9429-9437.
- Posner MI, Cohen Y (1984) Components of attention. In: *Attention and Performance* (Bouman H, Bowhuis D, eds), pp 531-556. Hillsdale, NJ: Erlbaum.
- Postle BR, Berger JS, Taich AM, D'Esposito M (2000) Activity in human frontal cortex associated with spatial working memory and saccadic behavior. *Journal of Cognitive Neuroscience* 12:2-14.
- Rafal R (1998) Neglect. In: *The attentive brain* (Parasuraman R, ed), pp 489-525. Cambridge, MA: MIT Press.
- Remington RW, Johnston JC, Yantis S (1992) Involuntary attentional capture by abrupt onset. *Percept Psychophys* 51:279-290.
- Rensink RA (2002) Change detection. *Annual Review of Psychology* 53:245-277.
- Rensink RA, O'Regan JK, Clark JJ (1997) To see or not to see: The need for attention to perceive changes in scenes. *Psychological Science* 8:368-373.
- Rosen AC, Rao SM, Caffarra P, Scaglioni A, Bobholz JA, Woodley SJ, Hammeke TA, Cunningham JM, Prieto TE, Binder JR (1999) Neural basis of endogenous and exogenous spatial orienting: a functional MRI study. *Journal of Cognitive Neuroscience* 11:135-152.
- Rosenkilde CE, Bauer RH, Fuster JM (1981) Single cell activity in ventral prefrontal cortex of behaving monkeys. *Brain Research* 209: 375-394.
- Rowe JB, Toni I, Josephs O, Frackowiak RS, Passingham RE (2000) The prefrontal cortex: Response selection or maintenance within working memory? *Science* 288:1656-1660.
- Sakai K, Rowe JB, Passingham RE (2002) Active maintenance in prefrontal area 46 creates distractor-resistant memory. *Nature Neuroscience* 5:479-484.
- Schmahmann JD (1996) From movement to thought: anatomical substrates of the cerebellar contribution to cognitive processing. *Human brain Mapping* 4:174-198.
- Shulman GL, Ollinger JA, Akbudak E, Conturo TE, Snyder AZ, Petersen SE, Corbetta M (1999) Areas involved in encoding and applying directional expectations to moving objects. *Journal of Neuroscience* 21:9480-9496.
- Smilek D, Eastwood JD, Merikle PM (2000) Does unattended information facilitate change detection? *Journal of Experimental Psychology - Human Perception and Performance* 26:480-487.
- Smith EE, Jonides JJ, Koeppe RA, Awh E, Schumacher EH, Minoshima S (1995) Spatial versus object working memory: PET investigations. *Journal of Cognitive Neuroscience* 7:337-356.
- Thach WT (1996) On the specific role of the cerebellum in motor learning and cognition: clues from PET activation and lesion studies in man. *Behavioral Brain Science* 19:411-431.
- Ungerleider LG, Christensen CA (1979) Pulvinar lesions in monkeys produce abnormal scanning of a complex visual array. *Neuropsychologia* 17:493-501.
- Ungerleider LG, Gaffan D, Pelak VS (1989) Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkeys. *Experimental Brain Research* 76:473-484.

Pessoa, L. & Ungerleider, L.G. (2004). Top-down mechanisms for working memory and attentional processes. In M. S. Gazzaniga (Ed.), *The New Cognitive Neurosciences, 3rd Edition*, pp. 919-930, MIT Press.

Vandenberghe R, Gitelman DR, Parrish TB, Mesulam M (2001) Location- or feature-based targeting of peripheral attention. *NeuroImage* 14:37-47.

Vandenberghe R, Duncan J, Dupont P, Ward R, Poline J, Bormans G, Michiels J, Mortelmans L, Orban GA (1997) Attention to one or two features in left or right visual field: a positron emission tomography study. *Journal of Neuroscience* 17:3739-3750.

Watanabe M (1986a) Prefrontal unit activity during delayed conditional go/no-go discrimination in the monkey I. Relation to the stimulus. *Brain Research* 382:1-14.

Watanabe M (1986b) Prefrontal unit activity during delayed conditional go/no-go discrimination in the monkey II. Relation to go and no-go responses. *Brain Research* 382:15-27.

Webster MJ, Bachevalier J, Ungerleider LG (1993) Subcortical connections of inferior temporal areas TE and TEO in macaques. *Journal of Comparative Neurology* 335:73-91.

Webster MJ, Bachevalier J, Ungerleider LG (1994) Connections of inferior temporal areas TEO and TE with parietal and frontal cortex in macaque monkeys. *Cerebral Cortex* 4:470-483.

Yantis S, Johnson DN (1990) Mechanisms of attentional priority. *Journal of Experimental Psychology: Human Perception & Performance* 16:812-825.

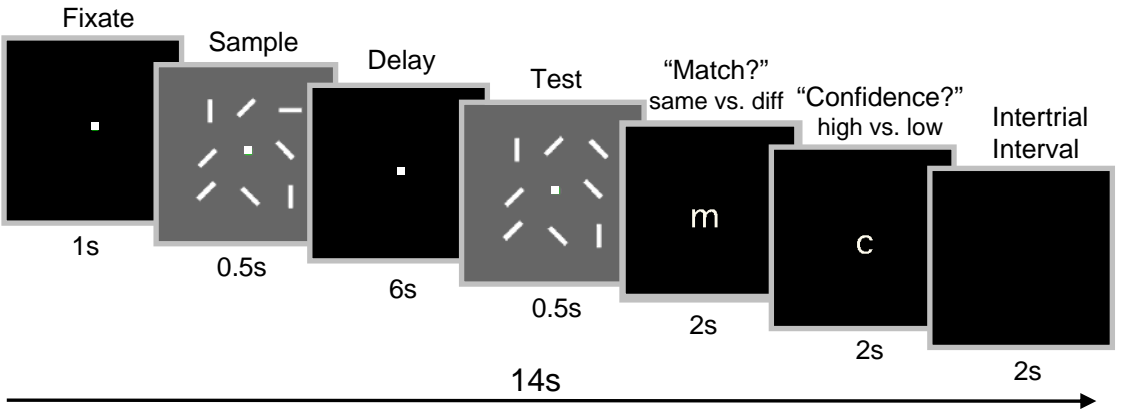


Figure 1

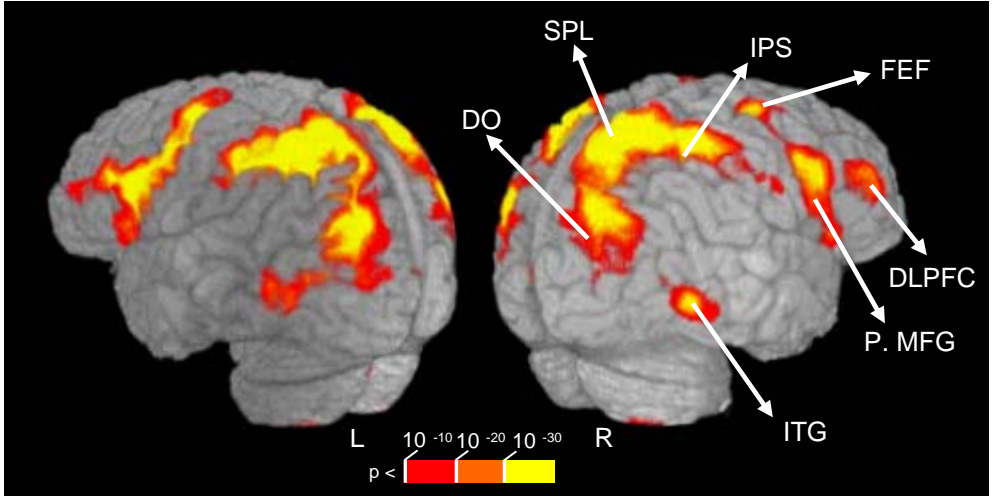


Figure 2

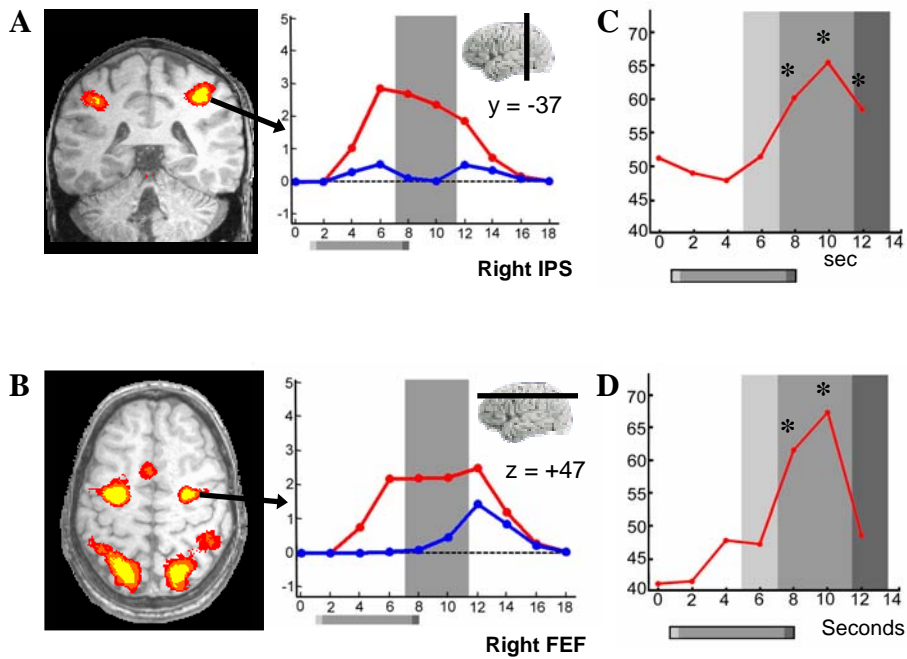
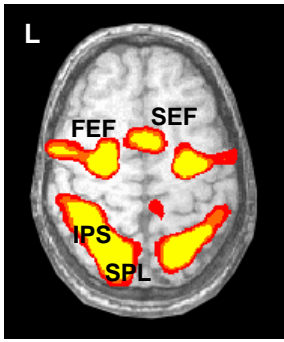


Figure 3

A. Encoding vs. rest



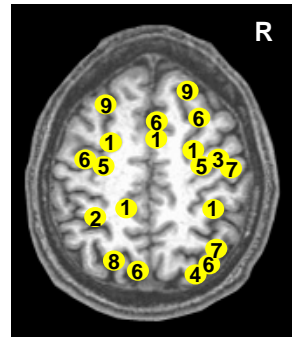
z = +47

B. Working Memory Network: Delay vs. rest



z = +47

C. Spatial Attention Network



z = +45

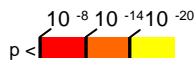
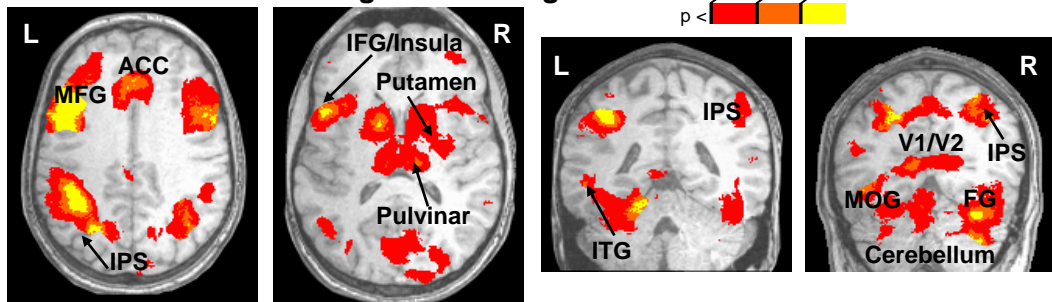


Figure 4

A. Correct at Test: Change > No change



B. Incorrect at Test: False Alarm > Miss

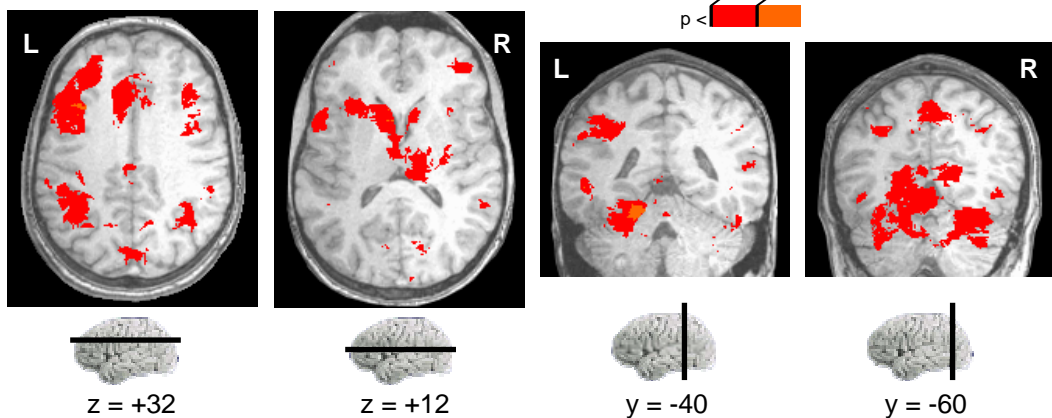


Figure 5