

CHAPTER X: A Hierarchical Biased-Competition Model of Domain-Dependent Working Memory Maintenance and Executive Control.

Authors: Susan M. Courtney, Jennifer K. Roth, Joseph B. Sala

X.1 INTRODUCTION: DEFINING WORKING MEMORY

Cognitive psychologists and neurophysiologists seem to have slightly different definitions of working memory, with the former tending to emphasize the “working” (executive control and manipulation of information) aspect of the term and the latter tending to emphasize the “memory” aspect. In this chapter we define “Working Memory” (WM) as the ability to maintain a limited amount of task-relevant information in an active representation so that it is able to influence current and upcoming behavior and cognition. There are a couple of key elements to this definition which must be emphasized in order to understand the role of working memory in cognition and behavior and the neural mechanisms that underlie this ability.

First, working memory is *capacity limited*. This limitation creates the need to maintain only the information that is most important for the current task. Effective capacity can be increased if one can select or create the most efficient and effective representation that will best achieve the current goals according to the current rules. Therefore the same information may be represented neurally in different ways in order to maximize the efficiency of this limited capacity. While working memory has traditionally been studied regarding the maintenance of stimulus-specific information such as locations, objects, or words, the selection and continued maintenance of this information must be guided by a maintained representation of the current rules and goals. In this chapter we will explore the

possibility that the same neural mechanisms that support working memory for stimulus-specific information may also be involved in the selection and maintenance of more abstract information, such as current rules and goals. The maintenance of such abstract information and its influence on the selective maintenance of more stimulus-specific information may form the basis of executive control -- the ability to optimally select, manipulate, and use the stimulus-specific information to be maintained.

The second key element in the definition of working memory is that the representation is active and therefore *flexible and transient*. Without active maintenance, information in the working memory buffer is overwritten by other competing information such as current sensory input, information retrieved from long-term memory, or other spontaneous thoughts. Much theorizing and experimentation has been directed at ascertaining whether information decays from the buffer directly due to the passage of time or whether it is necessarily replaced by interfering information (e.g. Doshier, 1999). Because this interference can come from internal as well as external sources, however, including random neurophysiological fluctuations, it is difficult to separate the effects of time *per se* from the interference that inevitably accumulates with time.

In order to selectively maintain only the most currently relevant information, one must have both a mechanism for protecting the information that is currently in working memory from interference and a mechanism for allowing information to enter and overwrite the current contents of working memory when the new information becomes more important to the task than the old information. This dynamic flexibility at a millisecond timescale necessarily implies that working

memory be instantiated through neural activity rather than the structural changes that accompany long-term memory encoding and storage.

In the brain, the signature of working memory has been considered to be the sustained neural activity over delays after the stimulus is no longer present. Sustained activity has been observed during single cell neurophysiological recordings in nonhuman primates (see reviews in Goldman-Rakic, 1995; Fuster, 2001) and using neuroimaging techniques in humans such as EEG (e.g. Ruchkin *et al.*, 1992; Mecklinger and Pfeifer 1996; McEvoy *et al.*, 1998) and fMRI (e.g. Courtney *et al.*, 1997; Cohen *et al.*, 1997; Zarahn *et al.*, 1999). Working memory performance depends on this sustained activity, particularly in prefrontal cortex (PFC) (e.g. Kubota and Niki, 1971; Miller *et al.*, 1996; Pessoa *et al.*, 2002). What precisely this sustained activity represents and what its role is during performance of working memory tasks, however, has been the subject of much debate (e.g. see reviews Levy and Goldman-Rakic 2000; Miller, 2000; Duncan, 2001; Fuster, 2001; Curtis and D'Esposito 2003; Passingham and Sakai, 2004; Courtney, 2004). Accumulating evidence suggests that the information represented and the role of sustained neural activity in task performance may be different for different brain regions and that these representations and roles may dynamically change according to task demands.

Sustained representations of the current task demands are thought to form the basis of the biasing signal in the biased competition model for attentional selection of perceptual information (Desimone and Duncan, 1995; Desimone, 1998). In this model, representations of current perceptual information compete for further processing through mutually inhibitory interactions. The biasing

signals enhance the strength of one of the representations, resulting in the inhibition of other possible representations. The needs of working memory are very similar to those of perceptual processing. Both systems require the selection of relevant information and the suppression of irrelevant information. Both systems also require the ability either to sustain the current state or to shift states when the task demands change. Current interpretations of the biased competition model for attentional selection presume that the biasing signal, representing such information as task demands and search target templates, is maintained via PFC and that this information (in combination with perceptual salience) creates attentional priority maps in parietal cortex and the frontal eye fields, which in turn increase or decrease the strength of the representations of different locations or objects in the perceptual input (e.g. Bichot and Schall, 1999; Bisley and Goldberg, 2003; Serences *et al.*, 2005). We propose that similar mechanisms may be operating in working memory, influencing the relative strength of different representations of information within WM. (See also Deco and Rolls, 2003; Almeida *et al.*, 2004).

X.2 SELECTIVE MAINTENANCE OF TASK RELEVANT INFORMATION

X.2.1 *Domain-Dependent PFC Organization: Stimulus-Specific Information versus “Executive” Information*

Ever since Baddeley and Hitch (1974) proposed their Multiple Component Model with two domain-dependent “slave systems” (i.e. the phonological loop and the visuospatial sketch pad) and a domain-independent “central executive”, most theories of working memory have posited both distinct and common neural

resources required for performance of working memory tasks involving the maintenance of different types of information (Miyake and Shah, 1999). Two tasks that both depend on the phonological loop, for example, will interfere with each other more than will two tasks that depend on different slave systems. However, even tasks that depend on separate slave systems are not entirely independent and are thus assumed to both require some common executive resources (Logie, 1995).

Models of working memory that include distinct systems for maintenance of verbal, spatial, and nonspatial visual information as well as a domain-independent resource necessary for all such tasks have been supported by recent neuroimaging studies. While common neural systems seem to be recruited by all of these types of WM tasks relative to nonmnemonic control tasks, double dissociations regarding the degree of activation in different cortical areas for maintenance of different types of information have also consistently been found (see Courtney, 2004 for review).

While it has long been known that sensory processing areas are information domain-dependent (for review see Ungerleider and Haxby, 1994), only recently has sufficient evidence accumulated to support the idea that the prefrontal cortex is also organized according to the type of information being processed or maintained. FMRI studies in humans clearly demonstrate that both dorsal and ventral frontal cortex show activation during both object and spatial working memory tasks relative to non-mnemonic control tasks (Baker *et al.*, 1996; Owen *et al.*, 1996; D'Esposito *et al.*, 1998; Nystrom *et al.*, 2000; Postle *et al.*, 2000a, 2000b; Stern *et al.*, 2000; Postle and D'Esposito, 1999). Many of these studies

failed to observe any dorsal-ventral organization within the PFC related to maintenance of object versus spatial information (Petrides, 1995b, 1995a, 1996; D'Esposito *et al.*, 1998; Nystrom *et al.*, 2000; Stern *et al.*, 2000; Postle and D'Esposito, 1999). More recent studies that have found such an organization, however, suggest that the lack of dissociation was likely due to either insufficient statistical power or recoding strategies (for review see Courtney 2004). Studies that do find a spatial/nonspatial functional topography demonstrate that a region near the posterior end of the superior frontal sulcus at the junction with the precentral sulcus is activated more during spatial working memory maintenance than during verbal or object working memory. Similarly, posterior ventrolateral PFC (BA 44/45) is activated more during verbal and object working memory than during spatial working memory (Courtney *et al.*, 1996, 1998; Munk *et al.*, 2003; Sala *et al.*, 2003; Gruber and Yves von Cramon, 2003; Sakai and Passingham, 2003). This spatial/nonspatial dissociation is not limited to the visual modality (Rämä *et al.*, 2004; Arnott *et al.*, 2005). Verbal working memory is usually left lateralized while both visual object working memory and spatial working memory tend to be right lateralized although these latter findings are less consistent (D'Esposito *et al.*, 1999; Smith and Jonides, 1999; Rämä *et al.* 2001; Sala and Courtney, in press), perhaps due to participants' tendencies to attempt to use verbal recoding strategies during such tasks. The functional significance of these fMRI activation differences, the nature of the representation of information in working memory, and the overall nature of the functional organization of prefrontal cortex, however, have remained unclear.

Studies of the effects of various prefrontal lesions in both human and nonhuman primates have also generally supported a distinction between spatial, object, and verbal working memory systems, although there are some caveats to consider (for review see Curtis and D'Esposito, 2004). In nonhuman primates, lesions limited to the principal sulcus and the nearby cortex dorsal to the sulcus cause deficits specifically in tasks that depend on the maintenance of spatial information across a memory delay (Mishkin *et al.*, 1969; Goldman and Rosvold, 1970; Goldman *et al.*, 1971; Petrides 1995;). These lesions do not cause deficits on tasks that require maintenance of nonspatial information or on spatial tasks that do not involve a memory delay.

By contrast, lesions of ventrolateral PFC do frequently cause impairments in delayed object-alternation and delayed object match-to-sample recognition tasks (Mishkin and Manning, 1978; Iverson and Mishkin, 1970; Passingham, 1975). However, deficits were also observed on similar spatial working memory tasks and were present for both spatial and nonspatial tasks even without a memory delay requirement (Iverson and Mishkin, 1970; Passingham, 1975). In humans, there is very little data with the lesion location specificity required to address this question. Some data do suggest that disruptions in the function of cortex within the posterior portion of the superior frontal sulcus in humans, either from stroke (Carlesimo *et al.*, 2001) or from transcranial magnetic stimulation (Mottaghy *et al.*, 2002) selectively disrupt spatial working memory, while disruptions of ventral PFC appear to selectively impair nonspatial working memory (Bechara *et al.*, 1998; Mottaghy *et al.*, 2002). However, both human and nonhuman primates with ventrolateral PFC lesions often have profound difficulties with inhibition of

prepotent responses and rule learning that interferes with performance on a wide variety of tasks, both spatial and nonspatial (e.g. Iverson and Mishkin, 1970; Stuss and Benson, 1986; Shallice and Burgess, 1991).

The lack of a symmetrical double-dissociation between the effects of posterior dorsal versus ventral PFC lesions may be the result of two, inter-related factors. First, it may be that the brain evolved separate systems governing working memory for spatial versus nonspatial working memory because the two types of information are fundamentally different and thus require different neural mechanisms. There are a limited number of spatial locations and spatial relationships and the representations of these types of information are intimately tied to the sensorimotor system. Many cells in parietal cortex, for example, receive both visual and somatosensory input and are important both for spatial perception and for reaching movements toward visual targets (Colby and Goldberg, 1999). For nonspatial (object and verbal) working memory, on the other hand, there is an unlimited number of possible stimuli which have a more indirect relationship to behavioral response through which we measure performance and impairment. Perhaps the neural mechanisms for representing this infinite variety of nonspatial information is necessarily more tied to the neural mechanisms that represent and implement task rules. Alternatively (or consequently) these functions may be implemented in separate cortical regions that are anatomically close together within the ventrolateral PFC and no lesion study has yet been able to distinguish them. This latter possibility is supported by the results of a study of individuals with damage in the ventral PFC by Thompson-Schill and colleagues (2002). As a group, the patients showed deficits

in verbal working memory relative to age-matched controls. However, one patient, RC, whose lesion extended slightly more anteriorly than any of the other patients, was the only one to have an abnormally greater difficulty with suppressing interference from memory sets presented in previous trials. Thus the ability to select currently relevant information in working memory may be functionally and neurally dissociable from those regions that subsequently maintain and use that information.

Neuroimaging studies also support the idea that there are separable regions for maintenance of spatial and nonspatial information and for executive functions that do not depend on the type of stimulus-specific information. Note that these other areas may also be considered “domain-dependent” if one considers such abstract information as task rules and goals as being another type of information domain. Of particular interest in the literature has been a mid-dorsolateral prefrontal region, likely corresponding to BA 46/9. In nonhuman primates it has been shown that many neurons in this region demonstrate sustained activity during working memory delays that is selective for the task rule (White and Wise, 1999; Wallis *et al.*, 2001), or stimulus category (Freedman *et al.*, 2003), rather than particular perceptual attributes of the sample or anticipated test stimuli. Neuroimaging studies suggest a similar interpretation. Although it is difficult to judge whether identical or merely nearby functional areas have been activated in different studies, this general region tends to be activated more when the task requires maintenance in the presence of distracting perceptual inputs (Sakai *et al.*, 2002), explicit manipulation of the maintained information (D’Esposito *et al.*, 1999), presumed recoding of the maintained

information under conditions of high WM load (Rypma *et al.*, 2002; Bor *et al.*, 2003), and a large variety of other “executive control” functions (e.g. Derrfuss *et al.*, 2004). This region has also been activated in very simple executive-type tasks involving the “refreshing” of recently presented information (Raye *et al.*, 2002). The magnitude of activation in this broadly defined region does not consistently distinguish between spatial and nonspatial tasks. Functional connectivity analyses suggest, however, that activity in this region may differentially influence the interactions among regions that are selectively involved in maintaining spatial versus nonspatial stimulus-specific information, depending on the task demands (Sakai and Passingham, 2003).

In summary, there is evidence for a domain-dependent neuroanatomical functional organization within the PFC that supports models of working memory that include both dissociable systems for the maintenance of spatial and nonspatial information and common resources for executive control of this information. The systems for spatial and nonspatial working memory are not isolated modules, however. These two systems may have different relationships with other systems for motor behavior, rule representation, and executive control. Thus the effects of lesions in these two systems may not be symmetrical. In addition, as explained in the next section, these two systems appear to change their interactions with other systems and with each other in a task-dependent manner in order to create integrated representations of spatial and nonspatial information, such as an object in its location.

X.2.2 Binding of Objects and their Locations in Working Memory

Despite the large literature from both human and nonhuman primate studies suggesting distinct neural systems for spatial and nonspatial information, outlined briefly above, there is an equally large literature suggesting that spatial and nonspatial information are integrated within the PFC. Single PFC neurons can integrate color and location information according to a pre-learned “rule” (White and Wise, 1999) or over the delays of delayed response tasks (Quintana, *et al.*, 1988; Yajeya *et al.*, 1988). PFC neurons also appear to make cross-modal associations (Fuster *et al.*, 2000). Prefrontal cooling implicates the prefrontal cortex specifically in the cross-temporal integration of spatial and nonspatial information (Quintana and Fuster, 1993). The most telling piece of information, however, was the demonstration that cells in both dorsal and ventral frontal cortex can show selective responses to either objects, locations, or both, dynamically changing their selectivity to reflect the current task demands (Rao, *et al.*, 1997; Rainer *et al.*, 1998).

Another critical piece of evidence in the puzzle over the nature of the representation of object and location information in working memory came from a pair of fMRI experiments that, similar to the nonhuman primate experiments, tested for changes in activation during object, location, and object-in-location working memory tasks. Sala and Courtney (in press) tested the ideas of a task-dependent information representation and a dynamic functional organization of the PFC in two experiments in which fMRI activation was measured while participants held in working memory either fractal-like patterns, the locations of those patterns, or both the patterns and their locations. In both of those

experiments, there was a dorsal/ventral, spatial/nonspatial functional topography such that the posterior part of the SFS had significantly greater activation for the location task and posterior inferior frontal cortex had greater activation for the pattern identity task. Significant activity relative to a fixation baseline or a sensorimotor control task was found in each PFC region during maintenance of both its preferred and nonpreferred information type, a result sometimes thought to be at odds with a domain-dependent functional organization. However, this activity during maintenance of that region's nonpreferred information could represent incidental encoding of the irrelevant information. Alternatively, this overlap of activation patterns could be interpreted as indicating the existence of intermixed spatially and nonspatially-selective cell populations with a greater percentage of primarily spatially-tuned neurons dorsally and a greater percentage of primarily object-tuned neurons ventrally, as has been previously proposed (e.g. Haxby *et al.*, 2000; Duncan, 2001).

This relative distributions account, however, is at odds with the results of the Sala and Courtney (in press) experiments for the task involving working memory maintenance of both the patterns and their locations. That task condition resulted in an activation level, in nearly every region activated by any of the tasks, that was greater than that for each region's nonpreferred (spatial or nonspatial) information type, but less than that for each region's preferred information type. If dorsal and ventral PFC areas contained a mixture of "what cells" and "where cells", then activity during object-in-location delays would be greater than the activity during maintenance of either information alone, because both cell

populations would now be active instead of only one or the other. Therefore, while the results of studies showing regional preferences for spatial versus nonspatial information are at odds with a stable domain-general organization, a stable domain-dependent, or even a domain-dependent organization with differential, rather than absolute, distributions of distinct cell types, has no way to account for a decrease in activity during “bound” object-in-location working memory maintenance.

INSERT FIGURE X.1 ABOUT HERE

The result that object-in-location working memory activity was significantly less than the preferred information type suggests a more selective, integrated representation of the information during this task, perhaps with a smaller number of cells active than during the region’s preferred task, but with those cells more active than during the region’s nonpreferred task. What is the neural mechanism that could simultaneously account for these fMRI results and the dynamic selectivity observed in the Rao *et al* (1997) and Rainer *et al.* (1998) studies?

X.2.3 Biased Competition Model for the Selective Maintenance of Task-Relevant Information.

A neural mechanism has recently been proposed that applies the principles of biased competition mechanisms for attentional selection to the problem of dynamically and selectively maintaining task-relevant information in working

memory (Sala and Courtney, in press). This model provides a single simple mechanism to explain both neuroimaging and single-cell physiology data regarding working memory maintenance of objects, locations, and the conjunction of an object and its location.

The model supposes domain-dependent inputs from parietal and inferior temporal cortices to dorsal and ventral PFC regions, respectively. Each of these PFC regions is proposed to then receive *task-dependent* input from the other. These excitatory inputs, combined with competitive interactions within each region, would result in the dual selectivity observed in the Rao *et al* (1997) and Rainer *et al.* (1998) studies. In this model, when only spatial locations are task relevant, the excitatory input is mainly from dorsal PFC to ventral PFC. In this case, all dorsal PFC cells which respond well to the to-be-remembered location are active, independent of their preferred object, because that object selectivity arises only when input is received from ventral PFC. When only object identities are task relevant, the excitatory input is mainly from ventral PFC to dorsal PFC. In this case, all ventral PFC cells which respond well to the to-be-remembered object are active, independent of their preferred location, because that location selectivity arises only when input is received from dorsal PFC. When the integrated representation of an object and its location is task relevant, then the excitatory inputs go in both directions and dual object and location selectivity is observed in both dorsal and ventral PFC. Cells would respond best *only* if the task trial required both the cell's preferred location and its preferred object to be remembered. This type of system would result in a greater number of cells in dorsal (or ventral) PFC being highly active during a task that only requires

memory for locations (objects, respectively) than when both an object and its location must be remembered. The fMRI activation, which depends on the average activity of all the cells in a region, would be expected to show the intermediate response for the object-in-location task that was observed by Sala and Courtney (in press).

An important feature of this model is that the strength and direction of the interactions between dorsal and ventral PFC are task dependent. A prediction of the model is that if the task requires that objects and locations be remembered independent of their relationship with one another (i.e. which object was in which location), then both dorsal and ventral PFC regions would be expected to be more active than during an task that required an integrated representation to be remembered. In addition, functional connectivity measures between dorsal and ventral PFC would be expected to be lower when objects and locations must be maintained independently than when an integrated representation is necessary.

The question remains how the strength and direction of these interactions are determined. A promising candidate is the other regions of the PFC whose activation levels do not appear to depend on the type of stimulus-specific information being maintained. As mentioned earlier, the level of activity in these regions appears to depend on the amount and complexity of the context and the rules governing task performance (e.g. Sakai *et al.*, 2002, D'Esposito *et al.*, 1999; Rypma *et al.*, 2002; Bor *et al.*, 2003; Derrfuss *et al.*, 2004). Even in simple tasks, however, these regions could provide biasing signals that control the type of information to be maintained or allowed access to WM (as in Raye *et al.*, 2002).

Thus, biased-competition-like interactions among PFC regions could create new representations by combining information from multiple sources according to the constraints of the current task rules. In the absence of these biasing signals and interactions both the information in WM and the resulting behavior would default to the most prepotent state, which would have been established through experience and previous behavior (see also Miller and Cohen, 2001).

X.3 INTERFERENCE-RESISTANT MAINTENANCE VERSUS UPDATING

Another realm of working memory where biased-competition-like mechanisms may be at work is in the updating of information in working memory. Successful working memory maintenance requires that interfering information that is not task-relevant be prevented from over-writing the current contents of the working memory buffer. Indeed, many accounts of the role of PFC in working memory maintenance emphasize the protection from interference aspect, rather than the storage of the information itself (e.g. Engle *et al.*, 1999; Sakai *et al.*, 2002). Some have suggested that working memory storage capacity is fundamentally a function of attentional control over interfering information (Kane and Engle, 2002). Simultaneously, however, the system must also allow the currently maintained information to be over-written with updated information quickly whenever the new information becomes more important to the current task than the previously maintained information. This concept of relative priority is again reminiscent of biased competition for attentional selection, and data from recent neuroimaging studies support the idea that a similar mechanism is at work.

Roth and her colleagues (Roth *et al.*, under review; Roth *et al.*, 2003) used fMRI to investigate the relationship between interference-resistant WM maintenance and updating the contents of WM with a new sample stimulus. They used a modified delayed-recognition task in which participants viewed a continuous stream of either faces or houses. The first object in each task block was the first sample to be maintained in WM. With the presentation of each subsequent stimulus, participants indicated with a button press whether the current stimulus matched the sample stimulus. Randomly, every 4-10 seconds, participants saw one of two well-memorized cue faces or houses. One of these cues instructed the participants that the old sample was now irrelevant and that they were to maintain in WM the next face or house that they saw and to make future match/nonmatch decisions in reference to this new sample stimulus. The other cue served as a control event. That cue instructed participants to continue to maintain the current sample stimulus. For both cue events, participants pressed a button to indicate that they recognized the cue stimulus. There were also control task blocks in which participants viewed the same stream of faces or houses, but did not need to maintain any one of them in WM. Instead, participants made a perceptual categorization decision (male/female for faces, garage/no garage for houses) for each stimulus as it was presented. Thus, the experimental design included both sustained activation components for memory blocks versus control blocks, related to WM maintenance, and transient activation components related to the update events. Contrasting the update events to the control cued maintenance events enabled identification of activity

related to replacing the current contents of WM with a current perceptual stimulus.

Independent of the type of object to be remembered (face or house), transient, update-related activations were observed primarily in middle and superior frontal regions and parietal cortex. These regions partially overlapped with those regions showing sustained, maintenance-related activity. Notably, the middle frontal region activated by both maintenance and updating appears to be the same region as has been previously implicated in WM maintenance under conditions of interference (Sakai *et al.*, 2002). A similar region of activation has been observed in other studies in which the task required actively maintained abstract information, such as rules, to influence cognition or behavior (Bunge *et al.* 2003; Derrfuss *et al.*, 2004; See Figure x.2.). In the Roth *et al* study, participants needed to continue to maintain the sample stimulus while making match/nonmatch and cue/not-cue decisions on highly similar stimuli. Thus, they had to attend to the current perceptual input for the purposes of immediate processing, but also keep that perceptual information from overwriting the contents of WM until an update cue was seen. The overlapping activations for interference-resistant maintenance and updating suggests that the same control mechanism may be involved for both purposes. The particular pattern of activity in this region and its interactions with other brain areas (including subcortical areas) may determine whether the current contents of working memory will be maintained or overwritten by new information (see also Rougier *et al.*, 2005).

Transient changes in activation have also been observed in a highly similar middle frontal region when research participants refreshed the mental

representation of a recently seen (but not actively maintained) stimulus (Raye, *et al.*, 2002; Johnson *et al.*, 2003; See Figure x.2.). Both this refreshing task and the update events in the Roth *et al.* study involve a change in the relative priority of current versus previously seen information. The other regions that showed both sustained, maintenance-related activity and transient, update-related activity in the Roth *et al.* study were in parietal and superior frontal cortex in regions highly similar to those that have been shown to have both sustained and transient activity related to maintaining and shifting attention, respectively (Yantis *et al.*, 2002; Serences *et al.*, 2004).

The existence of both sustained, maintenance-related activity, and transient, update-related activity in brain regions that have previously been implicated in protecting information in WM from interference and regions that have previously been implicated in controlling attentional selection among current perceptual stimuli, suggests that a common mechanism may be involved in all of these functions. We propose that the common requirement in all of these functions is the setting of relative priorities according to current task context and rules. Biased competition could be at work not only in selecting whether object identity or location or both would be attended in the perceptual input, but also which type of information would continue to be maintained during a WM delay. In addition, actively maintained information about task context and rules could also set the relative priorities for information already being maintained in WM versus current perceptual input. Changes in these relative priorities could result from either explicit instruction cues, as in the Roth *et al.* (under review) study or from unexpected reward feedback (see Rougier *et al.* 2005). Such resolution among

competing sources and representations of information is necessary because of the limited storage capacity of working memory.

X.4 SUMMARY AND FUTURE DIRECTIONS

Taken together, the studies reviewed in this chapter suggest a role for abstract contextual or rule information maintained via the mid-dorsolateral PFC to bias competitive interactions within and among other brain regions (including other regions within the PFC) in the service of selecting, creating, maintaining, and updating the optimal representation of the most important information for the current task. This select, more stimulus-specific information then in turn could serve as the biasing signal for selection of particular actions (Cisek and Kalaska, 2004; for reviews see Fuster 2001, Bunge 2004), selection of competing conceptual representations in long-term memory (Kan and Thompson-Schill, 2004), or for attentional selection, as in the original biased competition model (Desimone and Duncan, 1995; Desimone, 1998). This framework implies a hierarchical structure with domain-dependent information maintenance and selection via biased competition occurring at every level. The proposed model is shown in figure X.3.

INSERT FIGURE X.3 NEAR HERE

In the model there are mutually inhibitory connections within each level of the hierarchy and excitatory inputs across levels. Which representation will “win” that competition at each level depends on how the balance of competition is biased both by the saliency of feed-forward perceptual information and by

feedback signals from higher levels. The model allows for multiple representations to be active simultaneously, but it is their *relative* levels of activity that will ultimately determine their influence on other brain regions and, thus, on behavior (see also Bisley and Goldberg, 2003).

The most powerful aspect of the model is that it enables many aspects of perception, action, and cognition to be explained by a common mechanism: relative levels of sustained activity in one brain area biasing the interactions within mutually inhibitory neural networks in another brain area. While such mechanisms have been proposed before, the unusual aspect of the current proposal is that these interactions could occur *within* the PFC as well as between the PFC and perceptual or motor regions. Such a unifying framework could simplify discussions of working memory, cognitive control, and other “executive” processes. If the model holds true, the difference between the brain regions responsible for various types of executive processes or between the phonological loop and the visuospatial sketch pad would be defined primarily on the type of information represented (as determined by the inputs to that region) and the type of influence that the information in that region has on the rest of the system (as determined by the output targets of that region). The model is testable at many levels, from cellular physiology and anatomy to neuroimaging and behavioral analysis. The field of working memory has made great progress from identifying dissociations among different aspects of behavior and the associated neural systems. Perhaps it is now time to identify the common underlying mechanistic principles.

FIGURES

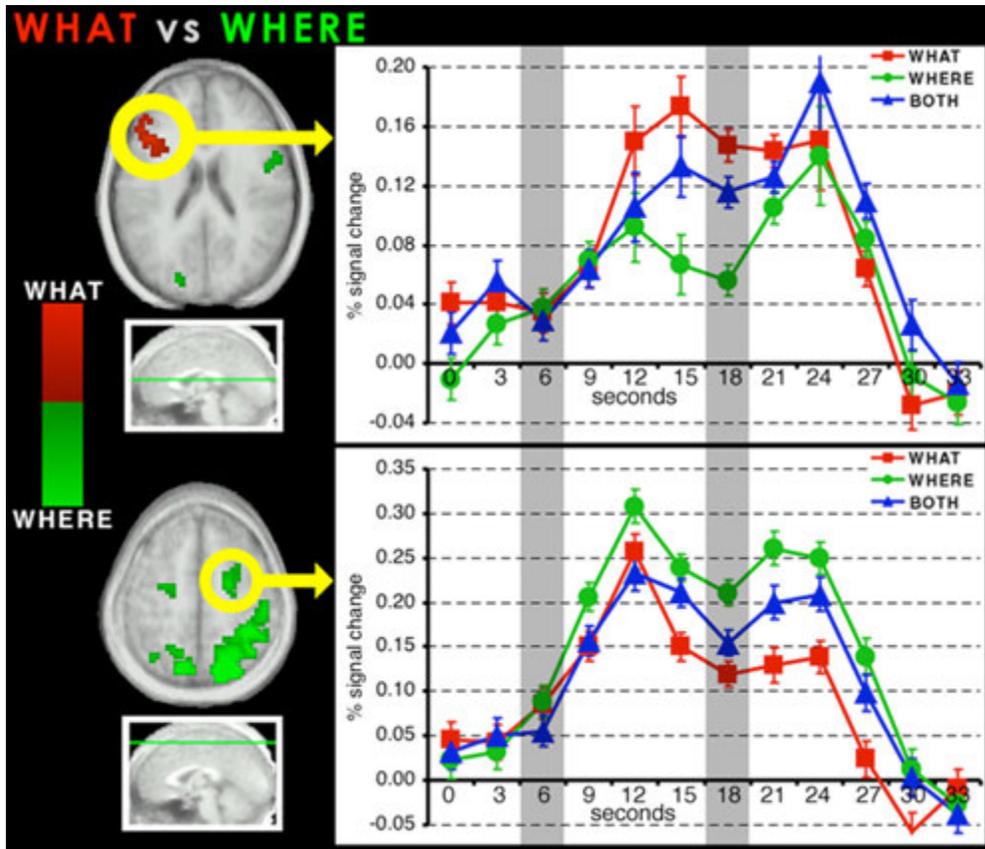


Figure X.1: FMRI activation patterns during working memory for fractal-like patterns (“WHAT”), the locations of those patterns (“WHERE”), or both the patterns and their locations (“BOTH”). There is a dorsal/ventral spatial/nonspatial topography for the what-only and where-only tasks, but the activation for the BOTH task is in between the levels of activation for the preferred and non-preferred information types, consistent with a more selective representation for an object-in-its-location, involving fewer cells than are active during maintenance of the preferred information, but with those cells more highly active than during maintenance of the non-preferred information. Reprinted with permission from Sala and Courtney (in press).

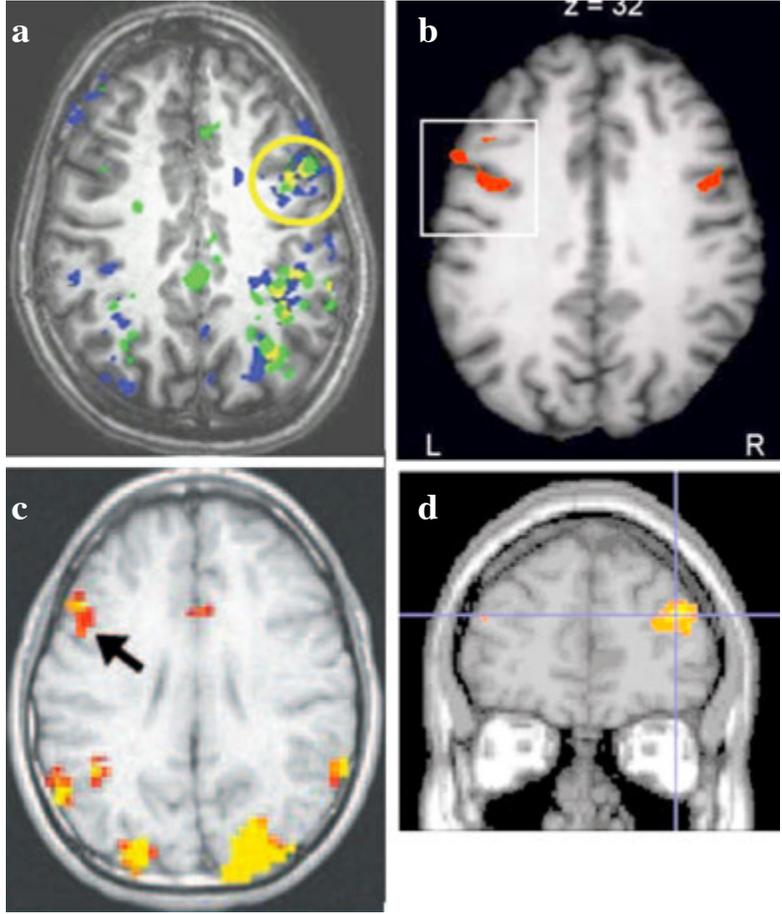


Figure X.2: Activation of middle frontal cortex (possibly Brodmann's Area 46) in several studies involving the prioritization of one type of information over another: **(a)** Updating (in green), WM maintenance (blue), and their overlap (yellow) (reprinted with permission from Roth *et al.*, under review), **(b)** Common activation for task-switching, Stroop task, and n-back working memory task (reprinted with permission from Derrfuss *et al.*, 2004), **(c)** Refreshing of just-seen information (reprinted with permission from Johnson *et al.*, 2003), **(d)** Interference-resistant WM maintenance (reprinted with permission from Sakai *et al.*, 2002).

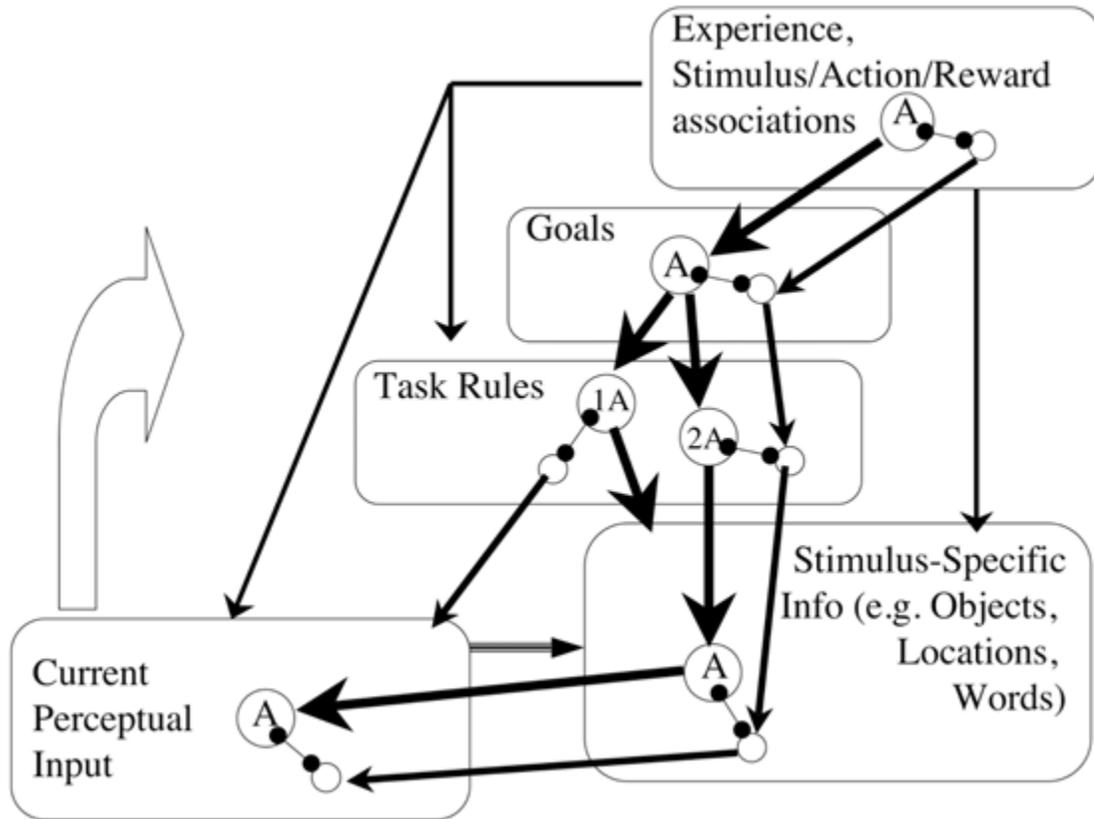


Figure X.3: Hierarchical biased-competition (HBC) model for working memory maintenance and cognitive control. “A” represents the current task schema with all of its associated goals, rules, and sensory information, each of which is proposed to be represented by activity in a different level of the hierarchy. Note that there are two parts to the rule representation (1A and 2A). The greater activation of 1A relative to other possible rules determines whether the current contents of working memory or the current perceptual input is more important for future maintenance in WM. The greater activation of 2A relative to other possible rules determines which objects, locations, or other stimulus-specific information will be maintained.

REFERENCES

- Almeida R, Deco G, and Stetter M. (2004) Modular biased-competition and cooperation: A candidate mechanism for selective working memory. *Eur J Neurosci*, 20: 2789-803.
- Arnott, S.R., Grady CL, Hevenor SJ, Graham S, Alain C. (2005) The functional organization of auditory working memory as revealed by fMRI. *Journal of Cognitive Neuroscience*. 17(5):819-31.
- Baddeley A and Hitch GJ. (1974) Working memory. In Bower G.A. (Ed.) *Recent advances in learning and memory*. New York: Academic Press, pp. 47-90.
- Baker SC, Frith CD, Frackowiak RS, and Dolan RJ. (1996) Active representation of shape and spatial location in man. *Cereb Cortex*, 6: 612-9.
- Bechara A, Damasio H, Tranel D, and Anderson SW. (1998) Dissociation of working memory from decision making within the human prefrontal cortex. *J Neurosci*, 18: 428-37.
- Bichot NP, Schall JD. (1999) Effects of similarity and history on neural mechanisms of visual selection. *Nat Neurosci*. 2(6):549-54.
- Bisley J.W., Goldberg, M.E. (2003). Neuronal activity in the lateral intraparietal area and spatial attention. *Science* 299, 81-86.
- Bor D, Duncan J, Wiseman RJ, Owen AM. (2003) Encoding strategies dissociate prefrontal activity from working memory demand. *Neuron*. 37(2):361-7.
- Bunge SA. (2004) How we use rules to select actions: a review of evidence from cognitive neuroscience. *Cogn Affect Behav Neurosci*. 4(4):564-79.
- Carlesimo GA, Perri R, Turriziani P, Tomaiuolo F, and Caltagirone C. (2001) Remembering what but not where: Independence of spatial and visual working memory in the human brain. *Cortex*, 37: 519-34.
- Colby CL, Goldberg ME. (1999) Space and attention in parietal cortex. *Annu Rev Neurosci*. 22:319-49
- Courtney SM. Attention and cognitive control as emergent properties of information representation in working memory. (2004) *Cognitive, Affective, & Behavioral Neuroscience*, 4(4): 501-516.
- Courtney SM, Petit L, Maisog JM, Ungerleider LG, and Haxby JV. An area specialized for spatial working memory in human frontal cortex. *Science*, 279: 1347-51, 1998.
- Courtney SM, Ungerleider LG, Keil K, and Haxby JV. (1996) Object and spatial visual working memory activate separate neural systems in human cortex. *Cereb Cortex*, 6: 39-49.
- Curtis CE, D'Esposito M. (2003) Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Science* 7(9):415-423.
- Curtis CE, D'Esposito M. (2004) The effects of prefrontal lesions on working memory performance and theory. *Cogn Affect Behav Neurosci*. 4(4):528-39.
- D'Esposito M, Aguirre GK, Zarahn E, Ballard D, Shin RK, and Lease J. (1998) Functional mri studies of spatial and nonspatial working memory. *Brain Res Cogn Brain Res*, 7: 1-13.

- D'Esposito M, Postle BR, Ballard D, and Lease J. (1999) Maintenance versus manipulation of information held in working memory: An event-related fmri study. *Brain Cogn*, 41: 66-86.
- D'Esposito M, Postle BR, and Rypma B. (2000) Prefrontal cortical contributions to working memory: Evidence from event-related fmri studies. *Exp Brain Res*, 133: 3-11.
- Deco G and Rolls ET. (2003) Attention and working memory: A dynamical model of neuronal activity in the prefrontal cortex. *Eur J Neurosci*, 18: 2374-90.
- Derrfuss J, Brass M, von Cramon DY. (2004) Cognitive control in the posterior frontolateral cortex: evidence from common activations in task coordination, interference control, and working memory. *Neuroimage*. 23(2):604-12.
- Desimone R. (1998) Visual attention mediated by biased competition in extrastriate visual cortex. *Philos Trans R Soc Lond B Biol Sci*, 353: 1245-55.
- Desimone R and Duncan J. (1995) Neural mechanisms of selective visual attention. *Annu Rev Neurosci*, 18: 193-222.
- Doshier BA, (1999) Item Interference and Time Delays in Working Memory: Immediate Serial Recall. *International Journal Of Psychology*, 34 (5/6): 276- 284.
- Duncan J. (2001) An adaptive coding model of neural function in prefrontal cortex. *Nat Rev Neurosci*, 2: 820-9.
- Engle RW, Kane MJ, Tuholski SW. (1999) "Individual Differences in Working memory capacity and what they tell us about controlled attention, general fluid intelligence, and functions of the prefrontal cortex" in Miyake A. and Shah P. (Eds.) *Models of Working Memory: Mechanisms of Active Maintenance and Executive Control*. pp. 102-134. Cambridge University Press.
- Freedman, D.J., Riesenhuber, M., Poggio, T., and Miller, E.K (2003) A comparison of primate prefrontal and inferior temporal cortices during visual categorization. *Journal of Neuroscience*, 23(12):5235-5246
- Fuster JM. (2001) The prefrontal cortex--an update: Time is of the essence. *Neuron*, 30: 319-33.
- Fuster JM, Bodner M, and Kroger JK. (2000) Cross-modal and cross-temporal association in neurons of frontal cortex. *Nature*, 405: 347-51.
- McEvoy LK, Smith ME, Gevins A.(1998) Dynamic cortical networks of verbal and spatial working memory: effects of memory load and task practice. *Cereb Cortex*. 8(7):563-74.
- Goldman PS, Rosvold HE, Vest B, Galkin TW. (1971) Analysis of the delayed-alternation deficit produced by dorsolateral prefrontal lesions in the rhesus monkey. *J Comp Physiol Psychol*. 77(2):212-20.
- Goldman and Rosvold (1970) Localization of function within the dorsolateral prefrontal cortex of the rhesus monkey. *Exp Neurol*. 27(2):291-304.
- Goldman-Rakic PS. Cellular basis of working memory. (1995) *Neuron*, 14: 477-85.
- Gruber & Yves von Cramon (2003) The functional neuroanatomy of human working memory revisited. Evidence from 3-T fMRI studies using classical domain-specific interference tasks. *Neuroimage*. 19(3):797-809.

- Iverson SD and Mishkin M. (1970) Perseverative interference in monkeys following selective lesions of the inferior prefrontal convexity. *Exp. Brain Res.* 11, 376-86.
- Johnson MK, Raye CL, Mitchell KJ, Greene EJ, and Anderson AW. (2003) Fmri evidence for an organization of prefrontal cortex by both type of process and type of information. *Cereb Cortex*, 13: 265-73.
- Kan IP, Thompson-Schill SL (2004) Selection from perceptual and conceptual representations. *Cogn Affect Behav Neurosci.* 4(4):466-82.
- Kane MJ, Engle RW (2002) The role of prefrontal cortex in working-memory capacity, executive attention, and general fluid intelligence: an individual-differences perspective. *Psychonomic Bull Rev.* 9(4):637-71.
- Kubota K, Niki H. (1971) Prefrontal cortical unit activity and delayed alternation performance in monkeys. *Journal of Neurophysiology.* 34:337-47
- Levy R and Goldman-Rakic PS. (2000) Segregation of working memory functions within the dorsolateral prefrontal cortex. *Exp Brain Res*, 133: 23-32.
- Logie R. (1995) *Visuo-spatial working memory*. Hove: Lawrence Erlbaum Associates, Inc.
- Mecklinger A, Pfeifer E (1996) Event-related potentials reveal topographical and temporally distinct neuronal activation patterns for spatial and object working memory. *Cognitive Brain Research* 4:211-224.
- Miller EK. (2000) The prefrontal cortex and cognitive control. *Nat Rev Neurosci*, 1: 59-65.
- Miller EK and Cohen JD. (2001) An integrative theory of prefrontal cortex function. *Annu Rev Neurosci*, 24: 167-202.
- Miller, E.K., Erickson, C.A., and Desimone, R. (1996) Neural mechanisms of visual working memory in prefrontal cortex of the macaque. *Journal of Neuroscience.* 16:5154-5167.
- Miyake A. and Shah P. (1999) *Models of Working Memory: Mechanisms of Active Maintenance and Executive Control*. Cambridge University Press,.
- Mottaghy FM, Gangitano M, Sparing R, Krause BJ, and Pascual-Leone A. (2002) Segregation of areas related to visual working memory in the prefrontal cortex revealed by rtms. *Cereb Cortex*, 12: 369-75.
- Munk M, Linden D, Muckli L, Lanfermann H, Zanella F, Singer W, and Goebel R. (2002) Distributed cortical systems in visual short-term memory revealed by event-related functional magnetic resonance imaging. *Cerebral Cortex*, 12: 866-87.
- Nystrom LE, Braver TS, Sabb FW, Delgado MR, Noll DC, and Cohen JD. (2000) Working memory for letters, shapes, and locations: Fmri evidence against stimulus-based regional organization in human prefrontal cortex. *Neuroimage*, 11: 424-46.
- Owen AM, Evans AC, and Petrides M. (1996) Evidence for a two-stage model of spatial working memory processing within the lateral frontal cortex: A positron emission tomography study. *Cereb Cortex*, 6: 31-8.
- Passingham, R. (1975). Delayed matching after selective prefrontal lesions in monkeys (*Macaca mulatta*). *Brain Research*, 92, 89-102.
- Passingham D, Sakai K. (2004) The prefrontal cortex and working memory: physiology and brain imaging. *Curr Opin Neurobiol.* 14(2):163-8.

- Pessoa L, Gutierrez E, Bandettini P, and Ungerleider L. (2002) Neural correlates of visual working memory: Fmri amplitude predicts task performance. *Neuron*, 35: 975-87.
- Petrides M. (1995a) Functional organization of the human frontal cortex for mnemonic processing. Evidence from neuroimaging studies. *Ann NY Acad Sci*, 769: 85-96.
- Petrides M. (1995b) Impairments on nonspatial self-ordered and externally ordered working memory tasks after lesions of the mid-dorsal part of the lateral frontal cortex in the monkey. *J Neurosci*, 15: 359-75.
- Petrides M. (1996) Specialized systems for the processing of mnemonic information within the primate frontal cortex. *Philos Trans R Soc Lond B Biol Sci*, 351: 1455-61.
- Postle BR and D'Esposito M. (1999) "What"-then-where" in visual working memory: An event-related fmri study. *J Cogn Neurosci*, 11: 585-97.
- Postle BR, Stern CE, Rosen BR, and Corkin S. (2000) An fmri investigation of cortical contributions to spatial and nonspatial visual working memory. *Neuroimage*, 11: 409-23.
- Postle BR, Zarahn E, and D'Esposito M. (2000) Using event-related fmri to assess delay-period activity during performance of spatial and nonspatial working memory tasks. *Brain Res Brain Res Protoc*, 5: 57-66.
- Quintana J, Fuster JM. (1993) Spatial and temporal factors in the role of prefrontal and parietal cortex in visuomotor integration. *Cereb Cortex*, 3: 122-32.
- Quintana J, Yajeya J, and Fuster JM. (1988) Prefrontal representation of stimulus attributes during delay tasks. I. Unit activity in cross-temporal integration of sensory and sensory-motor information. *Brain Res*, 474: 211-21.
- Rainer G, Asaad WF, and Miller EK. (1998) Memory fields of neurons in the primate prefrontal cortex. *Proc Natl Acad Sci U S A*, 95: 15008-13.
- Rämä, P., Poremba, A., Yee, L., Malloy, M., Mishkin, M., Courtney, S.M., (2004). Dissociable functional cortical topographies for working memory maintenance of voice identity and location. *Cerebral Cortex*, 14:768-780.
- Rämä, P., Sala, J.B., Gillen, J.S., Pekar, J.J., Courtney, S.M., (2001). Dissociation of the neural systems for working memory maintenance of verbal and nonspatial visual information. *Cognitive, Affective, and Behavioral Neuroscience* 1:161-171.
- Rao SC, Rainer G, and Miller EK. (1997) Integration of what and where in the primate prefrontal cortex. *Science*, 276: 821-4.
- Raye, C.L., Johnson, M.K., Mitchell, K.J., Reeder, J.A., Greene, E.J. (2002). Neuroimaging a single thought: dorsolateral PFC activity associated with refreshing just-activated information. *NeuroImage* 15, 447-453.
- Roth JK, Serences JT, Courtney SM. (2003) "Updating Versus Refreshing The Contents Of Working Memory For Houses And Faces: A Direct Comparison." Program No 343.4. 2003 Abstracts Viewer/Itinerary Planner. Washington, DC: Society for Neuroscience. CD-ROM.
- Roth JK, Serences JT, Courtney SM. "Neural system for controlling the contents of object working memory in humans", *under review*.
- Rougier NP, Noelle DC, Braver TS, Cohen JD, O'Reilly RC (2005) Prefrontal

- cortex and flexible cognitive control: Rules without symbols. *Proc. Natl. Acad. Sci.* 102(207): 338–7343
- Ruchkin DS, Johnson R Jr, Grafman J, Canoune H, Ritter W. (1992) Distinctions and similarities among working memory processes: an event-related potential study. *Brain Res Cogn Brain Res.* 1(1):53-66.
- Rypma B, Berger JS, D'Esposito M. (2002) The influence of working-memory demand and subject performance on prefrontal cortical activity. *J Cogn Neurosci.* 14(5):721-31.
- Sakai K and Passingham RE. (2003) Prefrontal interactions reflect future task operations. *Nat Neurosci,* 6: 75-81.
- Sakai K, Rowe JB, Passingham RE (2002) Active maintenance in prefrontal area 46 creates distractor-resistant memory *Nature Neuroscience.* 5(5):479-84.
- Sala, J.B. and Courtney, SM (in press) "Binding of What and Where during Working Memory Maintenance" *Cortex.*
- Sala JB, Rama P, and Courtney SM. (2003) Functional topography of a distributed neural system for spatial and nonspatial information maintenance in working memory. *Neuropsychologia,* 41: 341-56.
- Serences JT, Schwarzbach J, Courtney SM & Yantis S (2004) "Control of object-based visual attention in human cortex" *Cerebral Cortex.* 14: 1346-1357
- Serences JT, Shomstein S, Leber AB, Golay X, Egeth HE, Yantis S. (2005) Coordination of voluntary and stimulus-driven attentional control in human cortex. *Psychol Sci.* 16(2):114-22.
- Shallice T. and Burgess PW (1991) Deficits in strategy application following frontal lobe damage in man. *Brain* 114, 727-41.
- Smith EE and Jonides J. (1999) Storage and executive processes in the frontal lobes. *Science,* 283: 1657-61.
- Stern CE, Owen AM, Tracey I, Look RB, Rosen BR, and Petrides M. (2000) Activity in ventrolateral and mid-dorsolateral prefrontal cortex during nonspatial visual working memory processing: Evidence from functional magnetic resonance imaging. *Neuroimage,* 11: 392-9.
- Stuss DT and Benson DF (1986) *The frontal lobes.* New York: Raven Press.
- Thompson-Schill SL, Jonides J, Marshuetz C, Smith EE, D'Esposito M, Kan IP, Knight RT, Swick D. (2002) Effects of frontal lobe damage on interference effects in working memory. *Cogn Affect Behav Neurosci.* 2(2):109-20.
- Ungerleider LG, Haxby JV. (1994) 'What' and 'where' in the human brain. *Curr Opin Neurobiol.* 4(2):157-65.
- Wallis, J.D., Anderson, K.C., and Miller, E.K. (2001) Single neurons in the prefrontal cortex encode abstract rules. *Nature,* 411:953-956.
- White IM and Wise SP. (1999) Rule-dependent neuronal activity in the prefrontal cortex. *Exp Brain Res,* 126: 315-35.
- Yajeya J, Quintana J, and Fuster JM. (1988) Prefrontal representation of stimulus attributes during delay tasks: The role of behavioral significance. *Brain Res,* 474: 222-30.
- Yantis S, Schwarzbach J, Serences JT, Carlson RL, Steinmetz MA, Pekar JJ, Courtney SM (2002) Transient neural activity in human parietal cortex during spatial attention shifts. *Nature Neuroscience,* 5: 995 - 1002.
- Zarahn E, Aguirre GK, D'Esposito M. (1999) Temporal isolation of the neural

correlates of spatial mnemonic processing with fMRI. *Brain Res Cogn Brain Res.* 7(3):255-68