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## Working memory, cognitive control, and the prefrontal cortex: Computational and empirical studies

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**Abstract** - The dominant cognitive theory of working memory (WM) postulates a strict architectural segregation between components responsible for the short-term active maintenance of information and those responsible for the control and coordination of that information. Cognitive neuroscience research has provided strong evidence that the prefrontal cortex (PFC) serves as an important neural substrate of WM. However, the literature is mixed as to whether PFC should be considered a storage or control component. A theory is presented that attempts to resolve this conflict by postulating that PFC represents and actively maintains context information. These maintained representations provide a mechanism of control by serving as a top-down bias on the local competitive interactions that occur during processing. As such, it is suggested that storage and control functions are integrated within PFC. This theory is implemented as connectionist computational model. Simulation studies are described which demonstrate that the model can account for a wide range of behavioral data associated with performance of a simple task paradigm that probes both the storage and control functions of WM. Two neuroimaging studies are then presented which directly test the predictions of the model regarding the role of PFC in context processing. Taken together, the results provide new insights into the relationship between storage and control in WM, and the role of PFC in subserving these functions.

**Key words:** neuroimaging, neural network, frontal lobes, executive control.

### 1. Introduction

Research on working memory (WM) is currently one of the most active topics within cognitive psychology and cognitive neuroscience, as evidenced by the flurry of books (Gathercole, 1996; Logie, 1995), edited volumes (Logie and Gilhooly, 1998; Miyake and Shah, 1999; Richardson *et al.*, 1996), and special journal issues on this topic (*Memory and Cognition*, 1993; *Neuropsychology*, 1994; *Quarterly Journal of Experimental Psychology*, 1996). Much of the excitement regarding the



study of WM can be traced to the contributions of Alan Baddeley, whose theoretical and experimental work in this area has had a lasting and widespread influence on the field (Baddeley and Della Sala, 1996; Baddeley, 1986; Baddeley and Hitch, 1974; Baddeley and Hitch, 1994). Baddeley and colleagues have put forth a theoretical account regarding the architecture of WM, which has come to be the dominant model (Baddeley and Hitch, 1974). In this model, there are two domain-specific buffer systems – the phonological loop and the visuospatial scratchpad – whose activity is coordinated by a central control structure termed the “central executive”. The key aspect of this model is that both storage and control processes are included under the heading of WM, but that these processes are architecturally distinct and segregated. These theoretical distinctions between WM components within the Baddeley model have attracted cognitive psychologists, who were encouraged to study the properties of, and functional dissociations between the more tractable buffer systems, without feeling the need to first fully understand the characteristics of the more vaguely described central executive. In parallel, cognitive neuroscientists have been attracted by the prospects of discovering the neural substrates of each component within the model.

In cognitive neuroscience studies of WM, the prefrontal cortex (PFC) has been a particular area of focus. Studies of neuropsychological patients have long pointed to this brain region as being involved with behavioral and cognitive regulation (Damasio, 1985; Hecaen and Albert, 1978; Stuss and Benson, 1986). Thus, it is not surprising that many researchers have identified the PFC with the central executive component of Baddeley’s model. Indeed, a prominent neuropsychological theory, put forward by Shallice and colleagues, has specifically described the PFC as a Supervisory Attentional System that performs the control functions commonly attributed to the central executive (Norman and Shallice, 1986; Shallice, 1982; Shallice, 1988). Baddeley himself has incorporated SAS theory into his own model (Baddeley, 1986), thus reinforcing this linkage between PFC and the central executive component of WM. However, this neuropsychological perspective stands in stark contrast with studies arising out of the animal literature on PFC function. In this literature, PFC has been found to be critically involved in short-term active maintenance of information (Fuster, 1989; Goldman-Rakic, 1987). Goldman-Rakic, who has been one of the most active researchers in this area, has argued that sustained neuronal activity in PFC serves as the “cellular basis” of WM (Goldman-Rakic, 1995). Yet the functions ascribed to PFC by Goldman-Rakic seem to align more closely with the buffer system component of WM rather than the control system. Thus, the search for the neural substrates of WM have led to considerable controversy within cognitive neuroscience. Specifically, does the PFC subserve the storage or control functions of WM? Recently there has been an attempt to resolve this controversy using the newly developed techniques of functional neuroimaging. A number of investigators, arguing from meta-analyses of neuroimaging studies of WM, have suggested that there is an anatomical segregation within lateral PFC. In particular, it has been suggested that while ventral PFC regions may be involved directly with active maintenance functions, dorsal PFC regions are instead involved with the control aspects of WM rather than storage directly (D’Esposito *et al.*, 1998; Owen, 1997; Smith and Jonides, 1999).

In the current paper, we argue for a different, potentially more radical, resolution to this controversy. In particular, we take the perspective that the strict distinction between storage and control advocated by Baddeley does not map cleanly onto the architecture of the brain, in which processing and memory functions are typically distributed within, and performed by the same neural substrate (Rumelhart and McClelland, 1986). Specifically, we make the suggestion that PFC might subserve specific control functions precisely through active maintenance of certain types of information in WM. Our perspective on the role of PFC in WM is developed through a computational, mechanistically-explicit approach, relying on principles of neural information processing associated with the “connectionist” or neural network framework. We develop a model in which PFC subserves a specific computational function, that of *representing and actively maintaining context information*. We describe computer simulations which demonstrate how this model might provide an account of the role of PFC in a specific behavioral task known as the AX-CPT, which probes both the storage and control functions of WM. We then present two new functional neuroimaging studies which directly test this aspect of the model. The results of these studies provide support for the claim that dorsolateral PFC is involved with actively maintaining context information in WM, and that this information is critical for the control of behavior.

## 2. A theory of cognitive control

### 2.1. Context and cognitive control

We begin with a discussion of how the control of cognition might be exerted. We note that one of the most basic and fundamental cognitive control functions is the ability to flexibly adapt behavior to the demands of particular tasks, by facilitating processing of task-relevant information over other sources of competing information, and by inhibiting habitual, or otherwise prepotent responses which are inappropriate to the task. Because this control function is such a fundamental one, it occurs in even very simple task situations. As a specific example, take a situation where a speeded response is required to a particular stimulus, but only in a particular context (e.g., respond to the letter ‘X’ only if immediately following the letter ‘A’). If the context-stimulus pairing occurs frequently, the cognitive system should begin to exploit the contextual information to prime or facilitate processing of the subsequent stimulus. In contrast, in the rare situations where the stimulus occurs in a different context (e.g., X following the letter ‘B’), the system must rely upon the information provided by the context in order to inhibit the tendency to respond. As this example makes clear, the cognitive system needs some mechanism which can exploit task-relevant context in order to properly control processing and response selection.

In the current paper, we focus on this mechanism of cognitive control. In particular, we derive a theory that describes this mechanism in terms of both its computational properties and underlying neural substrates. The theory is composed of three central hypotheses: 1) PFC is specialized for the representation and maintenance of context information; 2) context representations act to mediate control by



modulating information flow along the pathways required to support performance of a task; and 3) context information is maintained in PFC as a stable and self-sustaining pattern of neural activity. All three hypotheses presented above focus on internal representations of context information. We define context as any task-relevant information that is internally represented in such a form that it can bias processing in the pathways responsible for task performance. Goal representations are one form of such information, which have their influence on planning and overt behavior. However, we use the more general term context to include representations that may have their effect earlier in the processing stream, on interpretive or attentional processes. For example, in the Stroop task, the context provided by the task instructions must be actively represented and maintained to bias attentional allocation and response selection towards the ink color dimension of a visually presented word. Thus, context representations may include a specific prior stimulus, or the result of processing a sequence of stimuli, as well as task instructions or a particular intended action. Representations of context are particularly important for situations in which there is strong competition for response selection. These situations may arise when the appropriate response is one that is relatively infrequent, or when the inappropriate response is dominant and must be inhibited (such as the word name in the Stroop task). Importantly, context representations are maintained on-line, in an active state, such that they are continually accessible and available to influence processing. Thus, context can be thought of as a component of WM. Specifically, context can be viewed as the subset of representations within WM which govern how other representations are used. In this manner, context representations simultaneously subserve both storage and control functions. As described above, this aspect of the model differentiates it from Baddeley's model of WM (e.g., Baddeley, 1986; Baddeley, 1993), which postulates a strict separation of representations for storage versus control.

## 2.2. A computational model of PFC function in WM and cognitive control

The theory of PFC involvement in context processing described above was developed within the connectionist, or parallel distributed processing framework (McClelland, 1993; Rumelhart and McClelland, 1986). The connectionist framework is a natural one for concomitantly studying the neural and psychological mechanisms of cognitive control, since it provides a computational architecture that is specified in neurobiological terms, and can be used to quantitatively simulate performance in cognitive tasks. In this framework, information is represented as graded patterns of activity over populations of simple units, processing takes place as the flow of activity from one set of units to another, and learning occurs through the modification of the connection strengths between these. From one perspective, connectionist models are highly simplified, capturing brain-style computation, without necessarily committing to the details of any particular neural system or sub-system. However, with appropriate refinement, such models offer the opportunity to build bridges between our understanding of the low-level properties of neural systems, and their participation in higher level (system) behavior.

The theory of cognitive control we put forward here can be schematized in the form of a simple canonical model, in which a context module serves as an indirect pathway that modulates processing in a direct stimulus-response pathway (see figure 1). This context processing module represents the functions of PFC. There are two critical features of this module that provide it with the capacity for control over processing. The first is that there is strong recurrent connectivity within the context layer, which allows for the active maintenance of information. Thus, input to the context layer can be sustained through activity recirculation along mutually excitatory connections, even when the external source of input is no longer present. The second critical feature of the context pathway is its feedback connection to the direct pathway. This provides a means for activity within the context module to provide an additional source of input, to the direct pathway which can modulate the flow of processing. In particular, feedback from the context layer serves to bias the local competition for representation that exists within each module, favoring one activation pathway or set of representations over their competitors. This biasing action of the context module can produce inhibitory effects on processing, by allowing a weak pathway to inhibit the more dominant one. Below, we review evidence regarding PFC function that supports these mechanisms of control in the model.

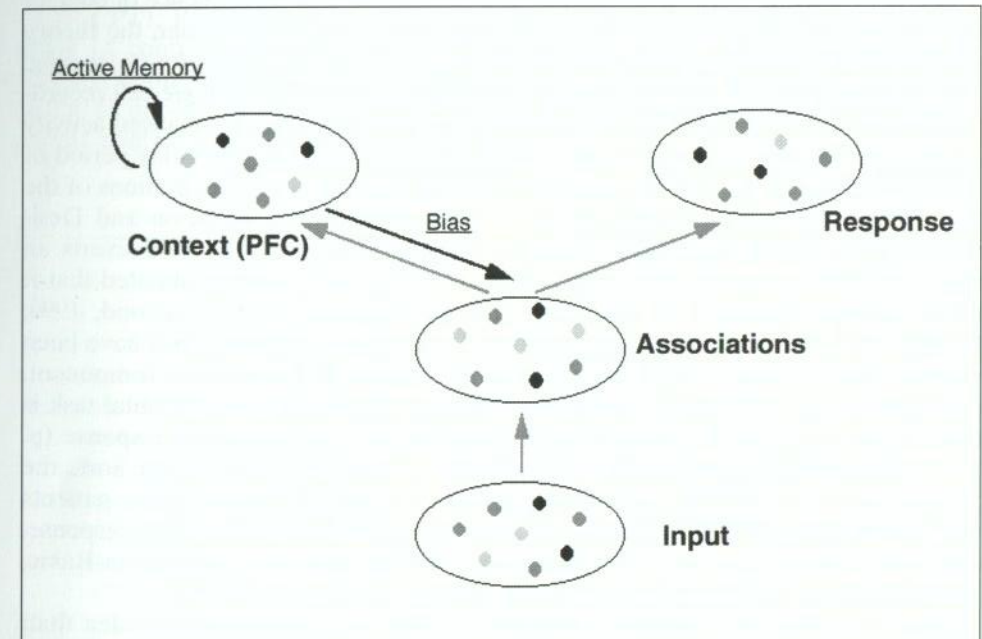


Fig. 1. Diagram of canonical model. Key computational principles of context processing mechanism are shown: 1) active memory through recurrent connections; and 2) top-down bias through feedback connections.



### 2.3. PFC and cognitive control

A critical component of our theory of cognitive control is that context representations are actively sustained over short periods of time within PFC. As mentioned above, the evidence that PFC is involved in WM has primarily come from both neurophysiological studies in non-human primates and more recently, from neuroimaging findings in humans. Primate studies have typically examined active maintenance in PFC through delayed-response paradigms, in which the animal must maintain a representation of a cue stimulus over some delay, in order to respond appropriately at a later point. It is now well-established that during performance of these tasks, populations of PFC neurons exhibit sustained, stimulus-specific activity during the delay period (e.g., Fuster and Alexander, 1971; Kubota and Niki, 1971). The mnemonic properties of these neurons have been demonstrated by showing that both local and reversible lesions to PFC impair performance on these tasks, and that performance errors in intact animals are correlated with reduced delay-period activity (Bauer and Fuster, 1976; Funahashi, Bruce and Goldman-Rakic, 1993; Fuster, 1973). Neuroimaging studies have begun to corroborate these findings in humans, by demonstrating that PFC activity is both modulated by active memory load (Braver *et al.*, 1997), and sustained throughout the period over which information must be maintained (Cohen *et al.*, 1997; Courtney, Ungerleider, Keil and Haxby, 1997).

In our theory, cognitive control emerges through the biasing influence of context representations that interact with task-specific processing. In particular, the theory suggests that context can exert both inhibitory and facilitory effects on processing. The facilitory effect of PFC activity has been directly observed in single-cell recording studies of primates. For example, Miller and colleagues found enhanced activity in cortical association areas (i.e., inferotemporal cortex) during the delay period of a delayed-response task which appeared to be dependent on representations of the cue maintained in PFC (Miller and Desimone, 1994; Miller, Erickson and Desimone, 1996). In the behavioral literature, it is well-accepted that PFC exerts an inhibitory influence over processing. Indeed, some theorists have postulated that it is the primary functions of this brain region (Dempster, 1992; Diamond, 1990; Fuster, 1989). In terms of cognitive performance, almost all tasks which have been shown to be sensitive to PFC function involve a response competition component. As Roberts *et al.* (1994) have noted, "a consistent feature of the prefrontal task is that it puts a prepotent tendency in competition with an alternative response (p. 375)". Examples of these types of tasks include: the Wisconsin Card Sort, the Stroop task, the A-not-B, and delayed alternation. In all of these tasks, patients with frontal damage show evidence of a failure to inhibit the prepotent response, even when the alternative is the appropriate one (Diamond and Goldman-Rakic, 1989; Freedman and Oscar-Berman, 1986; Milner, 1963; Perret, 1974).

Taken together, the empirical literature is very consistent with the idea that: 1) PFC plays a critical role in the active maintenance of information; and 2) information maintained in PFC acts to mediate control by biasing the processing of task-relevant information. However, stronger tests of this hypothesis could be

achieved through more focused studies that are directly motivated by the theory. For this reason, we have conducted simulation studies of the model to examine in more detail the mechanisms by which PFC might perform context processing functions during cognitive task performance. A task that we have used to demonstrate these context processing effects is a simple but informative paradigm – a version of the classic Continuous Performance Test (Rosvold, Mirsky, Sarason, Bransome and Beck, 1956), known as the AX-CPT (Cohen, Barch, Carter and Servan-Schreiber, 1999b; Servan-Schreiber, Cohen and Steingard, 1996). In the following sections, we describe our previous work in testing the predictions of our model through simulation and behavioral studies of AX-CPT performance. Then we present two new neuroimaging studies that directly test model predictions regarding the role of PFC in context processing functions.

### 3. Simulation and behavioral studies

#### 3.1. The AX-CPT paradigm

A primary feature of the AX-CPT is that it enables selective examination of the role of context processing in WM. In this task, sequences of letters are presented one at a time, as a series of cue-probe pairs (see figure 2). The object of the task is to make a target response to an X (the probe) but only when it follows an A (the cue), and a nontarget response in all other cases (hence the name "AX"-CPT). Performance in this task relies on the representation and maintenance of context information within WM, insofar as the correct response to X depends upon maintaining information from the previously presented cue stimulus (A or not-A). In our model, PFC is specialized for representing and maintaining the context provided by the cue stimulus.

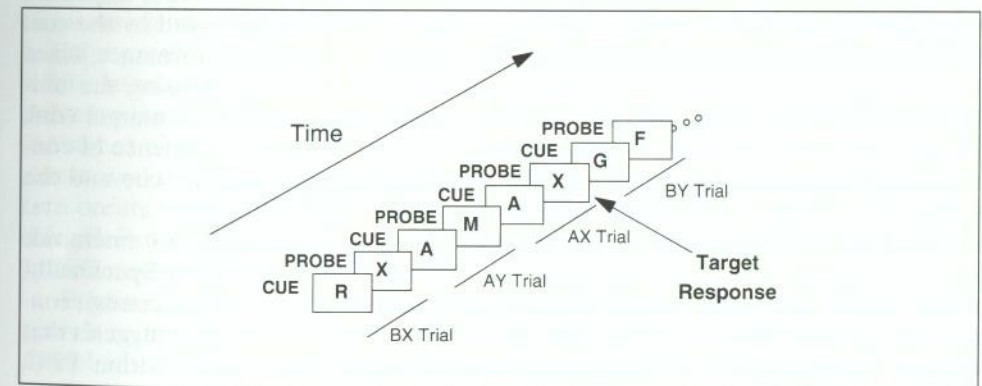


Fig. 2. Schematic of AX-CPT paradigm. Single letters are visually displayed as a series of cue-probe pairs. A target is defined as the occurrence of an "X" probe immediately following an "A" cue. There are three types of nontarget trials: BX, AY and BY (where "B" refers to any non-A cue, and "Y" refers to any non-X probe).



Importantly, the AX-CPT also provides behavioral measures for examining different aspects of context processing. In particular, within the AX-CPT, context information serves inhibitory, attentional, and WM functions. In the task, target (AX) trials occur with high frequency (70%). This induces two types of biases in subjects. The first is a bias to make a target response to the occurrence of an X probe. On those trials in which a target response should not be made to the X probe (i.e., "BX" trials, where B refers to any non-A cue), context information must be used in an *inhibitory* fashion to override the tendency to false alarm. The second bias that occurs in the AX-CPT is an expectancy to make a target response following the occurrence of an A cue. In this case, the context provided by the cue serves a predictive function which directs *attention* to a particular response (i.e., attention-to-action; Allport, 1989; Norman and Shallice, 1986). On those trials in which the cue is an invalid predictor of the response (i.e., "AY" trials, where Y refers to any non-X probe), this attentional function of context creates the tendency to false alarm. This type of cue validity effect is similar to others that have been well studied in the attentional literature (e.g., Posner, 1980). Thus, the integrity of context processing can be examined not only through performance on AX target trials, but also through an examination of performance on nontarget trials.

A key element of our theory is that both attentional and inhibitory functions in the AX-CPT should be subserved by a single underlying mechanism – the internal representation of context information within PFC. This assumption can be tested by examining the relationship of AY to BX performance. Note that on BX trials, the internal representation of context should *improve* performance, by inhibiting an inappropriate response bias. However, on AY trials, representation of context should *impair* performance, by creating an inappropriate expectancy bias. Thus, if context representations are intact, AY performance should be worse than BX performance (in terms of both errors and RT). Conversely, if context representations are impaired, BX performance should be worse than AY performance. Performance on AX target trials should also be poorer if context processing is impaired, since determination of targets is dependent upon the context provided by the cue. However, AX performance should not be as impaired as BX performance, since on AX trials, the response bias works in subjects' favor, by increasing the tendency to make the correct target response. Finally, a third type of nontarget trial, BY, provides a useful internal control, since in this condition the influence of context on performance should be relatively small (given that both the cue and the probe always map to a nontarget response).

The AX-CPT paradigm also provides a means for examining the mnemonic role of context information through the cue-probe delay duration. Specifically, under conditions in which there is a long cue-probe delay (e.g., 5-10 seconds), context information must be actively maintained within WM. Our theory suggests that context information is both represented and actively maintained within PFC. Thus, the same context processing mechanism that subserves inhibitory and attentional functions also subserves WM functions. Consequently, a strong prediction of the theory is that the effect of delay will interact with performance on AY and BX trials. If context maintenance is intact, then the strength of context represen-

tations should either hold constant or increase with delay (i.e., if it takes some period of time for context representations to reach full activation strength). Consequently, BX performance should remain constant or improve at long delays, while AY performance should remain constant or worsen with delay. Conversely, if context maintenance is impaired, then context representations should lose strength over time. This should lead to a worsening of BX performance with a delay, but an *improvement* in AY performance.

### 3.2. Simulations and behavioral performance

In our previous work, we have used our computational model of cognitive control to simulate performance in the AX-CPT task (Braver, Barch and Cohen, 1999; Braver, Cohen and Servan-Schreiber, 1995; Cohen, Braver and O'Reilly, 1996). By explicitly simulating performance in the task, we were able to directly and quantitatively compare the model with actual human behavior. Specifically, in comparing the model to empirical data collected from a normative study of over 200 young adults, we found that the model was able to successfully capture detailed aspects of behavioral performance. The model captured the relationship between AY and BX performance (i.e.,  $AY > BX$ , for both errors and RT), and the interaction of these effects with cue-probe delay duration (i.e., AY performance worsens with delay, while BX performance slightly improves). Moreover, the model also captures subtler effects in the data, such as the relationship between accuracy and response speed. Finally, it is important to note that the model not only captured the qualitative patterns in the data, but also quantitative relationships (see figure 3a and 3b).

An advantage of having implemented a computer simulation of the AX-CPT is that it can be used to explore the effects of impairments in context processing on model performance. We conducted such simulations with our AX-CPT model, by disrupting processing of the context module. This was done through manipulations of a specific model parameter, gain, which governs the responsivity of units to incoming input. By reducing gain in the model, context units showed both weak initial representation of context information, as well as a greater tendency for this information to decay over time (see figure 4). When we examined the influence of context processing disruptions in the AX-CPT task, we found substantial changes in the behavior of the model. For example, the model produces more BX than AY errors, and this effect becomes amplified with delay (see figure 3c). A similar pattern occurs for RTs (i.e., more slowing of BX than AY RT, and an amplification of this effect with delay). In contrast, BY performance is similar in the intact and disturbed model.

Because our theory postulates that the context module of the model corresponds to the functions of PFC in WM and cognitive control, the behavior of the model when context processing functions are impaired can be treated as specific predictions regarding the effects of PFC dysfunction on AX-CPT performance. In recent work, we have tested these predictions somewhat indirectly in a number of ways. First, we have examined AX-CPT performance in two different populations thought to suffer from disturbances in PFC – older adults and patients with schiz-



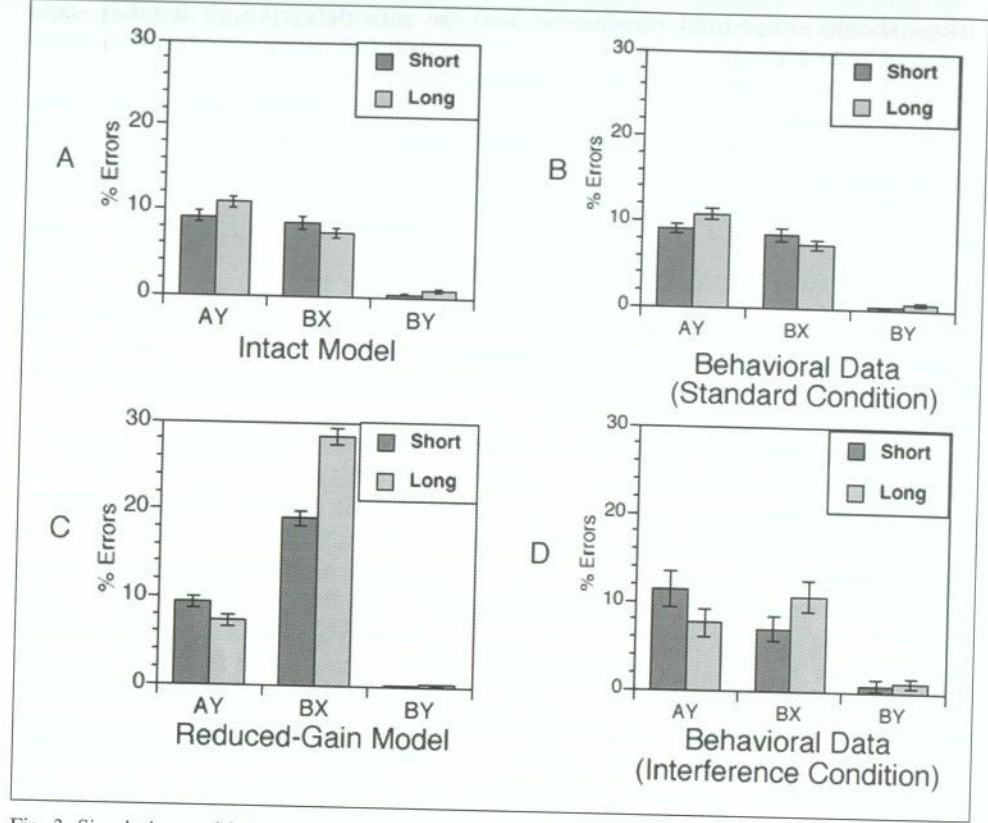


Fig. 3. Simulation and behavioral performance data from the AX-CPT. A. Simulation data from the intact computational model showing performance in each the 3 nontarget trial-types (AY, BX, and BY) under short (dark bars) and long delay conditions (light bars). B. Behavioral data obtained from a normative sample of over 200 healthy young adults performing the AX-CPT under standard conditions. C. Simulation data from the computational model with reduced gain on the context units. D. Behavioral data from young adults performing the AX-CPT under interference conditions. All data are taken from Braver *et al.* (1999).

izophrenia. In both populations, we found that participant performance was highly consistent with the predictions of the model (Braver *et al.*, 1999; Braver *et al.*, in press; Cohen, Barch, Carter and Servan-Schreiber, 1999a). An important aspect of the findings is that we confirmed a highly counter-intuitive prediction of the model, that we would observe not only performance impairments in these populations on the AX-CPT, but also relative performance improvements (i.e., on AY trials). Second, we additionally tested the predictions of the model in healthy young subjects, through the use of an experimental manipulation designed to disrupt context processing. Specifically, we had participants perform the AX-CPT under interference conditions, in which irrelevant distractor letters were presented during the

cue-probe delay period (Braver *et al.*, 1999). We hypothesized that this manipulation would produce changes in behavioral performance similar to that observed in the model and in populations suffering from physiological disturbances in PFC function. In fact, we did observe such an effect of interference. We found that under interference, the performance of healthy subjects looked similar to that produced by the reduced gain model. For example, performance on BX trials worsened with delay, while performance on AY trials improved, and these effects were strongest in the long delay condition there were more BX than AY errors (see figure 3d).

So, to summarize, our computer simulations of the AX-CPT provided support for our hypothesis that context processing within PFC might provide a mechanism for both storage and control in WM. We found that the normally functioning model was able to capture detailed aspects of behavioral data in healthy young adults, while disruptions of context processing in the model captured the specific patterns of performance change seen both in populations thought to suffer from PFC disturbance (older adults and schizophrenia patients), and in subjects performing the AX-CPT under interference conditions. In the following section, we present the results of two neuroimaging studies designed to more directly examine the role of PFC in context processing during WM.

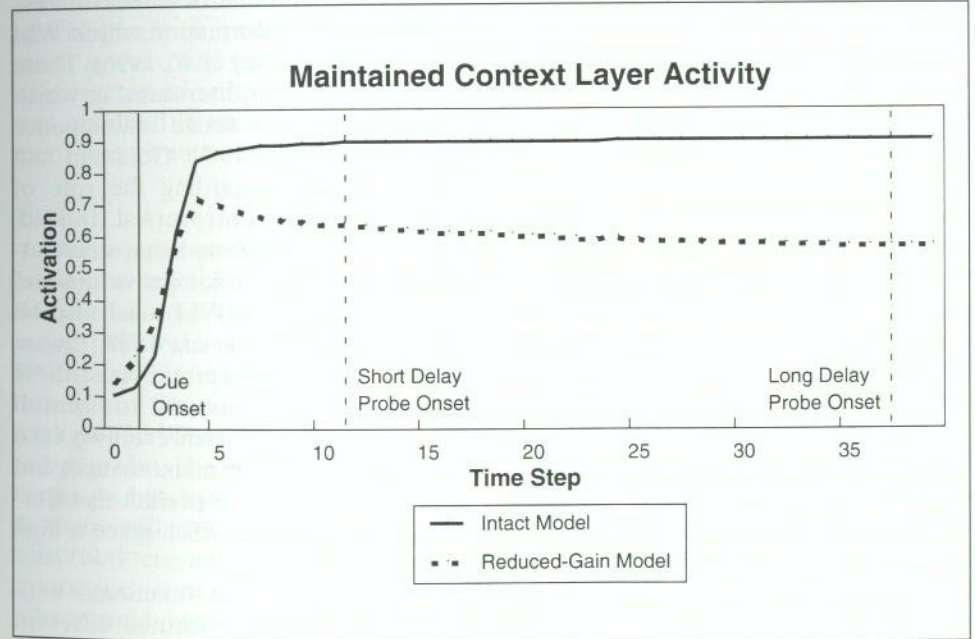


Fig. 4. Plot of average activity level in context units during the course of an AX-CPT trial in the intact and reduced-gain models. Note that context activity is attenuated in the reduced-gain model and further decays with delay.



#### 4. Neuroimaging studies

The results of the computer simulations and behavioral studies provide an important measure of support for our hypothesis regarding the role of context processing in WM. Specifically, the computational mechanisms postulated to underlie successful control over behavior in the AX-CPT – namely, the representation and active maintenance of context – were explicitly implemented in computer simulations and found to successfully account for and predict detailed aspects of behavioral performance in different populations during performance of the task. However, the model also makes claims about the neural substrates of these mechanisms of cognitive control. In particular, the model proposes that context information is represented in PFC, and is maintained there across delays as a sustained pattern of neural activity. Moreover, we suggest that it is the active maintenance of context information that directly enables the PFC to exert control over processing in many WM tasks. In the current studies, we attempted to test these claims directly using functional neuroimaging methods, which provide a means of examining brain activity during task performance.

Previous neuroimaging findings have already reliably demonstrated PFC activation during the performance of WM tasks and other tasks involving cognitive control (Cabeza and Nyberg, 2000). Typically, this activation has been located in dorsolateral regions of PFC (in the standard terminology of Brodmann's Areas (BA), in regions 46 and 9). There has been some indication that dorsolateral PFC activity is specifically related to the active maintenance of information within WM (Barch *et al.*, 1997; Cohen *et al.*, 1997; Courtney *et al.*, 1997; Fiez *et al.*, 1996). These findings are consistent with the data coming from the animal literature, in which the dorsolateral PFC region appear to be most critical for active maintenance functions (Butters, Pandya, Sanders and Dye, 1971; Fuster, 1989; Goldman and Rosvold, 1970; Goldman-Rakic, 1987). However, claims regarding the role of human dorsolateral PFC in active maintenance are not uncontroversial. Indeed, several recent meta-analyses of neuroimaging data have suggested that dorsolateral PFC regions are not engaged by the simple requirement for active maintenance, but rather only in conditions in which information in WM must also be manipulated or monitored in a specific fashion (D'Esposito *et al.*, 1998; Owen, 1997; Smith and Jonides, 1999). As mentioned above, one interpretation of these findings is that activity in dorsolateral PFC regions may correspond to "central executive"-like functions that do not directly involve storage. However, we take the position that the dorsolateral PFC is involved in active maintenance, but specifically active maintenance of context information. Thus, we predict that dorsolateral PFC will be most strongly activated in task situations which place a high demand on context representation and maintenance.

The present studies addressed this issue directly, by using functional neuroimaging methods to monitor brain activity while subjects performed different conditions of the AX-CPT. Two different studies were conducted, with separate groups of subjects. In Study 1, subjects performed the AX-CPT under short and long delay conditions. Because task requirements in the AX-CPT are identical in

both long and short delay conditions, they are only differentiated in terms of the duration over which context must be maintained. Thus, if the PFC maintains context information in WM, greater PFC activity should be observed in blocks of long delay trials than in blocks of short delay trials. Moreover, if context is maintained across the delay period, then analyses of PFC activity dynamics should reveal that activity is greatest during the period of the trial in which context is being maintained, and that the activity should be sustained across this period. In Study 2, subjects performed the AX-CPT under standard and interference conditions with a long delay. If PFC subserves context representation and maintenance, then disruption of context processing functions in the interference condition alter the dynamics of PFC activity. In particular, based on the simulation studies with the model (see figure 4), we predicted that activity in PFC would decay over the delay period during performance of the interference AX-CPT. Both of the present studies were conducted using functional magnetic resonance imaging (fMRI), which provides both high spatial resolution and temporal resolution that is sufficient to answer questions regarding the dynamics of activity within PFC.

#### 4.1. GENERAL METHODS

##### *Participants*

*Study 1.* 23 neurologically normal right-handed individuals (13 males and 10 females), with a mean age of 23.32 ( $SD = 9.27$ , Range 18 to 51 years). *Study 2.* 21 neurologically normal right-handed individuals (11 males and 10 females), with a mean age of 24.62 ( $SD = 5.08$ , Range 20 to 37 years). All participants had normal or corrected-to-normal vision and were native English speakers. Informed consent was obtained in accordance with the institutional review board, and a cash payment was given in return for participation.

##### *Task*

Participants performed trials of the AX-CPT task. Each "trial" consisted of a cue-probe sequence. These were presented in a continuous fashion, in pseudorandom order, such that target (AX) trials occurred with 70% frequency and non-target trials occurred with 30% frequency (evenly divided between AY, BX, and BY trials). Letters were presented on a visual display, occurring centrally with a duration of 500 msec, in 24 point uppercase Helvetica font, red against a black background. The letter A was used as the valid cue, and the letter X was the target probe. The remaining letters of the alphabet served as invalid cues and non-target probes, with the exception of the letters K and Y, which were excluded due to their similarity in appearance to the letter X. Subjects responded to every stimulus (both cue and probe), pressing one button for targets and another button for nontargets (cues were always considered non-targets). Responses were made using a hand-held response box with fiber-optic connections to a Macintosh computer in the scanner control room running PsyScope software (Cohen, MacWhinney, Flatt and Provost, 1993). Responses were made with the middle and index fingers of the right hand. Participants had 1.3 seconds from stimulus onset in which to



respond (regardless of interstimulus or intertrial interval). Responses that were slower than this limit were not recorded. Tasks were run on Apple Macintosh computers, using PsyScope software for stimulus presentation and data collection (Cohen *et al.*, 1993).

**Study 1.** Participants performed the standard AX-CPT under short and long delay conditions. The short delay lasted 1 sec and the long delay was 8 sec. Delay and ITI were counterbalanced across the two conditions, and cue and probe durations were 500 msec. Thus, total trial duration was 10 sec in both conditions. Eleven participants performed only these two primary delay conditions and the other 12 participants also performed a third delay condition, termed "extra-long". In the extra-long delay condition both the delay and ITI lasted 9.5 sec, yielding a total trial duration of 20 sec. The extra-long condition provided a means by which to dissociate cue-related activity from probe-related activity, discussed further below. Trials were blocked by delay condition, and an equal number of blocks were run in each of the conditions. Scanning occurred during performance of all blocks. For the 12 participants performing all 3 delay conditions, block duration was 4 minutes, and 4 blocks of each condition were performed. In the short and long delay conditions, each block contained 24 trials, while in the "extra long" delay condition each block contained 12 trials. For the other 11 participants, 6 blocks of each condition were performed, in 2 minute blocks containing 12 trials. Blocks were run in a pseudorandom order, such that all conditions were sampled once before starting the next cycle.

**Study 2.** Participants performed the "extra-long" delay condition of the AX-CPT with the same duration parameters were as in Study 1 (500 msec stimulus duration, 9.5 sec delay and ITI). The task was performed under both standard and interference conditions. In the interference condition, a total of 8 distractors (letters appearing in a different color) were presented during each trial, 4 during the delay period and 4 during the ITI. Distractors were presented in a sequential manner, for the same duration as cue and probe stimuli (i.e., 500 msec), with a 1500 msec ISI (regardless of whether the next stimulus was another distractor, a cue, or a probe). Thirteen participants performed 5 blocks each of the standard and interference conditions, and the remaining 8 participants performed 8 blocks of each of the two conditions. Blocks were run in a pseudorandom order, such that each condition was sampled once before starting the next cycle. Each block contained 10 trials, and scanning occurred during performance of each trial.

#### *MRI scanning procedures*

Images were acquired with a 1.5T GE Signa whole body scanner. Axial slices were acquired (3.75 mm<sup>3</sup> isotropic voxels) parallel to the AC-PC line. A spiral-scan pulse sequence was used, in which volume scans were acquired every 2.5s. Scans were synchronized to the start of every trial, in order to enable event-related analyses to be conducted. Prior to functional imaging, anatomical scans were acquired at the same locations as the functional images, using a standard T1-weighted pulse sequence.

**Study 1.** A 4-interleave spiral-scan pulse sequence (TR = 640 ms, TE = 35 ms, FOV = 24 cm, flip = 40°) (Noll, Cohen, Meyer and Schneider, 1995) was used which allowed 8 slices to be acquired during every 2.5s scan period. Four scans of 8 slice locations were acquired during each 10s trial (short and long delay conditions), and 8 scans of these locations acquired on every 20s trial (extra-long delay condition). In order to scan the whole brain volume (24 slices total), a first set of 8 locations was scanned for three consecutive trials, followed by two additional sets of 8 different locations, each scanned during three consecutive trials. Following this change of location, a fourth trial was presented in the absence of scanning, in order to allow the MRI signal to achieve steady state. This scanning procedure enabled 3 scans of all 24 slice locations to be acquired every 12 trials. The order in which slice locations were acquired was counterbalanced within subjects across blocks, as well as across subjects. This same scanning technique has been used in previous studies (e.g., Cohen *et al.*, 1997), to track the temporal dynamics of activation within each task trial.

**Study 2.** A 2-interleave spiral-scan pulse sequence (TR = 1250 ms, TE = 35 ms, FOV = 24 cm, flip = 60°) was used in order to simplify the acquisition procedure. The sequence enabled the acquisition of 8 scans at 16 slice locations during each 20s trial.

#### *Image analysis procedures*

Images were co-registered and pooled across subjects using a procedure similar to one used in PET studies (Woods, Mazziotta and Cherry, 1993). This procedure has been used successfully in previous fMRI studies to increase statistical power and permit direct quantitative identification of regions that change activity reliably across subjects (Barch *et al.*, 1997; Braver *et al.*, 1997; Cohen *et al.*, 1997). Participants' structural images were aligned to a reference brain using an automated algorithm (Woods, Cherry and Mazziotta, 1992). All functional images were corrected for movement and scaled to a common mean (to reduce the effect of scanner drift or instability). The functional images were then registered to the reference brain using the alignment parameters derived for the structural scans, and smoothed using an 8 mm FWHM Gaussian filter (to reduce the effects of anatomic variability across subjects).

**Study 1.** The imaging data, pooled across subjects, were analyzed in a voxel-wise manner with paired t-tests testing for greater activity in the long delay relative to the short. The statistical map generated by this procedure was then thresholded for significance using a cluster-size algorithm (Forman *et al.*, 1995), which takes account of the spatial extent of activation to correct for multiple comparisons. A cluster-size threshold of 8 voxels and a per-pixel alpha of 0.005 was chosen, thus ensuring that the image-wise false positive rate was 0.005. The anatomical location of each active region was then determined by reference to the Talairach atlas (Talairach and Tournoux, 1988). Finally, significant regions of interest (ROI) were subjected to an ANOVA analysis to examine event-related



activity. The time course of activation was analyzed statistically by examining the effect of scan-within-trial (1-4 or 1-8).

**Study 2.** Analyses were conducted in a confirmatory manner, using the ROIs derived from Study 1. The confirmatory analysis was carried out by co-registering the subjects of Study 2 to those of Study 1. The ROIs were then laid over each brain. The voxels corresponding to each ROI were averaged together and analyzed as a composite. ROI data were analyzed through an ANOVA with task condition (standard vs. interference) and scan-within-trial (scans 1-8) as factors. The primary effect of interest was the presence of a task x scan interaction. For ROIs showing significant effects, post-hoc analyses were conducted on individual voxels within the ROI.

#### 4.2. STUDY 1 RESULTS

**Delay effects.** Only three brain regions showed significantly greater activation in the long delay relative to the short delay condition. All of these regions were located within PFC: left middle frontal gyrus, right middle frontal gyrus, and left inferior frontal gyrus. As shown in Table 1, both middle frontal gyrus regions corresponded to dorsolateral PFC (DLPFC; BA 46/9), and the left inferior frontal gyrus region corresponded to Broca's area (BA 44/6). These findings regarding PFC are consistent with earlier reported results using a subset of 11 subjects from this group (Barch *et al.*, 1997).<sup>1</sup> Together, the results support the hypothesis that PFC is involved in actively maintaining context information provided by the cue during the delay period.

**Time Course Effects.** We next examined whether the delay effects observed in PFC were modulated during the time course of the trial. An ANOVA conducted on these 3 regions-of-interest (ROIs) revealed that none showed any interaction between delay and scan-within-trial (all  $ps > .1$ ; see figure 5), suggesting that the delay effect was sustained across the entire trial. A similar analysis was also conducted on the subset of subjects who performed the extra-long condition, in order to confirm the effect and to determine whether the sustained activity effect was specific to the delay period. Consequently, in the extra-long condition scans were subdivided into those corresponding to the delay period (scans 2-5) and those corresponding to the ITI (scans 6-8 and 1).<sup>2</sup> For the DLPFC ROIs (averaged together to increase statistical power), a trend-level main effect was observed for greater activity during the delay period than during the ITI period ( $F(1,11) = 4.41$ ,  $p = .06$ ) (see figure 6). In addition, the delay effect again did not interact with scan

<sup>1</sup> In contrast to the findings with PFC, an additional delay effect that was previously observed in parietal cortex failed to replicate. However, in the original observation, the delay effect was found to interact with scan-within-trial. Thus, it may be the case that the parietal region was either less reliably affected by the delay manipulation or functionally dissociable from the PFC regions.

<sup>2</sup> The coding of scans corresponding to delay and ITI periods was shifted forward by 1 scan, in order to take into account the approximately 3 second hemodynamic lag present in the fMRI response (Kwong *et al.*, 1992; Savoy *et al.*, 1995).

Table 1. Study 6: Significant activation as a function of delay.

Regions of interest	Brodmann area(s)	X <sup>a</sup>	Y <sup>a</sup>	Z <sup>a</sup>	Volume (mm <sup>3</sup> ) <sup>b</sup>	Maximum Z-score <sup>c</sup>
Left DLPFC	46/9	-30	47	26	701	3.06
Right DLPFC	46/9	32	41	32	2026	3.06
Left inferior frontal cortex	44/6	-54	9	17	1658	3.88

<sup>a</sup> X, Y, and Z are coordinates in a standard stereotactic space (Talairach and Tournoux, 1988) in which positive values refer to regions right of (X), anterior to (Y), and superior to (Z) the anterior commissure (AC).

<sup>b</sup> Volume refers to the number of voxels (converted to mm<sup>3</sup>) which reached statistical significance in each region of interest.

<sup>c</sup> F values were converted to Z-scores to provide a measure of effect size independent of sample size.

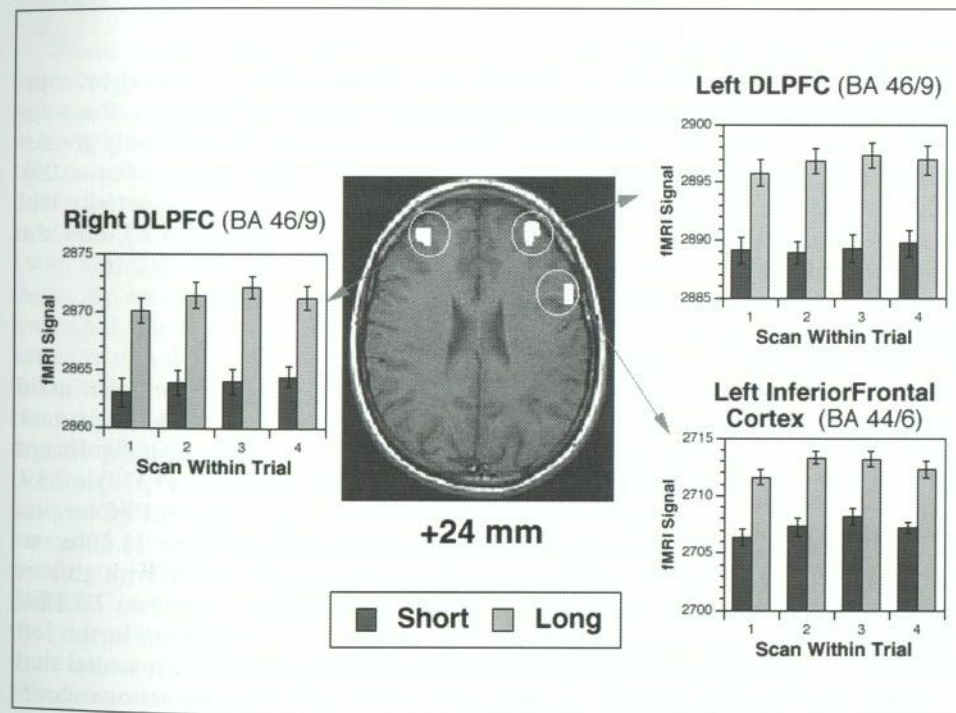


Fig. 5. Study 1: Delay related activity as a function of scan within trial for the three active regions within PFC in the short (dark bars) and long (light bars) delay conditions. Brain activation data is shown for a representative axial slice 24mm superior to the AC-PC plane.



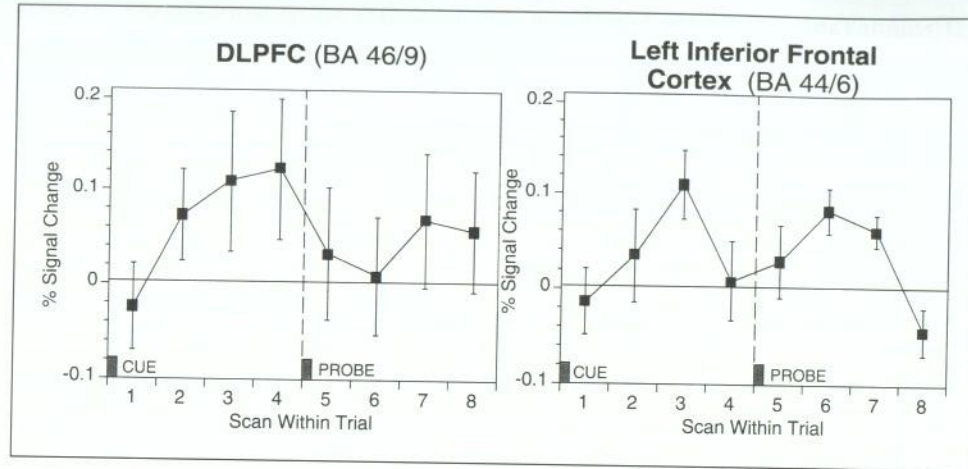


Fig. 6. Study 1: The time course of event-related activity in the PFC regions (the dorsolateral PFC regions are averaged together) in the extra-long delay condition. Note that the DLPFC regions show a sustained increase in activity during the cue-probe delay period that is greater than that seen during the ITI. The left inferior cortex region does not show this pattern.

( $F(3,33) = 0.05$ ,  $p > .1$ ). The main effect findings were further examined by computing "area under the curve" measures for each of the two events (i.e., the summed increase in signal across the 4 scans). This analysis revealed significantly greater area under the curve for delay-related vs. ITI-related activity ( $F(1,11) = 5.09$ ,  $p < .05$ ). The Broca's area ROI did not show the same pattern. Delay-related activity was not significantly greater than ITI-related activity ( $F(1,11) = 1.35$ ,  $p > .1$ ), and the interaction with scan was marginally significant ( $F(3,33) = 2.33$ ,  $p = .09$ ).

#### 4.3. STUDY 2 RESULTS

In the standard condition, all three PFC ROIs showed highly significant main effects of scan (all  $ps < .001$ ), suggesting that these regions were sensitive to task events. When comparing the standard and interference conditions, a significant task  $\times$  scan interaction was observed for the left DLPFC region ( $F(7,133) = 2.19$ ,  $p < .05$ ). This interaction was not significant for either the right DLPFC region ( $F(7,133) = 1.62$ ,  $p > .1$ ) or the left inferior region ( $F(7,133) = 0.847$ ,  $p > .1$ ). Interestingly, however, the left inferior region did show a main effect of task, with greater activity under interference ( $F(1,19) = 4.53$ ,  $p < .05$ ). Neither of the two DLPFC regions showed such effects (both  $ps > .1$ ). The task  $\times$  scan interaction in the left DLPFC was also followed up by post-hoc voxelwise analyses. These revealed that the effect was highly consistent, with 8 of the 9 voxels showing interactions significant at the  $p < .10$  level. The nature of this interaction can be seen in figure 7, which shows the pattern of activity dynamics in both task conditions for the two most significant voxels (averaged together).

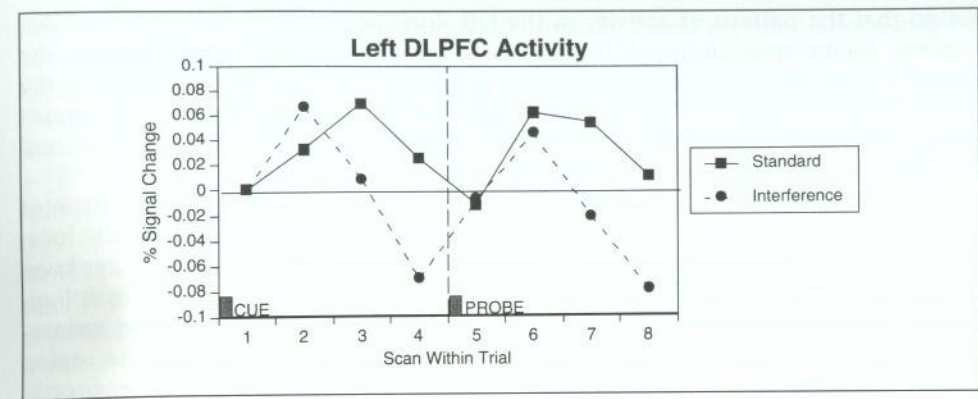


Fig. 7. Study 2: The time course of event-related activity in the left dorsolateral PFC region (extra-long delay condition) in both the standard and interference conditions. Activity decays more rapidly under the interference condition.

#### 4.4. DISCUSSION

These neuroimaging studies were conducted to directly test predictions of the model regarding the role of PFC in the representation and maintenance of context information. Using fMRI, we examined PFC activity during performance of the AX-CPT, which is postulated to rely on actively maintained context. Many previous neuroimaging studies have already demonstrated PFC involvement in both CPT tasks and others which rely upon the active maintenance of context (Cohen *et al.*, 1997; Cohen *et al.*, 1987; Courtney *et al.*, 1997; Fiez *et al.*, 1996; Seidman *et al.*, 1998; Smith, Jonides and Koeppel, 1996). However, the current findings go beyond these, by establishing the specific characteristics of PFC activity during task performance. First, we established that PFC activity increases when the duration of active maintenance increases. By comparing activity between short delay and long delay trials, we were able to hold all aspects of task processing constant except for the proportion of time over which context must be maintained. We identified PFC regions whose activity reliably and significantly increased in the long delay condition relative to the short. Second, we established that maintenance-related activity was selective to PFC. In the comparison of short and long delay performance across 23 subjects, only 3 regions were found whose activity significantly increased with delay. These 3 regions were all located within PFC – bilaterally in dorsolateral PFC, and in left inferior frontal cortex. Third, we determined that activity in the dorsolateral PFC (but not in left inferior frontal cortex) was selectively increased during the delay period relative to the ITI. Fourth, we established that the dynamics of PFC activity were consistent with a sustained increase in activity across the entire delay interval. The effect of delay was found to be constant across the entire trial when comparing the long delay condition against the short, and across the entire delay period when comparing delay against ITI. Fifth, we



round that the pattern of activity in the left dorsolateral PFC region showed disruption under conditions of interference. Specifically, under interference the event-related response to the cue appeared to decay more rapidly during the delay period. Thus, taken as a whole, the findings from this study strongly support the hypothesis that context information is selectively represented within PFC and is actively maintained there over delay periods.

The regions of PFC that satisfied all of the criteria for active maintenance of context were located dorsolaterally, in the middle frontal gyrus. The specific location of these regions corresponded to Brodmann's area (BA) 46/9, which has been an area long associated with active maintenance in both animal neurophysiological and human neuroimaging studies. The most reliable sites for detecting maintenance-related activity in primate single-cell recordings have been in the region around the principal sulcus (Goldman-Rakic, 1987), which appears to be directly homologous to BA 46 (Rajkowska and Goldman-Rakic, 1995). Moreover, this region has been observed to be critical for performance in delayed-response tasks, as impairment can be observed even following highly circumscribed lesions (Butters *et al.*, 1971). In humans, BA 46/9 has also been commonly observed in neuroimaging studies involving active maintenance and working memory (for reviews see, Fiez *et al.*, 1996; McCarthy, 1995; Cabeza and Nyberg, 2000). In particular, this region has been found to be engaged by tasks requiring maintenance of a wide range of stimuli including, faces (Courtney, Ungerleider, Keil and Haxby, 1996), letters (Cohen *et al.*, 1994), digits (Grasby *et al.*, 1994; Petrides, Alivisatos, Meyer and Evans, 1993b), locations (McCarthy *et al.*, 1994), and abstract shapes (Petrides, Alivisatos, Evans and Meyer, 1993a; Swartz *et al.*, 1995). More recently, a few neuroimaging studies which have attempted to isolate the maintenance component of working memory have also demonstrated activity in BA 46/9 (Cohen *et al.*, 1997; Courtney *et al.*, 1997; Fiez *et al.*, 1996). As such, the current results are consistent with previous findings, and provide more specific support for the hypothesis that dorsolateral PFC is responsible for actively maintaining representations of context information through sustained patterns of neural activity.

Nevertheless, the claim that dorsolateral PFC directly subserves active maintenance functions is not uncontroversial, as mentioned above. Recent reviews of the neuroimaging literature have led a number of investigators to suggest that dorsolateral PFC may not engaged by active maintenance itself, but rather the executive-control functions such as manipulation and/or monitoring that must occur in parallel with active maintenance in certain WM tasks (D'Esposito *et al.*, 1998; Owen, 1997; Smith and Jonides, 1999). The current findings have the potential to resolve this controversy. Specifically, we suggest that tasks which engage dorsolateral PFC are those which specifically require the maintenance of context information as opposed to the maintenance of other types of information. In particular, it may be that maintenance of context information is qualitatively different from the more domain-specific "buffer-type" of maintenance typically discussed in standard theories of working memory (Baddeley, 1992). For example, in traditional verbal working memory tasks (e.g., immediate serial recall), it may be sufficient to maintain stimulus information as an articulatory or phonologically-based representa-

tion. In contrast, such articulatory or phonologically based representations may be necessary, but not *sufficient*, to drive performance in the AX-CPT. Instead, AX-CPT performance is critically dependent upon transforming the cue stimulus into a context-based representation, which carries information about the consequences of the cue for future stimulus evaluation and response. For example, presentation of a "C" cue, sets up a context in which a non-target response should be made to a subsequent presentation of an X probe. This contextual information serves as a type of behavioral goal (i.e., "if X, then non-target") that must be internally represented and maintained over the delay period in order to bias future response selection. It is the representation and maintenance of information in this context-based code that we feel best characterizes the functional role of dorsolateral PFC. Tasks which are likely to engage dorsolateral PFC are those which place a high demand on representing and maintaining information in such a context-based code, such as when the context changes frequently or in which the context must be used to override a dominant response tendency. The AX-CPT is a prime example of such a task, both since the relevant context can change on a trial-to-trial basis and since context is required periodically to override target response tendencies on BX trials.

In contrast to the finding of context-related activity we observed in dorsolateral PFC, a different pattern of activity dynamics was observed in left inferior frontal cortex. Although this region showed increased activity in the long relative to short delay condition, in the event-related analysis left inferior frontal cortex did not appear to show a sustained response over the delay. Moreover, in the interference condition, left inferior frontal cortex showed *increased* rather than decreased activity. This dissociation between inferior and dorsolateral PFC is consistent with our previous findings using the n-back task (Cohen *et al.*, 1997). In that study, we observed that DLPFC showed sustained activity that was sensitive to working memory load. In the left inferior frontal cortex, activity was also load sensitive, but appeared to interact with scan, such that the activation was more sustained at higher levels of load. This potential functional dissociation between left inferior and dorsolateral PFC has also been observed by other investigators (e.g., Awh *et al.*, 1996). Many other studies have observed left inferior frontal cortex activation during language and verbal working memory tasks (Fiez *et al.*, 1996; Frackowiak, 1994; Zatorre, Meyer, Gjedde and Evans, 1996). In these studies, activity in this region has been typically interpreted as reflecting articulatory planning and rehearsal (e.g., Paulesu, Frith and Frackowiak, 1993). This interpretation would also be consistent with our delay effect, since it is plausible that participants engaged in rehearsal of the cue to improve maintenance over the delay. However, if this were the case we would expect to observe a more sustained pattern of activity dynamics in the event-based analysis, since rehearsal is presumably an ongoing, repetitive process. On the other hand, it is possible that the minimal load imposed by the cue (i.e., a single letter), did not require rehearsal to occur throughout the delay period. This latter interpretation is also consistent with the findings from the n-back study, in which left inferior frontal cortex showed a somewhat transient pattern of activity dynamics during the 1-back condition (which also only required maintenance of a single letter).



The results of the Study 2 provide further support for the predictions of the model regarding the role of dorsolateral PFC in context processing functions. The model suggested that under interference conditions the representation and maintenance of context would be weakened, and that this would be reflected in terms of a decay in PFC activity during the delay period of the AX-CPT. The use of a confirmatory analysis approach provided the strongest test of this hypotheses, both anatomically and conceptually, by forcing us to demonstrate that the dorsolateral PFC regions identified in Study 1 would: a) replicate the pattern of activity dynamics observed in the standard AX-CPT in a completely different group of participants; and b) also show effects of interference which were indicative of a delay-related decay in activity. These hypotheses were both confirmed by the data. We observed a significant task condition x scan interaction in the left DLPFC region. As figure 7 shows, the activity dynamics in the standard condition are similar to that observed in the extra-long condition of Study 1 (cf. figure 6). However, under interference, the cue-related activity decayed more rapidly during the delay period. As such, the results are fully consistent with the simulations performed under conditions when context representation and maintenance is disturbed. In those simulations, context-related activity was also found to decay over the delay period (see figure 4).

It is important to note that without benefit of the model, one might have predicted that the interference condition would have a different effect on PFC activity. For example, one plausible hypothesis is that under interference the PFC response would be one of enhancement rather decay. The logic of this hypothesis is that the interference condition increases active memory load, and that the response to this increased load would be increased PFC activity, as has been observed in other working memory tasks, such as the n-back (Braver *et al.*, 1997; Jonides *et al.*, 1997). The model makes clear that interference does not increase memory load *per se*, because no more information must be maintained as context. Rather, the model suggests that the presence of interfering items should serve to weaken the representation and maintenance of context, and that this effect should accumulate over the delay period.

As noted above, the current results are consistent with the model predictions that DLPFC should be decreased, rather than enhanced under interference. Nevertheless, the results do not rule out the possibility that compensatory strategies are employed by subjects to counteract the effects of interference. Indeed, the data provide some tantalizing hints in this regard. First, in the left DLPFC region it is interesting to note that although activity following the cue decays more quickly under interference, it rises more quickly as well. In particular, at scan 2 the cue-related response appears to be greater under interference than in the standard condition, although this effect was not statistically significant. One intriguing hypothesis is that under interference, the initial representation of context is amplified, possibly due to enhanced attentional allocation. This early enhancement may help to counteract the disruption and decay of context representation due to the subsequent presentation of distractor stimuli. A second indication of potential compensatory strategies in play during interference is the finding of increased

activity in the left inferior frontal cortex. If activity in this region represents the presence of articulatory planning and rehearsal, the increased activity under interference could reflect the increased use of this processing strategy during the interference condition. Indeed, it is well-documented that subjects use rehearsal as a primary strategy for maintaining information in the face of interference (e.g., Baddeley, 1986). However, these interpretations are still somewhat speculative and premature, given that they weren't the primary focus of this experiment. Nevertheless, they do make clear the need for a more systematic study of the relationship between subjects' strategies and brain activity patterns.

Another issue worth noting is the lack of a task x scan interaction in the right DLPFC region. In Study 1, this region had shown a pattern of effects which were almost identical to that observed for the left DLPFC region. Moreover, upon inspection, they appeared to be located in homologous regions of cortex. However, in study 2, these two regions showed very different patterns. Specifically, the activity dynamics looked virtually equivalent in right DLPFC in both standard and interference conditions, suggesting that the lack of a task x scan interaction was not simply due to a lack of statistical power. Although we have no explanation for this lack of an effect, it does suggest that the two regions might in fact be functionally dissociable. Obviously, further work is needed to provide support for this assumption, but the results do make clear the point that demonstration of dissociability between very similar cortical regions may require the use of systematic testing and subtle task manipulations.

The results of this study also have interesting implications for neuroimaging studies of patients suffering from PFC dysfunction, such as schizophrenia patients or older adults. We have suggested that the interference condition of the AX-CPT produces disturbances in the representation and maintenance of context information. This disturbance is reflected both in terms of behavioral performance and PFC activity dynamics. As discussed above, we have also suggested that performing the AX-CPT under interference puts healthy subjects in an experimental state that is somewhat analogous to that experienced by patients with PFC dysfunction. Thus, based on the current results, the model makes strong predictions about the pattern of brain activity that would be expected in neuroimaging studies of the AX-CPT conducted in populations suffering from PFC dysfunction. First, the model predicts that patients should show reduced delay-related activity in PFC during AX-CPT performance. Second, the model predicts that patients should show a pattern of PFC activity dynamics (in the baseline condition) similar to that observed in healthy subjects in the interference condition; that is, activation which appears to decay over the delay period. We have now begun to test these predictions empirically. In a study with schizophrenia patients we found exactly the predicted pattern – reduced left DLPFC activity in patients which further showed an interaction with scan-within-trial such that the activity reduction was greatest at the end of the delay period (Barch *et al.*, 2001). Future work will be required to determine whether similar patterns are observed in other populations suspected to suffer from PFC dysfunction, such as older adults.



## 5. General discussion

The studies presented in this paper have provided support for a theory regarding the relationship between storage and control in WM. Specifically, we have proposed that the PFC subserves both storage and control functions, by representing and maintaining prior context information. We suggested that context representations subserve control functions by biasing local competitive activity within task-specific pathways, but also subserve storage functions in WM, since they represent task-relevant information that is actively maintained over time. These storage and control functions were studied in the context of performance in the AX-CPT, a simple but informative task paradigm. Furthermore, the theory was implemented as an explicit model developed within the connectionist framework, such that simulations of task performance could be conducted. The findings from these studies demonstrate that the theory and model can account for performance data in the AX-CPT under a variety of conditions and in different populations. Moreover, we presented neuroimaging evidence that directly supports two key claims of the model: 1) that context information is actively maintained in PFC; and 2) that this information is relevant for control over behavior. As such, we believe that the theory presented here provides new insights into the relationship between WM and cognitive control, and the role of PFC in subserving these functions. Below, we discuss the implications of the model in greater detail.

### 5.1. Cognitive control

A primary component of the theory is that control is exerted by activation of a mechanism which serves to bias on-going processing by both facilitating task-appropriate information and responses, and by inhibiting competing information and responses which are task-inappropriate. In this respect, the theory makes claims similar to that of Posner and Snyder (1975) and Shiffrin and Schneider (1977), who also argue that the conscious control of cognition results in both costs and benefits in task performance. However, the mechanisms by which these costs and benefits accrue are largely left unspecified in traditional theories. In the theory presented here, the mechanism of control is that of biasing activation states through sustained representations of context. This mechanism is in agreement with Norman and Shallice (1986), who argue that the SAS mediates control in a purely modulatory fashion, that is "neither sufficient nor necessary to cause selection (p. 8)".

The current theory shares many other commonalities with the Norman and Shallice model, including a focus on response competition and selection and the assignment of control functions to PFC. However, this account goes beyond Norman and Shallice, by additionally beginning to specify the properties of PFC representations, and by implementing these ideas within simulation models. In particular, we have argued that PFC representations encode context information, which can be in an abstract form, such as that provided by task instructions, but may also be much more specific, such as that provided by prior stimuli (as in the AX-CPT). Furthermore, we have suggested that a critical property of PFC representa-

tions is that they can be actively maintained for short-periods of time, which enables them to modulate processing of subsequent inputs or selection of subsequent responses. Most importantly, through computer simulations, we have explicitly demonstrated that these ideas regarding PFC function can account for detailed aspects of behavioral and neuroimaging data from both healthy individuals and those with disorders affecting PFC (i.e., older adults, patients with schizophrenia).

### 6.1. Working memory

The theory presented in this paper provides new insights regarding the relationship between cognitive control and working memory. The most prominent model of working memory in the cognitive psychology literature has been the one put forward by Baddeley (1986). In Baddeley's framework, working memory is a triarchic system composed of two domain-specific buffers, the phonological loop and the visuospatial scratchpad, and a central executive that oversees and coordinates their operation. However, in Baddeley's model, the central executive largely serves as a catch-all designation for a number of control functions that remain for the most part undifferentiated in terms of their underlying mechanisms (but for recent progress in this area, see Baddeley, 1996). In contrast, the account that we have put forward has focused on a critical control function, the ability to facilitate task-relevant information and responses while inhibiting competing information and responses. In the studies presented, we have attempted to specify the nature and mechanisms of this function in terms of the: a) the task situations in which it is most critical (e.g., when context is frequently updated and is critical for overriding dominant response tendencies); b) its neural substrate (e.g., dorsolateral PFC) and c) the causes and consequences of its breakdown (e.g., the effects of interference manipulations).

Additionally, we have argued that a fundamental mechanism of cognitive control is the active maintenance of a particular type of task-relevant information, which we've referred to as context. Moreover, because context is actively maintained, it can act to influence how incoming information is represented and processed. In many ways, this account is consistent with the common definition of working memory as a system that involves both the temporary storage and manipulation of task-relevant information (Baddeley, 1986; Just and Carpenter, 1992). However, at least in the formulation of working memory advocated by Baddeley, storage and control are strictly segregated, with storage occurring only in the two buffers, and control operating through the central executive. The account we have proposed rejects the strong form of this distinction, by suggesting that storage and control can be intrinsically related. In particular, a primary feature of the model which provides the capacity for cognitive control is the active maintenance of context representations. Furthermore, active maintenance is a central aspect of control function, in that it allows a means for task-relevant information to be utilized in a manner that allows it to directly bias on-going processing. Indeed, this feature of the model leads to a number of new predictions regarding working memory. For example, the theory suggests that storage in working memory does not neces-



sarily require the operation of the two buffer systems. In particular, the studies we have presented in this paper argue that maintenance of cue-related information in the AX-CPT occurs within a context-processing module, which in Baddeley's terminology, could be thought of as a component of the central executive. Moreover, in healthy individuals under normal task conditions, we observed that maintenance was not subject to decay (at least over the delay intervals tested). In the model, this characteristic is due to the strong recurrent connectivity within the context layer that enables representations to be self-sustaining and robust to normal levels of noise. This property of context maintenance may differentiate it from maintenance within the two buffer systems. Specifically, it has been argued that information within the phonological loop decays in about 2 seconds, if not actively refreshed by a rehearsal process (Baddeley, Thomson and Buchanan, 1975).

## 6.2. PFC function

A central premise of the cognitive control model is that context information is represented and maintained within PFC. This idea is consistent with a wide range of data from neurophysiology, neuropsychology, and most recently, neuroimaging. Moreover, the model provides a reinterpretation of the literature on active memory in PFC. Goldman-Rakic (1987) has argued that PFC is specialized for actively maintaining sensory information in working memory, by demonstrating that neuronal activity in PFC shows sensitivity to specific sensory features, and that impairing this activity (e.g., through lesions or pharmacological manipulations) produces selective impairments in the maintenance of this information. The theory presented here is consistent with these findings, but further suggests that in at least dorsolateral PFC, active maintenance occurs for particular type of information, namely, context representations. Because only the behaviorally relevant aspects of prior information are stored in context representations, active maintenance in dorsolateral PFC is not likely to be equivalent to a short-term memory trace. As such, the representations may be insensitive to certain featural or response distinctions. Moreover, because context may be represented as a goal state or the end result of integrating a series of inputs, actively maintained representations in PFC might be very complex and not easily analyzed by the standard methods of sensory physiology (i.e., receptive fields mapping, post-stimulus histograms). Indeed, initial support for these hypotheses comes from the recent work of Miller and colleagues, who have demonstrated that neuronal activity in PFC: a) is responsive to only the behaviorally-relevant subset of information in a visual cluttered array (Rao, Rainer and Miller, 1997b); b) is insensitive to intervening, but irrelevant inputs, presented during the delay period between cue and probe (Miller *et al.*, 1996); and c) represents both spatial and object identity information in an integrated form when task demands require that both domains of information be maintained to respond appropriately (Rao, Rainer and Miller, 1997a). Future studies along these lines will help to shed more light on the specific characteristics of active memory as it occurs in PFC.

## 6.3. Other brain systems

An important issue that has not been addressed by the current model is the interaction between context representations in PFC and other brain systems specialized for memory. In particular, it seems likely that there are neural systems that are particularly specialized for the short-term maintenance of both temporal and spatial relationships. These systems may correspond to the STM buffers frequently described in both the verbal and spatial working memory literatures. In particular, inferior parietal cortex has often been associated with phonological storage, while superior parietal cortex is thought to play a role in visuospatial processing (Logie, 1995; Vallar and Shallice, 1990). Additionally, it is known that there are at least two neural systems responsible for maintaining information over longer term periods. One system is specialized for the rapid formation of arbitrary memory traces, and appears to be located within the hippocampal formation, while the other is slower, more structured, and involves the neocortex (McClelland, McNaughton and O'Reilly, 1995).

It would seem that the coordination of these systems in a task-appropriate manner is a control function that is necessary in many behavioral situations, and is one that has been noted by a number of investigators (Baddeley, 1996; Ericsson and Kintsch, 1995; Gupta and MacWhinney, 1997; Shallice, 1988). This type of coordination and organization of other brain systems may occur through the sustained influence of context representations. In short-term memory systems, it appears that representations decay quickly if not continually reactivated. Maintained representations of context within PFC may serve this function, by providing a sustained source of top-down input based on the current behavioral goal. Moreover, for both short and long-term memories, context representations may provide a mechanism for search and retrieval of particular subsets of information. However, the computational dynamics of these processes have not yet been well-worked out (Burgess and Hitch, 1992; Houghton, 1990; Kawamoto and Anderson, 1985). Nevertheless, relevant data on all of these issues can already be found in the neuroimaging literature. Specifically, both verbal and spatial working memory tasks appear to involve the coactivation of PFC with other brain regions thought to be specialized for verbal or spatial STM (inferior and superior parietal cortex, e.g., Smith *et al.*, 1996). Additionally, PFC activation is now a robust finding in tasks involving search and retrieval from episodic memory (Buckner and Koutstaal, 1998). More detailed information on the relationship between PFC and these other brain systems could be obtained from future studies which make use of time-course or correlational information about activation patterns between brain regions.

## Author notes

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