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# Cognitive Control and Schizophrenia

## *Psychological and Neural Mechanisms*

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Schizophrenia is a complex and debilitating psychiatric disorder that affects approximately one percent of the population. Lay conceptions of schizophrenia typically focus on symptoms such as hallucinations, delusions, and disorganized speech, which are often considered the hallmark features of this disorder. However, clinicians, researchers, and theorists have long noted that individuals with schizophrenia also commonly suffer from disturbances in memory and cognition, often severely so. Interestingly, recent research suggests that disturbances in social and occupational functioning in individuals with schizophrenia may be more influenced by the severity of their cognitive deficits than the severity of symptoms such as hallucinations and delusions (Green, Kern, Braff, & Mintz, 2000). Such findings have led to a resurgence of interest in identifying the nature of cognitive abnormalities in schizophrenia. A close examination of the types of symptoms and cognitive disturbances displayed by individuals suggests that many of these disturbances appear to reflect an inability to control or regulate their cognitive and emotional states. In this chapter, we review the evidence that one of the core cognitive disturbances in schizophrenia is a deficit in one or more components of executive function, which leads to disturbances in the ability to appropriately regulate thoughts and behavior in accordance with internal goals. More specifically, we suggest that individuals with schizophrenia suffer from a disturbance in a specific type of executive control process that we refer to as a deficit in the ability to represent and maintain context.

Researchers have long recognized that individuals with schizophrenia appear to show profound deficits on cognitive tasks that are thought to require what is collectively referred to as "executive functions" or cognitive control functions. For example, numerous studies have shown that individuals with schizophrenia are impaired on tasks, such as the Wisconsin Card Sorting Task, that require a number of different components of executive function, including problem solving, set switching, and working





memory (Weinberger, Berman, & Zec, 1986). At the same time, individuals with schizophrenia also display deficits in a number of other cognitive domains, including selective attention, inhibition, working memory, perceptual integration (Silverstein, Kovacs, Corry, & Valone, 2000), and sustained attention (Carter, Robertson, & Nordahl, 1992; Chapman & McGhie, 1962; Cornblatt & Keilp, 1994; Gold, Carpenter, Randolph, Goldberg, & Weinberger, 1997; Gold, Randolph, Carpenter, Goldberg, & Weinberger, 1992; Nuechterlein & Dawson, 1984; Park & Holzman, 1992). These findings of deficits in a broad array of task domains raised the question of whether individuals with schizophrenia have a number of independent (or at least semi-independent) cognitive deficits, or whether there is some fundamental or basic component of cognitive control that is impaired in this disorder, which in turn contributes to disturbances on tasks thought to measure many different cognitive domains. In prior work, we and our colleagues have put forth the hypothesis that one of the fundamental disturbances in cognitive control present in schizophrenia is a deficit in the ability to represent and maintain context information (Barch et al., 2001; Braver, Barch, & Cohen, 1999a; Braver & Cohen, 1999; Cohen & Servan-Schreiber, 1992) because of a disturbance in the function of dopamine in dorsolateral prefrontal cortex.

To develop more explicit theories and testable predictions about context processing deficits in schizophrenia, we have drawn upon computational modeling as a tool for specifying the neural mechanisms that support context processing (e.g., dorsolateral prefrontal cortex and the dopamine system) and how specific disturbances to these mechanisms lead to cognitive impairments (Braver, 1997; Braver et al., 1999a; Braver, Barch, & Cohen, 1999b; Braver & Cohen, 1999; Braver, Cohen, & McClelland, 1997; Braver, Cohen, & Servan-Schreiber, 1995; Cohen & Servan-Schreiber, 1992). These models were constructed within the parallel distributed processing (PDP), or "neural network" framework, allowing the quantitative simulation of human performance in cognitive tasks using principles of processing that are similar to those believed to apply in the brain (McClelland, 1993; Rumelhart & McClelland, 1986). The nature of these models and the results of simulations are discussed in detail elsewhere (Braver, 1997; Braver et al., 1999a, 1999b; Braver & Cohen, 1999; Braver et al., 1997; Braver et al., 1995).

## CONTEXT PROCESSING

As discussed in many of the other chapters in this volume, such as that by West and Bowry, cognitive control requires the ability to detect, adjust, and respond to changing contingencies and feedback in the environment and no doubt requires a number of different functions and mechanisms. In our own work, we focused on several such mechanisms that we think are important for cognitive control, including context representation, context

intenance, context updating, conflict detection, and subgoal process-
(Barch et al., 2001; Barch et al., 2001; Botvinick, Braver, Barch, Carter, &
hen, 2001; Braver et al., 1999a; Braver & Bongiolatti, 2002; Braver, Cohen,
Barch, 2002; O'Reilly, Noelle, Braver, & Cohen, 2002). In regards to under-
nding cognitive control deficits in schizophrenia, we argued that deficits
the representation, maintenance, and updating of context may be central
this disorder. By context information, we mean information that must
"actively" held in mind in a form that allows it to be used to mediate
sk appropriate behavior. In our models, representations of context are
ed specifically to support task-relevant information against sources of
terference that can occur simply as a function of time (e.g., noise accu-
ulating in the system) or because of specific competing processes (e.g.,
e need to process other stimuli, distractions). Context representations
n comprise a variety of different types of information, such as a specific
ior stimulus, the result of processing a sequence of prior stimuli, or more
stract information such as task instructions. As an example, take the fol-
wing sentence: "In order to keep pigs, you need a pen." In this sentence,
e first clause serves as context that biases you toward the appropriate
eaning of the word "pen" (a fenced enclosure) for this sentence, rather
an the more common meaning of the word "pen" (a writing instrument).
his is a case in which the result of processing the first part of the sentence
.g., a sequence of prior stimuli) creates a contextual representation that
an bias future behavior (e.g., semantic interpretation of the word "pen").
s another example, take the well-known Stroop task. In one condition
f this task, participants are shown color words written in different colors
.g., the word "RED" written in blue). In the absence of any other infor-
ation, a participant's natural response is to read the word rather than
name the color, as this is what one typically does when presented with
erbal stimuli. In other words, reading the word rather than naming the
olor is the prepotent response. However, in the Stroop task, participants
re given the instruction to ignore the word and instead read the color. We
vould argue that in this situation, the task instructions serve as context that
llows the participant to inhibit the prepotent response tendency to read the
vord.

In many ways, one might argue that such a definition of context could
e overly broad or inclusive, as almost any type of stimulus could be seen
s forming a context representation. However, we would argue that con-
ext information or representations can be distinguished, both theoreti-
ally and empirically, from other related concepts in important ways. As
an example, we argued that the representation and maintenance of con-
ext can be distinguished from both the constructs of short-term mem-
ory and working memory (Barch, Carter, & Cohen, 2003; Cohen, Barch,
Carter, & Servan-Schreiber, 1999; Cohen & Servan-Schreiber, 1992). Short-
term memory is often used to refer to processes necessary to temporarily



store recently presented information in a form somewhat close to the form in which it was presented (e.g., without conceptual transformation). Such information held in short-term memory may or may not have implications for how one should respond in a future situation. In contrast, our definition of context information is that it must be information that has relevance for later behavior, but it may not correspond to the actual identity of previously presented information. In fact, our assumption is that context representations are almost always transformations of the identity of specific stimuli into their meaning for behavior, which often may no longer include the initial identify of the stimulus. We do think context processing is much more closely aligned with conceptions of working memory, which is commonly defined as the collection of processes responsible for the on-line maintenance and manipulation of information necessary to perform a cognitive task (Baddeley, 1994). However, we do not believe that context processing and working memory are interchangeable constructs. Instead, we view context representations as a subset of representations within working memory, which govern how other representation held within either working memory or long-term memory are used.

An important insight that has emerged from our work is that the context processing functions of our model demonstrate how a single underlying mechanism, operating under different task conditions, might subserve three cognitive functions that are often treated as independent: attention (selection and support of task-relevant information for processing), active memory (on-line maintenance of such information), and inhibition (suppression of task-irrelevant information). When a task involves competing, task-irrelevant processes (as in the Stroop task), it is often assumed that a dedicated inhibitory function is responsible for suppressing, or overriding, these irrelevant processes. However, in our model, there is no dedicated mechanism for inhibition. Rather, context representations accomplish the same effect by providing top-down support for task-relevant processes, allowing these to compete effectively against irrelevant ones. In contrast, when a task involves a delay between a cue and a later contingent response, it is usually assumed that a working memory function is involved. Once again, there is no dedicated mechanism for this function in our model. Rather, the mechanism used to represent context information is used to maintain task relevant information against the interfering and cumulative effects of noise over time. Thus, both for tasks that tap "inhibition" and for those that tap "working memory," the same mechanism is involved; it is simply a matter of the behavioral conditions under which it operates (i.e., the source of interference) that lead us to label it as having an "inhibitory" or a "working memory" function. Furthermore, under both types of conditions, context representations serve an attentional function by selecting task-relevant information for processing over other potentially competing sources of information. Thus, in all circumstances, the

same context processing mechanism is involved. We hypothesize that this context processing mechanism is impaired in schizophrenia. Consequently, we suggest that disturbances in context processing may form a common basis for many of the deficits observed across multiple cognitive domains in schizophrenia, including attention, inhibition, working memory, and language processing.

In many ways, this notion of deficits in the representation of context is related to the notion of goal neglect discussed by West and Bowry in another chapter in this volume and in previous work (West, 1999; West & Alain, 2000). It is also related to similar ideas put forth by Duncan (Duncan, Emslie, Williams, Johnson, & Freer, 1996). For example, one can think of context information as representations of goals that are held in memory to guide and constrain ongoing processing. Difficulties in the sustained active maintenance of such representations can lead to a number of behavioral deficits on cognitive control tasks as described by West. As discussed in greater detail later, our model of context processing and the associated neurobiological mechanisms provides some hypotheses as to disturbances that might contribute to deficits in context processing and/or goal neglect.

Further, our hypotheses regarding the role of context processing in cognitive control (and the influence of such maintained context representations to overcome the negative influences of interference and conflict) are consistent with the role of "executive attention" in the working memory model put forth by Engle and colleagues (Engle & Kane, 2004). Specifically, Engle suggests the term executive attention refers to the ability to maintain even a single bit of information (e.g., a goal) in working memory in the face of a variety of sources of conflict. As with our theory, Engle and colleagues do not draw a strong line between mechanisms involved in the maintenance of information and those involved in the control and manipulation of ongoing processing. For example, Engle argues that although there may be multiple components of working memory capacity, the component most closely linked to success in a number of real-world outcomes (e.g., new vocabulary learning) is the ability to use attentional control to maintain goal-relevant information when there is interference or competition for other processes or stimuli. This is in contrast to the type of working memory model put forth by Baddeley, which does postulate a stricter segregation of storage/maintenance processes and central executive processes (Baddeley, 1996; Baddeley, 1986, 2000; Baddeley & Hitch, 1994), although more recently Baddeley emphasized the importance of attention control for working memory function (Baddeley, 1993; Baddeley & Logie, 1999). Thus, our model can be thought of as being highly compatible with that of Engle and colleagues. The primary differences between the models are ones of emphasis and the experimental domains upon which they have focused. Engle and colleagues have primarily focused on studies of healthy young adults, using both an individual differences approach and standard



cognitive psychology methodology. In contrast, our own model focused as heavily on special populations (i.e., schizophrenia, older adults) as on healthy young adults and integrated computational and cognitive neuroscience methodologies with cognitive experimental ones.

## CONTEXT PROCESSING IN SCHIZOPHRENIA

In many ways, our hypotheses about context processing deficits in schizophrenia are very similar to earlier suggestions about the nature of cognitive deficits in this disorder put forth by researchers such as Shakow (Shakow, 1962). For example, Shakow suggested that "we see particularly the various difficulties created by context . . . It is as if, in the scanning process which takes place before the response to a stimulus is made, the schizophrenic is unable to select out the material relevant for optimal response (p. 4)" (Shakow, 1962). There is now a growing body of evidence from a variety of different task domains that supports the idea that individuals with schizophrenia have a deficit in the ability to represent and maintain context information, including tasks drawn from the domains of working memory, selective attention, inhibition, and language processing.

### AX-CPT Task

One task that we used in numerous studies is a version of the classic Continuous Performance Test (Rosvold, Mirsky, Sarason, Bransome, & Beck, 1956) known as the AX-CPT (Cohen et al., 1999; Servan-Schreiber, Cohen, & Steingard, 1996). This test was specifically designed as a measure of context representation and maintenance. As shown in Figure 6.1a, in this task, participants are presented with cue–probe pairs and told to make a target response to an "X" (probe) but only when it follows an "A" (cue), and a nontarget response otherwise. A correct response to "X" depends upon maintaining the "context" provided by the cue ("A" or not-"A"). One change to the standard AX-CPT was to increase the frequency of target ("AX") trials so that they occur with a high frequency (70%, see Figure 6.1b), with the remaining 30% of trials distributed across 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). This creates two types of biases that can be used to probe the integrity of context processing. The first bias, or prepotent response, is that participants expect to make a target response when they see an "X" probe, because this is the correct response on most of the trials (87.5% of trials in which an X is presented). On "BX" trials, participants have to use to the context provided by the "B" cue to inhibit this bias to respond target to an "X" (which would lead to a false alarm). Thus, impaired context representations will lead to poor performance on "BX" trials, because the context provided by the "B" cue would not be available

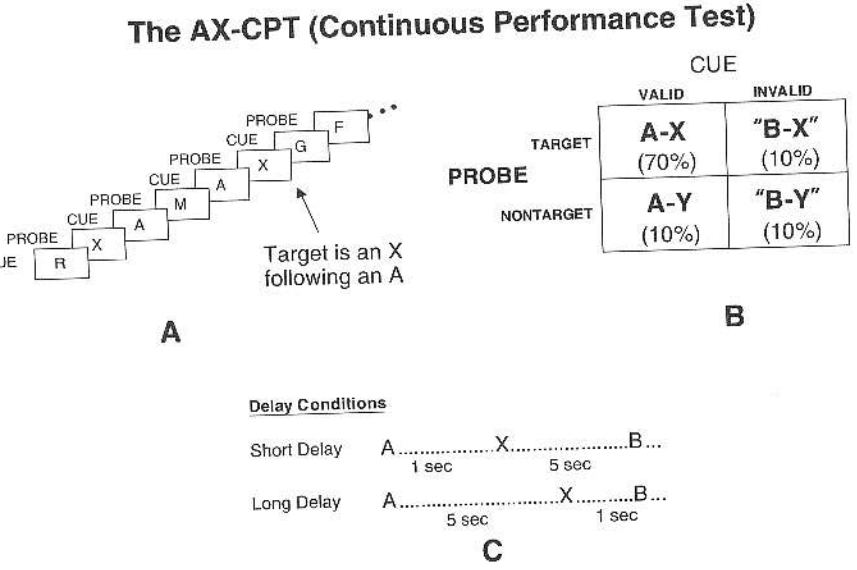


FIGURE 6.1. Panel A: Schematic of stimuli presentation across time in the AX-CPT. Panel B: Illustration of relative frequencies of different trial types in the AX-CPT. Panel C: Illustration of the timing of the stimuli in task conditions of the AX-CPT with either a short or a long delay between the cue and the probe.

to override the tendency to want to response target to the "X." The second bias is that participants expect to make a target response after they see an "A" cue, because most of the time an "X" follows the "A" cue (87.5% of "A" cue trials). However, on trials in which the "A" is not followed by an "X", this predictive aspect of context actually *creates* the tendency to false alarm. Thus, intact representations of context will hurt performance on "AY" trials, because context induces an invalid expectancy, leading to worse "AY" than "BX" performance. In contrast, individuals with impaired context representations should show worse "BX" than "AY" performance. In other words, individuals with impaired context representations (such as individuals with schizophrenia) should show worse "BX" performance, but *better* "AY" performance, than individuals with intact context representations.

A second manipulation included in the AX-CPT task is to examine maintenance of context information and the initial representation of context by manipulating the delay between the cue and probe (see Figure 6.1c). When the interval or delay between the cue and the probe is lengthened from, for example, 1 second to 5 or 10 seconds, context must be actively maintained within *working memory* (supported by prefrontal cortex in this and other theories of working memory function; see below). One prediction of



the context processing theory is that performance on "AY" and "BX" trials will vary as a function of delay (Braver et al., 1999a; Braver et al., 2002; Braver et al., 1995). When context can be maintained, then the strength of context representations should stay the same or increase with delay. If so, then "BX" performance should stay the same or even get better with longer delays because there is more time for context information to prepare the person to inhibit an incorrect response to the "X". In contrast, "AY" performance should stay the same or get worse with delay because there is more time for context representations to induce the participant to prepare for a target response, which must be inhibited when a "Y" rather than an "X" occurs. In contrast, if context maintenance is impaired, then "BX" performance should get worse with delay, but "AY" performance should actually *improve*.

A number of prior studies found results with this AX-CPT task that provide evidence consistent with an impairment in context processing in schizophrenia (Barch et al., 2001; Barch et al., 2003; Cohen et al., 1999; Javitt, Shelley, Silipo, & Lieberman, 2000; Servan-Schreiber et al., 1996; Stratta, Daneluzzo, Bustini, Casacchia, & Rossi, 1998; Stratta, Daneluzzo, Bustini, Prosperini, & Rossi, 2000). For example, earlier work in our lab (Barch et al., 2001) demonstrated that as predicted, individuals with schizophrenia (first episode, neuroleptic naïve; see Figure 6.2a) made significantly more "BX" errors than did healthy controls, but significantly *fewer* "AY" errors, particularly at the longer delay. This pattern of both impaired and improved performance suggests that context representations are less available or less able to influence processing in individuals with schizophrenia, leading to an inability to override the incorrect tendency to respond target to the "X" on "BX" trials. In addition, such impairments in the processing of context lead to less predictive use of context on "AY" trials (which normally leads to errors on "AY" trials). In addition, the individuals with schizophrenia were significantly slower than controls on correct "BX" trials (suggesting increased interference from the "X" cue when there is a need to override a prepotent response tendency). However, the individuals with schizophrenia were not significantly slower than controls on "AY" trials, despite the fact that patients are typically overall slower on all tasks (see Figure 6.2b). This lack of an RT difference on AY trials again suggests that patients did not use context in a predictive fashion, leading them to actually experience less of a context-induced interference effect.

Across a number of different studies, results with the AX-CPT have consistently demonstrated that individuals with schizophrenia have deficits in the representation of context, in that they show the predicted patterns of increased BX errors and RTs, but not increased AY errors (or even decreased) and RTs. However, the answer to the question of whether patients with schizophrenia have a deficit in the maintenance of context

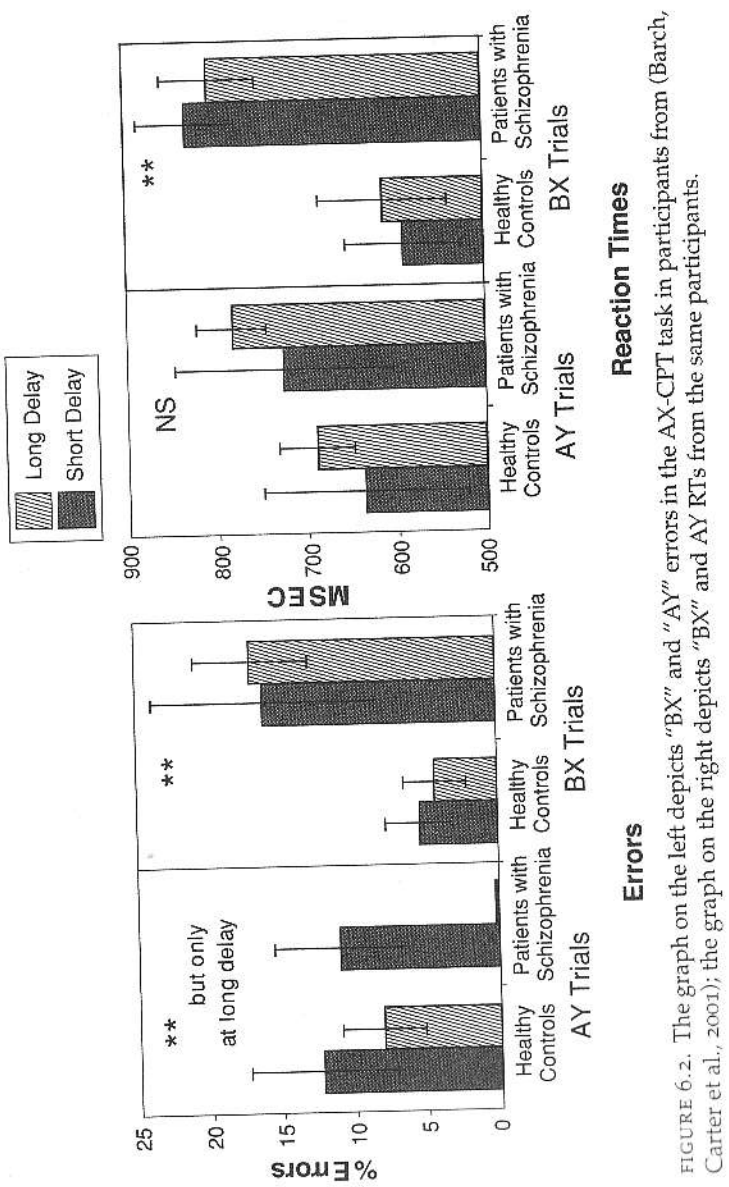


FIGURE 6.2. The graph on the left depicts "BX" and "AY" errors in the AX-CPT task in participants from (Barch, Carter et al., 2001); the graph on the right depicts "BX" and AY RTs from the same participants.



(e.g., effects exacerbated at the longer delay) and a deficit in the initial representation of context (e.g., deficits at short delay) is unclear. If patients with schizophrenia were primarily experiencing deficits in the representation of context, but not in maintenance, then performance deficits should be equal across the short and long delay. In contrast, if patients had deficits in representation and maintenance, then deficits should be worse at the long as compared to short delay. Some studies have shown that individuals with schizophrenia show an increase in context processing deficits at the long as compared to short delay (Cohen et al., 1999; Elvevag, Duncan, & McKenna, 2000; Javitt et al., 2000; Servan-Schreiber et al., 1996; Stratta et al., 1998; Stratta et al., 2000), whereas other studies have not (Barch et al., 2001; Barch et al., 2003; MacDonald et al., in submission; Perlstein, Dixit, Carter, Noll, & Cohen, 2003). However, close examination of the patterns of data across these different studies suggests that two different factors may be influencing whether context processing deficits are significantly greater at the long as compared to short delay in patients with schizophrenia as compared to controls. The first factor is whether the patients are early in the course of illness (e.g., first episode) or more chronic. To date, the studies with first episodic patients have not, for example, found significant increases in "BX" errors or RTs at the long as compared to the short delay (Barch et al., 2001; Barch et al., 2003; MacDonald et al., in submission) or have at least found smaller increases as a function of delay than in studies with chronic patients (Javitt et al., 2000). This suggests that early in the course of illness, patients with schizophrenia experience deficits in the initial representation of context but not further deficits in the maintenance of context. In contrast, studies with chronic patients do indicate that "BX" errors and RTs are significantly increased at the long as compared short delay (Cohen et al., 1999; Elvevag et al., 2000; Javitt et al., 2000; Servan-Schreiber et al., 1996; Stratta et al., 1998; Stratta et al., 2000), suggesting that chronic patients may have deficits in context maintenance and in initial context representation. A second factor is the performance of controls. In some studies with chronic patients, the controls also showed an increase in "BX" errors or RTs from the short to long delay, making it difficult to detect a differentially greater increase in patients (Cohen et al., 1999; Javitt et al., 2000). At this point, it is not entirely clear why some healthy controls show reductions in context processing at the long versus short delay, though it is possible that this may be related to some changes in the ability to represent and/or maintain context that occurs with age (see below for further discussion of aging and context processing) (Braver et al., 2001) or that can vary as a function of factors such as fluid intelligence (Burgess & Braver,). Additional studies more directly examining stage of illness effects or longitudinal changes in context processing among both patients with schizophrenia and healthy controls will help to clarify the magnitude of deficits in

FIGURE 6.3. The graph on the left depicts "BX" and "AY" errors in the AX-CPT task in participants from (Barch et al., 2003); the graph on the right depicts "BX" and "AY" RTs from the same participants.



the initial representation of context versus the maintenance of context in schizophrenia.

In other work, we also examined the degree to which such context processing deficits are specific to individuals with schizophrenia as compared to other psychiatric disorders. For example, one study compared chronic individuals with schizophrenia to individuals with nonpsychotic major depression and found that unlike individuals with schizophrenia, individuals with major depression did not show any evidence of impairments in context processing (Cohen et al., 1999). In more recent work (Barch et al., 2003), we compared the specificity of context processing deficits to individuals with schizophrenia versus individuals with other psychotic disorders (e.g., major depression with psychotic features, bipolar disorder, delusional disorder, psychotic disorder NOS). In this study, participants were entered into the study upon their first contact with psychiatric services and tested before they were ever administered antipsychotic medications. Participants were then followed longitudinally, with repeat testing after four weeks and a confirmation of their diagnostic status at six months. At study admission, the individuals with psychotic disorders other than schizophrenia demonstrated a very similar pattern of deficits in context processing to that shown by individuals with schizophrenia. This included more "BX" errors and slower "BX" RTs as compared to controls, but *the same or "AY"* errors and no difference in "AY" RTs. Again, this suggests that both the individuals with schizophrenia and the individuals with other psychotic disorders were less able to use context representations to inhibit an incorrect target response on "BX" trials and less able to use context to predict potential targets on "AY" trials.

However, at four weeks, the individuals with other psychotic disorders, but not the individuals with schizophrenia, began to show improvements in context processing. As shown in Figure 6.3, by four weeks, the individuals with other psychotic disorders no longer differed from controls in "BX" performance (either errors or RT), but they did show significantly performance differences when compared to individuals with schizophrenia. Taken together, we argued that such results suggest that context processing deficits are a more stable component of schizophrenia, perhaps forming part of the vulnerability to this disorder. In contrast, context processing deficits may be more state-related in other psychotic disorders (Barch et al., 2003).

Others research found that individuals at risk for schizophrenia, and who presumably share liability for this disorder, also display deficits in context processing on the AX-CPT task. For example, MacDonald and colleagues showed that nonpsychotic siblings of patients with schizophrenia show a similar performance pattern on the AX-CPT to that found with schizophrenia patients, demonstrating increased "BX" errors and RTs and decreased "AY" errors and no difference in "AY" RTs (MacDonald,

FIGURE 6.4. The graph on the left depicts "BX" and "AY" errors in the AX-CPT task in controls and individuals with schizotypal personality disorder (SPD) from (Barch, Mitropoulou et al., in press); the graph on the right depicts "BX" and "AY" RTs from the same participants.



Pogue-Geile, Johnson, & Carter, 2003). In our own work, we examined context processing deficits in individuals with schizotypal personality disorder, a disorder thought to share genetic liability with schizophrenia. As shown in Figure 6.4, we also found a pattern of deficits on the AX-CPT among individuals with schizotypal personality disorder that is indicative of a disturbance in context processing (Barch et al., in press). Like individuals with schizophrenia, the individuals with schizotypal personality disorder displayed increased "BX" errors, but not "AY" errors, combined with increased "BX" RTs, but not "AY" RTs. However, none of these effects were significantly exacerbated with delay in the individuals with schizotypal personality disorder. Taken together, these results suggest that individuals with schizotypal personality disorder also have difficulty utilizing contextual information to govern behavioral responding, but that this deficit is not worsened by increasing the delay over which such information must be maintained.

### Other Measures of Context Processing

A number of studies using tasks other than the AX-CPT also provided evidence for deficits in context processing in schizophrenia. For example, a growing number of studies suggest that deficits in context processing can be observed in the domain of language comprehension and production. Very interesting evidence for context processing deficits in schizophrenia comes from a number of studies examining an ERP component called the N400, which is thought to index the degree of consistency or relatedness between a stimulus (e.g., word) and the preceding context (which could be a single word, a sentence, or an entire discourse; Brown & Hagoort, 1993; Kutas & Hillyard, 1980). The N400 is a negative going component of an ERP waveform that occurs approximately 400 msec after the onset of the stimulus of interest. In cognitively intact individuals, words that are not consistent with the preceding context elicit a larger N400 than words that are consistent with the preceding context.

A number of such N400 studies using different types of paradigms have provided evidence for context processing deficits in schizophrenia. For example, Condray used a lexical decision task in which pairs of words were presented that were either semantically related or semantically unrelated (Condray, Steinhauer, Cohen, van Kammen, & Kasparek, 1999; for related studies, see Grillon, Ameli, & Glzer, 1991). Controls demonstrated a significant priming effect in N400s (larger N400s to unrelated as compared to related words), whereas drug-free individuals with schizophrenia did not show an N400 priming effect. This suggests that patients were unable to use the context provided the first word to bias processing of the second word. Salisbury (Salisbury, O'Donnell, McCarley, Nestor, & Shenton, 2000) used a paradigm in which he presented four-word sentences to participants,

of the form "THE *NOUN* WAS *ADJECTIVE/VERB*." In this paradigm, the adjective or verb was always congruent with the noun. Controls showed significantly reduced N400s to the sentence final adjective/verbs as compared to the nouns presented earlier in the sentence, consistent with the idea that the controls use the noun to generate contextual representations that can help facilitate processing of consistent semantic information. However, the patients with schizophrenia did not show any reduction in N400 to the sentence final words as compared to the nouns, suggesting that patients were unable to either develop or use such contextual representations.

In more recent work, Sitnikova and colleagues (Sitnikova, Salisbury, Kuperberg, & Holcomb, 2002) examined N400s in a paradigm involving two clause sentences. The first clause ended with a homograph that had asymmetrical meanings (a dominant meaning and a subordinate meaning), and the second clause started with a strong semantic associate of the dominant meaning of the homograph. On half the trials, the first clause biased the dominant meaning of the homograph (so that the second clause should be consistent and not elicit an N400). On the other half of the trials, the first clause biased the subordinate meaning of the homograph (so that the second clause should be inconsistent and should elicit an N400). The control participants demonstrated reliably larger N400s in the inconsistent second-clause condition as compared to the consistent second-clause condition. This suggests that controls were able to use the context in the first clause to facilitate processing of the subordinate meaning of the homograph and suppress the dominant meaning. In contrast, the patients with schizophrenia showed a significantly smaller N400 than controls to the dominant meaning of the homograph when it followed a context that should have biased the subordinate meaning, and in fact showed no differences in N400 to consistent and inconsistent second clauses (for related studies, see (Adams et al., 1993; Niznikiewicz et al., 1997; Ohta, Uchiyama, Matsushima, & Toru, 1999; Olichney, Iragui, Kutas, Nowacki, & Jeste, 1997; Strandburgh et al., 1997; Titone, Holzman, & Levy, 2002; Titone, Levy, & Holzman, 2000)). Again, such results suggest that the patients with schizophrenia were less able to use the context provided by the first part of the sentence to bias ongoing processing. Of note, we do not mean to imply that we think the N400 itself is necessarily generated by the same context representation and maintenance processes that support AX-CPT task performance. However, variations in the N400 (and the cognitive processes generating this ERP component) may be influenced by the integrity of such context representation mechanisms. If so, then examining variations in the N400 may allow one to make inference about context representation and maintenance processes that modulate the types of integration or semantic process that give rise to the N400.

Studies in the domain of selective attention have also been used as evidence for deficits in context processing. For example, a number of studies using the color–word Stroop task found that individuals with schizophrenia are less able to inhibit the prepotent response to read the word, as evidenced by increased errors in the incongruent condition (color and word conflict) or by an increase in the total Stroop effect in RT (Barch et al., 1999; Barch, Carter, Hachten, & Cohen, 1999; Carter et al., 1992; Chen, Wong, Chen, & Au, 2001; Cohen et al., 1999; Elvevåg et al., 2000; Henik et al., 2002; Taylor, Kornblum, & Tandon, 1996). Further, in recent work, we used the process dissociation techniques developed by Jacoby to estimate the contributions of both word naming and color reading to Stroop performance in schizophrenia and found that color reading estimates are reduced whereas word reading estimates increased (Barch, Carter, & Cohen, in press). As described previously, our theory posits that task instructions to attend to color and ignore words serve as context representations in the Stroop tasks that normally allow one to inhibit the tendency to read words. Thus, we argued that Stroop task deficits in schizophrenia are consistent with a deficit in context processing.



Silverstein and colleagues suggested that deficits in context processing and contextual integration among individuals with schizophrenia extend even to the level of basic perceptual processing. (Silverstein et al., 2000). It is not yet clear whether the type of contextual processing measured in these paradigms is the same as that measured in tasks such as AX-CPT. However, such results raise the intriguing possibility that deficits in context processing account for deficits among individuals with schizophrenia both on high-level cognitive tasks and in more basic sensory and perceptual domains.

## INTERRELATIONSHIP OF CONTEXT PROCESSING AND OTHER COGNITIVE CONSTRUCTS

As noted earlier, one of our hypotheses is that deficits in context processing serve as a common underlying impairment across a wide variety of cognitive domains, including working memory, inhibition/selective attention, and language processing. To test this hypothesis, we conducted a study in which we administered several different tasks to individuals with schizophrenia, along with healthy controls and depressed individuals (see Figure 6.5) (Cohen et al., 1999). We picked tasks that had traditionally been associated with different cognitive domains: (a) working memory with the AX-CPT; (b) inhibition/selective attention with the color–word Stroop; and (c) language processing with a lexical disambiguation task. However, each of the tasks included similar manipulations designed to increase their reliance on context representation and maintenance. As shown in Figure 6.5, each task included some type of contextual cue, a prepotency manipulation (either naturally occurring or induced in the task), and a delay manipulation (between the context and the need to use the context). The AX-CPT task was administered as described earlier. The Stroop task was modified to be a "switching" Stroop in which trials randomly

**Context Tasks**

In each task, there was:
1) a delay between the cue (context) and response
2) an asymmetry in the relative prepotency of competing responses

| Task | Context | Prepotency | Delay |
|---|---|---|---|
| AX-CPT | "A" or "Not-A" cue | 70% Target (A-X) Sequences | 1 or 5 sec cue-probe interval |
| Stroop | Word Reading or Color Naming Instruction | Word Reading more prepotent than color naming | 1 or 5 sec cue-stimulus interval |
| Lexical Disambiguation | Sentence that biases a dominant or subordinate completion<br>**Example:** race/rage ("ra_e")<br>**Race:** Fred and Bob dashed to the finish line in a tie.<br>**Rage:** Fred and Bob had bad tempers and often became quite angry. | One completion of an item ("ra_e") more frequent (race) in the absence of context than other completion (rage) | Sentence order, either:<br>neutral -> Bias<br>or<br>bias -> Neutral |

FIGURE 6.5. Description of the tasks and manipulations of context representation and delay (Cohen et al., 1999).

alternated from color-naming to word-reading, with the type of trial indicated by a cue (i.e., context) that occurred at the start of each trial. Thus, participants needed to use the context provided by this cue to inhibit the tendency to read the word on color naming trials and needed to update this context information on a trial-by-trial basis. In addition, we manipulated the delay between the cue and the onset of the stimulus in order to assess maintenance of context. In the lexical disambiguation task, participants were presented with words missing one letter that could be completed in one of two ways, with one completion occurring more frequently than another (in the general population). These "missing letter" stimuli were preceded by sentences that could bias the participant toward the more dominant completion or toward the less frequent completion. As such, participants needed to use the context provided by the preceding sentences to modulate the tendency to complete the letter strings with the dominant versus subordinate completion. As with the other two tasks, we also manipulated the delay between this contextual information and the occurrence of the missing letter stimuli to assess context maintenance.

The results of this study indicated that, for the most part, individuals with schizophrenia were impaired across all three cognitive domains and tasks in the conditions that we would argue most strongly tap the need to represent and maintain context information. For example, the patients with schizophrenia again demonstrated increased "BX" errors as compared to



the controls, but no increased AY errors, as well as no increased "AX" errors, especially with a long delay. On the Stroop task, the patients with schizophrenia demonstrated significantly more errors than did the controls, particularly in the incongruent condition of the color naming task, the condition we argue is most dependent on context processing. On the lexical disambiguation task, the individuals with schizophrenia demonstrated a clear pattern indicative of impaired context processing, which included: (a) demonstrating the same asymmetry in production of the dominant versus subordinate completions as the controls in the absence of any biasing context; (b) the production of fewer subordinate completions, particularly with a long delay, when the sentence context should have biased such completions; and (c) the production of fewer dominant completions than controls when the sentence context should have biased them toward such completions (ruling out the possibility that patients simply had a dominant response bias). More importantly, however, were the results of the analyses examining cross-task relationships. We found that among the total sample and just within the individuals with schizophrenia, performance on each of the three tasks in conditions dependent on context processing were strongly and selectively interrelated, whereas performance on conditions not dependent on context (but psychometrically matched) were not related. Such results provide support for the hypothesis that deficits in a wide variety of cognitive domains in schizophrenia may result from disturbances in contextual processing.

In other studies, we also found that performance on tasks specifically designed to measure context processing, such as the AX-CPT, are strongly correlated with performance on tasks measuring other cognitive processes, which we would argue are also dependent on context processing. For example, in a large sample of healthy younger and older adults, we found that performance on the AX-CPT was correlated with performance on a number of standard measures of working memory, including the reading span, a highly demanding digit span, and an "N-back" task (Keys, Barch, Braver, & Janowsky, submitted). In the study described previously with individuals who have schizotypal personality disorder, we found that AX-CPT performance was strongly correlated with performance on an "N-Back" task, which measures working memory, and on an Eriksson Flanker task, which measures selective attention (Barch et al., in press). Again, such findings are consistent with the hypothesis that deficits in context processing may contribute to disturbances in a variety of related cognitive domains.

## THE NEUROBIOLOGY OF CONTEXT PROCESSING

We hypothesized that the representation and maintenance of context processing are subserved by a specific set of neural mechanisms. In

particular, we postulate that representations of context information are housed within the dorsolateral portion of the prefrontal cortex (DL-PFC) and actively maintained there when task demands require such active maintenance (O'Reilly, Braver, & Cohen, 1999). Further, we hypothesize that the dopamine (DA) projections to DL-PFC regulate the access to such context information, insulating this information from the interfering effects of noise over intervals in which the information must be sustained, while at the same time allowing for the appropriate updating of such context information when needed (Braver & Cohen, 2000). These hypotheses are consistent with the broader neuroscience literature, in which active maintenance in the service of control is a commonly ascribed function to PFC (Fuster, 1989; Goldman-Rakic, 1987; Miller & Cohen, 2001), and the DA system is widely held to modulate the active maintenance properties of PFC (Cohen, Braver, & Brown, 2002; Luciana, Collins, & Depue, 1998; Sawaguchi, Matsumura, & Kubota, 1990; Williams & Goldman-Rakic, 1995). In our model, the context processing functions of cognitive control critically depend upon DL-PFC and DA system interactions. As a consequence, the model predicts that individuals and populations with impairments in either or both DL-PFC or the DA system should demonstrate specific patterns of impaired cognitive control related to the processing of context.

## ROLE OF PREFRONTAL CORTEX

As noted above, a large number of functional neuroimaging studies have demonstrated that prefrontal cortex is activated when individuals have to maintain information in working memory (Cabeza & Nyberg, 2000). However, the majority of these studies used tasks that may or may not tap context processing, and they were not specifically designed to selectively measure context processing. However, we and our colleagues conducted a number of neuroimaging studies using tasks, such as the AX-CPT and the switching Stroop, that were specifically designed to measure context processing. For example, our early research with the AX-CPT demonstrated that dorsolateral PFC and ventrolateral PFC showed selective increases in activity when context representations had to be maintained over a long delay as compared to short delay (Barch et al., 1997; Braver & Cohen, 2001). In contrast, these same PFC regions did not show increased activity when the AX-CPT task was made more difficult by degrading the stimuli (but not changing maintenance demands). This suggests that dorsolateral PFC regions are not simply activated whenever the task gets more challenging, although the anterior cingulate did respond to this difficulty manipulation, leading to subsequent research on the role of the anterior cingulate in conflict detection (Botvinick et al., 2001). Such findings dissociating the control processes subserved by the dorsolateral PFC relative to other



brain regions (such as the anterior cingulate) have been replicated by other studies as well (MacDonald, Cohen, Stenger, & Carter, 2000). Of interest, the only brain regions to show a sustained increase in activity when required to maintain context information were the dorsolateral and ventrolateral PFC regions. This is in contrast to the patterns of brain activity often found during working memory tasks, which is typically much more widespread, including regions such as the parietal cortex, frontomedial motor regions, and other subcortical regions (e.g., cerebellum, basal ganglia). We argued that this selective responsivity of PFC regions to the context maintenance manipulation provides strong support for their central role in supporting this particular component of cognitive control.

We also examined how challenging context processing in healthy individuals alters task-related PFC activity. For example, we developed a version of the AX-CPT in which participants are presented with distractor items during the delay between the cue and the probe. Our hypothesis was that if deficits on the AX-CPT among individuals with schizophrenia were due to disturbances in the ability to maintain context information, disturbing the ability to maintain context information in healthy adults should elicit the same types of task deficits as found in individuals with schizophrenia. Consistent with this hypothesis, we found that adding distractors during the delay between the cue and the probe in the long-delay conditions of the AX-CPT increased the number of "BX" errors (and slowed "BX" RTs) that healthy participants made, but *decreased* the number of "AY" errors, consistent with a reduced ability to use context information. In a subsequent functional neuroimaging study using the same task design, we found that the addition of distractions and impairments in task performance was accompanied by a selective decrease in dorsolateral PFC activity but no change or even an increase in ventrolateral PFC activity (Braver & Cohen, 2001). The results of this study and others have provided some clues about the different contributions that dorsolateral versus ventrolateral PFC play in context processing. More specifically, we argued that ventrolateral regions of PFC may serve a more general role in phonological processing or rehearsal that may in no way be selective or specific to context representations, an idea put forth by many other researchers as well. In contrast, it may be that dorsolateral PFC (particularly in the left hemisphere) may be more specifically involved in the development and/or maintenance of context representations.

We also examined the patterns of brain activity found in individuals with schizophrenia during the performance of tasks such as the AX-CPT. In one such study, medication naïve first episode individuals with schizophrenia and controls were presented with trials that had either a short- or a long-delay period between the cue and the probe (Barch et al., 2001). The trials were designed so that four images of the brain were acquired during each trial, allowing us to glean some rough information about the time course

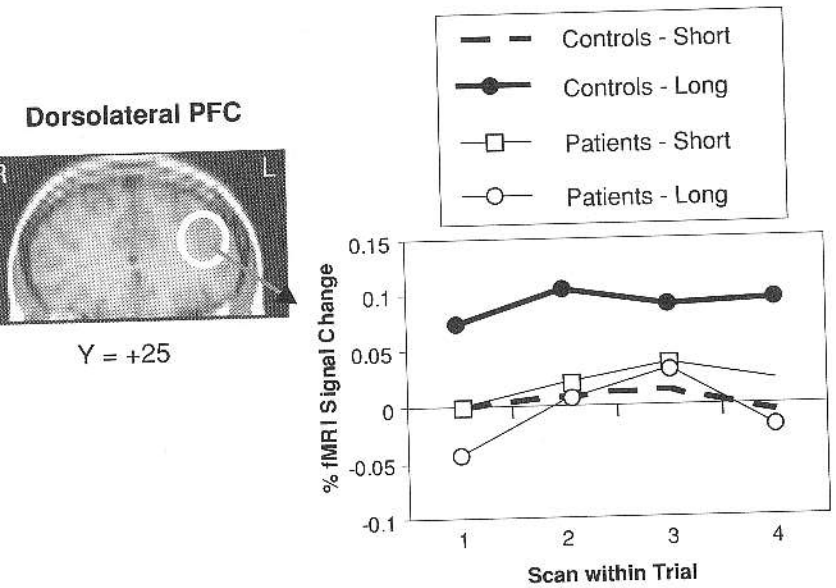


FIGURE 6.6. Illustration of task-related brain activity in dorsolateral PFC during the AX-CPT. The image displays a coronal slice through the brain 25 mm anterior to the anterior commissure plane. The graph illustrated percent fMRI signal change during each scan of the trial, relative to the first scan of the short delay condition, for each group in each condition.

of brain activity during context maintenance. As shown in Figure 6.6, the healthy controls once again demonstrated a sustained increase in dorsolateral PFC activity during the long as compared to short-delay condition. However, the medication naïve individuals with schizophrenia did not show any significant increased in dorsolateral PFC activity in response to the context maintenance demand. In contrast, as shown in Figure 6.7, the individuals with schizophrenia did show increased delay related activity in ventrolateral PFC regions, activity that did not differ in magnitude from controls. Again, this provides evidence for the fact that dorsolateral and ventrolateral regions of PFC play different roles in context processing and are differentially impaired in schizophrenia.

Such findings of impaired dorsolateral PFC activity during the performance of context processing tasks have now been replicated several times, in chronic and in first episode patients (MacDonald, in press; Perlstein, Dixit, Carter, Noll, & Cohen, 2003). Further, recent research suggests that such dorsolateral PFC deficits are specific to individuals with schizophrenia as compared to individuals with other psychotic disorders, who show a different pattern of potentially increased dorsolateral PFC activity (MacDonald et al., in submission).



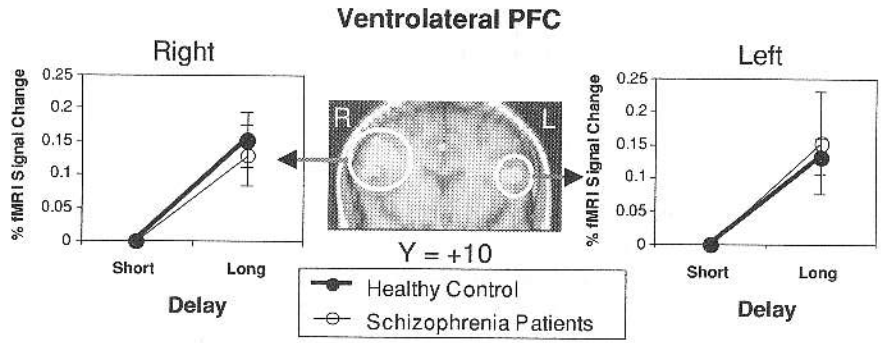


FIGURE 6.7. Illustration of task-related brain activity in ventrolateral PFC during the AX-CPT. The image displays a coronal slice through the brain 10 mm anterior to the anterior commissure plane. The graphs for both the left and right ventrolateral regions display the increase in task-related brain activity from the short- to the long-delay condition.

## ROLE OF DOPAMINE

As described above, our models also postulate a central role for dopamine in context processing and hypothesize that impaired dopamine function in dorsolateral PFC contributes to context processing deficits. There is a large body of evidence in nonhuman primates and humans suggesting that dopamine plays an important role in working memory more generally (Arnsten, Cai, Murphy, & Goldman-Rakic, 1994; Barch, in press; Brozoski, Brown, Rosvold, & Goldman, 1979; Cai & Arnsten, 1997; Castner, Williams, & Goldman-Rakic, 2000; de Sonneville, Njiokiktjien, & Bos, 1994; Goldman-Rakic, 1995; Kimberg & D'Esposito, 2003; Kimberg, D'Esposito, & Farah, 1997; Luciana & Collins, 1997; Luciana, Collins, & Depue, 1995; Luciana et al., 1998; Luciana, Depue, Arbisi, & Leon, 1992; Mattay et al., 1996; Mattay et al., 2000; Mattay et al., 2003; Mehta et al., 2000; Mehta, Swainson, Gogilvie, Sahakian, & Robbins, 2001; Mintzer & Griffiths, 2003; Muller, von Cramon, & Pollmann, 1998; Sawaguchi & Goldman-Rakic, 1994; Williams & Goldman-Rakic, 1995). This includes evidence that nonspecific dopamine agonists, such as amphetamine, can improve working memory in medicated patients with schizophrenia (Barch & Carter, in preparation; Daniel et al., 1991; Goldberg, Bigelow, Weinberger, Daniel, & Kleinman, 1991) and that changes in D1 receptor availability in DLPFC are associated with working memory impairment in schizophrenia (Abi-Dargham et al., 2002). Unfortunately, however, there is little direct evidence yet for a role for dopamine specifically in context processing in humans, as compared to working memory more generally. However, we have recently completed a double-blind placebo controlled study examining the influence of d-amphetamine on AX-CPT performance in healthy individuals.

In this study we used both our standard version of the AX-CPT and the nterference" version described previously, in which distractors appeared etween the cue and the probe. As noted earlier, including such distrac-ors normally elicits a pattern of performance in controls analogous to hat found in schizophrenia (e.g., increased "BX" errors and RT; decreased AY" errors). Participants were 12 healthy controls who participated in two xperimental sessions spaced no more than one week apart. In each ses-ion, participants performed both the baseline and interference conditions. t each session, participants were orally administered either placebo or )-AMP, at a dosage of 0.25 mg/kg of body weight, at the beginning of the ession. The drug on each day was administered in a double-blind manner with an unlabeled opaque capsule), and drug order was randomly coun-erbalanced across participants. Because D-AMP effects peak after one to wo hours, and are stable over the following one to two hours (Angrist, Corwin, Barlett, & Cooper, 1987) participants were tested approximately wo hours postingestion. To analyze the data, we examined a measure of ontext sensitivity that we refer to as d'-context, a signal-to-noise measure omparing hits to "AX" trials and false alarms to "BX" trials. As shown in Figure 6.8, we found that under placebo, the addition of distractors dur-ng the cue-probe period of long-delay trials reduced sensitivity to con-ext, as indexed by a reduced d'-context (e.g., increased "AX" misses and 'BX" false alarms). However, this effect was significantly reduced with d-amphetamine. More specifically, there was a significant main effect of d-amphetamine on d'-context ($F(1,11) = 6.41$, $p < .05$) and a significant drug ×condition interaction ($F(1,11) = 6.31$, $p < .05$). Planned contrasts revealed that under placebo, context sensitivity was reduced in the inter-ference condition ($F(1,11) = 18.39$, $p < .01$), but that there was no signifi-cant difference between the two conditions under D-AMP ($F(1,11) = 0.32$, $p > .10$) (see Figure 6.8). Results of studies such as this provide some more specific evidence for a relationship between dopamine function and context processing, at least in healthy individuals.

On a related note, the finding that dopaminergic agents can influence context processing may help to shed light on the mechanisms that by which stress influences working memory. In another chapter in this book, Sliwin-ski and colleagues review evidence that higher perceived levels of stress are associated with cognitive impairment, particularly impaired working memory, on both a between-person basis (i.e., comparing individuals with high and low levels of perceived stress) and a within-person basis (i.e., com-paring times with high and low perceived stress within the same person). Sliwinski and colleagues put forth the hypothesis that this relationship may reflect that fact that individuals coping with a stressor may use cogni-tive resources to suppress stress-related thoughts, leaving fewer resources available for other cognitive tasks. However, stress is also known to alter dopamine function, at least acutely, and some animal research has shown a



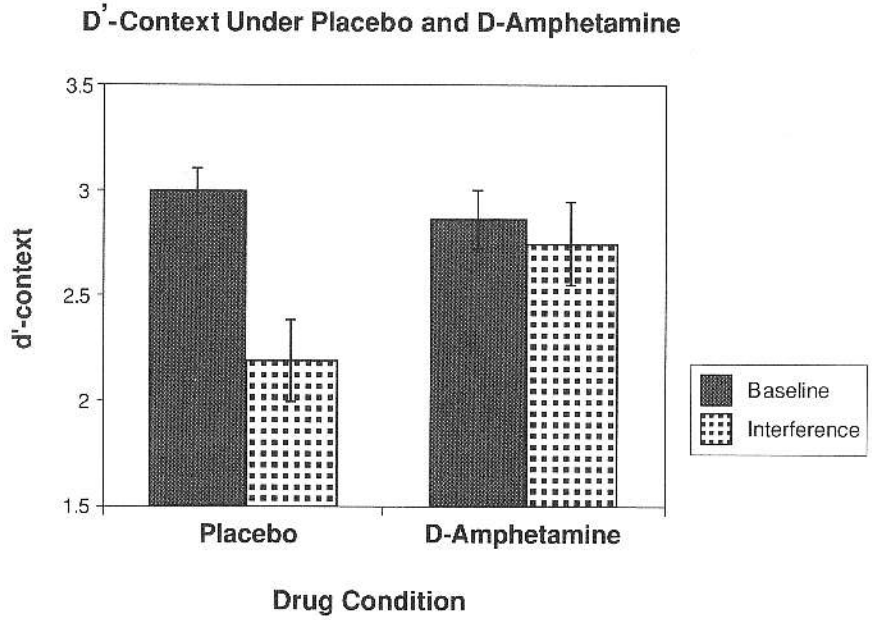


FIGURE 6.8. Graph illustrating change in d'-context as a function of adding interfering distractors, both under placebo and under d-amphetamine.

detrimental impact of stress on working memory via dopaminergic mechanisms in prefrontal cortex (Arnsten & Goldman-Rakic, 1998). As such, it is possible that stress influences working memory, and potentially context processing, via disruption of the dopamine system. This hypothesis is not meant to be an alternative to the one put forth by Sliwinski, but rather may provide a different level of explanation for the same mechanism.

## RELATIONSHIP OF CONTEXT PROCESSING TO CLINICAL SYMPTOMS IN SCHIZOPHRENIA

One important question that arises when discussing context processing deficits in schizophrenia is whether such disturbances are present in all individuals with schizophrenia with equal severity, or whether the severity of such context processing deficits are related to the severity of specific symptoms. We and others found that context processing deficits in schizophrenia appear to be strongly related to the severity of a constellation of behaviors referred to as disorganization symptoms, which include disorganized behavior (dressing in an unusual manner, behaving oddly in public), attentional problems, and difficulties in producing goal directed speech (e.g., loose associations (Barch et al., 1999; Barch & Carter, 1998; Barch

al., 2003; Cohen et al., 1999; MacDonald et al., in submission; Perlstein, rter, Noll, & Cohen, 2001; Perlstein et al., 2003; Stratta et al., 2000). Such dings are interesting in light of research suggesting that representations context information are important for guiding coherent ongoing lan- age production (Levelt, 1989). Further, such associations are consistent th the research reviewed above, suggesting that impairments in lan- age comprehension, homograph interpretation/meaning selection, and mantic priming may be related to impairments in the ability to use or aintain contextual information.

More recently, we also found some evidence that deficits in context pro- ssing may also be related to disturbances in the ability to regulate the fluence of emotion on cognitive processing in schizophrenia. More specif- ally, we found that individuals with impaired context processing show eater language production disruptions (in the form of unclear references) hen discussing affectively negative as compared to affective neutral top- s (Burbridge & Barch, 2002). There is a growing literature in affective neu- science examining the role that different cognitive control functions play emotional regulation and the role that dorsolateral PFC plays in emo- onal regulation (Gray, 2001; Gray, Braver, & Raichle, 2002; Ochsner, Bunge, ross, & Gabrieli, 2002). One hypothesis is that intact representations of ontext are also important for the regulation of emotionbecause such infor- nation provides clues as to what emotional responses are appropriate in iven situations and a means by which to alter emotional responses that are ot compatible with current task demands. As such, it will be interesting in uture research to examine the role that the representation and maintenance f context plays in successful emotional regulation and the potential influ- nce of disordered context processing on disturbed emotional functioning n disorders such as schizophrenia.

## CONTEXT PROCESSING IN OTHER POPULATIONS

ndividuals with schizophrenia are not the only population thought to xperience changes in prefrontal function that may be associated with hanges in dopamine function. For example, individuals with Parkinson's isease are known to have disturbances in dopamine function and distur- ances in tasks designed to measure working memory and other aspects of cognitive control (Zgaljardic, Borod, Foldi, & Mattis, 2003). In addition, ndividuals with attention deficit hyperactivity disorder are thought to suf- er from disturbances in dopamine function and prefrontal function and again show deficits on a range of cognitive control tasks (Casey et al., 1997; Aron, Dowson, Sahakian, & Robbins, 2003; Nigg, 2003). Of interest, healthy older adults represent a nonpathological population that also experiences cognitive control problems that may be related to changes in prefrontal and dopamine function. For example, a growing body of work suggests



that healthy aging involves systematic changes in prefrontal function as measured by functional imaging techniques (Cabeza, 2001; Grady, 1998) and involves changes in cognitive functions thought to be associated with prefrontal function (Balota, Dolan, & Duchek, 2000; Jacoby, Debner, & Hay, 2001), both of which may be associated with changes in dopamine function with aging (Arnsten et al., 1994; Arnsten, Cai, Steere, & Goldman-Rakic, 1995; de Keyser, De Backer, Vauquelin, & Ebinger, 1990; Goldman-Rakic & Brown, 1981; Suhara et al., 1991; Volkow et al., 1998)). Further, in many ways, the types of cognitive deficits shown by healthy older individuals are very similar to those found in individuals with schizophrenia. The chapter by West and Bowry in this volume nicely articulates many of the types of cognitive deficits shown by healthy older adults, which are similar to deficits seen in individuals with schizophrenia, For example, both individuals with schizophrenia and healthy older adults show increased incongruent errors in the Stroop and an increased total Stroop effect in RT (Spieler, Balota, & Faust, 1996; Verhaeghen & De Meersman, 1998; West & Baylis, 1998), and both populations have more difficulties with color naming in a switching Stroop that varies the task to be performed on a trial-by-trial basis, as compared to blocked trials of color naming (Cohen et al., 1999; West, in press). Similar to our interpretations of the source of these deficits in schizophrenia, West attributed such Stroop task deficit in healthy older adults to disturbances in context processing.

We directly studied context processing and related functions in healthy aging (e.g., working memory, inhibition) and also found evidence that healthy older adults show deficits in context processing (Braver et al., 2001), which are strongly correlated with deficits in measures of working memory and inhibition (Keys et al., submitted). For example, in recent work, we found that healthy young-older adults (ages 65 to 75) show deficits in context representation, in the form of increased "BX" RTs as compared to younger adults, but not increased "AY" RTS (Braver, Satpute, Keys, & Racine, in press). Further, healthy much older adults (76+) demonstrated additional deficits in context maintenance, in that their "BX" worsened as a function of delay, while "AY" performance improved.

## RELATIONSHIPS AMONG ANTERIOR CINGULATE, DOPAMINE FUNCTION, AND COGNITIVE CONTROL

In addition, West and others examined additional components of cognitive control in healthy aging, such as error processing as indexed by an ERP component referred to as the error related negativity (ERN). The ERN is thought to index either error monitoring and/or correction (Falkenstein, Hohnsbein, Hoorman, & Blanke, 1991; Falkenstein, Hoorman, Christ, & Hohnsbein, 2000; Gehring, Goss, Coles, Meyer, & Donchin, 1993) or conflict processing (Botvinick et al., 2001), critical components of cognitive

control. A number of researchers believe that one of the main generators of the ERN is the anterior cingulate, and that alterations in the ERN may also reflect changes in dopamine function in the anterior cingulate (Botvinick et al., 2001; Holroyd & Coles, 2002). As reviewed by West, the amplitude of the ERN is reduced in healthy older adults across a wide range of task paradigms (Band & Kok, 2000; Falkenstein, Hoorman, & Hohnbein, 2001; Nieuwenhuis et al., 2002; West, in press), a finding consistent with the research on reduced dopamine function in healthy aging. Similarly, a growing number of studies also suggest reduced ERNs in individuals with schizophrenia, even when there are no behavioral differences in conditions thought to be associated with increased conflict (Alain, McNeely, Yu, Christensen, & West, 2002; Bates, Kiehl, Laurens, & Liddle, 2002; Carter, MacDonald III, Ross, & Stenger, 2001; Kopp & Rist, 1999) and decreased anterior cingulate activity, a potential generator of the ERN (Carter et al., 2001). Again, such results in schizophrenia may reflect abnormalities in dopamine function, which influences anterior cingulate and dorsolateral PFC function. Such results suggest that both individuals with schizophrenia and healthy older adults may experience deficits in error monitoring/conflict processing and deficits in context processing.

Despite the many similarities in the profiles of cognitive disturbances shown by individuals with schizophrenia and healthy older adults, there are also intriguing differences. For example, in studies of context processing in healthy older adults using the AX-CPT task, deficits in at least the young-older adults are apparent primarily in RTs rather than errors. In contrast, individuals with schizophrenia manifest context-processing deficits in both errors and RTs on the AX-CPT. In the Stroop task, research examining process-dissociation estimates of color naming and word reading has found increased word reading estimates in older adults, but no changes in color naming estimates (Spieler et al., 1996). In contrast, in schizophrenia, we have found both increased word reading and decreased color naming estimates (Barch et al., in press). In addition, as noted by West, studies of healthy aging populations have not found increased correct trial related negativities in ERP studies (referred to as the CRN; Band & Kok, 2000; Falkenstein et al., 2001; West, in press), whereas studies of schizophrenia have reported such increased CRNs (Alain et al., 2002; Mathalon et al., 2002). One argument is that increased CRNs reflect additional conflict because of inadequate goal representations or context representations that normally serve to reduce conflict in information processing. These differences in the performance of individuals with schizophrenia and healthy older adults suggest that although these two populations may share some common cognitive and neurobiological disturbances, there are also important differences. For example, one possibility is that the severity of context processing deficits is simply worse in individuals with schizophrenia as compared to healthy adults. Such a hypotheses would be consistent with



the fact that individuals with schizophrenia show problems in both errors and RTs and alterations in both color and word processing estimates (alterations in only word processing estimates among older adults might reflect a less severe disturbance). However, it is somewhat less clear why a less severe context processing deficit would lead to reductions only in the ERN and not the CRN, as compared to the concurrent reductions in the ERN and the CRN found in schizophrenia. Future research more directly comparing the performance of individuals with schizophrenia and healthy older adults in the same exact paradigms may help clarify some of these issues and better delineate the similarities and differences in the profiles of cognitive disturbances found in these two populations.

It is not necessarily surprising that both individuals with schizophrenia and healthy older individuals show similar patterns of cognitive deficits if both populations experience changes in prefrontal function associated with dopamine changes. Although the source of the prefrontal cortex and dopamine changes in schizophrenia and healthy aging may be very different, it may still be the case that a final common pathway of changes in prefrontal function leads to somewhat similar cognitive deficits in schizophrenia and healthy aging. However, at the same time, it also clear that there are many differences between individuals with schizophrenia and healthy older adults, both in the severity of their cognitive deficits and the associated symptoms and phenomenology found in schizophrenia. Such differences may reflect several factors. First, many researchers believe that at least some aspects of the neurobiological pathology found in schizophrenia are neurodevelopmental in origin and are thus present throughout the life span. In contrast, changes in prefrontal function in healthy older adults may begin to occur much later in life, with intact prefrontal function early in life. The eventual outcome of neurodevelopmental changes in prefrontal function may be very different than changes that occur only later in life, because such prefrontal changes could then influence the course of learning, skill acquisition, and cognitive development in individuals with schizophrenia, which may have additional contributions to the profile of cognitive disturbances found in schizophrenia. Second, it is unlikely that changes in prefrontal cortex and dopamine function are the only neurobiological disturbances found in schizophrenia. As such, the interaction of multiple sources of neurobiological and cognitive abnormalities in schizophrenia may contribute to many of the cognitive deficits/symptoms found in schizophrenia that are not present in healthy aging (although healthy aging also may involves changes in brain regions other than prefrontal cortex).

## SUMMARY

In this chapter, we described our theory regarding one component of cognitive control, the representation and maintenance of context, that we argue is

nportant for the ongoing control of thoughts, behaviors, and emotion. We rgued that this particular component of cognitive control is supported by opamine function in dorsolateral prefrontal cortex. As described in more etail above, this theory regarding cognitive control is highly consistent ith the theories put forth by a number of authors of other chapters in is volume, including the ideas put forth by Engle, West, Sliwinski and eir colleagues. Further, we argued that populations that experience disurbances in either or both dopamine function and dorsolateral prefrontal ortex function experience deficits in the processing of context, and we eviewed empirical data supporting this assertion. One important area for uture research will be to better delineate the similarities and difference n the profiles of cognitive and neurobiological disturbances across popilations thought to suffer from disturbances in prefrontal and dopamine unction. By better understanding the relationships between specific types f cognitive control deficits and particular kinds of neurobiological disturbances, we can better validate, modify, and/or expand theories regarding he neurobiology of cognitive control. We have also suggested that the proesses involved in the representation and maintenance of context may play critical role in emotion regulation, though considerably more empirical nd theoretical work is needed to examine this hypothesis.

## Author Note

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