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Cognitive Control, Goal Maintenance, and Prefrontal Function in Healthy Aging

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Cognitive control impairments in healthy older adults may partly reflect disturbances in the ability to actively maintain goal-relevant information, a function that depends on the engagement of lateral prefrontal cortex (PFC). In 2 functional magnetic resonance imaging studies, healthy young and older adults performed versions of a task in which contextual cues provide goal-relevant information used to bias processing of subsequent ambiguous probes. In Study 1, a blocked design and manipulation of the cue–probe delay interval revealed a generalized pattern of enhanced task-related brain activity in older adults but combined with a specific delay-related reduction of activity in lateral PFC regions. In Study 2, a combined blocked/event-related design revealed enhanced sustained (i.e., across-trial) activity but a reduction in transient trial-related activation in lateral PFC among older adults. Further analyses of within-trial activity dynamics indicated that, within these and other lateral PFC regions, older adults showed reduced activation during the cue and delay period but increased activation at the time of the probe, particularly on high-interference trials. These results are consistent with the hypothesis that age-related impairments in goal maintenance abilities cause a compensatory shift in older adults from a proactive (seen in young adults) to a reactive cognitive control strategy.

Keywords: compensation, event-related, executive function, inhibition, working memory

Introduction

A growing body of research suggests that older adults show impaired performance in tasks that require a high degree of cognitive control, such as when information must be maintained within working memory (e.g., Craik et al. 1990; Salthouse 1990; Daigneault and Braun 1993), when attention must be endogenously focused particularly in the face of distraction or interference (e.g., Duchek et al. 1998), or when inappropriate response tendencies must be inhibited (e.g., Spieler et al. 1996; Zacks et al. 1996; West and Bell 1997; May et al. 1999). Theorists have put forth a range of ideas as to the mechanisms that lead to such age-related declines in cognitive controls tasks. These include generalized slowing (Cerella 1985; Myerson et al. 1990; Salthouse 1996), reduced processing resources (Craik and Byrd 1982), reduced working memory capacity (Salthouse 1990; Park 2000), inhibitory deficits (Hasher and Zacks 1988), and disturbed attentional control (Balota et al. 2000). In our own work, we have put forth the hypothesis that one of the mechanisms underlying age-related cognitive changes is a deficit in the ability to actively represent and maintain task goals. This goal maintenance deficit (which we have also previously referred to as a context processing impairment) has been found to account for a wide range of findings related to older adult behavioral performance (Braver et al. 2001; Braver and Barch 2002; Braver et al. 2005; Rush et al. 2006; Braver and West, forthcoming). The current study directly tested predictions from this goal maintenance account that relate to age-related changes in brain activation. Specifically, we examined whether deficits in task-goal maintenance among older adults are associated with disturbances in the functional activation of the prefrontal cortex (PFC).

We have argued that goal maintenance is a critical component of cognitive control that is required for successful performance in a wide variety of cognitive situations (Cohen et al. 1996; Braver and Cohen 2000; Braver et al. 2002). Goal representations contain information regarding the actions needed to bring about specific outcomes, which can help guide planning and behavior. However, these representations may also exert influence over perceptual or attentional processes. For example, in the Stroop task, task goals must be actively represented and maintained in a form that can bias attention allocation and response selection toward the ink color rather than the word. Goal representations are particularly important in situations with a strong competition for response selection. These situations arise when the appropriate response is one that is relatively infrequent (e.g., withholding a response to an infrequent "no-go" stimulus) or when the inappropriate response is dominant and must be inhibited (e.g., the word in a Stroop task). We argue that goal representations are maintained in an active online state and are continually available to influence processing. Consequently, goal representations can be thought of as the subset of representations within working memory that govern how other representations are used. Thus, goal representations can subserve both storage and control functions. This aspect of the theory differentiates it from classic accounts of working memory (e.g., Baddeley 1992), which postulate a stricter separation of representations for storage versus control.

Although there are a number of behavioral paradigms that can tap goal maintenance, we have frequently used a version of the classic continuous performance test (Rosvold et al. 1956) that operationalizes representation, maintenance, and updating of task goals in terms of the effects of contextual cues on task performance (Barch 1993; Servan-Schreiber et al. 1996; Braver and Cohen 1999; Cohen et al. 1999; Braver and Cohen 2000; Barch et al. 2001; Braver et al. 2001; Barch et al. 2003; Braver et al. 2005). In this AX version of the continuous performance task (AX-CPT), 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. Nontarget responses are required on all other trials. Because target (AX) trials occur with high

frequency (70%), 2 types of biases are present that assess the utilization of contextual cues to update task goals in different ways. First, goal-related utilization of contextual cues is critical for inhibiting a target response bias that occurs when an X-probe follows a non–A-cue ("BX" trials). Second, goal-related utilization of contextual cues produces an expectancy bias that primes and facilitates target responses following an A-cue. However, this expectancy bias can also impair performance when the A-cue is followed by a non–X-probe ("AY" trials). These biases can be measured behaviorally by contrasting performance in AY and BX trial types against a third type of nontarget trial, BY, which serves as a control condition because neither type of bias is present. Thus, intact representation and utilization of task goals should lead to impaired AY performance but enhanced BX performance. Conversely, individuals with impaired goal maintenance should show poorer performance on BX compared with AY trials. Importantly, these predictions distinguish a deficit in goal representation from a deficit in inhibitory control. Specifically, a deficit in inhibitory control would predict poor performance in both AY and BX trials because both trial types require the ability to overcome a strong tendency to execute a primed, but incorrect response (i.e., primed by the cue in AY trials and by the probe in BX trials). In contrast, a goal maintenance deficit should lead to reduced cue priming and thus not impair performance on AY trials.

The AX-CPT also provides a way to investigate active maintenance of task goals by manipulating the delay between the cue and probe. When the cue–probe delay is lengthened (e.g., 5–10 s as compared with 1 s), the ability to maintain access to goal-related information is challenged. A prediction of the goal maintenance theory is that the effect of delay will interact with performance on AY and BX trials. When task-goal information is actively maintained, then the strength of goal representations should stay the same or increase with delay (i.e., BX performance should stay the same or improve at longer delays, whereas AY performance should stay the same or worsen). In contrast, if goal maintenance is impaired, then BX performance should worsen with delay, but AY performance should actually improve.

In previous behavioral studies, we have observed a pattern of performance in older adults that was indicative of a selective deficit in goal representation and maintenance. Healthy older adults performed more poorly than young adults in both accuracy and reaction times on BX trials, which is the nontarget trial type in which goal representations are needed to prevent errors (Braver et al. 2001; Braver et al. 2005; Paxton et al. 2006). At the same time, older adults performed better on AY trials, which is the nontarget trial type in which intact goal representations lead to worse performance. Moreover, in the oldest adults, these effects were amplified at long cue–probe delays, suggesting a further impairment in goal maintenance (Braver et al. 2005). The AY trial effects are particularly interesting as they provide a unique example of a task situation in which older adults actually performed both more accurately and as quickly as young adults, though this "better" performance was theoretically predicted by the presence of a deficit in goal maintenance.

Our theory suggests that goal representations are housed within the lateral portion of the PFC and actively maintained there when task demands require such maintenance (Braver et al. 1999; Braver and Cohen 1999; O'Reilly et al. 1999; Braver and Cohen 2000). Further, we have postulated that deficits in goal maintenance arise from a disturbance in the function of the dopamine (DA) system in the PFC. Such a hypothesis is consistent with a growing literature on the neurobiology of healthy aging suggesting that the PFC and DA systems are among the most strongly affected by increasing age (Arnsten et al. 1995; Raz et al. 1997; Peters et al. 1998; Volkow et al. 1998; Cabeza 2001). The DA projections to lateral PFC are postulated to regulate the access to goal representations by insulating this information from the interfering effects of noise while allowing for the appropriate updating of task goals when needed (Braver and Cohen 2000). These assertions are consistent with the neuroscience literature in which active maintenance in the service of control is a commonly ascribed function of the PFC (Goldman-Rakic 1987; Fuster 1989; Miller and Cohen 2001), and the DA system is believed to modulate the active maintenance properties of the PFC (Sawaguchi et al. 1990; Williams and Goldman-Rakic 1995; Luciana et al. 1998). In a number of prior functional neuroimaging studies with the AX-CPT, we and others have shown that the lateral PFC is selectively active in response to the need for maintaining task goals across time (Barch et al. 1997; MacDonald et al. 2000; Barch et al. 2001; Braver and Cohen 2001; Braver and Bongiolatti 2002; MacDonald and Carter 2003). Additionally, pharmacological challenge studies have demonstrated that augmenting DA function can improve goal maintenance (Barch and Braver 2005).

The neuroimaging literature on lateral PFC function has recently been enhanced by a growing number of studies indicating that older adults tend to show patterns of either underrecruitment or enhanced recruitment of PFC regions. Underrecruitment refers to the finding that older adults show reduced activity in frontal regions, including lateral PFC, which is thought to be important for the performance of specific cognitive tasks (Grady et al. 1995; Cabeza et al. 1997; Rypma and D'Esposito 2000; Logan et al. 2002; Milham et al. 2002; Johnson et al. 2004; Persson et al. 2004). At the same time, other studies suggest enhanced activity in a number of prefrontal regions along with posterior cortical and subcortical areas during performance on a range of cognitive tasks (Grady et al. 1998; Haut et al. 2000; Rypma and D'Esposito 2000; Cabeza et al. 2002; Logan et al. 2002; Rosen et al. 2002; Langenecker and Nielson 2003; Cabeza et al. 2004; Langenecker et al. 2004; Persson et al. 2004; Colcombe et al. 2005; Townsend et al. 2006). In some cases, older adults showed enhanced activity in the same regions activated by young adults, but in other cases, the enhanced activity occurred in regions not recruited by young adults. Enhanced activity in lateral PFC regions has been interpreted as being either compensatory in that it is thought to be a response to reduced efficiency/integrity of activation (Cabeza et al. 1997; Grady 2000; Cabeza et al. 2002; Rosen et al. 2002; Cabeza et al. 2004; Park et al. 2004; Buckner 2005; Mattay et al. 2006) or an indication of nonselective recruitment of task regions that may not be particularly helpful for task performance (Li and Lindenberger 1999; Li et al. 2001; Logan et al. 2002; Tisserand and Jolles 2003).

These prior findings of abnormal lateral PFC activity in older adults are consistent with the hypothesis that goal maintenance deficits in older adults are due in part to altered function in this brain region. The goal of the current studies was to examine the hypothesis that healthy older adults would show a specific

impairment in the ability to activate lateral PFC regions in response to the need to represent and maintain task-goal information. In particular, our hypothesis suggests a possible explanation for the mixed findings in neuroimaging studies with older adults regarding overrecruitment versus underrecruitment in PFC regions. We suggest that older adults will show a general overrecruitment pattern in task-related activity in both PFC and other brain regions as an attempt to compensate for underrecruitment in the more focal PFC regions that are required to meet specific demands on goal maintenance and cognitive control tasks. Thus, a comparison of task conditions that isolates these specific demands on goal maintenance and cognitive control will reveal underrecruitment within focal regions of lateral PFC, whereas overrecruitment will be found more broadly in PFC and other cortical regions in task condition comparisons that isolate more general task-related processing demands.

Study 1 tested these hypotheses in a sample of healthy young and older adults performing a variant of the AX-CPT with standard blocked design functional magnetic resonance imaging (fMRI) methods. We predicted that an examination of general task-related activation (i.e., task vs. fixation) would reveal an enhanced pattern of overall PFC as well as posterior cortical and subcortical activation in older adults. In contrast, the goal maintenance account predicts that contrasting conditions with high versus low goal maintenance demands (long vs. short delay conditions) would reveal reduced activation within lateral PFC among older adults.

Study 1

Older and young adults performed 2 AX-CPT versions that varied only in the delay over which goal-related information provided by contextual cues had to be maintained (short vs. long delay). A blocked design procedure was used to identify brain regions showing age differences in either 1) general task-related activity (i.e., main effects of age independent of delay) or 2) activation specifically related to goal maintenance (i.e., age × delay interactions). In our previous work, the delay manipulation has been highly successful at isolating lateral PFC activity in healthy young adults (Barch et al. 1997; Barch et al. 2001; Braver and Cohen 2001; Braver and Bongiolatti 2002).

Method

Participants

Participants were 21 healthy young adults (M = 22.8, standard deviation [SD] = 3.7, range = 18–31) and 20 healthy older adults (M = 73, SD = 5.7, range = 66–83) recruited from participant pools maintained by the Department of Psychology at Washington University in St Louis. All participants provided written informed consent as outlined by the Washington University Human Studies Committee. All participants were right handed. The groups did not differ significantly in gender breakdown, $\chi^2 = 2.1$, degrees of freedom (df) = 1, $N = 41$, $P = 0.21$ (young adults: 10 females and 11 males; older adults: 14 females and 6 males). Participants were screened for any signs of medical disorders (including treated or untreated hypertension, diabetes, and thyroid problems), neurological disorders (including past head injuries involving loss of consciousness for 5 or more minutes or a documented concussion), psychiatric disorders, medication histories that could influence cognitive performance, or any other contraindication for magnetic resonance scanning. Older adults were administered the Blessed Orientation-Memory-Concentration Test (Katzman et al. 1983) over the telephone. Individuals obtaining 5 or more errors were not included. Participants were paid $25 per hour remuneration for their participation.

Behavioral Tasks

Participants performed a variant of our AX-CPT that retained the basic format of the original task but used words instead of letters (Word AX-CPT). The target was the word"LIME" when it occurred following the word"FATE." Thus, the Word AX-CPT is directly analogous to the original AX-CPT in that it requires subjects to actively maintain goal-related information arising from contextual cues but with the context cue being a specific word rather than a letter. The words were presented one at a time in cue–probe pairs. Target and nontarget trials appeared intermixed in a pseudorandom sequence. Target trials (FATE–LIME) occurred with 70% frequency, and nontarget trials occurred with 30% frequency. The frequency of nontarget trials was evenly distributed as follows: 10%"BX" trials (i.e., a word other than FATE followed by the word LIME) in which an invalid cue preceded the target; 10%"AY" trials (i.e., the word FATE followed by a word other than LIME) in which a valid probe was followed by a nontarget probe; and 10%"BY" trials (i.e., a word other than FATE followed by a word other than LIME) in which an invalid cue was followed by a nontarget probe. The frequencies of the various trial types replicates those used in most previous studies with our AX-CPT paradigm (Barch et al. 1997; Cohen et al. 1999; Barch et al. 2001; Braver et al. 2001; Braver and Cohen 2001; Barch et al. 2003; Braver et al. 2005). The young adults also performed 2 other variants of the AX-CPT in separate blocks, the results of which were the focus of another publication (Braver and Bongiolatti 2002).

We manipulated the delay over which participants had to engage in goal maintenance arising from presentation of a contextual cue. The short delay was 1 s in duration. In 12 of the young adults, the long delay was 5 s, and in the remaining 9 young adults and all the older adults, the delay was 7.5 s. None of the results presented below differed when only the young adults and older adults with the same trial duration were compared. Total trial duration was equated by counterbalancing the intertrial interval (ITI) with the cue–probe delay (e.g., the delay was 1 s and ITI was 5 or 7.5 s for the short delay version). Trials were presented to participants in a blocked manner, such that all trials in one imaging run were of the same delay type. Participants performed 2 runs of short delay trials and 2 runs of long delay trials, with order counterbalanced across participants. A total of 80 trials were performed (40 with a short cue–probe delay and 40 with a long cue–probe delay), of which 56 were AX trials and 8 each were AY, BX, and BY trials.

The words for the task were presented centrally on a visual display in 36-point Helvetica font. In addition to LIME and FATE, the remaining words were a set of repeated abstract and concrete nouns that were 3–7 letters in length and 1–2 syllables (the properties of the nontarget word stimuli satisfied constraints imposed by the other conditions examined in Braver and Bongiolatti 2002). Each word was presented for 750 ms. Participants responded to stimuli by pressing one button with their index finger for targets and another button with their middle finger for nontargets (and cues, to ensure

encoding) using a hand-held button box with a fiber optic interface to PsyScope. Visual stimuli were presented using PsyScope software (Cohen et al. 1993) running on an Apple PowerMac G4. Stimuli were projected to subjects with an AmPro LCD projector (model 150) onto a screen positioned at the head end of the bore. Participants viewed the screen through a mirror attached to the head coil.

Functional Imaging

Images were acquired on a Siemens 1.5-Tesla Vision System (Erlangen, Germany) with a standard circularly polarized head coil. A pillow and tape were used to minimize head movement. Headphones served to dampen scanner noise and provided a means of communication with the participants. Both structural and functional images were acquired at each scan. High-resolution (1.25 ×1 ×1 mm) structural images were acquired using a sagittal MP-RAGE 3D T_1-weighted sequence (time repetition [TR] = 9.7 ms, time echo [TE] = 4 ms, flip = 12, time to inversion = 300 ms) (Mugler and Brookeman 1990). Functional images were acquired using an asymmetric spin-echo echo-planar sequence (TR = 2500 ms, TE = 50 ms, flip = 90°). Each image consisted of 16 contiguous, 8-mm thick axial slices acquired parallel to the anterior–posterior commissure plane (3.75 × 3.75 mm in-plane), allowing complete brain coverage at a high signal-to-noise ratio (Conturo et al. 1996). Each of the 4 scanning runs consisted of alternating cycles of task (2 per run) and fixation (2 per run) blocks. Task blocks were 10 trials in duration. Fixation blocks (denoted by a centrally presented crosshair) were either 25 or 37.5 s in duration. The first 4 images in each scanning run were used to allow the scanner to reach a steady state and were discarded.

Data Analysis

Behavioral data were analyzed using error rates (misses and false alarms) and median correct RTs as dependent measures. A *z*-score transformation was applied to the RTs across all correct trials for each participant to correct for individual differences (including general slowing with age) in RT (Faust et al. 1999) and to increase power (Bush et al. 1993). Specifically, for each participant, a global mean RT and SD were computed using all trials for that participant. Then the RT for each trial was standardized by subtracting this global mean RT and dividing by the SD. This procedure equated all participants with respect to global reaction time (RT) and RT variance (i.e., global RT = 0, SD = 1 for each participant). The median *z*-transformed RTs for each experimental cell thus represent SDs from the participants' global RT. Performance was analyzed with analyses of variance (ANOVAs) conducted separately for target (AX) and nontarget (AY, BX, BY) trial types in an effort to avoid comparing target trials that were presented 70% of the time with nontarget trials that were presented 10% each. Nontarget trial ANOVAs were applied with age (young vs. older) as a between-subject factor and both trial type (AY, BX, BY) and delay (short vs. long) as within-subject factors. Target trial ANOVAs were applied with age (young vs. older) as a between-subject factor and delay (short vs. long) as a within-subject factor. A signal detection measure estimated sensitivity to the contextual impact of the cue given an X-probe (i.e., contrasting AX hits vs. BX false alarms). This measure is referred to as d'-context and has been used in previous AX-CPT studies to provide a more specific index of sensitivity to the goal-related implications of contextual cues (Servan-Schreiber et al. 1996; Cohen et al. 1999). Because of technical difficulties, behavioral data from one subject was unusable. Additionally, *z*-transformed RT data were excluded for 2 older adult participants because they did not produce any correct response on BX trials and RT analyses were computed using only correct trials.

Functional imaging data were preprocessed prior to statistical analysis. All functional images were first corrected for movement using a rigid-body rotation and translation correction (Friston et al. 1996; Snyder 1996) and registered to the participant's anatomical images (to correct for movement between the anatomical and function scans). The data were then scaled to achieve a whole-brain mode value (used in place of the mean because of its reduced sensitivity to variation in brain margin definition) of 1000 for each scanning run to reduce the effect of scanner drift or instability and spatially smoothed with a 9-mm full-width half-maximal Gaussian kernel. Participants' structural images were transformed into standard atlas space (Talairach and Tournoux 1988) using a 12-dimensional affine transformation (Woods et al. 1992; Woods et al. 1998). The functional images were then registered to the reference brain using the alignment parameters derived for the structural scans. General linear models (GLMs) for each participant were constructed to estimate task-related activation in each voxel using a boxcar function convolved with a canonical hemodynamic response, with separate estimates for short- and long-delay conditions. Parameter estimates from each participant's GLM were submitted to second-level tests treating participant as a random factor in *t*-tests and ANOVA.

We identified regions that showed either 1) age differences in general task-related activation, which was defined as greater activity in task compared with the fixation baseline irrespective of delay condition, or 2) age differences in delay-related activity, which was defined as regions that showed greater task-related activity in the long-delay as compared with the short-delay condition. Additionally, in the Supplementary Material, we report regions showing similar task-related and delay-related activity in both age groups. To identify regions showing these effects, an approach was applied involving multiple statistical tests applied in a voxel-wise manner. In order to be identified as significant, we required that multiple contrasts were satisfied. Each contrast was set at a relatively low threshold in order to optimize the trade-off between false-positive protection (Type 1 error) and sensitivity/power (Type 2 error). Thus, for a brain region to be accepted as selective for a particular effect, all voxels within the region were required to be statistically significant in all tests for that effect, which are described in detail below. The analysis was set up such that any voxel meeting criteria in all statistical tests would have alpha protection equivalent to $P < 0.0001$, although this value is likely to be an overestimate given nonindependence in the error terms in the statistical contrasts. Moreover, a region was considered significant only if it contained a cluster of 8 or more contiguous voxels. The additional cluster-size requirement ensured an overall image-wise false-positive rate of $P < 0.05$ (Forman et al. 1995; McAvoy et al. 2001). Finally, to increase interpretability, only positive activations (relative to baseline) were considered in all analyses.

The first analysis identified regions in which older adults showed greater"task-related activity" than young adults using the following tests: 1) greater activation in the task compared with the fixation baseline in older adults, 2) greater task-related activation for older compared with young adults, 3) no effect of

delay in older adults, and 4) no age by delay interaction. An analogous analysis was performed to also identify regions showing the reverse pattern (older < young). The second analysis identified regions in which older adults showed reduced delay-related activity than young adults using the following tests: 1) greater activity in the task compared with the fixation baseline for the long-delay condition in young adults, 2) greater activation in the long-delay compared with the short-delay condition in young adults, and 3) an age by delay interaction. Again an analogous analysis was performed to also identify regions showing the reverse pattern (older > young).

Results

Behavioral Data

The accuracy and RT data for task performance in the scanner is shown in Table 1. The ANOVA for nontarget accuracy indicated a significant age by trial type interaction, $F_{2,52} = 7.04$, $P < 0.01$, partial $\eta^2 = 0.16$, and a trend level age by trial type by delay interaction, $F_{2,64} = 2.46$, $P = 0.10$, partial $\eta^2 = 0.06$. Planned contrasts to follow up on the age by trial type interaction indicated that, as predicted, older adults made more errors than young adults on BX trials (older: M = 0.17; young: M = 0.03; $F_{1,38} = 5.8$, $P < 0.05$) but were less error prone on AY trials (though not statistically different; older: M = 0.05; young: M = 0.07; $F_{1,38} = 0.3$, $P > 0.5$). The trend level age by trial type by delay interaction reflected the fact that the delay-related increase in BX errors was larger for older adults (short: M = 0.11; long: M = 0.24) than young adults (short: M = 0.01; long: M = 0.06). The target accuracy ANOVA indicated a significant main effect of age group ($F_{1,38} = 5.23$, $P < 0.05$, partial $\eta^2 = 0.12$) and a trend level age group by delay interaction ($F_{1,38} = 3.68$, $P = 0.06$, partial $\eta^2 = 0.09$). Older adults (M = 0.08) made more AX errors than young adults (M = 0.02), and this effect was particularly prominent at the long delay (old: M = 0.12; young: M = 0.04). A similar pattern was observed in the RT data, which were first *z*-score transformed to control for general age-related slowing. The nontarget ANOVA indicated an age by trial type interaction ($F_{1.63,58.66} = 9.24$, $P < 0.01$, partial $\eta^2 = 0.20$). Relative to group mean-corrected reaction times, older adults had longer RTs on BX trials than young adults (older: M = 0.81, young: M = 0.01; $F_{1,38} = 10.30$, $P < 0.01$) but shorter RTs on AY trials (older: M = 0.74; young: M = 1.15; $F_{1,38} = 8.44$, $P < 0.01$). Age differences were not found for BY or AX target trials and did not further interact with delay.

The analysis of d′-context indicated a significant main effect of age, $F_{1,38} = 5.4$, $P < 0.05$, and an age by delay interaction, $F_{1,38} = 4.2$, $P < 0.05$. As can be seen in Table 1, older adults had a lower d′-context than young adults. The age by delay interaction reflected the fact that age-related differences in d′-context were greater at the long delay (effect size = 0.72) than at the shorter delay (effect size = 0.59). Also, the reduction in d′-context as a function of delay was greater for older (effect size = 1.08) than young (effect size = 0.55) adults. The pattern of performance observed for accuracy, RT, and d′-context replicates previous studies investigating age differences on the AX-CPT (Braver et al. 2001; Braver et al. 2005).

Imaging Data

General task-related activation. We began by examining regions showing significant differences between older and young adults in task-related activation. Of the total brain volume showing age differences in task-related activity (61 938 mm^3 total), a much greater proportion (82%) showed the older > young pattern. The brain-wide distribution of general task-related activity is shown graphically in Figure 1*A*; a full list of coordinates in text form is reported in the Supplementary Material. Older adults showed increased task-related activity in a number of frontal regions, such as right superior frontal gyrus, bilateral middle frontal gyrus, and right inferior frontal gyrus. In contrast, the frontal brain regions showing increased task-related activity in young adults were fewer and smaller in size.

Delay-related activation. Next, we examined regions showing significant age differences in delay-related activation with a focus on frontal activation (see Table 2). Whole-brain activations are reported in the Supplementary Material. As predicted, young adults showed significantly greater delay-related activation in a right dorsolateral region of PFC as well as in the inferior frontal junction (IFJ). As required by the analysis procedure, this dorsolateral PFC region showed a significant age × delay interaction ($F_{1,80} = 11.57$, $P < 0.01$, partial $\eta^2 = 0.13$), with older adults showing a trend toward decreased activity in the long-delay relative to the short-delay condition (see Fig. 1*B*). Interestingly, however, an analogous analysis identifying regions showing greater delay-related activation in older adults also revealed activation in a number of different frontal regions including the right superior frontal gyrus, right dorsolateral PFC, left medial frontal gyrus, left anterior cingulate gyrus, and bilateral motor cortex, but with dorsolateral regions conspicuously absent (Table 2). Thus, when considering the total brain volume showing age differences in delay-related activity (20 034 mm^3 total), a greater proportion (67%) still showed the older > young pattern.

Table 1
Errors and reaction times for young and older adults in Study 1 and Study 2

Trial type	Short delay		Long delay	
	Young	Older	Young	Older
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Study 1				
Errors				
AX	0.01 (0.01)	0.04 (0.08)	0.03 (0.07)	0.12 (0.16)
AY	0.06 (0.12)	0.05 (0.09)	0.07 (0.13)	0.05 (0.11)
BX	0.01 (0.04)	0.11 (0.21)	0.06 (0.13)	0.24 (0.31)
BY	0.01 (0.04)	0.02 (0.07)	0.05 (0.11)	0.03 (0.08)
Reaction times				
AX	465 (97)	541 (97)	508 (91)	633 (121)
AY	661 (117)	744 (107)	695 (138)	796 (116)
BX	525 (183)	770 (201)	540 (174)	782 (254)
BY	499 (156)	589 (132)	513 (130)	650 (110)
d′-Context	3.2 (0.2)	2.8 (0.9)	2.9 (0.6)	2.1 (1.3)
Study 2				
Errors				
AX			0.02 (0.03)	0.00 (0.01)
AY			0.02 (0.04)	0.04 (0.07)
BX			0.06 (0.08)	0.07 (0.25)
BY			0.01 (0.04)	0.01 (0.04)
Reaction times				
AX			552 (112)	592 (94)
AY			696 (169)	775 (117)
BX			530 (182)	605 (159)
BY			547 (128)	610 (115)
d′-context			3.54 (.42)	3.52 (1.15)

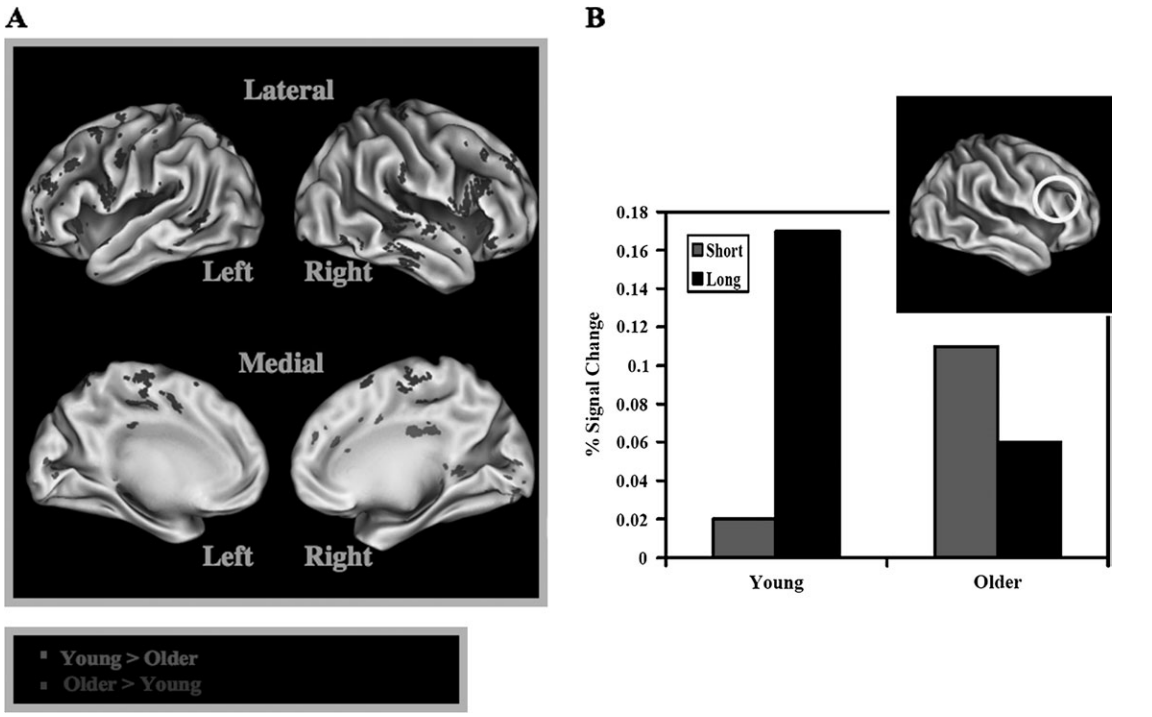

Figure 1. (*A*) Brain regions demonstrating age differences in general task-related activation (collapsing across delay condition) in Study 1. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain. Regions in red reflect greater blood oxygen level–dependent (BOLD) response in young compared with older adults, and regions in blue reflect greater BOLD response in older as compared with young adults. (*B*) Right DL-PFC ($x = 36$, $y = 24$, $z = 23$) region showing decreased activity at long delay for older adults.

Table 2
Frontal regions showing ages differences in delay-related activation in Study 1

Regions of interest	Brodmann area(s)	X^a	Y^a	Z^a	Volume (mm^3)[b]
Older < young					
Right middle frontal gyrus	46	36	24	23	621
Left inferior frontal junction	6	−38	−4	29	486
Older > young					
Left orbital frontal gyrus	47	−18	22	−22	216
Left medial frontal lobe	11	−11	36	−17	216
Right superior frontal gyrus	6	23	−5	66	351
	6	9	8	62	216
Right middle frontal gyrus	10	26	44	4	378
	6	42	11	49	378
Left medial frontal gyrus	6	−14	−2	59	945
Left anterior cingulate gyrus	32	−9	17	38	648
Right precentral gyrus	4	49	−2	48	756
	4	41	−11	57	432
	4	32	−23	55	2133
	6	57	−2	6	486
Left precentral gyrus	4	−41	−24	61	648
	4	−32	−27	55	1134

[a]*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.
[b]Volume refers to the number of voxels (converted to mm^3) that reached statistical significance in each region of interest.

Study 1 Discussion

The results of this study add to the growing literature on the role of brain activation changes in older adults and their relationship to age-related cognitive decline. Critically, the results provide new information on the contribution of goal maintenance deficits in cognitive aging. In terms of behavioral performance, the results were consistent with previous findings in demonstrating a clear pattern of age-related performance changes associated with a disturbance in goal maintenance (Braver et al. 2001; Braver et al. 2005). Older adults showed increased errors and RTs on BX trials, which is the trial type for which goal representations are most critically needed for intact performance. In contrast, older adults showed fewer errors and faster RTs (after correcting for general slowing) than young adults on AY trials, the trial type for which intact and active goal representation impairs performance. Further, the age differences for RT were much greater for BX than AY trials, and only the young adults showed slower AY than BX RTs. We found some evidence that older adults showed greater goal maintenance deficits at the long delay as compared with the short delay, primarily in the d′-context data. Our prior results suggest that delay-related aging effects are most pronounced in the older adults with the most advanced ages (>75 years old; Braver et al. 2005). In the current study, the majority of the participants (14/20) were in the young old age range (i.e., 65–75). Thus, the observed delay effects in the current study may actually be an underestimate of what would be seen in an even older sample. Unfortunately, the current data set was not large enough to subdivide and compare the older adults according to age. Still, such analyses will be important in future studies.

The present fMRI results are also highly consistent with the previous neuroimaging literature on cognitive aging, in showing both an overrecruitment and underrecruitment in older adults during task performance (Grady et al. 1998; Haut et al. 2000; Rypma and D'Esposito 2000; Cabeza et al. 2002;

Logan et al. 2002; Rosen et al. 2002; Langenecker and Nielson 2003; Cabeza et al. 2004; Langenecker et al. 2004; Persson et al. 2004; Colcombe et al. 2005; Townsend et al. 2006). Specifically, a number of brain regions, including those in lateral PFC showed greater overall task-related activity in older compared with young adults. This pattern of enhanced task-related activity in older adults was clearly a reliable one, in which the reverse contrast identified very few regions showing the pattern of greater task-related activity in young adults. In contrast, older adults showed reduced delay-related activation compared with young adults in the lateral PFC, including a region of right dorsolateral PFC. As noted earlier, greater activation of lateral PFC in the long-delay as compared with the short-delay conditions among young adults has been a consistent finding in prior AX-CPT studies (Barch et al. 1997; MacDonald et al. 2000; Barch et al. 2001; Braver and Cohen 2001; Braver and Bongiolatti 2002; MacDonald and Carter 2003). In several studies, this lateral PFC activity was on the left rather than the right, though studies have found bilateral PFC activation that included the right dorsolateral region identified in the current study (Braver and Cohen 2001).

A surprising aspect of the results was that we identified a number of additional frontal regions that showed the reversed pattern of enhanced delay-related activity in older adults. Some of these regions such as the right anterior PFC and anterior cingulate cortex tend to be engaged during the performance of cognitive control tasks. Nonetheless, the remaining prefrontal regions showing enhanced delay-related activation among older adults were not ones as commonly associated with the execution of cognitive control tasks and were more medial and/or orbital than those found in the young adults. Still, the delay-related results were not as selective as we had anticipated. In summary, Study 1 showed enhanced general task-related activity in older adults in various regions including PFC regions consistent with the results of a number of previous studies. In response to a specific demand to maintain context over a delay, however, we found evidence for decreased delay-related activity in dorsolateral PFC among older adults coupled with enhanced delay-related activity in more inferior, medial, and orbital PFC regions.

Unresolved Issues

Although the current results point to disturbances in the ability to appropriately utilize lateral PFC regions as a potential contributing factor in the goal maintenance deficits shown by older adults, a number of questions remain unanswered. First, although the current results are consistent with the previous findings from neuroimaging studies in cognitive aging demonstrating enhanced general task-related activity (including lateral PFC), it is still unclear why such a pattern emerges. This enhanced activation in older adults could be due to a general increase in activation across the task (e.g., global task demands) or an increase in activation related to specific events or processes occurring within the task. For example, recent work on the dynamics of the PFC during cognitive control tasks has highlighted the fact that such activity can either be sustained across trials within a task block (i.e., tonic) or transient (i.e., event-related). It has been suggested that this sustained activity may reflect the operation of general control processes during task performance or the maintenance of general task demands or instructions (Donaldson 2004; Dosenbach et al. 2006). In contrast, the transient or item-related activity may reflect specific processes operating in response to different trial types (i.e., AX, AY, BX, BY) and/or events within trial types (i.e., cue, delay, probe). Determining whether the enhanced task-related activity shown by older adults is sustained across trials or specifically trial-related (or both) may help identify the causes of such changes in brain function in older adults. If the increased task-related activity in older adults is due to greater sustained activation, then it may be that older adults are recruiting additional regions in order to maintain the general task goal or that they use brain resources in an inefficient and nonspecific manner. Conversely, if older adults show greater transient activation, then the increased task-related activation may reflect older adults' need to recruit additional PFC regions in order to process the event (cue and probe) information at the time that it occurs.

Second, although older adults show behavioral patterns consistent with a deficit in goal maintenance, they still are able to perform correctly on the majority of trials. A question thus arises as to why older adults show generally intact performance if they have difficulties representing goal-related information. One hypothesis is that they are using a different type of control process than young adults to perform demanding cognitive tasks. Recently, we have hypothesized that in tasks such as the AX-CPT, young adults encode the goal-related implications of the cue as soon as it is presented (e.g., prepare for an X and target response when they see an A or prepare for nontarget response when they see a B-cue) and actively maintain this information across a delay in lateral PFC (Braver et al. 2005). This approach has been referred to as a proactive form of cognitive control (Braver et al. 2007) and involves actively maintaining goal representations that allow young adults to respond rapidly and accurately on AX and BX trials, but also impairs performance on AY trials.

In contrast, older adults may not process the goal-related implications of cues when they are presented and/or may not actively maintain this information in the lateral PFC. Instead, older adults may use what is referred to as a reactive strategy, which involves transiently retrieving the cue information, processing its implications for responding, and then using this information to respond to the probe when it appears (Braver et al. 2007). Thus, older adults may need to reactivate task-goal information provided by the contextual cue following the onset of the probe and use this information to make correct responses on some trials. If so, then older adults may make errors when this information is not available quickly enough to inhibit a prepotent bias to make a target response when an X-probe appears after a non–A-cue. Moreover, they may be slow even when correct on BX trials because of the need to reactivate context information following the onset of the probe. Conversely, older adults may be less likely to make AY errors or be slowed on AY trials because they are not proactively representing this task-goal information.

The reactive versus proactive control hypothesis is one that leads to a specific set of predictions regarding age-related changes in brain activation that could be tested with an event-related design. Prior research suggests that the proactive use of the goal-related information provided by the contextual cue is associated with cue-related brain activity that is sustained across the trial (Braver and Cohen 2001; Carter et al. 2001; MacDonald and Carter 2003). Further, some research suggests that this activity may be greater for B- than A-cues, given that B-cues are needed to overcome a prepotent response tendency

(MacDonald and Carter 2003; Perlstein et al. 2003). In contrast, reactive control should be associated with greater probe-related activity, particularly when the probe produces a high degree of interference, such as on BX trials (Braver et al. 2007).

In Study 1, the use of a blocked design did not allow us to examine issues related to age-related changes in the dynamics of brain activity, particularly in lateral PFC. Previous neuroimaging studies using event-related designs have provided unique and highly informative data about cognitive aging. For example, one study demonstrated that lateral PFC activity was more pronounced in older adults during the encoding and retrieval phases of a working memory task than during the maintenance phase (Rypma and D'Esposito 2000). Such data are consistent with the idea of a shift from proactive to reactive control in older adults. Thus, in Study 2, we utilized event-related methods in conjunction with the AX-CPT to examine age-related changes in cognitive control more directly. Additionally, we investigated whether the generalized task-related increases in activity among older adults are primarily sustained across trials or trial specific using a mixed blocked/event-related design that enables decomposition of these 2 types of effects (Donaldson et al. 2001; Visscher et al. 2003; Donaldson 2004).

Study 2

In this study, a second set of older and young adults performed the AX-CPT in the long-delay condition. Two sets of analyses were conducted. The first decomposed general task-related activation into 2 components: 1) sustained activity that persisted across trials and was independent of trial events, and 2) transient activity that was selectively evoked by trial events. This analysis enabled us to investigate whether the increased task-related activity observed among older adults in Study 1 was primarily associated with the sustained or transient component of activation. The second analysis further decomposed trial-specific transient activity into cue-related and probe-related components. This analysis enabled us to examine whether older adults showed a pattern of activity dynamics consistent with reactive instead of proactive control. This hypothesis was associated with 4 specific predictions. First, we predicted that older adults would show less cue-related activity than young adults (particularly in lateral PFC regions) reflecting a reduced tendency to encode, maintain, and utilize task-goal information over the delay period. Second, this reduction in cue-related activity would be most apparent to B-cues as some prior research suggests greater need to proactively maintain B-cues to overcome the prepotent response tendencies associated with X-probes (MacDonald and Carter 2003; Perlstein et al. 2003). Third, older adults would show greater probe activity than young adults, reflecting an increased tendency to reactivate task-goal information at the time of probe presentation. Fourth, this increase in probe activity would be most prominent on BX trials as this is the condition most likely to elicit interference and require the reactivation of cue information to suppress inappropriate responding.

Method

Participants

Participants were 16 healthy young adults (M = 21.56, SD = 3.14, range = 18–28) and 16 healthy older adults (M = 72.38, SD = 6.51, range = 65–84) recruited from the same sources as Study 1. Participants underwent the same written consent process as described in Study 1. All participants were right handed. The groups did not differ significantly in gender breakdown, $\chi^2 = 1.25$, df = 1, $N = 32$, $P = 0.26$ (young adults: 9 females and 7 males; older adults: 12 females and 4 males). Participants were screened with the same inclusion/exclusion criteria used in Study 1 and paid $25 per hour for their participation. Two older adult participants also participated in Study 1.

Behavioral Tasks

Participants performed the long delay version of the original AX-CPT using letters and the same distribution of trial types as in Study 1 (70% were AX, 30% were nontarget trials). All participants performed 3 scanning runs of 40 trials each of the AX-CPT in the long-delay condition. Thus, they completed 84 AX trials and 12 of each of the trial types (AY, BX, and BY; nontarget cues and probes were randomly distributed across the rest of the alphabet, excluding B, H, K, V, W, Y), yielding a total of 120 trials. Trials were 7.5 s in duration and composed of a cue letter presented for 300 ms followed by an unfilled delay period of 4900 ms and then the probe letter was presented for 300 ms, with an additional 1000-ms response period. Following the probe response, a message appeared on the screen for 1000 ms saying "Trial over, get ready for the next one." The letters were presented in white 36-point uppercase bold Helvetica font on a black screen, and responses were made using the same procedures as Study 1. The young adults also performed the AX-CPT in 2 other conditions involving manipulation of financial incentives, the results of which are described elsewhere (Locke and Braver, Forthcoming 2007). The baseline AX-CPT condition that was the focus of interest here was always performed first, and participants were not aware of any other conditions or the incentive manipulation during baseline performance.

Functional Imaging

The functional and structural scanning protocol and parameters were identical to Study 1 except for a slight difference in whole-brain acquisition parameters (18 contiguous, 7-mm thick axial images acquired parallel to the anterior–posterior commissure plane with 3.75 × 3.75 mm in plain resolution). Data were acquired in runs of 237 images, using a mixed blocked/event-related design that allows the separate estimation of sustained and transient activation (Donaldson et al. 2001; Visscher et al. 2003; Donaldson 2004). During each run, 2 task blocks (94 frames each) and 3 fixation blocks (20 frames each) were administered. In each task block, trials occurred with a variable ITI (2.5–7.5 s in steps of 2.5 s), which enabled estimation of event-related responses and separation of these from sustained activation.

Data Analysis

Behavioral data were analyzed using the same method as described for Study 1. *z*-Transformed RT data were excluded for one older adult participant because the participant had no correct responses on BX trials, and RT analyses were computed using only correct trials. Functional imaging data were also preprocessed identically to Study 1. GLMs (Friston et al. 1995) for each participant were constructed in order to analyze event-related effects (item effects) and sustained activity across

the entire task block (state effects). Sustained effects were independently coded using an assumed shape of a long duration (i.e., boxcar convolved with a gamma function). This approach assumes that event-related effects will decay back to baseline during the ITI while sustained effects should remain constant. Event-related effects were analyzed with GLMs estimating values for the time points with an unassumed shape for the hemodynamic response function. This GLM approach involved estimation of a 25-s (10 TR) event-related response epoch for each trial type for each participant. Trials where the participant failed to make a response or made an incorrect response were not included in the analyses (i.e., were estimated separately). Parameter estimates from each participant's GLM were submitted to second-level tests treating participant as a random factor in the *t*-tests and ANOVAs used as part of the analyses.

The same multiple contrast approach to statistical analysis and identification of significant voxels used in Study 1 was also employed here. In each analysis, we identified regions showing significant age-related differences in activation. Additionally, in the Supplementary Material, we report the results of analyses that identified regions showing similar patterns of activation for young and older adults for each effect of interest. In all analyses, we defined cue/delay activity as the sum of activation at time points 3 and 4 (i.e., corresponding to 5–7.5 s after cue onset, which accommodates the well-known hemodynamic lag) and probe activity as the sum of activation at time points 5 and 6 (i.e., corresponding to 10–12.5 s after probe onset). The analyses examining whole-trial transient activity included time points 3–6. All event-related analyses included a contrast designed to compare activation at the time of interest (e.g., time points 3–4 for cue activity, 5–6 for probe activity, 3–6 for whole-trial activity) with pre-cue activity (sum of activation at time points 1–2) to ensure that regions identified demonstrated a difference in the event-related response to the stimulus as opposed to a baseline shift in activity. Figure 2 schematically illustrates the time points examined and the hypotheses for activation at time of cue and probe.

The first set of analyses examined age differences in sustained and whole-trial transient activation. To identify regions showing greater "sustained activity" in older adults, the following contrasts were employed: 1) significant sustained activation in older adults during the task compared with the fixation baseline and 2) significantly greater sustained activation in older compared with young adults. An analogous analysis was conducted to identify regions showing the reverse pattern (older < young sustained activity). To identify regions showing greater "whole-trial transient" activity in older adults, the following contrasts were employed: 1) significant whole-trial activation in older adults compared with the fixation baseline, 2) significant whole-trial activation in older adults compared with a pre-cue baseline, and 3) significantly greater whole-trial activation in older adults compared with young adults. An analogous conjunction analysis was conducted to identify regions showing the reversed pattern (older < young whole-trial transient activity).

The second set of analyses examined age differences in cue and probe activation. Our first primary hypothesis was reduced "cue-related activity" in older adults. To identify these regions, the following contrasts were employed: 1) significant cue-related activation in young adults compared with the fixation baseline (tested independently for each trial type), 2) significant cue-related activation in young adults compared with a pre-cue baseline (tested independently for each trial type), 3) significantly reduced cue activation (collapsed across trial type) in older adults compared with young adults, and 4) numerically reduced cue activation in older adults compared with young adults (tested independently for each trial type). A further analysis identified regions showing reduced "B-cue activity" in older adults. To identify these regions, the following contrasts were employed: 1) significant activation for B-cues in young adults compared with the fixation baseline, 2) significant activation for B-cues in young adults compared with a pre-cue baseline, 3) significantly greater activation for B-cues compared with A-cues for young adults, 4) no significant differences in pre-cue activity between A and B trials for young adults, 5) significant age × cue type interaction for cue activity, and 6) numerically lower activation for B-cue in older adults compared with young adults. Analogous analyses were performed to identify regions showing the reversed pattern (increased cue or B-cue–related activation in older adults).

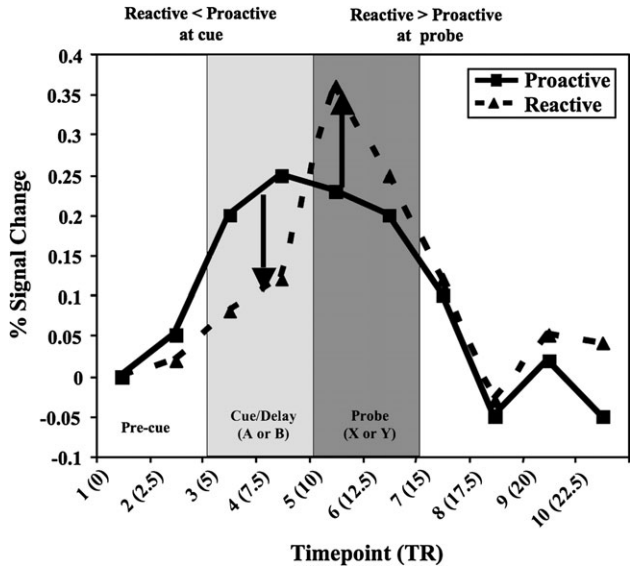

Figure 2. Time course illustrating time of the cue (A or B) and probe (X or Y). Plotted activation represent hypothesized pattern for proactive and reactive approaches across time.

Our second primary hypothesis was increased "probe-related activity" in older adults. To identify these regions, the following contrasts were employed: 1) significant probe-related activation in older adults compared with the fixation baseline (tested independently for each trial type), 2) significant probe-related activation in older adults compared with a pre-cue baseline (tested independently for each trial type), 3) a significant age difference in probe versus cue activity (i.e., age × time point [3/4 vs. 5/6] interaction) collapsed across trial type, and 4) numerically greater probe activation in older adults compared with young adults (tested independently for each trial type). An analogous analysis was conducted to uncover probe-related activity in young adults. A further analysis identified"BX-probe–selective" effects in older adults. To identify these regions, the following contrasts were employed: 1) significant probe-related activation on BX trials in older adults compared with the fixation baseline, 2) significant probe-related activation on BX trials in older adults compared with a pre-cue baseline, 3) significant age difference in probe versus cue activity on BX trials (age × time point interaction), 4) numerically greater

probe-related activation on BX trials in older compared with young adults, 5) significantly greater probe activity on BX versus BY trials in older adults, 6) no significant age difference in probe versus cue activity on BY trials (no BY age × time point interaction), and 7) no significant effect of probe type (X, Y) in older adults during the pre-cue period. Analogous analyses were performed to identify regions showing the reversed pattern (reduced probe or BX-probe–related activation in older adults).

In order to further explore cue and probe activation, we conducted a final analysis that identified regions showing both decreased cue-related activation and enhanced probe-related activation in older adults. In particular, we tested for the presence of a significant age by event type (cue vs. probe) crossover interaction with the following contrasts: 1) significant age by event type interaction when considering all trials or just BX trials (because these have the highest control demands at both cue and probe periods, 2) numerically greater cue responses in young adults when considering either all trials or just B-cue trials, and 3) numerically greater probe responses in older adults when considering either all trials or just BX trials. Then, as a further step, we created an inclusive mask composed of all regions identified in the 4 previous analyses comparing cue and probe effects discussed above (i.e., reduced cue-related activity in older adults, reduced B-cue activity in older adults, increased probe-related activity in older adults, and increased BX-probe activity in older adults). We then masked the voxels identified in the contrast test above with this inclusive mask to identify regions of interest. This final step ensured that all identified crossover effect regions were also a subset of the regions showing age differences in the previous analyses.

Results

Behavioral Data

The ANOVA for nontarget accuracy (see Table 1) showed no significant effects of age or an age by trial type interaction. When the effect of trial type was investigated separately for each age group, the effect size values (partial $\eta^2 = 0.06$ vs. 0.19, for older vs. young, respectively) suggest that there was a larger difference in performance among trial types for young than there was for older adults. Furthermore, the difference between AY and BX errors was greater for young adults, $F_{1,15} = 3.33$, $P = 0.09$, partial $\eta^2 = 0.18$, than it was for older adults, $F_{1,15} = 0.26$, $P = 0.62$, partial $\eta^2 = 0.02$. Moreover, on target trials, young adults made significantly more AX errors than older adults ($F_{1,30} = 4.99$, $P < 0.05$; young: M = 0.02, old: M = 0.00). The nontarget RT ANOVA (Table 1) on *z*-score–transformed data controlling for generalized slowing also indicated no significant age by trial type interaction. Planned contrasts indicated that both older and young adults were slower on AY trials as compared with BX trials ($F_{1,29} = 65.06$, $P < 0.0001$, partial $\eta^2 = 0.69$) and compared with BY trials ($F_{1,29} = 70.88$, $P < 0.0001$, partial $\eta^2 = 0.71$). Separate analyses on target trials and d′-context also revealed no significant main effects of age. These behavioral results somewhat diverge from Study 1 and our previous work in showing close to age-equivalent performance. However, a positive aspect of the results are that they enable a strong test of hypotheses regarding age-related changes in the underlying neural circuitry related to goal maintenance, as any age differences in neural activation will be unconfounded by age-related performance differences.

Imaging Data

Two sets of analyses were conducted, the first examining sustained versus whole-trial transient effects and the second examining cue-related versus probe-related activation. We focus the results on frontal activation, as this was our primary area of interest. Frontal activations showing age differences in cue and probe activation are presented in Table 3, and frontal activations showing both decreased cue and increased probe activation in older adults are shown in Table 4. Whole-brain activations are reported in the Supplementary Material.

Table 3
Frontal regions showing age differences in cue-related or probe-related activation in Study 2

Regions of interest	Brodmann area(s)	*X*[a]	*Y*[a]	*Z*[a]	Volume (mm^3)[b]
Cue					
Older < young					
Right middle frontal gyrus	46	26	41	15	756
Right middle/inferior frontal gyrus	45/46	24	22	22	5265
Left medial frontal gyrus	6	−2	4	50	15633
Right precentral gyrus	6	32	−7	40	918
Right superior frontal gyrus	6	32	−7	67	297
Left precentral gyrus	6	−42	−10	14	810
	4	−35	−25	53	1971
Older > young					
Left inferior frontal gyrus	47	−24	25	−14	297
Left cingulate gyrus	24	−18	21	−5	783
Specific to "B" cues					
Older < young					
Right medial frontal gyrus*	10/11	16	49	−10	3213
Left medial frontal gyrus	10	−35	40	−7	864
Right middle frontal gyrus**	9	31	37	33	9801
		49	10	35	6048
Right inferior frontal gyrus	45	55	19	16	675
Right inferior frontal junction*	44/6	38	−4	38	2592
Right corpus callosum		1	14	21	1404
Probe					
Older > young					
Left superior frontal gyrus	9	−36	44	32	837
Right middle frontal gyrus	9	42	17	29	243
	6	29	−6	55	945
Left middle frontal gyrus	6	−43	−9	53	1782
Right inferior frontal junction	44/6	40	6	34	486
Right precentral gyrus***	*6*	47	19	7	567
Specific to BX-probe					
Older > young					
Right superior frontal gyrus	8	25	27	51	999
Left superior frontal gyrus	6	−3	3	64	999
Right middle frontal gyrus	9	43	28	37	243
		54	7	36	297
Left inferior frontal gyrus	47	−48	27	−7	459
	44	−57	14	12	432
Right inferior frontal gyrus***	10/47	49	39	0	297
	47	53	22	0	1296
		34	20	−8	459
Right precentral gyrus***	4	15	−14	55	459
		31	−13	61	1053
Left precentral gyrus	4	−23	−14	52	1296
		−47	−8	42	1701

[a]*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.

[b]Volume refers to the number of voxels (converted to mm^3) that reached statistical significance in each region of interest.

*Indicates regions showing an age by trial type (AX vs. BX) interaction at $P < 0.05$.

**Indicates regions showing an age by trial type (AX vs. BX) interaction at $P < 0.10$.

***Indicates regions showing that were excluded in the analysis examining response slowing effects in which voxels demonstrating an AY > BX pattern in probe activation were masked out.

Table 4
Frontal regions showing a convergence of cue and probe effects in Study 2

Regions of interest	Brodmann area(s)	X^a	Y^a	Z^a	Volume (mm^3)[b]
Right middle frontal gyrus	8/9	24	27	50	999
	9/46	42	17	29	243
		43	28	37	243
Left middle frontal gyrus	9/46	−35	44	32	837
Right inferior frontal gyrus	47	37	20	−6	270
		51	21	0	1485
	47/10	49	39	0	297
Left inferior frontal gyrus	45/insula	−24	13	17	945
	44	−56	13	12	432
	47	−48	27	−7	459
Right inferior frontal junction	44/6	39	6	33	486
		53	6	36	297
Right superior frontal	6	29	−10	58	1269
Medial superior frontal gyrus	6	−3	−3	65	2592
(supplementary and premotor areas)		−46	−7	41	1485
	4	15	−14	54	459
		−29	−12	52	1944

[a]*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.
[b]Volume refers to the number of voxels (converted to mm^3) that reached statistical significance in each region of interest.

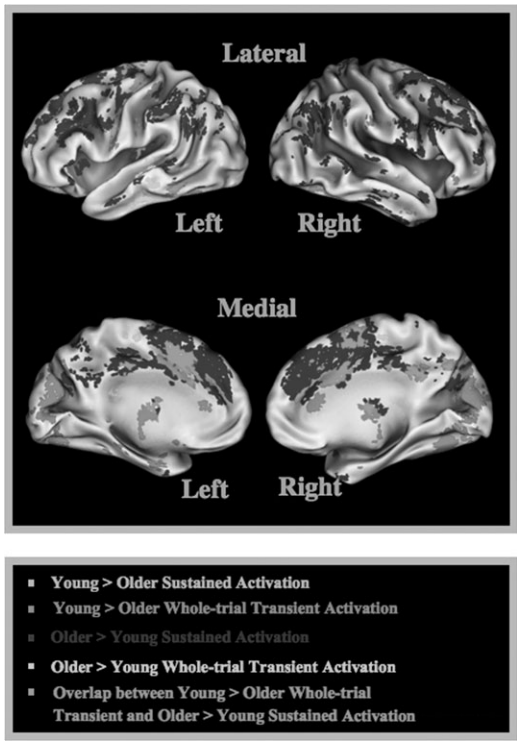

Figure 3. Brain regions showing age differences in sustained and transient activation in Study 2. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain. Regions in orange reflect greater blood oxygen level–dependent (BOLD) response for sustained activation in young adults compared with older adults, regions in red reflect greater BOLD response for whole-trial transient activation in young adults compared with older adults, regions in blue reflect greater BOLD response for sustained activation in older adults compared with young adults, regions in green reflect greater BOLD response for whole-trial transient activation in older adults compared with young adults, and regions in purple reflect overlap between greater BOLD response for whole-trial transient activation in young adults compared with older adults and sustained activation in older adults compared with young adults.

Sustained Effects

Age differences in sustained activity were observed throughout a large amount of total brain volume (208, 980 mm^3). Of this volume, almost all (96%) showed the older > young pattern. Older adults showed greater sustained activation compared with young adults in an extensive and widespread set of brain areas, including lateral PFC regions such as the dorsal, anterior, and inferior frontal cortex along with medial frontal regions such as the anterior cingulate and supplementary motor area (shown graphically in Fig. 3; a full list of coordinates in text form is reported in the Supplementary Material).

Whole-Trial Transient Effects

Like the analyses for sustained effects, age differences in whole-trial transient activation were also observed in an extensive amount of brain volume (120, 744 mm^3). Yet, in this analysis, the greater proportion of volume (71%) showed the reverse pattern of older < young. Older adults showed reduced whole-trial transient activation compared with young adults in a number of anterior and posterior cortical regions, including a number of PFC regions such as bilateral inferior frontal gyrus (Brodmann area [BA] 44 and 47), supplementary motor area (BA 6), and right premotor cortex (shown graphically in Fig. 3; a full list of coordinates in text form is reported in Supplementary Material). Although it was not the focus of this analysis, it is clear that some of the regions showing decreased whole-trial transient activation in older adults also displayed increased sustained activity, as can be observed in the amount of overlapping voxels displayed in Figure 3. Of the amount of brain volume showing increased sustained or transient activation in older or young adults (300, 024 mm^3), 9% showed overlap between increased sustained activation and decreased whole-trial transient activity in older adults. For instance, the 8127 mm^3 region in the anterior cingulate cortex (BA 32) showed this pattern. Finally, there were a small set of brain regions, including right anterior PFC (BA 10), left anterior cingulate gyrus (BA 32), and left primary motor cortex (BA 4), for which older adults showed increased whole-trial transient activity relative to young adults.

Cue-Related Activity

Our hypothesis predicts that if older adults have a reduction in the use of proactive control, then they should show reduced cue-related activity compared with young adults. We first examined activity that was present across both cue types (A and B). Of the total brain volume showing age differences in cue-related activity (109, 782 mm^3), almost all (87%) showed the older < young pattern (see Table 3 and Fig. 4*A*). This pattern of reduced cue activation in older adults compared with young adults was particularly prominent in regions of the frontal cortex including right dorsolateral PFC (BA 46), right superior frontal gyrus, right inferior frontal gyrus, and medial frontal cortex (pre-SMA). Moreover, one of the right dorsolateral PFC regions overlapped with the region identified in Study 1 that showed increased delay-related activation in younger adults. Only a left inferior frontal gyrus (BA 47) and anterior cingulate cortex (BA 24) showed the reversed pattern of increased cue-related activation in older adults. Next, we examined activation that was selective for B-cues as previous

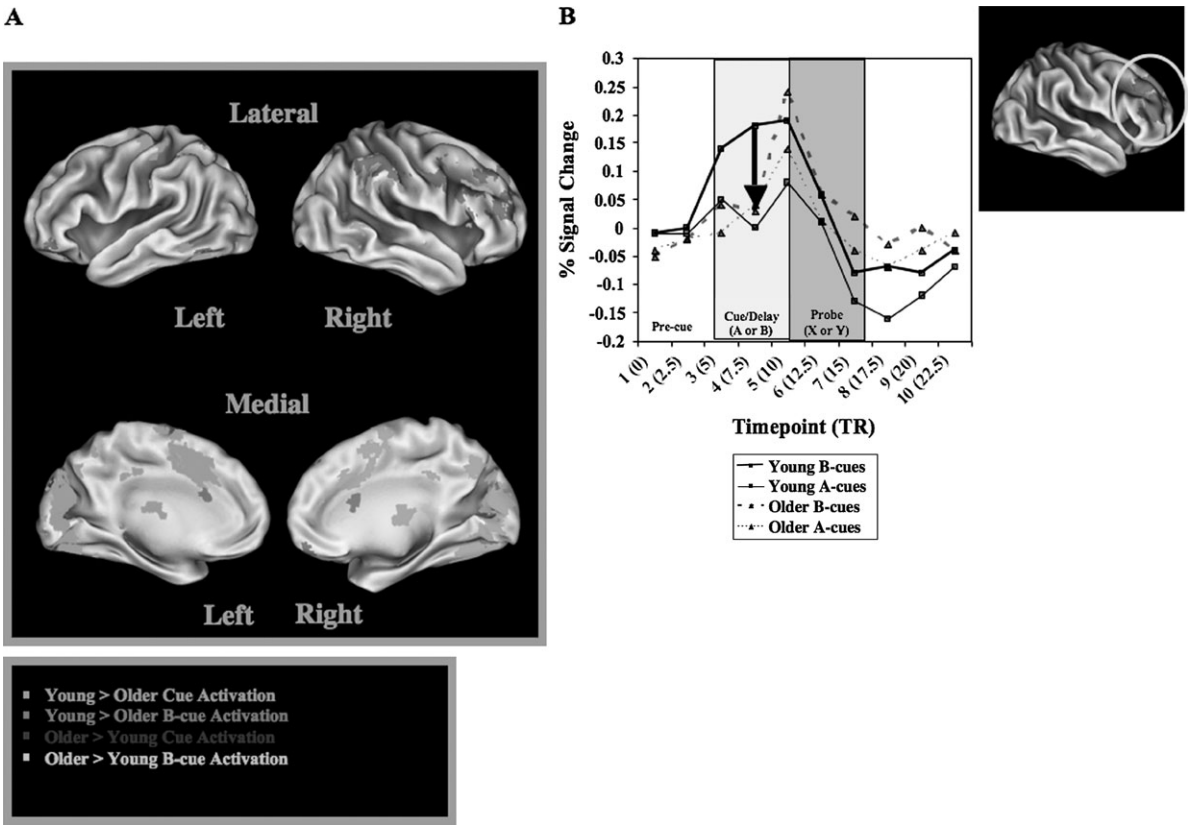

Figure 4. Brain regions showing age differences in cue activation in Study 2. (*A*) Activation shown on a surface rendering. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain. Regions in orange reflect greater blood oxygen level–dependent (BOLD) response at the time of the cue in young relative to older adults, regions in red reflect greater BOLD response specific to B-cues in young adults compared with older adults, regions in blue reflect greater BOLD response at the time of the cue in older adults compared with young adults, and regions in green reflect greater BOLD response specific to B-cue in older adults compared with young adults (*B*) Activation across time for young and older adults for A- and B-cues in right dorsolateral PFC region ($x = 31$, $y = 37$, $z = 33$) identified as showing increased B-cue activation in young adults compared with older adults.

literature has suggested B-cue–selective activation in lateral PFC, presumably associated with an increased demand for proactive maintenance of task-goal information on B-cue trials (MacDonald and Carter 2003; Perlstein et al. 2003). Thus, age-related differences in the proactive use of contextual cue information might be especially prominent on B-cue trials. Similar to the pattern observed with general cue-related activity, the pattern was skewed in the older < young direction (93%) across the total brain volume showing age differences in B-cue–selective effects (40, 041 mm^3 total). A large region of right dorsolateral PFC (BA 9) was identified that showed a selective reduction in B-cue activation among older adults (see Table 3 and Fig. 4*A*). This dorsolateral PFC region was similar in location to that identified in previous event-related AX-CPT studies (MacDonald and Carter 2003; Perlstein et al. 2003). In this region, young adults showed the expected enhanced response on B-cue relative to A-cue trials, whereas older adults showed weaker and equivalent activity for both cue types (see Fig. 4*B*).

The examination of age-related differences in cue-specific effects can be more strongly examined by directly comparing only AX and BX trials, as the probe stimulus is the same across both trial types. Thus, we conducted a follow-up analysis on the identified B-cue–selective frontal ROIs testing the age by cue type effect but restricting the analysis to just AX and BX trials. This analysis revealed that many of these identified regions, including the large right dorsolateral PFC region, were statistically significant (at least at the trend level) and with the same pattern observed as in the primary analyses (see Table 3).

Probe-Related Activity

In contrast to the cue-related activation pattern, we predicted that older adults would show greater probe activity than young adults, reflecting their use of a reactive processing strategy that involves reactivating cue information at the time of probe presentation. The results supported this prediction. Of the total brain volume showing age differences in probe-related activity (49, 437 mm^3 total), almost all (90%) showed the older > young pattern. Enhancement of probe-related activity was particularly prominent in lateral PFC, with right dorsolateral PFC (BA 9), middle frontal gyrus (BA 6), and left superior frontal gyrus showing the effect (see Table 3 and Fig. 5*A*). There were no frontal regions showing the reversed pattern of older < young. Lastly, we examined probe-related activity specific to BX trials as we predicted that the use of reactive control would have the highest demands on these trials in order to overcome interference related to the target response bias associated with X-probes. Again, of the total brain volume showing age differences in BX-probe–related activity (71, 982 mm^3 total), almost all (99%) showed the older > young pattern. As shown in Table 3 and Figure 5*A*, older adults showed significantly enhanced probe activation on BX trials compared with young

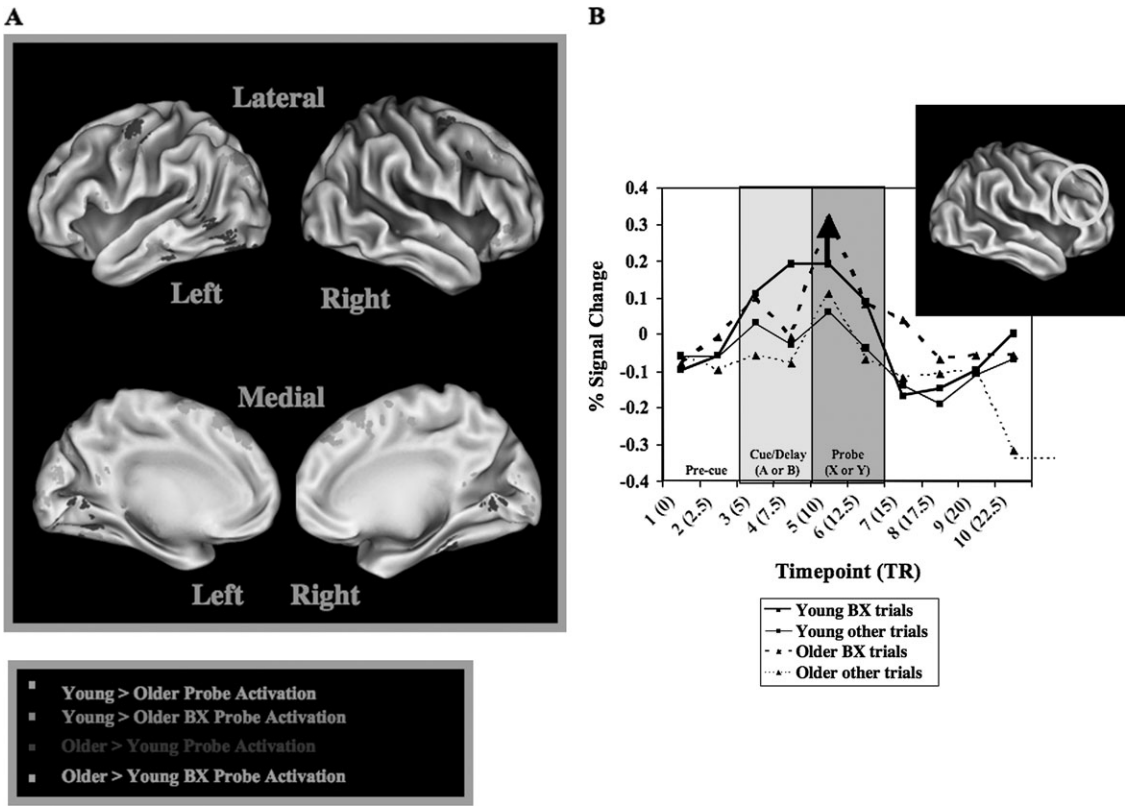

Figure 5. Brain regions showing age differences in probe activation in Study 2. (*A*) Activation shown on a surface rendering. The right side of the image is the right side of the brain, and the left side of the image is the left side of the brain. Regions in orange reflect greater blood oxygen level–dependent (BOLD) response at the time of the probe in young relative to older adults, regions in red reflect greater BOLD response specific to BX-probes in young as compared with older adults, regions in blue reflect greater BOLD response at the time of the probe in older adults compared with young adults, and regions in green reflect greater BOLD response specific to BX-probes in older adults compared with young adults. (*B*) Activation across time for young and older adults for BX trials and the average of the 3 other trial types (AX, AY, BY) in the right middle frontal gyrus region (x =43, y = 28, z = 37) identified as showing increased BX-probe activation in older adults compared with young adults.

adults in a number of lateral PFC regions including the right dorsolateral PFC (BA 9), bilateral ventrolateral PFC (BA 47), and bilateral premotor and supplementary motor cortex (BA 4). Figure 5*B* shows the time course of activation in the right middle frontal gyrus region illustrating the specific enhancement of BX-probe activity observed in older adults but not in young adults. Again, no frontal regions showed the reverse pattern of older < young adults.

A possible concern regarding the increased probe-related activation in older adults is that it does not reflect reactive control processes but rather may reflect the generally slower responses made by older adults. Thus, the increased activation among older adults at the time of the probe might reflect a general and nonspecific positive relationship between RT and activation. If so, then it should be the case that the trial types associated with slower RTs would also be associated with increased probe activation. In both older and young adults, AY trials had significantly slower RTs than BX trials; indeed, this trial-type effect on RT was much stronger than the effect of age on RT. Thus, to determine whether general RT slowing effects might have contributed to the results, we identified all voxels for which probe activation was numerically greater on AY compared with BX trials. We then masked these voxels from all the identified ROIs showing the older > young pattern in probe-related activity, including the BX-specific effects. It should be noted that this is an especially stringent control because we used a very loose criterion (i.e., numerically rather than statistically significant increased RTs on AY vs. BX trials), and it might be the case that voxels showing the AY > BX activation pattern do not necessarily reflect generalized slowing effects. Nevertheless, this analysis revealed that very few of the identified ROIs were excluded by this control analysis (see Table 3), suggesting that the increased probe activation among older adults in these regions cannot be fully explained in terms of general response slowing effects.

Convergence of Cue and Probe Effects

Visual inspection of the patterns of activation suggested that many regions showing decreased cue-related activation in older adults also showed increased probe-related activation in older adults (e.g., Fig. 5*B*). Consequently, we tested this pattern formally by searching for regions showing a significant crossover age by event type (cue/probe) interaction. Specifically, we tested for regions showing both reduced cue and increased probe effects in older adults from the regions identified in the first analysis showing 1 of the 2 effects. Indeed, a significant subset of the previously identified regions showed this pattern (see Table 4), including the right dorsolateral region (BA 9) shown in Figure 5*B*, along with additional bilateral dorsal (BA 9/46), ventral (BA 44, 45, and 47), and right posterior (BA 44/6 in the IFJ) regions of PFC.

Study 2 Discussion

One of the primary goals of Study 2 was to investigate patterns of sustained and transient brain activation in young and older

adults while completing the AX-CPT. More specifically, we were interested in determining whether previous findings of increased task-related activation in older adults (as in Study 1 and prior work) reflected increases in either sustained or transient activation or both. The second primary goal was to examine whether the dynamics of event-related brain activity shown by older adults corresponded to the predictions generated by the hypothesis that young adults use a proactive control approach, whereas older adults use a reactive control approach on the AX-CPT (Braver et al. 2001; Braver et al. 2005).

Using a mixed blocked/event-related design in Study 2, we found clear evidence that older adults showed enhanced sustained (i.e., tonic) activation across anterior and posterior brain regions relative to young adults. In contrast, young adults tended to show greater whole-trial transient or trial-related activity relative to older adults. As noted earlier, previous studies such as Study 1 have consistently found evidence for enhanced task-related activity in older adults (Grady et al. 1998; Haut et al. 2000; Rypma and D'Esposito 2000; Logan et al. 2002; Rosen et al. 2002; Langenecker and Nielson 2003; Cabeza et al. 2004; Langenecker et al. 2004; Persson et al. 2004; Colcombe et al. 2005; Townsend et al. 2006). Yet, a limitation of many of these studies is that they employed blocked designs. Such designs cannot disentangle the source of age-related enhancement in terms of trial-related activation or a more tonic process associated with task performance. The results of the current study suggest that enhanced task-related activity in older adults may primarily reflect increases in tonic or sustained components of task processes rather than trial-specific processing. This enhanced sustained activity among older adults may be due to several different factors. One possibility is that older adults have difficulty maintaining general task goals and need to activate additional regions to maintain such global task information. This would be consistent with recent findings indicating that a core network of regions including medial, anterior, and opercular frontal regions similar to those activated in the current study are tonically activated during cognitive task performance and interpreted as reflecting task-set maintenance (Dosenbach et al. 2006). Alternatively, it may be that older adults use brain resources in an inefficient and nonspecific manner leading to generalized increases in sustained task-related activity. Another possibility is that the tonic activation is related to components of task performance that are not purely cognitive in nature, such as increased arousal, motivation, or anxiety. Indeed, in separate analyses of the young adult data, it was found that increased motivation led to a significant increase in sustained brain activity in a number of regions, including the PFC (Locke and Braver, unpublished data). Finally, the finding that some regions show a pattern of both increased sustained and decreased whole-trial transient activation in older adults relative to young adults suggests that older adults may be compensating for a deficit in trial-related processing by recruiting more global activation across trials. Clearly, further research is needed to determine the cognitive and neural sources of enhanced sustained activity in older adults.

The second goal of Study 2 was to determine whether older adults showed patterns of event-related brain activity consistent with the hypothesis that, with age, a shift occurs from the proactive control strategy utilized by young adults to a more reactive approach. This hypothesis led to 2 specific predictions. First, the reduction in proactive control among older adults predicted decreased cue-related activity, which would indicate a reduction in the utilization and maintenance of task-goal information. Second, the increased reliance on reactive control among older adults predicted an increase in probe-related activity, which would be needed to reactivate task goals in order to determine whether a target response should be given. Moreover, we predicted that these effects might be most prominent on conditions involving B-cues and BX-probes as these are the ones that are the most challenging for goal utilization and reactivation.

The results were consistent with these predictions. In terms of total brain volume, an older < young pattern was found for general cue-related activation and B-cue–selective effects, but an older > young pattern was found for probe-related activation, especially on BX trials. Moreover, these patterns of age differences were highly prominent within the lateral PFC. Older adults showed a significant reduction in cue-related activity within a large region of the right dorsolateral PFC. Further, this region overlapped with the region identified in Study 1 showing reduced delay-related activation in older adults and was near to a region that showed greater activation specific to B-cues in young adults. These findings suggest that this reduction in delay-related activation in older adults in Study 1 might have been due to impaired encoding and maintenance of contextual cue information, a function that could be mediated by this right dorsolateral PFC region. During probe processing, however, older adults showed increased activation in additional PFC regions such as the ventral PFC and the IFJ. Further activation of bilateral ventrolateral PFC was observed specifically in the BX condition, which agrees with the proposal that activation in such regions, especially left ventrolateral PFC would represent reactive cognitive control (Braver et al. 2007). It is interesting that the regions showing increased BX-probe activity in older adults have been previously shown to be involved in transient forms of inhibition and interference control. For instance, studies have shown activation in the IFJ during Stroop incongruent trials (Derfuss et al. 2005). Also, inferior/ventrolateral PFC activation has been documented during nogo and stop-signal response inhibition trials (Menon et al. 2001; Durston et al. 2002; Li et al. 2006) and during probe-related interference in conditions of the Sternberg WM task requiring inhibition (Jonides et al. 2002; Zhang et al. 2003). Thus, these findings suggest that older adults needed to resort to this "late correction" form of reactive inhibition in order to suppress inappropriate responding at the time of the probe.

One potential concern regarding the results involves the behavioral performance in Study 2. In particular, contrary to the pattern observed in Study 1 as well as our previous studies of age differences in the AX-CPT, we did not find evidence of significantly impaired goal maintenance among the older adults in Study 2. It is possible that the reason we did not observe significant age-related behavioral effects in Study 2 was because the participants across Study 1 and Study 2 performed at different levels. It is not clear why the performance of participants across the 2 studies might have differed as both were sampled from the same population and had similar demographic characteristics. Nevertheless, it is possible that some of the subtle differences between the 2 studies such as the variable timing associated with the event-related design of Study 2 and the more explicit marking of the trial end (via the visual feedback message "Trial Over") might have contributed

to the changes in performance. It is also possible that these changes led to a reduction of proactive control in young adults (i.e., less ability to predict the occurrence of stimuli) but improved proactive control in older adults (i.e., slower pace of the tasks and better delineation of trials). Regardless of these differences, the general structure of performance remained the same for both older and young adults in Study 2, suggesting that any cognitive effects, if present, were subtle ones. Even if such effects were present, they would only have worked against our ability to see age-related changes in brain activation, and therefore, they do not present a serious concern for interpretation of the results.

In summary, Study 2 highlighted the utility of examining the dynamics of brain activity in older and young adults in terms of revealing the locus and nature of age differences. The pattern of overactivation in studies using blocked designs during cognitive tasks appeared to be due to age-related increases in sustained or across-trial activation, rather than trial-evoked responses, which tended to be reduced in older adults. Moreover, the event-related dynamics within task trials suggested that older adults showed reduced cue but increased probe-related activation, consistent with a shift in cognitive control strategy from a proactive to a reactive mode.

General Discussion

The results of the current series of studies contribute to the growing literature on the cognitive neuroscience of aging by both replicating and extending previous findings. First, our results are highly consistent with previous data pointing to the lateral PFC as a critical locus of age-related changes in functional brain activity (for a review see Buckner 2004). In both studies, we replicated the pattern of both PFC over- and underactivation in older adults that has been observed in a number of studies (Grady et al. 1995; Cabeza et al. 1997; Grady et al. 1998; Haut et al. 2000; Rypma and D'Esposito 2000; Cabeza et al. 2002; Logan et al. 2002; Milham et al. 2002; Rosen et al. 2002; Langenecker and Nielson 2003; Cabeza et al. 2004; Johnson et al. 2004; Langenecker et al. 2004; Persson et al. 2004; Colcombe et al. 2005; Townsend et al. 2006). As such, the findings support a theory of cognitive aging asserting that PFC functions decline with increasing age (Moscovitch and Winocur 1995; West 1996).

Also, our results significantly extend this previous work by helping to clarify the nature of abnormal PFC activation patterns. Our findings suggest that the overactivation pattern typically observed in blocked design studies might actually reflect sustained or tonic activation increases instead of, or in addition to, changes in trial-evoked activation. These widespread sustained activation patterns might indicate activation associated with more nonspecific processes such as increased arousal, motivation, or a more general strategy of nonselective cortical recruitment to meet cognitive demands. In addition, patterns of overactivation observed in event-related designs might reflect an increased dependence on reactive control among older adults. Such reactive control strategies would be marked by a transient increase in activation specifically during points when cognitive control demands become high due to interference or weak bottom-up activation. Conversely, the results also suggest that underactivation patterns might occur when proactive control strategies are especially critical, such as during the encoding and active maintenance of contextual cues or when preparatory biasing of attention and action is needed. Under such conditions, older adults might be less likely than young adults to engage in such proactive control processes, which would lead to an age-related underactivation pattern, particularly within lateral PFC.

An important take-home message of this study is that further elucidation of age-related brain activation changes may require paying close attention to the temporal dynamics of brain activity. Previous work on functional brain activity in aging has suggested that some or all the enhanced task-related brain activity found in older adults reflects compensatory activation in response to reduced efficiency/integrity of activation (Cabeza et al. 1997; Grady 2000; Cabeza et al. 2002; Rosen et al. 2002; Buckner 2004; Cabeza et al. 2004; Park et al. 2004; Mattay et al. 2006). The results of the current study may provide a more elaborated and mechanistic approach to the compensation theory and explain some of the variability in results across studies. In particular, our data suggests that "compensation" may occur even within a single trial for older adults (i.e., the crossover age × event type interaction). Our finding of lateral PFC regions showing reduced cue activation but increased probe activation in older adults indicates that in these individuals the increased activation during one part of the trial (i.e., time of the probe) might have compensated for underactivation during another time period of the trial (i.e., time of the cue). Similarly, older adults showed increased sustained and decreased whole-trial transient in several regions including the anterior cingulate cortex, suggesting that older adults may compensate for impaired trial-related responses with increased tonic activation. Also, it is worth noting that the equivalent behavioral performance observed between young and older adults in Study 2 might also support a compensatory theory. According to this account, older adults achieved equivalent performance to young adults by compensating for their reduced cue-related activity with an increase in probe-related and sustained activation. Studies using paradigms that enable examination of within-trial (or potentially across-trial) changes in activity dynamics have the potential to provide further information about whether our account of compensation within a single trial provides a more comprehensive explanation of age-related patterns of over- and underactivation.

It is also important to consider how our theory regarding age-related shifts in cognitive control strategy relates to other theories of cognitive aging. According to the theory, proactive cognitive control may be the optimal strategy to use in demanding tasks (Braver et al. 2007). The finding that older adults are less likely than young adults to adopt a proactive strategy parallels previous results, suggesting that older adults are impaired in strategy use (Hybertson et al. 1982; Touron and Hertzog 2004). Our data also support a reduced processing capacity theory of aging (Craik and Byrd 1982) in that the reduced neural resources may prevent older adults from processing the cue proactively and maintaining the cue information over the delay. Additionally, it could be that attentional control deficits (Balota et al. 2000; McDowd and Shaw 2000) explain older adults' inability to selectively attend to the cue at the time it appears or maintain the expectancy created by the cue information across the delay. In a related vein, DeJong (2001) proposed that age-related deficits in cognitive control are due to an inability to select and maintain an appropriate goal, which is supported by our findings that older adults have difficulty initiating and maintaining a goal to

use a proactive strategy. Similar ideas have also been put forward by West and colleagues (for a review see West and Bowry 2005). Our current findings do not support a generalized slowing account of age-related cognitive deficits (Cerella 1985; Myerson et al. 1990; Salthouse 1996). Older adults showed differences in brain activation compared with young adults during particular trials and trial events associated with faster responses (e.g., BX-probes) than in comparable events associated with slow responses (e.g., AY trials), which is not consistent with a generalized deficit in older adults. Also, the finding that older adults do not use a proactive strategy does not directly support or refute the inhibitory deficit theory of aging (Hasher and Zacks 1988) as we would expect to see impaired performance on both AY and BX trials in older adults if an inhibition difficulty was playing a significant role in performance. In contrast, such a generalized age-related difficulty in suppressing irrelevant stimuli was observed in a recent fMRI study and was related to working memory abilities (Gazzaley et al. 2005). Still, because reactive control is a less efficient and more vulnerable form of control via its reliance on late correction of interference effects, increased utilization of reactive versus proactive control might be a behavioral reflection of impairment in inhibition or interference control.

A question arises regarding whether age-related differences in PFC activation would be related to cognitive strategy use on tasks other than the AX-CPT. If a shift to a more reactive approach is a general characteristic of cognitive aging, then such a pattern should be evident in other task domains that allow for the dissociation of proactive and reactive approaches. For instance, when young adult participants were given instructions to read the word or name the color before each trial of a Stroop task, enhanced lateral PFC activity was detected during the instruction period to name the color and correlated with reduced interference influences on task performance (MacDonald et al. 2000). These results support the theory that the DL-PFC is involved in representing and maintaining goal information needed to correctly name the color on trials, which parallels the proactive processing observed when young adults show greater lateral PFC activation at the time of the cue during the AX-CPT. Thus, the next logical question would ask whether older adults show reduced lateral PFC activity during the instruction phase of color naming trials and increased lateral PFC activity later in the trial representing more reactive processing in older adults. Hence, additional research is needed to determine whether age-related differences in proactive and reactive processing show different relationships between behavioral measures and patterns of activation.

A related question concerns the causal relationship between older adults' use of a reactive strategy and age-related changes in PFC activity. First, it could be that fixed age-related structural abnormalities in the PFC lead to impaired use of a proactive strategy and increased use of a reactive strategy in older adults. Finding a reactive pattern of brain activation in older adults suggests that age-related changes in PFC activation may be due to changes in cognitive mechanisms such as strategy use, but does not rule out that such changes may reflect, at a different level of description, a primary age-related change in brain structural integrity. Previous studies have also suggested that use of different strategies modulate age-related activation changes (Logan et al. 2002). Another explanation suggests that older adults' use of a reactive strategy develops as a result of a primary inability to use a proactive strategy effectively, which results in changes in temporal dynamics of PFC activation in older adults (i.e., increased activation at the time of the probe and decreased activation at the time of the cue). Furthermore, young and older adults may use different cognitive approaches and show different patterns of brain activation due to abnormalities in neurotransmitter function such as the dynamics of how DA is inputted with neurons.

One way to assess the relationship between the strategy used on the task and altered PFC activation is to look at plasticity effects or the degree to which behavior and brain activity can be modified by experience. After gathering evidence that older adults use a reactive strategy whereas young adults use a proactive strategy, we have become interested in determining whether these different approaches are fixed or whether they can be modified through instructed training. In a previous behavioral study, we found that older adults' performance could be modified to be more similar to that of young adults through focused proactive strategy training as well as additional practice (Paxton et al. 2006). Our next question asks whether such focused training will result in differences in the pattern of brain activation in older adults. A recent study investigating the effects of training on a working memory task showed increased PFC activation after training (Oleson et al. 2004). Thus, we are interested in determining whether the pattern of neural activation in older adults after focused strategy training will more closely resemble the proactive pattern observed in the young adults identified in Study 2.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

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Notes

Conflicts of Interest: None declared.

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