Age Differences in Deactivation: A Link to Cognitive Control?

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Abstract

■ The network of regions shown by functional imaging studies to be deactivated by experimental tasks relative to nominally more passive baselines (task < baseline) may reflect processes engaged during the resting state or ''default mode.'' Deactivation may result when attention and resources are diverted from default-mode processes toward task processes. Aging is associated with altered patterns of deactivation which may be related to declining resources, difficulties with resource allocation, or both. These possibilities predict that greater task demand, which increases deactivation levels in younger adults, should exacerbate age-related declines in allocating resources away from the default mode. The present study investigated the magnitude and temporal properties of deactivations in young and older adults during tasks that varied in their demand for cognitive control. Two versions of a verb generation task that varied in their demand for selection among competing alternatives were compared to word reading and a fixation baseline condition. Consistent with our hypothesis, greater deactivations were found with increasing demand. Young and older adults showed equivalent deactivations in the minimal selection condition. By contrast, age differences in both the magnitude and time course of deactivation increased with selection demand: Compared to young adults', older adults' deactivation response showed less sensitivity to demand. Demand-related changes in deactivation magnitude correlated with performance changes, suggesting that individual and group differences in deactivation have functional significance. ■

INTRODUCTION

Task-induced deactivations, or less activity during an experimental task than during a passive baseline condition, have become the target of much investigation (Mazoyer et al., 2001; Binder et al., 1999; Shulman et al., 1997). Such deactivations are generally thought to reflect a switch away from unconstrained ''default-mode'' processing in the passive condition (thus deactivating regions supporting the default mode) to constrained processing during the task (producing positive activation [task > baseline] of regions that support task-related processing) (Raichle et al., 2001). Older adults often have difficulty with controlled processing, with some theories emphasizing an age-related deficit in keeping thought constrained to the relevant task (West, 1996; Hasher & Zacks, 1988). Recent evidence suggests that both normal aging (Grady, Springer, Hongwanishkul, McIntosh, & Winocur, 2006; Lustig et al., 2003) and Alzheimer's disease (Lustig et al., 2003) lead to reduced deactivations, and that these responses may be delayed in pathological aging (Rombouts, Goekoop, Stam, Barkhof, & Scheltens, 2005). The parameters of these effects, however, are not yet understood. Together, these possibilities suggest a potential relationship between age reductions in deactivation magnitude and age-related declines in cognitive control (e.g., Braver & Barch, 2002). We investigate this relationship by comparing the magnitude and time course of deactivations in younger and older adults during a verb generation task that varies cognitive control by manipulating selection demands (see, e.g., Kan & Thompson-Schill, 2004, for a review).

In young adults, deactivations are typically found in a network of regions that includes the medial frontal, medial and lateral parietal, and posterior cingulate cortex (Mazoyer et al., 2001; Binder et al., 1999; Shulman et al., 1997). The components of this network are relatively stable over a wide range of tasks. This stability suggests a coherent set of processes engaged during baseline conditions (the default mode) that is not dependent on the idiosyncracies of the particular experimental task or procedure. In addition, spontaneous fluctuations of activity (during relatively passive conditions) in the regions composing this network are tightly correlated, and are anticorrelated with frontal (and other) regions typically involved in active task processing (Fox et al., 2005; Fransson, 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001). Both the stability of this network and its anticorrelation with active-task regions buttress the idea that this network

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supports default-mode processing from which participants switch away to focus on the active task. Further supporting the idea that this network is involved in default-mode processing, these regions, particularly the medial parietal/posterior cingulate components, show very high metabolism under rest conditions as measured using fluorodeoxyglucose positron emission tomography (FDG-PET; Phelps et al., 1981). Default-mode processes have not been precisely characterized, but they are thought to include attending to external environmental stimuli, monitoring one's own internal state and emotion, and autobiographical/episodic memory processing (Gusnard, Akbudak, Shulman, & Raichle, 2001; Raichle et al., 2001; Binder et al., 1999; Andreasen et al., 1995). Deactivations may occur when the participant switches from these unconstrained processes into the specific processes demanded by the active task.

Although the components of the deactivation network are stable across tasks, the magnitude of deactivation is responsive to task difficulty (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003). Specifically, increasing task difficulty by increasing factors such as stimulus presentation rate or memory load results in greater deactivation (greater distance from baseline) (McKiernan et al., 2003). Furthermore, under equivalent difficulty conditions, greater deactivations during learning are associated with successful encoding as demonstrated by subsequent memory (Daselaar, Prince, & Cabeza, 2004). These findings support the idea that deactivations reflect a reallocation of processing resources away from default-mode processing and toward the demands of the experimental task. Providing further support for this idea, experimental manipulations that reduce the ability to engage cognitive control result in reduced deactivations (Choo, Lee, Venkatraman, Sheu, & Chee, 2005; Chee & Choo, 2004).

Adult aging is thought to be associated with reduced cognitive control (see Braver & Barch, 2002), which can adversely affect the ability to constrain attention to a relevant task (e.g., Jennings & Jacoby, 1993; Hasher & Zacks, 1988). Almost all functional neuroimaging studies of aging and cognitive control have focused on age differences in the positive activation of active-task regions (see recent reviews by Rajah & D'Esposito, 2005; Reuter-Lorenz & Lustig, 2005; Buckner, 2004; Hedden & Gabrieli, 2004). However, recent evidence suggests that both healthy aging and dementia are also associated with altered deactivations of the default-mode network (Grady et al., 2006; Rombouts, Barkhof, Goekoop, Stam, & Scheltens, 2005; Lustig et al., 2003). Are age differences in deactivations linked to age differences in cognitive control?

The present report addresses this question by examining the magnitude and time course of deactivations during a task that manipulates the demand for control by varying the requirement to select among competing conceptual representations (Kan & Thompson-Schill, 2004). Participants completed a verb generation task, during which they are instructed to generate an appropriate verb in response to a visually presented noun (Persson et al., 2004; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997). Within the verb generation task, two levels of selection demand were used. In the high-selection condition, items were nouns with many appropriate associated responses (e.g., BALL—THROW, KICK, BOUNCE, etc.), but without a clear dominant response. In the low-selection condition, items were nouns with one clear dominant response, or a few associated responses (e.g., SCISSORS—CUT). The high-selection condition is presumed to place greater demands on processes involved in resolving competition between multiple possible alternatives to determine which will ultimately be given as a response. This results in an ''interference effect,'' or longer reaction times (RTs) in the high-selection condition than in the low-selection condition. In addition to the rest baseline, a read condition was used as an active-task condition with minimal selection demands. In a previous report based on a subset of the same subjects performing the same generation task, we documented age-related differences in positive (task > baseline) activation (Persson et al., 2004). In particular, older adults showed less activation in the left inferior frontal gyrus (IFG) coupled with more activation in the right IFG compared to young adults, possibly reflecting compensation.

In light of recent findings, we investigated deactivation within the same dataset (plus several additional participants), and we hypothesized that deactivation magnitudes should be larger in the high-selection demand conditions than in the low-demand conditions (cf. McKiernan et al., 2003). Also, if age differences in deactivation reflect age differences in the ability to reallocate resources, age differences in deactivation should be most evident in the high-demand conditions. We further tested the idea that deactivation is related to the reallocation of processing resources by correlating deactivation magnitude with activation in frontal regions, and with behavioral performance. Finally, exploratory analyses characterized the time course of deactivations as a function of region, age, and selection demand.

METHODS

Participants

Thirty-two young adults (15 men; age range: 18–30 years) and 28 senior adults (14 men; age range: 60–81 years) were recruited from local newspapers and posted advertisements, and completed a self-report health screening and neuropsychological tests. All participants were right-handed native English speakers who reported no existing neurological or psychiatric illness. Vision was normal or corrected to near normal using MRI-compatible glasses or contact lenses. None of the participants reported

medical conditions (e.g., high blood pressure) or medications that could affect blood-oxygen levels. Seniors' scores on the neuropsychological tests were in the normal range for this age group. Senior participants were excluded if they scored below 25 on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975). None of the participants that attended the prescanning session were excluded based on this criterion. Although one senior participant did score a 25 on the MMSE, the scores were overall high (mean = 28.6, *SD* = 1.29). All participants were paid $10–20 per hour for the experiment, and senior participants were additionally paid for their travel time to campus.

Behavioral Methods

The study consisted of two separate sessions: neuropsychological pretesting (for senior adults only) and fMRI scanning with neuropsychological posttesting. Neuropsychological testing included standardized tests such as the MMSE, the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993), and the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987) (see Table 1). The tasks used in the scanning session required participants either to generate a verb related to a visually presented noun or to simply read the noun. For each of the nouns, the participants responded by pressing a button with their right hand after they had covertly generated a single verb response in the ''generate task,'' or after they had read the noun in the ''read task.'' The nouns in each of the conditions (MANY, FEW, READ) were presented only once. Due to the nature of the task, the words used in the three conditions were different, but were of similar length (3–8 letters) and frequency (Kucera-Francis range from 0 to 591).

Table 1. Mean Scores and Standard Deviation (*SD*) for the Demographic and Neuropsychological Data

	Young	*Senior*
Demographics		
n	32	28
Age	21.7 (2.5) (18–30 years)	68.1 (5.8) (60–81 years)
Gender (M:F)	15:17	12:16
Education[a] (years)	3.0 (1.4)	3.1 (2.6)
Neuropsychological		
Fluency		
Semantic	23.3 (5.2)	18.0 (4.9)
First-letter cue	47.7 (10.9)	43.4 (12.2)
Vocabulary	53.5 (5.5)	54.9 (7.7)
Letter–number sequencing	14.4 (2.3)	11.2 (2.1)
MMSE[b]	–	28.6 (1.3)

[a]Number of years after high school.

[b]MMSE collected as a screening criterion for senior (min = 25).

The high- and low-selection conditions were blocked, and participants were not informed about this selection manipulation. They also completed a low-level baseline condition in which participants gazed at a central fixation cross. Four nouns were presented in each 16-sec block (except for REST), with each word presented for 4 sec. The study was divided into two runs, each with eight alternating sets of MANY, FEW, and READ blocks (24 blocks total), as well as four baseline blocks. Before each task block began, an instruction was placed on the screen for 2 sec (i.e., ''GENERATE'' or ''READ''). The order of the blocks was counterbalanced. Before noun presentation, a small letter ''G'' or ''R'' was displayed for 500 msec in the center of the screen to remind participants of the task at hand. Further details of the behavioral methods have been reported elsewhere (Persson et al., 2004).

In all behavioral analyses, an effect was considered significant if it reached a threshold of $p < .05$.

fMRI Methods

Images were acquired using a 3-T whole-body MRI scanner (General Electric) equipped with a standard quadrature head coil. Functional T2* blood oxygenation level-dependent (BOLD) images were acquired using a spiral sequence with 25 contiguous axial 5-mm slices (repetition time [TR] = 1500 msec, echo time [TE] = 25 msec, flip angle = 90°, and a field of view [FOV] = 24 cm). A T1-weighted gradient-echo (GRE) anatomical image was also acquired by using the same parameters and slices as were used in the functional scans (TR = 275 msec, TE = 35 msec, and flip angle 90°). In addition, a 60-slice high-resolution set of anatomical images was acquired by using spoiled gradient-recalled acquisition in steady state (SPGR) imaging (TR = 35 msec, TE = 3 msec, flip angle = 35°, and FOV = 24 cm, 2.5 mm slice thickness, 3.75 × 3.75-mm in-plane resolution). Experimental tasks were presented using E-Prime (Psychology Software Tools, Pittsburgh, PA) and the IFIS 9.0 system (MRI Devices, Waukesha, WI), and responses were collected using two 5-button glove-like response pads. Subsequent preprocessing and analyses were done using SPM99 (Wellcome Department of Cognitive Neurology, London, UK). Further details of the methods for the fMRI session have been reported elsewhere (Persson et al., 2004).

All conditions (high, low, and read) were modeled as a fixed response (box-car) waveform convolved with the hemodynamic response function. Statistical parametric maps were generated using *t* statistics to identify regions deactivated according to the model. Group data were then analyzed using a random-effects model. All reported overall deactivations passed a threshold corrected

for multiple comparisons of $p < .01$, and deactivation in the group comparisons (young vs. old) passed an uncorrected threshold of $p < .005$. Regions of interests were functionally defined on the voxels that showed peak deactivations in a comparison of the combined selection conditions (HIGH and LOW) versus resting (fixation) baseline in the current dataset, and that corresponded to typical deactivation/default-mode regions in the literature. Each region was created by including activated voxels ($p < .01$, corrected) within a 10-mm sphere around the peak voxel corresponding to default-mode regions reported in the literature. Each ROI contained a minimum of 40 contiguous voxels. Peak coordinates are presented in Table 2 (coordinates in bold are those used as seeds for the ROIs) and corresponding regions in Figure 3. They included the medial and lateral parietal cortex (LPC), the medial frontal cortex, and medial-temporal regions. For each ROI, effect sizes (% signal change) for the different conditions were then extracted for each age group separately. The effect sizes represent an average of the time points across the task blocks versus the average across the fixation blocks.

RESULTS

Behavioral Data

Reaction time data were collected for the three behavioral tasks (high, low, and read) during scanning (Figure 1). Four participants (2 seniors) were excluded from the analysis due to technical problems. An analysis of variance (ANOVA) of these data, including age group as a between-subjects variable and task condition as a within-subjects variable, indicated that the senior adults' responses were slower than those of younger adults [$F(1, 54) = 6.20, p < .05$]. The task condition main effect was also significant [$F(2, 54) = 328, p < .001$]. Paired comparisons of the task conditions indicated that response times for high and low selection were significantly different [$t(55) = 14.7, p < .001$], as were the differences between low selection and read [$t(55) = 16.7, p < .001$], and high selection and read [$t(55) = 20.4, p < .001$]. The Age by Task interaction was not significant [$F(2, 54) = 0.16, p = .85$].

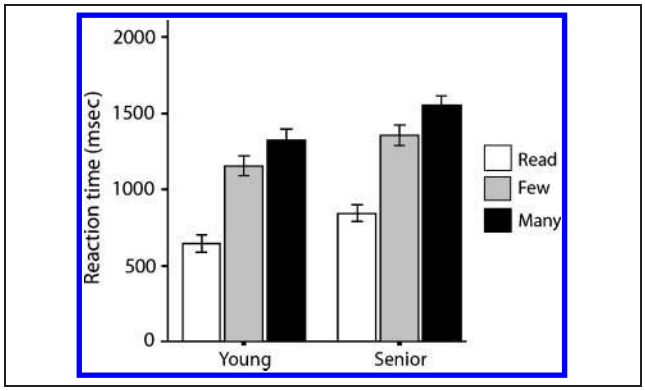

Figure 1. Mean RTs as a function of age group and task condition based on median RTs for each participant. Error bars represent standard error of the mean.

For the neuropsychological tests, senior participants performed significantly worse on the semantic fluency test [$t(56) = 3.99, p < .001$] and letter–number sequencing [$t(45) = 5.08, p < .001$]. Performance was equivalent for senior and young adults in WAIS-III Vocabulary [$t(55) = 0.81, p = .42$] and first-letter fluency [$t(56) = 1.42, p = .16$]. Education level was also equivalent [$t(51) = 0.58, p = .89$].

Table 2. Talairach Coordinates for Areas that Show Maximal Deactivation ($p < .01$, Corrected for Multiple Comparisons)

Anatomical Localization	*BA*	*x*	*y*	*z*	*Z*
R precuneus	**7**	**11**	**−57**	**30**	**14.70**
R lateral parietal	**39**	**49**	**−61**	**17**	**14.30**
L precuneus	**30**	**−15**	**−68**	**26**	**13.31**
L precuneus	31	−11	−52	49	12.10
R precuneus	31	11	−52	49	12.07
L posterior cingulate	31	−15	−35	39	11.49
L superior temporal	22	−41	−22	0	10.95
R superior frontal gyrus	6/8	22	22	55	9.01
R medial temporal		**30**	**−45**	**−5**	**7.85**
L inferior parietal	40	−59	−28	29	7.47
R medial frontal	**9/10**	**11**	**49**	**21**	**7.14**

L = left; R = right; BA = Brodmann's area; *x*, *y*, *z* = stereotactic coordinates. The regions in **bold** were selected for ROI analyses.

fMRI Results

To investigate deactivation related to task selection based on the two age groups combined, we contrasted the rest baseline with the verb generation conditions (high and low selection combined). The results from this contrast are presented in Figure 2 and Table 2. Consistent with previous findings (e.g., McKiernan et al., 2003; Mazoyer et al., 2001), task-induced deactivations were found in multiple cortical regions including a medial prefrontal region (PFC; Brodmann's area [BA] 9/10), bilateral medial parietal regions (posterior cingulate cortex [PCC]; BA 30/31), the precuneus (BA 7), and a right lateral temporo-parietal region (BA 39). Consistent with some previous findings (e.g., Greicius, Srivastava, Reiss, & Menon, 2004), we also found deactivation in a region of the medial-temporal lobe (MTL). Based on this whole-brain analysis (baseline > verb generate), five regions were functionally determined using Marsbar (http://marsbar.sourceforge.net). These regions have typically been associated with task-induced deactivations

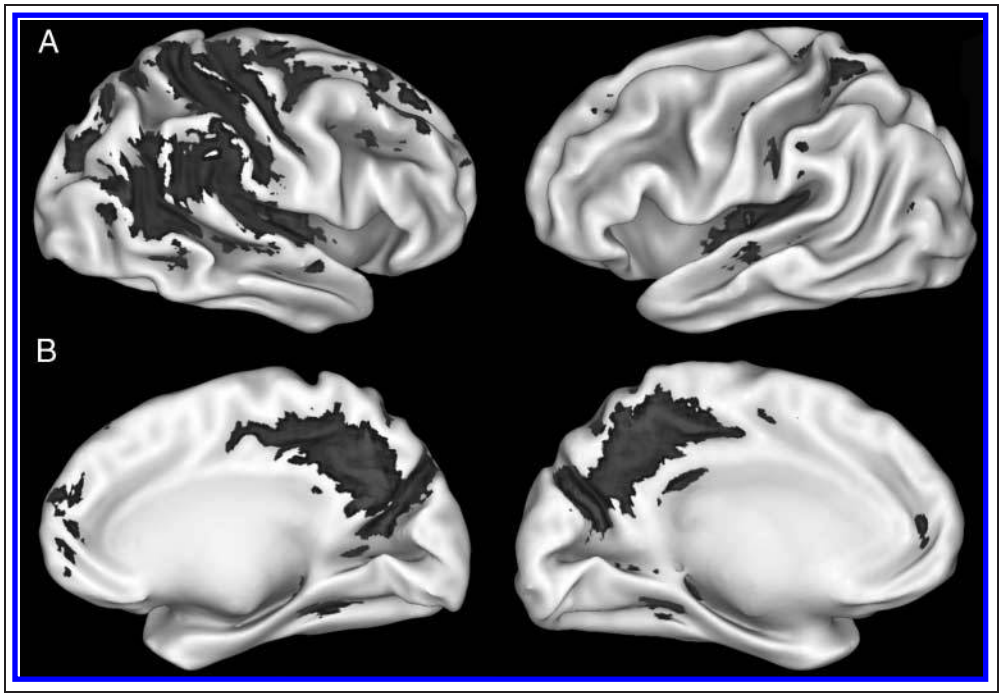

Figure 2. Statistical activation map for deactivations (baseline > verb generation; corrected threshold at $p < .01$) across all subjects.

(Mazoyer et al., 2001; Binder et al., 1999; Shulman et al., 1997), and were selected for additional ROI analyses. For all subsequent ROI analyses, we focused on these five regions (Figure 3).

ROI Analyses

The primary objective for the ROI analyses was to investigate age-related differences in magnitude and temporal properties in regions associated with the default-mode network. A critical feature of these analyses was to investigate whether age-related differences in deactivation varied as a function of task demand. Separate Group (young, senior) by Condition (read, few, many) ANOVAs were performed for each of the ROIs. In the analysis of deactivation magnitude for the medial frontal region (Figure 3A), there was a main effect of condition [$F(2, 54) = 29.6$, $p < .001$)]. Deactivation became greater (task − baseline values became more negative) as a function of task demand. The Condition × Age interaction was also significant [$F(2, 54) = 4.33$, $p < .05$)], indicating that age differences in deactivation magnitude changed as a function of demand. Follow-up analyses showed that young participants had greater deactivation than seniors in the MANY condition [high-selection demand: $t(54) = 2.40$, $p < .05$], whereas deactivations for the FEW condition [low selection demand: $t(54) = 0.776$, $p = .441$] and the read condition [$t(54) = 0.769$, $p = .445$] were nonsignificant. These results suggest that as processing demand increases, the magnitude of medial prefrontal deactivation in this region increases accordingly. Moreover, age differences emerge when higher levels of selection are required.

The same pattern was evident for the right LPC (Figure 3B). The main effect for condition [$F(2, 54) = 44.97$, $p < .001$], and the Task × Age interaction [$F(2, 54) = 3.76$, $p < .05$] were both significant. The deactivation was greater during more demanding task conditions; older adults showed less deactivation than young adults in the high-selection condition [$t(54) = 2.85$, $p < .01$], but not in the low-selection or read conditions [$t(54) = .487$, $p = .628$; $t(54) = .003$, $p = .998$].

Data for the left PCC (Figure 3C) yielded a significant Condition × Age interaction [$F(2, 54) = 4.03$, $p < .05$]. The main effects for condition and age were not significant. In contrast to the observation of greater deactivation for more demanding conditions in young participants, senior participants did not show variations due to task demand. In line with the findings for the medial PFC region and the lateral parietal region, age differences were found in the most demanding condition [$t(54) = 2.26$, $p < .05$], but not in the condition with low-selection demands [$t(54) = 1.28$, $p = .203$] or the read condition [$t(54) = 0.017$, $p = .986$].

In the analysis of the magnitude of deactivation in the right PCC (Figure 3D), the main effect of condition was significant [$F(2, 54) = 15.9$, $p < .001$]. The main effect of age was not significant, and the Condition × Age interaction showed a trend [$F(2, 54) = 2.71$, $p < .071$] indicating that the age differences were exacerbated with increasing selection demand. Once again, a significant group difference was present for the high-selection condition [$t(54) = 1.73$, $p < .05$], whereas neither the low-selection [$t(54) = 0.318$, $p = .751$] nor the read condition [$t(54) = 0.048$, $p = .962$] differed between groups.

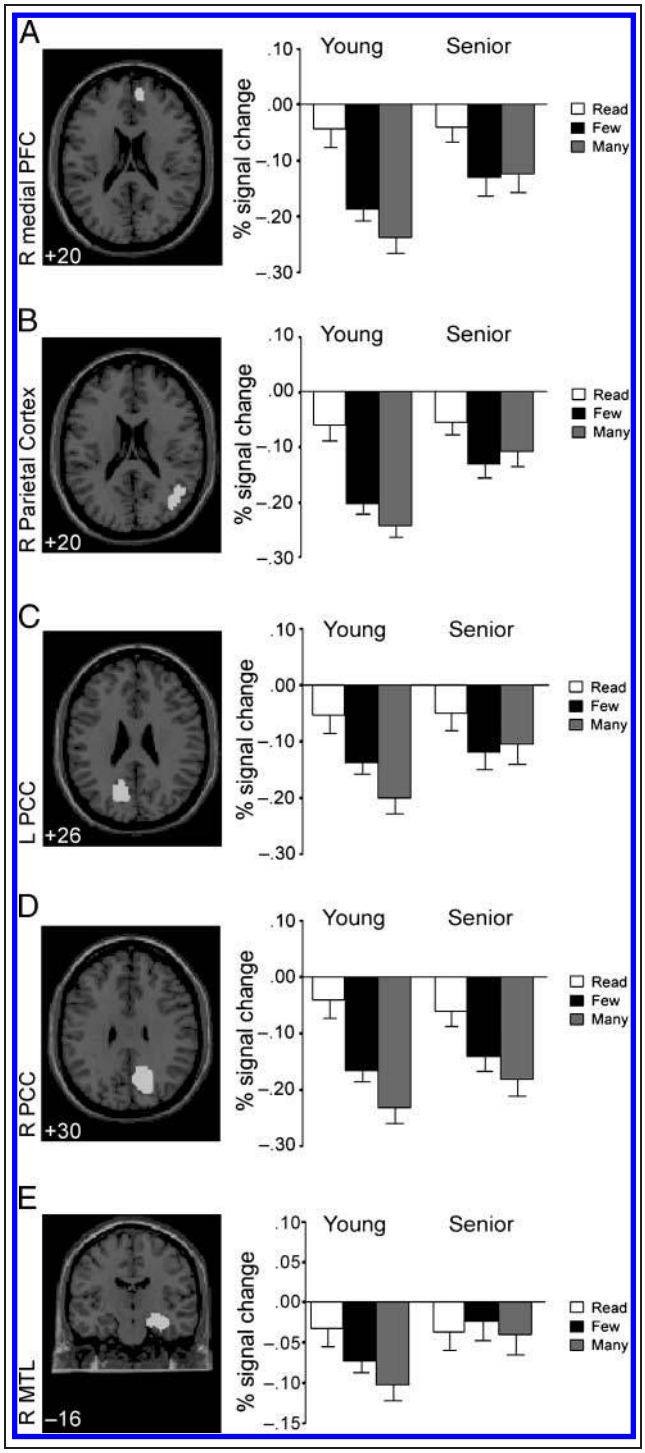

Figure 3. Transverse sections depict the location of the areas used for the ROI analyses. Bar graphs represent the average percent signal change for young and senior participants for each of the conditions (READ, FEW, MANY) compared to a rest baseline. Error bars represent standard error of the mean.

The results for the right MTL region (Figure 3E) showed a significant Condition × Age interaction [$F(2, 54) = 5.93, p < .01$]. The main effects for condition and age were not significant. Also, the group difference for neither the selection condition nor the read condition were significant. The Condition by Age interaction suggests that although younger individuals show more deactivation in more demanding selection conditions, older individuals show similar levels of deactivation across selection demands.

Time Course Analyses

Although time course analyses are most frequently performed for event-related designs, they can also be informative about temporal properties in block designs (Fox, Snyder, Barch, Gusnard, & Raichle, 2005; Konishi, Donaldson, & Buckner, 2001; Friston, Frith, Turner, & Frackowiak, 1995). Konishi et al. suggested that effects linked to the transition between baseline and task blocks could reflect updating or changing the behavioral mode (i.e., ''task set''), or alternatively might reflect competition between brain regions (and their respective cognitive processes) to control performance during the task. Either of these possibilities would require cognitive control in order to activate the appropriate task processes or to inhibit inappropriate ones. Lustig et al. (2003) noted qualitative variations in the temporal profile of deactivations as a function of region (medial prefrontal, lateral parietal, or posterior cingulate/medial parietal) and group (young, old, or Alzheimer's), but did not conduct formal analyses (see also Rombouts, Goekoop, et al., 2005, for a comparison of early vs. late phases of the BOLD response in an event-related analysis of data from healthy older adults, mildly cognitively impaired older adults, and Alzheimer's patients).

We investigated age differences in the magnitude and shape of the time courses for each of the ROIs (Figure 4). An analysis of the time courses for the low-selection condition (FEW) revealed a significant Time × Group interaction for the medial PFC [Figure 4A; $F(18, 54) = 2.25, p < .05$]. For the high-selection condition (MANY), a similar pattern was evident for the medial PFC [Figure 4A; $F(18, 54) = 2.49, p < .01$], the right LPC [Figure 4B; $F(18, 54) = 7.29, p < .001$], and the left PCC [Figure 4C; $F(18, 54) = 2.72, p < .001$]. No Time × Group difference was found for the visual cortex (BA 17; data not shown) in either the high- or low-selection condition, suggesting that the differences in time courses for the default-mode regions are not related to general aspects of changes in the hemodynamic response that occur with age. The significant interaction between time and age indicates that the time course of the response in that region had a different shape for young compared to senior participants. In addition to the findings of less deactivation for senior adults, inspection of Figure 4 suggests that there is a slight delay in deactivation for senior adults compared to young adults.

In order to investigate possible age and condition differences in positive activation–deactivation dynamics, we also plotted activation time courses from the right IFG (BA 45/46; $x, y, z = 41, 15, 5$) region that was associated

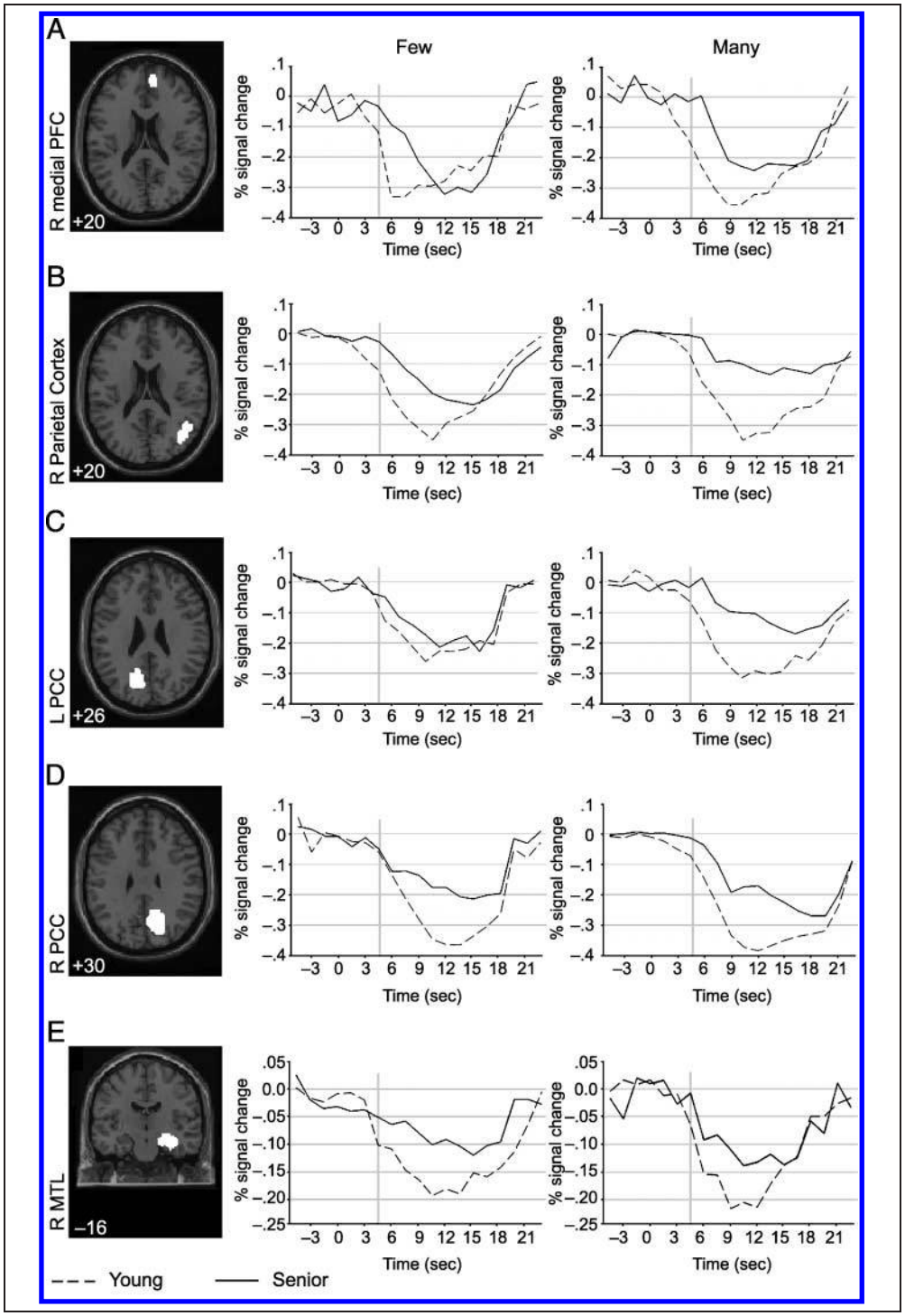

Figure 4. Transverse sections depict the location of the areas used for the ROI analyses. The graphs represent time courses for each of the verb generate conditions (FEW, MANY).

with age differences in activation in our previous analyses of the positive activations on this dataset (Persson et al., 2004), together with deactivation time courses for the two medial PCC regions (Figure 5). Visual inspection of these time courses revealed only small age differences in the low-selection condition, with the peak of activation occurring before the peak of deactivation. Although young adults maintain this pattern in the high-selection demand condition, older adults show a more extended frontal activation with a later peak. Power at this sample size does not allow for strong statements about whether this age difference interacts with selection difficulty. However, the more consistent findings of age differences in deactivation in the high-selection condition than in the low-selection condition are suggestive in this regard.

We also asked whether deactivations in our ROIs might be related to positive activations in regions that

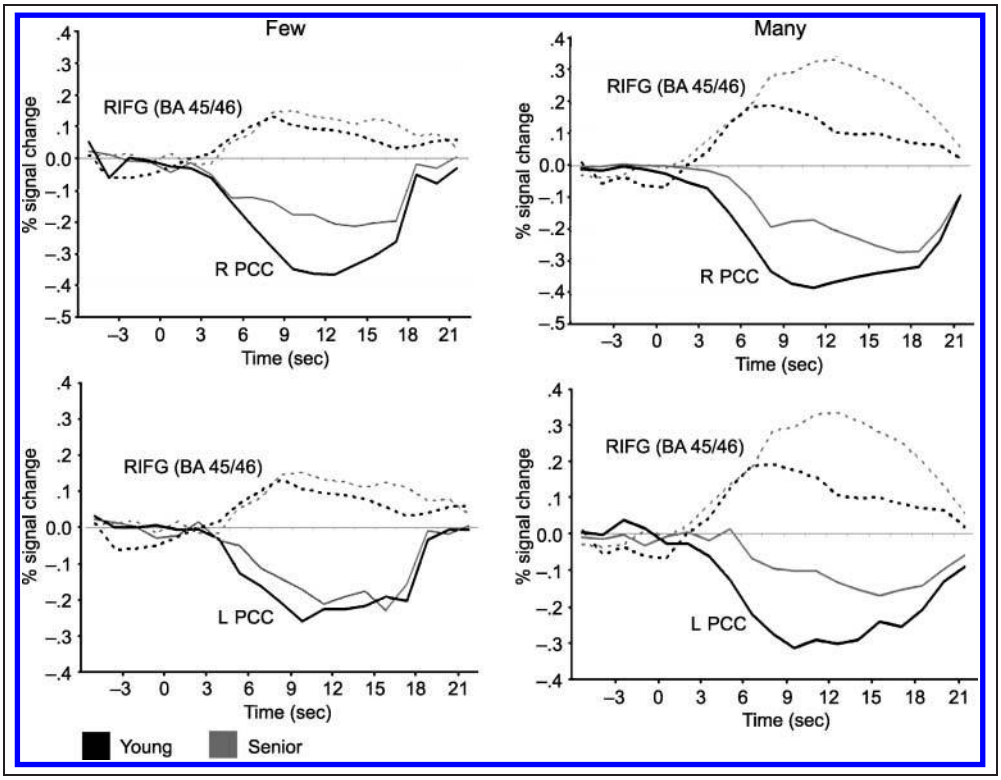

Figure 5. The graphs represent time courses for each of the high- and low-selection conditions for the right IFG region together with the medial PCC regions for each age group.

are typically associated with cognitive control. To test this hypothesis, we examined potential correlations between the deactivation ROIs used here and a region in the left IFG (BA 45/46; $x, y, z = -49, 26, 15$) that showed positive activation in the analysis by Persson et al. (2004), and a region in the right IFG (BA 45/46; $x, y, z = 41, 15, 5$) that showed an age-related increase in that analysis. Neither of these regions correlated with any of the deactivation ROIs.

Correlation Analyses of Behavioral Data

Do individual differences in deactivation correspond to individual differences in behavior? The right PCC showed a significant correlation ($r = .40$, $p < .01$) between changes in deactivation magnitude and changes in response time between the high- and low-selection conditions (Figure 6). Those participants who showed the *smallest* difference in deactivation magnitude between the high- and low-selection conditions were those who showed the *largest* interference effects, as reflected by longer response time. This pattern is consistent with the idea that deactivation magnitudes correspond with an individual's response to demands for selection or resolving interference.

Whole-brain Analyses

Although ROI analyses allow the rigor of a priori hypothesis testing and increased sensitivity, they run the risk of missing effects elsewhere in the brain. We therefore conducted exploratory whole-brain analyses to confirm and extend the a priori ROI analyses. To display the effects of age at each level of task difficulty, we conducted three separate Group (young vs. old) × Condition (active task vs. fixation baseline) voxelwise ANOVAs, one for each level of demand (Figure 7).

For each of these analyses, we distinguished between regions showing more deactivation by young adults versus those showing more positive activation by older adults. Consistent with the ROI analyses, age differences in deactivation magnitude were most apparent in the

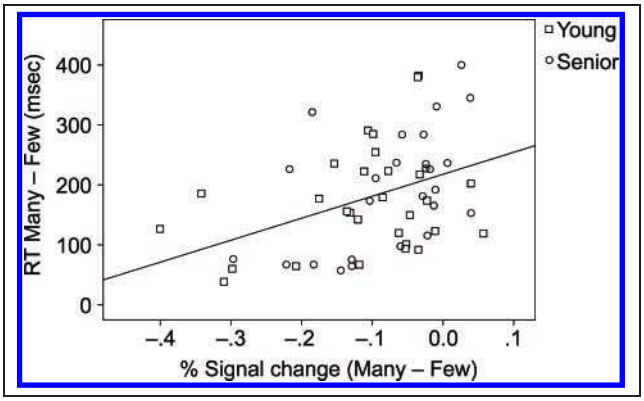

Figure 6. Correlation between the behavioral interference effect (MANY vs. FEW) and the magnitude of interference in deactivation (MANY vs. FEW) in the right PCC.

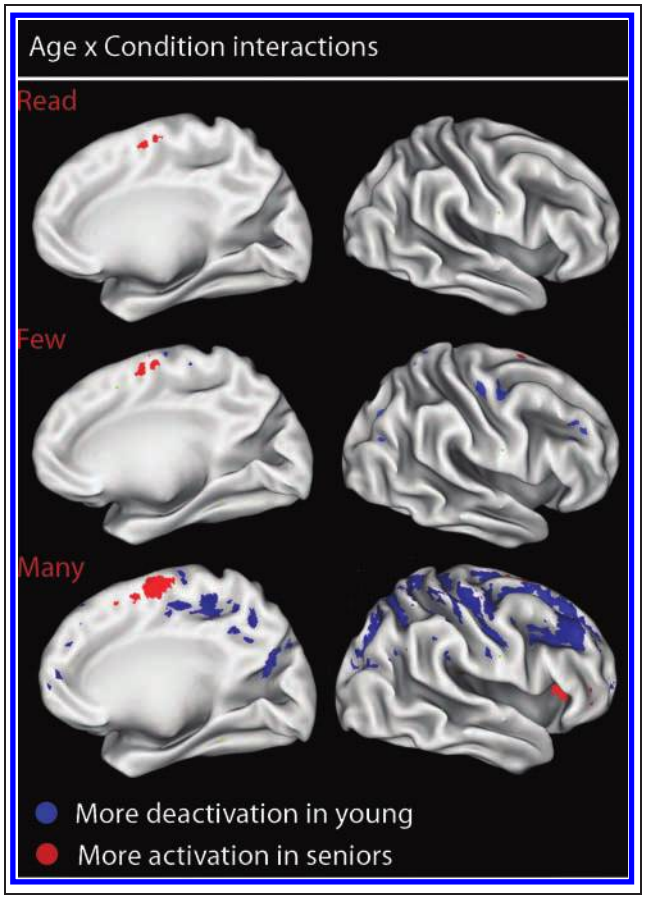

Figure 7. Map of statistically significant group differences across the brain for each of the conditions (i.e., baseline > read/few/many). Each interaction was masked by an overall contrast to indicate the direction of effects.

high-selection condition. Regions showing age differences in deactivation included the postcentral sulcus, the medial PFC, the LPC, and the PCC (Figure 7). Age differences in deactivation magnitude are unlikely to reflect a simple lack of responsiveness by older adult brains: Older adults show greater positive activations than do young adults in a medial dorsal frontal region (SMA; BA 6) and right IFG (BA 45/46). The age difference in the right IFG was specific to the high-selection condition (see also Figure 5), also discounting a generic ''positive bias'' account of age differences in activation and deactivation.

DISCUSSION

Several significant findings emerged from these results. First, age differences in deactivation were not present in an active task with minimal selection demands, and overall deactivations were small in this condition. Both overall deactivation magnitude and the size of age differences in deactivation became greater as a function of the demand for cognitive control (specifically, selection between competing alternatives). Additionally, inspection of the time courses suggested that deactivations are not only reduced in magnitude but also slower for older adults than for young adults under high control demand conditions, suggesting a slower reallocation of attention or resources. Furthermore, control-related changes in deactivation in the right PCC correlated with control-related changes in performance. To our knowledge, this is the first report of individual-level correlations between deactivation change and performance change, and it provides support for the idea that deactivations have functional significance.

The most likely explanation for deactivation-performance links is that deactivations reflect a diversion of attention away from so-called default mode processes and toward the experimental task. Spontaneous (non-task-related) activity in regions associated with task-induced deactivations and default-mode processing correlates negatively with spontaneous activity in regions associated with task-induced positive activations, suggesting the existence of two competing networks (Fox et al., 2005). Other manipulations of difficulty (target discriminability, stimulus presentation rate, and short-term memory load) also lead to changes in deactivation magnitude similar to those seen here (McKiernan et al., 2003). Greater deactivations at encoding are related to subsequent memory, again suggesting a reallocation of attentional resources away from default mode processes and toward learning and memory (Daselaar et al., 2004). The group- and individual-differences level data reported here converge with the network-level, task-level, and item-level findings to suggest that deactivations reflect important processes related to cognitive control.

Difficulties with cognitive control are a major feature of cognitive aging, but only a few prior studies have specifically examined the effects of aging on default mode functioning (Rombouts, Barkhof, et al., 2005; Lustig et al., 2003). Although the specifics differ between these studies and ours (e.g., by including Alzheimer's disease patients), the overall pattern of age-related changes in deactivation magnitude is generally consistent with the current findings. For example, the observation of reduced medial parietal and frontal deactivations in older adults found here during a verb generation task replicates and extends previous findings of age differences using a semantic classification task (Lustig et al., 2003). These regions also show alterations in individuals with mild cognitive impairment (Rombouts, Barkhof, et al., 2005) and Alzheimer's disease (Rombouts, Barkhof, et al., 2005; Lustig et al., 2003), suggesting a relation between disruption of the default-mode network and dementia severity. However, reduced deactivations are likely a characteristic of normal aging as well as dementia, as recent work suggests that a reduction in deactivation magnitude is apparent even in middle age (Grady et al., 2006). An important question for future work is whether age differences in deactivation interact with the

type as well as the level of task demands; the selection demands of the verb generation task revealed age differences in lateral parietal deactivation that were not found in previous studies focusing on memory encoding and retrieval (Grady et al., 2006; Lustig et al., 2003).

The Age by Condition interactions represent an advance over previous studies because they links age differences in deactivation magnitude to increased demand for cognitive control, rather than to more general age differences in the hemodynamic response implied by main effects for age (see, e.g., Johnson, Mitchell, Raye, & Greene, 2004; Buckner, Snyder, Sanders, Raichle, & Morris, 2000 for other examples of Age by Condition interaction logic). Young and old adults were remarkably similar during low-demand conditions. Age differences were only strongly revealed when demand was relatively high. The control demand specificity of age differences in deactivation magnitude supports the idea that they reflect age differences in the cognitive control required to divert attention away from task-irrelevant default-mode processing.

The failure to find Age by Condition interactions in performance might at first seem to argue against this conclusion. Indeed, the possibility exists that reduced deactivations by older adults in the high demand conditions may even reflect a form of compensation, as age differences in *positive* activation in the absence of behavioral age differences are often interpreted as compensatory (e.g., Cabeza, Anderson, Locantore, & McIntosh, 2002; Reuter-Lorenz et al., 2000; Grady et al., 1994). However, correlations with performance provide evidence against the compensation explanation of reduced deactivations. The inverse relationship between deactivation in the right PCC and interference scores (many − few difference) indicates that, at a particular level of task complexity, greater deactivation may be related to more efficient task performance.

Given that only a few studies have examined age differences in deactivation, it is too early to rule out a possible compensatory role. However, we speculatively propose the opposite hypothesis: Failures to divert attention or resources away from default-mode processing (as reflected by slower and reduced deactivations) may, in fact, be part of what older adults are compensating *for* (as reflected by increased or additional frontal activations). Spared performance may result when older adults recruit additional (prefrontal) regions to compensate for lingering default-mode processes during the experimental task (see Rombouts, Barkhof, et al., 2005 for a more extreme version of this pattern in Alzheimer's disease patients).

The hypothesis that increased frontal activations may reflect compensation for failures to divert attention from or inhibit default-mode processes receives tentative but convergent support from several recent findings. Mirroring the control-demand specificity of age differences in deactivation magnitude and time course found here, Velanova et al. (2007) recently reported that extended positive activation in the right IFG for older adults was specific to a high control-demand retrieval condition, and did not occur under low-demand conditions. Within the current dataset, greater right IFG activation was found for seniors compared to young adults in the high-selection condition (Persson et al., 2004). Comparison of time courses for right IFG and medial PCC regions across conditions (Figure 5) reveals a similar time course of frontal activation for young and old adults in the low-selection demand condition, replicating Velanova et al., and for both age groups, the peak of frontal activation occurs before the point of greatest deactivation. Young adults maintain this pattern in the high-selection demand condition, but older adults show a more extended frontal activation with a later peak, which may be related to their slower deactivation time course. Of interest, aging is not the only condition that is associated with disruptions in cognitive control and its neuroimaging correlates, including deactivations: Some parallels exist between the present results and those found due to sleep deprivation (Chee & Choo, 2004). Although this area of research is relatively new, the findings seem to converge on the hypothesis that successful task execution results from a coordinated pattern of activation in task-relevant areas and deactivation of task-irrelevant ones.

Given the increased RT with task difficulty, one alternative explanation for the findings of greater deactivation in conditions with high demands for cognitive control is increased time on task. RTs and demands for cognitive control are typically tightly linked, making it difficult to rule out this explanation at all levels of analysis. However, it is unlikely to apply as a general principle. First, a simple time-on-task account of deactivations would have difficulty explaining why older adults showed similar changes in RT across conditions as did young adults, but not similar changes in deactivation magnitude. Second, overall older adults had longer RTs than did young adults (spent more time on task), but had smaller deactivations. Furthermore, a time-on-task account would predict that even within an age group, the fastest subjects should show the smallest deactivations. Our results trended in the opposite direction (data not shown). Finally, a comparison of the conditions in which young and older adults were matched on response time (young − many versus old − few) results in *larger* age differences in deactivation magnitude. Taken together, these patterns make it very difficult to support an account whereby greater deactivations represent generic effects of greater difficulty or greater time on task. Instead, we suggest that greater deactivations represent greater responsiveness to cognitive control demands—here instantiated as a demand on selection processes.

In conclusion, these findings suggest that advanced age alters the functional properties of task-induced

deactivations, and that age-related differences are most pronounced in conditions with greater demand for cognitive control. Observations of an inverse relationship between deactivation in specific regions and interference suggest that deactivations may be related to the degree of cognitive efficiency. Reduced deactivation for older adults in high-control conditions may indicate a reduction in cognitive efficiency stemming from difficulty disengaging from or inhibiting internal processes in order to reallocate attention to the task at hand.

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