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Under-Recruitment and Nonselective Recruitment: Dissociable Neural Mechanisms Associated with Aging

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Summary

Frontal contributions to cognitive decline in aging were explored using functional MRI. Frontal regions active in younger adults during self-initiated (intentional) memory encoding were under-recruited in older adults. Older adults showed less activity in anterior-ventral regions associated with controlled use of semantic information. Under-recruitment was reversed by requiring semantic elaboration suggesting it stemmed from difficulty in spontaneous recruitment of available frontal resources. In addition, older adults recruited multiple frontal regions in a nonselective manner for both verbal and nonverbal materials. Lack of selectivity was not reversed during semantically directed encoding even when under-recruitment was diminished. These findings suggest two separate forms of age-associated change in frontal cortex: under-recruitment and nonselective recruitment. The former is reversible and potentially amenable to cognitive training; the latter may reflect a less malleable change associated with cognitive decline in advanced aging.

Introduction

Cognitive difficulties, including those involving memory, are a common complaint of older adults. In laboratory settings, older adults routinely perform worse than younger adults on a variety of tasks that tap episodic memory and place demands on controlled, effortful processing (Kausler et al., 1988; Nyberg et al., 1996; Park et al., 1996). Age-associated cognitive decline has been attributed, in part, to structural and functional changes in the prefrontal cortex (e.g., Dempster, 1992; Moscovitch and Winocur, 1995; Stuss et al., 1996; West, 1996; for review, see Greenwood, 2000). Several findings support this attribution. Older adults show volumetric reduction in frontal cortex that is proportionately larger than in some other brain regions (Raz et al., 1997; for review, see Raz, 2000). Cognitive difficulties in older adults present as mild variants of impairments observed after frontal damage (Dempster, 1992; Moscovitch and Winocur, 1995; Stuss et al., 1996; West, 1996). Finally, when younger adults perform multiple tasks simultaneously (e.g., divided attention), frontal activity is attenuated and task performance becomes impaired paralleling that observed in older adults under full attention conditions (Fletcher et al., 1998; Iidaka et al., 2000; Shallice et al., 1994). Here we explore mechanisms that may underlie age-associated cognitive decline using functional MRI (fMRI) focusing on the role of frontal cortex in episodic memory encoding.

Prior imaging studies have suggested that older adults often fail to recruit specific frontal regions during memory encoding to the same extent as younger adults, in particular during intentional encoding where effective encoding strategies must be spontaneously initiated (e.g., Anderson, et al., 2000; Cabeza et al., 1997; Grady et al., 1995, 1999; Madden et al., 1999b; for review, see Grady and Craik, 2000). For instance, using PET, Grady and colleagues (1995) observed that older adults did not significantly activate left frontal regions activated in younger adults during an intentional encoding task involving faces. In addition, Cabeza and colleagues (1997), exploring intentional encoding of verbal materials using PET, found that left prefrontal and occipitotemporal regions were more active during encoding for younger adults than older adults. Attenuated activity in frontal regions may partly underlie age-related cognitive decline (Anderson et al., 2000; Cabeza et al., 1997; Grady and Craik, 2000; Grady et al., 1995, 1999; Iidaka et al., 2001; Madden et al., 1999b; Reuter-Lorenz et al., 2000; Rypma and D'Esposito, 2000).

In addition to less activation in regions associated with successful episodic encoding, several studies have reported, somewhat paradoxically, that older adults activate certain frontal regions during encoding more than younger adults. This effect has been observed in a variety of tasks requiring controlled, effortful (executive) processes, including studies of verbal and spatial working memory (Reuter-Lorenz et al., 2000), verbal encoding (Anderson et al., 2000; Cabeza et al., 1997; Madden et al., 1999b), and episodic retrieval (e.g., see Cabeza et al., 1997; Bäckman et al., 1997; Madden et al., 1999b; Schacter et al., 1996) (for review see Cabeza, 2002; Reuter-Lorenz et al., 2001; Park et al., 2001). For example, Cabeza et al. (1997) demonstrated that older adults showed less activity (relative to young adults) in some frontal regions and also *more* activity in other regions, including bilateral insular cortex.

Several distinct mechanisms could underlie the complex patterns of data discussed above. Models of age-associated cognitive decline have distinguished between resources that are no longer available (absent) and those that are available but not spontaneously engaged, referring to the latter situation as a "production deficiency" (e.g., Craik and Byrd, 1982). Attenuated frontal cortex activation could be related to either of these two possibilities. The central idea of an *absence* hypothesis is that aging is associated with an irreversible loss of frontal (executive) resources that leads to cognitive decline, perhaps due to atrophy or other changes at the

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cellular level. A second possibility is an *under-recruitment* hypothesis, namely that available frontal resources are present but, under certain conditions, are inadequately recruited (see also Gershberg and Shimamura, 1995).

Under-recruitment might occur if age-related decreases in the level of frontal activity emerge *only under specific conditions*. That is, unlike a decrease resulting from an irreversible absence or reduction in available resources, under-recruitment would manifest as a context-dependent decrease that could be reversed in task conditions that encourage older adults to exploit all available resources. Evidence that context-dependent under-recruitment is a plausible possibility comes from studies which have shown that, during attentionally demanding tasks, older adults benefit from cues or other explicit instructions on task strategies (Craik, 1977; Craik and Simon, 1980; Park et al., 1990). External presentation of task strategies and cues is referred to as *environmental support*. In the present studies, we test between absence and recruitment hypotheses by exploring whether diminished activation can be ameliorated during tasks that provide considerable environmental support for encoding.

A second form of inappropriate recruitment might exist and relate to the activity increases that have been observed in older adults. *Nonselective* recruitment might occur if multiple frontal regions are recruited but in a manner atypical of healthy, younger adult task performance (see Cabeza, 2002; Reuter-Lorenz et al., 2001). In the present studies, the level of nonselective recruitment in older adults during tasks promoting verbal and nonverbal encoding is explored, as well as the degree to which nonselective recruitment relates to activation decreases. One possibility is that nonselective recruitment is directly associated with attenuated activation: to the degree appropriate regions are less accessible (either because of absence or recruitment mechanisms), nonselective recruitment may occur, perhaps as a form of compensation (see Reuter-Lorenz et al., 2001 for discussion). Alternatively, nonselective recruitment may be characteristic of aging independent of attenuated activation responses. In the present studies, the association between decreased activation in frontal cortex and nonselective recruitment is explored by determining whether they track each other across multiple encoding conditions and across different older adult age groups.

Several findings regarding the specific frontal regions associated with effective memory encoding in younger adults provide a basis for the present studies. Brain imaging studies in younger adults have suggested at least three specific frontal regions that are involved in episodic memory encoding (Demb et al., 1995; Fletcher et al., 1998; Kapur et al., 1994, 1996; Kelley et al., 1998; McDermott et al., 1999; Wagner et al., 1998a, 1998b; see also Buckner, 1996; Petersen et al., 1988; Poldrack et al., 1999). Verbal encoding associates with two functionally dissociated frontal regions along left inferior frontal gyrus, including a posterior-dorsal region near Brodmann areas (BA) 6/44 and a second anterior-ventral region near BA 45/47. Activation of left BA 45/47 has been particularly associated with semantic (meaning-based) elaboration on verbal information, a process known to promote encoding (Buckner et al., 1999; Demb et al., 1995; Kapur et al. 1996; Petersen et al., 1988; Poldrack et al., 1999). Nonverbal encoding often additionally associates with a third right-lateralized frontal region homologous to left BA 6/44 (Kelley et al., 1998; McDermott et al., 1999; Wagner et al., 1998a). Moreover, studies examining encoding on a trial-by-trial basis demonstrate that activity within left BA 6/44 and 45/47 predicts successful word encoding whereas activation of right BA 6/44 predicts successful encoding of pictorial stimuli (Wagner et al., 1998a; Brewer et al., 1998; Kirchhoff et al., 2000; Buckner et al., 2001; Otten et al., 2001; Baker et al., 2001). Because of their consistent association with episodic memory encoding in younger adults, these three regions (labeled L BA 6/44, R BA 6/44, and L BA 45/47) were selected for hypothesis-directed analyses in the present studies.

The current studies investigate the mechanisms underlying age-related changes in neural correlates of episodic encoding. Emphasis is placed on the specific frontal regions, mentioned above, that are consistently associated with successful episodic encoding in younger adults. In Experiment one, younger and older adults intentionally memorized words and faces. Experiment two examined whether age effects in frontal resource recruitment observed in Experiment one could be ameliorated by providing subjects with environmental support at encoding, e.g., by giving them an effective encoding strategy of meaning-based (semantic) elaboration.

Results

Experiment One

Behavioral Results

Corrected recognition rates were computed as hits (responding "old" to a previously studied item) minus false alarms (responding "old" to an unstudied item). Mean corrected recognition performance for word encoding was 86.2% in young and 67.2% in older adults, $t(24) = 1.96$, $p = .06$. Recognition performance for face encoding was 82.3% in young and 38.4% in older adults, $t(24) = 3.99$, $p < .005$. Using corrected recognition, older adults showed poorer memory performance than younger adults, $F(1, 24) = 11.59$, $MSE = 1102.96$, $p < .005$. Memory performance was better overall in word than face encoding, $F(1, 24) = 12.00$, $MSE = 287.80$, $p < .005$. There was also an age group x encoding task interaction, $F(1, 24) = 6.95$, $MSE = 287.80$, $p < .05$, such that older adults were differentially impaired in face compared to word encoding. The poor memory scores for face encoding may be due, in part, to differences in visual acuity between the groups as older adults, almost always, required magnet-compatible corrective lenses. For this reason, we do not interpret strongly the disproportionate impairment of older adults for face recognition in the context of the functional imaging results.

Neuropsychogical test results are summarized for the older adults in Table 1. For reference, while neuropsychological test results were not obtained for younger adults in this study, it should be noted that the young older adults performed *similarly* to young adult normative data with two exceptions. Our older adults performed exceptionally well on the information test compared to previously published data for young adults and

Table 1. Neuropsychological Test Scores for Older Adults by Experiment and Age

	Experiment 1[a]	Experiment 2[b]	<73 years old[c]	>73 years old[d]
	M (SD)	M (SD)	M (SD)	M (SD)
Mental control	7.5 (1.7)	7.2 (2.4)	**8.5 (1.1)	**6.1 (2.1)
Digit span (combined)	12.3 (2.0)	12.3 (2.4)	12.3 (1.9)	12.3 (2.5)
Associate memory (recall)	16.9 (3.3)	16.8 (4.3)	17.1 (3.5)	16.5 (4.0)
Trailmaking A (in s)	37.5 (8.2)	33.7 (9.3)	35.9 (7.6)	36.0 (10.1)
Trailmaking B (in s)	75.6 (21.7)	67.6 (34.0)	**62.1 (21.2)	**84.3 (29.2)
WAIS information	22.7 (2.5)	21.1 (4.0)	22.4 (2.7)	21.6 (3.9)
Block design	32.3 (8.0)	34.4 (9.0)	33.9 (8.2)	32.4 (8.7)
Digit symbol	49.7 (7.2)	54.4 (7.7)	53.9 (7.6)	49.0 (7.0)
Boston naming	57.1 (4.4)	57.6 (2.5)	58.1 (2.1)	56.3 (4.8)
Word fluency (S + P)	35.4 (12.9)	36.7 (7.2)	35.9 (8.0)	35.9 (13.7)

Note: experiments 1 and 2 are mean scores from all available subjects in each study. <73 and >73 represent the same data but combining both studies and separating subjects by age (corresponding to functional analyses in Figures 4 and 5).

[a]N = 14; [b]N = 10; [c]N = 13; [d]N = 11; **significant difference, $p < .05$, two-tailed t test between young-old and old-old.

even previously published norms for older adults (e.g., Hulicka, 1966; Zagar et al., 1984). This may reflect the careful screening for any signs of dementia as well as the tendency for our older adults to be highly educated. Second, the older adults performed slower than is typical for young adults (on Trail Making A and Trail Making B), a phenomenon consistent with the large literature on cognitive slowing in the elderly (Myerson et al., 1990; Salthouse, 1996) and prior norms for the Trial Making tests. In general, the neuropsychological data were consistent with a sample of well-educated, healthy older adults.

fMRI Results

Activity levels in the three a priori defined frontal regions were explored by comparing younger to older adults for both the verbal (words) and nonverbal (unfamiliar faces) intentional encoding tasks. Two specific hypotheses were explored. First, we explored whether older adults would show under-recruitment in frontal regions typically recruited by younger adults during encoding. In particular, the anterior-ventral region in left frontal cortex (near BA 45/47) has been most consistently associated with meaning-based elaboration and effective encoding strategies (Buckner et al., 1999; Kapur et al., 1996). Would older adults appropriately recruit this region under intentional encoding conditions when they must self-initiate their own strategies? Second, we explored whether older adults would show nonselective recruitment, e.g., recruit frontal regions in a manner that is atypical of younger adults in a given task. In the current experiment, older adults could show such nonselective recruitment by disproportionately recruiting right frontal regions during word encoding and left frontal regions during face encoding.

Under-Recruitment of Frontal Regions

Using younger adults' mean regional activity levels as a baseline, under-recruitment was defined as less activity in older adults compared to younger adults. In word encoding, as shown in Figure 1A, there was a main effect of age group for the left frontal regions, $F(1, 26) = 6.24$, $MSE = .04$, $p < .05$. In particular, older adults significantly under-recruited L BA 45/47, an area involved in meaning-based processing (see Figure 1A; $t(26) = 2.94$, $p < .01$). L BA 6/44 did not show a significant under-recruitment effect ($t(26) = 1.35$, $p=.19$). However, the region x age group interaction for left frontal regions was also not significant ($F(1, 26) = 2.78$, $MSE = .01$, $p = .11$), making interpretation of L BA 6/44 less clear. In face encoding, activity for R BA 6/44 was not significantly different between younger and older adults, $t(26) = .37$.

Thus, significant under-recruitment was observed in older adults for left frontal regions, in particular L BA 45/47, during intentional word encoding.

Nonselective Recruitment of Frontal Regions

Using younger adults' mean regional activity levels as a baseline, nonselective recruitment was defined as relative increases in activity in regions not typically activated in younger adults in a given encoding condition, i.e., activity in right frontal regions during word encoding or activity in left frontal regions during face encoding. For these analyses, the homologous frontal regions near BA 6/44 in the left and right hemispheres were compared. These regions typically show domain-preferential specialization (Kelley et al., 1998; McDermott et al., 1999; Wagner et al., 1998b). As expected, there was a main effect of region in word encoding such that L BA 6/44 was more active than R BA 6/44, $F(1, 26) = 24.09$, $MSE = .01$, $p < .001$, replicating prior studies. Relevant to nonselective recruitment, as shown in Figure 2A, there was a trend toward a region x age group interaction, $F(1, 26) = 3.35$, $MSE = .01$, $p = .08$, such that older adults showed proportionately greater recruitment of R BA 6/44 relative to L BA 6/44 for verbal materials, compared to younger adults. A reversed pattern was found for face encoding. As expected, there was a main effect of region such that R BA 6/44 was more active than L BA 6/44, $F(1, 26) = 6.07$, $MSE = .01$, $p < .05$. More importantly, there was a significant region x age group interaction, $F(1, 26) = 6.96$, $MSE = .01$, $p < .05$; older adults showed greater relative recruitment of L BA 6/44 for nonverbal materials, compared to younger adults (see Figure 2B). Thus, nonselective recruitment was observed for both verbal and nonverbal encoding. However, as noted above, the findings from the nonverbal encoding condition should be interpreted cautiously because of the low behavioral performance.

Exploratory Analyses

Exploratory analyses based on whole-brain statistical activation maps reinforced the hypothesis-driven regional analyses (Figure 3). Figure 3A shows statistical

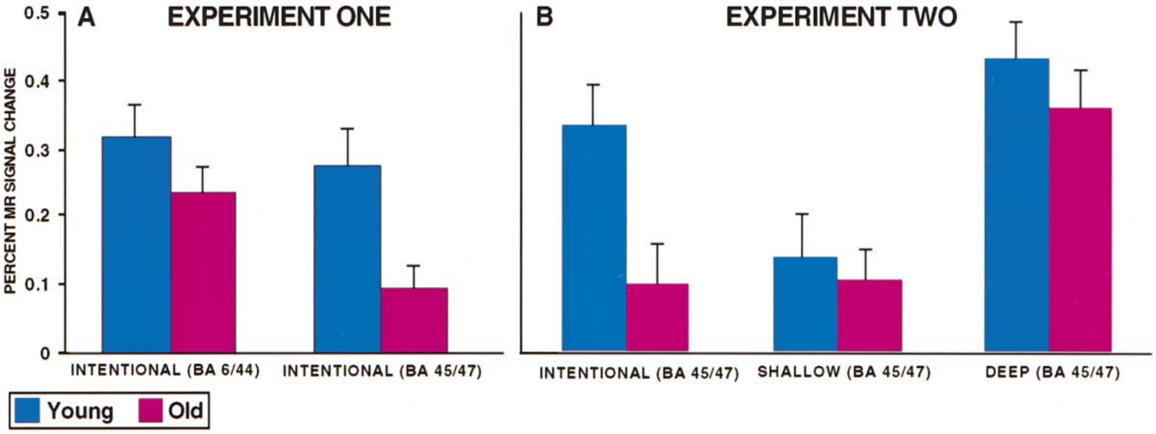

Figure 1. Regional Activity Levels Show Under-Recruitment of Frontal Cortex in Older Adults during Verbal Encoding

Mean activity levels plot as percent signal change in blue for younger adults and in red for older adults. Error bars show standard error of the mean. (A) Mean activity levels are displayed for L BA 6/44 (posterior-dorsal) and L BA 45/47 (anterior-ventral) regions from the intentional encoding condition of Experiment one. A significant decrease is observed in L BA 45/47. (B) Mean activity levels are displayed for L BA 45/47 across encoding conditions of Experiment two, with a significant age group x Condition interaction. There was a significant decrease in *intentional* encoding in older adults compared to younger adults, replicating Experiment one. *Shallow* encoding significantly decreased younger adult activity levels but had minimal effect on older adults. *Deep* encoding significantly increased older adult activity levels above *intentional* encoding with no difference in DEEP encoding between younger and older adults.

activation maps of frontal activation across the verbal condition for younger and older adults. The maps show activation of L BA 45/47 in younger adults and the absence (under-recruitment) of BA 45/47 in older adults during intentional verbal encoding (versus fixation). (Complete tables of peak coordinates of activation are available from the authors upon request.)

Summary

Taken together, these patterns indicate two separate effects associated with aging. First, when employing

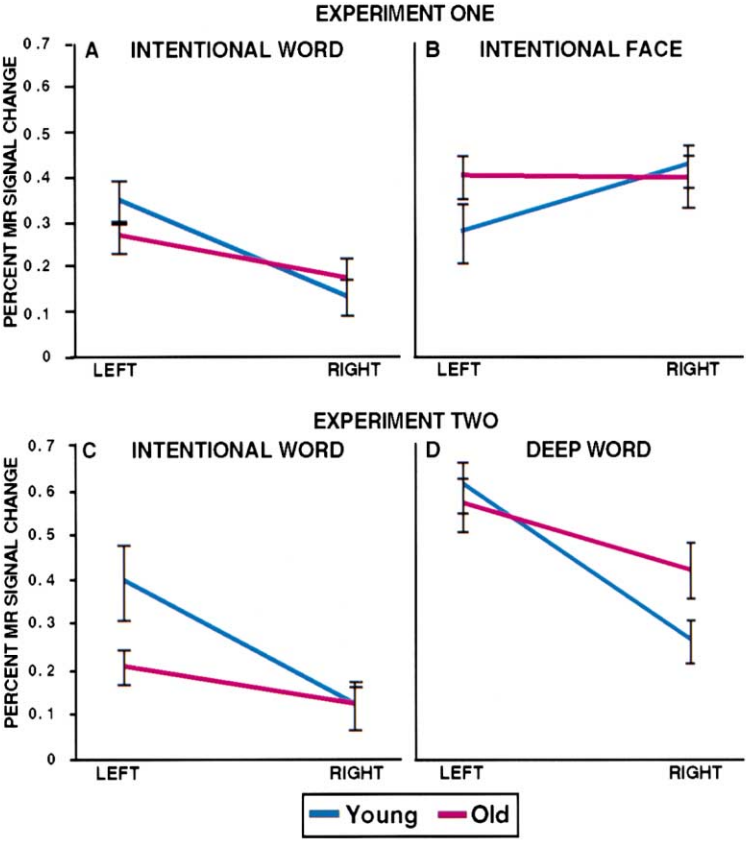

Figure 2. Regional Activity Levels Show Nonselective Recruitment of Frontal Cortex in Older Adults

Mean activity levels plot as percent signal change in blue for younger adults and in red for older adults. Error bars show standard error of the mean. *Left* and *right* correspond to the L BA 6/44 and R BA 6/44. (A) *Intentional* encoding of words in Experiment one showed a pattern for older adults to activate R BA 6/44 disproportionately more than younger adults, relative to activity in L BA 6/44. (B) *Intentional* encoding of faces in Experiment one showed a significant interaction in the opposite direction to that of verbal materials. (C) *Intentional* encoding in Experiment two replicates the effect observed in Experiment one. (D) *Deep* encoding in Experiment two also showed nonselective recruitment, with preserved levels of activity in left frontal regions.

their own self-initiated strategies, older adults do not fully recruit frontal resources associated with effective encoding strategies. In particular, recruitment differences occurred prominently (but not necessarily exclusively) in L BA 45/47, a region that has repeatedly been associated with semantic elaboration. Second, older adults recruit regions in a nonselective manner not typically associated with effective intentional encoding in younger adults.

Experiment Two

Several questions were raised in Experiment one. First, a key unresolved issue concerns the mechanism behind the loss of activation observed in L BA 45/47 in older adults. The observed decreases could be due to an irreversible loss of frontal resources (e.g., associated with atrophy or regional dysfunction). Alternatively, the decreases could be due to an ineffective recruitment of available resources. The latter implies a more context-dependent under-recruitment of available frontal resources, such that older adults *could* recruit left frontal resources to a similar extent as younger adults *under more supportive encoding conditions*.

Second, it is similarly unclear whether nonselective recruitment is under the control of the subject and is related to an adaptive strategy (e.g., compensation) or reflects an irreversible pattern associated with aging. The alternatives were explored by contrasting frontal activation across three verbal tasks including two new tasks (deep and shallow incidental encoding) and the same intentional encoding task as used in Experiment one.

Behavioral Results

Performance is reported for both the scanned encoding tasks (for the deep and shallow incidental encoding tasks) and recognition following the scanning session (for all three encoding conditions). Task performance (e.g., abstract/concrete decisions) during deep and shallow encoding was high (above 90%) for both age groups for both tasks. In the shallow encoding task, there was no significant difference in task accuracy between younger (96.3%) and older adults (94.4%) adults, $t(28) = 1.53$. In the deep encoding task, there was a trend toward a significant difference in performance between younger (94.3%) and older (91.0%) adults, $t(28) = 1.81$, $p = .09$. Overall, performance in the shallow encoding task was significantly higher than in the deep encoding task, $t(29) = 2.34$, $p < .05$. With regard to response latencies, decisions made in the shallow encoding task (1071 ms) took longer than those in the deep encoding task (954 ms), $t(29) = 4.57$, $p < .001$. In the shallow encoding task, older adults (1133 ms) were significantly slower than younger adults (1017 ms), $t(28) = -2.47$, $p < .05$. In the deep encoding task, younger adults (943 ms) did not significantly differ from older adults (967 ms), $t(28) = -0.60$.

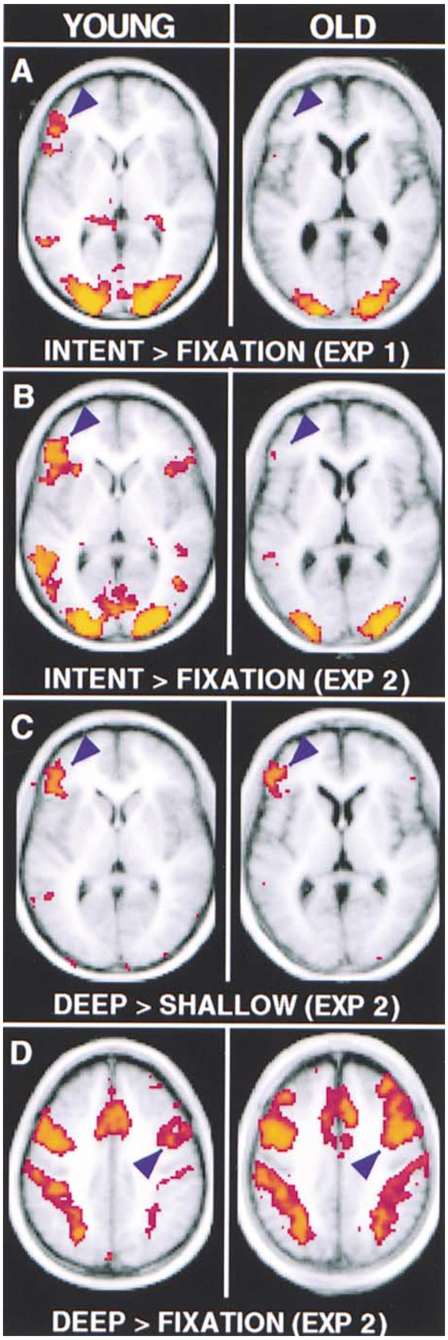

Figure 3. Statistical Activation Maps Show Frontal Activation across All Verbal Encoding Conditions for Younger and Older Adults

Each image represents the average statistical map for the age group plotted on their own group-averaged anatomy image with increasing color intensity reflecting increasing Z value (threshold = 4.4; maximum = 10.0). The left side of the brain is plotted to the left. These maps are complementary to the targeted-statistical analyses that directly compare older to younger adults (Figures 1 and 2). Blue arrows point to the regions being highlighted. (A) Transverse sections (4 mm above the AC-PC plane) show activation of L BA 45/47 in younger adults and the under-recruitment of L BA 45/47 in older adults during intentional encoding (versus fixation) in Experiment one. (B) L BA 45/47 under-recruitment is replicated during intentional encoding in Experiment two. (C) The direct comparison between deep and shallow encoding in Experiment two reveals that under-recruitment of L BA 45/47 can be reversed. L BA 45/47 is selectively active in both younger and older adults. (D) Transverse sections (36 mm above the AC-PC plane) show activation of BA 6/44 in both younger and older adults during deep encoding (versus fixation), with relatively greater (nonselective) activation of R BA 6/44 in older adults.

In recognition test performance, there was a main effect of encoding condition, F(2, 56) = 58.10, MSE = 112.98, $p < .001$, such that recognition was greater overall in deep compared to intentional [t(29) = 5.510, $p < .001$] or shallow encoding [t(29) = 9.638, $p < .001$], and recognition was greater in intentional compared to shallow encoding, t(29) = 6.24, $p < .001$. There was a main effect of age group, F(1, 28) = 7.76, MSE = 370.18, $p < .01$, such that recognition was poorer overall for older adults than younger adults. The age group x encoding task interaction was not significant ($F < 1$) but there was a qualitative trend for older adults to benefit more from deep encoding than did younger adults. For recognition following intentional encoding, older adults (25.4%) performed worse than younger adults (39.6%), t(28) = 2.59, $p < .05$. Recognition following deep encoding was 40.4% in older adults and 51.9% in younger adults, t(28) = 1.92, p = .07. Recognition following shallow encoding for older adults (12.4%) and younger adults (20.7%) was significantly different, t(28) = 2.21, $p < .05$.

Neuropsychogical test results are summarized in Table 1.

fMRI Results

The same regions as in Experiment one were explored for evidence of under-recruitment and nonselective recruitment, as well as whether the two forms of age-associated functional change dissociated.

Under-Recruitment of Frontal Regions

For mean regional activity levels in left frontal regions, there was a main effect of encoding task, F(2, 56) = 19.15, MSE = .04, $p < .05$, such that activity was highest in the deep encoding task. There was no main effect of age group, F(1, 28) = 1.69, MSE = .22. Importantly, there was an age group x encoding task interaction, F(2, 56) = 3.93, MSE = .10, $p < .05$, in which older adults showed evidence of under-recruitment in left frontal regions only in the intentional encoding task, F(1, 28) = 6.72, MSE = .04, $p < .05$, as shown in Figure 1B. By direct contrast, the under-recruitment was minimally present in the deep encoding task. As in Experiment one, the greatest decline in older adults' activity in intentional encoding was in L BA 45/47. Further post hoc analyses revealed that L BA 45/47 activity was significantly different between younger and older adults in the intentional encoding task (t[28] = 2.79, $p<.01$) while L BA 6/44 showed a trend (t[28] = 1.97, p=.06). Consistent with the interaction, neither region approached showing a significant age group difference in the deep encoding task.

The finding of a significant interaction across conditions is particularly important because it also suggests that the observed under-recruitment was not a product of global differences in hemodynamic response properties, as might confound interpretations in between-group studies (D'Esposito et al., 1999; Buckner et al., 2000).

Nonselective Recruitment of Frontal Regions

As in Experiment one, L BA 6/44 and R BA 6/44 were examined during word encoding (Figures 2C and 2D). Replicating Experiment one, during intentional encoding, there was an age group x region interaction, F(1, 28) = 5.03, MSE = .02, $p < .05$, such that older adults showed more bilateral activation in BA 6/44 compared to younger adults. As in Experiment one, nonselective recruitment also was observed in the presence of diminished activation in the older adults, t(28) = 1.97, p =.06. However, during deep encoding, there was also an age group x region interaction, F(1, 28) = 4.69, MSE = .03, $p < .05$, but, in this instance, in the presence of nearly identical activity levels in left frontal cortex. That is, significant nonselective recruitment was observed when under-recruitment was reversed. Consistent with this pattern, older adults paradoxically showed a trend toward an increase in R BA 6/44 activity compared to younger adults, t(28) = 2.00, p = .06.

Exploratory Analyses

Exploratory analyses based on whole-brain statistical activation maps reinforced the hypothesis-driven regional analyses. Figures 3B, 3C, and 3D show statistical activation maps of frontal activation across intentional and incidental encoding for younger and older adults, generated with the same parameters that were used for Experiment one (Figure 3A). Figure 3B shows that under-recruitment of L BA 45/47 is replicated during intentional encoding. The direct comparison between deep and shallow encoding, shown in Figure 3C, reveals that under-recruitment of L BA 45/47 can be reversed under more supportive encoding conditions (e.g., meaning-based encoding). L BA 45/47 is selectively active in both younger and older adults. With regard to nonselective recruitment, Figure 3D shows activation of L BA 6/44 in both younger and older adults during deep encoding (versus fixation), but relatively greater (nonselective) activation in R BA 6/44 in older adults. It should also be noted that nonselective recruitment appears to extend beyond homologous regions (see Park et al., 2001 for discussion). In older adults, right frontal activation is significant extending into BA 9. However, this observation should be considered tentative and await future quantitative analysis that directly compares groups. (Complete tables of peak coordinates of activation are available from the authors upon request.)

Summary

Experiment two replicated and extended findings from Experiment one in several ways. As in the first experiment, Experiment two showed evidence of both under-recruitment and nonselective recruitment in healthy aging. During intentional encoding, older adults showed less activity in left frontal regions, prominently in L BA 45/47 which is associated with semantic elaboration, suggesting again a decreased ability to use self-initiated strategies to recruit appropriate frontal resources. During shallow incidental encoding, which discouraged semantic elaboration, L BA 45/47 activity levels in younger adults decreased to levels observed in older adults. Poor memory performance was also observed. That is, younger adults became much like older adults. By contrast, during deep incidental encoding which directly required semantic elaboration, L BA 45/47 activity increased in older adults to nearly the same level as measured in younger adults indicating frontal resources were available but seemingly not recruited during self-initiated encoding. Thus, by providing environmental support that encouraged semantic elaboration, older adults became much like younger adults in terms of left frontal activity levels. Memory performance improved in the older adults but not fully to levels observed in the younger adults.

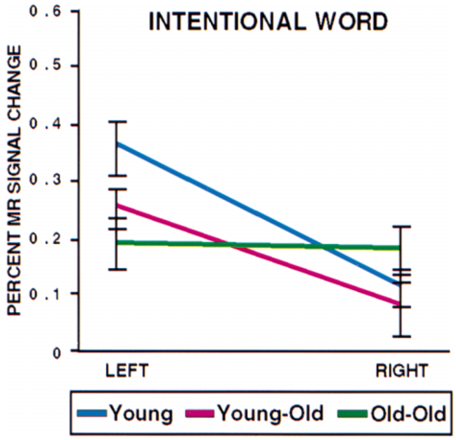

Figure 4. Regional Activity Levels Show Nonselective Recruitment of Frontal Cortex in Older Adults 73 Years of Age or Older (Old-Old Group) during Intentional Verbal Encoding

Mean activity levels plot mean percent signal change in blue for younger adults, red for young-old adults (under 73 years old), and green for old-old adults. Error bars show standard error of the mean. *Left* and *right* correspond to L BA 6/44 and R BA 6/44. Old-old adults showed more bilateral frontal activation, recruiting R BA 6/44 to the same extent as L BA 6/44, whereas young and young-old adults were left lateralized, recruiting L BA 6/44 significantly more than R BA 6/44 during intentional verbal encoding.

With regard to nonselective recruitment, as in Experiment one, older adults showed a disproportionate reliance on R BA 6/44 compared to L BA 6/44 during intentional encoding of verbal materials. Critically, even under deep encoding when the under-recruitment observed in left frontal regions was remedied, nonselective recruitment of R BA 6/44 was still prominently observed (Figure 2D).

Combined Analyses Exploring Effects of Advanced Aging

In order to further examine the relation of age and the ability to recruit frontal regions associated with successful encoding strategies, data were combined across the two experiments for the intentional word encoding condition that was included in both. For this analysis, intentional word encoding data were divided by age groups: younger adults (young) ($N = 30$), older adults under 73 years of age (young-old) ($N = 14$; Mean age $= 67.5$ years), and older adults 73 years of age or older (old-old) ($N = 14$; Mean age $= 80.0$ years). The age cutoff for young- and old-old was selected based on our sample to provide for equal numbers of subjects in each older adult group. Behaviorally, there was a slight, but nonsignificant, decrement in recognition score for the old-old (37.1%) as compared to young-old (42.6%) (corrected recognition scores for this comparison were weighted by the number of subjects from each experiment).

The fMRI data showed an interaction between age group and region [$F(2, 55) = 7.22$, $MSE = .02$, $p < .005$]. As shown in Figure 4, both young and young-old adults showed patterns of left lateralization in recruiting frontal regions, i.e., activating L BA 6/44 significantly more than R BA 6/44, [young, $t(29) = 5.76$, $p < .001$; young-old $t(13) = 8.36$, $p < .001$]. By contrast, the oldest adults were more bilateral; activity levels of L BA 6/44 and R BA 6/44 were almost equivalent in old-old adults, $t(13) = .25$. Thus, nonselectivity emerged, in this study, only with advanced aging.

Of interest, the division by age may also provide another dissociation between under-recruitment and nonselective recruitment. Both young-old and old-old individuals appear to show under-recruitment of L BA 6/44 even though they dissociate in terms of nonselective recruitment (see Figure 4). However, a t test showed only a weak trend for under-recruitment of L BA 6/44 in the young-old ($p = .18$). To further explore this possible dissociation, L BA 45/47 was also examined by age (as noted in previous sections, L BA 45/47 showed the greatest effect of under-recruitment during verbal encoding). The mean percent signal change was .30, .10, and .09 for the young, young-old, and old-old adults for L BA 45/47, respectively. Post hoc analysis revealed under-recruitment was significant in the young-old referenced to the young [$t(42) = 2.99$, $p < .005$]. Thus, under-recruitment was present in the young-old adults and nearly equivalent in magnitude to that of the oldest adults.

Taken together, these results tentatively suggest an age difference in the onset of under-recruitment and nonselective recruitment. Under-recruitment emerges in the sixth decade of life, if not earlier, while nonselective recruitment does not become prominent until the seventh and eighth decades. Neuropsychogical test results for the young-old and old-old groups are summarized in Table 1, and show some suggestions of more prominent cognitive decline in the oldest individuals.

Exploratory Analyses

Exploratory analyses based on whole-brain statistical activation maps reinforced the regional analysis (Figure 5). Statistical activation maps in Figure 5, with the same parameters as Figure 3, show BA 6/44 activation during intentional encoding (versus fixation) for young, young-old, and old-old adults. Old-old adults show activation (nonselective) in R BA 6/44.

Discussion

The current study found evidence for two separate age-associated changes in neural correlates of memory encoding: under-recruitment and nonselective recruitment of specific regions within frontal cortex (see also Anderson et al., 2000; Cabeza et al., 1997; Grady and Craik, 2000; Grady et al., 1995, 1999; Madden et al., 1999a, 1999b). For descriptive purposes, under-recruitment and nonselective recruitment are quantitatively summarized in Table 2 for all of the verbal encoding conditions across the two studies.

In both studies older adults showed a deficit in recruiting frontal resources associated with effective verbal encoding strategies when left to execute their own strategies, that is, during intentional encoding. A key question of the current study was whether such frontal activity losses in older adults reflected a true absence of frontal resources, or rather reflected an ineffective utilization of available frontal resources, compared to younger adults. In Experiment two, providing environmental support by requiring semantic elaboration during

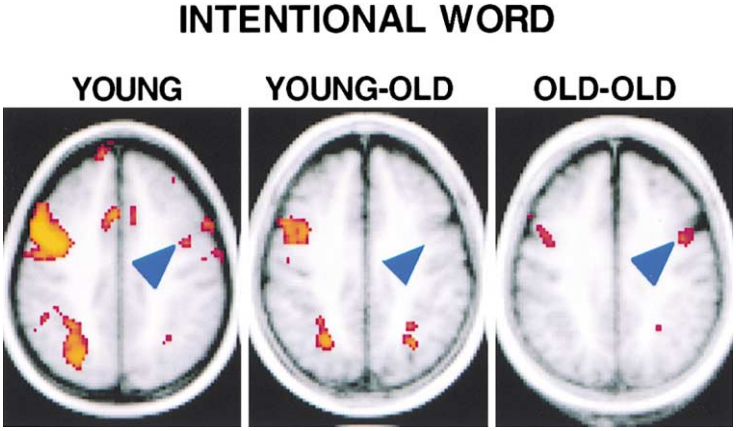

Figure 5. Statistical Activation Maps Show Frontal Activation in Advanced Aging

Statistical activation maps, with the same format as Figure 4, show frontal activation of BA 6/44 during intentional encoding (versus fixation) for young, young-old, and old-old adults, collapsed across Experiments one and two. Transverse sections (36 mm above the AC-PC plane) show relatively greater (nonselective) activation in R BA 6/44 in old-old adults compared to either young or young-old adults. Because different numbers of subjects contribute to each image, the differences in Z scales across images should not be directly interpreted.

encoding revealed that reduced frontal activation could be ameliorated and effectively reversed in older adults. This finding supports an under-recruitment hypothesis in healthy aging, namely that frontal resources are present to a larger degree than has previously been appreciated, but are not recruited effectively when self-initiated encoding strategies are required.

In addition to under-recruitment, older adults also tended to recruit regions that are not typically associated with effective encoding in younger adults (see also Anderson et al., 2000; Cabeza et al., 1997; Madden et al., 1999b). This particular pattern of nonselective recruitment was observed under a variety of encoding conditions, including intentional verbal (Experiments one and two), intentional nonverbal (Experiment one), and incidental meaning-based verbal encoding (Experiment two). Even when under-recruitment in left frontal regions was remedied in an environmentally supported task condition, nonselective recruitment persisted in older adults. Thus, the current study reveals a dissociation of under-recruitment and nonselective recruitment in healthy aging. The implications of these data patterns are discussed in more detail below.

Under-Recruitment Can Be Reversed with Supportive Task Conditions

The current study finds that older adults do not fully recruit frontal regions associated with semantic elaboration under verbal task conditions in which subjects rely on their own self-initiated strategies, consistent with the notion of a production deficiency (Craik and Byrd, 1982). Under-recruitment in older adults during verbal encoding was most prominent in L BA 45/47, a region implicated in semantic elaboration of verbal materials (other regions, including L BA 6/44, may also show such effects). It is notable that several earlier studies demonstrating attenuated frontal activity in older adults during episodic memory encoding utilized intentional encoding procedures (Anderson et al., 2000; Cabeza et al., 1997; Grady et al., 1995, 1999).

The findings from this and other such studies support under-recruitment as one mechanism associated with cognitive decline. In this specific instance, the prominent under-recruitment of L BA 45/47 suggests memory difficulties may result, in part, because of failure to appropriately elaborate on the meaning of words—a common and effective organizational strategy spontaneously adopted by younger adults. The finding that under-recruitment was reversible suggests that significant frontal resources are available to healthy older adults and also suggests that prominent loss of activity in such regions is not necessarily an inevitable consequence of aging. Additional data consistent with this notion of reversible under-recruitment come from studies in which older adults do not significantly recruit a given region during one task, but do recruit the region under other task conditions (Cabeza, 2002; Cabeza et al., 1997). For instance, Cabeza et al. (1997) noted that older

Table 2. Quantification of Under-Recruitment and Nonselective Recruitment

	Mean Magnitude Estimates[a]									
	L BA6/44		R BA6/44		L BA45/47		Asymmetry[b]		Old Relative to Young	
	Yng	Old	Yng	Old	Yng	Old	Yng	Old	Selectivity[c]	Recruitment[d]
Int 1	.32	.24	.10	.14	.27	.09	3.01	1.69	56%	75%/33%
Int 2	.39	.21	.12	.12	.33	.10	3.26	1.74	53%	54%/30%
Deep	.60	.57	.28	.43	.43	.36	2.15	1.33	62%	95%/84%

Notes: all estimates are from verbal (word) encoding conditions. Int 1 is from intentional encoding of Experiment one, Int 2 is from intentional encoding of Experiment two, and Deep is from deep encoding of Experiment two.

[a] Estimates in percent signal change.

[b] Asymmetry is the ratio of left (L) to right (R) BA 6/44 magnitude estimates.

[c] Selectivity is the percentage of asymmetry that the older adults achieve, referenced to the younger adults.

[d] Recruitment is the percentage of activation magnitude that the older adults achieve, referenced to the younger adults; the two values reflect recruitment for L BA6/44 and L BA45/47, respectively.

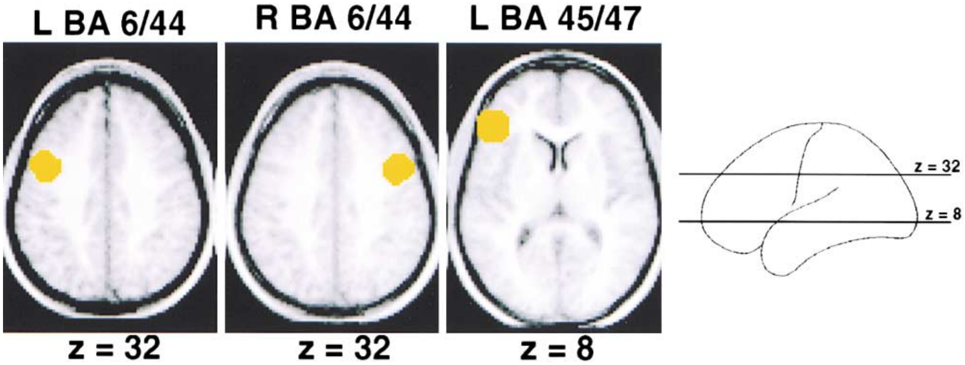

Figure 6. Transverse Sections Show the Location of the Three Frontal Regions Used for All Hypothesis-Driven Analyses, Including Posterior-Dorsal L BA 6/44 (Left), Posterior-Dorsal R BA 6/44 (Middle), and Anterior-Ventral L BA 45/47 (Right)

Z axis labels are given at the bottom of each section in relation to their plane in the Talairach and Tournoux (1988) atlas. Regions were derived a priori from a meta-analysis of frontal regions active during intentional episodic encoding of words and faces (see Konishi et al., 2001; Buckner and Logan, 2002).

adults did not significantly recruit certain left frontal regions during encoding (as younger adults did) yet did recruit these regions during retrieval (contrary to younger adults who did not). Rypma and D'Esposito (2000) also demonstrate such an effect within the context of a working memory task.

Similarly, under-recruitment was not detected during face encoding in the present study. However, findings associated with the face encoding condition are difficult to interpret because of the poor behavioral performance associated with this condition (see behavioral results section of Experiment one). The most straightforward interpretation is that the difficulty of the task, perhaps because of differential perceptual demands on the older adults, encouraged frontal recruitment. Two related findings suggest a more speculative, alternative explanation. First, relative to words, it has often been difficult to find robust task (levels of processing) effects on encoding of complex, nonverbal materials. That is, the mere presentation of a scene or face can sometimes promote almost as good encoding as when a subject is explicitly instructed to memorize. This behavioral observation suggests that certain nonverbal materials may directly promote forms of elaboration even without an intentional or task-directed strategy employed by the subject (but see Grady et al., 1995). Second, following repeated exposure to stimuli, which leads to automated responding, frontal activity reduces to near baseline levels for words but not for faces (R.L. Buckner, unpublished observation). This latter finding also suggests that faces, in healthy young adults, spontaneously elicit more extensive frontal participation. While speculative, the present findings of under-recruitment for words but not faces in older adults may be another example of the more direct route complex nonverbal materials have to frontal processing.

The finding that under-recruitment for verbal materials can be largely reversed and is context dependent has interesting implications for efforts in cognitive rehabilitation. It may be possible to train individuals who reveal under-recruitment of frontal regions associated with successful encoding strategies to recruit these regions spontaneously, i.e., in a self-initiated manner, leading to a functional recovery of brain regions previously underutilized during encoding or other cognitively demanding tasks. For instance, Savage et al. (2001) have observed increased frontal activity in younger adults when they are explicitly instructed in the use of an effective encoding strategy (semantic clustering) compared to when they must spontaneously initiate an effective encoding strategy for the same types of materials. Patients with Parkinson's disease and obsessive-compulsive disorder have also been found to benefit from explicit instruction in appropriate task strategies (e.g., Knoke et al., 1998). The long-term maintenance of such strategy use remains unclear. The present findings may indicate the amenability of healthy aging to memory training designed to explicitly instruct or implicitly shape effective strategy use and semantic elaboration during episodic memory tasks (e.g., see Camp et al., 2000).

Nonselective Recruitment Persists across Conditions and Onsets with Advanced Aging

In addition to under-recruitment, older adults consistently showed nonselective recruitment of frontal regions with a relatively high activity level in R BA 6/44 during verbal encoding and relatively high activity in L BA 6/44 during nonverbal encoding. These findings are consistent with prior neuroimaging studies of memory and aging that show older adults often recruit regions not typically recruited by younger adults for a given task (Anderson et al., 2000; Cabeza et al., 1997; Cabeza, 2002; Madden et al., 1999b; Reuter-Lorenz et al., 2000, 2001).

Unlike under-recruitment, nonselective recruitment persisted even during deep encoding where environmental support was maximized and under-recruitment was reversed, implying an age-associated change that persists across a range of task conditions. Interestingly, nonselective recruitment was most pronounced in older adults 73 years of age and older. Thus, it appears that advancing age may predict nonselective recruitment in frontal cortex (but see Dixit et al., 2000). The emergence of nonselective recruitment only in advanced aging also provides a further dissociation with under-recruitment, which was already significant and prominent in the older adults under the age of 73 (for L BA 45/47).

It is unclear from the current data what causes the nonselective recruitment observed or what effect nonselective recruitment may have on an individual's cognitive performance. One possibility is that nonselective recruitment may reflect activation which compensates for failures or difficulties in recruiting more typical brain regions activated during a task (Cabeza et al., 1997; Cabeza, 2002; Grady et al., 1995; Madden et al., 1999a, 1999b; McIntosh et al., 1999; Nielson et al., 2002; Reuter-Lorenz et al., 2000, 2001; for review see Grady and Craik, 2000; Park et al., 2001) or compensates for evolving perceptual difficulties (Baltes and Lindenberger, 1997; see also Buckner et al., 2000). Stroke patients often activate adjacent regions in the damaged hemisphere and homologous regions in the opposite hemisphere when performing a task that typically relies on the injured brain areas—an effect that may reflect compensation (Buckner et al., 1996; Cao et al., 1999; Gold and Kertesz, 2000; Honda et al., 1997; Ohyama et al., 1996; Rosen et al., 2000; Sohlberg and Mateer, 2001; Thulborn et al., 1999; Weiller et al., 1995). Older adults may be engaging a more subtle form of compensation. Relevant to this possibility, Reuter-Lorenz and colleagues (2001) have demonstrated a modest relation in older adults between right frontal recruitment and performance on verbal working memory tasks. However, other studies have not shown a link between recruitment of additional brain regions and improved performance (Madden et al., 1999b) or have even shown negative correlation between activity in atypical regions and performance (Cabeza et al., 1997). The current study was not designed to explicitly test whether nonselective recruitment was compensatory for under-recruitment. Nonetheless, it is interesting to note that young and old adults are almost matched in terms of their regional activity in L BA 6/44 and L BA 45/47 during deep incidental encoding, yet old-old adults still disproportionately recruit R BA 6/44.

A second hypothesis, which we believe is more likely, is that *nonselective recruitment reflects a breakdown in the appropriate selection of regions associated with controlled task performance* (Buckner and Logan, 2002). While younger adults may selectively recruit left frontal regions most efficient for verbal processing, excluding participation of other regions, older adults may fail to allocate resources in such a selective manner. For instance, Konishi, Donaldson, and Buckner (2001) examined the temporal evolution of left and right frontal recruitment during intentional word encoding and found an initial, transient increase in right frontal activity. One interpretation of their findings is that younger adults initially recruit multiple, potentially useful regions at encoding (e.g., both left and R BA 6/44), but then quickly resolve to select those regions most appropriate for task performance (e.g., L BA 6/44 and not R BA 6/44). Older adults may be failing to resolve competition among brain regions. Such a pattern might be indicative of the neural bases of a general impairment in controlled or inhibitory processing often observed behaviorally in older adults (e.g., Balota et al., 2000; Hasher and Zacks, 1988; Hasher et al., 1999; Kausler et al., 1988; Nyberg et al., 1996).

It also seems likely that nonselective recruitment may be associated with physiological changes that accompany advanced aging—what Cabeza (2002) has called a *neurogenic* origin. While it is speculative to suggest what such an origin might be, it is noteworthy that a recent study has found aging to be associated with changes in the white matter. Using diffusion tensor imaging (DTI), O'Sullivan et al. (2001) found evidence for reduced tract integrity (as measured by anisotropy) and increased water diffusion in white matter in older adults (see also Sullivan et al., 2000; Raz, 2000). These white matter changes were maximally represented in anterior regions. Based on these findings, the authors suggest that age-related changes in white matter integrity may be related to a decrease in functional integration between cortical brain regions (e.g., cortical "disconnection") (O'Sullivan et al., 2001). The functional outcome of this change in white matter, or yet other unspecified physiological change, may be the nonselective recruitment of processing regions as observed here, which in turn may lead to controlled processing difficulties so often associated with aging.

Experimental Procedures

Overview

Two fMRI studies imaged younger and older adults during memory encoding. The first study explored *intentional encoding*, requiring self-initiated memorization strategies. Both verbal and nonverbal materials were used. The second study explored possible mechanisms behind observed age-associated changes. Intentional encoding and two new verbal encoding conditions based on incidental encoding were used: a *shallow encoding* condition constructed to discourage use of meaning-based elaboration (which impairs memory formation) and a *deep encoding* condition constructed to encourage use of meaning-based elaboration (which aids memory encoding; Craik and Lockhart, 1972; Craik and Tulving, 1975). The idea behind this manipulation is that deep incidental encoding, because of its well-defined task goals, maximizes the opportunity for older adults to recruit appropriate brain regions for encoding.

Subjects

Sixty-two subjects served across the two studies and were paid for participation in accordance with guidelines of the Washington University Human Studies Committee. Older adults were recruited from either the Washington University Alzheimer's Disease Research Center (ADRC) or through advertisements associated with the Washington University community. When recruited through the ADRC, only nondemented individuals were enrolled as assessed by the Clinical Dementia Rating (CDR) scale (all CDR 0) (Hughes et al., 1982; Morris, 1993) and therefore would be considered atypically healthy, exhibiting no signs of mild cognitive impairment. Older adults recruited from the broader community were administered neuropsychological tests that revealed high level functioning (see Neuropsychological Testing below). Younger adults were recruited through advertisement. All subjects were right-handed, native English speakers, and had no reported neurological problems that might cause dementia. Vision was normal or corrected to near normal using magnet compatible glasses or contact lenses.

fMRI Data Acquisition

Scanning was performed using a Siemens 1.5 Tesla Vision scanner (Erlangen, Germany). Cushions and a thermoplastic face mask were used to reduce movement. Headphones dampened scanner noise and were used to communicate with the subject. Responses were collected from a fiber-optic button-press device held in one hand (Experiment one) or two hands (Experiment two) and linked to a PsyScope button box attached to a Power Macintosh computer (Apple, Cupertino, CA) controlled by PsyScope software (Cohen et al., 1993). Stimuli were projected (AmPro model LCD-150) on to a screen at the head of the bore, viewed by the subject via a mirror attached to the head coil. Magnet compatible glasses or contact lenses were used to aid vision. Individuals were fit with lenses prior to imaging based on their subjective report of improved visual acuity.

Structural images were acquired first including a scout image to center the field of view on the subject's brain. Then a high-resolution ($1 \times 1 \times 1.25$ mm) structural T1-weighted image (MP-RAGE sequence; TR = 9.7 ms, TE = 4 ms, flip angle = 10°, TI = 20 ms, TD = 500 ms) was acquired. Functional images were acquired using an asymmetric spin-echo sequence sensitive to blood oxygenation-level dependent (BOLD) contrast (T2*) (TR = 2.68 s or 2.50 s, T2* evolution time = 50 ms). Subjects performed four (Experiment one) or six (Experiment two) blocked-task paradigm functional runs consisting of between 102 (Experiment two) and 128 (Experiment one) sequential whole-brain acquisitions (16 contiguous slices, 8 mm thickness, 3.75×3.75 mm in-plane resolution, aligned to the anterior-posterior commissure plane). The first four images acquired in each functional run were excluded from analysis to allow stabilization of longitudinal magnetization.

General fMRI Data Analyses

Functional data were first preprocessed. Each volume within each run was corrected for odd/even slice intensity differences and then corrected for motion between volumes using a rigid-body rotation and translation correction (Snyder, 1996). To account for between-slice timing differences induced by differences in acquisition order, the data were interpolated using ideal sinc interpolation. The linear slope was removed on a voxel-by-voxel basis to accommodate linear drift (Bandettini et al., 1993). Then each subject's whole-brain signal intensity was normalized to 1000 for each run. Finally, anatomic and functional data for each subject were placed in stereotaxic atlas space (Talairach and Tournoux, 1988) using procedures similar to McDermott et al. (1999). One difference in the present procedure was that the image-mask used to align the structural image to the target was relaxed (enlarged) to allow a better registration for the older adults. The atlas-transformed anatomic image for each subject (young and old) was then checked against a reference average to ensure appropriate registration. Reconstructed atlas voxel size was $2 \times 2 \times 2$ mm.

Following preprocessing, magnitude estimates for effects of interest were computed for each subject based on an implementation of the general linear model (see McDermott et al., 1999). For this analysis, task-related activity was modeled as an extended γ function (Boynton et al., 1996) with run mean and slope coded as effects of no interest, and scaled to percent signal change. The model was computed for each voxel separately. The result was a Z statistic map and estimated magnitude map for each encoding condition versus reference (e.g., intentional word encoding; intentional face encoding). These maps were then used for hypothesis-driven (magnitude maps) and exploratory analyses (Z statistic maps).

Hypothesis-Driven Analyses

For both studies, hypothesis-driven analyses were performed using three a priori defined frontal regions based on regions consistently activated during tasks promoting memory encoding (Buckner et al., 1999). These regions were generated previously from a large sample of young adults pooled across three separate fMRI studies of word and face encoding (see Konishi et al., 2001; see also Buckner and Logan, 2002). The peak locations of the two left frontal regions were −43, 3, 32 and −45, 29, 6, corresponding to L BA 6/44 (posterior-dorsal) and L BA 45/47 (anterior-ventral), respectively. The third right frontal region's peak location was 43, 3, 32, corresponding to R BA 6/44. Regions including all activated voxels within 12 mm of each of these peaks were then generated. Regions are shown in Figure 6.

Using data from the present study, magnitude estimates were computed for each of these regions for each condition within each subject. Individual magnitude estimates were then entered into statistical analyses based on a random-effects model. These tests were constructed, where possible, to include either a region-by-group or condition-by-group interaction. The reason for examining interactions is that such analyses are less affected by baseline differences in hemodynamic response properties, such as might be observed for between-population comparisons either because of intrinsic physiological properties or external properties of the analysis (e.g., misregistration) (Buckner et al., 2000; D'Esposito et al., 1999).

Exploratory fMRI Data Analyses

A second exploratory phase of analysis was conducted that made no assumptions about which brain regions would be active. Whole-brain activation maps were constructed for each group on a voxel-by-voxel basis by averaging and scaling the individual Z maps using a fixed-effect model. This analysis allowed the full activation pattern to be observed but with less power (and using a more liberal statistical model) than the hypothesis-directed analyses above. Based on our prior work (Konishi et al., 2001), regions of activation were identified using a significance threshold set at $p < .0001$ with 19 or more contiguous significant voxels activated (152 mm^3). All interpreted results were identified in the hypothesis-driven analyses above using a random-effects statistical model that included age group as a factor. Exploratory analyses were used to liberally identify possible findings for future investigation.

Neuropsychological Testing

Neuropsychological tests were administered to older adults as part of their ongoing participation for the ADRC or separately in a 2 hr session (for those participants recruited from the general community). Four participants from Experiment two were not tested. Memory was assessed with the Wechsler Memory Scale (WMS; Wechsler and Stone, 1973) Associate Recall subscales (paired-associate learning). Forward and backward digit span from the WMS were also assessed. Subjects were given the WMS Mental Control test (Wechsler and Stone, 1973), which assesses the ability to quickly produce a well-rehearsed letter or digit sequence, such as the alphabet, in a specified amount of time. Subjects also received the Word Fluency Test, which asks subjects to name as many words as possible beginning with a given letter (e.g., *s* and *p*) in a 60 s time period (Thurstone and Thurstone, 1949). General intelligence measures included three subtests of the Wechsler Adult Intelligence Scale (Wechsler, 1955): Information, Block Design, and Digit Symbol. Visual perceptual-motor performance was assessed by Trail Making Form A, in which subjects must connect numerically ordered circles that result in a specific pattern. In Trail Making Form B, a test requiring working memory and planning, subjects must connect numerically ordered and alphabetically ordered circles in an alternating sequence (e.g., 1, A, 2, B). Subjects completed the Boston Naming Test (Goodglass et al., 1983), which reflects semantic-lexical retrieval processes in naming simple line drawings.

Experiment One

Fourteen younger adults (mean age = 21.1 years, range 18–24; 5 male) and 14 older adults (mean age = 74.9 years, range 66–89; 5 male) participated. *Intentional encoding* was examined for verbal (words) and nonverbal (unfamiliar faces) stimuli. Subjects were instructed to memorize the items. No specific strategies were suggested.

A blocked-task paradigm was employed similar to McDermott et al. (1999) with four runs per subject. For the two verbal encoding runs, blocks alternated between intentional word encoding and fixation for 42.88 s and 26.80 s, respectively. Each of four blocks per run contained eight words (4.0 s stimulus duration, 1.36 s intertrial interval) for a total of 32 words per run. Words were concrete nouns presented in large (oversized), uppercase Geneva font. Run structure was similar for the two nonverbal encoding runs except that high-resolution color faces were presented. Two sequential word encoding runs were performed by each subject, counterbalanced with two similar face encoding runs using identical presentation parameters except that unfamiliar faces were presented as stimuli. Immediately following each run, within the scanner, memory performance was tested using a fixed-paced old/new recognition test in which participants pressed a single button when they saw a previously studied item.

Experiment Two

Eighteen younger adults (mean age = 25.0 years, range 18–31; 6 male) and 16 older adults (mean age = 72.2 years, range = 61–82, 3 male) performed three tasks: intentional encoding, shallow incidental encoding, and deep incidental encoding. Three subjects (two young, one old) were excluded from fMRI data analyses because of failure to reach 75% performance during incidental encoding or because of recognition memory performance below 10% following all encoding conditions. A fourth older adult was excluded because their fMRI magnitude estimates were greater than three standard deviations from the mean.

Only verbal materials were used in Experiment two. In the *shallow encoding* task (nonsemantic judgment), subjects decided whether the first or last letter of each word came earlier in the alphabet. In the *deep encoding* task (semantic judgment), subjects decided whether each word represented an abstract or concrete entity. In both the shallow and deep encoding tasks, responses for each word were made with either the left index finger (response for "first letter" or "abstract") or the right index finger (response for "last letter" or "concrete"). The semantic judgment task was expected to require attention to word meaning while the nonsemantic judgment task was not (Demb et al., 1995). Subjects were unaware that their memory would be tested for the incidentally encoded words.

A blocked-task paradigm was employed with six runs per subject (two runs per condition). For each run, blocks alternated between fixation and one of the word-encoding conditions for 22.50 s and 30.00 s, respectively. Each of the three encoding blocks per run contained 12 words (2.0 s stimulus duration, .5 s intertrial interval) for a total of 36 words per run. Order of task was counterbalanced across subjects.

The same words were counterbalanced across the three encoding conditions with only the task instructions differing between conditions. The stimuli were based on a subset of 480 words representing abstract and concrete entities used by Demb et al. 1995. Nine lists of 36 words each were created such that half of the words were abstract and half also had the first letters of the words come earlier in the alphabet than the last letters (e.g., GHOST, where "G" comes before "T" in the alphabet). Lists were balanced for word length (mean = 5.89), frequency (as determined by Kucera and Francis, 1967; mean = 22.69), and syllable number (mean = 1.87). Following all fMRI runs, subjects were removed from the scanner and administered a self-paced old/new recognition memory test.

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References

Anderson, N.D., Iidaka, T., Cabeza, R., Kapur, S., McIntosh, A.R., and Craik, F.I.M. (2000). The effects of divided attention on encoding- and retrieval-related brain activity: A PET study of younger and older adults. J. Cogn. Neurosci. *12*, 775–792.

Bäckman, L., Almkvist, O., Andersson, J., Nordberg, A., Winbald, B., Reineck, R., and Langstrom, B. (1997). Brain activation in young and older adults during implicit and explicit retrieval. J. Cogn. Neurosci. *9*, 378–391.

Baker, J.T., Sanders, A.L., Maccotta, L., and Buckner, R.L. (2001). Neural correlates of verbal memory encoding during semantic and structural processing tasks. Neuroreport *12*, 1251–1256.

Balota, D.A., Dolan, P.O., and Duchek, J.M. (2000). Memory changes in healthy older adults. In The Oxford Handbook of Memory, E. Tulving and F.I.M. Craik, eds. (New York: Oxford University Press), pp. 395–410.

Baltes, P.B., and Lindenberger, U. (1997). Emergence of powerful connection between sensory and cognitive functions across the adult life span: A new window to the study of cognitive aging? Psychol. Aging *12*, 12–21.

Bandettini, P.A., Jesmanowicz, A., Wong, E.C., and Hyde, J.S. (1993). Processing strategies for time-course data sets in functional MRI of the human brain. Magn. Reson. Med. *30*, 161–173.

Boynton, G.M., Engel, S.A., Glover, G.H., and Heeger, D.J. (1996). Linear systems analysis of functional magnetic resonance imaging in human V1. J. Neurosci. *16*, 4207–4221.

Brewer, J.B., Zhao, Z., Desmond, J.E., Glover, G.H., and Gabrieli, J.D.E. (1998). Parahippocampal and frontal responses to single events predict whether those events are remembered or forgotten. Science *281*, 1185–1187.

Buckner, R.L. (1996). Beyond HERA: Contributions of specific prefrontal brain areas to long-term memory retrieval. Psychon. Bull. Rev. *3*, 149–158.

Buckner, R.L., and Logan, J.M. (2002). Frontal contributions to episodic memory encoding in the young and elderly. In The Cognitive Neuroscience of Memory Encoding and Retrieval, A.E. Parker, E.L. Wilding, and T. Bussey, eds.(Philadelphia: Psychology Press), in press.

Buckner, R.L., Corbetta, M., Schatz, J., Raichle, M.E., and Petersen, S.E. (1996). Preserved speech abilities and compensation following prefrontal damage. Proc. Natl. Acad. Sci. USA *93*, 1249–1253.

Buckner, R.L., Kelley, W.M., and Petersen, S.E. (1999). Frontal cortex contributes to human memory formation. Nat. Neurosci. *2*, 311–314.

Buckner, R.L., Snyder, A.Z., Sanders, A.L., Raichle, M.E., and Morris, J.C. (2000). Functional brain imaging of young, nondemented and demented older adults. J. Cogn. Neurosci. *12* Suppl. *2*, 24–34.

Buckner, R.L., Wheeler, M.E., and Sheridan, M.A. (2001). Encoding processes during retrieval tasks. J. Cogn. Neurosci. *13*, 406–415.

Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. Psychol. Aging, in press.

Cabeza, R., Grady, C.L., Nyberg, L., McIntosh, A.R., Tulving, E., Kapur, S., Jennings, J., Houle, S., and Craik, F.I.M. (1997). Age-related differences in neural activity during memory encoding and retrieval: A positron emission tomography study. J. Neurosci. *17*, 391–400.

Camp, C.J., Bird, M.J., and Cherry, K.E. (2000). Retrieval strategies as a rehabilitation aid for cognitive loss in pathological aging. In Cognitive Rehabilitation in Old Age, R.D. Hill, L. Bäckman, and A.S. Neely, eds. (New York: Oxford University Press), pp. 224–248.

Cao, Y., Vikingstad, E.M., George, K.P., Johnson, A.F., and Welch, K.M.A. (1999). Cortical language activation in stroke patients recovering from aphasia with functional MRI. Stroke *30*, 2331–2340.

Cohen, J.D., MacWhinney, R.C., Flatt, M., and Provost, J. (1993). An interactive graphic system for designing and controlling experiments in the psychology laboratory using Macintosh computers. Behav. Res. Methods Instrum. Comput. *25*, 257–271.

Craik, F.I.M. (1977). Age differences in human memory. In Handbook of Psychology and Aging, 3rd ed., J.E. Birren and K.W. Schaie, eds. (New York: Van Nostrand Reinhold Company), pp. 384–420.

Craik, F.I.M., and Byrd, M. (1982). Aging and cognitive deficits: The role of attentional resources. In Aging and Cognitive Processes, F.I.M. Craik and S. Trehub, eds. (New York: Plenum), pp. 191–211.

Craik, F.I.M., and Lockhart, R.S. (1972). Levels of processing: A framework for memory research. J. Verbal Learn. Verbal Behav. *11*, 671–684.

Craik, F.I.M., and Simon, E. (1980). Age differences in memory: The roles of attention and depth of processing. In New Directions in Memory and Aging: Procedures of the George A.Talland Memorial Conference, L.W. Poon, J.L. Fozard, L.S. Cermak, D. Arenberg, and L.W. Thompson, eds. (Hillsdale, NJ: Lawrence Erlbaum Associates), pp. 95–112.

Craik, F.I.M., and Tulving, E. (1975). Depth of processing and the retention of words in episodic memory. J. Exp. Psychol. Gen. *104*, 168–294.

Demb, J.B., Desmond, J.E., Wagner, A.D., Baidys, C.J., Glover, G.H., and Gabrieli, J.D.E. (1995). Semantic encoding and retrieval in the left inferior prefrontal cortex: A functional MRI study of task difficulty and process specificity. J. Neurosci. *15*, 5870–5878.

Dempster, F.N. (1992). The rise and fall of the inhibitory mechanism: Toward a unified theory of cognitive development and aging. Dev. Rev. *12*, 45–75.

D'Esposito, M., Zarahn, E., Aguirre, G.K., and Rypma, B. (1999). The effect of normal aging on the coupling of neural activity to the BOLD hemodynamic response. Neuroimage *10*, 6–14.

Dixit, N.K., Gerton, B.K., Dohn, P., Meyer-Lindenberg, A., and Berman, K.F. (2000). Age-related changes in rCBF activation during an N-back working memory paradigm occur prior to age 50. Neuroimage *11*, S94.

Fletcher, P.C., Shallice, T., and Dolan, R.J. (1998). The functional roles of prefrontal cortex in episodic memory I: Encoding. Brain *121*, 1239–1248.

Gershberg, F.B., and Shimamura, A.P. (1995). Impaired use of organizational strategies in free recall following frontal lobe damage. Neuropsychologia *33*, 1305–1333.

Gold, B.T., and Kertesz, A. (2000). Right hemisphere semantic processing of visual words in an aphasic patient: an fMRI study. Brain Lang. *73*, 456–465.

Goodglass, H., Kaplan, E., and Weintraub, S. (1983). Boston Naming Test Scoring Booklet (Philadelphia: Lea & Febiger).

Grady, C.L., and Craik, F.I.M. (2000). Changes in memory processing with age. Curr. Opin. Neurobiol. *10*, 224–231.

Grady, C.L., McIntosh, A.R., Horwitz, B., Maisog, J.M., Ungerleider, L.G., Mentis, M.J., Pietrini, P., Schapiro, M.B., and Haxby, J.V. (1995). Age-related reductions in human recognition memory due to impaired encoding. Science *269*, 218–221.

Grady, C.L., McIntosh, A.R., Rajah, M.N., Beig, S., and Craik, F.I.M. (1999). The effects of age on neural correlates of episodic encoding. Cereb. Cortex *9*, 805–814.

Greenwood, P.M. (2000). The frontal aging hypothesis evaluated. J. Int. Neuropsychol. Soc. *6*, 705–726.

Hasher, L., and Zacks, R.T. (1988). Working memory, comprehension, and aging: A review and new view. In The Psychology of Learning and Motivation, G.H. Bower, ed. (San Diego, CA: Academic Press), pp. 193–225.

Hasher, L., Zacks, R.T., and May, C.P. (1999). Inhibitory control, circadian arousal, and age. In Attention and Performance XVII: Cognitive Regulation of Performance: Interaction of Theory and Application, D.E. Gopher and K. Koriat, eds. (Cambridge, MA: MIT Press), pp. 653–675.

Honda, M., Nagamine, T., Fukuyama, H., Yonekura, Y., Kimura, J., and Shibasaki, H. (1997). Movement-related cortical potential and regional cerebral blood flow change in patients with stroke after motor recovery. J. Neurol. Sci. *146*, 117–126.

Hulicka, I.M. (1966). Age differences in Wechsler Memory Scale scores. J. Genet. Psychol. *109*, 135–145.

Hughes, C.P., Berg, L., Danziger, W.L., Coben, L.A., and Martin, R.L. (1982). A new clinical scale for the staging of dementia. Br. J. Psychiatry *140*, 566–572.

Iidaka, T., Anderson, N.D., Kapur, S., Cabeza, R., and Craik, F.I.M. (2000). The effect of divided attention on encoding and retrieval in episodic memory revealed by positron emission tomography. J. Cogn. Neurosci. *12*, 267–280.

Iidaka, T., Sadato, N., Yamada, H., Murata, T., Omori, M., and Yonekura, Y. (2001). An fMRI study of the functional neuroanatomy of picture encoding in younger and older adults. Cogn. Brain Res. *11*, 1–11.

Kapur, S., Craik, F.I.M., Tulving, E., Wilson, A.A., Houle, S., and Brown, G.M. (1994). Neuroanatomical correlates of encoding in episodic memory: Levels of processing effects. Proc. Natl. Acad. Sci. USA *91*, 2008–2011.

Kapur, S., Tulving, E., Cabeza, R., McIntosh, A.R., Houle, S., and Craik, F.I.M. (1996). The neural correlates of intentional learning of verbal materials: A PET study in humans. Cogn. Brain Res. *4*, 243–249.

Kausler, D.H., Salthouse, T.A., and Saults, J.S. (1988). Temporal memory over the adult lifespan. Am. J. Psychol. *101*, 207–215.

Kelley, W.M., Miezin, F.M., McDermott, K.B., Buckner, R.L., Raichle, M.E., Cohen, N.J., Ollinger, J.M., Akbudak, E., Conturo, T.E., Snyder, A.Z., and Petersen, S.E. (1998). Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal encoding. Neuron *20*, 927–936.

Kirchhoff, B.A., Wagner, A.D., Maril, A., and Stern, C.E. (2000). Prefrontal-temporal circuitry for episodic encoding and subsequent memory. J. Neurosci. *20*, 6173–6180.

Knoke, D., Taylor, A.E., and Saint-Cyr, J.A. (1998). The differential effects of cueing on recall in Parkinson's disease and normal subjects. Brain Cogn. *38*, 261–274.

Konishi, S., Donaldson, D.I., and Buckner, R.L. (2001). Transient activation during block transition. Neuroimage *13*, 364–374.

Kucera, H., and Francis, W.N. (1967). Computational analysis of present-day American English (Providence, RI: Brown University Press).

Madden, D., Gottlob, L., Denny, L., Turkington, T., Provenzale, J., Hawk, T., and Coleman, R. (1999a). Aging and recognition memory: Changes in regional cerebral blood flow associated with components of reaction time distributions. J. Cogn. Neurosci. *11*, 511–520.

Madden, D.J., Turkington, T.G., Provenzale, J.M., Denny, L.L., Hawk, T.C., Gottlob, L.R., and Coleman, R.E. (1999b). Adult age differences in the functional neuroanatomy of verbal recognition memory. Hum. Brain Mapp. *7*, 115–135.

McDermott, K.B., Buckner, R.L., Petersen, S.E., Kelley, W.M., and Sanders, A.L. (1999). Set- and code-specific activation in the frontal cortex: an fMRI study of encoding and retrieval of faces and words. J. Cogn. Neurosci. *11*, 631–640.

McIntosh, A.R., Sekuler, A.B., Penpeci, C., Rajah, M.N., Grady, C.L., Sekuler, R., and Bennett, P.J. (1999). Recruitment of unique neural systems to support visual memory in normal aging. Curr. Biol. *9*, 1275–1278.

Morris, J.C. (1993). The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology *43*, 2412–2414.

Moscovitch, M., and Winocur, G. (1995). Frontal lobes, memory, and aging. Ann. NY Acad. Sci. *769*, 119–150.

Myerson, J., Hale, S., Wagstaff, D., Poon, L.W., and Smith, G.A. (1990). The information-loss model: A mathematical theory of age-related cognitive slowing. Psychol. Rev. *97*, 475–487.

Nielson, K.A., Langenecker, S.A., and Garavan, H.P. (2002). Differences in the functional neuroanatomy of inhibitory control across the adult lifespan. Psychol. Aging, in press.

Nyberg, L., Bäckman, L., Erngrund, K., Olofsson, U., and Nilsson, L. (1996). Age differences in episodic memory, semantic memory, and priming relationships to demographic, intellectual, and biological factors. J. Gerontol Psychol. Sci. *51B*, P234–P240.

Ohyama, M., Senda, M., Kitamura, S., Ishii, K., Mishina, M., and Terashi, A. (1996). Role of the nondominant hemisphere and undamaged area during word repetition in poststroke aphasics. Stroke *27*, 897–903.

O'Sullivan, M., Jones, D.K., Summers, P.E., Morris, R.G., Williams, S.C.R., and Markus, H.S. (2001). Evidence for cortical "disconnection" as a mechanism of age-related cognitive decline. Neurology *57*, 632–638.

Otten, L.J., Henson, R.N., and Rugg, M.D. (2001). Depth of processing effects on neural correlates of memory encoding: Relationship between findings from across- and within-task comparisons. Brain *124*, 399–412.

Park, D.C., Smith, A.D., Morrell, R.W., Puglisi, J.T., and Dudley, W.N. (1990). Effects of contextual integration on recall of pictures by older adults. J. Gerontol. Psychol. Sci. *45*, 52–57.

Park, D.C., Smith, A.D., Lautenschlager, G., Earles, J.L., Frieske, D., Zwahr, M., and Gaines, C.L. (1996). Mediators of long-term memory performance across the life span. Psychol. Aging *11*, 621–637.

Park, D.C., Polk, T.A., Mikels, J.A., Taylor, S.F., and Marshuetz, C. (2001). Cerebral aging: Integration of brain and behavioral models of cognitive function. Dialogues in Clinical Neuroscience *3*, 151–166.

Petersen, S.E., Fox, P.T., Posner, M.I., Mintun, M.A., and Raichle, M.E. (1988). Positron emission tomographic studies of the cortical anatomy of single-word processing. Nature *331*, 585–589.

Poldrack, R.A., Wagner, A.D., Prull, M.W., Desmond, J.E., Glover, G.H., and Gabrieli, J.D.E. (1999). Functional specialization for semantic and phonological processing in the left inferior prefrontal cortex. Neuroimage *10*, 15–35.

Raz, N. (2000). Aging of the brain and its impact on cognitive performance: Integration of structural and functional findings. In The Handbook of Aging and Cognition, F.I.M. Craik and T.A. Salthouse, eds. (Mahwah, NJ: Lawrence Erlbaum Associates, Inc., Publishers), pp. 1–90.

Raz, N., Gunning, F.N., Head, D., Dupuis, J.H., McQuain, J., Briggs, S.D., Loken, W.J., Thornton, A.E., and Acker, J.D. (1997). Selective aging of the human cerebral cortex observed in vivo: Differential vulnerability of the prefrontal gray matter. Cereb. Cortex *7*, 268–282.

Reuter-Lorenz, P.A., Jonides, J., Smith, E.E., Hartley, A., Miller, A., Marschuetz, C., and Koeppe, R.A. (2000). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. J. Cogn. Neurosci. *12*, 174–187.

Reuter-Lorenz, P.A., Marshuetz, C., Jonides, J., and Smith, E.E. (2001). Neurocognitive ageing of storage and executive processes. Eur. J. Cogn. Psychol. *13*, 257–278.

Rosen, H.J., Petersen, S.E., Linenweber, M.R., Snyder, A.Z., White, D.A., Chapman, L., Dromerick, A.W., Fiez, J.A., and Corbetta, M.D. (2000). Neural correlates of recovery from aphasia after damage to left inferior frontal cortex. Neurology *55*, 1883–1894.

Rypma, B., and D'Esposito, M. (2000). Isolating the neural mechanisms of age-related changes in human working memory. Nat. Neurosci. *3*, 509–515.

Salthouse, T.A. (1996). The processing-speed theory of adult age differences in cognition. Psychol. Rev. *45*, 403–428.

Savage, C.R., Deckersbach, T., Heckers, S., Wagner, A.D., Schacter, D.L., Alpert, N.M., Fischman, A.J., and Rauch, S.L. (2001). Prefrontal regions supporting spontaneous and directed application of verbal learning strategies. Brain *124*, 219–231.

Schacter, D.L., Savage, C.R., Alpert, N.M., Rauch, S.L., and Albert, M.S. (1996). The role of hippocampus and frontal cortex in age-related memory changes: A PET study. Neuroreport *7*, 1165–1169.

Shallice, T., Fletcher, P., Frith, C.D., Grasby, P., Frackowiak, R.S.J., and Dolan, R.J. (1994). Brain regions associated with acquisition and retrieval of verbal episodic memory. Nature *368*, 633–635.

Snyder, A.Z. (1996). Difference image versus ratio image error function forms in PET-PET realignment. In Quantification of Brain Function Using PET, D. Bailey and T. Jones, eds. (San Diego: Academic Press), pp. 131–137.

Sohlberg, M.M., and Mateer, C.A. (2001). Cognitive Rehabilitation: An Integrative Neuropsychological Approach (New York: The Guilford Press).

Stuss, D.T., Craik, F.I.M., Sayer, L., Franchi, D., and Alexander, M.P. (1996). Comparison of older people and patients with frontal lesions: Evidence from word list learning. Psychol. Aging *11*, 387–395.

Sullivan, E.V., Adalsteinsson, E., Hedehus, M., Ju, C., Moseley, M., Lim, K.O., and Pfefferbaum, A. (2000). Equivalent disruption of regional white matter microstructure in ageing healthy men and women. Neuroreport *12*, 99–104.

Talairach, J., and Tournoux, P. (1988). Co-Planar Stereotaxic Atlas of the Human Brain (New York: Thieme Medical Publishers, Inc.).

Thulborn, K.R., Carpenter, P.A., and Just, M.A. (1999). Plasticity of language-related brain function during recovery from stroke. Stroke *30*, 749–754.

Thurstone, L.E., and Thurstone, T.G. (1949). Examiner Manual for the SRT Primary Mental Abilities (Chicago: Science Research).

Wagner, A.D., Poldrack, R.A., Eldridge, L.L., Desmond, J.E., Glover, G.H., and Gabrieli, J.D.E. (1998a). Material-specific lateralization of prefrontal activation during episodic encoding and retrieval. Neuroreport *9*, 3711–3717.

Wagner, A.D., Schacter, D.L., Rotte, M., Koutstaal, W., Maril, A., Dale, A.M., Rosen, B.R., and Buckner, R.L. (1998b). Building memories: Remembering and forgetting of verbal experiences as predicted by brain activity. Science *281*, 1188–1191.

Wechsler, D. (1955). WAIS Manual (New York: Psychological Corporation).

Wechsler, D., and Stone, C.P. (1973). Manual: Wechsler Memory Scale (New York: Psychological Corporation).

Weiller, C., Isensee, C., Rijntsjes, M., Huber, W., Muller, S., Bier, D., Ditschka, K., Woods, R.P., Noth, J., and Diener, H.C. (1995). Recovery from Wernicke's Aphasia: A positron emission tomography study. Ann. Neurol. *37*, 723–732.

West, R.L. (1996). An application of prefrontal cortex function theory to cognitive aging. Psychol. Bull. *120*, 272–292.

Zagar, R., Arbit, J., Stuckey, M., and Wengel, W.W. (1984). Developmental analysis of the Wechsler Memory Scale. J. Clin. Psychol. *40*, 1466–1473.