The Effects of Divided Attention on Encoding- and Retrieval-Related Brain Activity: A PET Study of Younger and Older Adults

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Abstract

■ Divided attention (DA) disrupts episodic encoding, but has little effect on episodic retrieval. Furthermore, normal aging is associated with episodic memory impairments, and when young adults are made to encode information under DA conditions, their memory performance is reduced and resembles that of old adults working under full attention (FA) conditions. Together, these results suggest a common neurocognitive mechanism by which aging and DA during encoding disrupt memory performance. In the current study, we used PET to investigate younger and older adults' brain activity during encoding and retrieval under FA and DA conditions. In FA conditions, the old adults showed reduced activity in prefrontal regions that younger adults activated preferentially during encoding or retrieval, as well as increased activity in prefrontal regions young adults did not activate. These results indicate that prefrontal functional specificity of episodic memory is reduced by aging. During encoding, DA reduced memory performance, and reduced brain activity in left-prefrontal and medial-temporal lobe regions for both age groups, indicating that DA during encoding interferes with encoding processes that lead to better memory performance. During retrieval, memory performance and retrieval-related brain activity were relatively immune to DA for both age groups, suggesting that DA during retrieval does not interfere with the brain systems necessary for successful retrieval. Finally, left inferior prefrontal activity was reduced similarly by aging and by DA during encoding, suggesting that the behavioral correspondence between these effects is the result of a reduced ability to engage in elaborate encoding operations. ■

INTRODUCTION

Cognitive studies indicate that aging impairs episodic encoding and retrieval (for reviews see Craik, Anderson, Kerr, & Li, 1995; Burke & Light, 1981); however, these processes are difficult to isolate in behavioral studies because age-related memory decrements could be due to impairments of encoding, retrieval, or both. Functional neuroimaging techniques such as positron emission tomography (PET) allow a more direct examination of encoding and retrieval processes and how they change with normal aging, because it is possible to obtain separate measures of brain activity during encoding and retrieval.

PET studies in young and old adults have identified age-related decreases in brain activity in regions that young adults typically activate during encoding and retrieval. Specifically, Grady et al. (1995) found that activity in left prefrontal cortex (PFC) and right medial-temporal areas was reduced by aging during the encoding of unfamiliar faces, and Cabeza et al. (1997) found a

similar age-related decline in left PFC during the encoding of word pairs. By contrast, Madden et al. (1999) had subjects make semantic judgments about words, a task that facilitates elaborate encoding (Craik & Tulving, 1975), and encoding-related brain activity in left PFC and medial-temporal regions did not interact with age. Together, these studies indicate that age-related reductions in encoding-related brain activity exist when the task requires complex self-initiated encoding, but not when the task guides and supports elaborate encoding.

Retrieval-related brain activity is also reduced in old adults in some cases. It is generally accepted that controlled and automatic processes mediate retrieval (e.g., Jacoby, 1991; Hasher & Zacks, 1979; Atkinson & Juola, 1974), and that retrieval cues facilitate automatic processes, or diminish the extent to which controlled, attention-demanding processes must be engaged (Craik, 1986). Furthermore, behavioral studies find that controlled processes decline with age, while automatic processes are relatively spared (e.g., Jennings & Jacoby, 1993; Hasher & Zacks, 1979). Neuroimaging studies have found congruent results. Namely, in tasks that arguably relied on more controlled than automatic processes (cued recall and associative recognition of moderately related word pairs in Cabeza et al., 1997; word stem cued recall of perceptually encoded words in Schacter, Savage, Alpert, Rauch, & Albert, 1996), right PFC activity was reduced by aging. By contrast, in tasks that arguably relied on more automatic than controlled processes (item recognition in Grady et al., 1995 and Madden et al., 1999; word stem cued recall of semantically encoded words in Bäckman et al., 1997), right PFC activity during retrieval did not differ with age or was more extensive in the old adults. In summary, it seems that age-related reductions in right PFC activity during retrieval exist when controlled, attention-demanding retrieval operations must be engaged, but not when automatic forms of retrieval are engaged.

Neuroimaging studies have also found that aging is associated with *increased* brain activity in regions that are typically not activated by young adults during encoding or retrieval (e.g., Madden et al., 1999; Bäckman et al., 1997; Cabeza et al., 1997; Schacter, Savage, Alpert, Rauch, & Albert, 1996). The interpretation of these findings is still unclear, however, as increased brain activity in old adults has occurred both in the context of comparable behavioral performance in young and old adults (e.g., suggesting the engagement of compensatory strategies, Cabeza et al., 1997), and in the context of poorer behavioral performance in the old than young adults (e.g., suggesting an age-related increase in the attentional demands of the memory task, Madden et al., 1999).

Craik (1983, 1986) hypothesized that controlled encoding and retrieval processes are impaired by normal aging because they require the allocation of a substantial amount of attentional resources, and that many factors including normal aging and divided attention (DA) reduce the amount of attentional resources available to fuel complex cognitive operations. Evidence in support of this view includes the fact that age-related memory decrements are greater on recall tests than on recognition tests (Schonfeld & Robertson, 1966), because recognition tests provide more retrieval support and, therefore, rely less on self-initiated retrieval operations. Furthermore, when the attentional resources available for encoding are reduced in young adults by DA, their pattern of memory performance mimics that of old adults performing under full attention (FA) conditions (Anderson, Craik, & Naveh-Benjamin, 1998; Jennings & Jacoby, 1993; Craik, 1982; Rabinowitz, Craik, & Ackerman, 1982).

This behavioral evidence suggests that the effects of aging and DA during encoding have a common neurocognitive cause. At the cognitive level, this cause has been described as a reduction in attentional resources (Craik, 1983, 1986), but what is its identity at the neural level? Following the suggestion made by Anderson et al. (1998) that the neural correlate of attentional resources may be increased in cerebral blood flow in particular brain regions in response to a cognitive challenge, it follows that DA and aging should similarly reduce encoding-related brain activity. The evidence in support of this hypothesis is striking but indirect. Specifically, separate experiments have demonstrated that DA during encoding (Iidaka, Anderson, Kapur, Cabeza, & Craik, 2000; Fletcher, Frith, & Grasby, et al., 1995; Fletcher, Shallice, & Dolan, 1998; Shallice et al., 1994) and normal aging (Cabeza et al., 1997; Grady et al., 1995) are associated with a similar reduction in left PFC activity. Finally, although DA during encoding impairs later memory performance, memory performance is relatively immune to the effects of DA during retrieval (Craik, Govoni, Naveh-Benjamin, & Anderson, 1996; Baddeley, Lewis, Eldridge, & Thomson, 1984). In a recent PET study with young adults, we demonstrated that the asymmetric effects of DA on encoding and retrieval hold at the level of brain activity—DA during encoding disrupted memory performance and encoding-related brain activity, but DA during retrieval left memory performance and retrieval-related brain activity intact (Iidaka et al., 2000).

In the current study, we used PET to image younger and older adults' brain activity during episodic encoding and retrieval under FA and DA conditions. The memory task was derived from the cued recall task of Cabeza et al. (1997). Participants were shown lists of word pairs (e.g., ''dentist–glove'') to try to encode, and then at retrieval were given the first word as a cue to recall the second word. Scanning took place during encoding or retrieval, while participants performed a secondary auditory task that was easy (respond to a repeated low tone) or difficult (respond to differentially low and high tones). Given the relatively automatic nature of the easy version of the auditory task, we regarded it as the FA condition, and given the complexity of the difficult task, we re-

garded it as the DA condition (c.f., Fletcher, Frith, & Grasby, et al., 1995; Shallice et al., 1994). We analyzed the PET data using partial least squares (PLS), a multivariate technique that identifies patterns of brain activity that distinguish experimental conditions.

The young adults' data are reported by Iidaka et al. (2000). The goal of the present article is to address four main questions regarding the effects of aging on brain activity. (1) Does encoding-related or retrieval-related brain activity differ with age? Given that we used the same complex, attention-demanding memory task used by Cabeza et al. (1997), we expected age-related differences in both encoding- and retrieval-related brain activity in FA conditions. (2) Do the effects of DA on encoding-related brain activity differ with age? Aging (Cabeza et al., 1997; Grady et al., 1995) and DA during encoding (Fletcher, Frith, & Grasby, et al., 1995; Fletcher, Shallice, & Dolan, 1998; Iidaka et al., 2000; Shallice et al., 1994) both reduce left PFC activity, and the effects of DA during encoding on memory performance are comparable for young and old adults (Anderson et al., 1998). Thus, we hypothesized that young and old adults would show similar effects of DA on encoding-related brain activity, although aging and DA may have distinct effects on activity in regions that are not typically associated with encoding. (3) Do the effects of DA on retrieval-related brain activity differ with age? Because DA during retrieval has little effect on memory performance for either age group (Anderson et al., 1998) and has little effect on retrieval-related brain activity in young adults (Iidaka et al., 2000), we predicted minimal effects of DA on retrieval-related brain activity in both age groups, although age and DA may have distinct effects on activity in regions that are not usually associated with retrieval. (4) Does the similarity between aging and the effects of DA during encoding in young adults hold at the level of brain activity? We expected it would, and predicted that there would be encoding-related brain activity similarly affected by aging and by DA during encoding in young adults. Specifically, given the previous results described above (Iidaka et al., 2000; Cabeza et al., 1997; Fletcher, Frith, & Grasby, et al., 1995; Flethcher et al., 1998; Grady et al., 1995; Shallice et al., 1994) we expected that both aging and DA during encoding in young adults would be associated with similar reductions in left PFC activity.

RESULTS

Memory Performance

Table 1 shows memory performance in each of the experimental conditions. The temporal placement of the scanning did not influence FA memory performance for either age group (FA Encoding vs. FA Retrieval, $p > .50$ for both age groups). A $2 \times 2 \times 2$ ANOVA with Young/Old, Encoding/Retrieval, and FA/DA as variables showed that memory performance was better for the young adults than for the old adults [$F(1, 22) = 10.02$, $p = .004$], and that DA disrupted encoding more than retrieval [Encoding/Retrieval × FA/DA, $F(1, 22) = 23.97$, $p < .001$], similarly for young and old adults [Young/Old × Encoding/Retrieval × FA/DA, $F(1, 22) < 1$]. Furthermore, the magnitude of memory costs, measured in absolute (full − divided) or relative [(full − divided) / full] terms, did not differ between the two age groups [$F(1,22) < 1$].

PET Results

We initially included all of the conditions in an omnibus PLS analysis. This analysis yielded four significant LVs, each representing a three-way interaction among Young/Old, Encoding/Retrieval, and FA/DA. To interpret these complex interactions, and to address our specific hypotheses more directly, we conducted three two-way PLS analyses: (1) Young/Old × Encoding/Retrieval under FA conditions; (2) Young/Old × FA/DA during encoding; and, (3) Young/Old × FA/DA during retrieval. These results are reported in tables below; in most cases, the peak voxel in each cluster is reported, but for large clusters that extended over more than one brain region, the peak voxel in each region is reported. To aid the interpretation of the analyses, univariate analyses (*t* tests) were performed for the peak voxels identified in the PLS analyses. Although these two methods correspond in most cases, there are cases in which they differ mainly because of the reduced sensitivity to distributed effects in univariate analyses (McIntosh, Bookstein, Haxby, & Grady, 1996).

Table 1. Mean Proportion of Words Correctly Recalled and DA Costs

		Attention condition		*Memory cost*	
Age group	*Memory condition*	*Full*	*Divided*	*Absolute*	*Relative*
Young	Encoding	.79 (.12)	.58 (.20)	.21 (.19)	.26 (.24)
	Retrieval	.78 (.10)	.75 (.04)	.03 (.09)	.04 (.13)
Old	Encoding	.60 (.24)	.36 (.05)	.24 (.17)	.36 (.32)
	Retrieval	.59 (.22)	.51 (.20)	.08 (.15)	.09 (.29)

Note: Standard deviations in parentheses. Absolute memory cost = FA − DA. Relative memory cost = (FA − DA) / FA.

Inferences were based on the permutation and bootstrap tests described in Methods.

For comparisons in which brain activity differed between young and old adults, we show the main-effect image for each age group, rather than the interaction image. Interaction images are difficult to comprehend, as each cluster could represent a main effect in one group only, or could represent a crossover interaction. By showing the images for each group separately, the main effects and interactions are obvious simultaneously. Clusters that appear in both age groups represent main effects, and the clusters appears in one group but not the other or show opposite effects in the two groups represent interactions. These results are also presented in the tables: Main effects are labeled as ''in young and old'', effects in one group but not the other are labeled as ''in young only'' or ''in old only'', and crossover interactions are labeled as ''in young only'' for one effect (e.g., encoding > retrieval), and as ''in old only'' for the opposite effect (e.g., retrieval > encoding). Nevertheless, it is important to keep in mind that all results reported and discussed were obtained from the between-groups analyses.

Young/Old × Encoding/Retrieval in FA Conditions

To test whether encoding- or retrieval-related brain activity differed with age, we conducted a PLS analysis of Age and Encoding/Retrieval under FA conditions. The first LV ($p < .001$; Figure 1A) represented the Encoding/

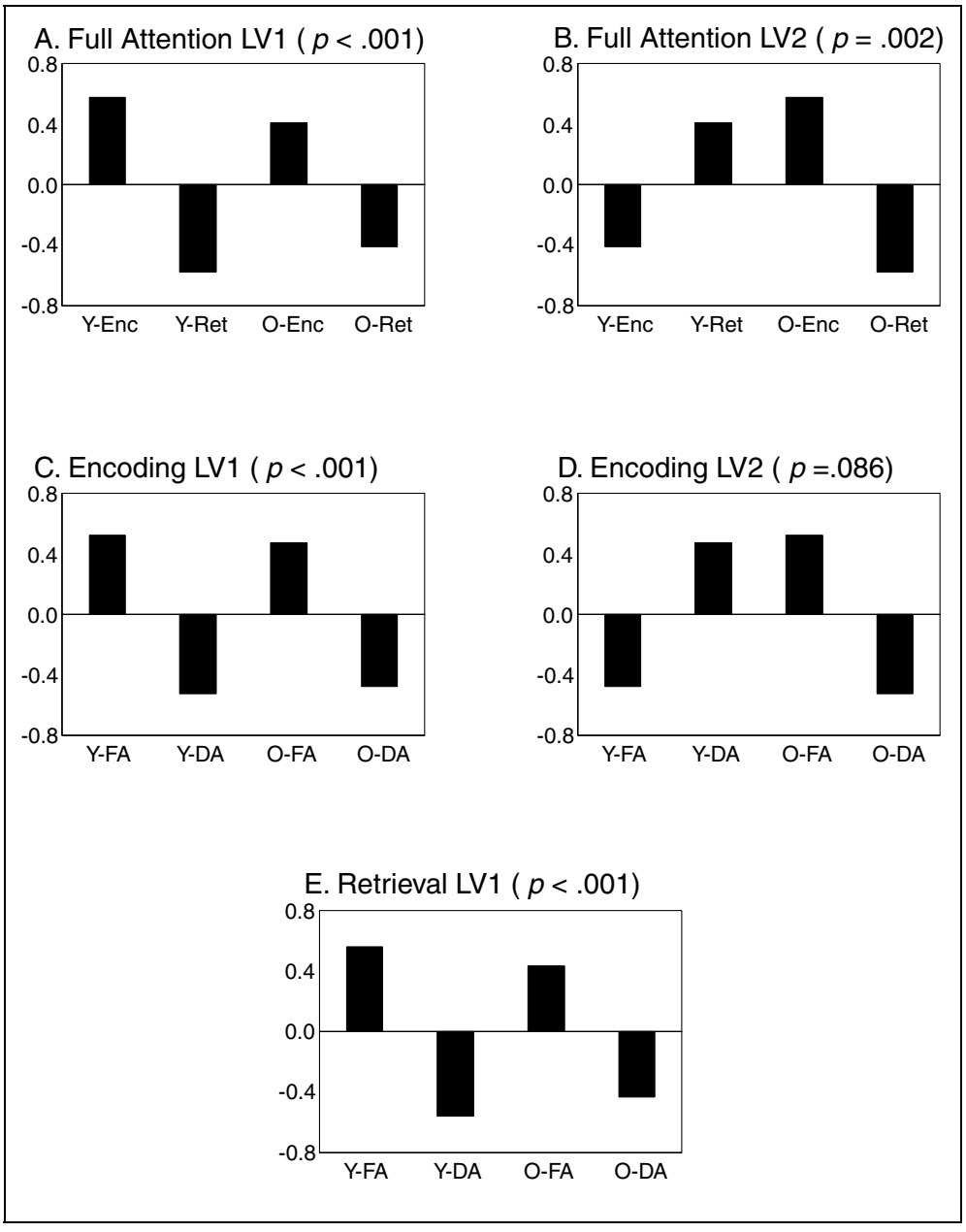

Figure 1. Design scores for each LV in each analysis. Top row: LVs from the analysis of Young/Old × Encoding/Retrieval under FA conditions. (A) LV1 distinguished areas that were more active during encoding (Enc) than retrieval (Ret) from areas that were more active during retrieval than encoding. (B) LV2 represented an Encoding/Retrieval × Young/Old interaction. Middle row: LVs from the analysis of Young/Old × FA/DA during encoding. (C) LV1 distinguished areas that were more active during FA than DA conditions from areas that were more active during DA than FA conditions. (D) LV2 represented an FA/DA × Young/Old interaction. Bottom row: (E) LV1 from the analysis of Young/Old × FA/DA during retrieval. This LV distinguished areas that were more active during FA than DA conditions from areas that were more active during DA than FA conditions. Note that the second LV (the interaction of Young/Old × FA/DA during retrieval) was not significant.

Table 2. Regions That Were More Active During Encoding Than Retrieval Under FA Conditions

Region	*Side*	*BA*	*x*	*y*	*z*	*Boot*	*Y-t*	*O-t*
Encoding > Retrieval in Young and Old								
Middle frontal gyrus	L	9/10/46	−34	40	20	5.08	3.58	3.66
Superior temporal gyrus	L	22	−50	−36	12	4.66	2.97	2.91
Middle temporal gyrus	L	37	−40	−60	12	6.22	3.74	4.27
Middle temporal gyrus	L	21	−54	−10	−12	6.62	3.42	6.48
Fusiform gyrus	L	20	−40	−16	−24	5.62	2.71	5.63
Inferior parietal lobule	L	40	−50	−40	28	8.56	7.71	4.10
Inferior occipital gyrus	L	18	−26	−90	0	4.00	2.52	3.06
Inferior temporal/Fusiform gyrus	R	37/19	42	−66	0	6.04	4.82	3.22
Fusiform gyrus	R	20	36	−16	−28	5.62	3.52	2.74
Inferior parietal lobule	R	40	34	−36	40	4.91	2.89	2.68
Encoding > Retrieval in Young Only								
Medial Frontal gyrus		6	0	−12	44	4.57	3.00	−2.75
Inferior frontal gyrus	L	45/46	−50	36	16	4.38	2.50	−2.51
Inferior frontal gyrus	L	44	−42	14	24	4.82	3.05	−2.39
Inferior frontal gyrus	L	47	−44	38	−8	3.45	2.09	−2.14
Fusiform gyrus	L	37	−48	−46	−12	3.35	3.84	−1.43
Superior temporal gyrus	L	38	−30	10	−28	4.80	3.93	0.80
Inferior frontal gyrus	R	44	54	14	8	5.13	3.02	−3.06
Precentral gyrus	R	4/6	52	2	20	4.33	4.74	1.52
Superior temporal gyrus	R	22	60	−4	0	4.00	3.24	−1.79
Middle temporal gyrus	R	21	52	6	−20	4.35	2.70	−2.95
Lingual gyrus	R	18	18	−58	4	2.99	4.95	−0.56
Fusiform gyrus	R	18	36	−90	−12	3.35	2.43	−1.60
Brainstem	R		12	−20	−16	3.57	2.83	−1.82
Encoding > Retrieval in Old Only								
Middle temporal gyrus	L	20	−36	−12	−16	3.52	−1.04	3.44
Middle temporal gyrus	L	37	−58	−58	8	3.41	−0.24	3.46
Fusiform gyrus	L	19	−28	−52	−4	3.66	−1.95	2.98
Inferior parietal lobule	L	40	−58	−28	36	4.19	−1.16	4.44
Middle frontal gyrus	R	9/10/46	38	42	12	4.24	−2.00	2.85
Superior temporal gyrus	R	22	48	−38	20	3.09	0.03	4.98
Transverse gyrus	R	41	36	−36	4	4.21	−1.37	3.53
Insula	R		34	−22	−8	3.54	−1.37	4.18
Inferior parietal lobule	R	40	42	−32	28	3.92	−0.39	4.98
Brainstem	R		16	−34	−28	3.27	−0.21	3.76
Putamen	R		18	4	−12	3.72	−2.23	2.26

Note: BA = Brodmann's Area; Boot = bootstrap ratio; Y-*t* = *t* value for young adults; O-*t* = *t* value for older adults. Positive *t* values represent greater values during encoding than retrieval; negative *t* values represent greater values during retrieval than encoding. $t(11) \geq |2.22|$, $p < .05$.

Retrieval main effect that was numerically although not significantly stronger for the young adults. The second LV (p = .002; Figure 1B) represented an interaction between Encoding/Retrieval and Age. The regions that were more active during encoding than retrieval are listed in Table 2 and are shown in yellow and red in Figure 2A and B, for the young and old adults, respectively. Although the left middle frontal gyrus (BA 9/10/46) was more active during encoding than retrieval in both age groups, this activity extended into the left inferior frontal gyrus (BA 44/45/46/47) only for the young adults. Similarly, both age groups activated the inferior parietal lobule (BA 40) more during encoding than retrieval, but this activation, particularly in the right hemisphere, was more extensive in the old than young adults.

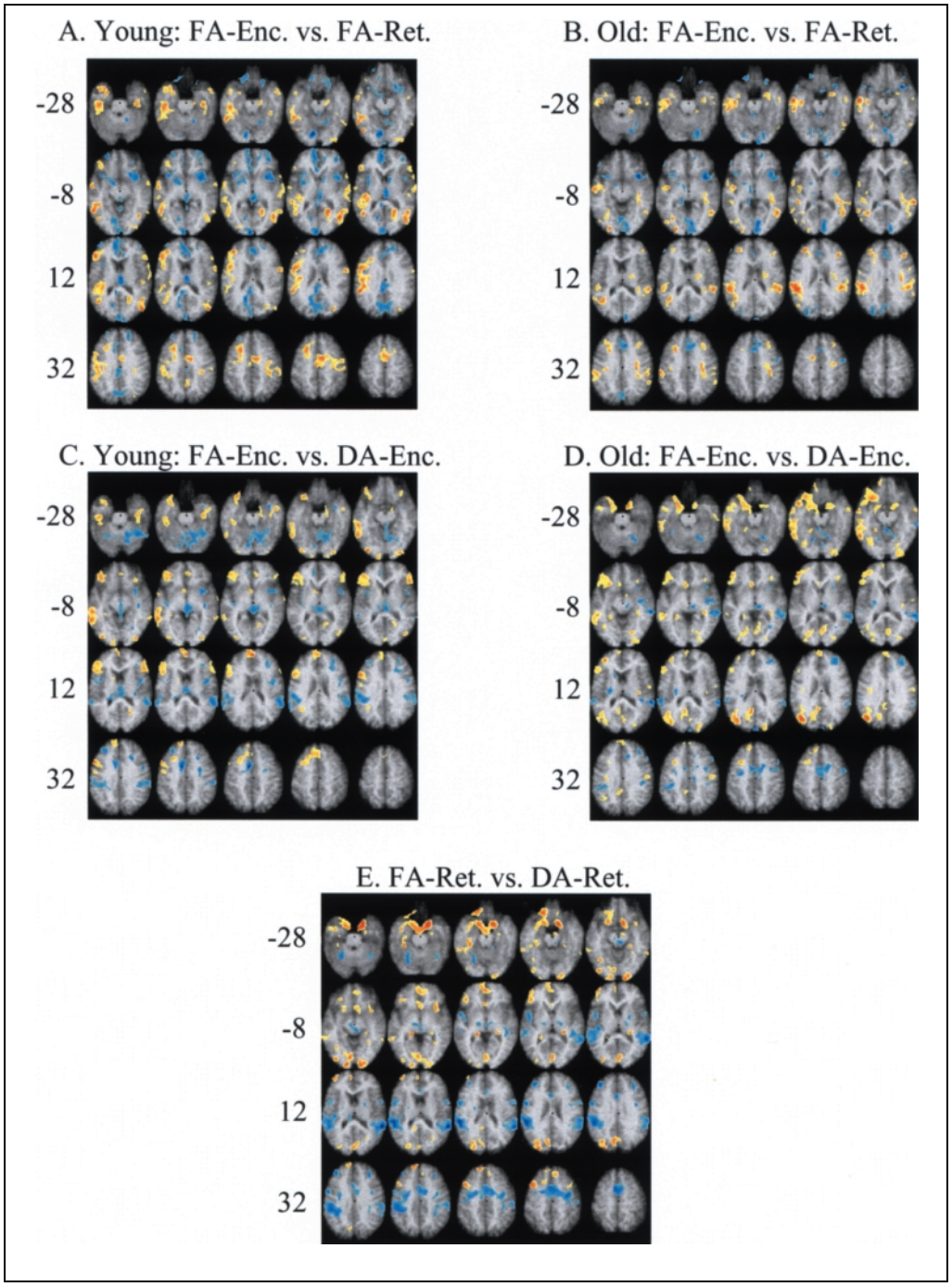

Figure 2. Top row: Panels A and B show images from FA conditions, for young and old adults, respectively. Regions that were more active during FA encoding than FA retrieval are shown in yellow and red (see Table 2 and Figure 1A), and regions that were more active during FA retrieval than FA encoding are shown in blue (see Table 3 and Figure 1B). Middle row: Panels C and D show images from the FA and DA during encoding conditions, for young and old adults respectively. Regions that were more active during FA than DA encoding are shown in yellow and red (see Table 4 and Figure 1C) and regions that were more active during DA than FA encoding are shown in blue (see Table 5 and Figure 1D). Bottom row: Panel E shows the image from the retrieval conditions for both age groups. Regions that were more active during FA than DA retrieval are shown in yellow and red (see Table 6 and Figure 1E), and regions that were more active during DA than FA retrieval are shown in blue (see Table 7 and Figure 1E). The data are not shown for the two age groups separately because the interaction of age and FA/DA was not significant. Note that the images in top and middle rows are shown separately for the two age groups to facilitate comparison, but that the results described in the text and tables were derived from the between-groups analysis. The PET data have been superimposed on standard MR images, plotted from z = −28 to z = +48 mm relative to the AC–PC line, in 4 mm increments. Numbers on the left of each panel represent the z value of the first image in each column. The left side of each image represents the left side of the brain.

Table 3. Regions That Were More Active During Retrieval Than Encoding Under FA Conditions

Region	*Side*	*BA*	*x*	*y*	*z*	*Boot*	*Y-t*	*O-t*
Retrieval > Encoding in Young and Old								
Orbital frontal gyrus	L	11	−14	32	−20	4.80	−3.81	−2.78
Anterior cingulate	L	32	−4	38	24	4.88	−3.04	−3.39
Insula	L		−36	14	−4	5.69	−4.75	−2.95
Precuneus	L	18	−8	−70	28	5.05	−4.20	−2.51
Cerebellum	L		−6	−74	−12	5.89	−5.46	−2.73
Putamen	L		−20	4	−4	4.74	−4.14	−1.73
Orbital frontal gyrus	R	47	20	22	−20	5.10	−4.35	−2.74
Medial frontal gyrus	R	10	14	52	0	4.46	−2.50	−2.98
Insula	R		32	12	−8	8.36	−4.88	−6.74
Precuneus	R	18	2	−70	28	5.95	−4.05	−3.03
Brainstem			0	−38	−16	5.24	−3.60	−3.00
Retrieval > Encoding in Young Only								
Middle frontal gyrus	L	10	−26	56	−8	5.30	−4.09	−0.79
Medial frontal gyrus	L	10	−16	48	8	4.00	−3.07	2.03
Posterior cingulate	L	23	−12	−54	20	3.40	−4.57	1.42
Cuneus	L	18	−10	−94	8	3.85	−3.73	1.34
Middle frontal gyrus	R	10	38	42	12	4.24	−2.00	2.85
Medial frontal gyrus	R	9	6	46	24	3.69	−2.81	2.00
Cerebellum	R		14	−58	−20	3.83	−4.38	−1.70
Thalamus			0	−20	12	5.15	−4.88	−1.24
Retrieval > Encoding in Old Only								
Anterior cingulate		32	0	18	44	4.18	1.26	−3.89
Inferior frontal gyrus	L	45/46	−50	36	16	4.38	2.50	−2.51
Inferior frontal gyrus	L	47	−44	38	−8	3.32	2.09	−2.14
Middle occipital gyrus	L	19	−26	−76	28	3.37	0.96	−3.39
Brainstem	L		−8	−16	−4	3.62	1.71	−2.88
Precentral gyrus	R	4	44	−4	44	5.69	3.26	−4.11
Striate	R	17	2	−92	0	3.66	−0.50	−4.50

Note: BA = Brodmann's Area; Boot = bootstrap ratio; Y-*t* = *t* value for young adults; O-*t* = *t* value for older adults. Positive *t* values represent greater values during encoding than retrieval; negative *t* values represent greater values during retrieval than encoding. $t(11) \geq |2.22|, p < .05$.

Regions that were more active during retrieval than encoding are listed in Table 3 and are shown in blue in Figure 2A (young) and B (old). There was retrieval-related activity in orbital and medial aspects of the frontal lobes in both age groups. In addition, the young adults activated bilateral PFC regions more during retrieval than encoding, although it should be noted that the young adults' left PFC activity was more medial than was their encoding-related activity. By contrast, the regions that old adults activated more during retrieval than encoding included the anterior cingulate and lateral aspects of the left-inferior-frontal gyrus, two regions that the young adults activated more during encoding than retrieval.

Young/Old × FA/DA During Encoding

To examine whether the effects of DA on encoding-related brain activity differ with age, we conducted a PLS analysis that included Age and FA/DA during encoding as

factors. The first LV ($p < .001$; Figure 1C) represented a FA/DA main effect, about equally for the two age groups. The second LV ($p = .086$; Figure 1D) represented an interaction between FA/DA and Age. Regions that were more active during FA than DA conditions in both age groups are listed in Table 4 and are shown in yellow and red in Figure 2C for the young and in Figure 2D for the old. These regions were mainly left-lateralized in the PFC, except at more superior slices where the young adults showed FA-related right PFC (BA 46) activity.

Table 4. Regions That Were More Active Under FA Than DA Conditions During Encoding

Region	*Side*	*BA*	*x*	*y*	*z*	*Boot*	*Y-t*	*O-t*
Full > Divided in Young and Old								
Inferior frontal gyrus	L	47	−32	20	−16	7.02	4.06	5.00
Inferior frontal gyrus	L	45/46	−48	40	4	5.00	3.49	5.42
Medial frontal gyrus	L	10	−4	58	20	5.48	3.87	3.50
Middle frontal gyrus	L	6/8	−26	16	40	5.03	2.74	4.29
Parahippocampal gyrus	L	36	−26	−42	−8	3.48	2.00	2.92
Inferior temporal gyrus	L	37	−54	−56	−12	6.57	4.46	6.04
Inferior frontal gyrus	R	47	28	26	−8	3.90	3.18	2.64
Inferior occipital gyrus	R	18	28	−92	−12	5.83	4.64	3.68
Lingual gyrus	R	18	10	−62	0	4.89	3.84	2.23
Full > Divided in Young Only								
Middle frontal gyrus	L	9	−52	12	36	3.94	4.39	−0.58
Inferior temporal gyrus	L	20	−40	−20	−28	4.70	4.76	1.44
Caudate	L		−6	8	0	3.88	3.33	−1.44
Striate	L	17	−14	−104	−8	3.75	3.38	2.16
Inferior frontal gyrus	R	46	42	28	12	3.08	2.17	−1.41
Anterior cingulate	R	24	4	38	−4	3.02	2.90	1.53
Inferior temporal gyrus	R	20	38	−12	−28	3.62	3.33	1.77
Middle temporal gyrus	R	21	58	−48	−4	4.20	3.74	−1.75
Parahippocampal gyrus	R	28	16	−16	−20	3.42	3.31	−1.01
Full > Divided in Old Only								
Orbital frontal gyrus	L	11	−14	48	−16	4.90	0.63	4.84
Anterior cingulate	L	24	−6	18	−4	5.60	0.36	5.02
Precentral gyrus	L	4	−34	−20	32	4.25	−1.64	3.58
Inferior temporal gyrus	L	20	−40	−4	−28	2.82	−0.68	2.44
Inferior temporal gyrus	L	20	−56	−24	−20	2.92	−1.71	2.23
Angular gyrus	L	39	−42	−68	24	6.35	0.52	7.90
Posterior cingulate	L	31	−6	−44	32	4.59	2.21	4.04
Cuneus	L	31	−14	−58	24	3.06	−1.48	2.45
Middle occipital gyrus	L	17/18	−24	−76	4	3.59	−1.12	3.09
Middle occipital gyrus	L	19	−34	−82	20	4.39	2.02	4.40
Cerebellum	L		−30	−68	−16	3.06	−1.13	2.68

(continued)

Table 4. *(continued)*

Region	*Side*	*BA*	*x*	*y*	*z*	*Boot*	*Y-t*	*O-t*
Full > Divided in Old Only								
Precentral gyrus	R	4	48	−14	28	4.60	0.36	4.38
Hippocampus	R		30	−34	−4	6.30	−0.59	4.84
Middle temporal gyrus	R	21	52	−2	−16	3.09	2.08	2.60
Insula	R		30	−22	12	5.78	−3.20	4.22
Middle occipital gyrus	R	19	18	−94	16	3.82	−1.20	4.12
Caudate	R		14	4	−12	3.71	2.10	3.25

Note: BA = Brodmann's Area; Boot = bootstrap ratio; Y-*t* = *t* value for young adults; O-*t* = *t* value for older adults. Positive *t* values represent greater values during FA than DA conditions. Negative *t* values represent greater values during DA than FA conditions. $t(11) \geq |2.22|, p < .05$.

Other areas that were more active in FA than DA conditions included inferior and medial temporal lobe regions, and a number of occipital regions. Regions that were more active during DA than FA conditions in both age groups are listed in Table 5 and are shown in blue in Figure 2C and D. These included the anterior cingulate, bilateral postcentral gyri, and cerebellum in both age groups. In addition, regions that were more active

Table 5. Regions That Were More Active Under DA Than FA Conditions During Encoding

Region	*Side*	*BA*	*x*	*y*	*z*	*Boot*	*Y-t*	*O-t*
Divided > Full in Young and Old								
Anterior cingulate	L	24	−8	2	40	8.03	−8.83	−3.93
Superior temporal gyrus	L	22	−56	−42	16	5.21	−4.12	−2.98
Inferior parietal lobule/Postcentral gyrus	L	40/3/1/2	−36	−34	32	5.36	−4.30	−3.08
Middle frontal gyrus	R	9	28	38	24	4.92	−3.19	−3.50
Superior temporal gyrus	R	22	52	−40	16	6.54	−5.12	−3.50
Insula (anterior)	L		28	10	−4	3.85	−3.93	−1.59
Inferior parietal lobule/Postcentral gyrus	R	40/3/1/2	38	−28	32	5.11	−3.38	−3.63
Cerebellum	R		14	−58	−24	5.83	−4.51	−3.90
Brainstem	R		2	−26	0	4.32	−4.19	−2.46
Divided > Full in Young Only								
Middle frontal gyrus	L	8/9	−30	36	36	2.94	−3.28	−0.60
Medial frontal gyrus	L	10	−10	46	4	4.04	−4.38	−1.50
Precentral gyrus	L	6	−40	4	12	5.40	−3.32	2.27
Insula (posterior)	L		−38	−22	−4	3.30	−2.97	0.52
Insula (posterior)	R		30	−22	12	5.78	−3.20	4.22
Divided > Full in Old Only								
Thalamus	L		−24	−16	12	3.92	0.48	−4.37
Cerebellum	L		−18	−64	−16	3.16	0.67	−4.24
Anterior cingulate	R	24	4	−16	40	4.47	2.47	−2.53
Middle temporal gyrus	R	21	50	−14	−4	5.19	−1.67	−3.02
Insula (middle)	R		34	−14	−8	4.63	−0.91	−4.00

Note: BA = Brodmann's Area; Boot = bootstrap ratio; Y-*t* = *t* value for young adults; O-*t* = *t* value for older adults. Positive *t* values represent greater values during FA than DA conditions. Negative *t* values represent greater values during DA than FA conditions. $t(11) \geq |2.22|, p < .05$.

Table 6. Regions That Were More Active Under FA Than DA Conditions During Retrieval, and Regions That Were More Active Under DA Than FA Conditions During Retrieval

Region	*Side*	*BA*	*x*	*y*	*z*	*Boot*	*Y-t*	*O-t*
Full > Divided in Young and Old								
Anterior cingulate		24	0	18	−4	3.31	2.08	2.51
Orbital frontal gyrus	L	11	−18	30	−16	4.85	3.15	2.43
Medial frontal gyrus	L	10	−2	50	0	4.04	2.89	2.26
Middle frontal gyrus	L	46	−40	50	8	4.13	3.76	1.51
Middle frontal gyrus	L	8	−40	14	44	4.62	2.74	2.55
Superior frontal gyrus	L	8	−12	48	40	5.09	4.59	1.92
Parahippocampal gyrus	L	35	−16	−36	−4	5.63	2.45	5.89
Posterior cingulate	L	30	−8	−48	20	3.40	2.81	1.41
Striate	L	17	−14	−94	−8	5.19	2.91	3.93
Fusiform gyrus	L	19	−36	−64	−12	4.04	5.24	1.01
Cuneus	L	18	−8	−80	24	3.98	2.48	2.91
Middle occipital gyrus	L	19	−28	−76	24	3.87	2.52	3.61
Medial frontal gyrus	R	8	4	36	44	3.52	2.11	2.31
Inferior frontal gyrus	R	47	30	16	−4	4.07	2.65	2.43
Parahippocampal gyrus	R	36	22	−34	−12	3.44	2.72	1.22
Inferior temporal gyrus	R	37	54	−48	−12	3.54	3.05	1.58
Lingual gyrus	R	17	12	−100	−12	5.42	4.74	1.12
Fusiform gyrus	R	19	28	−52	−8	3.42	1.90	3.15
Cuneus	R	18	24	−64	16	3.41	2.59	2.09
Brainstem	R		12	10	−16	6.01	3.38	2.73
Divided > Full in Young and Old								
Middle frontal gyrus	L	46/9	−36	40	28	6.73	−3.76	−4.57
Precentral gyrus	L	4/6	−52	2	28	5.73	−4.68	−2.14
Transverse gyrus	L	41	−38	−24	12	4.93	−2.46	−4.38
Superior temporal gyrus	L	22	−52	−42	16	7.89	−4.40	−8.75
Inferior parietal lobule	L	40	−46	−26	32	6.07	−5.62	−2.83
Cerebellum	L		−24	−56	−28	4.37	−3.62	−2.73
Middle frontal gyrus	R	9	28	34	32	4.93	−3.37	−2.49
Anterior cingulate	R	24	8	2	44	5.22	−2.83	−3.40
Precentral gyrus	R	4/6	58	4	20	3.33	−4.33	−1.28
Superior temporal gyrus	R	22	54	−44	12	10.38	−8.14	−6.00
Inferior parietal lobule	R	40	54	−32	24	5.57	−5.04	−2.21
Cerebellum	R		30	−52	−28	3.32	−3.72	−0.90
Brainstem	R		4	−28	−12	4.61	−4.23	−1.16

Note: BA = Brodmann's Area; Boot = bootstrap ratio. Y-*t* = *t* value for young adults; O-*t* = *t* value for older adults. Positive *t* values represent greater values during FA than DA conditions. Negative *t* values represent greater values during DA than FA conditions. $t(11) > |2.22|$, $p < .05$.

during DA than FA conditions included left PFC regions, insular cortex, and the inferior parietal lobule for the young, and the anterior cingulate, thalamus, and caudate for the old.

Young/Old × FA/DA During Retrieval

To address the question whether the effects of DA on retrieval-related brain activity differ with age, we conducted a PLS analysis with FA/DA at retrieval and Age as factors. The first LV ($p < .001$; Figure 1E) represented a FA/DA main effect. The second LV representing the interaction between FA/DA and Age was not significant ($p = .59$). Regions that were more active during FA than DA conditions during retrieval (Table 6, top) are shown in yellow and red in Figure 2E. These included bilateral, medial, and orbital PFC regions (BA 8/10/11), a region in the posterior portion of the right inferior frontal gyrus (BA 47), in addition to medial-temporal regions, and regions in occipital cortex. Regions that were more active in DA than FA conditions during retrieval (Table 6, bottom) are shown in blue in Figure 2E. These included bilateral PFC regions (BA 46/9), the transverse gyrus, and bilateral aspects of the superior temporal gyrus, inferior-parietal lobule, and cerebellum.

DISCUSSION

Does Encoding- or Retrieval-Related Brain Activity Differ With Age?

Our first goal was to replicate and extend previous research on age differences in encoding- and retrieval-related brain activity. In FA conditions, some regions were more activated during encoding than retrieval in both age groups. In PFC, encoding-related brain activity was found in the left middle frontal gyrus (BA 9/10/46), which is situated very near to the peak ($x, y, z = -38, 34, 24$) reported by Nyberg et al. (1996) to be more activated by encoding than retrieval. The temporal regions that were more activated by encoding than retrieval (BA 20/21/37) are part of the visual pathway involved in object perception (Ungerleider & Mishkin, 1982); these activations were more extensive in the left hemisphere, which is consistent with other reports that link left-temporal regions to semantic (word meaning) knowledge (e.g., Martin, Haxby, LaLonde, Wiggs, & Ungerleider, 1995; Martin, Wiggs, Ungerleider, & Haxby, 1996; Kapur et al., 1994). The inferior-parietal lobule (BA 40) is involved in integrating information over multiple modalities (Barbas, 1992), and has been associated with working memory (Cohen et al., 1997; Petrides, Alivisatos, Evans, & Meyer, 1993; Petrides, Alivisatos, Meyer, & Evans, 1993). The greater activation of this area bilaterally during encoding than retrieval presumably reflects greater working memory demands during episodic encoding than retrieval. Finally, the activation of visual areas during encoding presumably reflects greater visual processing or visual attention paid to the two words presented during encoding, relative to the one word presented during retrieval.

Some encoding-related activations differed between the two age groups. First, only the young adults activated left inferior PFC regions (BA 44/45/46/47) more during encoding than retrieval, a pattern that is consistent with previous reports (Madden et al., 1999; Cabeza et al., 1997; Grady et al., 1995). Second, although both age groups activated the inferior parietal lobe (BA 40) bilaterally more during encoding than retrieval, these activations were more extensive in the old adults. This area has been implicated in working memory (e.g., Petrides, Alivisatos, & Evans, 1993; Petrides, Alivisatos, & Meyer, 1993), specifically in the functioning of the phonological loop (Paulesu, Petrides, Evans, & Meyer, 1993). These results may reflect the fact that encoding places greater working memory demands on the old than young adults. Alternatively, these results may indicate that there is a greater reliance on shallow, phonological encoding rather than deep, semantic encoding in old age (Craik, 1982).

Retrieval-related PFC regions included bilateral orbital (BA 11 and 47) and medial (BA 10 and the anterior cingulate) regions for both age groups, regions that are frequently activated during episodic memory tasks and other attention-demanding tasks (see Grady, 1999; Cabeza and Nyberg, 1997). The precuneus was also activated by both age groups more during retrieval than encoding. The precuneus has been linked to memory retrieval, in particular to retrieval success (Rugg et al., 1998; Buckner, Raichle, Miezin, & Peterzen, 1996), and to the use of visual imagery during retrieval (Fletcher, Frith, & Baker, et al., 1995; Fletcher, Shallice, Frith, Frackowiak, & Dolan, 1996; Kapur et al., 1995). Another region that both age groups activated more during retrieval than encoding was the insular cortex, which has reciprocal connections with other frontal, temporal, parietal, and limbic areas (Augustine, 1996), and has been found to be activated by retrieval (Buckner et al., 1996, 1998), and thus is likely part of a larger distributed retrieval network.

Only the young adults activated BA 10 of the right middle frontal gyrus more during retrieval than encoding, the region that is most consistently associated with episodic retrieval (Grady, 1999; Cabeza & Nyberg, 1997). In addition, however, retrieval-related PFC activity was also present in the left hemisphere (BA 10) of the young adults, and was strictly left-lateralized (BA 45/46/47) in the old adults. Bilateral retrieval-related PFC activity has been reported in several studies (for reviews and discussion, see Buckner, 1996; DesGranges, Baron, & Eustache, 1998). A reasonable interpretation of these findings is that when episodic retrieval failed, participants generated associates to the cue words as candidate responses, an operation that activates left PFC regions (e.g., Buckner et al., 1995; Frith, Friston, Liddle,

& Frackowiak, 1991; Petersen, Fox, Posner, Mintum, & Raichle, 1989). This interpretation is consistent with a recent hypothesis that left PFC regions are recruited during difficult episodic retrieval tasks, such as the systematic generation of retrieval cues when the retrieval information provided is insufficient (Nolde, Johnson, & Raye, 1998).

In summary, the PFC showed the most prominent difference between the young and old adults' brain activity during encoding and retrieval. The young adults activated inferior left PFC regions more during encoding than retrieval, but their old counterparts did not. In addition, the PFC regions that were more activated during retrieval than encoding were bilateral in the young adults, but left-lateralized in old adults. These findings are consistent with other reports (Madden et al., 1999; Cabeza et al., 1997; Schacter et al., 1996), and suggest that aging is associated with reduced functional specialization of episodic memory.

Do the Effects of DA on Encoding-Related Brain Activity Differ With Age?

DA during encoding impairs later memory performance (Craik et al., 1996), similarly for young and old adults (Table 1; Anderson et al., 1998), and reduces encoding-related left PFC activity in young adults (Iidaka et al., 2000; Fletcher, Frith, & Grasby, et al., 1995; Shallice et al., 1994). Our second question was, given the similar effects of DA on memory performance for the two age groups, are the effects of DA on encoding-related brain activity also similar for young and old adults? In both young and old adults, a large region in left PFC was more active during FA than DA conditions during encoding. These results replicate those of Shallice et al. (1994) and Fletcher, Frith, and Grasby, et al. (1995), who also found that left PFC activity during encoding was reduced by DA, and show that this finding extends to old adults. Furthermore, the left dominance of these PFC clusters under FA conditions is in line with the hemispheric asymmetry of encoding and retrieval (HERA, Tulving et al., 1994), and is probably due to the greater degree of semantic processing achieved during FA than DA conditions. This result is important for two reasons. First, it demonstrates a strong brain–behavior relationship, in that both memory performance and left prefrontal brain activity were reduced similarly by DA during encoding in both young and old adults. Second, although the old adults activated left inferior frontal gyrus more during retrieval than encoding (rather than the other way around; see previous analysis), the old adults did indeed activate left inferior PFC during encoding, and this activity was disrupted by the secondary task.

A number of additional regions were more active during FA than DA encoding. Both age groups activated regions of the medial temporal lobes (the parahippocampal gyrus by both age groups and the hippocampus by the old) more during FA conditions; the fact that these regions are important for memory has been known for some time (Scoville & Milner, 1957), and their appearance here is probably tied to the greater amount of encoding that occurred in FA than DA conditions. Finally, FA encoding was associated with activity in the left middle temporal gyrus and in bilateral inferior-temporal gyri. These temporal regions are part of a larger neural network that is recruited during reading and writing; this network, which includes the angular gyrus (BA 39) in the left hemisphere for right-handed persons, and extrastriate cortex (BA 18/19), is functionally disconnected in dyslexic patients (Horwitz, Rumsey, & Donohue, 1998). Together, these findings suggest that more visual word encoding occurred under FA than DA conditions.

Many of the regions that were more active during DA than FA conditions during encoding appear related to the secondary task itself, or to the generally greater central processing demands in the DA condition. The activation of secondary auditory association cortex (BA 22), the postcentral gyri, and the cerebellum may be linked to the auditory secondary task. The activation of the right middle frontal gyrus (BA 9) during DA encoding should be contrasted with the activation of the right-inferior-frontal gyrus (BA 47) during FA encoding. This dissociation provides support for the hypothesis made by Petrides (1995) and Petrides, Alivisatos, and Evans (1995) that ventrolateral PFC regions (e.g., BA 47) mediate strategic encoding and retrieval operations, and mid-dorsolateral PFC regions (e.g., BA 9), mediate control operations, such as the need to monitor information in DA situations. Finally, the anterior cingulate (BA 24) was more activated during DA than FA encoding, which is consistent with the results of Fletcher, Frith, and Grasby, et al. (1995) and probably reflects the role of the anterior cingulate in response selection (e.g., Corbetta, Miezin, Dobmeyer, Shulman, & Petersen, 1991; Pardo, Pardo, Janer, & Raichle, 1990).

In summary, although the effects of DA on brain activity interact in some brain regions, we suggest that their effects on *encoding-related* brain activity are generally similar for the two age groups. Specifically, DA during encoding interferes with left PFC function that mediates encoding (Fletcher, Frith, & Grasby, 1995; Fletcher et al., 1998; Shallice et al., 1994), and with medial temporal lobe activity associated with successful encoding (e.g., Rugg, Fletcher, Frith, Frackowiak, & Dolan, 1997; Nyberg et al., 1996), but these effects are broadly similar in young and old adults.

Do the Effects of DA on Retrieval-Related Brain Activity Differ With Age?

DA during retrieval has very little effect on episodic memory performance (Craik et al., 1996; Baddeley et al., 1984) for either young or old adults (Anderson et al.,

1998). Furthermore, young adults' retrieval-related brain activity is undisrupted by DA during retrieval (Iidaka et al., 2000). The goal of our third analysis was to determine if retrieval-related brain activity is similarly immune to disruption in old adults. Indeed, the analysis revealed no interaction between age and the effects of DA on the pattern of retrieval-related brain activity. Brain regions that were more active during FA than DA conditions during retrieval in both age groups included a number of PFC regions in both hemispheres. The presence of left PFC activation during FA retrieval likely reflects the generation of associates to the cue words, an operation that has been linked to left PFC activity (e.g., Buckner et al., 1995; Martin et al., 1995; Martin et al., 1996; Petersen et al., 1989). More importantly, of the seven PFC regions in which activity was reduced by DA, only one of these was preferentially active during retrieval relative to encoding (see Table 4); that was the left orbital frontal gyrus (BA 11), in which activity is associated with a variety of cognitive operations, including retrieval, working memory, perception, and classical conditioning (see Grady, 1999). On balance, these data demonstrate that retrieval-related PFC brain activity was immune to disruption in both age groups.

By contrast, bilateral parahippocampal activity was reduced by DA during retrieval. The behavioral results indicate that the DA-related disruption of parahippocampal activity during retrieval did not interfere with the success of retrieval from episodic memory, but may reflect a compromised encoding of the retrieval cue. This suggestion is bolstered by the fact that the other regions in which activity was reduced by DA during retrieval—inferior temporal gyrus, lingual gyrus, fusiform, cuneus, and middle occipital gyrus—all mediate visual object perception. Thus, it appears that while DA during retrieval may reduce visual encoding, it has very little effect on retrieval-related brain activity for young or old adults.

Finally, some regions were more activated in DA than FA conditions during retrieval. These included the bilateral middle frontal gyri in BA 46 and 9, consistent with the model of Petrides et al. (1995) that mid-dorsolateral (BA 46/9) PFC regions are recruited when higher-order working memory operations such as retrieval monitoring are required. The other regions that were more active during DA than FA conditions appear to be related to perceptual and motor demands of the task, or to the greater degree of task complexity in the DA conditions. For example, the activation of primary (BA 41) and secondary (BA 22) auditory regions, premotor cortex (BA 4/6), cerebellum, and brainstem can be tied to the auditory/manual secondary task demands, while the activation of bilateral BA 40 may be linked to the greater working memory demands of the dual task situation (Paulesu et al., 1993; Petrides, Alivisatos, & Evans, 1993; Petrides, Alivisatos, & Meyer, 1993). In summary, DA during retrieval had very small effects on retrieval-related brain activity in both young and old adults. These results are consistent with the behavioral finding that DA during retrieval has little or no effect on memory accuracy (Craik et al., 1996; Baddeley et al., 1984) in either age group (Anderson et al., 1998).

Does the Similarity Between Aging and the Effects of DA During Encoding in Young Adults Hold at the Level of Brain Activity?

As we described in the Introduction, when young adults are required to encode information under DA conditions, their pattern of memory performance resembles that of old adults' encoding under FA conditions (e.g., Jennings & Jacoby, 1993; Craik, 1982; Rabinowitz et al., 1982). The current data replicated this effect: Under FA conditions, the old adults recalled on average 60% of the words, and in DA conditions during encoding, the young adults' recall was reduced to 58%. This finding is consistent with the suggestion that there is a common mechanism by which aging and DA reduce memory performance, and at the cognitive level, this mechanism has been described as a reduction in attentional resources available for complex cognitive tasks (Craik, 1983, 1986).

The present results demonstrate that the similarity between aging and DA during encoding in young adults holds at the level of brain activity. First, there was an age-related reduction in left inferior PFC activity during encoding. Only the young adults activated left inferior PFC more during encoding than retrieval, with the peak

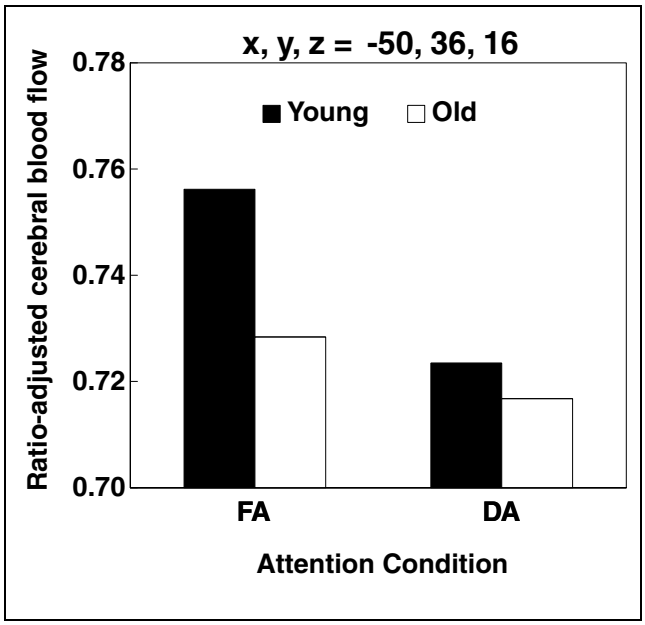

Figure 3. Ratio-adjusted blood flow values during encoding at x, y, $z = -50$, 36, 16 as a function of age group and attention condition. FA = full attention, DA = divided attention.

in BA 45/46, at $x, y, z = -50, 36, 16$; indeed, the old adults activated this same region more during retrieval than encoding (see Table 3). Second, activity in left inferior PFC was reduced by DA during encoding; the peak of this effect was also in BA 45/46, at $x, y, z = -48, 40, 4$ (Table 5), which is very near to the same effect reported by Fletcher, Frith, and Grasby, et al. (1995) in BA 45/46, at $x, y, z = -48, 34, 8$. Figure 3 illustrates the fact that DA during encoding reduces young adults' left inferior PFC activation to the level demonstrated by old adults encoding under FA conditions (Young DA vs. Old FA at $x, y, z = -50, 36, 16, p > .80$). Thus, we conclude that the reduction in the attentional resources available for episodic encoding caused by aging and by DA during encoding maps on to a reduction in left inferior PFC activity during encoding. Together with a recent report that DA interferes with conceptual priming relying on the activation of semantic information but has no effect of perceptual priming which operates nonsemantically (Mulligan, 1998), and with the linking of left PFC regions with the encoding of semantic information (Tulving et al., 1994), these results suggest that the effects of aging and of DA during encoding are similar because both reduce the ability to engage in elaborate, semantic processing.

CONCLUSIONS

This study compared encoding-related and retrieval-related brain activity in young and old adults, under FA and DA conditions. Four major results were found. First, consistent with previous research on aging (e.g., Madden et al., 1999; Cabeza et al., 1997), in FA conditions there was evidence both for age-related decreases in encoding- and retrieval-related PFC activity and for age-related increases in PFC activation of regions that were not activated during encoding and retrieval by the young adults. These results indicate that *during a complex, attention-demanding memory task,* normal aging is associated with a reduction in the functional specialization of PFC. We emphasize the nature of the memory task because we believe that when the memory task requires less allocation of controlled processes (e.g., semantic orienting tasks during encoding, or item recognition tasks), then there should be fewer age-related differences in frontally mediated mnemonic control functions. Second, DA during encoding reduced memory performance, and reduced left PFC and medial-temporal lobe activity in both age groups, suggesting that DA compromises elaborative encoding of semantic information. Third, DA during retrieval did not impair memory performance, and had very little effect on retrieval-related brain activity in either age group. These results indicate that although DA during retrieval may interfere with some processes (e.g., encoding of the retrieval cue, working memory), it does not interfere with the operations necessary for retrieval success. Finally, activity in inferior left PFC regions (BA 45/46) was reduced similarly by aging and by DA during encoding; thus, the effects of aging and DA during encoding on memory performance are similar because they reduce the amount of attentional resources available to engage in the elaborative encoding of semantic information.

METHODS

Subjects

Twelve subjects between 21 and 31 years of age and 12 subjects between 63 and 76 years of age participated in the study after giving informed consent. Sex, mean age, and mean years of formal education are shown in Table 7. The young subjects were students at the University of Toronto, and the old subjects were independently living old adults. No subject had a history of cerebrovascular disorders, cardiopulmonary disease, head trauma, neurological or psychiatric disorders, or drug use affecting cerebral blood flow. All subjects spoke English fluently and were right-handed. As shown in Table 7, the young adults outperformed the old adults on the WAIS-R digit symbol test, the California Verbal Learning Test, the Culture Fair Test of fluid intelligence, and Trails B, but did not differ in vocabulary, letter fluency, or Trails A. The old adults made more perseverative errors on the Wisconsin Card Sorting Test, although this difference was only marginally significant ($p < .10$).

Experimental Tasks

The memory task consisted of lists of 20 moderately related word pairs (e.g., dentist–glove). During encoding, the word pairs were presented on a computer monitor suspended about 70 cm in front of the subject. The word pairs were presented at a rate of 5 sec per pair, with a 1-sec interstimulus interval (ISI). The subject was instructed to read the second word of each pair aloud, and to make a visual image connecting the two words because this would facilitate memory for the word pairs. During the retrieval phase, the second word of each pair was replaced by ''word?'' (e.g., dentist–word?). These retrieval cues were presented at a 5-sec rate with a 1-sec ISI, in a random order with respect to the order in which the words were presented during encoding. The subject was instructed to recall the original word or say ''pass''. The encoding and retrieval phases each lasted 2 min. In between the encoding and retrieval phases, a simple arithmetic task was performed in order to reduce recency effects. A three-digit number was read to the subject, and the subject counted by threes from this number for 1 min.

The secondary task consisted of tones presented by speakers placed behind the PET scanner so that they

Table 7. Demographic Characteristics and Neuropsychological Performance

	Young subjects	*Old subjects*
N	12 (3 male, 9 female)	12 (3 male, 9 female)
Age (years)	24.4 (3.0)	68.5 (4.0)
Education (years)	16.7 (1.7)	15.9 (3.8)
Digit symbol*	75.0 (12.8)	53.8 (5.1)
CVLT (total of five trials)*	67.3 (3.7)	59.2 (8.6)
Vocabulary	15.2 (2.4)	16.7 (1.6)
FAS Letter Fluency	45.3 (9.5)	48.3 (8.4)
WCST perseveration errors (%)	12.2 (7.0)	19.3 (11.7)
Culture Fair Fluid Intelligence*	115.4 (20.6)	94.4 (21.0)
Trails A (sec)	28.3 (7.9)	39.2 (22.1)
Trails B (sec)*	50.5 (10.7)	77.9 (22.2)

Notes: CVLT = California Verbal Learning Test; WCST = Wisconsin Card Sorting Test. Standard deviations in parentheses.

*$p < .01$, two-tailed.

were heard in the midline. The speaker volume was adjusted to be comfortable for each subject, but it was approximately the same for all subjects. The duration of each tone was 500 msec with a 1.5-sec ISI. In the FA condition, a low tone (220 Hz) was presented every 2 sec, and subjects pressed the left mouse button with their right index finger in response to each tone. In the DA condition, the low tone and a high tone (660 Hz) were presented randomly every 2 sec, and subjects pressed the corresponding mouse button (left button with the right index finger for the low tone, right button with the right middle finger for the high tone).

Design and Procedure

The study employed a 2 (Young/Old) × 2 (Encoding/Retrieval) × 2 (FA/DA) experimental design, with Age between-subjects, and Encoding/Retrieval and FA/DA within-subjects. Within each age group, the names of the experimental conditions refer to when scanning took place, and were: (1) FA at encoding, (2) DA at encoding, (3) FA at retrieval, and (4) DA at retrieval. In each experimental condition, scanning took place during one phase (encoding or retrieval), while the other phase took place under FA conditions in the interval between scans. That is, in the FA at encoding and DA at encoding conditions, retrieval was conducted under FA conditions in the postscan interval, and in the FA at retrieval and DA at retrieval conditions, encoding was conducted under FA conditions in the prescan interval. Subjects performed each experimental condition twice, once in each half of the experimental session. Four orders of experimental conditions were created for the first half of the experimental session, and to reduce order effects the conditions were administered in reverse order in the second half of the session. The four experimental orders were counterbalanced across subjects.

PET Methods

PET scans were obtained with a GE PC2048-15B scanner that acquired 15 axial images of the brain. The axial resolution was 6.9 mm (FWHM) and the inplane resolution was 5 mm. After taking a transmission scan using a rotating pin source, 60-sec emission scans were performed following a bolus injection of 35 mCi of $H_2{}^{15}O$. Integrated tissue radioactivity counts were used as a measure of cerebral blood flow to eliminate the need for arterial blood sampling. During the scan the subject's head was fixed to the scanner bed using a thermoplastic facemask to minimize head movement. Scans were conducted 11 min apart, and each task was started approximately 30 sec before the start of the 60-sec emission scan and continued for 2 min.

Image and Statistical Analysis

To prepare the data for statistical analysis, the PET scans from each subject were realigned to the first scan using AIR (Woods, Mazziotta, & Cherry, 1993). Following alignment all images were transformed into a standard space (Talairach & Tournoux, 1988) using SPM95 (Friston et al., 1995, Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks, MA, USA). The images were smoothed using an isotropic Gaussian kernel of 10-mm FWHM and the two scans from each condition were averaged. Because there

are general age-related differences in brain metabolism (see Madden & Hoffman, 1997), the age group main effect was removed from the data prior to analysis; the ratio-adjusted rCBF data (rCBF at each voxel divided by whole brain CBF) were residualized onto the age group vector and the predicted rCBF value was subtracted from rCBF in each voxel.

The image data were analyzed using PLS, a multivariate statistical method (McIntosh et al., 1996). A design matrix consisting of orthonormal Helmert contrasts representing task condition comparisons and the ratio-adjusted image data matrix were submitted to singular value decomposition. Each resulting latent variable (LV) provided a matrix of design saliences that specified how strongly the effects coded in the design contrast were represented in the pattern of brain activity for that LV, and a matrix of image saliences that specified the relation (positive or negative) of each voxel to the experimental effect. To assist in the interpretation of each LV, design scores were computed by multiplying the design saliences by the original contrast vectors. Permutation tests (McIntosh et al., 1996; Edgington, 1980) were performed to test the statistical significance of each LV. In each of 500 trials, the subjects' images were randomly assigned to experimental conditions, and a new singular value decomposition was performed. The probability that the singular value exceeded that obtained in the original PLS was computed; given that this probability is exact (vs. based on inferential statistics), we set the statistical significance level at $p < .10$. Finally, the reliability of each LV was determined using bootstrap estimation (Sampson, Streissguth, Barr, & Bookstein, 1989; Efron & Tibshirani, 1986). On 100 trials, subjects were randomly resampled with replacement (within each age group), and a new PLS was performed. The ratio of the original saliences to the standard error of the saliences obtained from the bootstrap was calculated, and a ratio of 2.5 or greater was considered reliable. Reliable clusters that were larger than 75 voxels are reported in terms of brain region, gyrus, bootstrap ratio, and Brodmann's area (BA) as defined by the Talairach & Tournoux (1988) atlas.

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