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Adult Age Differences in the Functional Neuroanatomy of Verbal Recognition Memory

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Abstract: Adult age differences are frequently observed in the performance of memory tasks, but the changes in neural function mediating these differences are largely unknown. We used $H_2{}^{15}O$ positron emission tomography (PET) to measure changes in regional cerebral blood flow (rCBF) during Encoding, Baseline, and Retrieval conditions of a recognition memory task. Twelve young adults (20–29 years) and 12 older adults (62–79 years) participated. During each task condition, participants made a two-choice manual response to each of 64 words. Analyses of the performance data yielded evidence of age-related slowing of encoding and retrieval processes, and an age-related decline in the accuracy of yes/no recognition (*d'*). The rCBF activation associated with both encoding and retrieval was greater for older adults than for young adults, but this pattern was more clearly evident for memory retrieval. For young adults, rCBF activation during retrieval occurred primarily in right prefrontal cortex, whereas older adults exhibited a more bilateral pattern of prefrontal activation. Regression analyses predicting reaction time in the memory task from regional PET counts confirmed that the neural system mediating memory retrieval is more widely distributed for older adults than for young adults. Both age groups exhibited some decrease in rCBF activation in the second half of the test session, relative to the first half. The practice-related decrease in rCBF activation was more prominent for young adults, suggesting that the older adults' recruitment of additional neural systems reflects a more continual allocation of attention to support task performance. *Hum. Brain Mapping 7:115–135, 1999.*

Key words: neuroimaging; aging; vision; reaction time; information processing; cortical activation

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INTRODUCTION

Older adults often express concern with a decline in the ability to remember, a concern that is in many respects substantiated by investigations of age-related changes in the performance of memory tasks [Kausler, 1994; Light, 1991; Salthouse, 1991; Smith, 1996]. As Craik and Jennings [1992] noted, age effects are difficult to characterize in terms of a single dimension and appear instead to represent a complex interaction of participants, materials, and encoding and retrieval variables. Age-related decline is most frequently observed when the task is both episodic, in the sense of referring to a particular learning context, and explicit, in the sense of involving specific instructions to remember.

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Both encoding and retrieval processes appear to contribute to age-related changes in episodic memory. The role of encoding is implicated by studies finding that young adults benefit more than older adults from conditions optimizing the depth of processing [Craik and Lockhart, 1972] of the items to be remembered. That is, in these experiments, encoding the items in a meaningful and distinctive manner amplified the age-related deficit in episodic memory performance [Craik, 1977; Rabinowitz, 1989; but cf. Burke and Light, 1981]. The importance of retrieval processes is suggested by the finding that although an age-related decline has been reported for both recall and recognition measures of memory, the decline is typically greater for recall [Burke and Light, 1981; Erber, 1974; Perlmutter, 1979].

Age-related changes in basic aspects of information processing, such as attention and speed of processing, may be a critical component of the age-related decline in memory functioning. Investigations of memory performance under dual-task conditions suggest that the attentional demands of both encoding and retrieval are greater for older adults than for young adults, although this age difference is most pronounced for retrieval [Anderson et al., 1998; Craik and McDowd, 1987; Whiting and Smith, 1997]. An age-related slowing of cognitive performance, which has been observed across a wide variety of tasks [Cerella, 1990; Myerson et al., 1990; Salthouse, 1996], would both lead to less effective encoding and increase the time required to retrieve stored information.

Neuroimaging investigations, focusing primarily on the performance of young adults, have yielded important information on the functional neuroanatomy of memory processes [Buckner and Tulving, 1995; Cabeza and Nyberg, 1997]. The results of several experiments using positron emission tomography (PET) to measure regional cerebral blood flow (rCBF) have suggested that different patterns of rCBF activation are associated with encoding and retrieval processes. These experiments have been incorporated into the hemispheric encoding/retrieval asymmetry (HERA) model by Tulving et al. [1994a] and Nyberg et al. [1996a]. According to this model, the left prefrontal cortex is more involved than the right prefrontal cortex in both the encoding of episodic information and the retrieval of semantic (context-independent) information. The right prefrontal cortex, in contrast, is more involved than the left prefrontal cortex in the retrieval of episodic information [cf. Buckner, 1996].

Other investigators have pointed out that the performance of memory tasks involves the coordination of multiple neural systems besides the prefrontal cortex. For example, task-related changes in rCBF have been observed for the medial temporal lobe and hippocampal regions, though not consistently [Buckner et al., 1995; Rugg et al., 1997; Squire et al., 1992]. Activation in the parietal lobe may mediate the recollection of spatial and temporal context required by episodic memory tasks [Andreasen et al., 1995; Tulving et al., 1994b]. It is also important to note that memory functioning may be reflected in rCBF deactivation as well as in activation. A decrease in rCBF during memory retrieval may occur either as a result of a reduction in processing for repeated items [Buckner et al., 1995; Squire et al., 1992] or as a result of inhibition from active neural regions [Nyberg et al., 1996b].

Neuroimaging studies have begun to identify the age-related changes in functional neuroanatomy contributing to adult age differences in memory performance. Grady et al. [1995], using a face recognition task, concluded that an age-related decline in recognition memory performance for faces was related primarily to encoding processes. Age differences in rCBF activation for retrieval processes are more prominent in experiments using verbal materials, although a consistent pattern is not apparent. Schacter et al. [1996] and Bäckman et al. [1997] both measured rCBF changes during recall of word lists. In the Schacter et al. experiment, recall was associated with bilateral activation of prefrontal cortex for both young and older adults, but the regions activated within the prefrontal area varied across the age groups. Bäckman et al. found that the pattern of retrieval-related activation in prefrontal cortex was similar for young and older adults. Young adults, however, exhibited relatively greater activation in left cerebellum and Wernicke's area. Cabeza et al. [1997] investigated rCBF activation during the encoding, recall, and recognition of word pairs. The young adults' rCBF activation in prefrontal cortex was left lateralized during encoding and right lateralized during retrieval, as predicted by the HERA model. The older adults exhibited reduced prefrontal activation during encoding and a more bilateral pattern of prefrontal activation during retrieval. Cabeza et al. proposed that age-related changes in neural functioning involve both decreases in activation, which may represent less efficient processing, and increases in activation, which may represent functional compensation.

The present experiment, like those of Schacter et al. [1996], Bäckman et al. [1997], and Cabeza et al. [1997], investigated age-related changes in rCBF during episodic memory for verbal material. These previous experiments all measured participants' memory performance in terms of accuracy of recall, although Cabeza et al. also measured recognition accuracy. We were particularly interested in age-related changes in the speed of processing, and in the relation of these changes to rCBF activation. To facilitate the measurement of the duration of encoding and retrieval processes, we presented a series of single words in each task condition and measured memory retrieval by means of yes / no recognition rather than by recall. One feature of the Cabeza et al. data is that recognition accuracy during the PET testing was comparable for young and older adults. We consequently used a greater number of items to be remembered (64 words) than did Cabeza et al. (24 word pairs), so that the task would be more likely to elicit the age-related decline typically observed in the performance of episodic memory tasks [Craik and Jennings, 1992; Smith, 1996]. In view of the Cabeza et al. findings, we hypothesized that the pattern of rCBF activation for encoding would be more prominent for young adults than for older adults. Retrieval-dependent activation, in contrast, was expected to involve a more widely distributed neural system for older adults than for young adults.

We were also interested in potential changes in rCBF activation as a function of practice. Raichle et al. [1994] reported that even relatively brief (15 min) practice in a verb generation task led to a substantial change in the pattern of rCBF activation. There was a practice-related decrease in the level of activation for neural regions mediating performance at the beginning of the task, accompanied by an increased activation in other regions. Raichle et al. proposed that this change occurred as a result of participants' responses becoming more automatic (i.e., less reliant on feedback and control). It is consequently important to determine whether practice leads to comparable changes in rCBF activation for young and older adults. If the attentional demands of memory retrieval are greater for older adults than for young adults [Anderson et al., 1998; Whiting and Smith, 1997], then it is possible that older adults maintain the same pattern of rCBF activation at early and later stages of practice, and that young adults exhibit greater practice-related change in the neural systems mediating the retrieval component of memory performance.

METHODS

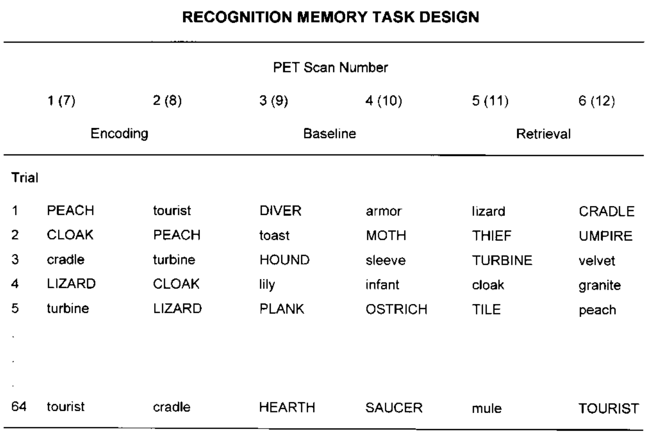
Participants

The participants were 12 young adults (six of each gender) between 20 and 29 years of age (mean = 23.17 years, SD = 2.86) and 12 older adults (seven women, five men) between 62 and 79 years of age (mean = 71.0 years, SD = 4.67). All participants gave written informed consent prior to the experiment, and the research procedures were approved by the Institutional Review Board of the Duke University Medical Center.

All participants were right handed and had completed at least a high school education. Binocular visual acuity for near point (corrected) was tested with a Keystone (Davenport, IA) Ophthalmic Telebinocular Vision Tester, and acuity for all participants was at least 20 / 40. Participants were free from major health problems as indicated by a screening questionnaire [Christensen et al., 1992]. Each participant was also administered a neurologic screening exam by a physician. This latter exam included a brief clinical history, recitation of a seven- digit numerical sequence, visual field testing by confrontation, testing for abnormalities of motor strength in face and limbs, sensory testing by light touch, and finger-to-nose and rapid alternating movement examination and evaluation for gait abnormalities.

Several psychometric tests were administered in a separate testing session, prior to the PET studies. All participants scored 28 or higher (out of 30) on the Mini-Mental State Exam [Folstein et al., 1975] and no higher than 6 (out of 63) on the Beck Depression Inventory [Beck, 1978]. The mean raw score on the Digit Symbol Substitution subtest of the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981), a measure of perceptual-motor speed, was significantly higher for young adults (mean = 78.17, SD = 5.86) than for older adults (mean = 48.75, SD = 7.09) ($t = 11.08$, $P < .0001$). The mean raw score on the WAIS-R Vocabulary subtest, a measure of verbal knowledge, did not differ significantly for the two groups (young adults' mean = 57.67, SD = 4.94; older adults' mean = 61.0, SD = 5.46). This age-related decline in perceptual-motor speed and preservation of verbal knowledge is consistent with previous findings obtained with these psychometric tests [Salthouse, 1982].

Magnetic resonance (MR) imaging was conducted prior to PET testing, and the MR images were examined by a neuroradiologist for evidence of significant cerebral atrophy or structural abnormality. Transaxial MR scans were acquired with a General Electric (Milwaukee, WI) 1.5 Tesla Signa scanner. Acquisitions were made with 3 mm slice thickness and no interslice gap. T1-weighted images had a repetition time (TR) of 600 msec and an echo delay time (TE) of 20 msec, and two excitations (NEX). T2-weighted images had a TR of 2.50 sec, TE values of 20 msec and 80 msec, and 1 NEX. The following exclusion criteria were applied to both age groups: any signal abnormality indicating a mass, ventricular enlargement or atrophy atypical for age,



RECOGNITION MEMORY TASK DESIGN

	PET Scan Number					
	1 (7)	2 (8)	3 (9)	4 (10)	5 (11)	6 (12)
	Encoding		Baseline		Retrieval	
Trial						
1	PEACH	tourist	DIVER	armor	lizard	CRADLE
2	CLOAK	PEACH	toast	MOTH	THIEF	UMPIRE
3	cradle	turbine	HOUND	sleeve	TURBINE	velvet
4	LIZARD	CLOAK	lily	infant	cloak	granite
5	turbine	LIZARD	PLANK	OSTRICH	TILE	peach
.						
.						
.						
64	tourist	cradle	HEARTH	SAUCER	mule	TOURIST

Figure 1.

Task conditions for the recognition memory task performed during the PET scans. Participants performed each of three task conditions: Encoding, Baseline, and Retrieval, during four PET scans (two scans in the first half of the testing, and two scans in the second half). During each PET study, 64 words (32 uppercase, 32 lowercase) were presented sequentially for 3 sec each. In the Encoding condition, participants made a living/nonliving decision regarding each word and were instructed to remember each word for a subsequent memory test. In the Baseline condition, participants made an uppercase/lowercase decision regarding each word and were instructed that memory for the Baseline words would not be tested. In the Retrieval condition, participants made a yes/no decision regarding whether each word had been presented during the Encoding condition. Each block of trials in the Encoding condition used the same set of 64 words, in a different randomized sequence. In the Retrieval condition, the uppercase/lowercase format of words that had been presented during Encoding was reversed. That is, for example, words presented in uppercase during encoding were presented in lowercase during retrieval.

flow signal abnormality within intracranial vessels, extra-axial fluid collection, and any focal signal abnormality within caudate, putamen, globus pallidus, thalamus, brain stem, or cerebellum. For young adults, any focal area of hyperintensity on T2-weighted images was also an exclusion criterion, whereas for older adults, the criterion was the presence of focal supratentorial hyperintense white matter signal abnormalities greater than 3 mm.

Recognition memory task

The design of the recognition memory task is illustrated in Figure 1. During each of 12 PET scans, participants viewed a series of 64 words (presented sequentially) and pressed one of two response buttons at the onset of each word. The words were concrete nouns that were relatively high in their frequency of occurrence in printed text, with a Standard Frequency Index [Carroll et al., 1971] ranging between 45.0 and 51.9 (mean = 47.84, SD = 1.82). Words contained between 2 and 11 letters (mean = 6.05 letters, SD = 1.78). Items were selected to be readily categorizable as referring to either “living” or “nonliving” objects. Examples of words in the “living” category are “peach,” “lizard,” and “tourist.” Examples of words in the nonliving category are “cloak,” “cradle,” and “turbine.” Each word was presented either in all uppercase letters or all lowercase letters. Each block of 64 trials contained 16 words for each combination of the case type and living / nonliving variables.

There were four blocks of trials in each of three task conditions: Encoding, Baseline, and Retrieval. In the Encoding trial blocks, participants made a living/ nonliving judgment regarding each word and were informed that memory for these items would be tested later. Encoding tasks that direct attention to the meaning of the items to be remembered tend to provide the best support for later retrieval [Craik and Lockhart, 1972; Craik and Tulving, 1975]. In the Baseline blocks, participants made an uppercase / lowercase response to each item and were informed that they would not need to remember these words. Thus, the case type variable was irrelevant on Encoding trials, and the living / nonliving variable (indeed, word meaning in general) was irrelevant on Baseline trials. In the Retrieval trial blocks, participants made a yes / no response to each word, in terms of whether they believed the word had been presented during the Encoding trials.

In the Retrieval blocks, the trials were a randomized sequence of 32 items that had been presented during encoding, and 32 new words that had not been presented during either the Encoding or the Baseline conditions. Although, in this design, memory retrieval could be successful on a maximum of 50% of the trials, every trial in the Retrieval condition required an assessment of whether the presented word was located in episodic memory. Our interest was in the process of episodic retrieval regardless of its success [Nyberg et al., 1995]. Each “old” item in the Retrieval condition was presented in the opposite case type relative to its original presentation. The purpose of this latter manipulation was to encourage participants to use a deliberate search of memory, rather than a visual matching strategy, as a basis for their decisions in the Retrieval blocks. A different set of 32 “new” words was used in each of the four Retrieval blocks, and a different set of 64 words was used in each of the Baseline blocks. In each task condition, the instructions encouraged participants to respond as rapidly as possible while maintaining accuracy.

There were two blocks of test trials for each task condition in each half of the testing session (six PET scans; Fig. 1). The task conditions in each half of the testing session were always presented in the following order: Encoding, Baseline, and Retrieval. Within participants, the same set of 64 words was repeated (in a different randomized sequence) across the four Encoding trial blocks. Each of these words was included (in the opposite case type) as an ‘‘old’’ item in two Retrieval blocks, once in the first pair of Retrieval blocks (PET scans 5 and 6) and once in the second pair of Retrieval blocks (PET scans 11 and 12). Each Retrieval block used a different set of 32 ‘‘new’’ words. Four different sets of 64 words were used for the Baseline blocks.

The set of words used in the recognition memory task comprised 448 words, 224 items in each of the ‘‘living’’ and ‘‘nonliving’’ categories, and the words in these two categories were equivalent in terms of familiarity and number of letters. Individual words were counterbalanced (across participants) for their appearance in the task conditions. Seven lists of the 448 words were constructed, and each of the words occurred in one of the lists as an Encoding item, in four of the lists as a Baseline item, and in two of the lists as a ‘‘new’’ item in the Retrieval condition. Each participant viewed one list. Within the age groups, each of the seven lists was administered to one to three participants.

Presentation of the words and measurement of participants’ responses were controlled by a Tangent (Burlingame, CA) 386-processor microcomputer and Zenith (St. Joseph, MI) video monitor. The monitor was positioned above the gantry opening of the PET scanner, facing downward at an approximately 45-degree angle. At the viewing distance of approximately 40 cm, the words were 2 degrees high and ranged from 2 degrees to 11 degrees in length. Presentation duration was 3 sec per word; the interval between words varied randomly from 600 msec to 1 sec, to reduce onset predictability. Participants responded on each trial by means of a two-button response box connected to the game port of the microcomputer. Participants rested the index and middle fingers of the right hand on the two response buttons. Reaction time (RT) was measured from the onset of the word on each trial. Within participants, the ‘‘living,’’ ‘‘uppercase,’’ and ‘‘yes’’ responses were always assigned to the same response button. The assignment of these responses to either the left or right button was alternated across participants, so that six participants in each age group used each of the response button assignments.

Positron emission tomography

Regional CBF was measured by PET using a General Electric Advance whole-body tomograph containing 18 detector rings [DeGrado et al., 1994]. Data were acquired simultaneously from 35 imaging planes (18 direct planes and 17 cross planes) separated by 4.25 mm. The axial field of view was 15.2 cm, and the intrinsic in-plane and axial spatial resolutions were approximately 5 mm FWHM. Data acquisition was performed in the three-dimensional mode (septa out).

An intravenous catheter was placed in the participant’s left arm, for radiotracer injection, at the beginning of the testing session. The participant was positioned in the tomograph with his or her head aligned in a plane approximately parallel to the glabella-inion line. Alignment was conducted with the assistance of a low-power laser. Prior to the emission scans, a 5 min transmission scan was performed using a pair of 3–10 mCi ^{68}Ge rotating pin sources. Following the transmission scan, participants performed three blocks of practice trials, one block for each of the Encoding, Baseline, and Retrieval conditions. The practice blocks each contained 12 trials, and none of the words was used in the test trials during the PET scans. The practice trial data were not included in the task performance analyses.

There were 12 emission scans; the radiotracer was administered as an intravenous bolus injection of approximately 10 mCi of $H_2{}^{15}O$. Prior to each radiotracer injection, participants were reminded of the instructions and response button assignment for the upcoming task condition. Presentation of the words in each task condition required 4 min and was initiated approximately 30 sec prior to radiotracer injection. The PET data acquisition began automatically when the radioactivity count rate exceeded a preset threshold of 75,000 counts / sec (random-corrected) and continued for 1 min. Successive scans were separated by 10 min. In each set of six PET scans, the interval between the end of the second Encoding block and the beginning of the first Retrieval block was approximately 28 min. Reconstruction of the PET image data was performed with filtered back-projection using a Hann filter transaxially and a ramp filter axially [Kinahan and Rogers, 1990]. Images comprised 128×128 pixels (2×2 mm^2) for each of 35 slices. The data were corrected for random coincidences, attenuation, scattered radiation, and dead time.

Changes in rCBF between task conditions were analyzed with the 1995 version of the Statistical Parametric Mapping (SPM) software [Friston et al., 1995]. The scans for each subject were realigned using the first scan as a reference. The scans were normalized and transformed, after realignment, into a standard stereotaxic space [Talairach and Tournoux, 1988]. This procedure began with a 12 parameter affine transformation, followed by piece-wise (contiguous transverse slices) nonlinear matching, constrained by a set of smooth basis functions [Friston et al., 1996]. The spatially normalized images were smoothed with an additional 15 mm FWHM isotropic Gaussian kernel.

The SPM analyses used analysis of covariance (ANCOVA), applied to the PET counts on a voxel by voxel basis, to remove the effect of global activity [Friston et al., 1990]. The increase in rCBF between task conditions was represented by a linear contrast (i.e., image subtraction), which was reversed to yield the corresponding decrease in rCBF. The resulting set of voxel t values for each subtraction constitute the statistical parametric map SPM t. The SPM t values were transformed to the unit normal distribution SPM and thresholded at 2.33 ($P = .01$, uncorrected). The resulting foci were then characterized in terms of the spatial extent (k) and peak height (u) of local maxima. The local maxima were defined as voxels with Z values greater than all voxels within 12 mm. Significance was estimated using distributional approximations from the theory of Gaussian fields. This characterization is in terms of the probability that a region of the observed number of voxels or greater would have occurred by chance ($P[\mathrm{n}^{\max} > \mathrm{k}]$), and the probability that the observed peak height of the local maximum of activation is greater than would be expected by chance ($P[\mathrm{Z}^{\max} > \mathrm{u}]$). The estimates were applied to the entire volume analyzed (i.e., a corrected P value). Up to three local maxima are provided for each region.

Two contrasts, Encoding minus Baseline and Retrieval minus Baseline, were of primary interest as estimates of encoding and retrieval processes, respectively. (The Retrieval minus Encoding contrast was also analyzed. These data are useful for a complete evaluation of rCBF activation, but our interest was in comparing these two conditions relative to the same baseline, rather than to each other. We have consequently not included the results of the Retrieval minus Encoding contrast in the present article.) The Encoding minus Baseline and Retrieval minus Baseline contrasts were examined within each age group. To assess the age differences associated with each of these subtractions, the CBF data for the two age groups were combined, and interaction contrasts were constructed that included two simultaneous linear contrasts: one representing the subtraction of interest and the other representing the difference between the two age groups. The resulting SPM map for these interaction contrasts contained those voxels that differed as a joint function of age group and task condition. A similar approach was adopted to examine the effects of practice within each age group: simultaneous linear contrasts were constructed that represented the subtraction of interest plus the difference between the first and second halves of the testing session.

The individual contrasts (i.e., main effects) were considered to be statistically significant if the region of rCBF change included at least 50 voxels and if the Z value for the peak height (u) of the local maximum was greater than 4.13 ($P < .05$, corrected). As noted in the previous paragraph, each interaction term was a simultaneous contrast that combined two subtraction effects. In the SPM algorithms, corrected probability levels are not estimated for simultaneous contrasts. We therefore used $Z = 2.33$ as a significance level for the interpretation of interactions. Because the two component contrasts within each interaction term were thresholded independently at $Z = 2.33$ ($P = .01$, uncorrected), however, a Z value of 2.33 for an interaction contrast is significant at the more conservative level of $P < .0001$, uncorrected (i.e., the joint probability of the component contrasts). It is important to note that the SPM analyses used a fixed effects model, and thus results for the interaction terms that involve random effects (i.e., the age differences) should be interpreted with caution. In addition, the task conditions were presented in a fixed order (Encoding, Baseline, Retrieval); conclusions regarding the task condition main effects consequently apply only to this presentation order.

RESULTS

Recognition memory performance

Reaction time

The data of primary interest in the analyses of task performance were the RTs for correct responses. We analyzed these data using a mixed models analysis of variance [ANOVA; Littell et al., 1996], which is an extension of the general linear model allowing a more flexible specification of the covariance matrix for error effects. Trials and participants were treated as random effects; age group and task condition were treated as fixed effects. Practice was also included as a fixed effect, contrasting the first half of the testing session (PET scans 1–6) with the second half (PET scans 7–12).

The RT data are presented in Figure 2. With all three task conditions included, the ANOVA of the RT data yielded significant main effects for age group ($F =$

13.97, $P < .001$), task condition ($F = 3{,}113.59$, $P < .0001$), and practice ($F = 252.89$, $P < .0001$). These effects represent, respectively, a higher RT for older adults (984 msec) than for young adults (832 msec), a variation across task condition from 679 msec in the Baseline condition to 978 msec in the Encoding condition and to 1,066 msec in the Retrieval condition, and a higher RT for the first half of the PET session (941 msec) than for the second half (874 sec).

Three interaction terms were also significant: age group × practice ($F = 5.41$, $P < .05$), condition × practice ($F = 46.71$, $P < .0001$), and age group × condition ($F = 19.17$, $P < .0001$). The interaction of age group and practice represents a greater decrease in RT, between the first and second halves of the testing session, for older adults (77 msec) than for young adults (57 msec), although the percentage decrease was similar for the two groups (young adults = 6.63%; older adults = 7.53%). The condition × practice interaction represents a greater practice-related decrease in RT for the Encoding and Retrieval conditions (89 msec and 102 msec, respectively) than for the Baseline condition (10 msec). The age group × condition interaction occurred because the increase in RT associated with the Encoding and Retrieval conditions, relative to the Baseline condition, was greater for older adults than for young adults.

To examine the age group × condition interaction further, we conducted separate analyses for the Encoding vs. Baseline and Retrieval vs. Baseline contrasts. Relative to the Baseline RT, the increase in RT was greater for the older adults than for the young adults in both the Encoding condition ($F = 21.54$, $P < .0001$) and the Retrieval condition ($F = 35.72$, $P < .0001$). Expressed as a percentage increase in RT relative to the Baseline RT, however, the two age groups were similar for both Encoding (young adults = 45.0%, older adults = 43.72%) and Retrieval (young adults = 57.42%, older adults = 56.78%).

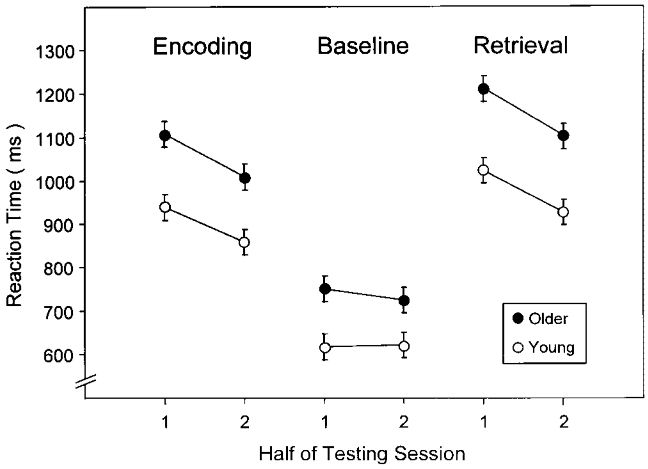


Figure 2.
Mean reaction time of correct responses in each of the three task conditions as a function of age group and practice. Each half of the testing session included two PET scans per condition, yielding a total of 1,536 observations per data point in the figure.

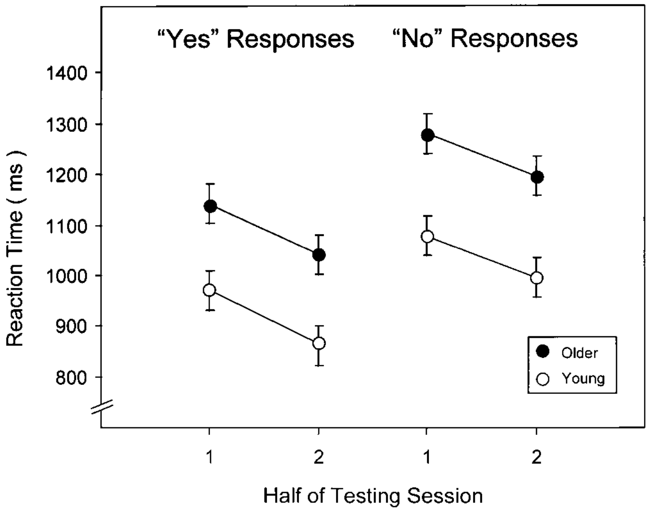


Figure 3.
Mean reaction time of correct responses in the Retrieval condition as a function of age group, response type, and practice.

We also examined the RT for correct responses on "yes" and "no" trials in the Retrieval condition. Previous studies of recognition memory have often found that RT is relatively higher for "no" responses, presumably because participants can respond "yes" as soon as a match is found in memory for the presented item, whereas a "no" response requires a more exhaustive comparison process [Ratcliff, 1978]. These data are presented in Figure 3. The analysis yielded a main effect of response type ($F = 242.49$, $P < .001$), reflecting a higher RT for "no" responses (1,137 msec) than for "yes" responses (997 msec). The response type × practice interaction was significant ($F = 3.99$, $P < .05$) because the decrease in RT from the first half of the testing session to the second half was greater for "yes" responses (119 msec) than for "no" responses (83 msec). Expressed as a percentage change, this RT decrease was also greater for "yes" responses (11.27%) than for "no" responses (7.04%). The age group × response type interaction was also significant ($F = 4.76$, $P < .05$). Although the magnitude of the response type effect was greater for older adults (161 msec) than for young adults (121 msec), the percentage increase in RT associated with the "no" response was similar for

TABLE I. Mean proportion hits and false alarms in the retrieval condition as a function of age group and practice*

	First half of testing session		Second half of testing session	
	Mean	SD	Mean	SD
Young adults				
Hits	.886	.087	.962	.047
False alarms	.068	.060	.040	.060
Older adults				
Hits	.845	.084	.931	.056
False alarms	.147	.069	.079	.060

* Hits, proportion correct responses on "yes" trials; false alarms, proportion incorrect responses on "no" trials; first half of testing session, PET scans 1–6; second half of testing session, PET scans 7–12. Each half of the testing session contained two PET scans per task condition.

the two age groups (young adults = 13.21%, older adults = 14.95%).

Memory discrimination and response bias

In the Baseline and Encoding conditions, the proportion of correct responses was at least .97 for each age group and was not analyzed further. For the Retrieval condition, the mean proportions of hits (correct responses on "yes" trials) and false alarms (incorrect responses on "no" trials) are presented in Table I. Signal-detection estimates of discrimination (*d*') and bias (β) were calculated from the hit and false alarm rates, assuming that one component of participants' responses in the Retrieval condition is an evaluation of each word along a dimension of familiarity [Parks, 1966; Snodgrass and Corwin, 1988]. These data are presented in Figure 4. The *d*' measure consequently represents the accuracy of memory discrimination, in terms of the degree of separation between the distributions of "old" and "new" words on the familiarity dimension. The bias measure β represents the placement of a criterion (i.e., the degree of familiarity required for a "yes" response). The *d*' and β values were obtained for each participant in each task condition. Prior to analysis, the β values were transformed logarithmically, for ease of interpretation. Log β has the property of being 0 when bias is neutral. Liberal placement of the criterion (i.e., less familiarity required for a "yes" response) yields negative log β values, and conservative bias yields positive log β values [McNicol, 1972].

The ANOVA of the *d*' values yielded significant main effects of age group ($F = 11.06$, $P < .01$) and practice ($F = 57.81$, $P < .0001$). These effects represent a higher level of memory discrimination for young adults (3.45) than for older adults (2.68), and an improvement in discrimination between the first (2.61) and second (3.52) halves of the testing session. The interaction term was not significant. The ANOVA of the log β data did not yield any significant effects, and the mean log β value did not differ from 0 for either age group.

Cortical volume

Cortical gray matter volume was estimated from each subject's MRI, using methods described by Madden et al. [1996]. Separate estimates were obtained for the total gray matter of the left and right cerebral hemispheres (excluding the basal ganglia) and for the total volume (gray and white matter) of the left and right cerebellar hemispheres. We performed an ANCOVA of the cortical gray and cerebellar volumes, using each participant's height as a covariate [Raz et al., 1997, 1998]. Age group and hemisphere (left vs. right) were treated as fixed effects, with participants as a random effect. The mean cortical gray values (per hemisphere) were comparable for young adults (348 cm^3, SD = 45.16) and older adults (347 cm^3, SD = 31.20), and the analysis of the cortical gray data did not yield a significant main effect for either age group or hemisphere. The age group × hemisphere interaction, however, was significant ($F = 5.17$, $P < .05$), because the left hemisphere volumes were slightly greater for

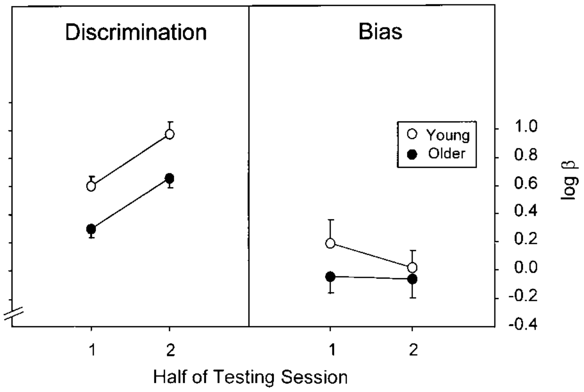


Figure 4.
Memory discrimination (*d*') and response bias (log β) in the Retrieval condition as a function of age group and practice. Increasing *d*' represents increasing discriminability of "old" and "new" words. Negative log values represent liberal bias; positive values represent conservative bias.

the young adults than for the older adults, whereas the reverse was true for the right hemisphere volumes. Simple main effect tests, however, indicated that the age difference was not significant for either hemisphere considered individually. No effects were significant in the analysis of the cerebellar volume data, and the mean values (per hemisphere) were comparable for young adults (70 cm^3, SD = 6.61) and older adults (68 cm^3, SD = 6.22).

Cerebral blood flow

The rCBF activations associated with the task condition subtractions are presented in Figure 5. To indicate background activation, the threshold for the gray scale (main effect) voxels in the figures was set to a more liberal criterion ($Z = 2.99$, $P = .001$, uncorrected) than was used for statistical significance. The local maxima of these increases in rCBF are listed in Table II. The corresponding decreases in rCBF (obtained by reversing the linear contrast for each subtraction) are presented in Table III. Tables II and III also list the coordinates of the local maxima in the standard stereotaxic space of Talairach and Tournoux [1988], the Brodmann's area (BA) designation, and the gyral location.

Increases in rCBF between task conditions

Encoding minus Baseline

This subtraction represents participants' categorizing the words presented during the Encoding condition as ''living'' or ''nonliving'' and attempting to remember the items for subsequent recognition. This subtraction did not yield any significant activation for young adults, but the older adults exhibited significant rCBF increases in prefrontal cortex bilaterally, and in several regions (thalamus, fusiform gyrus, and parahippocampal gyrus) of the left hemisphere. The interaction contrast, however, indicated that only the thalamic activation was significantly greater for the older adults than for the young adults.

Retrieval minus Baseline

This subtraction represents participants' deciding whether the words presented in the Retrieval condition had occurred previously during the Encoding decision. Relative to the Baseline condition, the most pronounced activation for the young adults was in right prefrontal cortex (BA 10). Activations were also evident in the left medial frontal gyrus (BA 8) and thalamus. For the older adults, there was extensive activation bilaterally in the prefrontal cortex (BAs 8, 10, 11) and in the inferior parietal lobule (BA 40), near the superior occipital gyrus. The older adults also exhibited activation in left inferior temporal cortex (BA 21) and in the left cerebellar hemisphere. The comparison of the two age groups indicated that the young adults' thalamic activation was greater than that of the older adults. Activation in several regions in prefrontal cortex of both the left and right hemispheres was greater for older adults than for young adults.

Decreases in rCBF between task conditions

Encoding minus Baseline

For the young adults, there were no regions of significant decrease in rCBF for the Encoding minus Baseline subtraction. The older adults exhibited decreases in the left anterior cingulate and in the inferior parietal lobule (BA 40) of the right hemisphere, near the lateral sulcus. There was no age-related change in the rCBF decrease.

Retrieval minus Baseline

The young adults' Retrieval minus Baseline subtraction yielded a significant rCBF decrease primarily in the right hemisphere, with local maxima in the medial occipital gyrus (BA 19) and inferior parietal lobule (BA 40; near the lateral sulcus). The older adults exhibited decreases in both hemispheres, with local maxima in BA 40 (near the lateral sulcus), and in several regions of the occipital and temporal lobes. The contrasts testing for age differences did not yield any significant voxels.

Effects of practice on rCBF

Within each age group, we compared the difference between the first and second halves of the testing session, for each task condition contrast. Analyses of the young adults' Encoding minus Baseline contrast did not reveal any significant changes in rCBF as a function of practice. For the other contrasts, the practice-related effects associated with the rCBF increases (activation) are presented in Figure 6 and Table IV. Practice-related effects associated with the rCBF decreases are presented in Table V. The older adults' Encoding minus Baseline activation included several local maxima in occipitotemporal cortex (BA 37) for which there was greater activation in the first half of the testing session than in the second half. Analyses of the Retrieval minus Baseline subtraction indicated that

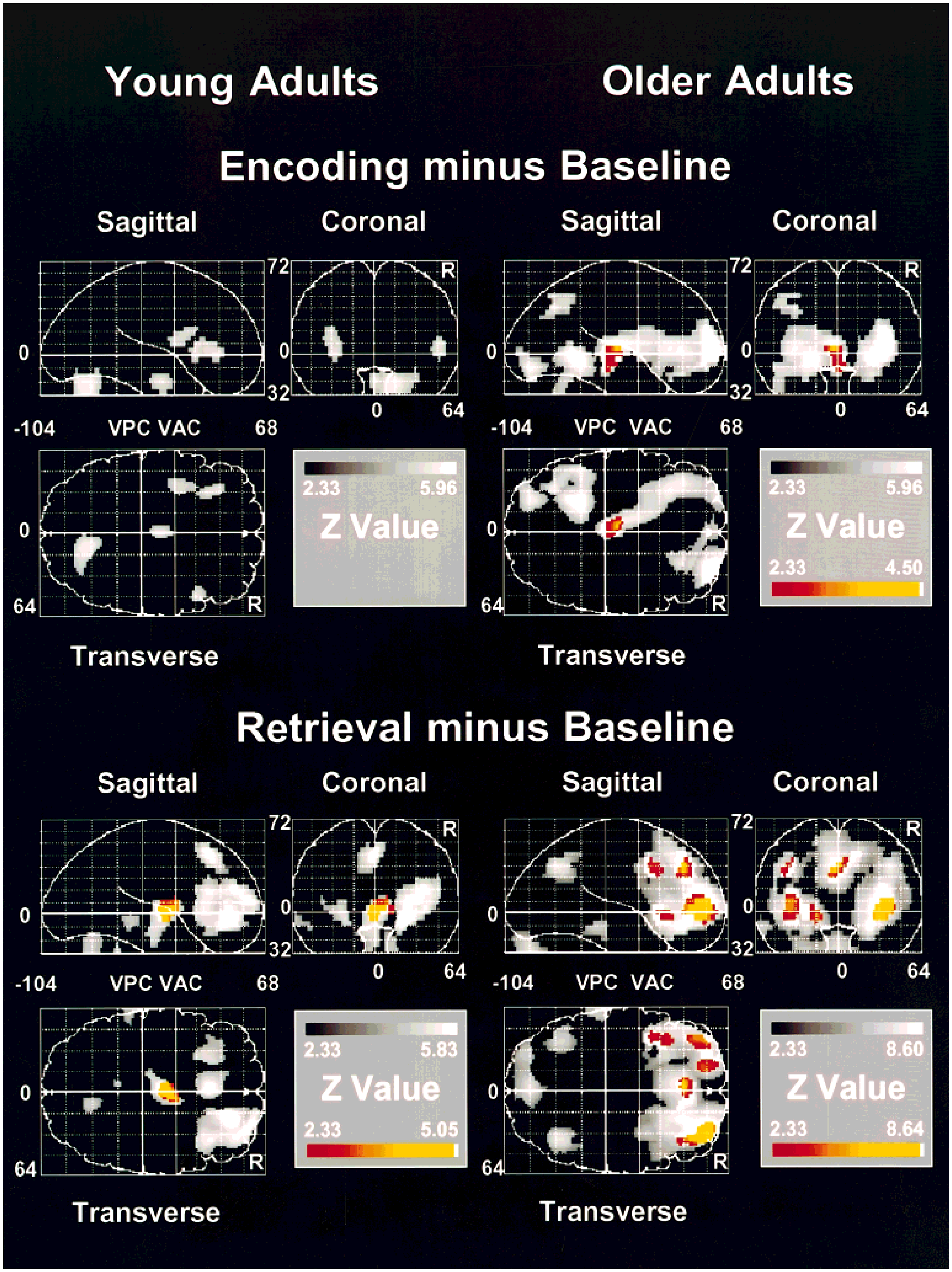

Young Adults
Older Adults
Encoding minus Baseline
Sagittal
Coronal
Sagittal
Coronal
72
R
0
0
32
0
64
-104
VPC VAC
68
0
64
R
2.33
5.96
Z Value
2.33
4.50
Transverse
Transverse
Retrieval minus Baseline
Sagittal
Coronal
Sagittal
Coronal
2.33
5.83
Z Value
2.33
5.05
2.33
8.60
Z Value
2.33
8.64
Transverse
Transverse

Figure 5.

several regions in prefrontal cortex exhibited relatively greater activation in the first half of the testing session. For the young adults, these regions were the middle and superior frontal gyri of the right hemisphere (BA 10) and the medial frontal gyrus of the left hemisphere (BA 8). For the older adults, activation in the left superior frontal gyrus (BA 10) was greater during the first half of the testing session than during the second half. The only activation that was relatively greater in magnitude during the second half of the testing session was the young adults' cerebellar activation for the Retrieval minus Baseline subtraction.

The decrease in rCBF in the right inferior parietal lobule (near the lateral sulcus), for the older adults' Encoding minus Baseline subtraction, was relatively greater during the first half of the testing session. Young adults' rCBF decrease in a similar, though somewhat more lateral, region of parietal cortex, for the Retrieval minus Baseline subtraction, was relatively greater during the second half of the testing session. The young adults also exhibited an rCBF decrease in the superior temporal gyrus, for the Retrieval minus Baseline subtraction, that was relatively greater in the first half of the testing session.

Relation between rCBF and reaction time

We used a stepwise multiple regression analysis [Neter et al., 1990] to determine the relation between rCBF and RT during task performance. Radioactivity counts were obtained for the voxels corresponding to the local maxima of each of the significant changes in rCBF, within each age group (i.e., the voxels listed in Tables II and III). The PET counts and mean RT were obtained for each of the 12 PET scans for each participant. Mean brain count values were determined for each PET study by calculating the mean voxel value of the whole image volume, and then calculating a brain mean from those voxels above 80% of the image mean. The voxel counts associated with a particular subtraction were used as independent variables predicting the dependent variable, RT. For the young adults, only the data for the Baseline and Retrieval conditions were used, because the young adults' Encoding minus Baseline subtraction did not yield any significant local maxima in the SPM analyses. For the older adults, one analysis was conducted on data in the Encoding and Baseline conditions, and another analysis was conducted on data in the Baseline and Retrieval conditions. Thus, the regression analyses developed a model for predicting the change in RT across the pair of task conditions, from the count values of the individual voxels. The voxels corresponding to all local maxima (both increases and decreases in rCBF) were included in each regression model.

The variables entered the model sequentially on the basis of their ability to improve the accountable variance (R^2) in the overall model. The threshold for entry into the model was an increase in R^2 that was significant at $P < .01$. At each step, the increment in accountable variance associated with each variable was estimated, covarying all predictors entered in previous steps. In each model, the mean count value for the whole brain was entered as the first predictor variable, to control for changes in global CBF. Variables entered in a previous step (except for the whole brain mean count) could be eliminated if they did not contribute significantly to the current step. The stepwise regression analyses were conducted on the data for both halves of the testing session combined.

The results of the stepwise regression analyses are presented in Table VI. A parameter estimate (*B*) with a positive value represents an increase in PET counts as a function of increasing RT; a negative B represents decreasing counts as a function of increasing RT. For the young adults' Baseline and Retrieval conditions, the counts in the right middle frontal gyrus (BA 10) were related positively to RT. The model for the older adults' Encoding and Baseline conditions included activation in both the left parahippocampal gyrus (BA 37) and right middle frontal gyrus (BA 10) as predictors. Several regions were predictors in the model for the older adults' Baseline and Retrieval conditions.

Figure 5.

Areas of increased rCBF between task conditions, as a function of age group. See the legend to Figure 1 for a description of task conditions. The Encoding minus Baseline subtraction represents the processes involved making a semantic (living/nonliving) decision regarding each of a series of words and attempting to remember the words for a subsequent memory test. The Retrieval minus Baseline subtraction represents the processes involved in making a yes/no decision regarding whether each of a series of words was presented previously during the Encoding condition. The results are presented as SPM voxel maps in the sagittal, coronal, and transverse planes, using the stereotaxic space of Talairach and Tournoux [1988]. The images are presented in standard neurologic orientation, so that the right half of the coronal image and the lower half of the transverse image correspond to the participant's right hemisphere. The rCBF increases for each age group are presented in the gray scale values (thresholded at $P < .001$, uncorrected). Within each age group, those voxels that differed significantly from those of the other age group are presented in the color scale values (thresholded at $P < .0001$, uncorrected). Cortical areas of significant rCBF increase are listed in Table II.

TABLE II. Regions of rCBF increase as a function of age group and task condition subtraction*

Region size (k)	P ($n^{max} > k$)	Z	P ($Z^{max} > u$)	x	y	z	BA	Location
Encoding minus Baseline, rCBF increase for young adults								
No significant voxels								
Encoding minus Baseline, rCBF increase for older adults								
675	.091	5.96	.0001	32	56	0	10	middle frontal gyrus
860	.044	4.94	.002	−22	−48	−4	37	parahippocampal gyrus
2,063	.001	4.86	.003	−4	−22	0		thalamus
		4.21	.044	−32	24	4	45	inferior frontal gyrus
302	.424	4.22	.043	−24	−84	−12	19	fusiform gyrus
Encoding minus Baseline, rCBF increase with young > older								
No significant voxels								
Encoding minus Baseline, rCBF increase with older > young								
147		4.50	.0001	−4	−18	4		thalamus
		3.33	.0001	0	−24	−12		red nucleus
Retrieval minus Baseline, rCBF increase for young adults								
1,537	.002	5.83	.0001	22	40	−4	10	middle/superior frontal gyri
		4.54	.014	30	52	12	10	middle frontal gyrus
		4.43	.022	36	42	20	10	middle frontal gyrus
410	.230	5.31	.0001	0	−12	0		thalamus
298	.391	4.80	.005	−2	24	44	8	medial frontal gyrus
Retrieval minus Baseline, rCBF increase for older adults								
8,011	.0001	8.60	.0001	32	46	4	10	middle frontal gyrus
		6.84	.0001	−4	32	36	8	medial frontal gyrus
		6.69	.0001	24	32	−8	11	middle frontal gyrus
262	.499	5.78	.0001	38	−62	36	40	inferior parietal lobule (near superior occipital gyrus)
398	.284	5.29	.0001	−2	−84	−28		cerebellum
		4.50	.015	−26	−88	−28		cerebellum
212	.605	4.80	.004	−36	−62	32	40	inferior parietal lobule (near superior occipital gyrus)
87	.892	4.46	.017	−60	−34	−12	21	inferior temporal gyrus
Retrieval minus Baseline, rCBF increase with young > older								
97		5.05	.0001	−4	−12	0		thalamus
		4.10	.0001	6	−6	4		thalamus
Retrieval minus Baseline, rCBF increase with older > young								
145		8.64	.0001	32	52	8	10	middle frontal gyrus
157		7.15	.0001	−2	32	36	8	medial frontal gyrus
		3.97	.0001	10	30	44	8/9	superior frontal gyrus
247		5.99	.0001	−38	46	4	10	middle frontal gyrus
		5.50	.0001	−16	48	−4	10	superior frontal gyrus
84		5.13	.0001	−40	22	0	47	inferior frontal gyrus
		4.88	.0001	−40	10	36	6/8	middle frontal gyrus

* See Methods section for a description of task conditions. Region size (k), number of voxels; P ($n^{max} > k$), probability that a region of k voxels or greater would have occurred by chance; Z, *t* value of local maximum of activation scaled to a unit normal distribution; P ($Z^{max} > u$), probability that the observed peak height of local maximum of activation is greater than would be expected by chance; x, y, z, coordinates in mm in the standard stereotaxic space of Talairach and Tournoux [1988]; x, right/left hemisphere, negative indicates left hemisphere; y, anterior/posterior coordinate, negative indicates posterior to the zero point (anterior commissure); z, superior/inferior coordinate, negative indicates inferior to the AC–PC line; BA, Brodmann's area. Probability levels of less than .0001 have been rounded to .0001.

TABLE III. Regions of rCBF decrease as a function of age group and task condition subtraction*

Region size (k)	P $(n^{max} > k)$	Z	P $(Z^{max} > u)$	x	y	z	BA	Location
Encoding minus Baseline, rCBF decrease for young adults								
No significant voxels								
Encoding minus Baseline, rCBF decrease for older adults								
3,935	.0001	6.67	.0001	−12	−18	36	24	anterior cingulate
		5.24	.0001	44	−28	24	40	inferior parietal lobule (near lateral sulcus)
		4.77	.003	−6	32	12	24	anterior cingulate
Encoding minus Baseline, rCBF decrease with young > older								
No significant voxels								
Encoding minus Baseline, rCBF decrease with older > young								
No significant voxels								
Retrieval minus Baseline, rCBF decrease for young adults								
67	.935	4.30	.036	42	−66	8	19	medial occipital gyrus
1,096	.012	4.27	.041	54	−42	24	40	inferior parietal lobule (near lateral sulcus)
Retrieval minus Baseline, rCBF decrease for older adults								
1,450	.026	5.60	.0001	52	−30	24	40	inferior parietal lobule (near lateral sulcus)
		5.04	.001	54	−46	16	22	superior temporal gyrus
		4.37	.015	46	−22	40	2	postcentral gyrus
1,475	.024	5.48	.0001	16	−58	12	30	posterior cingulate
		4.45	.011	16	−84	24	19	superior occipital gyrus
		4.15	.034	40	−76	12	19	medial occipital gyrus
1,652	.016	4.65	.005	−58	−38	28	40	inferior parietal lobule (near lateral sulcus)
		4.64	.005	−38	−16	12		insular cortex
		4.43	.012	−42	−32	16	41	transverse temporal gyrus
156	.719	4.31	.019	12	−102	4	18	cuneus
Retrieval minus Baseline, rCBF decrease with young > older								
No significant voxels								
Retrieval minus Baseline, rCBF decrease with older > young								
No significant voxels								

* See Methods for a description of task conditions. See footnote to Table II for a description of column headings.

The strongest predictor of RT was an increase in counts in the right middle frontal gyrus (BA 10). This model also included several posterior cortical regions, for which decreasing rCBF was associated with increasing RT.

DISCUSSION

Recognition memory performance

The RT data (Fig. 2) demonstrated that both the encoding and retrieval processes associated with the present task are subject to age-related slowing. The age group × condition and age group × practice interactions in the analysis of all three task conditions, and the age group × response type interaction in the analysis of the Retrieval condition, indicate that the absolute magnitude of the effects of these variables was greater for the older adults than for the young adults. The proportional changes in RT, however, were comparable for the two age groups. Compared to RT in the Baseline condition, both young and older adults' RTs increased by approximately 44% in the Encoding condition and by 57% in the Retrieval condition. Similarly, the decrease in RT between the first and second halves of the testing session was 7% for both

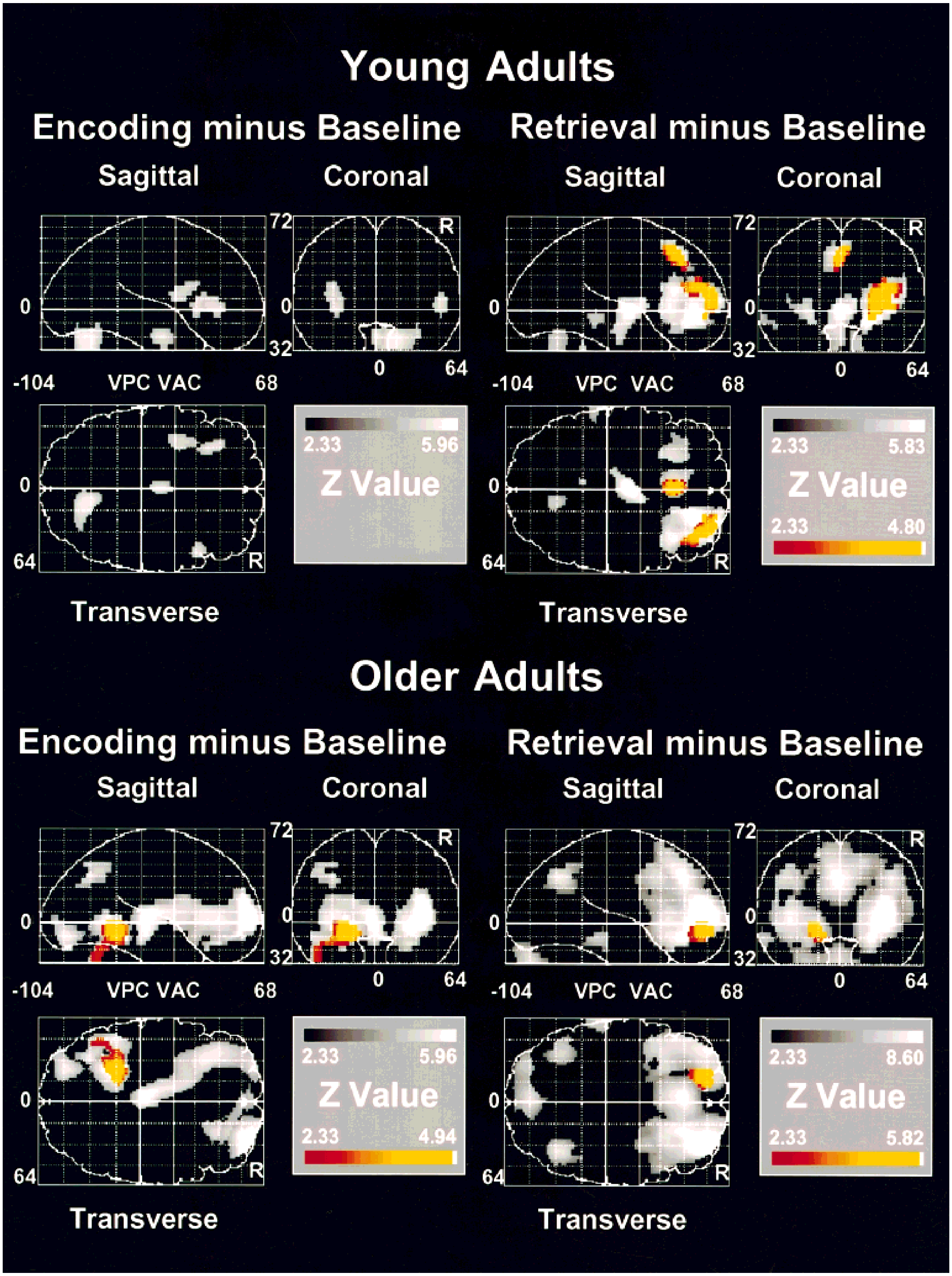


Figure 6.

Areas of change in rCBF activation as a function of practice. See the legend to Figure 1 for a description of task conditions, and the legend to Figure 5 for a description of the voxel thresholding and image orientation. The rCBF increases for each age group, averaged over the two halves of the testing session, are presented in the gray scale values. Within each age group, those voxels with significantly greater activation in the first half of the testing session than in the second half are presented in the color scale values. Cortical areas of significant change, as a function of practice, are listed in Tables IV (rCBF increases) and V (rCBF decreases).

TABLE IV. Regions of change in rCBF increase as a function of practice*

Region size (k)	Z	x	y	z	BA	Location
Encoding minus Baseline for older adults, rCBF increase for first half > second half						
264	4.94	−22	−48	−4	37	parahippocampal gyrus
	3.20	−38	−44	−16	37	fusiform gyrus
	3.06	−46	−56	−20	37	inferior temporal gyrus
Encoding minus Baseline for older adults, rCBF increase for second half > first half						
No significant voxels						
Retrieval minus Baseline for young adults, rCBF increase for first half > second half						
73	4.80	−2	24	44	8	medial frontal gyrus
225	4.60	22	46	−4	10	superior frontal gyrus
	4.54	30	52	12	10	middle frontal gyrus
	4.43	36	42	20	10	middle frontal gyrus
Retrieval minus Baseline for young adults, rCBF increase for second half > first half						
52	2.91	10	−64	−24		cerebellum
Retrieval minus Baseline for older adults, rCBF increase for first half > second half						
117	5.82	−18	50	−4	10	superior frontal gyrus
Retrieval minus Baseline for older adults, rCBF increase for second half > first half						
No significant voxels						

* See Methods for a description of task conditions. First half, PET scans 1–6; second half, PET scans 7–12. Each half of the testing session contained two PET scans per task condition. See footnote to Table II for a description of column headings.

groups, and the increase in ‘‘no’’ responses relative to ‘‘yes’’ responses in the Retrieval condition was 13–15%. This pattern of results suggests that the older adults were completing the component operations of the task in a similar manner as the young participants, but at a slower rate [Cerella, 1990; Myerson et al., 1990; Salthouse, 1996].

The signal detection analyses of participants' hits and false alarms in the Retrieval condition (Fig. 4) revealed an age-related decline in recognition memory performance. The *d*' measure of memory discrimination was higher for young adults than for older adults, whereas log β was near zero for both age groups. Assuming that the ‘‘old’’ and ‘‘new’’ words in the Retrieval condition are represented by separate distributions on a familiarity dimension [Parks, 1966], the age difference in d' suggests that these distributions are more widely separated for young adults than for older adults, yielding better discrimination of ‘‘old’’ and ‘‘new’’ words by young adults. Although age-related decline is typically greater in magnitude when tested by recall than by recognition [Craik and McDowd, 1987], age differences have been obtained previously with recognition testing [Gordon and Clark, 1974; Madden, 1986; Perlmutter, 1979], and the present finding of an age-related deficit in memory discrimination is consistent with these previous reports. The near-zero value of log β for the two age groups indicates that both age groups were using a relatively neutral response criterion in evaluating the familiarity of the words in the Retrieval condition.

Several models of recognition memory have proposed that recognition judgments involve a deliberate retrieval of specific trace information as well as an assessment of item familiarity [Atkinson and Juola, 1974; Mandler, 1980; Yonelinas, 1994, 1997]. The role of the retrieval component would be maximal during the initial recognition trials; repetition of the items to be remembered would increase their strength on the familiarity dimension [Smith and Halgren, 1989]. In the present experiment, each of the Encoding conditions was a repeated presentation (in a different order) of the same list of 64 words to be remembered. The increase in *d*' between the first and second halves of the testing session is consistent with an enhancement of the familiarity assessment.

TABLE V. Regions of change in rCBF decrease as a function of practice*

Region size (k)	Z	x	y	z	BA	Location
Encoding minus Baseline for older adults, rCBF decrease for first half > second half						
120	4.25	38	−34	24	40	inferior parietal lobule (near lateral sulcus)
	3.91	28	−36	40	40	inferior parietal lobule (near lateral sulcus)
Encoding minus Baseline for older adults, rCBF decrease for second half > first half						
No significant voxels						
Retrieval minus Baseline for young adults, rCBF decrease for first half > second half						
103	3.85	38	6	−20	22	superior temporal gyrus
Retrieval minus Baseline for young adults, rCBF decrease for second half > first half						
221	4.01	56	−38	28	40	inferior parietal lobule (near lateral sulcus)
	3.83	58	−28	16	40	inferior parietal lobule (near lateral sulcus)
	3.65	40	−28	12	41	transverse temporal gyrus
Retrieval minus Baseline for older adults, rCBF decrease for first half > second half						
No significant voxels						
Retrieval minus Baseline for older adults, rCBF decrease for second half > first half						
No significant voxels						

* See Methods for a description of task conditions. First half, PET scans 1–6; second half, PET scans 7–12. Each half of the testing session contained two PET scans per task condition. See footnote to Table II for a description of column headings.

The fact that the practice-related decrease in RT in the Retrieval condition was greater for ‘‘yes’’ responses than for ‘‘no’’ responses (Fig. 3) may also be related to the familiarity component. Because a different set of ‘‘new’’ items was used in each Retrieval condition, whereas the ‘‘old’’ items were repeated across the Encoding conditions, only the ‘‘yes’’ responses could benefit from the increased familiarity of individual items. Both the improvement in *d*’ with practice and the differential change in ‘‘yes’’ RTs with practice were comparable for young and older adults, which suggests that the age effects in this recognition memory task reflect a decline in the efficiency of the retrieval component rather than a change in familiarity assessment.

Cortical volume

Although the age × hemisphere interaction was significant in the ANCOVA of participants’ cortical gray matter volume, the age difference was not significant for either hemisphere considered individually, and there was no effect of age in the analysis of the cerebellar volumes. It consequently appears that the age-related changes in rCBF obtained in the present experiment are not related to substantial age differences in cortical volume (i.e., partial volume effects). Raz et al. [1997, 1998], using larger samples of participants (>100) than in the present experiment (24), have been able to detect an age-related decline in the volume of several cortical regions, especially prefrontal gray matter.

Cerebral blood flow

The analyses of rCBF yielded several changes as a function of task condition and age group (Fig. 5). For the older adults, the Encoding condition was associated with activation (relative to Baseline) in prefrontal cortex bilaterally. The prefrontal activation of the left hemisphere is consistent with the HERA model [Nyberg et al., 1996a; Tulving et al., 1994a], which emphasizes the differential involvement of left prefrontal cortex in encoding during episodic memory tasks. The activation of the older adults’ right prefrontal cortex, however, would not be predicted by the HERA model. In addition, several regions outside of the prefrontal cortex (left thalamus, left fusiform gyrus, left parahippocampal gyrus) were activated during the older adults’ performance in the Encoding condition. The

TABLE VI. Summary of stepwise regression analysis of reaction time, using PET counts of individual voxels as predictors*

Voxel location	*B*	*SE B*	Δr^2	model R^2
Baseline and Retrieval conditions for young adults				
BA 10 (R middle frontal gyrus)	2.70	0.66	.150	.159
Encoding and Baseline conditions for older adults				
BA 37 (L parahippocampal gyrus)	2.16	0.45	.112	.178
BA 10 (R middle frontal gyrus)	2.64	0.65	.124	.302
Baseline and Retrieval conditions for older adults				
BA 10 (R middle frontal gyrus)	2.59	0.62	.170	.171
BA 18 (R cuneus)	−3.37	0.55	.097	.268
BA 41 (L transverse temporal gyrus)	−3.63	0.76	.10	.368
BA 30 (R posterior cingulate)	−2.22	0.55	.084	.452
BA 40 (R inferior parietal lobule, near lateral sulcus)	−2.58	0.75	.065	.517

* See Methods for a description of task conditions. *B*, raw parameter estimate; *SE B*, standard error of estimate; Δr^2, increment in model R^2 associated with predictor variable in current step; model R^2, accountable variance in reaction time for model with variables in current and previous steps. BA, Brodmann's area; R, right hemisphere; L, left hemisphere. Voxel counts were thresholded for entry into the regression model at $P < .01$, covaried for global CBF (mean count of whole image volume).

thalamic activation may represent increased attention during the Encoding condition [LaBerge, 1995]. The fusiform and parahippocampal gyri are part of the occipitotemporal pathway that is critical for the mediation of form identification [Haxby et al., 1993; Ungerleider and Mishkin, 1982]. The left hemisphere pathway is particularly important for the identification of visually presented words [Petersen et al., 1990].

Although we had initially expected the rCBF activation associated with encoding to be greater for young adults than for older adults, the Encoding minus Baseline subtraction did not yield any regions of significant activation for the young adults. Both Grady et al. [1995] and Cabeza et al. [1997], in contrast, found that rCBF activation during memory encoding was greater for young adults than for older adults. Participants in the present experiment made few errors in the living / nonliving discrimination task used in the Encoding condition, and it is possible that this task was not sufficiently difficult to elicit rCBF activation for the young adults [Grady et al., 1996]. Only the thalamic activation, however, was significantly greater for the older adults than for the young adults, so it cannot be definitely concluded that the age groups differ in the magnitude of prefrontal and occipitotemporal activation during encoding. Low-level activation in these regions, for young adults, may have reduced the magnitude of the age interaction. The present findings suggest that age-related decline in rCBF activation does not necessarily occur during memory encoding and may be related to specific task requirements.

The Retrieval minus Baseline subtraction yielded extensive rCBF activation, for both age groups, in prefrontal cortex. It is interesting that the recognition memory task led to rCBF activation even though a successful retrieval occurred on a maximum of 50% of the trials in the Retrieval condition (''yes'' trials). Previous investigations manipulating the degree of success during memory performance have suggested that the right prefrontal cortex mediates a ''retrieval mode,'' which involves processes that occur regardless of the accuracy of individual retrieval events [Nyberg et al., 1995; but cf. Rugg et al., 1996, 1997]. There is in addition evidence that right prefrontal activation is more closely related to postretrieval verification and monitoring processes than to the initiation of a retrieval attempt [Schacter et al., 1997].

The rCBF data for the Retrieval condition confirmed our hypothesis of an age-related increase in prefrontal activation. The young adults' activation was located primarily in the middle frontal gyrus (BA 10) of the right hemisphere, although a local maximum was also present in BA 8 of the left hemisphere. This pattern is consistent with the HERA model, which emphasizes the role of right prefrontal cortex in the retrieval of episodic information. The older adults exhibited a more bilateral pattern of activation during retrieval. There were consequently several regions in left prefrontal cortex, and one region in right prefrontal cortex, exhibiting greater activation for older adults than for young adults (Table II and Fig. 5). Only one region, in the thalamus, exhibited relatively greater activation for young adults. The present results resemble those of Cabeza et al. [1997] in that the young adults' retrieval-related activation was located primarily in right prefrontal cortex, whereas the older adults' activation included prefrontal regions of both hemispheres. Our findings replicate the general pattern observed by Cabeza et al. for memory retrieval and support these authors' conclusion that the HERA model does not hold for older adults. The present results in addition extend this pattern of age differences to conditions under which an age-related decline was evident in recognition memory performance.

Cabeza et al. [1997] interpreted the age differences they observed as a form of ‘‘functional compensation,’’ in which age-related increases in some brain regions compensate for the decreases occurring in other regions [Grady et al., 1994, 1995]. Cabeza et al. also reported an age-related decline in right prefrontal activation, however, which was not observed in the present experiment. In addition, activation during the Encoding condition was at least as prominent for older adults as for young adults. The concept of functional compensation is thus less applicable to the present data. Our results indicate that aging is associated with the recruitment of additional neural systems to support memory encoding and retrieval, but the recruitment in the present context did not appear to be a compensation for a decreased level of activation.

It is also important to note that the older adults exhibited retrieval-related activations in the posterior aspect of the inferior parietal lobule (near the superior occipital gyrus) bilaterally, in left inferior temporal cortex (BA 21), and in the cerebellum, although these activations were not significant in the age difference contrast. The parietal lobe has been implicated in the assessment of context during episodic retrieval [Tulving et al., 1994b], and the cerebellum appears to contribute to performance in a variety of cognitive tasks [Leiner et al., 1995; Schmahmann, 1996]. The anatomical connections between the frontal and parietal lobes [Goldman-Rakic, 1987], as well as these functional activations, support the concept of a widely distributed memory system extending beyond prefrontal cortex [Andreasen et al., 1995].

In the analyses of the decreases in rCBF (Table III), the local maxima were more numerous for older adults than for young adults, but none of the age difference contrasts was significant. For both young and older adults, there were decreases in rCBF in right occipital cortex (BA 19) during the Retrieval trials, which is consistent with a reduction of perceptual processing for recognized items (i.e., priming [Badgaiyan and Posner, 1996; Buckner et al., 1995; Squire et al., 1992]). Both age groups also exhibited decreased rCBF in the inferior parietal lobule (BA 40). For the young adults, this decrease occurred in the right hemisphere, during the Retrieval condition. The older adults’ BA 40 decreases were located in the right hemisphere during encoding and in both hemispheres during retrieval. The local maxima of these decreases in rCBF were located in parietal cortex but were near the lateral sulcus, suggesting that they may represent the suppression of auditory information [Shulman et al., 1997].

Changes in cerebral blood flow with practice

Examination of the differences in rCBF between the first and second halves of the testing session (Tables IV and V, and Fig. 6) indicated several effects associated with practice. It is difficult to compare the age groups’ practice effects for the Encoding minus Baseline subtraction, because the young adults did not exhibit any significant rCBF change for both halves of the session combined. The older adults’ rCBF changes for the Encoding condition, both the increases and the decreases, tended to be greater in the first half of the testing session than in the second half. The practice-related changes associated with the Retrieval condition were more prominent for young adults than for older adults. For the young adults’ Retrieval minus Baseline subtraction, both the increases in rCBF in prefrontal cortex (right BA 10 and left BA 8), and the decreases in rCBF (right BA 40), were greater in the first half of the testing session than in the second half. In contrast, practice led to a change for only one of the older adults’ rCBF activations in the Retrieval condition (left BA 10). These findings support the observation of Raichle et al. [1994] that rCBF changes associated with early stages of practice tend to decline as task performance improves and less attentional control is required. In the Retrieval condition, these effects of practice were more apparent for young adults than for older adults, which suggests that the young adults were more efficient at reducing the attentional demands of the recognition memory task [Anderson et al., 1998; Whiting and Smith, 1997].

Relation of rCBF to reaction time

The goal of the stepwise regression analyses (Table VI) was to determine the relative importance of the activated regions as predictors of RT. Although previously in this Discussion we noted that the older adults’ left prefrontal activation in the Encoding condition was consistent with the HERA model [Nyberg et al., 1996a], voxel counts in this regions were not correlated significantly with the older adults’ RT in the Baseline and Encoding conditions. Instead, the activations in the left parahippocampal and right middle frontal gyri were more important as predictors of RT. The HERA model fares somewhat better in the analysis of the Baseline and Retrieval conditions. Right prefrontal cortex (BA 10) was the best predictor of RT for both young and older adults in these conditions. The older adults' regression model, however, also included several posterior cortical regions, for which increasing RT was associated with decreasing voxel counts. This finding is additional evidence that the neural system mediating episodic retrieval is more widely distributed for older adults than for young adults. At least some of the rCBF decreases (e.g., those near the lateral sulcus) that emerged as predictors may represent inhibitory processes. Nyberg et al. [1996b] emphasized that the neural mediation of memory performance comprises both excitatory and inhibitory components.

CONCLUSIONS

The present experiment demonstrated age differences in rCBF under conditions of age-related decline in both the speed and accuracy of recognition memory performance. The neural systems mediating task performance were associated with an increased level of activation, in more cortical regions, for older adults than for young adults. Encoding in the present task occurred without significant rCBF activation for young adults, and the relevant regions for older adults included the occipitotemporal pathway and prefrontal cortex bilaterally. Retrieval processes were associated with right prefrontal activation for both age groups. The older adults' retrieval-related changes in rCBF involved both activation and deactivation of several additional regions, including left prefrontal cortex and the inferior parietal lobule bilaterally. This recruitment of additional neural regions may represent the continual allocation of attention to task control, especially for memory retrieval, which young adults relinquish to some extent with increased practice.

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