



Neural correlates of memory for object identity and object location: effects of aging

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Abstract

The purpose of this study was to investigate the effects of aging on memory for object identity and object location to determine whether aging affects both posterior neocortical areas that are *domain-specific* and other brain regions, such as pre-frontal cortex, that are involved in encoding and retrieval regardless of the information that is processed (*domain-general*). We used positron emission tomography (PET) to measure changes in regional cerebral blood flow (rCBF) in younger and older participants while they were engaged in encoding and retrieving information about object identity and object location. Compared to young adults, older adults showed decreased activation in domain-specific regions of inferior parietal and inferior temporal cortex while engaged in processing (encoding and retrieving) information about object location and object identity, respectively. This decreased specificity in the older adults was accompanied by greater domain-general activation in right prefrontal and premotor cortex during perceptual encoding than during retrieval. Conversely, the younger participants showed greater domain-general activation in right extrastriate cortex (Brodmann area (BA) 18) during retrieval. Moreover, we found that medial temporal and frontal lobes were synergistically activated in younger adults but not in older adults. The pattern of decreased specificity of activation in posterior neocortex with greater activation in anterior neocortex suggests that, with age, compensatory domain-general mechanisms in anterior neocortex are recruited to mitigate altered domain-specific processes. Thus, the results of the present study indicate that the relation between the presumed integrity of various structures, such as the hippocampus, prefrontal cortex, and posterior neocortex, and their pattern of activation, is a complex one that is influenced by age, by the perceptual and cognitive demands of the task and their interaction. © 2002 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The effects of aging on episodic memory have been amply documented by behavioral [2,10,38,70,75] and, to a lesser extent, by neurometabolic research [5,6,15,19,22,60]. Recent brain imaging studies in young adults indicate that the brain regions involved in encoding and retrieval overlap with many of the same cortical regions that process domain-specific, perceptual information such as that associated with objects, words, faces or locations. Following Fodor [16] see also [41,43,46,47], we use the term *domain-specificity* to refer to a characteristic or attribute of *modules* which are neocortical structures that are dedicated to processing and representing only one type of informa-

tion or material. In addition to modules, other areas are recruited that are engaged preferentially at either encoding or retrieval no matter what information is being processed. We refer to the latter areas as *domain-general, central system* structures whose operation is defined not by the type of information that they process but by the function they have, such as encoding or retrieval, or its sub-components, such as monitoring or verification. The distinction between modules and central systems has been fruitful in developing neuropsychological theories and guiding research, and in stimulating debate about brain organization and function [7,16,44]. For example, Köhler et al. [35] showed that dorsal and ventral extrastriate cortical regions that are involved in recovering domain-specific information about object identity and location are coextensive with those involved in perceptual processing of the corresponding domains. Conversely, domain-general neocortical structures are hypothesized to operate across sensory modalities and

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information domains. Thus, the frontal lobes have been shown to be involved during episodic, semantic and working memory tasks, regardless of the type of information that is processed [35,41,47,55,71,77] but see Levy and Goldman-Rakic [36] and Moscovitch and Umiltà [46], for evidence of domain-specificity in the frontal lobes. In this paper, we examine the effect of aging on encoding and retrieval to distinguish between its effects on domain-specific and domain-general neocortical structures that mediate encoding and retrieval of information about object identity and location. We chose to examine object identity and location for two reasons: (1) they occupy a central place in neuropsychological theories of vision and memory, and (2) there is ample evidence, from human and animal models, that they are mediated by neuroanatomically distinct visual pathways, during both perceptual encoding and memory, which makes them ideally suited for investigation of age-related changes by neuroimaging.

The existence of separate extrastriate visual pathways for object recognition and spatial localization was described in primates almost two decades ago [74]. Regional cerebral blood flow (rCBF) studies using positron emission tomography (PET) confirmed this division in human participants in both young [25,34,52] and older adults [20]. This dichotomy was shown to extend to memory in a series of experiments by Köhler et al. [35] and Moscovitch et al. [45]. They showed that, in young participants, domain-specific areas in the extrastriate visual cortex that were differentially activated during perception and encoding of object location, as compared to object identity, were also differentially activated in memory retrieval of both types of information. For object identity, there was increased rCBF in portions of the bilateral lingual and fusiform gyri whereas for object location, there was increased rCBF in the right middle occipital gyrus, supramarginal gyrus and superior temporal sulcus [35]. Domain-general activations, by contrast, were found in right prefrontal cortex, bilateral middle and inferior frontal gyri and precuneus at retrieval and in superior temporal cortex at encoding. The data from these studies, and those from previous studies with face stimuli [20,26], suggest that explicit memory in young adults depends on networks of domain-specific (anterior inferotemporal cortex and posterior inferior parietal) and domain-general regions (medial temporal lobe and frontal structures) involved in episodic memory for object identity and location [35]. While the evidence is still equivocal, there is some suggestion that the two visual pathways remain functionally segregated and project to separate areas in the frontal lobe, where they produce domain-specific frontal activations related to working memory processes [8].

The distinction between domain-specific and domain-general regions figures prominently in theories of aging and memory. Traditionally, explicit, episodic memory loss in older adults has been ascribed to deficits in encoding and retrieval associated with deterioration of the medial temporal and frontal lobes which are considered domain-general

structures [1,11,14,60] (see also [49,78]). Because perceptual encoding is relatively less impaired by aging than is episodic memory, and because performance on perceptual implicit tests of memory is equivalent, or very nearly so, in older and younger adults [28,37,40,41], it is assumed that domain-specific, perceptual representation systems or modules in posterior neocortex should function at a similar level in both groups. According to these views, domain-specific modules in posterior neocortex that are associated with object identity and location should be affected less by aging than domain-general, central system structures in anterior, frontal regions.

There is little evidence concerning the operation of the dorsal and ventral pathways serving object identity and location in older adults, especially with regard to memory, but the few relevant studies that have been published yield provocative results. During perception of object (face) identity and spatial location, Grady et al. [20] found that both young and older adults showed activation in domain-specific regions of extrastriate areas sensitive to processing of object identity (Brodmann area (BA) 37) and spatial location (BA 19 and BA 7). The older adults, however, showed greater activation in BA 37, even on tests of spatial location, suggesting that domain-specific regions were not as clearly differentiated as they were in young adults. There were also some unexpected findings given the general consensus that frontal functions tend to deteriorate with age [59,64]; see [78] for review. Grady et al. [20] found that, in comparison to younger adults, older participants showed greater activations in prefrontal cortex, for both object identity and spatial location, but less activation in BA 18 of extrastriate cortex. One interpretation of these findings is that the frontal lobes, which have been considered to be domain-general regions, are recruited in older adults to compensate for reduced processing efficiency in extrastriate cortex. Similar frontal compensatory mechanisms seem to be operating at retrieval, though the evidence is based on just a few studies, most of them concerned with verbal memory [5,6,60]. Some studies, however, have also found decreased activation in the frontal lobes during memory retrieval in older adults [5,60].

The paucity of information makes it difficult to know whether aging also affects domain-specific processes at retrieval, either differentially or to the same extent in one domain as in another, and whether these effects interact with compensatory mechanisms in the frontal lobes. To address this problem, we decided to compare, within the same study, patterns of brain activation in younger and older adults during encoding and retrieval of object identity and object location. Our purpose was to examine whether these pathways remained segregated, i.e. showed the typical pattern of domain-specific activation, and worked synergistically, that is in a linked, complementary manner, in old age as in youth. By also using the same stimuli for both tasks, we circumvented difficulties associated with cross-experimental comparisons that use different materials, tasks and participants.

We measured rCBF while subjects engaged in perceptual matching of either the spatial location or the identity of line drawings of objects. Perceptual matching also involved incidental encoding of the presented novel visual information [72]. We, therefore, refer to this condition as “perceptual encoding”. Subsequently, rCBF was measured while subjects retrieved the location or the identity of the previously encountered objects from episodic memory in the context of forced-choice recognition memory tasks. We refer to this condition as “retrieval/memory”. The same type of stimuli were used in all tasks; experimental conditions differed only in terms of the kind of judgments required (perceptual encoding or retrieval/memory), the type of information on which these judgments had to be based (object location or object identity) and the age of the individuals (young or old) who participated in the study.

Based on the idea that domain-specific modules associated with perceptual encoding are affected less by aging than domain-general, central systems, we expected that rCBF changes associated with aging would be more noticeable in anterior frontal regions than in posterior neocortex. It was difficult to predict, however, whether any potential change in frontal activation would be a decrease accompanying deterioration or an increase reflecting compensatory responses. It was also difficult to predict how age effects on activation in domain-general regions would compare for the retrieval and perceptual encoding tasks. Potentially,

we predicted the possibility of a synergistic pattern of activation, i.e. a closely linked and complementary pattern of activation during perceptual encoding and subsequent retrieval in these regions. In posterior neocortex, we expected greater activation for both groups in ventral than dorsal pathways on tests of object identity than of location, and the reverse on tests of object location when compared to identity. Although age-related structural changes in posterior neocortical modules are shown to be relatively small, there is some evidence that strategic control processes mediated by the frontal lobes can affect their operation [33]. Consequently, it is possible that some age-related changes in rCBF may also be observed in these structures.

2. Methods

2.1. Overview

Fig. 1 shows an overview of the stimulus arrangements and tasks conditions in the present study.

2.2. Participants

A total of 24 right-handed individuals participated in this study (12 participants in each group). Participants were screened to rule-out any history of current medical,

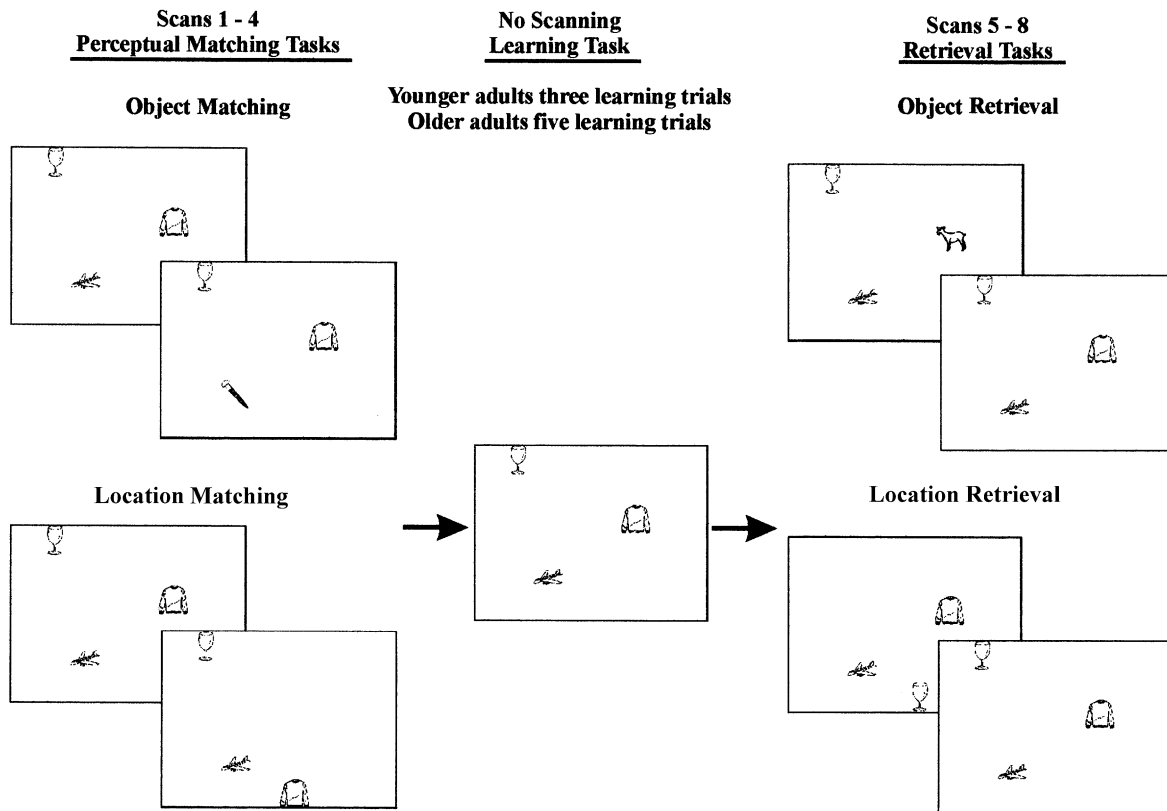


Fig. 1. Schematic diagram of experimental procedure and stimulus arrangements (see Section 2 for further details, adapted from Köhler [35]).

neurological or psychiatric disorder. The sample consisted of two groups; younger (12 men, mean age 25.3 years, S.D. 4.7) and older adults (11 men and one woman, mean age 70.17 years, S.D. 3.86, mean education 15.92 years, S.D. 2.54). All participants were right-handed. The data from the young adults were obtained from a previous PET study, details of which have been presented elsewhere [35] and re-analyzed for the purposes of the present study. Informed consent was obtained from all participants. The study was approved by the Human Participants Use Committee of Baycrest Center.

2.2.1. *Material*

The materials were identical to those used by Köhler et al. [35]. The stimuli were representational line drawings of common objects taken from Snodgrass and Vanderwart [66] set of normed pictures. Each display was composed of three drawings of semantically-unrelated objects. The drawings were presented at 44 different locations on a 14 in. computer screen of an IBM-compatible personal computer at a distance of 60 cm. To cover all possible locations, the area of the screen was divided into a 6×8 matrix which was not visible during presentation of any of the items. Every display contained drawings of unique objects presented in unique spatial configurations. The configurations were unique in terms of the combination of the particular angles and distances that were used. The pool of target displays contained two lists of 22 items. Both lists were used in the perceptual matching tasks. The items of one of the lists were selected as targets for the retrieval tasks.

The test displays for the perceptual matching and retrieval tasks were created by altering the target displays (see Fig. 1). Test displays for the location tasks were created by moving one of the three objects to a location different from the one used in the corresponding target display. Test displays for the object-based tasks were created by replacing one of the drawings of objects with a drawing of a novel object. For the four blocks of perceptual matching tasks, the two lists of target displays were paired with one set of spatially-altered test displays and one set of object-altered test displays each. For the four blocks of retrieval tasks, the single selected list of target displays was paired with two different sets of spatially-altered test displays and two different sets of object-altered test displays.

2.2.2. *Behavioral procedure*

A pilot study was conducted with a sample of 10 age-matched, right-handed older adults to determine if the presentation durations used for the young participants were adequate for the older participants. Results from this preliminary study showed that the original presentation durations resulted in accuracy scores of 80% or more in the older adults. Therefore, these presentation durations were also used in the PET study with the sample of older participants.

All participants were familiarized with the study tasks 24–48 h prior to scanning in a practice set of tasks with

items that were different from those in the actual experiment. Participants were asked to perform the perceptual matching tasks and the subsequent retrieval tasks for practice.

On the day of scanning, experimental testing started with a phase in which the perceptual matching tasks were presented while PET scans were taken. The perceptual matching tasks were always presented first so that they could also serve as incidental encoding tasks for information that had to be recovered in the retrieval tasks. Performance on the perceptual matching tasks themselves, however, did not require nor benefit from episodic memory retrieval. Two versions of the perceptual matching task for object identity and two for spatial location were administered in counter-balanced order. In each of these tasks, pairs of displays were presented in sequence and participants had to indicate whether the members of a pair were the same or different. Each pair consisted of two displays presented for 1 s each with a 0.75 s inter-display interval. The inter-pair interval was 2.25 s. Participants reported their responses by pressing the keys of a computer mouse with the right hand. In ‘same’ trials, which made up half of the trials of both tasks, identical target displays were presented twice in succession. In ‘different’ trials of the object matching tasks, a target display was paired with an object-altered test display. In ‘different’ trials of the spatial matching tasks, a target display was paired with a spatially-altered test display. For each block, participants were informed in advance whether the task required matching of spatial location or object identity.

After performing the perceptual matching tasks, participants underwent a learning phase while no PET scans were taken. Participants were re-exposed to a subset of target displays from the perceptual matching tasks. This was done in order to raise their subsequent memory performance for these displays to a level that was comparable to that observed in an earlier PET study [45]. The target displays which had been selected for memory testing were presented for 3 s each. The entire list of 22 displays was repeated five times for the older participants and three times for the younger participants. Based on the results of the pilot study, older participants were given two additional learning trials to ensure the formation of a sufficiently strong memory trace. Participants were instructed to memorize the displays and to pay attention to the identity and spatial location of the drawings of objects that formed a group in each display.

Memory testing started 10 min after the end of the learning phase. Participants were administered four blocks of trials in which two versions of the retrieval task for object identity and two versions of the retrieval task for spatial location were administered in counter-balanced order while PET scans were taken. The retrieval tasks were two-alternative, forced choice recognition memory tests because they are considered the best procedure for minimizing possible response bias. Pairs of displays were presented in sequence. Presentation durations and manual response requirements were identical to those in the perceptual matching tasks. In the object retrieval tasks, one display in each pair had been

studied previously and the other was a test display which was altered in terms of object identity. In the location retrieval task, one display of each pair had been studied previously and the other was a spatially-altered test display. In both retrieval tasks, participants had to indicate whether the first or the second display was the altered one in comparison to the studied display. The altered display was presented first in 50% of the trials. In each block of trials, participants were informed which kind of test displays was used.

2.3. PET scanning

Participants were scanned in a GEMS-PC-2048-15B scanner with a custom-fitted thermoplastic face-mask. Eight scans were obtained per subject. Each scan was acquired after a bolus injection of 40 mCi (1.48 Gbq) of $[O^{15}]$ -H₂O in the left forearm vein through an in-dwelling catheter [27]. The cognitive task was started 30 s prior to the 60 s data acquisition period for each scan. All scans were 11 min apart except for the fourth and fifth scans which were 22 min apart to accommodate the intentional learning trials. The PET images were attenuation-corrected using a transmission scan acquired prior to the first PET scan. The scans were reconstructed using a Hanning filter with a cut-off frequency of 0.5 Hz. Normalized integrated regional counts were used as an index of rCBF.

2.4. Data analysis

Images were realigned using AIR 3.0 software [79]. Other pre-processing steps were performed using the Statistical Parametric Mapping technique (SPM95), with software provided by Wellcome Department of Cognitive Neurology (UK). Software was implemented in MATLAB (Mathworks Inc. Sherborn, MA, USA). The realigned images from each subject were transformed into a standard stereotactic space [69] by matching them to a reference image that already conforms to the standard space. The images were subsequently smoothed using an isotropic Gaussian kernel with a full width at half-maximum of 10 mm in all dimensions. Changes in global blood flow were corrected for by proportional scaling.

The effects of cognitive tasks on rCBF were estimated using a three-factorial ANOVA in SPM96. Effects of interest were the main effects of 'type of information' (space versus object) and 'task' (retrieval versus perceptual encoding), the two-way interactions between these two factors and between each of them and 'group' (older versus younger), as well as the three-way interaction between 'group', 'type of information', and 'task'. It should be noted that the main effect of group is not interpretable in the context of the type of analyses performed on the present blood-flow data. Threshold for the resulting images was set at $P < 0.001$ level (uncorrected); only regions that consisted of at least 10 contiguous voxels above threshold were interpreted in the analysis. To shed more light on the patterns of activation

reflected in the ANOVA interaction terms, additional post-hoc comparisons were performed on the peaks of regions identified with the SPM interaction images. For these post-hoc comparisons, rCBF values were extracted for all experimental conditions at the relevant peaks; separate ANOVAs were performed on these extracted data in both groups to determine differences related to processing of location versus object information during perceptual encoding and retrieval. The significance level for post-hoc comparisons was set at $P < 0.01$.

3. Results

3.1. Behavioral task

Mean response accuracy (hits) for each experimental condition is displayed in Fig. 2 for both groups. An ANOVA revealed that the main effect of age (younger versus older) was significant [$F(1, 22) = 26.8, P < 0.001$], with the older participants showing generally lower performance scores than the younger participants. The interactions between 'task \times group' and 'type of information \times group', were not significant, although there was a trend in the type of information by group interaction [$F(1, 22) = 3.15, P = 0.09, ns$], suggesting that the older participants showed a tendency to be more impaired on object than location processing.

3.2. Neuroimaging

An analysis of group differences in blood flow across the entire brain and across all tasks was conducted to rule-out the confounding influence of global flow on activation. There was no significant global blood flow difference between the two groups, across tasks [$F(1, 95) = 1.129, ns$].

Three of the interaction terms computed with the three-factorial ANOVA were relevant for the examination of age-related group differences that are of primary concern to the present investigation (interactions: task \times group,

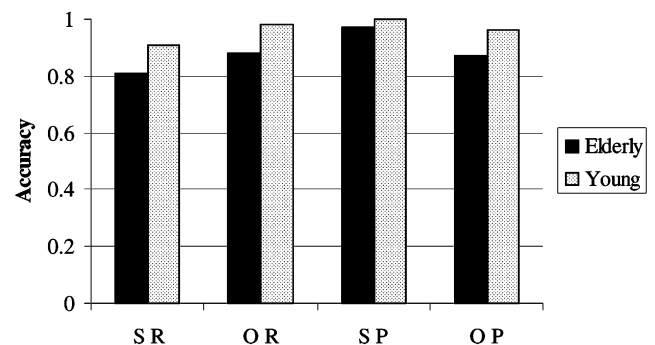


Fig. 2. Mean accuracy for older and younger participants on perceptual encoding and retrieval of object identity and object location. Older adults were significantly less accurate than younger adults across all conditions ($P < 0.001$). SP: spatial retrieval, OR: object retrieval, SP: spatial perception, OP: object perception.

information \times group, task \times information \times group). The corresponding results will be described subsequent to a brief summary of effects that were found across both groups, i.e. irrespective of group membership (main effect task, main effect information, interaction task \times information).

3.3. Main effect of information (object identity versus object location)

With this effect, brain regions were identified that showed domain-specific activation during perceptual encoding and retrieval in both groups. Younger and older participants showed increased rCBF during processing of location than of object identity in the right middle temporal gyrus and in the right dorsal occipital lobe. In contrast, processing of object identity resulted in greater activations of bilateral fusiform gyri and right ventral occipital lobe regions (see Table 1).

3.4. Main effect of task (retrieval versus perceptual encoding)

Brain regions were identified that showed domain-general activation in both groups. There were greater regional activations in the right superior temporal gyrus, the right superior frontal gyrus, the left inferior parietal lobule, the left middle temporal gyrus and the left anterior cingulate gyrus

during perceptual encoding than during memory retrieval. Portions of bilateral middle frontal gyri, the left middle temporal gyrus, the right middle occipital gyrus and the posterior cingulate gyrus showed higher rCBF during retrieval than perceptual encoding (see Table 1).

3.5. Task by information interaction

The image associated with this interaction term identified those brain regions that showed domain-specific activations in both groups that were specific to retrieval or perceptual encoding. The only region that demonstrated such a pattern was the medial aspect of the cerebellum (see Table 2). It displayed an increase in rCBF during object as compared to location processing during perceptual encoding but no parallel increase during retrieval.

3.6. Group by task interaction

The image associated with this interaction term identified those brain regions that showed domain-general activations that differed between both groups. Older participants showed greater activation in frontal regions during perceptual encoding as compared to retrieval that was not apparent in younger subjects. The peaks for these regions were located in the gyrus precentralis and right premotor cortex (see Table 2 and Fig. 3) but the observed cluster of

Table 1
Regions of activation for main effects of task and information^a

Region	BA ^b	Hem ^c	x	y	z	Cluster-level {k, Z}
Retrieval > perceptual encoding						
Middle frontal gyrus	9	Bil	-42	22	28	2237, 7.66
	46		40	30	24	731, 7.22
Middle frontal gyrus	47	R	24	46	-8	100, 5.99
Middle temporal gyrus	39	L	-32	-64	28	690, 5.74
Middle temporal gyrus	21	L	-58	-38	-12	47, 4.73
Middle occipital gyrus	19	R	30	-80	20	180, 5.61
Cingulate gyrus	23		0	-40	24	25, 3.85
Perceptual encoding > retrieval						
Superior temporal gyrus	22	R	54	-48	12	2252, 7.69
Inferior parietal lobule	40	L	-58	-44	24	196, 5.25
Middle temporal gyrus	21	L	-46	-18	-16	96, 5.20
Superior frontal gyrus	10	R	4	58	24	125, 5.04
Cingulate gyrus	24	L	-8	26	-4	222, 4.40
Thalamus		R	12	-20	-16	27, 4.05
Location > object						
Superior occipital gyrus	19	R	38	-80	20	68, 4.93
Middle temporal gyrus	21	R	48	-56	8	111, 4.17
Object > location						
Fusiform gyrus	37	Bil	-36	-84	-16	180, 4.60
			34	-54	-8	27, 3.83
Lingual gyrus	19	R	22	-96	-16	195, 4.56
Cuneus	17/18	L	-4	-92	8	122, 4.03

^a Coordinates are listed in millimeters according to Talairach and Tournoux [69].

^b BA: Brodmann area.

^c Hem: hemisphere.

Table 2
Regions of activation for interaction effects^a

Region	BA ^b	Hem ^c	x	y	z	Cluster-level {k, Z}
Group by task interaction						
Precentral gyrus/inferior frontal gyrus	6/8/44	R	52	0	20	126, 5.09
Premotor cortex	6	R	30	-10	36	41, 4.05
Inferior occipital gyrus	18	R	24	-86	-8	20, 3.74
Inferior parietal lobule	40	R	46	-28	28	34, 3.72
Middle temporal gyrus	21	L	-58	-44	-8	62, 3.99
Group by information interaction						
Fusiform gyrus	19	L	-42	-70	-12	54, 4.09
Fusiform gyrus	37	L	-38	-46	-16	63, 4.04
Supramarginal gyrus	40	R	56	-44	28	23, 2.3*
Task by information interaction						
Cerebellum	-	L	-6	-54	-16	60, 4.08
Group by information by task interaction						
Middle occipital gyrus	19	R	44	-64	-4	19, 3.82
Inferior frontal gyrus	47	L	-34	30	-8	20, 4.37
Hippocampus	-	L	-24	-30	-4	77, 4.01

^a Coordinates are listed in millimeters according to Talairach and Tournoux [69].

^b BA, Brodmann area.

^c Hem: hemisphere.

* Significant at $P < 0.05$.

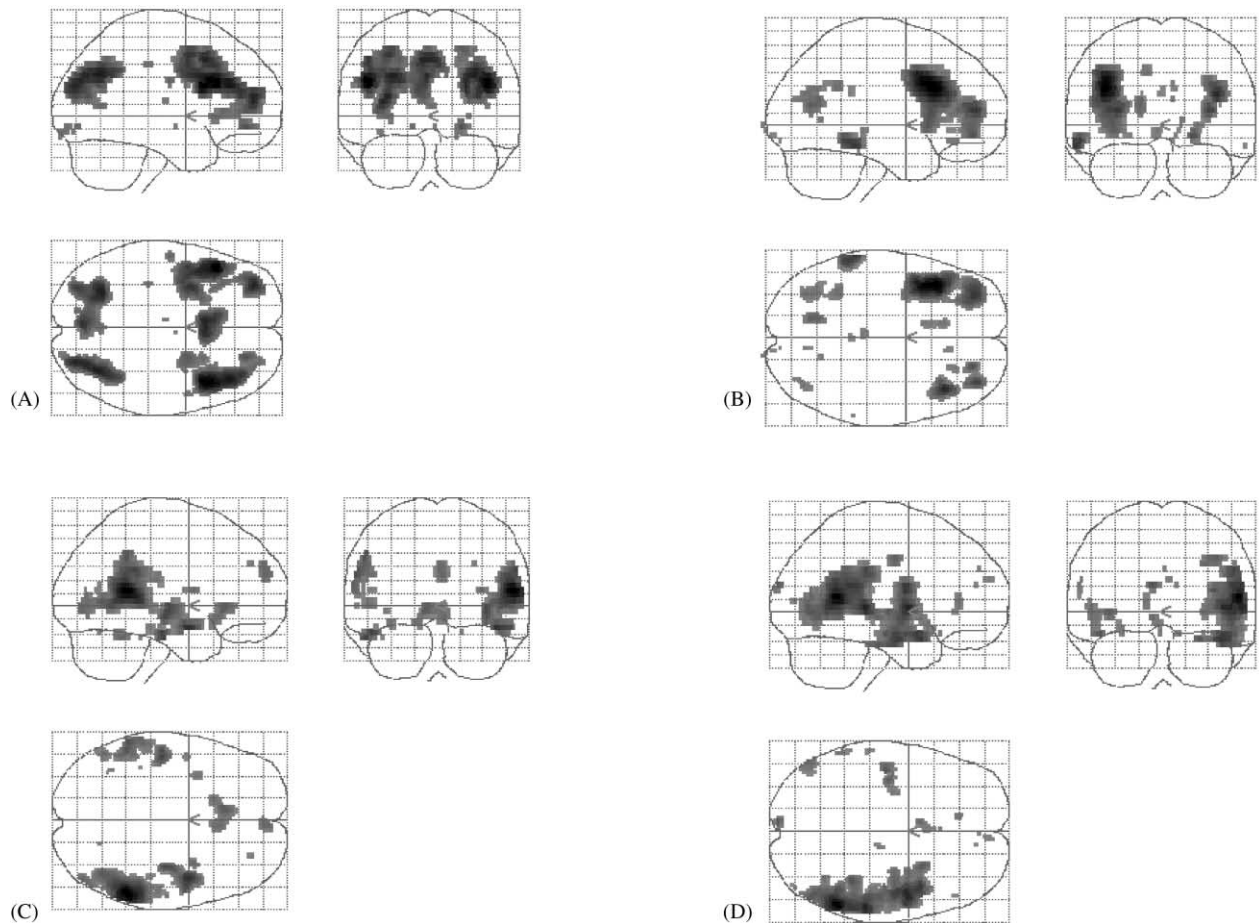


Fig. 3. Sagittal, coronal and transversal sections showing cerebral regions that show increased rCBF (at $P < 0.001$) when comparing retrieval and perceptual encoding in young and old adults. Top: retrieval minus perception in (A) younger participants and (B) older participants. Bottom: perceptual encoding minus retrieval in (C) younger participants and (D) older participants. Activations are superimposed on coordinates from the Talairach and Tournoux atlas [69] (see Table 2 for listing of observed activations).

pre-central activation extended into the inferior frontal gyrus of prefrontal cortex (BA 44). Post-hoc analyses confirmed that there was a significant simple main effect of task in the right precentral cortex peak in older [$F(1, 11) = 13.633$, $P < 0.01$] but not in younger subjects [$F(1, 11) = 2.263$, $P = 0.161$, ns]. Post-hoc comparisons for the peak in right premotor cortex yielded the same pattern of results, with non-significant findings in younger participants [$F(1, 11) = 3.911$, $P = 0.074$, ns] but significant differences in the older adults [$F(1, 11) = 19.519$, $P < 0.01$]. Another brain region in the right inferior parietal lobule showed a statistical trend with the same pattern, namely greater activation at perceptual encoding than retrieval in the older adults [for peak $F(1, 11) = 8.973$, $P = 0.012$, ns] but not in younger participants [$F(1, 11) = 0.508$, $P = 0.491$, ns].

There was also evidence for domain-general increases in activation related to retrieval that occurred only in the older adults. This activation was found in the left middle temporal gyrus. Post-hoc comparisons for the peak revealed greater activation at retrieval than perceptual encoding in the elderly

[$F(1, 11) = 9.484$, $P < 0.01$] but not in younger participants [$F(1, 11) = 0.842$, $P = 0.379$, ns].

Finally, we identified a region in the right occipital cortex with this interaction, in which there was domain-general activation, i.e. a significant main effect of task, for younger participants [for peak, $F(1, 11) = 10.282$, $P < 0.01$] that was not present in older adults [$F(1, 11) = 3.644$, $P = 0.083$, ns]. In this region, rCBF was greater during retrieval than perceptual encoding for young participants only.

3.7. Group by information interaction

The image associated with this interaction term identified those brain regions that showed domain-specific activations that differed between both groups (see Table 2 and Fig. 4). All three regions identified displayed domain-specific activation that was present in young participants only. Two regions were located in ventral aspects of occipito-temporal cortex. Post-hoc comparisons for the peak in left inferior occipital gyrus confirmed a significant simple main effect

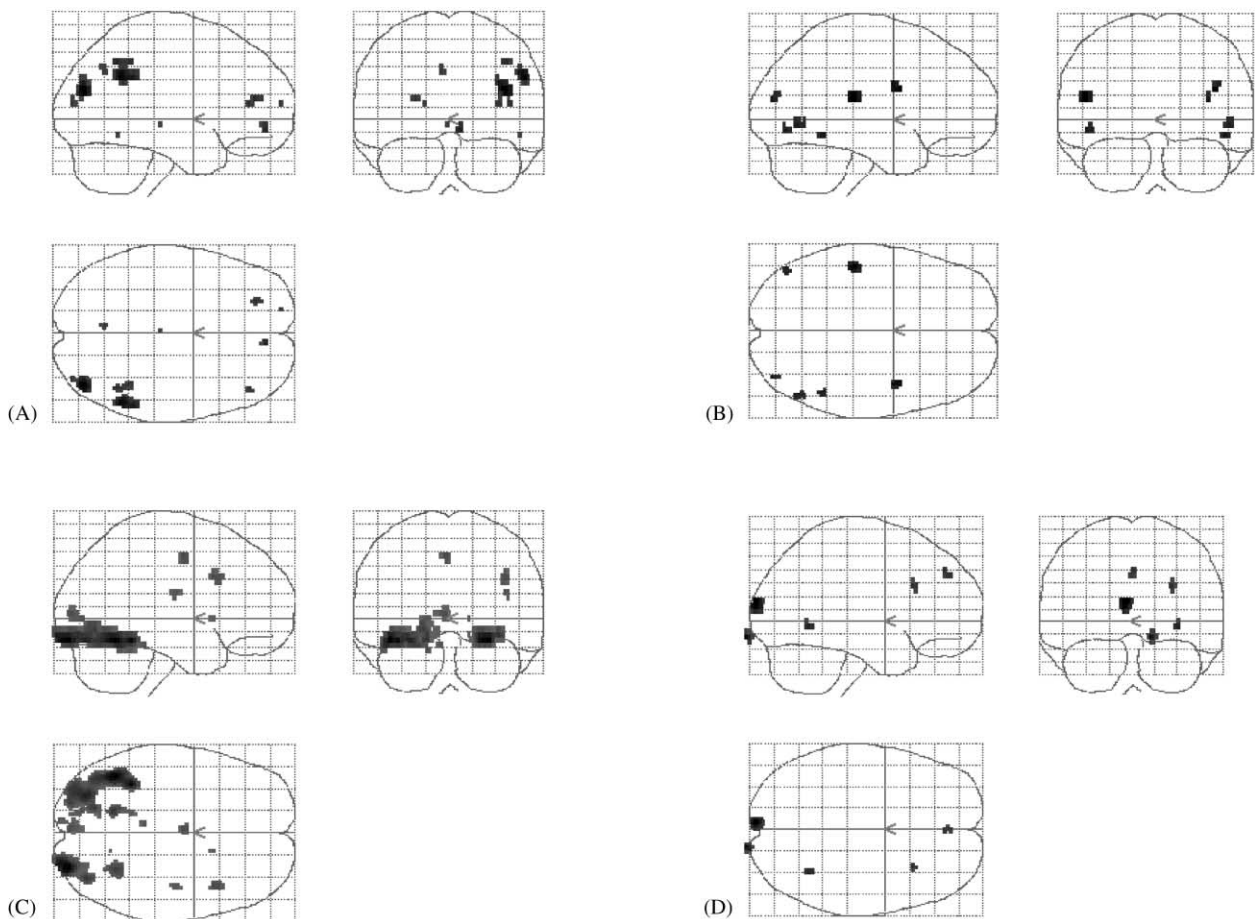


Fig. 4. Sagittal, coronal and transversal sections showing cerebral regions that show increased rCBF (at $P < 0.001$) when comparing spatial location and object identity in young and old adults. Top: spatial location minus object identity in (A) younger participants and (B) older participants. Bottom: object identity minus spatial location in (C) younger participants and (D) older participants. Activations are superimposed on coordinates from the Talairach and Tournoux atlas [69] (see Table 2 for listing of observed activations).

of type of information in younger participants [$F(1, 11) = 21.233, P < 0.01$] with greater rCBF during object identity than object location processing. At this peak, rCBF in the older participants displayed a statistical trend for the opposite response pattern (higher rCBF for location than object processing [$F(1, 11) = 7.720, P = 0.018, ns$]). Similar results were obtained for the peak in left fusiform gyrus, where younger subjects showed greater rCBF activation for object identity than object location processing [$F(1, 11) = 28.316, P < 0.01$] while the older adults failed to demonstrate differential activation [$F(1, 11) = 0.939, P = 0.353, ns$].

Additional analyses were conducted at a lowered statistical threshold in the right inferior parietal lobule as this contrast had proven to be theoretically important in our previous study [35,45]. At this lowered statistical threshold, there was activation in the younger participants in the region of the right supramarginal gyrus that reflected higher rCBF during object location than object processing [for peak, $F(1, 11) = 12.793, P < 0.01$]. The older participants did not show such a domain-specific effect in this location [$F(1, 11) = 0.035, P = 0.855, ns$].

3.8. Three way interaction

The image associated with this interaction term identified brain regions that showed group effects relating to domain-specific activations that differed for perceptual encoding and retrieval (see Table 2 and Fig. 4). Post-hoc

comparisons performed on the peak in the right middle occipital gyrus revealed domain-specific activation in younger participants at retrieval [$F(1, 11) = 10.928, P < 0.01$] but not at perceptual encoding [$F(1, 11) = 2.452, P = 0.146, ns$]. In contrast, the older participants showed significant domain-specific activations in this region at perceptual encoding [$F(1, 11) = 9.318, P < 0.01$] but not at retrieval [$F(1, 11) = 1.242, P = 0.289, ns$]. Younger participants showed an increase in rCBF during retrieval of location as compared to object identity whereas the older participants showed greater activation during perceptual encoding of object location than object identity.

Activations obtained in two additional regions proved to be especially informative because they revealed a synergistic pattern of activation between the left hippocampus and a left inferior frontal gyrus region in the young but not the older adults (Fig. 5). In both regions, the young adults showed opposite patterns of activation for location and object processing during perceptual encoding and retrieval. During retrieval, activation was greater for object than location processing whereas during perceptual encoding the activation was greater for location than object processing. In stark contrast, there were no signs of differential activation in the left hippocampus of older adults. In the left inferior frontal region, older participants showed a tendency for a pattern of activation that was opposite to that observed in the young participants (greater activation in location than object processing during retrieval and greater activation in object

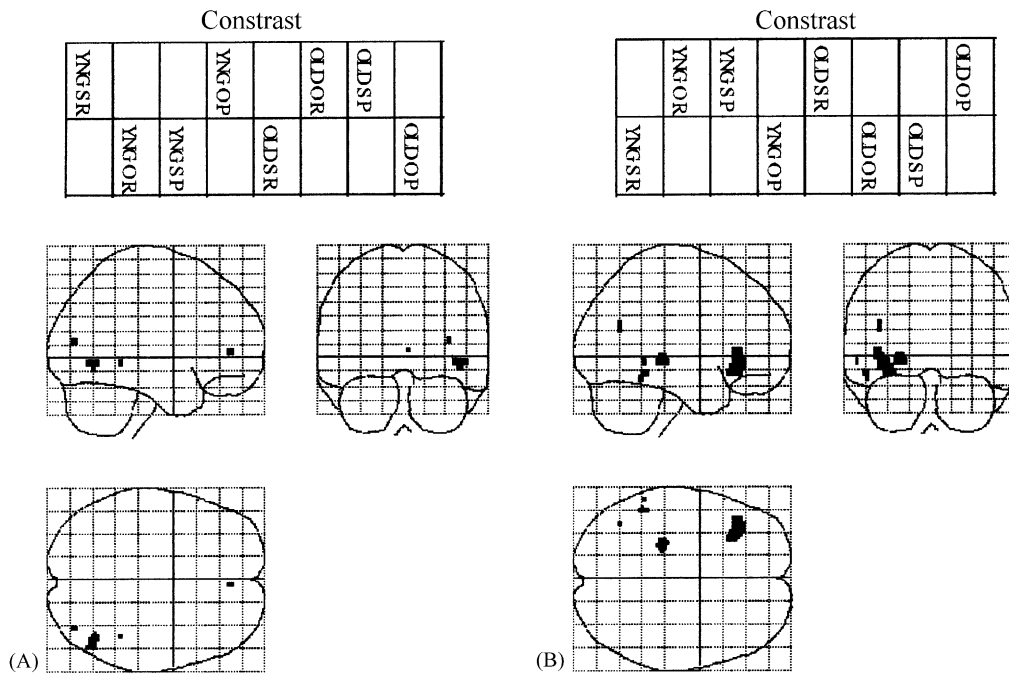


Fig. 5. Sagittal, coronal and transversal sections showing cerebral regions with increased rCBF (at $P < 0.001$) in the three way interaction (A) contrast revealing activation in middle occipital gyrus and (B) contrast revealing activation in left hippocampus and inferior frontal lobe. OLD: older participants; YNG: younger participants; SR: spatial location retrieval; OR: object location retrieval; SP: spatial location perceptual encoding; OP: object location perceptual encoding. Activations are superimposed on coordinates from the Talairach and Tournoux atlas [69] (see Table 2 for listing of observed activations).

than location processing at perceptual encoding; see Fig. 5). Post-hoc comparisons revealed that the changes in the left hippocampal peak in young adults were significant at retrieval [$F(1, 11) = 10.047, P < 0.01$] and showed a trend towards significance, in the opposite direction, at perceptual encoding [$F(1, 11) = 4.069, P = 0.069, ns$]. Conversely, older participants showed no significant rCBF change at this peak, neither at retrieval [$F(1, 11) = 0.238, P = 0.635, ns$] nor at perceptual encoding [$F(1, 11) = 1.435, P = 0.256, ns$]. For the peak observed in the left inferior frontal region, comparisons in young participants revealed a statistical trend for differences between object and location processing at retrieval [$F(1, 11) = 5.756, P = 0.035, ns$] but not at perceptual encoding [$F(1, 11) = 2.477, P = 0.144, ns$]. Older adults showed a trend towards differential activation at retrieval [$F(1, 11) = 4.216, P = 0.065, ns$] and a significant effect, in the opposite direction, at perceptual encoding [$F(1, 11) = 13.534, P < 0.01$].

4. Discussion

The results of the present study show that aging affects activation of domain-general regions, primarily in anterior cortex, that are activated selectively during encoding and retrieval irrespective of the domain of information involved. In addition, however, age-related changes were also observed in domain-specific regions of posterior neocortex that are specialized in processing object identity or object location. In comparison to young adults, older adults showed decreased specificity of activation in regions of inferior parietal and inferior temporal cortex while they were engaged in processing information about object location and object identity, respectively. This decreased specificity was observed regardless of whether the task at hand required perceptual encoding or retrieval of the relevant information and was accompanied by greater domain-general activation in various areas of right premotor and prefrontal cortex during perceptual encoding in older adults. Conversely, younger adults showed greater domain-general activation in right inferior occipital cortex during retrieval. We also found that the medial temporal and frontal lobes were synergistically activated in younger but not in older adults. At the behavioral level, the older participants performed more poorly than the young in all conditions, suggesting that they had greater difficulty processing information about object identity. We will discuss each of these findings in turn.

4.1. Behavior

Even though the older adults were well-educated and high functioning, the reduction in their memory performance was not unexpected. Despite the considerable effort we made to equate the performance of the older adults with that of the younger adults by giving the former additional learning trials, the older adults still had poorer performances than

younger adults, somewhat more so on the object than location tasks. Importantly, the older adults also performed more poorly than the young during the initial perceptual/encoding phase in which they had to match one three-item display with another one which was presented 750 ms earlier. Because the identity and location of the items in the display were unpredictable, the older adults may have had difficulty registering all the information from the displays before they disappeared. There is a suggestion that the difficulty was greatest in the object identity task where it was necessary to scan all the objects before reaching a decision whereas any displacement in location was easily noticed given the short delay between displays. In addition, even if all the information in the object task were registered, holding the first display in mind while comparing it with the second, even for a very short delay, likely invoked working-memory processes and may have strained those more in older than younger adults. The neuroimaging results, as we will show, are consistent with both interpretations.

4.2. Neuroimaging

As mentioned above, global blood flow was equivalent for both younger and older adults, thus, any differences favoring the younger group could not be ascribed to a global perfusion deficit in the older adults.

4.2.1. Age-related changes and task-specific activation of prefrontal cortex and posterior neocortex

The hypothesis that aging would affect domain-general, central system structures was supported by our finding of age-related changes in frontal function associated with task demands. There was greater activation in regions of right premotor and prefrontal cortex during perceptual encoding as compared to retrieval in the older adults, but not in the young. At first sight, the pattern of greater right frontal activation during perceptual encoding than retrieval that we found in older adults would seem to contradict the hemispheric encoding/retrieval asymmetry model (HERA). According to HERA, which is based on regularities observed in studies with young participants [6,12,71], greater rCBF is typically noted in left than right prefrontal regions during perceptual encoding, whereas the opposite occurs at retrieval. It should be noted, however, that we observed the typical right-sided activation in the analysis of main effects of retrieval, which concur with the previously reported hemispheric encoding/retrieval asymmetry (HERA). Indeed, a peak was observed for both groups in the right middle frontal gyrus (BA 47). In the older adults, this retrieval-related right prefrontal activation was complemented by more dorsally located frontal activation (BA 6, 8 and 44) related to perceptual encoding. The regions of differential right-frontal activation during perceptual encoding in the older adults are in the vicinity of those that have been reported to be activated, even in young adults, during perceptual encoding of non-verbal stimuli, such as faces [29], and during tests of

non-verbal working memory [30], although the activation in this study was more anterior than that reported for non-verbal paired associates by these authors. Moreover, the region of activation in premotor cortex corresponds to the one that Petit et al. [54] reported to be active during visual saccades, suggesting that older adults may have engaged in increased scanning during perceptual encoding in the present study.

In light of these findings, the pattern of right frontal activation during perceptual encoding in older adults suggests that older and young adults deal differently with identical stimuli and task demands. One interpretation of the age differences we found is that deterioration of frontal function in the elderly effectively increases the load on visuo-spatial working memory needed to hold the displays while comparing them during encoding. Older adults may scan the displays more than young adults because they have difficulty holding and encoding the information in working memory. As a result, they may attend to spatial aspects of the displays even when they are not required to do so, as in tests of object identity. This *spatial* interpretation is supported by the tendency for older adults to show greater activation in the right inferior parietal lobule during perceptual encoding than retrieval, which accords with observations that this region is activated on tests requiring processing of location information in three-item displays [45].

Whereas older adults showed greater activation primarily of anterior cortical regions during perceptual encoding, the group by task interaction indicated that younger adults displayed greater activation in ventrolateral occipital portions of posterior neocortex during retrieval. It is difficult to know whether these differences in activation result from age-related *structural* changes in posterior neocortex, from deteriorating frontal and medial-temporal functions that lead to age-related differences in processing and representation of the information that is retrieved, or from both. Whatever the cause, the patterns of activation in ventrolateral occipital cortex suggest that older adults are not as efficient at handling the visual processing demands of the task as are young adults, which may account for their decreased accuracy. This interpretation is reinforced by our finding of additional reductions in domain-specific posterior neocortical activation, associated with age.

4.2.2. Age and domain-specific activation in posterior neocortex

Young and older adults showed greater activation in inferotemporal cortex, i.e. bilateral fusiform gyrus, on tests of object identity than of location whereas they showed the reverse activation pattern in dorsal portions of right lateral occipital cortex. These results are consistent with previous reports that in both humans and monkeys, the dorsal visual pathways process information related to object location and the ventral pathways process information related to object identity [25,45,73,74,80]. Although results revealed that domain-specific activations in ventral and dorsal extrastriate cortex were present in both young and older adults, we

also found evidence indicating reduced domain-specificity in posterior neocortex of older adults. Most notably, older adults, unlike the younger participants of the study, showed no signs of domain-specific activation in inferior right parietal cortex in relation to processing of object location. In addition, there was an absence, in older adults, of differential activation related to processing of object identity in left-sided portions of anterior fusiform gyrus. This reduction of domain-specific activation in posterior neocortex in older adults was accompanied, as previously mentioned, by greater activation in prefrontal cortex during perceptual encoding.

It is unlikely that the reduced domain-specific activation in posterior neocortex in older adults results from a loss of regional differentiation with age, though some loss of efficiency has been reported [4,40,50,61]. Grady et al. [20] obtained the typical pattern of dorsal and ventral pathway activation in older adults on spatial and object tasks, respectively, although they also found some activation in the ventral pathway on a spatial task in older adults. A crucial difference between the present study and Grady et al. [20] is that they used stimuli from different domains (different materials) in each task, whereas we used identical stimuli. Because the correspondence between stimuli and task demands was readily apparent in Grady et al. study, it may have been easier for their participants to focus on the necessary decision-making information in each task. In contrast, in our study, because identical stimuli were used in both tasks, participants had to process information about objects and locations in both cases, but base their decision on only one type of information, that type being determined by the demands of the task. For example, in the object identity task participants had to compare objects at each spatial location but base their decision only on object identity. In this task, as in many others [23,24,63,76], younger adults may have found it easier than older ones to hold all the information in mind, focus on the required information and ignore, or inhibit, the information that was irrelevant [31,32]. Frontal-lobe deterioration accompanying old age affects all these functions and may have made the task especially difficult for older adults. The greater frontal activation observed in older adults here and by Grady et al. [20] may reflect this added effort. The domain-specific pattern of brain activation attests to the younger adults success in parsing object and location information, whereas the decreased specificity in older adults indicates that they were less able to do so. Thus, according to this interpretation, the primary cause leading to decreased specificity is not loss of differentiation in posterior neocortex but rather changes in (strategic) processes mediated by the frontal lobes [58].

4.2.3. Age and hippocampal/frontal activation

One of the more interesting results of the present study was that the hippocampus and frontal lobe were synergistically activated in younger adults, but less so, if at all, in older adults. By synergy, as stated above, we mean a closely linked and complementary interaction. For the young, there was an

inverse relationship between activation of these regions at encoding and at retrieval that was specific to the type of information being processed. However, caution needs to be exercised in considering this conclusion in view of the fact that significant differences on post-hoc tests were found only at retrieval. Nonetheless, the inverse relationship could suggest that the more the information is processed in these regions at encoding, the less processing will be required to recover the information at retrieval. Thus, these results provide novel suggestive evidence for the relation between encoding and retrieval in the same medial temporal lobe regions.

It is interesting that both the spatial (location) and non-spatial (object identity) condition were capable of producing hippocampal activation, the effect being most evident in the non-spatial condition at retrieval in the young. Although the hippocampus has long been implicated in memory for allocentric spatial information [51], it is controversial whether the hippocampus is needed for memory of object identity [3,17]. In our study, however, memory for object identity may have benefited from participants' forming configural associations among the three items in the display. Such an interpretation would be consistent with the hypothesis that the hippocampus is necessary for encoding, retention, and retrieval of relational or configural associations among items rather than for memory of any single item or simple association [13,68].

In keeping with our observations of age-related differences in domain-specific processing strategies, the type of information that leads to differential activation of the hippocampus and frontal lobes at encoding and retrieval differs between young and older adults. In young adults, greater hippocampal/frontal activation is associated with recovery of information about object identity at retrieval. At encoding, greater activation is associated with location processing, though the effect only approaches significance. This inverse relationship suggests that the more hippocampal/frontal processing is invested at encoding one type of information (i.e. object location), the less is needed for retrieving it. Conversely, more hippocampal/frontal activation is needed to recover information encoded with less investment (i.e. object identity). The same inverse relationship is not observed in older adults. If anything, they show small, non-significant effects in the opposite direction with greater hippocampal/frontal activation during encoding of object identity than of spatial location which may be indicative of the slight difficulty they have in encoding object identity and the greater effort they may exert in doing so. In older adults, the almost complete absence of this synergistic pattern may reflect the absence of clear-cut domain-specificity combined with deteriorating hippocampal function. The latter would be consistent with Mitchell et al.'s [39] and Grady's [19] observation of decreased hippocampal activation in the elderly. Though Mitchell et al. attribute the decrease to age-related deficits in binding information about objects and their location, the impairment may be more far-reaching and include deficits in any tests of explicit

memory that require relational processing. Our own findings would be consistent with either interpretation.

The complexity of the interaction makes it difficult to ascribe these age-related differences in hippocampal activation only to structural changes in the medial temporal lobes, though such changes may contribute to the effects. Instead, as with posterior neocortex, our findings suggest that age-related differences in hippocampal activation may also be determined by different processing strategies used by young and older adults when confronted with different types of materials and task demands. Indeed, the most likely interpretation is that structural and functional changes interact with one another to produce age-related differences in patterns of activation. The synergy between the frontal lobes and hippocampus in young adults, and the influence of material and task demands, suggest that age-related changes in the frontal lobes play a pivotal role in mediating these altered processing strategies. In addition, our study indicates that the relation between activation at encoding and at retrieval needs to be taken into account in interpreting age-related differences.

In light of these considerations, it is not surprising that age-related changes in regional brain activation on memory tests may vary from study to study. Thus, Grady [18] found less hippocampal activation in older than younger adults on a face-recognition task but only at encoding, Schacter et al. [60] found equal activation on successful word recognition at retrieval, and Backman et al. [1] found greater activation in older than younger adults at retrieval in a recall test with word stems as cues. Rather than view these results as inconsistent with one another, a better interpretation is that they are indicative of the different effects that variations in stimulus material, task demands, and processing strategies, have on patterns of brain activity in younger and older adults. Such an interpretation fits well with an extensive cognitive literature showing that age-related differences in memory are influenced by these very same variables, and can vary widely depending on the interplay among them [9].

The results are also consistent with a *component-processing approach to memory* which states that performance on a memory task depends on the contribution of various component processes each of which is mediated by different brain structures [41,42,48,49] which, in turn, can influence each other. Exactly which components and structures are engaged by each task will depend on the stimulus material and the demands of the task, as well as on the integrity of the structures that are engaged. For example, there is some neuroanatomical evidence indicating that the prefrontal cortex degenerates earlier with age than the posterior neocortex [53,57]. Nonetheless, contrary to expectation, we and others [19,20,58] found greater activation under some conditions in prefrontal cortex in the older adults than in the young, and a reduced, less differentiated pattern of activation in posterior neocortex. One plausible interpretation of these results is that frontal-lobe deterioration, combined with small, but noticeable deficits in sensory processes in the

older adults either at the receptor level [62,65] or centrally [4,40], are sufficient to force the older adults to commit greater (frontal) cognitive resources (attention, scanning) to stimulus analysis needed for encoding and thereby compensate for the sensory loss (see Grady et al. [21]). Indeed, Grady et al. [21], found that under conditions of stimulus degradation, such as occurs in attempting to perceive faces through noise, frontal activation increased even in younger adults. Because the allocation and deployment of cognitive resources and consequent action is associated with frontal function, the frontal lobes are activated more during perceptual encoding in the older adults than in the young, even though the frontal lobes may be less viable in the older adults. In addition, perceptual tasks, such as comparing two displays sequentially, that ostensibly have minimal working memory requirements in the young, may thus, impose a greater load on working memory in older adults which also would be reflected in greater, compensatory frontal activity [58]. In reaction, older adults may also adopt different processing strategies than young adults to deal with the same material and task demands. By committing cognitive resources to sensory analysis and adopting less appropriate or efficient processing strategies, older adults have fewer resources to process information deeply and their memory suffers as a result [56,67]. These processing changes, in turn, may be reflected in changes in activation patterns, in memory structures such as the hippocampus, just as structural changes influence the processing strategies that are adopted.

5. Conclusion

Age-related differences in activation were found in domain-specific structures in posterior neocortex as well as in domain-general structures such as the prefrontal cortex. In general, there was less domain-specificity in older than in younger adults, and greater frontal activation, indicative of a synergy between anterior and posterior structures in older adults. The synergy between frontal and hippocampal activation in younger adults, however, was much reduced, if not absent, in older adults, possibly because there was a general reduction in hippocampal activation in the older adults, accompanied by a loss of domain-specificity.

The results of the present study, and those in the literature on aging, indicate that the relation between the presumed integrity of various structures, such as the hippocampus, prefrontal cortex, and posterior neocortex, and their pattern of activation, is a complex one that is influenced by the perceptual and cognitive demands of the task and the interaction among brain regions. Thus, even if deterioration with age is limited to only one structure, it can give rise to a cascade of events, influenced by stimulus material and task demands, which are likely to be reflected in age-related changes of activation in many other areas. It is unlikely, therefore, that there is a single marker of aging that will be revealed by functional

neuroimaging, even if such a marker exists. By showing that different neural networks are activated in young and older adults when confronted with the same materials and task demands, neuroimaging studies force one to consider that young and older adults process and represent information differently even when their performance is equivalent. It is left for future research to determine whether the difference is related to structural changes in the affected regions or, as we believe is more likely, to differences in resource allocation and processing strategy, caused by structural changes in only some regions but influenced by environmental and psychological factors.

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