Task-independent and Task-specific Age Effects on Brain Activity during Working Memory, Visual Attention and Episodic Retrieval

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It is controversial whether the effects of aging on various cognitive functions have the same common cause or several different causes. To investigate this issue, we scanned younger and older adults with functional magnetic resonance imaging (fMRI) while performing three different tasks: working memory, visual attention and episodic retrieval. There were three main results. First, in all three tasks, older adults showed weaker occipital activity and stronger prefrontal and parietal activity than younger adults. The occipital reduction is consistent with the view that sensory processing decline is a common cause in cognitive aging, and the prefrontal increase may reflect functional compensation. Secondly, older adults showed more bilateral patterns of prefrontal activity than younger adults during working memory and visual attention tasks. These findings are consistent with the Hemispheric Asymmetry Reduction in Older Adults (HAROLD) model. Finally, compared to younger adults, older adults showed weaker hippocampal formation activity in all three tasks but stronger parahippocampal activity in the episodic retrieval task. The former finding suggests that age-related hippocampal deficits may have a global effect in cognition, and the latter is consistent with an age-related increase in familiarity-based recognition. Taken together, the results indicate that both common and specific factors play an important role in cognitive aging.

Keywords: frontal, hippocampus, lateralization, magnetic resonance imaging, recollection, reserve

Introduction

As we age, we become less able to manage several pieces of information at the same time, to filter distracting internal and external stimuli, and to remember what we did and what we have to do. Behavioral studies have carefully described and measured these age-related deficits in working memory, attention, episodic memory, and other cognitive functions (for reviews, see Craik and Salthouse, 2000). A basic issue is whether these various kinds of age-related cognitive deficits have the same common cause or several different causes. Thus far, this issue has been investigated primarily using statistical analyses of behavioral data. In the present study, we approached this problem from the new perspective provided by functional neuroimaging techniques.

A long-standing controversy in the cognitive aging literature is the one between common and specific factor theories. According to common factors theories, age-related sensory and cognitive changes can be accounted for by a common, biologically based factor (Lindenberger and Baltes, 1994; Anstey *et al.*, 2001; Christensen *et al.*, 2001). Common factor theories are attractive because they provide a parsimonious account of a large amount of empirical findings. At the same time, it has been noted that common causes cannot easily account for all manifestations of sensory and cognitive aging (Lindenberger and Baltes, 1994; Li and Lindenberger, 2002). There is much evidence that age effects can vary considerably across tasks (see Light, 1991), which may be more in line with specific factor theories.

From a cognitive neuroscience perspective, it is reasonable to assume that both common and specific factors are necessary for a full account of aging on sensory and cognitive functioning. On one hand, some forms of cerebral aging are likely to affect most cognitive tasks regardless of their nature (task-independent age effects). For example, age-related deficits in white matter integrity (for a review, see Raz, 2000) may reduce conduction speed and slow down responses in most cognitive tasks (Salthouse, 1996). On the other hand, other forms of cerebral aging are likely to affect only certain kinds of tasks (task-specific age effects). For instance, age-related deficits in dorsolateral prefrontal cortex (PFC) function are likely to have a greater impact on tasks that are highly dependent on executive functions (for reviews, see Moscovitch and Winocur, 1992; West, 1996), such as context memory (e.g. Cabeza *et al.*, 2000). Thus, rather than trying to decide between common and specific factor theories, our more modest goal was to distinguish between task-independent and task-dependent age effects on brain activity using functional neuroimaging (cf. Esposito *et al.*, 1999; Grady, 2002).

If one reviews functional neuroimaging studies of cognitive aging (e.g. Cabeza, 2001a,b), one can identify at least two consistent task-independent age effects. First, several studies have found an age-related decrease in occipital activity across a variety of tasks, including face matching (Grady *et al.*, 1994), lexical decision (Madden *et al.*, 1996), word-pair encoding (Cabeza *et al.*, 1997) and retrieval (e.g. Anderson *et al.*, 2000), temporal-order memory (e.g. Cabeza *et al.*, 2000) and letter working memory (e.g. Rypma *et al.*, 2001). Age-related decreases in occipital cortex activity have been attributed to inefficient sensory processing in the ventral (occipito-temporal) pathway (Grady *et al.*, 1994; Madden *et al.*, 1996). Second, several studies have found an age-related increase in PFC activity across a variety of tasks, such as face matching (e.g. Grady *et al.*, 1994), lexical decision (Madden *et al.*, 1996), word recognition (Madden *et al.*, 1999), verbal working memory (e.g. Rypma and D'Esposito, 2000) and problem-solving (Esposito *et al.*, 1999). Age-related increases in PFC activity have been typically attributed to functional compensation (e.g. Grady *et al.*, 1994; Madden *et al.*, 1996; Rypma and D'Esposito, 2000). Relating both types of effects, Grady *et al.* (1994) suggested that during perception older adults might compensate for deficits in sensory processes mediated by occipital regions by recruiting strategic processes mediated by PFC regions. Similarly, Li and Lindenberger (2002) noted that

the results from a number of studies suggest that older adults use cognitive processes to compensate for compromised sensory information.

When reviewing functional neuroimaging studies of cognitive aging, one can also identify task-specific age effects. For example, many studies have found an age-related contralateral PFC recruitment (for a review, see Cabeza, 2002), that is, older adults show greater PFC activity in the side of PFC that was less activated in younger adults. PFC lateralization differs across tasks, and age-related contralateral PFC recruitment does too. For example, in tasks associated with left PFC activity in young adults, such as episodic encoding, older adults show contralateral recruitment in right PFC (e.g. Logan and Buckner, 2001; Morcom *et al.*, 2003), whereas in tasks associated with right PFC activity in younger adults, older adults shows contralateral recruitment of left PFC (Bäckman *et al.*, 1997; Cabeza *et al.*, 1997; Madden *et al.*, 1999; Grady *et al.*, 2002).

The main problem with the foregoing list of task-independent and task-specific age effects is that it is based on cross-experiment comparisons. In the case of task-independent age effects, it is unclear if the putative common region was actually the same area of the brain in all studies. In the case of task-specific age effects, it is uncertain if the different age effects reflected the nature of the tasks employed or other methodological differences in the methods employed (participants, stimuli, procedures, etc.). In order to clearly distinguish between task-independent and task-specific age effects on brain activity, it is critical to compare age-related differences on brain activity on several different tasks, within-subjects and under similar conditions. This was the overall goal of the present study.

Extending, to aging, a cross-function approach (Cabeza and Nyberg, 2002) that we have previously investigated in young adults (Cabeza *et al.*, 2002a, 2003b; Nyberg *et al.*, 2002, 2003), we employed event-related fMRI to directly compare the effects of aging on the neural correlates of three cognitive tasks: working memory (WM), visual attention (VA) and episodic retrieval (ER). As illustrated by Figure 1, trials had two phases in all tasks. During the first phase of WM trials participants encoded and sustained a memory set of four words, and during the second phase they indicated if a probe word was part of the memory set or a new word. During the first phase of VA trials participants sustained attention to a symbol on the screen to determine if it blipped once, twice, or never during a 12 s interval, and during the second phase they indicated the presence or absence of blips. In most VA trials there was no blip during Phase 1, and only these no-blip trials were included in the fMRI analyses. Given that in the trials analyzed participants stared at the screen but nothing happened, the working memory component of the VA condition is minimal. During the first phase of ER trials participants generated the mental set of ER (retrieval mode; Tulving, 1983), and during the second phase they made the decision about whether or not a cue word was studied before the scanning session.

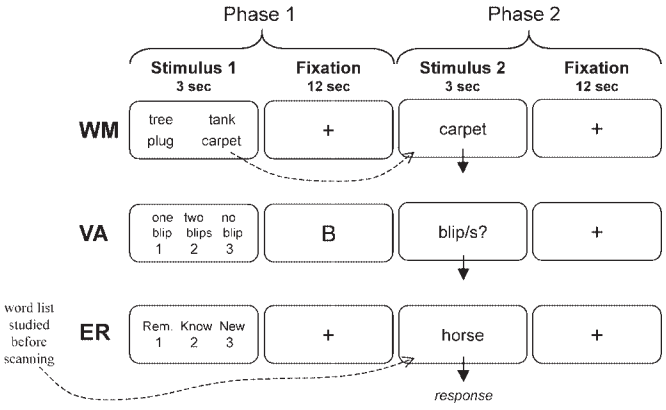

Figure 1. Behavioral paradigm. WM was investigated with a word delayed-response test, VA with a sustained attention task, and ER with a word recognition task.

The analyses of fMRI data identified task-independent and task-specific age effects. To identify task-independent age effects, we used a conjunction procedure that isolated age-related differences in activity that occurred in each and every cognitive task. On the basis of prior findings, we predicted that all three tasks would show age-related decreases in occipital activity and age-related increases in PFC activity. To identify task-specific age effects, we used a masking procedure that excluded from the age-related differences in activations of each task those previously identified as task-independent (conjunction analysis). Given that in younger adults, PFC activity tends to be left lateralized for verbal WM (for a review, see Smith and Jonides, 1999) and right lateralized for sustained VA (for reviews, see Coull, 1998; Sarter *et al.*, 2001), we predicted age-related contralateral recruitment in right PFC for WM but in left PFC for VA.

Materials and Methods

Subjects

The subjects were 20 younger adults (13 males) and 20 older adults (10 males). All participants were healthy, right-handed, native English speakers, with no history of neurological or psychiatric episodes. No participant was taking medications or had a medical condition that could affect cerebral blood flow (e.g. hypertension). All participants gave informed consent to a protocol approved by Duke University Institutional Review Board. Younger adults were Duke University students and staff with a mean age of 22.6 years (SD = 3.7). Older adults were community dwelling high-functioning individuals with a mean age of 70.3 years (SD = 6.3). Older adults were selected from a pool of senior research volunteers at Duke University and screened for health problems and conditions that could affect blood flow (e.g. hypertension, certain medications) using a questionnaire, and for signs of mild cognitive impairment or dementia using a test battery. The selected group of older participants performed within the normal range in the Mini-mental Status Exam (mean = 28.9) and in all other tasks in the battery.

Materials

The critical materials were concrete words selected from the MRC Psycholinguistic Database (http://www.psy.uwa.edu.au/mrcdatabase/mrc2.html). The words were four to six letters in length and of moderate frequency. Half of the words referred to living things and half to nonliving things.

Procedure

After completing health and MRI screening questionnaires and practicing the tasks to be performed in the scanner, subjects were placed in the scanner and anatomical scans were conducted. Following the anatomical scans and before the functional scans, subjects studied a list of 40 words (36 targets, two primacy fillers, two recency fillers), presented at a rate of 3 s/word. Subjects made a living/nonliving decision for each word and were also instructed to remember the words for a subsequent memory test. In the scanner (1.5 T GE LX Nvi), all stimuli were projected using an LCD projector to a screen located ~70 cm behind the subjects' crown, which subjects could see via an

angled mirror. When necessary, vision was corrected using MRI-compatible lenses that matched the prescription used by the participant. Responses were recorded using a three-button MR-compatible response box. During functional scanning, subjects performed WM, VA and ER trials in random order. Each trial lasted 30 s and had two phases, each consisting of a stimulus (3 s) followed by fixation (12 s). In all three tasks, subjects made a three-choice response to the second stimulus, which was always a single letter string. They were encouraged to respond while the word was on the screen (3 s) and trials with RTs beyond this interval were excluded from the analyses.

In WM trials, the first stimulus was a memory set of four words, presented in two columns, and the second stimulus was a probe word which subjects recognized as being in one of the two columns in the memory set or as a new word. In VA trials, the first stimulus was the instruction to perform the VA task, and the second stimulus was a response screen. Following the instruction screen, subjects had to stare continuously at the fixation symbol (a letter 'B') in order to determine if it 'blipped' (a brief disappearance) once, twice, or never during the 12 s interval. When the response screen was presented, subjects entered their response (once, twice, never). Only no-blip trials were included in the analyses. In ER trials, the first stimulus was the instruction to perform the ER task, and the second stimulus was the cue word. Subjects responded to the cue word by indicating whether they remembered having read the word in the study list before scanning ('Remember' response), whether they believed the word was in the study list but could not retrieve any specific detail about its occurrence within the list ('Know' response), or whether they thought the word was not included in the study list ('New' response). The Remember–Know paradigm was not included to compare Remember and Know trials, which was precluded by the total number of old words scanned (36), but to encourage subjects to use a recollection-based retrieval strategy.

Functional scanning consisted of 12 runs, and each run included nine critical trials: three WM trials with words from the memory set, three VA trials with no blips, and three ER trials with studied words. Additionally, each run contained several 'catch trials' which were not included in the analyses: an average of 0.5 WM trials with new words, 0.5 VA trials with blips, and 1.0 ER trial with new words. Across the 12 runs, there were a total of 36 old-word WM trials, 36 no-blip VA trials, and 36 old-word ER trials. Only trials in which the word was correctly classified as part of the intra-trial memory set (WM) trials, the pre-scanning study list (ER trials), or in which the absence of blips was correctly noted (VA trials) were included in the analyses. With accuracy levels of ~86–97%, subjects contributed ~30–35 trials to each condition.

fMRI Methods

Anatomical Scanning

A T_1-weighted sagittal localizer series was first acquired. The anterior (AC) and posterior commissures (PC) were identified in the mid-sagittal slice, and 34 contiguous oblique slices were prescribed parallel to the AC–PC plane. High-resolution T_1-weighted structural images were acquired with a 450 ms T_R (repetition time), a 9 ms T_E (echo time), a 24 cm FOV (field of view), a 256 × 256 matrix, and a slice thickness of 3.75 mm. A second series of 46 oblique T_1-weighted images perpendicular to the AC-PC was then acquired using the same imaging parameters.

Functional Scanning

Thirty-four contiguous gradient-echo echoplanar images (EPIs) sensitive to blood-oxygen level dependent (BOLD) contrast were acquired parallel to the AC–PC plane, using the same slice prescription described above for the near-axial structural images. The EPIs were acquired with a 3 s T_R, 40 ms T_E, one radio frequency excitation, 24 cm FOV, 64 × 64 image matrix, and a 90° flip angle. Slice thickness was 3.75 mm, resulting in cubic 3.75 mm^3 isotropic voxels.

Image Preprocessing

All image preprocessing and statistical analyses were performed using SPM99 (http://www.fil.ion.ucl.ac.uk/spm/). Time series were corrected for differences in slice acquisition times, and realigned to correct for motion artifacts. Anatomical images were coregistered with the first functional images for each subject, and then both anatomical and functional images were spatially normalized to a standard stereotactic space, using the Montreal Neurological Institute (MNI) templates implemented in SPM99. The coordinates were later converted to Talairach and Tournoux (1988) space using software available online (http://www.mrc-cbu.cam.ac.uk/imaging/mnispace/html). Subsequently, the functional images were spatially smoothed using an 8 mm isotropic Gaussian kernel. They were proportionally scaled to the whole-brain signal, which was not significantly correlated with any of the activations identified by subsequent statistical contrasts.

Statistical Analyses

Phase 1 and Phase 2 were modeled separately. For each subject, task-related activity was identified by a convolving vector of the onset times of the stimuli with a synthetic hemodynamic response function (HRF) and its temporal derivative. The general linear model, as implemented in SPM99, was used to model the effects of interest and other confounding effects (e.g. head movement, and magnetic field drift). We assessed statistical parametric maps (SPMs) for each individual subject by applying linear contrasts to the parameter estimates for the events of interest, resulting in a *t*-statistic for every voxel. Trials associated with correct and incorrect responses were modeled separate, and only the results for the former are reported. Group averages and group comparisons were calculated for each condition by employing a one-sample *t*-test without constant term (random effects) on the resulting contrast images, in which the variances of the young and old groups were pooled. This type of analysis allows inclusive masking and conjunction analyses over the effects of interest (see below).

Age-independent Activations

These were first identified for ER, VA, and WM by performing conjunction analyses over the voxels that were activated in both groups as compared to an implicit baseline, which were thresholded at $P < 0.0005$, uncorrected with a cluster size > 5.

Task-independent Age Effects

These were assessed at an uncorrected threshold of $P < 0.001$. First, we calculated group differences for each task at a threshold of $P < 0.1$, uncorrected. Next, to make sure that these group differences were not due to deactivations, we masked them (inclusively) with the voxels that were activated in each group compared to the baseline at $P < 0.05$, uncorrected. Finally, the conjunction of the group differences (global age effects) was calculated by multiplying the resulting *t*-maps. The probability of finding a voxel that is independently activated in each and all contrasts, i.e. the joint probability, can be estimated by multiplying the probabilities for each contrast (e.g. Allan *et al.*, 2000): $0.1 \times 0.1 \times 0.1 = P < 0.001$, uncorrected.

Task-specific Age Effects

Thesewere assessed by thresholding the group differences at $P < 0.001$, uncorrected with a cluster size > 5. Next, in order to remove the regions that showed common age differences across tasks, we not only masked them (inclusively, $P < 0.05$, uncorrected) with the voxels that were activated in each group relative to baseline, but additionally, we used the *t*-map comprising the conjunction of group differences as an exclusive mask.

Results

Behavioral Results

The proportion of correct responses in WM, VA, and ER tasks are listed in Table 1. A 2 (group: younger, older) × 3 (task: WM, VA, ER) analysis of variance (ANOVA) on accuracy data, yielded significant effects of task [$F(2,38) = 11.1$, $P < 0.0001$], but no reliable main effect of age [$F(1,38) = 3.0$, $P > 0.05$] or age × task interaction [$F(2,38) = 2.6$, $P > 0.05$]. The task effect

Table 1
Behavioral results in WM, VA and ER tasks

	Younger		Older	
	Mean	SD	Mean	SD
Accuracy (proportion correct)				
Working memory	0.92	0.1	0.91	0.9
Visual attention	0.97	0.6	0.96	0.7
Episodic memory	0.93	0.8	0.86	0.7
RTs (ms)				
Working memory	1485	263	1776	338
Visual attention	993	199	969	180
Episodic memory	1711	250	2241	405

reflected greater accuracy in the VA task than in the WM task [$t(39) = 3.7$, $P < 0.001$] and ER tasks [$t(39) = 4.2$, $P < 0.0001$], with no difference between WM and ER tasks ($t < 1$). In sum, accuracy was greater in the VA task, but similar for young and older adults.

For the ER task, we conducted additional analyses on corrected recognition scores and Remember/Know responses. The proportion of false alarms was 0.26 in younger adults and 0.22 in older adults. Neither false alarms nor corrected recognition scores (hits–false alarms) differed across groups ($t < 1$ for both). The proportions of Remember and Know responses in the ER task were 0.77 and 0.23, respectively, for younger adults, and 0.65 and 0.35, respectively, for older adults. Thus, older adults showed less Remember responses and more Know responses than younger adults [$t(38) = 2.0$, $P < 0.05$]. This result suggests that during ER older adults relied less on recollection and more on familiarity than younger adults.

RTs in WM, VA, and ER tasks are listed in Table 1. A 2 (group: younger, older) × 3 (task: WM, VA, ER) ANOVA on RTs yielded significant effects of age [$F(1,38) = 13.929$, $P < 0.001$] and task [$F(2,38) = 208.0$, $P < 0.0001$], as well as a reliable age × task interaction [$F(2,38) = 15.8$, $P < 0.0001$]. The effect of age reflected faster responses for younger than for older adults, and the effect of task, faster responses in the VA task than in the WM task [$t(39) = 12.9$, $P < 0.0001$] and ER tasks [$t(39) = 13.8$, $P < 0.0001$], and faster responses in the WM task than in the ER task [$t(39) = 6.965$, $P < 0.0001$]. The age × task interaction reflected a more pronounced age effect for ER than for WM and VA, and for WM than for VA. In sum, older adults were slower than younger adults, particularly in the ER task.

Imaging Results

Age-independent Activations

Table 2 shows brain regions where both younger and older adults showed significant activations in each of the three tasks. The role of each of these regions in each of the three tasks has been previously discussed (Cabeza *et al.*, 2002a, 2003b) and is beyond the scope of the present report, which focuses on the effects of aging. However, it is important to emphasize the despite the existence of significant age-related differences in activation, activation patterns in healthy older adults were remarkably similar to those displayed by young adults. As shown by Table 2, the two groups showed activations in many of the same brain regions. In addition to supporting the reliability of our data, this finding suggests that the effects of healthy aging on the neural correlates of cognition are relatively modest, leaving untouched a large proportion of the neural activity underlying fundamental cognitive functions such as WM, VA, and ER.

Task-independent Age Effects

Table 3 lists brain regions that showed significant age-related differences in activity in all three tasks. Consistent with our predictions, older adults showed weaker activity in occipital regions and stronger activity in PFC regions in all tasks (see Fig. 2). Age-related decreases in occipital activity were found in lateral (BA 19, 18) and medial (BA 31) extrastriate cortex, and age-related increases in PFC activity were found both left (BA 6) and right (BA 44/45) prefrontal regions. Beyond our predictions, interesting task-independent age effects were found in the hippocampal formation (subicular region), which was more activated in younger than in older adults, and in parietal regions, which were more activated in older than in younger adults.

Task-specific Age Effects

Table 4 lists brain regions that showed significant age-related differences in activity that were specific to WM, VA, or ER tasks. Consistent with our predictions, age-related contralateral PFC recruitment was found in right PFC for WM and in left PFC for VA (see Fig. 3). The age-related increase in left PFC activity during VA was identified using a more lenient threshold ($P < 0.01$). Beyond our predictions, an interesting task-specific age effect was in bilateral parahippocampal regions, which during ER were more activated in older than in younger adults (see Fig. 4). Other task-specific age effects included age-related decreases in striate cortex (BA 17) activity during WM, and in posterior cingulate activity during ER.

Discussion

The study yielded three main findings. First, consistent with our predictions, task-independent age effects included an age-related reduction in occipital activity coupled with an age-related increase in PFC activity. Secondly, also consistent with our predictions, task-specific age effects included age-related contralateral recruitments in right PFC during WM and in left PFC during VA. Finally, there was a dissociation between two medial temporal lobe (MTL) regions: the hippocampal formation, which showed weaker activity in older adults across all tasks, and the parahippocampal gyrus, which showed stronger activity in older adults during ER. Below, we discuss these three main results.

Age-related Decreases in Occipital Activity versus Age-related Increases in PFC

As illustrated by Figure 2, task-independent age effects included age-related decreases in occipital activity coupled with age-related increases in PFC activity. The co-occurrence of these two age effects extends to verbal working memory, visual sustained attention, and verbal episodic recognition memory tasks a finding originally reported by Grady *et al.* (1994) using a face matching task (see also Grady, 2002). Importantly, the present study demonstrates that exactly the same occipital and PFC regions can display identical age-related changes in activity across different cognitive tasks.

Table 2
Activations during WM, VA, and ER tasks shared by younger and older adults

Region of activation		Lat	BA	Ph	Coordinates			*t*-value	
					x	*y*	*z*	Younger	Older
Working memory									
Occipital ctx	Extrastriate	L	19	2	–49	–63	–9	5.5	3.3
.	Striate ctx	R	17	2	15	–91	–2	5.4	4.3
		R	17	1	11	–91	–2	12.0	16.0
PFC	Ventrolateral	L	47	2	–34	23	6	4.0	4.6
		R	47	2	49	18	–8	5.4	3.5
		L	9	1	–45	5	31	3.5	6.1
	Dorsolateral	L	6	1	–4	7	55	8.9	5.9
		L	6	2	–4	4	56	5.0	4.7
Parietal ctx		L	40	2	–41	–41	47	6.8	8.9
Cerebellum		R		2	30	–56	–22	8.3	5.2
		L		2	–38	–53	–23	6.3	5.9
Thalamus		L		2	–11	–18	8	11.0	7.2
		R		2	11	–14	8	5.7	6.7
Lateral temporal ctx		L	22	2	–55	8	–4	5.9	5.9
Visual attention									
Occipital (extrastriate) ctx		R	18	1	34	–83	1	10.6	11.1
		L	19	1	–30	–87	8	10.7	9.9
		R	18	2	34	–84	–3	11.6	8.1
		L	18	2	–34	–88	–2	9.5	9.0
PFC	Dorsolateral	L	6	2	–4	–1	49	12.1	9.6
		R	6	2	45	2	45	7.3	6.5
	Anterolateral	R	10	2	34	45	19	4.7	4.4
Thalamus		L	–	2	–15	–18	5	10.9	6.6
		R	–	2	11	–14	8	7.4	5.5
Caudate nucleus		L	–	2	–11	4	7	4.5	4.4
Episodic retrieval									
Occipital ctx	Extrastriate	L	18	2	–30	–88	–2	8.6	5.6
		R	18	2	30	–88	–2	8.9	6.4
	Striate	R	17	1	11	–88	–2	11.0	14.0
PFC	Ventrolateral	R	47	2	34	22	–8	5.5	6.3
		L	47	2	–34	22	–4	5.4	5.1
	Dorsolateral	L	6	2	–4	13	48	9.5	7.9
		L	9	2	–49	9	35	5.0	6.5
		R	46	2	49	24	26	3.4	4.7
	Anterolateral	L	10	2	–34	55	7	4.7	3.9
Thalamus		L	–	2	–8	–18	5	7.6	6.7
Parietal ctx		L	40	2	–41	–31	43	4.6	7.0
		L	7	2	–38	–60	48	4.3	7.4
Cerebellum		R	–	2	34	–63	–25	6.0	4.5
		L	–	2	–34	–59	–22	6.9	3.6
Parahippocampal gyrus		L	27	1	–23	–29	–5	8.3	3.3

Lat, lateralization; BA, Brodmann Area; Ph, phase; coordinates from Talairach and Tournoux (1988).

These task-independent findings are consistent with common factor theories of aging, although as discussed below, inconsistent task-specific age effects were also observed. Weaker visual cortex activity in older adults across all tasks fits well with the theory that age-related sensory processing plays a major role in cognitive aging (Baltes and Lindenberger,

Table 3
Age-related differences common across WM, VA and ER tasks

Region of activation		Lat	BA	Ph	Coordinates			*t*-values		
					x	*y*	*z*	WM	VA	ER
Younger > older										
Occip. (extrastriate) ctx	Lateral	L	19	2	–45	–77	–5	4.3	2.8	3.1
		L	18	2	–23	–84	–8	2.8	4.9	3.4
		R	18	2	23	–81	–9	3.1	3.8	3.0
	Medial	R	31	1	19	–62	10	4.9	3.9	4.7
Anterior cingulate		M	32	2	0	20	30	1.8	4.1	2.5
Precuneus		M	7	2	0	–16	46	2.7	2.4	1.5
Hippocampal formation (subiculum)		L		1	–19	–29	–2	6.6	5.0	4.0
		R		1	19	–29	1	4.8	4.8	3.4
Motor ctx		L	4	2	–38	–23	53	5.4	4.9	3.8
Cerebellum (hemisphere)		R		2	23	–48	–17	3.3	2.7	2.9
Older > younger										
PFC		L	6/9	2	–45	–6	38	6.7	3.0	2.7
		R	44/45	2	41	12	21	2.7	2.0	2.0
Inferior parietal ctx		L	40	2	–45	–35	37	2.7	2.9	2.0
Parieto-occipital ctx		L	19	1	–26	–75	42	2.0	2.3	2.0
		R	19	1	30	–71	45	3.1	2.7	2.2
Brain stem		R		2	4	–26	–8	2.3	3.7	3.2
Cerebellum		R		1	15	–82	–21	2.4	2.2	2.7
		L		1	–26	–56	–22	1.6	2.7	2.3

See Table 2 for abbreviations.

1997). As noted before, this theory is supported by evidence of strong correlations between age-related sensory/perceptual decline and age-related cognitive decline (e.g. Lindenberger and Baltes, 1994; Baltes and Lindenberger, 1997). There are three main explanations for the close link between sensory and cognitive deficits in older adults (Lindenberger and Baltes, 1994; Baltes and Lindenberger, 1997; Schneider and Pichora-Fuller, 2000): (i) sensory deficits cause cognitive deficits (sensory deprivation hypothesis); (ii) cognitive deficits cause sensory deficits (cognitive load on perception hypothesis); and (iii) sensory and cognitive deficits are both caused by a third underlying mechanism (common cause). The age-related decrease in visual cortex activity seems more consistent with the sensory deprivation hypothesis (Lindenberger and Baltes, 1994), but predicting activation data from the three views is not straightforward.

As for task-independent age-related increases in PFC activity, they suggest that some forms of functional compensation in older adults may be common across tasks. Given that lateral PFC regions are recruited by a variety of cognitive tasks (Cabeza and Nyberg, 2000, 2002), it is not surprising to find task-independent age effects in these areas. As mentioned before, Grady *et al.* (1994) suggested that age-related increases in PFC activity could compensate for age-related decreases in visual cortex activity (Grady *et al.*, 1994; Madden *et al.*, 1996). Although we did not find significant correlations between PFC activations and older adults' performance, we did find a reliable negative correlation between the effect size of age-related decrease in occipital activity (x, y, z = –23, –84, –8) and age-related increases in PFC activity (x, y, z = –45, –6, 38) in the WM task (r = –0.5, P < 0.02). In other words, in the WM condition, those older adults who showed the weakest occipital activations also showed in some cases the strongest PFC activations. This finding is consistent with Grady *et al.*'s hypothesis.

As shown in Table 3, older adults showed task-independent increases in activity not only in PFC but also in parietal regions. Age-related increases in parietal activity have been previously found during episodic memory (Anderson *et al.*, 2000; Grady *et al.*, 2002), but in the present study they were also found during WM and VA. Given that the recruitment of parietal regions occurred in combination with weaker activity in visual occipital regions, the results suggest an age-related shift from the ventral (occipitotemporal) stream to the dorsal (occipitoparietal) stream, which are pathways respectively associated with object and spatial processing (Ungerleider and Mishkin, 1982). Like PFC recruitment, parietal recruitment in older adults could reflect compensatory mechanisms. Another alternative is that the ventral/dorsal differentiation is less pronounced in older adults, an idea supported by behavioral (Chen *et al.*, 2002) and functional neuroimaging evidence (Grady *et al.*, 1994) and consistent with the notion of age-related dedifferentiation (Li and Lindenberger, 1999).

Age-related Contralateral PFC Recruitment

Not all age-related increases in PFC activity were task-independent; some were task-specific, including the recruitment of contralateral PFC regions. As illustrated by Figure 3, in the case

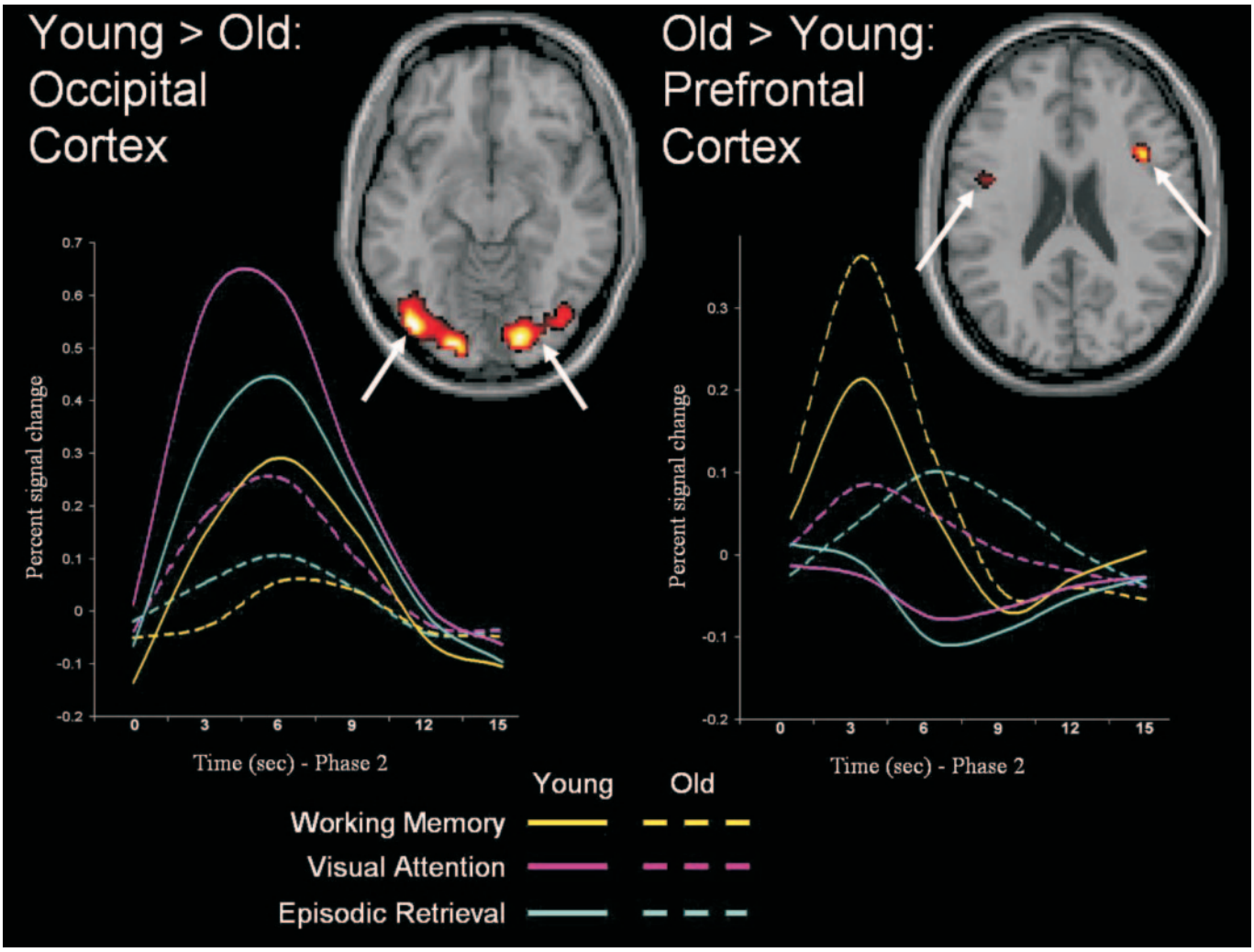

Figure 2. Task-independent age effects. Compared to younger adults, older adults showed weaker activity in occipital cortex but greater activity in frontal regions. The time-course plots are from left BA19 ($x, y, z = -23, -84, -8$) and right BA45 ($x, y, z = 41, 12, 21$).

of WM, older adults showed greater activity than younger adults in right PFC, whereas in the case of VA, older adults showed greater activity in left PFC during VA. Since PFC activity during ER in younger adults was largely bilateral, contralateral recruitment could not be observed. In contrast, in the case of WM and VA some PFC regions were lateralized in young adults, and contralateral recruitment yielded a more bilateral pattern of activity in older than in younger adults (see Fig. 3). This pattern, known as 'Hemispheric Asymmetry Reduction in Older Adults' or HAROLD, has been found in variety of cognitive tasks, including perception, episodic memory, semantic memory, working memory, language, and inhibition tests (for a review, see Cabeza, 2002). These studies show that when PFC activity is left lateralized in younger adults, older adults may recruit additional activity in right PFC and when PFC activity is right lateralized in younger adults, older adults may recruit additional activity in left PFC. As illustrated by Figure 3, we found both forms of contralateral recruitment in the same participants and within the same experiment (see also, Reuter-Lorenz *et al.*, 2000).

Age-related contralateral PFC recruitment may be beneficial for cognitive performance (compensation view, Cabeza *et al.*, 1997, 2002b; Reuter-Lorenz *et al.*, 2000; Rosen *et al.*, 2002), or it may reflect a difficulty in recruiting specialized neural mechanisms (dedifferentiation view, Li and Lindenberger, 1999; Logan *et al.*, 2002). Recent studies comparing brain activity in high- and low-performing older adults have provided evidence supporting the compensation view (Cabeza *et al.*, 2002b; Rosen *et al.*, 2002). If one assumes this view, one may ask about the differential contributions of left versus right PFC recruitment to older adults' cognitive performance. In the episodic retrieval domain, we have recently proposed that left PFC is differentially more involved than right PFC in semantically guided production processes, whereas right PFC is more involved than left PFC in monitoring processes (Cabeza *et al.*, 2003a). If the production-monitoring distinction can be extended beyond the episodic retrieval domain — and there is preliminary evidence that it can (Cabeza *et al.*, 2002a, 2003b), then the results in Figure 3 would suggest that older adults compensate for production deficits in left PFC by recruiting monitoring processes in right PFC, and vice versa.

Table 4
Age-related differences in brain activity specific to WM, VA, or ER tasks

Region of activation	Lat	BA	Ph	Coordinates			*Z*-value
				x	*y*	*z*	
Working memory							
Younger > older							
Occipital (striate) ctx	L	17	2	–11	–80	11	3.7
Older > younger							
PFC	L	6	2	–26	6	51	4.0
	L	46	2	–45	41	19	3.7
	R	9	2	45	24	26	4.0
Parietal ctx	R	40	2	41	–45	44	4.8
	R	7	2	30	–74	45	3.8
	L	7/40	2	–45	–56	48	3.6
Parieto-occipital ctx	L	19	2	–34	–79	39	4.4
Premotor ctx	R	8	2	23	13	44	4.8
Somatosensory ctx	L	1/2/3	1	–45	–17	36	3.6
Visual attention							
Younger > older							
No reliable differences							
Older > younger							
PFC	R	46	2	49	30	20	3.9
	L	45	2	–34	23	6	2.4*
Parietal ctx	L	40	2	–34	–42	37	3.8
Episodic retrieval							
Younger > older							
Posterior cingulate gyrus	M	23/31	2	0	–28	29	4.0
Older > younger							
Parahippocampal gyrus	R	36	2	19	–37	–7	4.0
	L	36	2	–26	–34	–11	4.2
Lateral temporal ctx	L	21	1	–45	–9	–19	4.7
	R	21	1	45	–5	–19	3.9
Parieto-occipital ctx	L	19	2	–30	–71	31	5.0
Thalamus	L	–	2	–11	–32	12	3.8
Cerebellum	L	–	1	–8	–41	–20	5.3

See Table 2 for abbreviations. *$P < 0.01$.

Age-related Decrease in Hippocampal Activity and Increase in Parahippocampal Activity

The third main finding of the study was a dissociation between two MTL regions (see Fig. 4): the hippocampal formation, which showed decreased activity in older adults across all tasks, and the parahippocampal gyrus, which showed increased activity in older adults during ER. Age-related decreases in hippocampal activity have been previously found for episodic memory (e.g. Grady *et al.*, 1995; Daselaar *et al.*, 2003; Morcom *et al.*, 2003) but not across several different cognitive functions. The present task-independent decrease suggests that a decline in hippocampal integrity during healthy (Raz *et al.*, 1997) and pathological (e.g. Kohler *et al.*, 1998; Du *et al.*, 2001) aging could affect other cognitive functions besides episodic memory, including working memory and attention. Three recent fMRI studies found significant hippocampal activity during working memory tasks (Ranganath and D'Esposito, 2001; Stern *et al.*, 2001; Cabeza *et al.*, 2002a), suggesting that the indexing function of the hippocampus applies to both long-term and short-term memory representations (Cabeza *et al.*, 2002a). Although it may be argued that hippocampal activity during WM reflected episodic memory encoding, this idea cannot easily account for the involvement of the hippocampus in the VA task. Given that only no-blip trials were included in the fMRI analyses, the memory component of the VA task was minimal. Participants had to maintain the goal of the task in working memory but this kind of sustained activity is unlikely to account for the event-related activations observed. In contrast, the hippocampal activation during VA fits very well with the idea that the hippocampus is involved in attentional orienting (e.g. Williams *et al.*, 2000; Oswald *et al.*, 2002) and novelty detection (e.g. Tulving *et al.*,

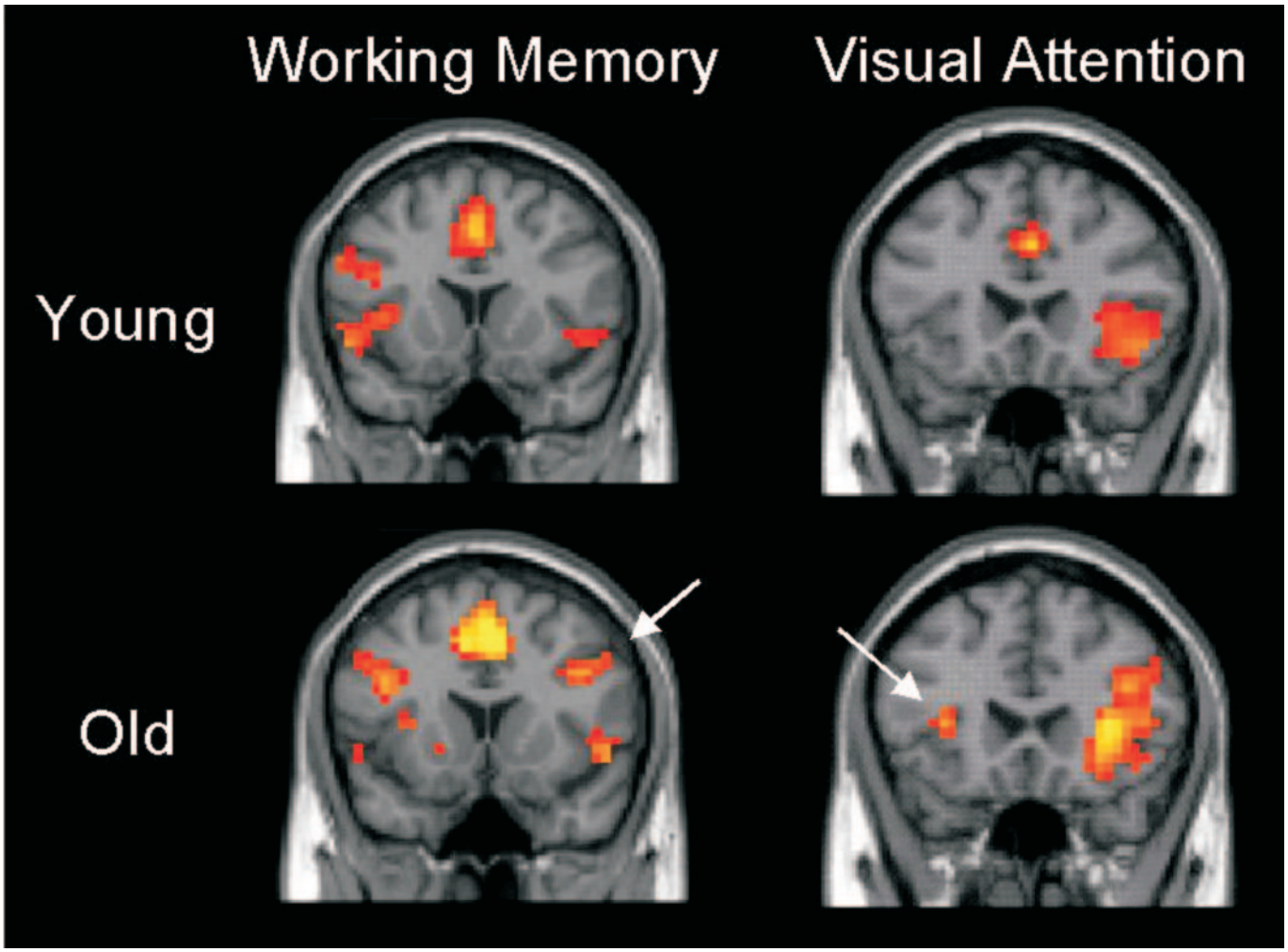

Figure 3. Task-specific age effects. Older adults showed contralateral recruitment in right PFC during WM and in left PFC during VA. As a result of these changes, activity in certain PFC regions was more bilateral in older than in younger adults ('Hemispheric Asymmetry Reduction in Older Adults' or HAROLD).

1994; Knight, 1996). Thus, the age-related decrease in hippocampal activity across the three tasks could reflect an age-related deficit in attentional orienting and/or novelty detection processes.

Whereas the hippocampal formation showed weaker activity in older than in younger adults, a left parahippocampal region showed stronger activity in older than in younger adults (see Fig. 4). This dissociation is consistent with the combination of two types of evidence: evidence that these two MTL regions are differentially involved in recollection and familiarity, and evidence that recollection and familiarity are differentially affected by aging. The results of lesion and functional neuroimaging research (for reviews, see Aggleton and Brown, 1999; Yonelinas, 2002) have linked the hippocampus to recollection (retrieval of specific details) and the surrounding perirhinal/parahippocampal cortex to familiarity (feeling of knowing). In general, older adults tend to be impaired in recollection but not in familiarity (Parkin and Walter, 1992; Jennings and Jacoby, 1993; Mantyla, 1993; Java, 1996; Searcy *et al.*, 1999). Moreover, in the Remember/Know paradigm, older adults have been found to show less 'Remember' responses (reduced recollection) but more 'Know' responses (increased familiarity) than younger adults (Parkin and Walter, 1992). This finding was replicated in the present study. Thus, it is reasonable to speculate that the present MTL dissociation reflected an age-related reduction in hippocampal-based recollection coupled with an age-related increase in parahippocampal-based familiarity. To test this idea, we calculated the correlation between the effect size of the age-related increase in parahippocampal activity (x, y, z = –26, –34, –11) and the number of Know responses in older adults. Consistent with the familiarity account, the correlation was positive and significant (R = 0.50, $P < 0.05$). Although further research is obviously required, this is probably the first evidence directly linking age-related differences in MTL activity to differential effects of aging on recollection and familiarity.

Conclusions

In summary, the study yielded three main results. First, consistent with our predictions, task-independent age effects included an age-related reduction in occipital activity coupled with an age-related increase in PFC. The former finding is consistent with the common factor view that age-related cognitive deficits are in great part due to a decline in sensory processing, and the latter finding suggests that some forms of compensatory PFC recruitment are common across tasks.

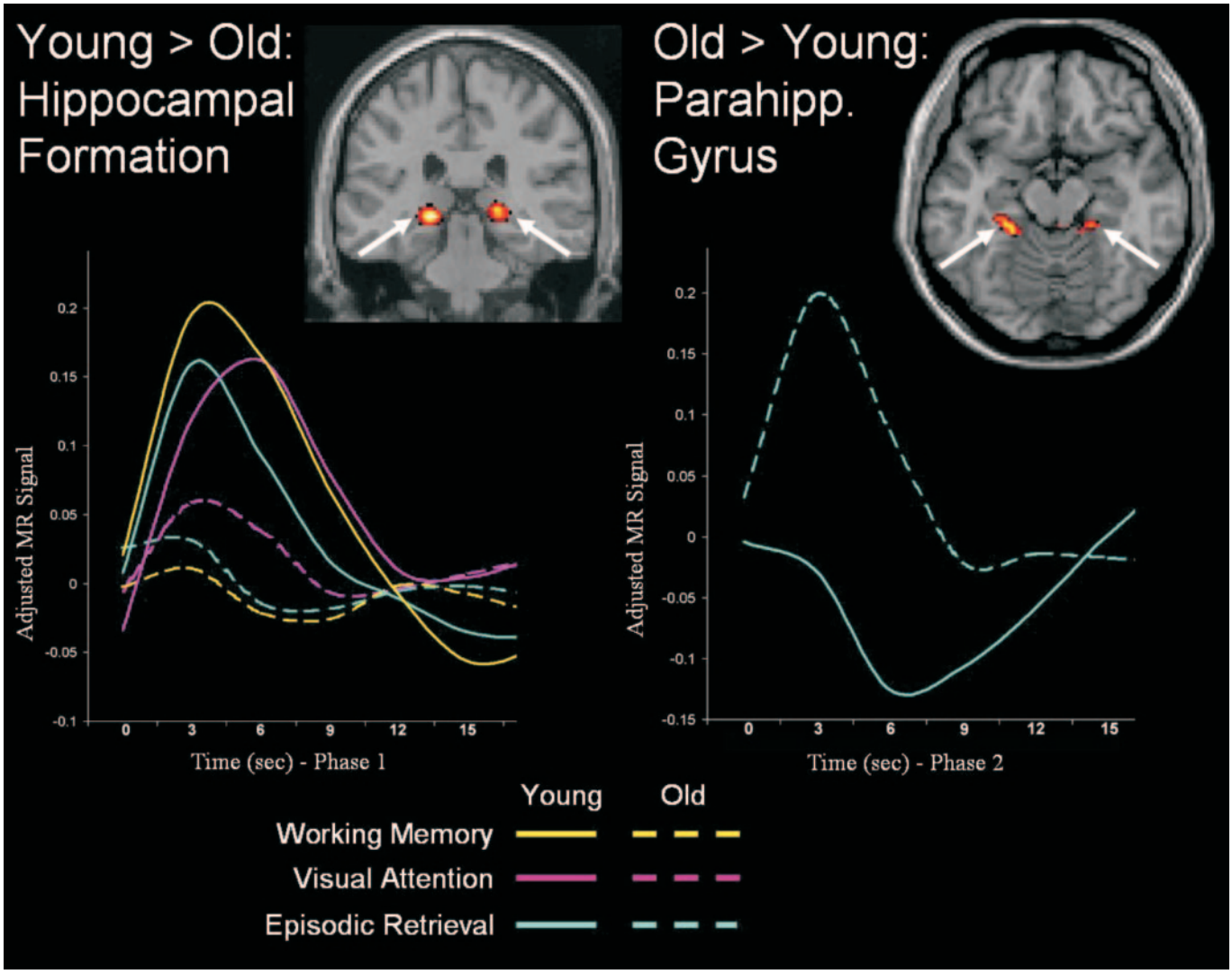

Figure 4. Dissociation between two medial temporal lobe regions. The hippocampal formation, bilaterally, was more activated in younger than in older adults during all tasks (task-independent age effect), whereas the parahippocampal gyrus, bilaterally, was more activated in older than in younger adults during the ER task (task-specific age effect). The time-course plots are from the left hippocampal formation ($x, y, z = -19, -29, -2$) and the left parahippocampal gyrus ($x, y, z = -26, -34, -11$).

Secondly, also consistent with our predictions, task-specific age effects included age-related contralateral recruitments in left PFC during WM and in right PFC during VA. This result suggests that older adults may compensate for deficits in production processes by recruiting monitoring processes, and vice versa. Finally, there was a dissociation between two MTL regions: the hippocampal formation, which showed decreased activity in older adults across all tasks, and the parahippocampal gyrus, which showed increased activity in older adults during ER. The task-independent decrease in hippocampal activity suggests that age-related deficits in hippocampal function may account for age-related cognitive decline beyond the episodic memory domain. The age-related increase in parahippocampal activity could reflect older adults' reliance on familiarity-based responding. Thus, the present results indicate that both common factors and specific factors play an important role in cognitive aging.

Notes

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