

Age-related Changes in Object Processing and Contextual Binding Revealed Using fMR Adaptation

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Abstract

■ Using fMR adaptation, we studied the effects of aging on the neural processing of passively viewed naturalistic pictures composed of a prominent object against a background scene. Spatially distinct neural regions showing specific patterns of adaptation to objects, background scenes, and contextual integration (binding) were identified in young adults. Older adults did not show adaptation responses corresponding to binding in the medial-temporal areas. They also showed an adaptation deficit for objects whereby their lateral occipital

complex (LOC) did not adapt to repeated objects in the context of a changing background. The LOC could be activated, however, when objects were presented without a background. Moreover, the adaptation deficit for objects viewed against backgrounds was reversed when elderly subjects were asked to attend to objects while viewing these complex pictures. These findings suggest that the elderly have difficulty with simultaneous processing of objects and backgrounds that, in turn, could contribute to deficient contextual binding. ■

INTRODUCTION

It has been widely demonstrated in the cognitive aging literature that difficulty in binding target information to its context is a primary cause of poor memory function in older adults (Mitchell, Johnson, Raye, Mather, & D'Esposito, 2000; Naveh-Benjamin, 2000; Chalfonte & Johnson, 1996; Spencer & Raz, 1995; Park, Puglisi, & Sovacool, 1984). For example, the recognition of objects placed in an array was comparable between young and old adults (an example of item memory), but recognition of the *combination* of item and its position in the array was poorer in elders, reflecting deficiency in binding operations (Chalfonte & Johnson, 1996).

Lesion data suggest that binding operations whereby objects are associated with their spatial locations are critically dependent on hippocampal and parahippocampal regions (Squire, Stark, & Clark, 2004; Burgess, Maguire, & O'Keefe, 2002). Functional imaging has shown engagement of the hippocampus and parahippocampal region when stimulus elements require relational encoding (binding processes), but not when they were encoded individually (Henke, Weber, Kneifel, Wieser, & Buck, 1999; Henke, Buck, Weber, & Wieser, 1997), and that hippocampal activation is tied to successful associative encoding (Jackson & Schacter, 2004; Sperling, Chua, et al., 2003). Additionally, functional imaging of objects that differ in their strength of con-

textual relationship to a particular place suggests that the parahippocampal and retrosplenial regions mediate contextual relations between objects and their contexts (Bar & Aminoff, 2003). Older adults have shown decreased hippocampal activation relative to young adults in associative encoding tasks involving objects in arrays (Mitchell, Johnson, Raye, & D'Esposito, 2000) and face–name pairs (Sperling, Bates, et al., 2003). Collectively, these observations suggest that decline in medial-temporal function contributes to impaired contextual binding in the elderly.

In the present work, we present data that support the notion that in addition to deficits in medial-temporal function, deficits in visual processing at earlier stages along the ventral visual pathway may contribute to age-related decline in binding.

Although alterations in the central processing of visual and auditory information have been shown to account for much of the age-related variance on a broad array of higher-order cognitive tests, including speed of processing, memory, verbal fluency, and reasoning (Baltes & Lindenberger, 1997; Lindenberger & Baltes, 1997), the neuroanatomical bases for these age-related sensory changes remains relatively unexplored.

Earlier functional neuroimaging studies on the aged visual system have shown a reduced amplitude of blood oxygenation level dependent (BOLD) response in the occipital cortex in response to a red flash (Ross et al., 1997) and to checkerboard stimuli (Huettel, Singerman, & McCarthy, 2001; Buckner, Snyder, Sanders, Raichle,

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& Morris, 2000). These reductions in stimulus response have been attributed to changes in neurovascular coupling or increased noise in the BOLD signal obtained from the elderly, and it is unclear how decreased BOLD signal relates to deficient information processing, if at all.

Recently, Park et al. (2004) demonstrated decrease in selectivity of the ventral visual cortex with age to four categories of visually presented stimuli. In contrast to older adults, young adults showed more distinctive activation patterns that represented a more differentiated neural representation for each class of stimuli. Park et al. suggested that the reduced uniqueness of stimulus representations could play an important role in age-related degradation of speed of processing, particularly perceptual speed.

In the present work, we further characterized age-related changes in processing along the ventral visual stream using a functional magnetic resonance adaptation (fMR-A) paradigm to study the visual processing of objects appearing in a naturalistic background context (Goh et al., 2004). Studying visual processing of objects in their natural contexts was motivated by the finding that responses of ventral visual neurons differ when an object is presented in a plain background and when it is presented in a visually rich environment (Rolls, Aggelopoulos, & Zheng, 2003). Furthermore, examining object processing in context allows us to simultaneously evaluate how aging affects visual item processing and contextual binding.

Advantages of Using fMR-A to Study Age-related Changes in Visual Processing

fMR-A reveals spatially separable brain regions sensitive to the selective repetition of particular stimulus types or stimulus features (Grill-Spector & Malach, 2001; Grill-Spector et al., 1999). More important, adaptation to repeated stimulus presentation is not automatic. Rather, the size of the adaptation effect is modulated by available processing resources and behavioral goals (Dobbins, Schnyer, Verfaellie, & Schacter, 2004; Eger, Henson, Driver, & Dolan, 2004; Ishai, Pessoa, Bickle, & Ungerleider, 2004; Murray & Wojciulik, 2004; Henson, Shallice, Gorno-Tempini, & Dolan, 2002). Attending to a particular stimulus type or stimulus feature generally results in greater initial activation followed by a more pronounced reduction in activation (adaptation) in response to repeated presentation of the test item. The converse of this is that failure to attend to a test item results in reduced adaptation.

A potential advantage of using the adaptation paradigm with older adults as opposed to merely examining activation is that adaptation magnitude is the difference in response to two stimuli presented sequentially. As such, this measure better reflects neural processing.

In contrast, merely measuring activation in response to a single stimulus relative to a baseline (as occurs in most neuroimaging paradigms) is more susceptible to vascular (“plumbing”) deficits that may occur in the elderly.

We hypothesized that older adults would evidence a reduced selectivity in adaptation responses in the ventral visual pathway by showing a decreased adaptation response to either objects or to background scenes, as well as a diminished response in the site that binds objects to backgrounds (Goh et al., 2004). The use of passive viewing in Experiment 1 enabled us to compare how the young and elderly adults process objects in the context of background scenes without biasing attention to either visual element.

By comparing the results of adaptation to undirected passive viewing of objects presented against background scenes (Experiment 1) to results obtained from viewing objects without a background (Experiment 2) and when attention was biased toward objects presented against complex backgrounds (Experiment 3), we isolated specific age-related functional changes in the ventral visual pathway that play a role in poorer binding or integration of picture elements in the elderly. In keeping with prior findings that contextual binding is impaired in elders (Sperling, Bates, et al., 2003; Chalfonte & Johnson, 1996), we also expected a reduction in adaptation responses characterizing binding in medial-temporal regions.

METHODS

Experiment 1

Participants

Seventeen healthy, right-handed, elderly volunteers (6 men, mean age 67 years, range 60–75 years) gave informed consent for this study. Data from 20 young volunteers (7 men, mean age 21 years, range 20–24 years) that were previously reported (Goh et al., 2004) were included for comparison. Elderly adults were screened for neurological, psychiatric, and medical conditions and participated only if they had well-controlled medical conditions. A battery of neuropsychological tests was administered to ensure that persons with mild cognitive impairment or dementia were not included in the study. All volunteers had normal vision or corrected visual acuity of 6/9. Refractive correction was performed where necessary using a set of magnetic-resonance-compatible eyeglasses. Prior to functional magnetic resonance imaging (fMRI), we ensured that the elderly volunteers were able to identify the prominent object in a test picture while in the magnet. All 17 elderly and 18 of 20 young adult volunteers underwent a battery of clinical neuropsychological tests (Table 1) following scanning.

Table 1. Demographic Information and Neuropsychological Test Scores of Young and Elderly Subjects

	<i>Young</i>		<i>Elderly</i>		<i>p Value</i>
	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	
<i>n</i>	20	17			
Sex	7 men	6 men			
Age (years)	21.3 (1.11)	66.9 (4.25)			.000
Years of education	14.0 (1.45)	12.6 (2.06)			.035
Trail-Making Test A (sec)	18.1 (4.54)	37.6 (9.09)			.000
Trail-Making Test B (sec)	38.4 (8.45)	80.8 (22.1)			.000
Pattern Matching	39.9 (5.50)	22.3 (4.06)			.000
Dot Comparison	16.6 (3.01)	7.76 (3.47)			.000
WAIS-R Digit-Symbol	82.7 (8.66)	50.0 (11.2)			.000
WAIS-R Information	20.2 (4.39)	17.7 (4.10)			ns
WAIS-R Comprehension	21.3 (3.72)	23.3 (4.45)			ns
MMSE	29.4 (.92)	28.7 (1.05)			.048
WMS-III Forward Spatial Span Score	10.2 (1.80)	8.35 (1.90)			.011
WMS-III Backward Spatial Span Score	9.67 (1.68)	7.59 (1.94)			.000
WAIS-III Forward Digit Span Score	12.4 (2.38)	10.4 (1.91)			.005
WAIS-III Backward Digit Span Score	9.22 (2.44)	6.41 (1.73)			.002

WAIS-R = Wechsler Adult Intelligence Scale—Revised; WMS-III = Wechsler Memory Scale—Third Edition; MMSE = Mini Mental State Exam.

Stimuli

A total of 200 full-color pictures, each containing a prominent object placed against a complex background (e.g., a bear in the foreground against a background of a lake and mountains) were used in a hybrid block, event-related fMRI experiment where quartets of picture stimuli comprising object–scene pairings were presented (Goh et al., 2004; Figure 1). Briefly, there were four conditions in this experiment: (a) OO: “old object, old scene,” where subjects saw four repetitions of a single picture containing the same object and background scene across all four repetitions; (b) ON: “old object, new scene,” where an identical central object was repeated four times but the background scene changed across the four pictures; (c) NO: “new object, old scene,” where the background scene was repeated across four pictures, but there was a novel central object that changed in the repeated background (e.g., a bear, fawn, dog, or elk); or (d) NN: “new object, new scene,” where four novel objects were paired with four novel background scenes. The prominent objects subtended

visual angles ranging from $0.5^\circ \times 1.0^\circ$ (minimum) to $2.5^\circ \times 5.5^\circ$ (maximum), and the background scenes subtended a fixed visual angle of $4.6^\circ \times 6.3^\circ$.

The four pictures within each quartet were presented consecutively and for 1500 msec each (stimulus duration [SD]). Pictures were separated by an interval of 250 msec (interpicture interval [IPI]). Between each quartet was an interquartet interval (IQI) that randomly varied between 6000, 9000, and 12,000 msec, with a mean of 9000 msec. A fixation cross was shown during the IPIs and IQIs when there was no picture on display. The order in which each experimental condition was presented was randomized for each subject such that a given condition did not occur more than three times consecutively. Each subject underwent four experimental runs that each lasted 348 sec. A run comprised 20 quartets that were preceded and followed by periods of fixation that lasted 30 sec. Each subject viewed 20 quartets of each experimental condition.

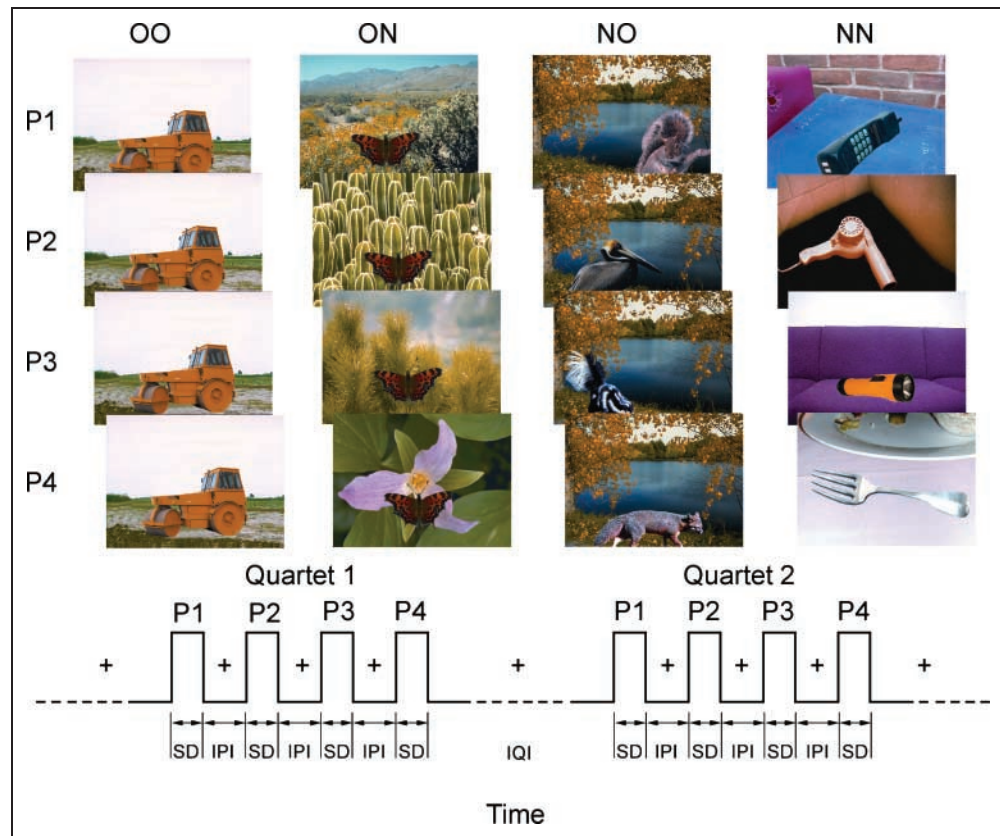
Imaging Protocol

The fMRI experiments were conducted using a 3.0T Allegra MR scanner (Siemens, Erlangen, Germany). Functional scans (116) were acquired in each using a gradient-echo EPI sequence with TR of 3000 msec, FOV 19.2×19.2 cm, and 64×64 matrix. Thirty-six oblique axial slices approximately parallel to the AC–PC line and 3 mm thick (0.3-mm gap) were acquired. High-resolution coplanar T2 anatomical images were also obtained. Stimuli were projected onto a screen at the back of the magnet and participants viewed the screen using a mirror.

Data Analysis

Functional images were processed using Brain Voyager QX (Brain Innovation, Maastricht, Holland) customized with in-house scripts. Details concerning image preprocessing have been described in the prior study on young adults (Goh et al., 2004). Functional imaging data were analyzed using a general linear model (GLM) in which the hemodynamic response associated with each of the four experimental conditions was modeled using 28 finite impulse response (FIR) predictors, 7 for each condition, across all 37 subjects. The fourth predictor of each condition (equivalent to 9 sec from onset of the first stimulus in this FIR design) was used for subsequent analyses, as this was identified as the peak response in the estimated signal time courses. Conjunction analyses of specific contrasts, entered into a random effects analysis, were used to identify voxels showing statistically significant adaptation effects across both young and elderly groups (Nichols, Brett, Andersson, Wager, & Poline, 2005). This means that for a given voxel, the statistical value reported in the conjunction analysis is the one associated with the *smallest relevant difference* between the estimates, for example, between

Figure 1. Picture stimuli and presentation sequence used in this study. Each picture (P) consisted of an object placed within a background scene. Pictures were presented in quartets with objects and scenes selectively repeated. Four types of quartets were used: (A) four repeated, identical pairings of object and background scene (OO); (B) an identical object repeated in four novel background scenes (ON); (C) novel objects in each of four repeated background scenes (NO); or (D) four novel objects paired with four novel background scenes (NN). Each picture was presented for an SD of 1500 msec with an IPI of 250 msec. Quartets were presented with a mean IQI of 9000 msec.



the ON and OO curves for object processing in the elderly (Figure 3)—hence the conservative nature of this analysis.

A statistical threshold of $p < .001$ (uncorrected) was used except for the hippocampus, where a reduced threshold of $p < .005$ was used. This latter threshold was used because of the lower signal to noise in the medial-temporal region (Strange, Otten, Josephs, Rugg, & Dolan, 2002; Eldridge, Knowlton, Furmanski, Bookheimer, & Engel, 2000; Ojemann et al., 1997).

Regions involved in object processing were defined as those showing adaptation when the object in a picture was repeated but not when the accompanying scene was repeated (i.e., voxels jointly fulfilling $NN > OO$, $NN > ON$, $NO > OO$, and $NO > ON$), using a strict definition of conjunction inference (Nichols et al., 2005). An additional criterion was that t tests of the parameter estimates in these regions should not yield significant differences in BOLD signal between the OO and ON or between NN and NO conditions, indicating that adaptation was related to object repetition and not scene repetition. We indexed adaptation magnitude related to central object repetition by the difference in parameter estimates between NN and ON conditions obtained from within “object-processing” regions defined above.

Regions involved in scene processing were denoted as those showing adaptation when the scene in a picture was repeated but not when the object was repeated (i.e., voxels jointly fulfilling $NN > OO$, $NN > NO$, $ON > OO$,

and $ON > NO$). These voxels were chosen on the basis that they did not show a significant difference in signal between OO and NO conditions or between ON and NN, indicating that adaptation was related to scene repetition and not object repetition. The difference between parameter estimates for the NN and NO conditions in these “background-processing” regions was used as a measure of background-repetition-related adaptation.

Regions involved in binding were identified as those showing (1) adaptation only when both objects and scenes were repeated but not when any element in a picture was novel ($NN > OO$, $ON > OO$, and $NO > OO$) and (2) adaptation to repeated object–scene pairs that was greater than the sum of object and scene adaptation effects ($[NN - OO] > [(NN - ON) + (NN - NO)]$). Fulfillment of both criteria differentiates regions showing adaptation to a particular combination of object and scene from those showing independent, weak adaptation to *both* object and scenes. The difference between parameter estimates for the NN and OO conditions was used as a measure of the magnitude of object–scene repetition related adaptation in these “binding” regions. Parameter estimates of signal change for each region of interest in each group (young and elderly) were used to plot the activation time course for each condition.

To determine the extent to which individuals in each group demonstrated spatial congruity of the three functional regions (object, background, binding) studied in the experiment, Talairach coordinates of points showing

maximal adaptation of interest were obtained from each individual subject. We computed the Euclidean distance between points showing maximal adaptation within each functional area for each group. This analysis addressed the possibility that individual differences in location of activation could account for age-related loss of adaptation effects: that is, more dispersed regions showing adaptation in the elderly.

Finally, we constructed penetrance maps to show the extent to which functional regions showing adaptation to objects and backgrounds overlapped across individuals in the two groups following the method outlined by Xiong et al. (2000). Briefly, a penetrance map is one that shows voxels where at least n subjects fulfill the condition of interest. In this study we set $n = 4$, so that the voxels revealed indicate that at least 20% (young subjects) or 23.5% (elderly) show overlapping adaptation in the conditions of interest.

Experiment 2

This was conducted to assess evidence for object-processing areas and background-processing areas in the ventral visual cortex when the objects and backgrounds were presented in isolation, rather than as two elements presented jointly within a single scene. Stimuli were not repeated. This was not an adaptation experiment; instead, it used a “localizer scans” protocol described in other work relating to higher visual processing (Kanwisher, McDermott, & Chun, 1997).

Participants

Seven healthy, right-handed, elderly (4 men, mean age 67 years, range 60–75 years) and 7 young (2 men, mean age 23 years, range 21–26 years) volunteers, who were a subset of those studied in Experiment 1, participated.

Stimuli and Procedure

Full-color pictures of 100 objects in a plain white background and 100 scenes without a central object were used in a blocked fMRI experiment. Subjects engaged in passive viewing of the stimuli. Pictures were presented for 2000 msec each (SD) and separated by an interval of 1000 msec (IPI). Each block consisted of either five object or five scene pictures. There were four blocks for each of the two conditions (object and scene) separated by an interval of 21,000 msec. A fixation cross was shown during the IPI when there was no picture on display. Each subject underwent five experimental runs that lasted 327 sec each. The visual angles subtended by objects and scenes were identical to those of the previous experiment.

Because of the smaller number of volunteers, fixed-effects analyses were used to identify voxels showing statistically greater activation for either objects or scenes.

A statistical threshold of $p < .001$ (uncorrected) was used. Individual parameter estimates of signal change for regions showing greater activation for objects than scenes (“object” areas) and those showing greater activation for scenes relative to objects (“scene” areas) were plotted for both groups.

Experiment 3

This experiment was conducted to evaluate the effect of biasing attention to objects on adaptation responses recorded from the lateral occipital complex (LOC).

Participants

Ten healthy, right-handed, elderly (4 men, mean age 67 years, range 62–75 years) volunteers who were a subset of those studied in Experiment 1 participated. Studying the same participants ensured that the inferences made from this experiment could not be attributed to the selection of a different segment of Singaporean elders available for study.

Procedure

Exactly the same experimental stimuli as in Experiment 1 were used and an identical image analysis pipeline was engaged. The experiment was run about 3 months after the completion of Experiment 1. The critical difference in this experiment was that volunteers were explicitly instructed to note that each picture comprised a prominent object set in a background and that they were to pay attention to the object in that background.

RESULTS

Behavioral Data

Young and elderly adults were compared on a number of standard neuropsychological tests in order to demonstrate that young and elderly were drawn from cohorts of similar intelligence and ability and that the sample of elderly exhibited the expected age-related declines in speed of processing and executive function. In comparing psychometric performance across young and elderly adults, young adults performed significantly better in tests of processing speed (Digit Symbol, Pattern Matching, Dot Comparison, Trails A), memory span (forward and backward spatial and digit span), and executive function (Trails B) (Table 1). There were no significant differences in knowledge-based tests that measured verbal IQ. Although Mini Mental State Exam (MMSE) scores showed a small significant difference between the two groups, no elder had a score less than 27 (out of a maximum of 30).

As volunteers were asked only to view pictures, no response-related behavioral data were collected.

Experiment 1: Delineating Regions that Showed Adaptation to Objects, Background Scenes, and “Binding” Operations in Young and Old Adults

Background Scene Processing

Regions involved in scene processing were denoted as those showing adaptation when the scene in a picture was repeated but not when the object was repeated (i.e., voxels jointly fulfilling NN > OO, NN > NO, ON > OO, and ON > NO).

In young adults, right (R) and left (L) parahippocampal areas adapted to background scene viewing, Brodmann’s area (BA) 19; R: $t(19) = 3.89, p < .001$, L: $t(19) = 5.38, p < .001$. These regions correspond to the parahippocampal place area (PPA) (Epstein & Kanwisher, 1998). Like young adults, elderly adults evidenced a well-defined adaptation response to background scenes, BA 19; R: $t(16) = 3.86, p < .001$; L: $t(16) = 4.84, p < .001$ (Table 2, Figures 2 and 3). In addition, there was no significant difference in the magnitude of adaptation to background repetition between the young and the elderly, R: $t(35) = 0.33, ns$; L: $t(35) = 0.65, ns$ (Figure 4).

Object Processing

Regions involved in object processing were defined as those showing adaptation when the object in a picture was repeated but not when the accompanying scene was repeated (i.e., voxels jointly fulfilling NN > OO, NN > ON, NO > OO, and NO > ON) using a strict definition of conjunction.

In young adults, adaptation in response to object presentation was significant in the right and left fusiform areas, BA 37; R: $t(19) = 5.80, p < .001$, L: $t(19) = 4.46, p < .001$, as well as the bilateral inferior occipital gyri, BA 19; R: $t(19) = 6.14, p < .001$, L: $t(19) = 5.81, p < .001$ (Table 2, Figure 2). These regions broadly correspond to the functionally defined LOC (Grill-Spector, Kourtzi, & Kanwisher, 2001; Malach et al., 1995) and fusiform face area (FFA) (Kanwisher et al., 1997; Haxby et al., 1996; Puce, Allison, Asgari, Gore, & McCarthy, 1996).

In elderly volunteers, no region fulfilled the conjunction of responses specifying an object region (Figure 2 and see Methods for details). Examination of the time course curves for the elderly group in the LOC (Figure 3) revealed the following: (1) The comparison of responses to NO and OO showed object adaptation, R: $t(16) = 4.01, p < .001$, L: $t(16) = 7.36, p < .001$, although there was greater adaptation to object repetition in the young relative to the elderly, R: $t(35) = 3.82, p < .001$, L: $t(35) = 2.87, p < .001$ (Figure 4). (2) Responses to NN and NO were of approximately the same magnitude, R: $t(16) = 0.88, ns$; L: $t(16) = 1.51, ns$, indicating that the LOC is

Table 2. Talairach Coordinates of Voxels in Young and Elderly Subjects Showing the Largest fMR-A Effects in the Conjunction Analyses for (a) Object Processing, (b) Background Scene Processing, and (c) Object and Background Scene Binding

Brain Region	BA	x	y	z	t Value
<i>Young</i>					
(a) Object processing (NN > OO, NN > ON, NO > OO, and NO > ON)					
R fusiform gyrus	37	39	-49	-10	4.34
R inferior occipital gyrus	19	36	-70	-5	4.50
L fusiform gyrus	37	-42	-51	-11	3.71
L inferior occipital gyrus	19	-36	-80	-5	4.36
(b) Background scene processing (NN > OO, NN > NO, ON > OO, and ON > NO)					
R parahippocampal gyrus	19	26	-34	-5	3.37
L parahippocampal gyrus	19	-27	-44	-4	4.16
L lingual gyrus	19	-9	-82	-5	3.41
(c) Object and background scene binding (NN > OO, NO > OO, ON > OO, and NN - OO > [(NN - ON) + (NN - NO)])					
R hippocampus	35	33	-4	-18	2.82
R parahippocampal gyrus	37	30	-25	-10	3.82
L parahippocampal gyrus	36	-27	-34	-11	2.94
L fusiform gyrus	37	-36	-52	-5	4.10
L superior parietal lobule	7	-24	-73	47	2.92
<i>Elderly</i>					
(a) Object processing (NN > OO, NN > ON, NO > OO, and NO > ON)					
No area fulfilled this conjunction of conditions.					
(b) Background scene processing (NN > OO, NN > NO, ON > OO, and ON > NO)					
R parahippocampal gyrus	37	27	-49	-9	3.55
R parahippocampal gyrus	19	30	-33	-11	3.19
L parahippocampal gyrus	19	-27	-50	-8	3.66
L occipitoparietal sulcus	19	-30	-83	19	3.00
R middle occipital gyrus	17	12	-91	11	2.94
(c) Object and background scene binding (NN > OO, NO > OO, ON > OO, and (NN - OO) > [(NN - ON) + (NN - NO)])					
R fusiform gyrus	19	34	-64	-11	3.30
L fusiform gyrus	37	-42	-41	-14	3.19
R occipitoparietal sulcus	7	33	-76	25	3.30
L occipitoparietal sulcus	7	-27	-64	31	2.98

The specific contrasts considered in each conjunction analysis are shown in parentheses. BA = Brodmann’s area; NN = new object, new background; NO = new object, old background; ON = old object, new background; OO = old object, old background; R = right; L = left.

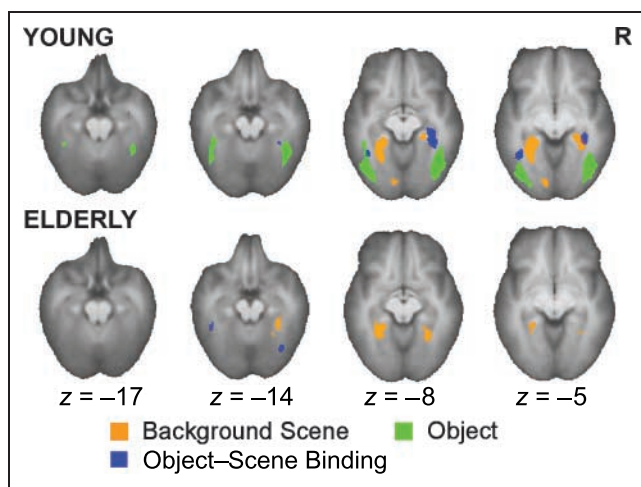


Figure 2. Maps showing results of the conjunction analyses (adaptation responses) illustrating areas involved in object processing, background scene processing, and object and background scene binding in young and elderly subjects.

capable of responding to novel objects, albeit to a lesser extent than younger volunteers. (3) More important, elders response to ON did not show the expected adaptation to repeated objects relative to NN in the LOC, $t(16) = 1.22$, *ns*. Failure of this condition to be met resulted in the nonfulfillment of the fourfold conjunction specifying an object-adapting region.

Further analysis of the elders' data indicated the absence of a region showing selective adaptation to objects relative to background scenes (indicated by the equivalence of ON and OO) was *not* a result of increased spatial dispersion of regions showing such a response in the elderly. Both the analysis of activation overlap using penetrance maps (Figure 5) and analysis of the Euclidean distance (data available on request) between voxels showing maximal adaptation to object repetition did not show increased spatial separation of object-sensitive areas in the elderly. Furthermore, the degree of overlap in voxels showing adaptation to background scenes was similar in young and elderly adults.

Figure 3. Time course plots of signal change obtained from regions participating in object processing, background scene processing, and object and background scene binding. Regions were obtained from omnibus conjunction analyses that considered both young and elderly subjects together. Threshold $p < .005$ (uncorrected) for illustration.

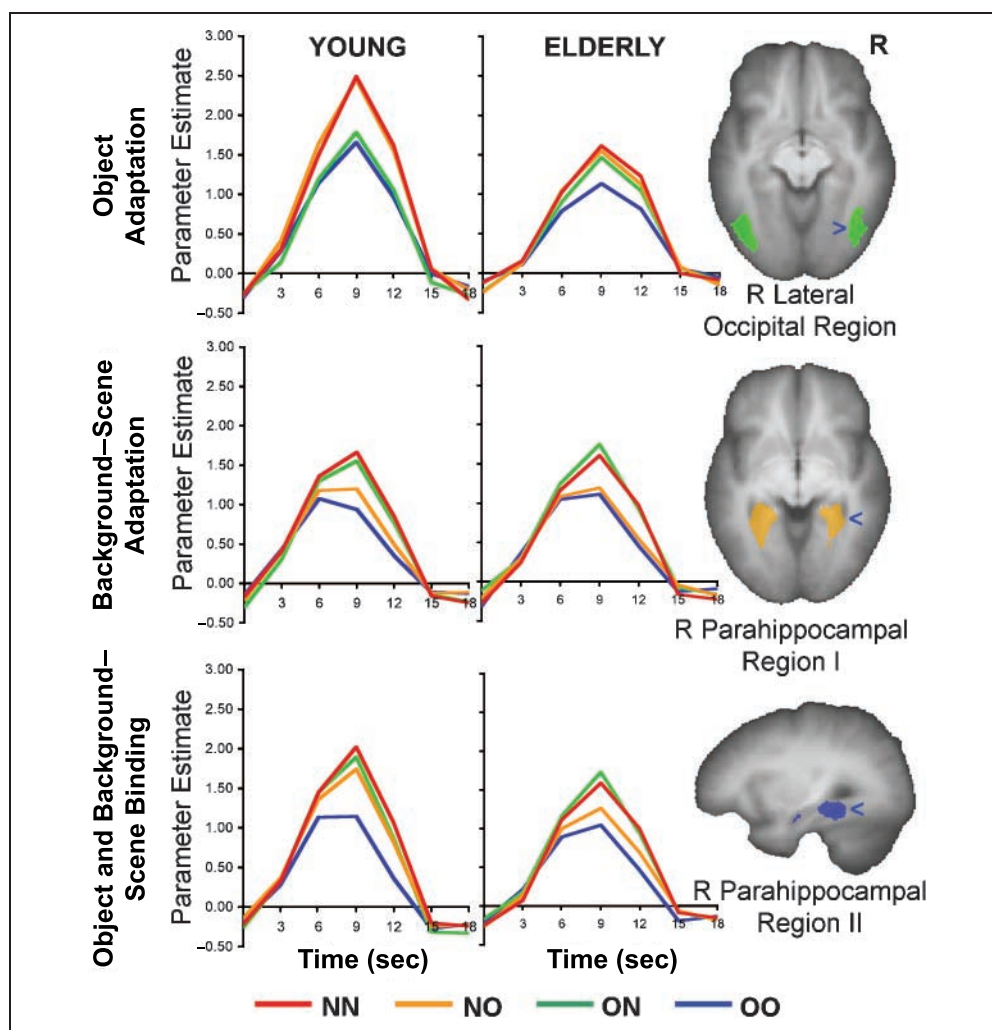
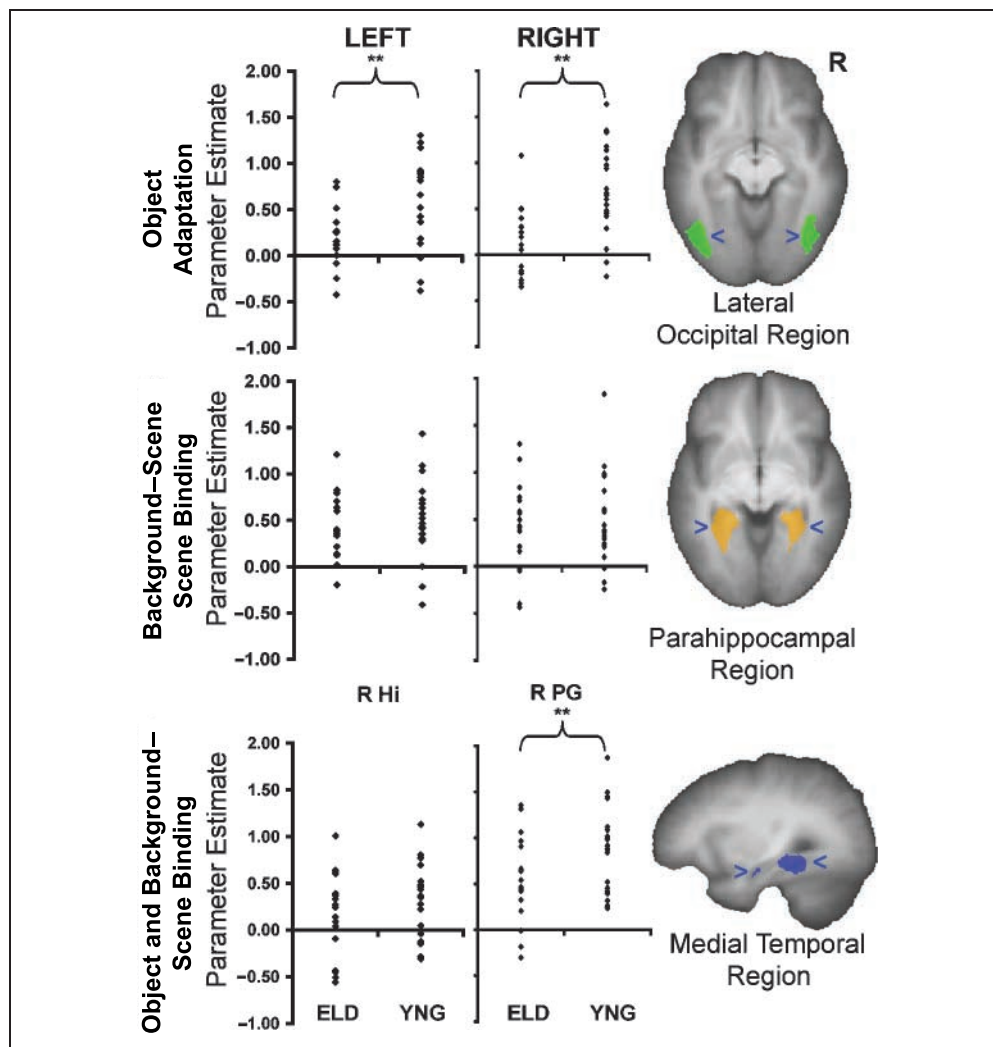


Figure 4. Scatterplots of adaptation magnitudes indexed by parameter estimates of the difference between the NN and ON (for object-processing regions, top), NN and NO (for background scene processing regions, middle), and NN and OO (for binding regions, bottom) conditions for each subject. $**p < .05$. Regions: R Hi = right hippocampus; R PG = right parahippocampal gyrus. ELD = elderly; YNG = young.



The most parsimonious explanation for this series of observations is that age compromises the processing of objects, in the context of novel backgrounds. We posit that older adults, due to limited visual processing resources, were unable to simultaneously process object and background information, and thus directed more attention to backgrounds than to objects. This would explain why ON elicited only insignificant adaptation in the LOC for the elderly. That NO represents a true response to novel objects is suggested by the similarity of responses to NO and NN. Notably, in NO, there is no distracting change in background scene to draw attention away from object processing. Similarly, adaptation was present in OO, a condition in which background scenes did not change. The NO and OO responses in the elderly show that the LOC in the elderly is capable of responding to objects when there is no change taking place in the background, an issue more explicitly addressed in Experiment 2.

In sum, although there was reduction of adaptation in the object-processing regions during passive viewing

of complex pictures, background processing in the PPA was preserved in the elderly.

Contextual Binding

In young adults, regions fulfilling the strict conjunction of conditions specified to define binding operations (see Methods) lay in the right and left parahippocampal areas, BA 36, 37; R: $t(19) = 4.66, p < .001$, L: $t(19) = 3.26, p < .001$; in the left fusiform area distinct from that involved in object-processing area, BA 37; $t(19) = 5.23, p < .001$; as well as a region at the head of the right hippocampus, BA 35, $t(19) = 3.10, p = .003$ (Table 2, Figures 2 and 3). For the older adults, there was a conspicuous absence of this selective pattern of adaptation in the anterior parahippocampal and right hippocampal regions present in the young. Two factors contributed: (1) Adaptation to completely repeated pictures (OO) relative to completely novel pictures (NN) was greater in the young compared to the elderly in the right parahippocampal region, $t(35) = 2.17,$

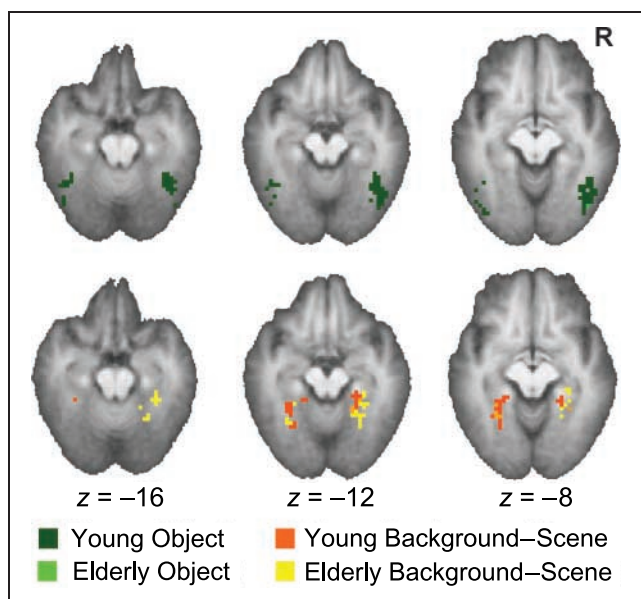


Figure 5. Penetrance maps showing the degree of voxel overlap for object processing and background scene processing across young and elderly subjects. Each colored square represents a voxel in which at least four or more subjects within each group showed object adaptation (top) and background scene adaptation (bottom). The threshold of significant adaptation effects was set very low ($p < .01$, uncorrected) to accommodate the possibility of lower effect sizes in elderly subjects. Even so, equivalent voxel overlap was observed for background scene processing in the young and elderly, but the overlap for object processing was negligible in the elderly compared to the young.

$p < .05$ (Figure 4). (2). There was significant adaptation to NO in the elderly, whereas this was insignificant in young adults. This buttresses the suggestion that object processing is faulty in elders and that it contributes to reduced engagement of medial-temporal areas in binding operations.

In the elderly, as in the young, binding areas in the fusiform were identified, but the effect was bilateral and more extensive, in contrast to the left-lateralized engagement observed in young adults, BA 19, 37; R: $t(16) = 4.06, p < .001$, L: $t(16) = 3.93, p < .005$ (Table 2, Figure 2).

Experiment 2: Preservation of Selective Responsiveness to Objects and Scenes when Objects and Scenes Are Presented in Isolation

Because the absence of adaptation responses corresponding to object processing within the LOC in old adults was unexpected, we conducted a second experiment to determine whether older adults would evidence an object area when they were viewing individual objects without an associated background scene. To this end, we were able to locate a subset of the subjects who participated in Experiment 1 and assess them for the presence of an object area and background area. When this subset of seven elderly and seven young adult

volunteers passively viewed objects against a plain white background and passively viewed scenes without a prominent object, lateral occipital areas maximally sensitive to objects versus scenes were demonstrated in both old and young volunteers (Figure 6). This result confirms that in elderly adults there was an intact “object area” (as defined by responses to the isolated presentation of object pictures).

Furthermore, the result underscores the value of studying the visual processing of objects presented within a meaningful context (Aggelopoulos, Franco, & Rolls, 2005; Bar, 2004; Rolls et al., 2003), as this may uncover differences in processing not evident when studying neural responses to isolated objects or backgrounds.

Experiment 3: The Effect of Selective Attention on Adaptation Responses

This experiment was conducted to evaluate the effect of biasing attention to objects on adaptation responses recorded from the LOC. When the elderly were instructed to attend to objects presented against a background using the stimuli from Experiment 1, adaptation responses fulfilling the definition of an object area were observable in the LOC, BA 18; $t(9) = 5.92, p < .001$ (Figure 7). The difference between NN and ON responses in the attend-objects condition, signifying adaptation to repeated objects when the background changed, was greater than during passive viewing, $t(9) = 2.29, p < .05$ (scatterplot in Figure 7).

These result lends further support to the notion that adaptation effects are not automatic and that they can be modulated by attention (Yi & Chun, 2005; Murray &

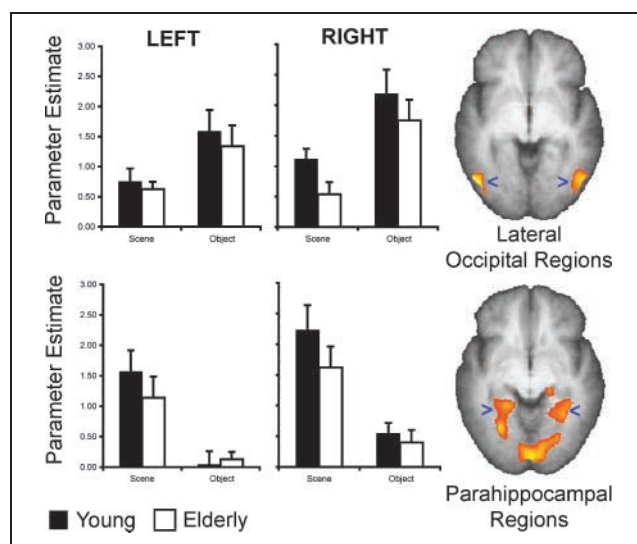


Figure 6. BOLD signal response when young and elderly volunteers viewed isolated objects and isolated scenes in regions sensitive to objects; LOC (top: object > scene) and scenes; PPA (bottom: scene > object). Threshold $p < .001$ (uncorrected).

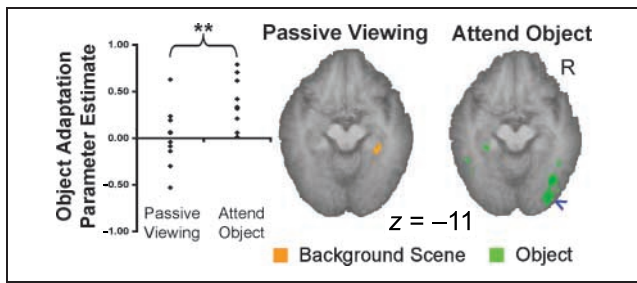


Figure 7. Scatterplot showing greater magnitude of object-related adaptation in elderly individuals ($n = 10$) when they attended to objects in the pictures (voxel map: right axial slice) compared with when they passively viewed the same pictures (voxel map: left axial slice). Object adaptation magnitudes were indexed by the difference between parameter estimates for the NN and ON conditions in the LOC (arrow) identified by conjunction analyses. Threshold of voxel maps set at $p < .005$ (uncorrected) for illustration. $**p < .05$.

Wojciulik, 2004). Also, in keeping with prior results that show that enhancement of neural activity in brain regions supporting processing of the attended feature is accompanied by suppression of neural activity in areas irrelevant to processing that feature (Gazzaley, Cooney, McEvoy, Knight, & D’Esposito, 2005), it can be seen that adaptations in the “background” area were modulated such that this area was not revealed when attention was biased to objects. (Compare axial slices for “passive viewing” and “attend object” in Figure 7.)

A further observation related to this trade-off between object and background emphasis in processing is the continued absence of binding adaptation in the medial-temporal region. This result could also indicate that age-related dysfunction of contextual processing in the parahippocampal region is an independent factor contributing to the loss of binding adaptation.

DISCUSSION

There were three main findings in the present study that relate to the aging ventral visual pathway. The first is that aging is associated with a loss of fMR-A effects in the medial-temporal region, supporting the notion that contextual binding is altered in the elderly. The second is the age-related loss of adaptation to repeated objects presented in the context of changing backgrounds but not to repeated objects presented in isolation, indicating that there is deficient concurrent visual processing of both object and backgrounds. Third, this selective loss of adaptation to objects in older adults is a result of biased attention to background scenes at the expense of object processing.

Decreased Binding in Medial Temporal Areas

Although multiple lines of evidence point to the hippocampus (Rolls, Xiang, & Franco, 2005) and parahippo-

campal regions as being responsible for contextual binding (Cohen et al., 1999) or contextual processing without specific reference to binding (Bar, 2004; Bar & Aminoff, 2003), this is the first study to show age-related reduction in engagement of these regions during the *passive viewing* of pictures. The present findings complement recent observations from memory studies whereby older adults showed decreased hippocampal engagement and compensatory frontal activation while actively encoding complex scenes (Gutchess et al., 2005; Park et al., 2003). In the present study, we did not observe any differences in frontal activation as a function of adaptation condition or as a function of age, probably because the passive viewing and rapid presentation times in the present study made low demands on the frontal lobe in contrast to the active judgments and long presentation times used in two prior studies where more distributed frontal activation with age was observed (Gutchess et al., 2005; Park et al., 2003).

The fMR-A procedure did result, however, in an extension of binding patterns of adaptation in older adults to more posterior regions in the visual processing system in the fusiform gyri and the occipitoparietal sulci bilaterally. We speculate that the enlargement of fusiform adaptation with age could represent an adaptive response to the loss of recruitment of medial-temporal regions for binding. We note that the fusiform area has been shown to be sensitive to the conjunction of features relevant to object processing (Schoenfeld et al., 2003) and that neurophysiology in primates has also revealed the existence of neurons sensitive to conjunctions of object features (Brincat & Connor, 2004; Baker, Behrmann, & Olson, 2002), adding credibility to this argument. Although the contribution of fusiform areas to *successful relational encoding* of visual stimuli is not certain, the critical role of the parahippocampal region and posterior hippocampus in relating an object to its place in the environment is well established (Bar & Aminoff, 2003; Burgess et al., 2002). Thus, the possibility that fusiform areas may play a compensatory role for binding processes in the elderly requires further investigation.

Impaired Object Processing in the Elderly Could Contribute to Deficient Binding

Although impaired binding is plausibly a product of age-related structural involution of medial-temporal structures (Raz, Rodrigue, Head, Kennedy, & Acker, 2004; Petersen et al., 2000) and depressed functional activation of the same during associative encoding (Sperling, Bates, et al., 2003), an alternative explanation for degraded binding is a trading of attention to contextual information at the expense of object processing due to reduced processing resources in the elderly. It is critical to reiterate that the difference in adaptation patterns within the LOC between young and elderly

groups in our study does not mean that the elderly were *unable* to process objects. Rather, *incomplete* processing of objects in the LOC, resulting in insufficient information to complete the binding operation in medial-temporal regions, can explain the present findings.

Reversibility of Object Adaptation: Possibility of Compensation?

Further support for this explanation comes from Experiment 3, where biasing attention to the object in the scene appeared to reverse the deficit in adaptation to objects in the context of a changing background. This finding suggests that alteration in perceptual bias may help elders capture more of the information that is available in complex pictures, although more work is warranted: Biasing attention to objects did not restore responses associated with contextual binding in the aged medial-temporal region.

In the broader context of memory phenomena, the extent of adaptation observed may relate to the extent to which a stimulus is encoded. Greater fMR-A in response to picture repetition may point to additional processing during the initial presentation of the picture (Yi & Chun, 2005) that, in turn, may relate to the laying down of more enduring or accessible memories (Epstein, Higgins, & Thompson-Schill, 2005). This is an area of emerging interest because whereas the behaviorally measured mnemonic benefit of even short-term exposure to pictures has been clearly related to the magnitude of priming/repetition-related neural response reduction (Zago, Fenske, Aminoff, & Bar, 2005; Maccotta & Buckner, 2004), we know much less about how the magnitude of repetition-related reduction in neural responses relates to long-term memory (van Turennout, Ellmore, & Martin, 2000) and, in particular, real-world cognitive capabilities. This may be changing; to illustrate, among observers who viewed repeated pictures containing a prominent object, those in whom adaptation in the PPA was greater for repeated pictures were also those who also had higher spatial navigation skills, that is, better visuospatial memory (Epstein et al., 2005). In the context of the present experiment, reduced adaptation to objects in the elderly, when they are not explicitly told to pay close attention to these, could relate to reduced priming to objects when presented in changing contexts and poorer memory in tasks that require the elderly to bind object and location, such as remembering where one left the car keys.

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The data reported in this experiment have been deposited with the fMRI Data Center (www.fmridc.org). The accession number is 2-2005-1209K.

REFERENCES

- Aggelopoulos, N. C., Franco, L., & Rolls, E. T. (2005). Object perception in natural scenes: Encoding by inferior temporal cortex simultaneously recorded neurons. *Journal of Neurophysiology*, *93*, 1342–1357.
- Baker, C. I., Behrmann, M., & Olson, C. R. (2002). Impact of learning on representation of parts and wholes in monkey inferotemporal cortex. *Nature Neuroscience*, *5*, 1210–1216.
- Baltes, P. B., & Lindenberger, U. (1997). Emergence of a powerful connection between sensory and cognitive functions across the adult life span: A new window to the study of cognitive aging? *Psychology and Aging*, *12*, 12–21.
- Bar, M. (2004). Visual objects in context. *Nature Reviews Neuroscience*, *5*, 617–629.
- Bar, M., & Aminoff, E. (2003). Cortical analysis of visual context. *Neuron*, *38*, 347–358.
- Brincat, S. L., & Connor, C. E. (2004). Underlying principles of visual shape selectivity in posterior inferotemporal cortex. *Nature Neuroscience*, *7*, 880–886.
- Buckner, R. L., Snyder, A. Z., Sanders, A. L., Raichle, M. E., & Morris, J. C. (2000). Functional brain imaging of young, nondemented, and demented older adults. *Journal of Cognitive Neuroscience*, *12*(Suppl. 2), 24–34.
- Burgess, N., Maguire, E. A., & O'Keefe, J. (2002). The human hippocampus and spatial and episodic memory. *Neuron*, *35*, 625–641.
- Chalfonte, B. L., & Johnson, M. K. (1996). Feature memory and binding in young and older adults. *Memory & Cognition*, *24*, 403–416.
- Cohen, N. J., Ryan, J., Hunt, C., Romine, L., Wszalek, T., & Nash, C. (1999). Hippocampal system and declarative (relational) memory: Summarizing the data from functional neuroimaging studies. *Hippocampus*, *9*, 83–98.
- Dobbins, I. G., Schnyer, D. M., Verfaellie, M., & Schacter, D. L. (2004). Cortical activity reductions during repetition priming can result from rapid response learning. *Nature*, *428*, 316–319.
- Eger, E., Henson, R. N., Driver, J., & Dolan, R. J. (2004). BOLD repetition decreases in object-responsive ventral visual areas depend on spatial attention. *Journal of Neurophysiology*, *92*, 1241–1247.
- Eldridge, L. L., Knowlton, B. J., Furmanski, C. S., Bookheimer, S. Y., & Engel, S. A. (2000). Remembering episodes: A selective role for the hippocampus during retrieval. *Nature Neuroscience*, *3*, 1149–1152.
- Epstein, R., & Kanwisher, N. (1998). A cortical representation of the local visual environment. *Nature*, *392*, 598–601.
- Epstein, R. A., Higgins, J. S., & Thompson-Schill, S. L. (2005). Learning places from views: Variation in scene processing as a function of experience and navigational ability. *Journal of Cognitive Neuroscience*, *17*, 73–83.
- Gazzaley, A., Cooney, J. W., McEvoy, K., Knight, R. T., & D'Esposito, M. (2005). Top-down enhancement and suppression of the magnitude and speed of neural activity. *Journal of Cognitive Neuroscience*, *17*, 507–517.

- Goh, J. O., Siong, S. C., Park, D., Gutchess, A., Hebrank, A., & Chee, M. W. (2004). Cortical areas involved in object, background, and object-background processing revealed with functional magnetic resonance adaptation. *Journal of Neuroscience*, *24*, 10223–10228.
- Grill-Spector, K., Kourtzi, Z., & Kanwisher, N. (2001). The lateral occipital complex and its role in object recognition. *Vision Research*, *41*, 1409–1422.
- Grill-Spector, K., Kushnir, T., Edelman, S., Avidan, G., Itzhak, Y., & Malach, R. (1999). Differential processing of objects under various viewing conditions in the human lateral occipital complex. *Neuron*, *24*, 187–203.
- Grill-Spector, K., & Malach, R. (2001). fMR-adaptation: A tool for studying the functional properties of human cortical neurons. *Acta Psychologica*, *107*, 293–321.
- Gutchess, A. H., Welsh, R. C., Hedden, T., Bangert, A., Minear, M., Liu, L. L., & Park, D. C. (2005). Aging and the neural correlates of successful picture encoding: Frontal activations compensate for decreased medial-temporal activity. *Journal of Cognitive Neuroscience*, *17*, 84–96.
- Haxby, J. V., Ungerleider, L. G., Horwitz, B., Maisog, J. M., Rapoport, S. I., & Grady, C. L. (1996). Face encoding and recognition in the human brain. *Proceedings of the National Academy of Sciences, U.S.A.*, *93*, 922–927.
- Henke, K., Buck, A., Weber, B., & Wieser, H. G. (1997). Human hippocampus establishes associations in memory. *Hippocampus*, *7*, 249–256.
- Henke, K., Weber, B., Kneifel, S., Wieser, H. G., & Buck, A. (1999). Human hippocampus associates information in memory. *Proceedings of the National Academy of Sciences, U.S.A.*, *96*, 5884–5889.
- Henson, R. N., Shallice, T., Gorno-Tempini, M. L., & Dolan, R. J. (2002). Face repetition effects in implicit and explicit memory tests as measured by fMRI. *Cerebral Cortex*, *12*, 178–186.
- Huettel, S. A., Singerman, J. D., & McCarthy, G. (2001). The effects of aging upon the hemodynamic response measured by functional MRI. *Neuroimage*, *13*, 161–175.
- Ishai, A., Pessoa, L., Bickle, P. C., & Ungerleider, L. G. (2004). Repetition suppression of faces is modulated by emotion. *Proceedings of the National Academy of Sciences, U.S.A.*, *101*, 9827–9832.
- Jackson, O., III, & Schacter, D. L. (2004). Encoding activity in anterior medial temporal lobe supports subsequent associative recognition. *Neuroimage*, *21*, 456–462.
- Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *Journal of Neuroscience*, *17*, 4302–4311.
- Lindenberger, U., & Baltes, P. B. (1997). Intellectual functioning in old and very old age: Cross-sectional results from the Berlin Aging Study. *Psychology and Aging*, *12*, 410–432.
- Maccotta, L., & Buckner, R. L. (2004). Evidence for neural effects of repetition that directly correlate with behavioral priming. *Journal of Cognitive Neuroscience*, *16*, 1625–1632.
- Malach, R., Reppas, J. B., Benson, R. R., Kwong, K. K., Jiang, H., Kennedy, W. A., Ledden, P. J., Brady, T. J., Rosen, B. R., & Tootell, R. B. (1995). Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex. *Proceedings of the National Academy of Sciences, U.S.A.*, *92*, 8135–8139.
- Mitchell, K. J., Johnson, M. K., Raye, C. L., & D'Esposito, M. (2000). fMRI evidence of age-related hippocampal dysfunction in feature binding in working memory. *Brain Research, Cognitive Brain Research*, *10*, 197–206.
- Mitchell, K. J., Johnson, M. K., Raye, C. L., Mather, M., & D'Esposito, M. (2000). Aging and reflective processes of working memory: Binding and test load deficits. *Psychology and Aging*, *15*, 527–541.
- Murray, S. O., & Wojciulik, E. (2004). Attention increases neural selectivity in the human lateral occipital complex. *Nature Neuroscience*, *7*, 70–74.
- Naveh-Benjamin, M. (2000). Adult age differences in memory performance: Tests of an associative deficit hypothesis. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *26*, 1170–1187.
- Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J. B. (2005). Valid conjunction inference with the minimum statistic. *Neuroimage*, *25*, 653–660.
- Ojemann, J. G., Akbudak, E., Snyder, A. Z., McKinstry, R. C., Raichle, M. E., & Conturo, T. E. (1997). Anatomic localization and quantitative analysis of gradient refocused echo-planar fMRI susceptibility artifacts. *Neuroimage*, *6*, 156–167.
- Park, D. C., Polk, T. A., Park, R., Minear, M., Savage, A., & Smith, M. R. (2004). Aging reduces neural specialization in ventral visual cortex. *Proceedings of the National Academy of Sciences, U.S.A.*, *101*, 13091–13095.
- Park, D. C., Puglisi, J. T., & Sovacool, M. (1984). Picture memory in older adults: Effects of contextual detail at encoding and retrieval. *Journal of Gerontology*, *39*, 213–215.
- Park, D. C., Welsh, R. C., Marshuetz, C., Gutchess, A. H., Mikels, J., Polk, T. A., Noll, D. C., & Taylor, S. F. (2003). Working memory for complex scenes: Age differences in frontal and hippocampal activations. *Journal of Cognitive Neuroscience*, *15*, 1122–1134.
- Petersen, R. C., Jack, C. R., Jr., Xu, Y. C., Waring, S. C., O'Brien, P. C., Smith, G. E., Ivnik, R. J., Tangalos, E. G., Boeve, B. F., & Kokmen, E. (2000). Memory and MRI-based hippocampal volumes in aging and AD. *Neurology*, *54*, 581–587.
- Puce, A., Allison, T., Asgari, M., Gore, J. C., & McCarthy, G. (1996). Differential sensitivity of human visual cortex to faces, letterstrings, and textures: A functional magnetic resonance imaging study. *Journal of Neuroscience*, *16*, 5205–5215.
- Raz, N., Rodrigue, K. M., Head, D., Kennedy, K. M., & Acker, J. D. (2004). Differential aging of the medial temporal lobe: A study of a five-year change. *Neurology*, *62*, 433–438.
- Rolls, E. T., Aggelopoulos, N. C., & Zheng, F. (2003). The receptive fields of inferior temporal cortex neurons in natural scenes. *Journal of Neuroscience*, *23*, 339–348.
- Rolls, E. T., Xiang, J. Z., & Franco, L. (2005). Object, space, and object-space representations in the primate hippocampus. *Journal of Neurophysiology*, *94*, 833–844.
- Ross, M. H., Yurgelun-Todd, D. A., Renshaw, P. F., Maas, L. C., Mendelson, J. H., Mello, N. K., Cohen, B. M., & Levin, J. M. (1997). Age-related reduction in functional MRI response to photic stimulation. *Neurology*, *48*, 173–176.
- Schoenfeld, M. A., Tempelmann, C., Martinez, A., Hopf, J. M., Sattler, C., Heinze, H. J., & Hillyard, S. A. (2003). Dynamics of feature binding during object-selective attention. *Proceedings of the National Academy of Sciences, U.S.A.*, *100*, 11806–11811.
- Spencer, W. D., & Raz, N. (1995). Differential effects of aging on memory for content and context: A meta-analysis. *Psychology and Aging*, *10*, 527–539.
- Sperling, R., Chua, E., Cocchiarella, A., Rand-Giovannetti, E., Poldrack, R., Schacter, D. L., & Albert, M. (2003). Putting names to faces: Successful encoding of associative memories activates the anterior hippocampal formation. *Neuroimage*, *20*, 1400–1410.
- Sperling, R. A., Bates, J. F., Chua, E. F., Cocchiarella, A. J., Rentz, D. M., Rosen, B. R., Schacter, D. L., & Albert, M. S. (2003). fMRI studies of associative encoding in young and

- elderly controls and mild Alzheimer's disease. *Journal of Neurology, Neurosurgery and Psychiatry*, 74, 44–50.
- Squire, L. R., Stark, C. E., & Clark, R. E. (2004). The medial temporal lobe. *Annual Review of Neuroscience*, 27, 279–306.
- Strange, B. A., Otten, L. J., Josephs, O., Rugg, M. D., & Dolan, R. J. (2002). Dissociable human perirhinal, hippocampal, and parahippocampal roles during verbal encoding. *Journal of Neuroscience*, 22, 523–528.
- van Turennout, M., Ellmore, T., & Martin, A. (2000). Long-lasting cortical plasticity in the object naming system. *Nature Neuroscience*, 3, 1329–1334.
- Xiong, J., Rao, S., Jerabek, P., Zamarripa, F., Woldorff, M., Lancaster, J., & Fox, P. T. (2000). Intersubject variability in cortical activations during a complex language task. *Neuroimage*, 12, 326–339.
- Yi, D. J., & Chun, M. M. (2005). Attentional modulation of learning-related repetition attenuation effects in human parahippocampal cortex. *Journal of Neuroscience*, 25, 3593–3600.
- Zago, L., Fenske, M. J., Aminoff, E., & Bar, M. (2005). The rise and fall of priming: How visual exposure shapes cortical representations of objects. *Cerebral Cortex*, 15, 1655–1665.