

Aging Does Not Affect Brain Patterns of Repetition Effects Associated with Perceptual Priming of Novel Objects

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Abstract

■ This study examined how aging affects the spatial patterns of repetition effects associated with perceptual priming of unfamiliar visual objects. Healthy young ($n = 14$) and elderly adults ($n = 13$) viewed four repetitions of structurally possible and impossible figures while being scanned with blood oxygenation level-dependent functional magnetic resonance imaging. Although explicit recognition memory for the figures was reduced in the elder subjects, repetition priming did not differ across the two age groups. Using multivariate linear modeling, we found that the spatial networks of regions that demonstrated repetition-related increases and decreases in activity were identical in both age groups, although there was a trend for smaller magnitude repetition effects in these net-

works in the elder adults for objects that had been repeated thrice. Furthermore, repetition-related reductions in activity in the left inferior frontal cortex for possible objects correlated with repetition-related facilitation in reaction time across both young and elder subjects. Repetition-related increases of an initially negative response were observed for both object types in both age groups in parts of the *default network*, suggesting that less attention was required for processing repeated stimuli. These findings extend prior studies using verbal and semantic picture priming tasks and support the view that perceptual repetition priming remains intact in later adulthood because the same spatial networks of regions continue to show repetition-related neural plasticity across the adult life span. ■

INTRODUCTION

It is well established that normal aging is associated with a decline in *episodic memory*, or the ability to consciously recognize or recollect past experiences (Cabeza, Nyberg, & Park, 2005; Craik, 1994). Age-related deficits in implicit memory tasks, which do not require conscious recollection, are less pronounced and sometimes absent (Light, Prull, La Voie, & Healy, 2000; Fleischman & Gabrieli, 1998). *Repetition priming* is a type of implicit memory and refers to a change in the ability to classify, identify, or produce an item as a result of prior exposure to that item. According to some investigators, age-related deficits in repetition priming tend to be somewhat larger on priming tasks that require the semantic or conceptual analysis of stimuli, whereas age deficits on perceptual priming tasks tend to be minimal (Stuart, Patel, & Bhagrat, 2006; Rybash, 1996; Jelicic, 1995, but see Mitchell & Bruss, 2003).

Evidence from neuroimaging and patient studies suggest that repetition priming is supported by different neural mechanisms than episodic memory, which could explain the differential effects of aging on the two types of memory (Schacter & Buckner, 1998). Thus, medial-temporal lobe structures and parts of the prefrontal cor-

tex have been shown to be vital for explicit memory (Davachi, 2006; Hwang & Golby, 2006), and both areas demonstrate age-related structural and functional changes that may be associated with age-related decreases in episodic memory (Nordahl et al., 2006; Persson et al., 2006; Hedden & Gabrieli, 2005; Rajah & D'Esposito, 2005). The neural mechanisms underlying repetition priming are still not fully understood, but a consistent finding is that repeated stimuli elicit a smaller neural response than new stimuli in a subset of those brain regions that are initially engaged in task performance (for a review, see Henson, 2003). This is also referred to as *repetition suppression (RS)*. It has been proposed that RS represents the neural mechanism that gives rise to repetition priming (Henson, 2003; Wiggs & Martin, 1998), although dissociations between the two phenomena have been reported (Sayres & Grill-Spector, 2006; Henson, Rylands, Ross, Vuilleumeir, & Rugg, 2004).

Based on the behavioral evidence, it has been conjectured that the networks of brain regions that support repetition priming, particularly perceptual priming, remain functionally intact in older adults. Somewhat surprisingly, only three neuroimaging studies, to date, have explored the effects of aging on the neural correlates of priming and their results were somewhat mixed (Daselaar, Veltman, Rombouts, Raaijmakers, & Jonker, 2005; Lustig & Buckner, 2004; Backman, Almkvist, Andersson, & Nordberg,

1997). Furthermore, no study has examined the effects of aging on a relatively “pure” perceptual priming task. Finally, prior studies did not employ data-analytic methods that could unambiguously test the hypothesis that the spatial networks of brain regions that show priming-related neural plasticity (i.e., RS) are identical in the young and elder subjects (see below for an explanation).

Thus, both Daselaar et al. (2005) and Backman et al. (1997) examined the effects of aging on word-stem completion priming, a test that appears to rely not only on perceptual processes but also on conceptual and phonemic processes (Brooks, Gibson, Friedman, & Yesavage, 1999; Rueckl & Mathew, 1999). Backman et al. (1997) reported no age difference in priming and similar RS for young and elder subjects in the extrastriate cortex. Daselaar et al. (2005), by comparison, reported less priming in the elder subjects and differential RS effects across the two age groups in some brain regions. In particular, the left inferior frontal cortex showed comparable RS effects for both age groups, the left superior temporal gyrus and left cerebellum showed reliable RS effects only for the young subjects, the right occipital lobe showed a larger RS effect for the young than older subjects, and the right inferior frontal gyrus showed a reliable RS effect only in the older sample. In addition, the peak coordinates for areas showing comparable RS effects in the two groups differed by as much as 2.5 cm, suggesting that the spatial network of regions showing priming-related RS effects may not have been identical in the two age groups. Lustig and Buckner (2004) used a semantic repetition priming task and reported no effect of aging on priming and no effect of aging on the magnitude of RS in two a priori–defined ROI regions in the prefrontal cortex. Formal results of whole-brain analyses were not reported.

Taken together, these studies suggest that priming-related repetition effects are not affected by aging in at least some brain regions. It is not clear, however, whether the entire network of regions that shows priming-related repetition effects is identical in the young and elder subjects. Thus, it is possible that preserved behavioral performance in the elder adults is partially attributable to beneficial compensatory activity in certain regions that overcomes potential deterioration in networks that show age-related pathology. Such compensatory recruitment in elder adults has been observed in other memory tasks (Stern et al., 2005; Scarmeas et al., 2003; Cabeza, Anderson, Locantore, & McIntosh, 2002). If it is correct that the networks of brain regions that support repetition priming, particularly perceptual priming, remain functionally intact in older adults, then the following two predictions can be made: First, young and elder participants should show priming-related neural repetition effects in the same network of brain regions. Second, the magnitude of repetition effects in this network should be the same across age groups. The goal of this study was to test these predictions.

In the current study we used multivariate linear modeling (MLM), an imaging analysis method that, unlike statistical parametric mapping (SPM), can unambiguously test the hypothesis that the spatial pattern of brain regions that shows neural repetition effects is identical for two groups of subjects (Worsley, Poline, Friston, & Evans, 1997). The reason that SPM is ambiguous with respect to the hypothesis that two brain activation patterns are identical is that even pure scaling differences between two groups could lead to the existence of true voxelwise intensity differences between groups (see Figure 1 for an illustration). Likewise, two thresholded SPM maps (one per brain activation pattern) can look quite distinct from each other even when these spatial patterns are identical to within a scaling factor. Group by Task interactions can also be ambiguous in this regard, as they can arise when the scaling factors between two groups differ in Task 1 and Task 2 (although within each task, the brain activation patterns of Groups A and B are scaled versions of one another). Another approach, region-of-interest laterality indices (Cabeza, 2002), does provide a valid test of identical patterns of region-of-interest effects in noiseless data, but because it involves ratios of estimated activation, it can be unstable in practice. Moreover, region-of-interest approaches do not compare entire brain activation patterns. In contrast, MLM can validly assess whether whole-brain activation patterns are identical by explicitly determining the number of latent spatial patterns required to summarize them (see Methods). We emphasize that the main hypothesis of this study concerns the identity of brain activation

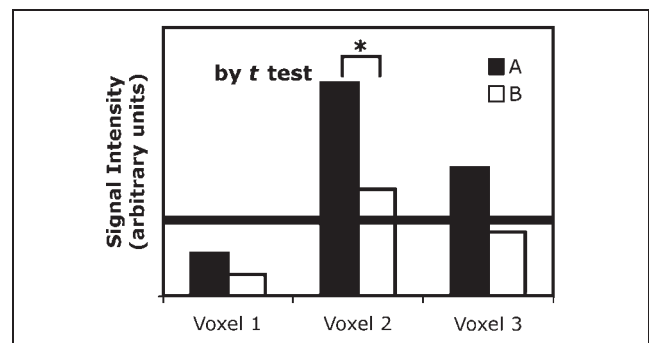


Figure 1. This example (adapted from Zarahn et al., 2007) illustrates how neither visual inspection of thresholded maps nor group comparisons via *t* test formally assess whether brain activation patterns in two groups are identical to within a scaling factor. Groups A and B express identical brain activation patterns, with the expression of this pattern in Group A being twice that in Group B. A visual comparison of thresholded maps might lead to the incorrect conclusion that brain activation patterns are different in the two groups because suprathreshold activation in Voxel 3 is present in Group A, but not in Group B. When directly comparing voxelwise intensity differences between groups via *t* tests, one might incorrectly conclude that brain activation patterns are different because only Voxel 2 tends to be detected as having a difference in intensity between Groups A and B. (* Indicates high probability of detecting a difference between groups via *t* test).

patterns in young and older adults, not other hypotheses that can be validly assessed using other methods.

To measure perceptual repetition priming, we used the possible/impossible object-decision test, a relatively “pure” perceptual test. It uses pre-experimentally unfamiliar visual objects. Consequently, priming effects are unlikely to index modifications of preexisting semantic or conceptual representations.

METHODS

Subjects

Fourteen healthy, young subjects (age range = 19–29 years) and 14 healthy, elderly subjects (age range = 67–81 years) participated in this study. The data from one elderly subject were excluded from analyses because of a large artifact in the magnetic resonance imaging (MRI) data. All subjects reported having normal or corrected-to-normal vision, being right-handed, and being free of neurological and psychiatric diseases, as assessed via questionnaire. The young subjects were recruited through flyers posted at the Columbia University campus, whereas the elderly subjects were recruited from senior centers in the New York City area. All elderly subjects were classified as nondemented and without serious cognitive impairment, on the basis of their performance on the Dementia Rating Scale—2 (all ≥ 138). The groups did not differ significantly in terms of the mean number of years of education ($p = .09$), verbal IQ ($p = .5$), as estimated by the North American Adult Reading Test (NART), and verbal fluency (CFL; $p = .7$) (see Table 1 for a complete list of participant demographic and neuropsychological characteristics).

Table 1. Demographic and Neuropsychological Variables

	Young ($n = 14$)	Elder ($n = 13$)
Female/Male	7/7	5/8
Age**	23.6 (3.2)	73.1 (4.3)
Education (years)	15.7 (1.4)	17.2 (2.3)
DRS-2*	143.9 (0.3)	141.4 (2.4)
NART-IQ	121.3 (3.8)	118.1 (12.3)
SRT*	63.6 (6.2)	53.7 (11.6)
WAIS letter-number sequencing**	15.8 (2.2)	9.9 (2.8)
Verbal fluency—CFL	48.1 (10.7)	46.6 (10.3)

Means and standard deviations (in parentheses) for demographic variables and neuropsychological test scores. DRS-2 = Dementia Rating Scale-2; NART-IQ = North American Adult Reading Test estimated IQ; SRT = Selective Reminding Test; WAIS = Wechsler Adult Intelligence Scale.

*Significant difference between groups, $p < .05$.

**Significant difference between groups, $p < .0001$.

Stimuli

Subjects viewed 39 line drawings of unfamiliar structurally possible (P) three-dimensional objects and 39 line drawings of structurally impossible (I) figures, which could not be rendered as coherent three-dimensional structures. The 78 stimuli were divided into three object sets of 13 P and 13 I objects each, such that the mean classification accuracy for P and I objects did not differ across object sets, as determined by prior behavioral pilot experiments. An additional 10 figures served as buffer items at the beginning of blocks and as practice items (see Figure 2 for examples of P and I figures used in this study).

Behavioral Procedure

We used an event-related functional magnetic resonance imaging (fMRI) design that consisted of three blocks, each with a distinct set of 13 P and 13 I objects. The order of blocks was counterbalanced between subjects. Each block was exactly 8 min in duration and consisted of four buffer trials, followed by an intermixed series of 52 presentations of P objects (13 objects \times 4 presentations/per object) and 52 presentations of I objects. Each object was viewed in one of three different repetition sequences, such that two, four, or six items intervened between stimulus repetitions. The lag between stimulus repetitions was kept relatively low so as to maximize the likelihood of generating sufficiently robust repetition effects (Henson et al., 2004). The following sequences were used: [2, 4, 6], [4, 6, 2], and [6, 2, 4]. Use of different sequences lowers the predictability of stimuli to participants. The three repetition sequences, which were counterbalanced over stimuli across subjects in a Latin square, were distributed equally throughout the experiment. However, given that 13 objects of each type were presented in a block, each block had five repetition sequences of one type and four of each of the two

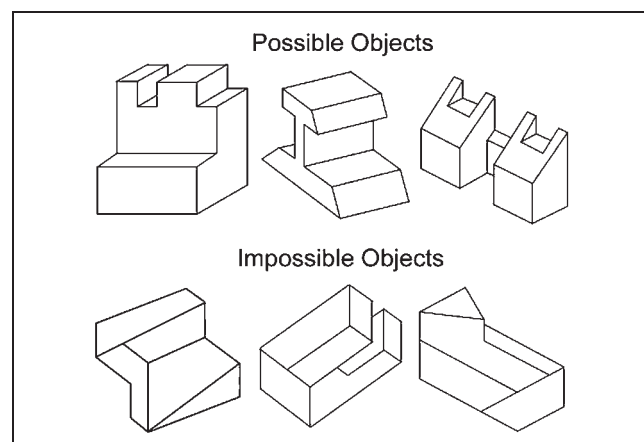


Figure 2. Examples of possible and impossible figures used in this study.

others. An additional 52 blank trials were interspersed throughout each block to provide a comparison to baseline and to maintain the required object spacing. During blank trials, the fixation cross was presented, but no stimulus followed and no response was required.

Each trial, including blank trials, lasted 3 sec and began with a 500-msec intertrial interval, followed by a 500-msec fixation cue. Fifty milliseconds after the offset of the fixation cue, the stimulus was presented for 1000 msec. A response interval started coterminously with the stimulus presentation and lasted for 1950 msec. Subjects were asked to indicate via differential button press (LUMItouch button boxes; Photon Control Company) whether a given stimulus depicted a “possible” or “impossible” object. A right index finger button press was used for P objects and a left index finger press for I objects. Both speed and accuracy were emphasized. Task administration and data collection were controlled with PsyScope 1.2.5. All timing was facilitated by the use of the external PsyScope Button Box, which interfaced directly with the PsyScope software, the LUMItouch button boxes, and the MRI acquisition computer. Stimulus presentations were automatically synched to the video retrace signal. Prior to scanning, subjects viewed examples of P and I objects and completed five practice trials. The experiment started only when subjects did not express uncertainty regarding the distinction between P and I objects. Participants were not informed that the procedure was a memory test.

Following the object-decision test, a subset of the participants (12 young, 8 elder) also performed an old–new recognition test to assess their explicit memory for the objects. In this test, subjects were shown all 78 objects presented in the object-decision test, as well as 78 new objects (39 P, 39 I). The task was to indicate which of these objects they had seen previously during the object-decision test phase and which objects were new. Subjects who completed the old–new recognition test did not differ significantly from the total sample of young or older subjects in demographic characteristics or neuropsychological test performance (all $p > .1$), indicating that recognition performance for this subgroup may be generalized to the total sample. This subgroup also showed the same pattern of priming in the object-decision test as the total sample.

fMRI Acquisition and Preprocessing

A 1.5-T magnetic resonance scanner (Phillips) was used to acquire functional T2*-weighted images using a gradient-echo, echo-planar imaging pulse sequence (TE = 50 msec; TR = 3 sec; flip angle = 90°; 64 × 64 matrix, 400 cm² field of view) and a standard quadrature head coil. At the end of the experiment, high-resolution (in-plane) T2 images were also acquired from each subject at the same slice locations as in the fMRI run using a fast echo-spin sequence (TE = 100 msec;

TR = 3 sec; 256 × 256 matrix; 400 cm² field of view). Task stimuli were back-projected onto a screen located at the foot of the MRI bed using an LCD projector. Subjects viewed the stimuli via a mirror system located in the head coil.

The data were processed using SPM99 (Wellcome Department of Cognitive Neurology, London) and in-house code written in Matlab 5.3 (Mathworks, Natick, MA). For each subject, images were first corrected for timing of slice acquisition (slice acquisition was ascending, interleaved). All functional volumes were then realigned to the first volume of the first session. The T2 structural image was then coregistered to the first functional volume using the mutual information coregistration algorithm implemented in SPM99. This coregistered high-resolution image was then used to determine parameters (7 × 8 × 7 nonlinear basis functions) for transformation into a Talairach standard space defined by the Montreal Neurological Institute (MNI) template brain supplied with SPM99. These normalization parameters were then applied to the functional data using sinc interpolation to reslice the images to 2 × 2 × 2 mm³.

fMRI Time-series (i.e., First-level) Modeling

The regressors for the first-level general linear model (GLM) were constructed by convolving the default SPM99 hemodynamic response function with the basis functions for each trial type (a rectangular pulse) aligned with stimulus onset. For each subject, the GLM contained one regressor for each crossing of object type (2), presentation (4), and block (3) (correct trials only). Additional regressors were included for incorrect trials in each block. High-pass filtering eliminated information below 1/117 Hz. Next, eight linear contrast images (one for each crossing of object type and presentation, implicitly with respect to baseline) were computed for each subject, averaging across blocks. All contrast images were intensity normalized by dividing each voxel by its time-series average, spatially smoothed using a Gaussian kernel of 8 mm full width at half maximum, masked with an image that had a gray matter prior probability of >.25 (to eliminate ventricles from the search volume), and then used for subsequent second-level (i.e., population-level inference) analysis. This second-level GLM had eight repeated measures per subject per voxel and one between-subjects factor (age). Its covariance matrix (S in Worsley et al., 1997) was estimated by spatially averaging voxelwise covariance estimates.

Multivariate Linear Modeling

MLM is an extension of the SPM framework that provides a multivariate test of the spatial null hypothesis that there is no common latent whole-brain image pattern of blood oxygenation level-dependent activation common

to two or more contrast images. Like SPM, MLM involves voxelwise application of the GLM, but instead of statistically testing for effects of interest (i.e., repetition effects for P and I objects) at each voxel, the statistical testing assesses the existence of any such effects simultaneously at all voxels in other words, in a spatially omnibus fashion. For this reason, MLM will tend to have superior detection power compared with SPM voxelwise testing in the presence of spatially distributed effects, without inflating Type I error. A second advantage of MLM over SPM is that MLM can explicitly test hypotheses regarding the number of spatial patterns required to summarize the effects of interest. MLM does not itself provide localized tests of blood oxygenation level-dependent contrast values. However, because MLM is an extension of SPM, localization information is easily recovered from the univariate GLM. Because the goal of this study was to formally test the hypothesis that the spatial patterns of repetition effects are identical for young and older subjects, we chose MLM over the more standard SPM approach. However, traditional SPM analyses were also performed to follow up on some of the MLM results (see below).

In order to compare the brain patterns of repetition effects across the two age groups, six sets of two effects of interest (young vs. elder) were analyzed with MLM, comprising the following contrasts for young and elder subjects: (1) fMRI signal difference between the first and second presentation of P objects, (2) fMRI signal difference between the second and fourth presentation of P objects, (3) fMRI signal difference between the first and fourth presentation of P objects, and (4–6) the corresponding contrasts for I objects. Repetition effects at the second and fourth stimulus presentation relative to Presentation 1 were assessed separately to see if young and elders showed similar patterns of neural plasticity following a single repetition compared to three repetitions of a stimulus.

Six additional MLM analyses were performed to identify the spatial networks of regions where both young and elder subjects showed similar correlations between neural repetition effects and reaction time (RT) priming (i.e., latent spatial patterns of repetition effects that correlated with RT priming for both age groups). The same types of contrasts were used as for the first set of MLM analyses, but the corresponding RT reductions were included as behavioral covariates in the GLM. (Accuracy was not used as a covariate because young subjects did not show significant priming as measured by accuracy.) Thus, these MLM analyses comprised the following six sets of contrasts for young and elder subjects: (1) fMRI signal difference between the first and second presentation of P objects that correlated (across subjects) with the difference in RT between the first and second presentation of P objects; (2) fMRI signal difference between the first and fourth presentation of P objects that correlated with the difference in RT between the first

and fourth presentation of P objects; (3) fMRI signal difference between the second and fourth presentation of P objects that correlated (across subjects) with the difference in RT between the second and fourth presentation of P objects; and (4–6) the corresponding contrasts for I objects.

In this study, the effects of interest are said to have dimensionality $k = 2$ because two effects of interest were specified for each MLM analysis (i.e., one contrast for young subjects, and the corresponding one for elder subjects). In MLM, singular value decomposition decomposes the k -dimensional effects of interest into k latent components (some of which might contain only noise, and others of which might contain signal plus noise), each comprising a latent spatial pattern and its latent expression (over subjects in this context). The first component explains the greatest amount of variance; the second explains the greatest amount of variance after accounting for the first, and so on. To statistically assess the number of latent components containing some signal, a sequential latent root testing procedure is performed that uses parametric approximations (F statistics), which have been validated using computer simulations (Worsley et al., 1997). Thus, MLM concerns statistical inference on the number of unique spatial patterns of signal in the effects of interest.

Repetition effects for P and I objects were examined separately, as previous neuroimaging and electrophysiological studies have reported differences in the processing of P and I objects (Habeck, Hilton, Zarahn, Brown, & Stern, 2006; Soldan, Mangels, & Cooper, 2006; Schacter et al., 1995). The possible outcomes of an MLM analysis for two effects of interest are 0, 1, or 2 latent spatial patterns. For this set of effects of interest, zero latent spatial patterns would indicate that there were no neural repetition effects, as assessed by a spatially omnibus null hypothesis. One latent spatial pattern would signify that a main effect of repetition was detected, as assessed by a spatially omnibus null hypothesis, and that this effect occurred in the same spatial network of brain regions for the young and elder subjects. Two latent spatial patterns would indicate that the spatial patterns of repetition effects were not identical for the young and elderly participants (i.e., nonscaled versions of one another).

Significant latent spatial patterns are presented for descriptive and display purposes (analogous to SPM t images; Worsley et al., 1997) in all tables and figures at a t value corresponding to $p < .001$, uncorrected for multiple comparisons and a cluster size of 10 voxels. This threshold does not control mapwise statistical significance at $\alpha = .05$ (Worsley et al., 1996), and so is only meant to provide a somewhat condensed description of the significant latent spatial patterns. MNI coordinates were converted to Talairach coordinates using the `mni2tal` Matlab function and Talairach Daemon was used to provide anatomic labels for nearest gray

matter cluster maxima (<http://ric.uthscsa.edu/projects/talairachdaemon.html>).

SPM Analysis

Following up on some of the MLM results, additional voxelwise SPM comparisons were performed to localize regions showing a main effect of repetition or differences between young and elder subjects. Contrasts of the parameter estimates from single-subject models were entered into random effects analyses (two-tailed one-sample *t* tests) comparing the mean parameter estimate over subjects to zero. Results were corrected for multiple comparisons across the whole brain using the Bonferroni correction for the number of resolution elements (Worsley et al., 1996).

RESULTS

Parts of these data (young subjects only, Presentations 1 to 3) have been published previously using a different data-analytic technique (Habeck et al., 2006). Differences in the repetition effects for P and I objects were not specifically explored in this article, as these were investigated by Habeck et al. (2006).

Behavioral Performance

Mean accuracy and RT data from the P/I object-decision test were analyzed using repeated measures analysis of variance (ANOVA) with object type (P vs. I) and presentation (1–4) as within-subject factors and group (young vs. elder) as a between-subjects factor (Figure 3, top). Overall, accuracy was higher for young than elder subjects, as indicated by an effect of group [$F(1, 25) = 15.02, p < .001$]. For accuracy, there was also an effect of object type [$F(1, 25) = 23.64, p < .0001$], indicating better performance for P than for I objects. There was a clear effect of presentation on accuracy [$F(3, 75) = 7.51, p < .001$], as well as an interaction between presentation and group [$F(3, 75) = 4.12, p = .015$]. No other effects were significant (all $p > .14$). Post hoc contrasts showed that accuracy increased from Presentation 1 to Presentation 4 in the elder subjects [$t(13) = 2.77, p < .02$], with the major change occurring from the first to the second presentation. For the young group, accuracy did not increase significantly from Presentation 1 to Presentation 4, although the trend was in the same direction [$t(13) = 1.50, p = .16$]. The apparently greater increase in accuracy for the elder compared to the young group may stem from the fact that accuracy for P objects was at ceiling in the young group (96% at Presentation 1), thereby restricting priming. For I objects, accuracy was lower in the young subjects (87%) and a marginal priming effect was observed from Presentations 1 to 4 [$t(13) = 2.13, p = .05$].

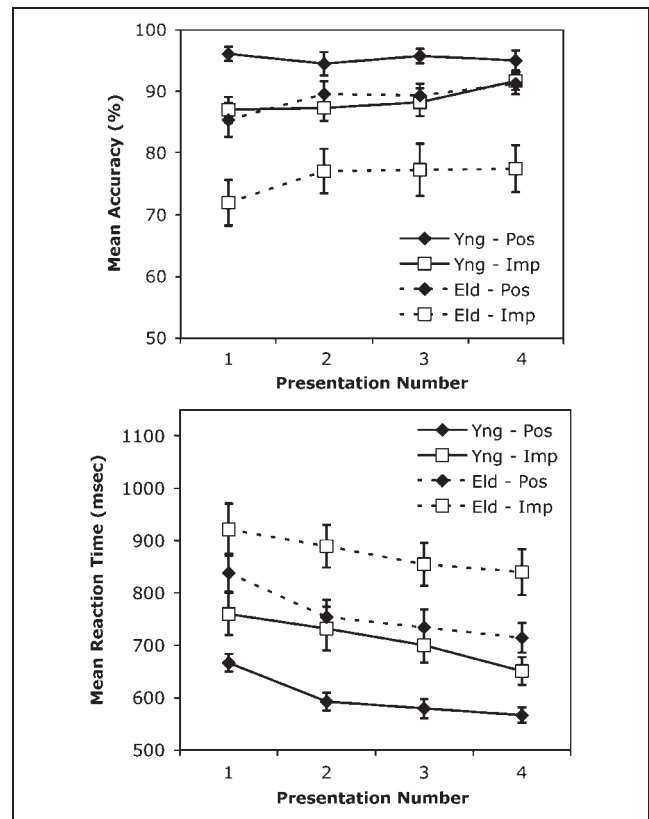


Figure 3. Preserved repetition priming in elder adults. Object-based performance as a function of presentation for possible and impossible objects in the young and elder participants: mean classification accuracy (top) and reaction time (bottom). Error bars represent the standard error of the mean. Yng = young participants; Eld = elder participants; Pos = possible objects; Imp = impossible objects.

The analysis of subjects' RT revealed that young subjects responded significantly faster than elder subjects [$F(1, 25) = 16.14, p < .001$] (Figure 3, bottom). There was also an effect of object type [$F(1, 25) = 27.20, p < .0001$], indicating faster RTs for P than for I objects. The effect of presentation was also significant [$F(3, 75) = 62.69, p < .0001$], as was the interaction between presentation and object type [$F(3, 75) = 4.67, p = .007$]. There were no other significant effects or interactions (all $p > .23$). Post hoc profile contrasts showed that RTs, collapsed across object type and group, decreased with each stimulus repetition [from Presentations 1 to 2: $F(1, 25) = 77.22, p < .0001$; Presentations 2 to 3: $F(1, 25) = 20.93, p < .0005$; and Presentations 3 to 4: $F(1, 25) = 15.74, p < .001$]. However, from Presentations 1 to 2, the decrease in RT (i.e., priming) was larger for P than for I objects [$F(1, 25) = 12.95, p < .005$], whereas for subsequent repetitions, there was no difference in priming between P and I objects (both $p > .17$). An additional analysis indicated that the variability in RT was not significantly greater in the elder group than in the young group [$F(1, 25) = 1.75, p = .20$]. There were no correlations between measures of priming and neuro-

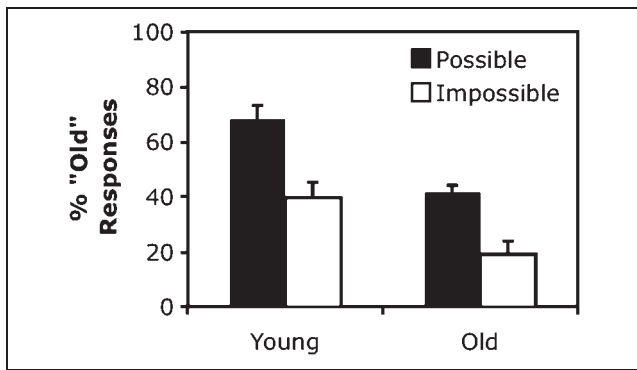


Figure 4. Impaired recognition performance in elder adults. Mean corrected recognition performance (hits minus false alarms) of possible and impossible objects in young and elder subjects. Error bars represent the standard error of the mean.

psychological test performance in either the young or old group.

For the old–new recognition test, corrected recognition scores (hits – false alarms) were computed and submitted to a repeated measures ANOVA with object type as a within-subjects factor and group as a between-subjects factor. This analysis showed that, in stark contrast to the preserved priming effects in the two age groups, old–new recognition performance was markedly lower for the elder than the young subjects (Figure 4), as indicated by an effect of group [$F(1, 18) = 14.81, p = .001$]. Furthermore, performance was lower for I than for P objects [$F(1, 18) = 32.58, p < .0001$], but there was no interaction between object type and group ($F < 1, p = .51$). There were no significant correlations between subjects' corrected recognition scores and subjects' priming scores from Presentations 1 to 4 (i.e., mean RT, Presentations 1–4, or mean percent correct,

Presentations 1–4) for either P or I objects within the two groups or across groups (all $p > .13$).

fMRI Results: Repetition Effects in Young and Elders

One latent spatial pattern was detected for each of the six sets of effects of interest representing the difference in fMRI amplitude between the first and second presentation, the second and fourth presentation, and the first and fourth presentation of stimuli (see Table 2 for the sequential latent root testing results). Thus, the results indicate identical patterns of fMRI repetition effects for the young and elder groups for both P and I objects. Furthermore, the magnitude of pattern expression did not differ significantly in the young and elder groups for any of the six sets of effects of interest (all $p > .05$). However, there was a nonsignificant trend for smaller expressions in the elderly of the patterns representing the repetition effects from Presentations 1 to 4 for both P and I objects (see Table 2). The latent spatial patterns of repetition effects from Presentations 1 to 2 and 1 to 4, as well as their corresponding expressions, are shown in Figure 5. The latent spatial patterns of repetition effects from Presentations 2 to 4 are not depicted and discussed further because the regions that showed repetition effects from Presentations 2 to 4 were largely overlapping with regions showing repetition effects from Presentations 1 to 4. The relatively gradual increase or decrease in activation/deactivation across the four presentations can be seen in Figure 6.

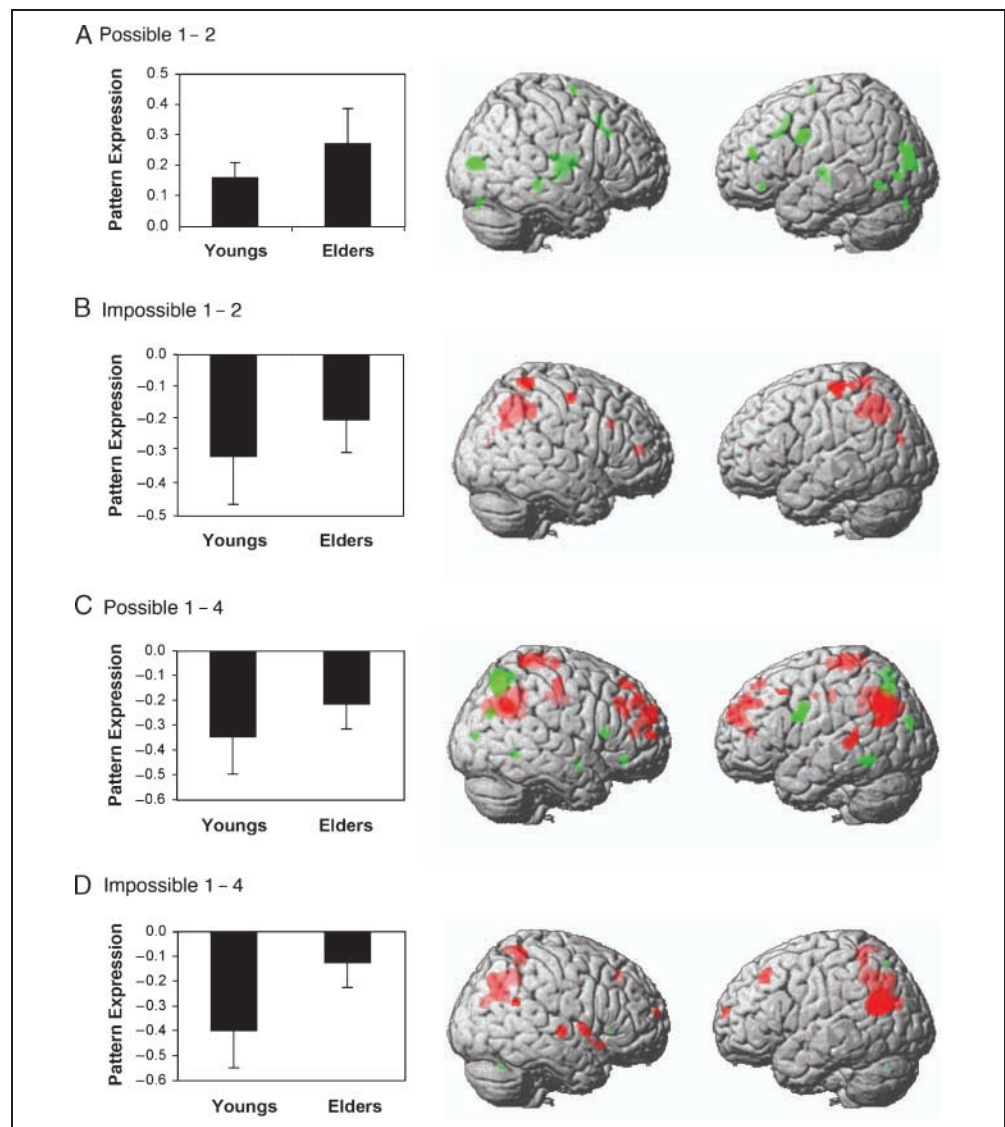
For the latent spatial pattern of repetition effects for P objects from Presentations 1 to 2, the largest spatial weights were all positive, indicating that they represented RS effects. These were observed in regions previously

Table 2. Sequential Latent Root Testing Results for Contrasts Representing Young and Elder Neural Repetition Effects of Possible and Impossible Objects, as well as Contrasts Representing Young and Elder Baseline (i.e., Presentation 1) Activation for Possible and Impossible Objects

Effects of Interest	Test for at Least One Component		Test for Two Components		Inferred Number of Latent Spatial Patterns	Age Difference in Expression	
	$F(653, 12,854)$	p	$F(327, 8597)$	p		$t(25)$	p
Possible 1	6.22	<.0001	1.07	.20	1	1.64	.11
Possible 1–2	1.19	.0009	0.84	.98	1	0.95	.37
Possible 2–4	1.42	<.0001	1.04	.29	1	0.86	.40
Possible 1–4	1.67	<.0001	1.06	.22	1	1.85	.08
Impossible 1	3.64	<.0001	1.20	.008	2	1.24	.23
Impossible 1–2	1.19	.0007	0.92	.86	1	0.64	.52
Impossible 2–4	1.20	.0003	0.89	.92	1	1.36	.19
Impossible 1–4	1.18	.001	0.81	.99	1	2.04	.05

Last column contains results for two-tailed independent-samples t tests comparing the magnitude of expression of the first (i.e., common) latent spatial pattern in young and elder subjects.

Figure 5. Scaled latent spatial patterns of repetition effects (red: voxels showing repetition enhancement; green: voxels showing repetition suppression) and subject-wide expressions of the corresponding pattern in young and elder subjects. Error bars represent the standard error of the mean. (A) Difference in fMRI amplitude between Presentations 1 and 2 of possible objects; (B) difference in fMRI amplitude between Presentations 1 and 2 of impossible objects; (C) difference in fMRI amplitude between Presentations 1 and 4 of possible objects; and (D) difference in fMRI amplitude between Presentations 1 and 4 of impossible objects.



reported to show RS during repetition priming tasks, including the precentral gyrus (BA 6), thalamus, cuneus (BA 17), parahippocampal gyrus (BA 36), middle occipital gyrus (BA 19), and precuneus (BA 7). The latent spatial pattern of repetition effects for P objects from Presentations 1 to 4 had both large positive and negative spatial weights, indicating the presence of both RS effects and *repetition enhancement* (RE) effects. RS effects were present in similar regions as at Presentation 2, whereas the largest RE contributions occurred in the inferior parietal lobule (BA 39), superior temporal gyrus (BA 39), cuneus (BA 7, 19), precuneus (BA 7, 31), and medial frontal gyrus (BA 9). All brain regions with large weights in the latent spatial pattern representing the repetition effects for I objects from Presentations 1 to 2 and 1 to 4 contributed an RE effect. These were observed in largely overlapping regions as the RE effects for P objects. For both P and I objects, these RE effects generally represented decreases in task-induced deactivation relative to

baseline, rather than increases of an initially positive response (Figure 6). A detailed tabular description of the brain regions strongly weighted in these latent spatial patterns is not provided, as this is not of direct relevance to the hypothesis under investigation.

An informal inspection of the signal amplitude in regions with large weights in these latent spatial patterns indicated that the magnitude of RS was comparable for the two age groups, whereas the magnitude of RE tended to be slightly larger for the young subjects (see Figure 6). Note that an SPM voxelwise comparison of the repetition effects between young and elder subjects did not detect any significant difference in the magnitude of either RS or RE at the whole-brain-corrected threshold for P or I objects. Only when the threshold was lowered ($p < .001$, $k = 10$) were a few regions detected, which showed larger RE from Presentations 1 to 4 for young than older adults: the bilateral superior temporal gyrus and the inferior parietal lobule for P objects and the

right insula and the left medial precuneus for I objects. There was no group difference in the magnitude of RS at this threshold.

Post hoc correlations showed that individual subjects' expressions of the latent spatial patterns of repetition effects did not correlate with the magnitude of priming (i.e., RT reductions or accuracy increases) in either the young or elder group. There were also no correlations between neuropsychological test performance and individual pattern expressions.

Next, we examined which of those regions that contributed strong RS/RE effects for both young and elder participants also showed a correlation between the magnitude of this RS/RE effect and RT priming for both age groups. The purpose of this analysis was to examine which brain regions might be particularly relevant for mediating preserved priming effects in old age. All analyses regarding correlations between behavioral and neural repetition effects were performed collapsing across age groups because the spatial patterns of neural repetition effects were deemed identical for the two groups by MLM.

First, we used MLM to test if there exist spatial patterns of RT correlated repetition effects where both young and elder subjects showed similar correlations between RS/RE and RT priming. Common spatial networks of repetition effects that correlated with RT priming for young and elders were detected for P objects from Presentations 1 to 2, 2 to 4, and 1 to 4 and for I objects from Presentations 1 to 4 [test for one or more latent spatial patterns, all $p < .0007$], data not shown. Next, we determined the overlap between the latent spatial patterns representing the fMRI repetition effects (thresholded at $p < .001$, $k = 10$ voxels) and the common (for young and elder subjects) latent spatial patterns of fMRI repetition effects that correlated with RT priming (thresholded at $p < .05$, $k = 5$ voxels). (A lower threshold was chosen for the second pattern to increase sensitivity in detecting correlations between behavioral and neural repetition effects.)

One area was identified where the magnitude of the RS effect from Presentations 1 to 4 for P objects correlated with RT priming for P objects at Presentation 4, collapsing across age groups: the left inferior frontal gyrus

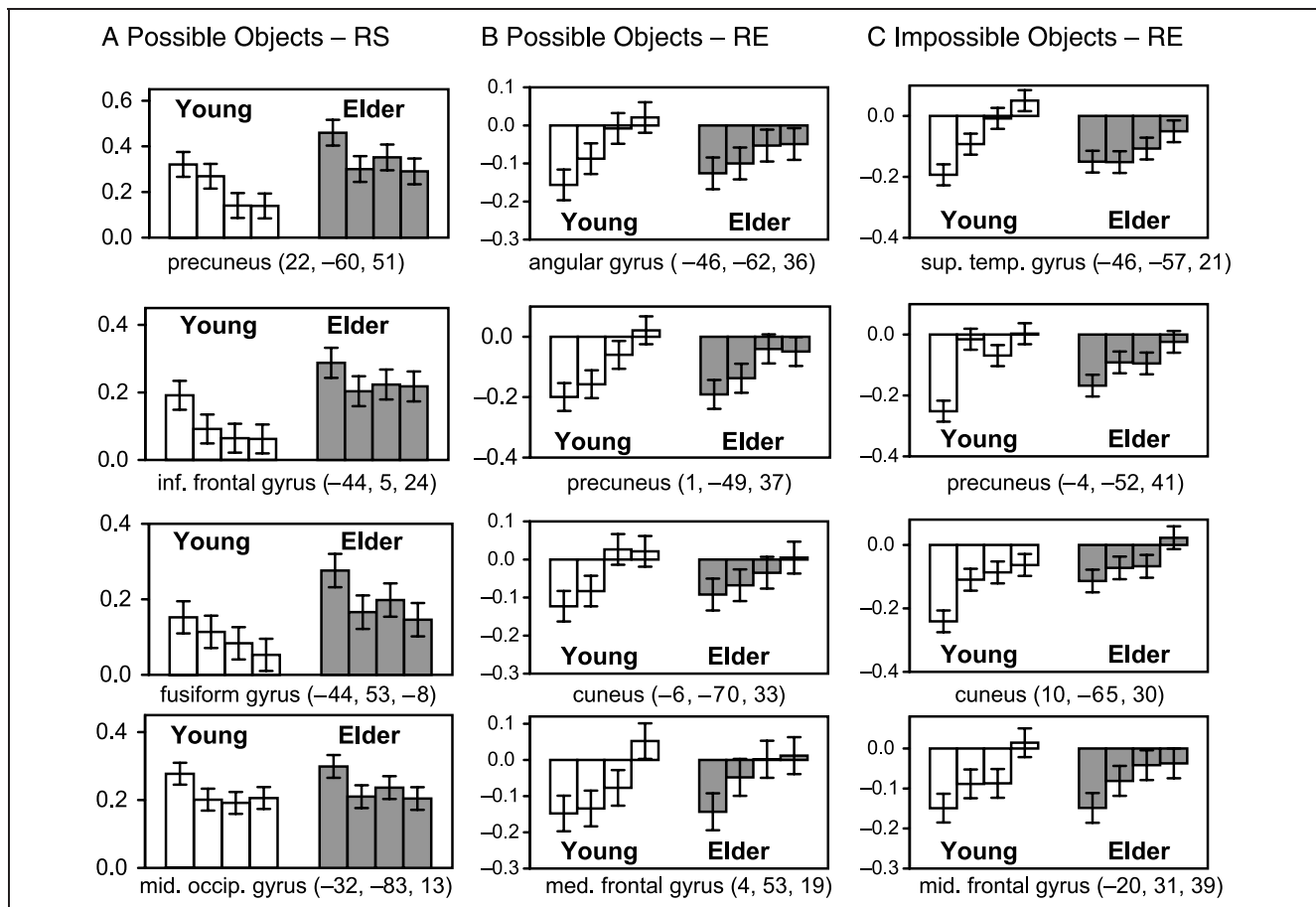


Figure 6. Graphs show mean fMRI signal change (on y-axis) at four cluster maxima with strong weights for the latent spatial patterns of repetition effects for young and elder subjects from Presentations 1 to 4 for possible objects (A, B) and impossible objects (C) as a function of presentation number (on x-axis). Repetition suppression (A) and repetition enhancement (B) effects for possible objects are plotted separately. For impossible objects, only repetition enhancement (C) is shown because there were no clusters with large repetition suppression effects.

(BA 9, cluster maximum: $x = -48, y = 1, z = 22; r = .48, p < .05; k = 11$ voxels; Figure 7A). The magnitude of the RT priming effect for P objects at Presentation 4 also correlated with the magnitude of the RE effect for P objects from Presentations 1 to 4 in the left cuneus (cluster maximum: $x = -18, y = -82, z = 30; r = .45, p < .05; k = 6$ voxels; Figure 7B). The left cuneus also showed a correlation between the magnitude of the RE effect for I objects from Presentations 1 to 4 and RT priming for young and elder adults (cluster maximum: $x = -8, y = -74, z = 26; r = .56, p = .002; k = 81$ voxels; Figure 7C).

Next, we conducted follow-up SPM voxelwise comparisons (i.e., second-level group GLM described in the Methods section) to confirm that the regions identified in the MLM analysis to show a correlation between RS/RE and RT priming, indeed, showed a significant main effect of repetition (either RS or RE). P objects showed a significant RS from Presentations 1 to 4 (collapsing across young and elder subjects) in the left inferior frontal gyrus ($x = -50, y = 1, z = 22; t = 5.59, p < .05$, corrected), and a significant RE from Presentations 1 to 4 in the left cuneus ($x = -26, y = -80, z = 26, t = 4.91, p < .05$, corrected). The left cuneus also showed a significant RE for I objects ($x = -12, y = -73, z = 24, t = 4.40, p < .05$ corrected).

Additional post hoc correlational analyses were performed between individuals' corrected recognition memory scores and the magnitude of RE from Presentations 1 to 4 in the four regions contributing the largest RE effects to the latent spatial patterns of repetition effects from Presentations 1 to 4 for young and elder subjects. These analyses were performed separately for P and I objects, but collapsed across age group. None of these correlations were significant. Because older subjects sometimes show differences in their initial response to stimuli (i.e., Presentation 1 vs. baseline), we also compared fMRI activations across the two groups at Presentation 1. Using MLM, we found that there was only one latent spatial pattern representing the fMRI

activation for P objects at Presentation 1 for both young and elders, indicating that both groups activated the same spatial network (see Table 2 for sequential latent root testing results). The magnitude of pattern expression did not differ for the two groups, although there was a trend for greater magnitude expression in the elder group (mean expression = 0.70, $SE = 0.20$) than the young group (mean expression = 0.55, $SE = 0.15$) [$t(25) = 1.64, p = .11$]. An inspection of mean activation values of heavily weighted regions suggested that there was no age difference in the magnitude of deactivation, but that older adults tended to show greater magnitude activations relative to baseline in some areas. Follow-up SPM analysis of the same contrasts confirmed that there were two regions where older adults showed more positive activation than young ones: left inferior frontal gyrus (BA 45) and left postcentral gyrus (BA 2). Neither of these two regions demonstrated reliable RS or RE at Presentation 2 or 4 ($p > .001$, uncorrected).

An MLM analysis comparing fMRI activation for I objects at Presentation 1 across the two groups indicated the presence of two significant latent spatial patterns (see Table 2 for sequential latent root testing results). The first latent spatial pattern had the same sign of expression for both groups and expression magnitude did not differ for young (mean expression = 0.52, $SE = 0.14$) and elder subjects (mean expression = 0.66, $SE = 0.19$) [$t(25) = 1.24, p = .23$]. The second pattern had opposite signs of expression for the young (mean expression = $-0.27, SE = 0.07$) and elder participants (mean expression = 0.25, $SE = 0.07$). Whereas elder subjects tended to contribute positive activations relative to baseline, young subjects contributed deactivations or nil activation to this pattern (data not shown). Regions above our display threshold were the left inferior frontal gyrus (BA 9), which was activated by the elder subjects, but not by the young, and the left middle temporal gyrus, the left superior temporal gyrus, and the left posterior insula, which all contributed an activation effect for the elder group and a deactivation effect for

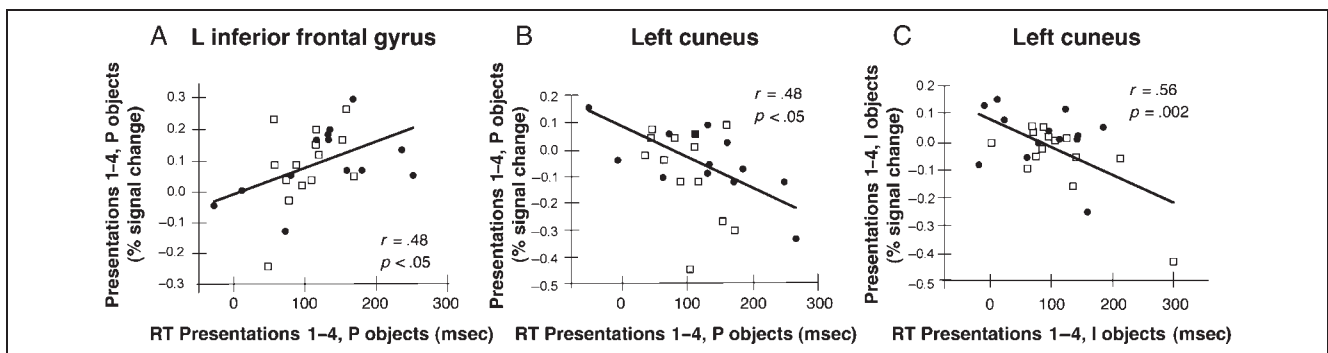


Figure 7. Scatterplots of correlations between behavioral priming and neural repetition effects for both young (\square) and elder (\bullet) subjects. The magnitude of priming for P objects from Presentations 1 to 4 was correlated with the magnitude of repetition suppression in the left inferior frontal gyrus, BA 9 (A). The left cuneus showed a correlation between priming and repetition enhancement from Presentations 1 to 4 for both possible objects (B) and impossible objects (C).

the young group. Follow-up SPM analyses showed that only one of these regions, the left inferior frontal gyrus, showed a significant age difference at the corrected threshold. None of these regions showed RS or RE at Presentation 2 or 4 for either group, even at a liberal threshold ($p < .001$), indicating that they were not reliably modulated by repetition.

DISCUSSION

This study investigated how aging affects patterns of neural repetition effects associated with perceptual priming of unfamiliar visual objects. Critical in this investigation was the usage of MLM, rather than SPM, to test whether the brain networks that display neural repetition effects are identical in young and elder adults. Behaviorally, young and elder adults showed similar repetition priming effects across three stimulus repetitions for structurally possible and impossible figures, despite impaired recognition memory in the elder individuals. The brain networks that showed repetition effects (both RS and RE) were identical in both age groups. Furthermore, the magnitude of repetition effects in these networks did not differ significantly across the two groups, although there was a trend for greater magnitude repetition effects, particularly RE, in young subjects for stimuli that had been repeated thrice. These findings support the view that perceptual repetition priming remains intact across the adult life span because the same networks of brain regions continue to show neural plasticity during repetition priming tasks in young and older adults. There was no evidence for age-related compensatory reorganization of the brain networks that demonstrated repetition-related changes in activity. Previous studies have not been able to unambiguously test this hypothesis.

The finding of preserved patterns of neural repetition effects is interesting in light of the fact that, during the initial presentation of stimuli, older adults tended to activate some brain regions more than young adults, particularly in the frontal cortex. Given that we were unable to detect reliable repetition effects in these regions, they may not support repetition priming (i.e., learning). Rather, their recruitment in the elder subjects may reflect compensatory activity related to the overall performance of the task. Thus, it is possible that because older adults experienced greater difficulty with this task, as indexed by lower accuracy, they showed greater effort-related activation in some regions. A similar interpretation was offered by Lustig and Buckner (2004), who also reported greater frontal activation in older compared to young adults during semantic priming. Increased and potentially compensatory brain activity in older adults has been reported for other types of memory tests as well (e.g., Cabeza et al., 2002; Reuter-Lorenz, 2002). One possibility is that regions that show greater activation in old than young adults but no or weak ef-

fects of repetition may reflect generalized control processes, whereas regions that show repetition effects but no effect of age are more specifically related to the processing of individual stimuli in this task. However, given that the absence of a reliable repetition effect in the former set of regions reflects a null finding, caution needs to be exercised when interpreting these results.

The findings from this study indicate that the persistence of priming in later adulthood and its neural correlates are not restricted to familiar stimuli, such as words and everyday objects, but extends to pre-experimentally unfamiliar visual objects with and without a globally coherent three-dimensional structure. Because the priming effects observed in this study necessarily involve newly formed object representations, the associated neural changes do not simply reflect the reactivation of preexisting knowledge, but the formation of new implicit memories. Furthermore, even if the priming effects in this study were supported the learning of highly specific stimulus-response associations (Dobbins, Schnyer, Verfaellie, & Schacter, 2004), these associations must involve, at least to some extent, newly acquired perceptual features of the stimuli. These data thus confirm previous reports that elder adults can show intact priming for newly acquired information (Light, La Voie, & Kennison, 1995; Schacter, Cooper, & Valdiserri, 1992). The finding that the elder adults were, overall, less accurate and slower than the younger participants may be attributable to a more general problem of slowed information processing (Salthouse, 1985) that impairs performance on tasks that involve brief stimulus exposures.

In support of the view that RS in some brain regions may be causally related to repetition priming (Henson, 2003; Wiggs & Martin, 1998), we found that the magnitude of RS in the left inferior frontal gyrus from Presentations 1 to 4 for structurally coherent 3-D objects correlated with repetition-related decreases in RT for both young and elder adults. This relation was similarly strong for both age groups. This finding is consistent with previous studies that have linked individual differences in RS in the left prefrontal cortex to differences in the behavioral benefit of repetition in both young and healthy older adults, as well as in individuals in the early stage of dementia of the Alzheimer's type (Daselaar et al., 2005; Dobbins et al., 2004; Lustig & Buckner, 2004; Maccotta & Buckner, 2004). These prefrontal RS effects have been observed with a variety of stimuli and tasks, but appear to require that the same task be performed during the first and repeated presentations of stimuli (Dobbins et al., 2004; Wagner, Koutstaal, Maril, Schacter, & Buckner, 2000). It has been postulated that they reflect a reduced need for controlled, strategic processing that occurs with repetition (Dobbins et al., 2004; Lustig & Buckner, 2004). The present results are consistent with this hypothesis and further suggest that the type of processing performed by these regions is not limited to verbal material and familiar objects. A related

possibility is that these prefrontal RS effects index a reduction in effortful response-selection mechanisms, which have also been shown to involve left prefrontal regions (Jiang & Kanwisher, 2003; Schumacher, Elston, & D'Esposito, 2003).

It is noteworthy that most of the regions with large spatial weights in the latent patterns that represented the repetition effects for I objects for young and elder adults contributed an increase in activity (i.e., RE rather than RS). At the same time, both groups of subjects showed significant behavioral priming effects across the four presentations of I objects. This pattern of results differs from most prior neuroimaging studies, which usually report RS during repetition priming tasks (for a review, see Henson, 2003).

Although the repetition of I objects predominantly led to RE, it is, nonetheless, possible that the behavioral priming effects for I objects in this study were exclusively based on RS. This could occur if the locations of RS effects for I objects were too variable across subjects to be detected in the group analysis. This variability across subjects may stem from the fact that there are no specialized brain regions for processing I objects, as they are not encountered in everyday life. In this scenario, the RE effects would be co-occurring with, but not causally related to, repetition priming. Another possibility is that the RS effects for I objects occurred in similar regions across subjects, but were simply of a smaller magnitude than that for P objects and the experiment lacked sufficient power to detect them. However, if priming for both P and I objects was indeed mediated by RS only, but with smaller magnitude RS for I than P objects, this would imply that similar-magnitude behavioral priming can be associated with different magnitude RS effects within the same task, depending on the physical characteristics of the stimulus. This, in turn, would suggest that either not all aspects of RS for P objects were directly related to the behavioral priming effects or, probably less likely, that I objects required less RS than P objects in order to obtain the same priming effects. Differentiating between these alternative explanations would likely require the modeling of subject-specific information (for a more detailed discussion on this issue, as well as differences in the neural patterns of repetition effects for P and I objects, see Habeck et al., 2006). Interestingly though, the present findings do suggest that many regions that typically show RS, particularly in the occipital-temporal cortex, are sensitive to the global 3-D structure of objects because large RS contributions to the latent spatial patterns of repetition effects were not observed for I objects.

Notably, the RE effects in this study generally occurred in regions that were deactivated relative to baseline at Presentation 1 and did not increase above baseline levels across the three repetitions (see Figure 6). This argues against the view that they index the formation of new memory representations, which has been proposed to

occur in some priming studies using pre-experimentally unfamiliar stimuli (Soldan, Zarahn, Hilton, & Stern, 2008; Fiebach, Gruber, & Supp, 2005; Henson, 2003; Henson, Shallice, & Dolan, 2000). Thus, the formation of new representations would appear to require RE to above-baseline levels, indexing stimulus- and task-related processing. Moreover, none of the regions with large RE effects for P or I objects were located in the occipital-temporal cortex (Figure 5), arguing against the view that new perceptual representations of the figures were formed. The RE effects in this study are also unlikely to reflect the incidental explicit recognition of repeated stimuli, as the magnitude of RE from Presentations 1 to 4 did not correlate with subjects performance on the old-new recognition test.

These RE effects for P and I objects in this study occurred in many of the same regions that have been referred to as the *default network* (Raichle et al., 2001). This network of regions is thought to be active when subjects are at rest and appears to be related to “mind wandering” or the “stream of consciousness” that is disrupted when subjects engage in an attention-demanding task (Mason et al., 2007; McKiernan, D'Angelo, Kaufman, & Binder, 2006). Default network activity has also been shown to decrease as difficulty decreases (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003). The observed increase in default network activity with stimulus repetition in the present study is therefore consistent with the view that task performance became less difficult or more automatic with stimulus and task repetition. In other words, as task performance became easier and/or required less processing time (as evidenced by reductions in RT), task-related processing decreased (as evidenced by RS) and task-unrelated activity increased (as evidenced by greater default network activity). Consistent with this interpretation, the magnitude of RE in the left cuneus from Presentations 1 to 4 was correlated with the magnitude of RT priming from Presentations 1 to 4.¹ This region was initially deactivated relative to baseline and its activity increased with repetition to reach baseline levels at Presentation 4. We hypothesize, therefore, that increased default-network activity is a by-product of facilitated task performance that results from learning in other networks, particularly those showing RS. A between-subjects correlation between the magnitude of deactivation and RT in a cognitive task was also recently reported by Persson, Lustig, Nelson, and Reuter-Lorenz (2007), who suggested that the ability to deactivate default network regions might actually be beneficial to task performance, as it reflects important cognitive control processes.

Decreases in task-induced deactivation during repetition priming tasks have been reported previously (Orfanidou, Marslen-Wilson, & Davis, 2006; Simons, Koutstaal, Prince, Wagner, & Schacter, 2003; Koutstaal et al., 2001), but these effects are usually not as large as in the present study. The reason that relatively large repetition-related

changes in default network activity were observed in the present study could be related to the usage of unfamiliar stimuli, particularly the I objects, a class of stimuli with which our visual system has virtually no experience. Thus, although subjects can perform the P/I classification task well above chance, these stimuli are more difficult to process than familiar objects, leading to larger decreases in default network activity during the initial stimulus encounter. Consistent with this interpretation, familiar stimuli tend to elicit much smaller task-induced deactivations than globally unfamiliar stimuli (Soldan et al., 2008).

Important for the purpose of this investigation is the finding that young and elder adults showed task-induced deactivations in the same spatial network of regions and of a similar magnitude, but with a trend for smaller repetition-related decreases in deactivation from Presentations 1 to 4 in the older individuals. There is a small but growing body of research investigating age-related changes in deactivation during cognitive tasks. Current evidence suggests that when task demands are relatively low, older and younger adults show similar magnitude task-induced deactivations; however, for more difficult tasks, young adults tend to show greater magnitude deactivations than older individuals (Persson et al., 2007; Grady, Springer, Hongwanishkul, McIntosh, & Winocur, 2006; Lustig et al., 2003). The reason for the absence of an age difference in deactivation during the initial performance of the P/I object-decision task could be related to the fact that, although this task is more difficult than other priming tasks, it was still relatively easy for both the young and older participants. Thus, despite accuracy not being at ceiling, response times were relatively low (650 to 950 msec), suggesting that task-related processing was not very resource demanding for both age groups.

Another possibility is that the elder subjects were simply unable to further deactivate the default network at Presentation 1 due to some age-related physiological deficit, despite experiencing greater difficulty with the task than the young adults, as indexed by their lower accuracy. This would be consistent with the finding of smaller deactivations in normal aging and may also explain why the older subjects showed increased activation in other regions at Presentation 1. Specifically, Persson et al. (2007) proposed that the inability to sufficiently deactivate task-unrelated processes is what elder subjects are compensating for when they show increased activation in other, primarily frontal regions. This interpretation would also explain why the repetition-related decrease in deactivation from Presentations 1 to 4 tended to be slightly smaller in the older adults than in the young subjects. Thus, although the elder subjects may have been unable to sufficiently deactivate at presentation 1 (i.e., in proportion to the greater difficulty they experienced relative to the young subjects), they showed smaller decreases in deactivation with repetition because the task continued to be more resource demanding for them

than for the young subjects. This account, however, is speculative and should be tested in future investigations.

In conclusion, the present study supports the hypothesis that perceptual repetition priming is preserved in elder adults because the brain networks that show repetition-related neural plasticity largely retain their functional integrity. Importantly, these networks support the learning of novel information, which opens potential avenues for developing learning strategies that remediate age-related memory deficits.

Acknowledgments

This work was supported by NIA grant RO1-AG16714 to Yaakov Stern.

We thank Oksana Tatarina for research assistance.

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Note

1. These results corroborate those reported by Habeck et al. (2006), who applied ordinal trend canonical variates analysis (OrT CVA) to the data. They identified a spatial covariance pattern of regions showing RS and RE effects in the young subjects whose expression across subjects correlated with RT priming for P objects.

REFERENCES

- Backman, L., Almkvist, O., Andersson, J., & Nordberg, A. (1997). Brain activation in young and older adults during implicit and explicit retrieval. *Journal of Cognitive Neuroscience*, *9*, 378–391.
- Brooks, J. O., III, Gibson, J. M., Friedman, L., & Yesavage, J. A. (1999). How to drastically reduce priming in word stem completion—and still present the words. *Memory & Cognition*, *27*, 208–219.
- Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: The HAROLD model. *Psychology and Aging*, *17*, 85–100.
- Cabeza, R., Anderson, N. D., Locantore, J. K., & McIntosh, A. R. (2002). Aging gracefully: Compensatory brain activity in high-performing older adults. *Neuroimage*, *17*, 1394–1402.
- Cabeza, R., Nyberg, L., & Park, D. C. (2005). *Cognitive neuroscience of aging*. New York: Oxford University Press.
- Craik, F. I. M. (1994). Memory changes in normal aging. *Current Directions in Psychological Science*, *3*, 155–158.
- Daselaar, S. M., Veltman, D. J., Rombouts, S. A., Raaijmakers, J. G., & Jonker, C. (2005). Aging affects both perceptual and lexical/semantic components of word stem priming: An event-related fMRI study. *Neurobiology of Learning and Memory*, *83*, 251–262.
- Davachi, L. (2006). Item, context and relational episodic encoding in humans. *Current Opinion in Neurobiology*, *16*, 693–700.
- 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.

- Fiebach, C. J., Gruber, T., & Supp, G. G. (2005). Neuronal mechanisms of repetition priming in occipitotemporal cortex: Spatiotemporal evidence from functional magnetic resonance imaging and electroencephalography. *Journal of Neuroscience*, *25*, 3414–3422.
- Fleischman, D. A., & Gabrieli, J. D. E. (1998). Repetition priming in normal ageing and Alzheimer's disease: A review of findings and theories. *Psychology and Ageing*, *13*, 88–119.
- Grady, C. L., Springer, M. V., Hongwanishkul, D., McIntosh, A. R., & Winocur, G. (2006). Age-related changes in brain activity across the adult lifespan. *Journal of Cognitive Neuroscience*, *18*, 227–241.
- Habeck, C., Hilton, H. J., Zarahn, E., Brown, T., & Stern, Y. (2006). An event-related fMRI study of the neural networks underlying repetition suppression and reaction time priming in implicit visual memory. *Brain Research*, *1075*, 133–141.
- Hedden, T., & Gabrieli, J. D. (2005). Healthy and pathological processes in adult development: New evidence from neuroimaging of the aging brain. *Current Opinion in Neurology*, *18*, 740–747.
- Henson, R., Shallice, T., & Dolan, R. (2000). Neuroimaging evidence for dissociable forms of repetition priming. *Science*, *287*, 1269–1272.
- Henson, R. N. (2003). Neuroimaging studies of priming. *Progress in Neurobiology*, *70*, 53–81.
- Henson, R. N., Rylands, A., Ross, E., Vuilleumeir, P., & Rugg, M. D. (2004). The effect of repetition lag on electrophysiological and haemodynamic correlates of visual object priming. *Neuroimage*, *21*, 1674–1689.
- Hwang, D. Y., & Golby, A. J. (2006). The brain basis for episodic memory: Insights from functional MRI, intracranial EEG, and patients with epilepsy. *Epilepsy Behavior*, *8*, 115–126.
- Jelicic, M. (1995). Aging and performance on implicit memory tasks: A brief review. *International Journal of Neuroscience*, *82*, 155–161.
- Jiang, Y., & Kanwisher, N. (2003). Common neural substrates for response selection across modalities and mapping paradigms. *Journal of Cognitive Neuroscience*, *15*, 1080–1094.
- Koutstaal, W., Wagner, A. D., Rotte, M., Maril, A., Buckner, R. L., & Schacter, D. L. (2001). Perceptual specificity in visual object priming: Functional magnetic resonance imaging evidence for a laterality difference in fusiform cortex. *Neuropsychologia*, *39*, 184–199.
- Light, L. L., La Voie, D., & Kennison, R. (1995). Repetition priming of nonwords in young and older adults. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *21*, 327–346.
- Light, L. L., Prull, M. W., La Voie, D. J., & Healy, M. R. (2000). Dual process theories of memory in old age. In T. J. Perfect & E. A. Maylor (Eds.), *Models of cognitive ageing* (pp. 238–300). Oxford, UK: Oxford University Press.
- Lustig, C., & Buckner, R. L. (2004). Preserved neural correlates of priming in old age and dementia. *Neuron*, *42*, 865–875.
- Lustig, C., Snyder, A. Z., Bhakta, M., O'Brien, K. C., McAvoy, M., Raichle, M. E., et al. (2003). Functional deactivations: Change with age and dementia of the Alzheimer type. *Proceedings of the National Academy of Sciences, U.S.A.*, *100*, 14504–14509.
- 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.
- Mason, M. F., Norton, M. I., Van Horn, J. D., Wegner, D. M., Grafton, S. T., & Macrae, C. N. (2007). Wandering minds: The default network and stimulus-independent thought. *Science*, *315*, 393–395.
- McKiernan, K. A., D'Angelo, B. R., Kaufman, J. N., & Binder, J. R. (2006). Interrupting the “stream of consciousness”: An fMRI investigation. *Neuroimage*, *29*, 1185–1191.
- McKiernan, K. A., Kaufman, J. N., Kucera-Thompson, J., & Binder, J. R. (2003). A parametric manipulation of factors affecting task-induced deactivation in functional neuroimaging. *Journal of Cognitive Neuroscience*, *15*, 394–408.
- Mitchell, D. B., & Bruss, P. J. (2003). Age differences in implicit memory: Conceptual, perceptual, or methodological? *Psychology and Aging*, *18*, 807–822.
- Nordahl, C. W., Ranganath, C., Yonelinas, A. P., Decarli, C., Fletcher, E., & Jagust, W. J. (2006). White matter changes compromise prefrontal cortex function in healthy elderly individuals. *Journal of Cognitive Neuroscience*, *18*, 418–429.
- Orfanidou, E., Marslen-Wilson, W. D., & Davis, M. H. (2006). Neural response suppression predicts repetition priming of spoken words and pseudowords. *Journal of Cognitive Neuroscience*, *18*, 1237–1252.
- Persson, J., Lustig, C., Nelson, J. K., & Reuter-Lorenz, P. A. (2007). Age differences in deactivation: A link to cognitive control? *Journal of Cognitive Neuroscience*, *19*, 1021–1032.
- Persson, J., Nyberg, L., Lind, J., Larsson, A., Nilsson, L. G., Ingvar, M., et al. (2006). Structure–function correlates of cognitive decline in aging. *Cerebral Cortex*, *16*, 907–915.
- Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences, U.S.A.*, *98*, 676–682.
- Rajah, M. N., & D'Esposito, M. (2005). Region-specific changes in prefrontal function with age: A review of PET and fMRI studies on working and episodic memory. *Brain*, *128*, 1964–1983.
- Reuter-Lorenz, P. (2002). New visions of the aging mind and brain. *Trends in Cognitive Sciences*, *6*, 394.
- Rueckl, J. G., & Mathew, S. (1999). Implicit memory for phonological processes in visual stem completion. *Memory & Cognition*, *27*, 1–11.
- Rybash, J. M. (1996). Implicit memory in ageing: A cognitive neuropsychological perspective. *Developmental Neuropsychology*, *12*, 127–179.
- Salthouse, T. (1985). *A theory of cognitive aging*. Amsterdam: North-Holland.
- Sayres, R., & Grill-Spector, K. (2006). Object-selective cortex exhibits performance-independent repetition suppression. *Journal of Neurophysiology*, *95*, 995–1007.
- Scarmeas, N., Zarahn, E., Anderson, K. E., Hilton, J., Flynn, J., Van Heertum, R. L., et al. (2003). Cognitive reserve modulates functional brain responses during memory tasks: A PET study in healthy young and elderly subjects. *Neuroimage*, *19*, 1215–1227.
- Schacter, D. L., & Buckner, R. L. (1998). On the relations among priming, conscious recollection, and intentional retrieval: Evidence from neuroimaging research. *Neurobiology of Learning and Memory*, *70*, 284–303.
- Schacter, D. L., Cooper, L. A., & Valdiserri, M. (1992). Implicit and explicit memory for novel visual objects in older and younger adults. *Psychology and Aging*, *7*, 299–308.
- Schacter, D. L., Reiman, E., Uecker, A., Polster, M. R., Yun, L. S., & Cooper, L. A. (1995). Brain regions associated with retrieval of structurally coherent visual information. *Nature*, *376*, 587–590.
- Schumacher, E. H., Elston, P. A., & D'Esposito, M. (2003). Neural evidence for representation-specific response selection. *Journal of Cognitive Neuroscience*, *15*, 1111–1121.

- Simons, J. S., Koutstaal, W., Prince, S., Wagner, A. D., & Schacter, D. L. (2003). Neural mechanisms of visual object priming: Evidence for perceptual and semantic distinctions in fusiform cortex. *Neuroimage*, *19*, 613–626.
- Soldan, A., Mangels, J. A., & Cooper, L. A. (2006). Evaluating models of object-decision priming: Evidence from event-related potential repetition effects. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *32*, 230–248.
- Soldan, A., Zarahn, E., Hilton, H. J., & Stern, Y. (2008). Global familiarity of visual stimuli affects repetition-related neural plasticity but not repetition priming. *Neuroimage*, *39*, 515–526.
- Stern, Y., Habeck, C., Moeller, J., Scarmeas, N., Anderson, K. E., Hilton, H. J., et al. (2005). Brain networks associated with cognitive reserve in healthy young and old adults. *Cerebral Cortex*, *15*, 394–402.
- Stuart, G. P., Patel, J., & Bhagrath, N. (2006). Ageing affects conceptual but not perceptual memory processes. *Memory*, *14*, 345–358.
- Wagner, A. D., Koutstaal, W., Maril, A., Schacter, D. L., & Buckner, R. L. (2000). Task-specific repetition priming in left inferior prefrontal cortex. *Cerebral Cortex*, *10*, 1176–1184.
- Wiggs, C. L., & Martin, A. (1998). Properties and mechanisms of perceptual priming. *Current Opinion in Neurobiology*, *8*, 227–233.
- Worsley, K. J., Marrett, S., Neelin, P., Vandal, A. C., Friston, K. J., & Evans, A. C. (1996). A unified statistical approach for determining significant signals in images of cerebral activation. *Human Brain Mapping*, *4*, 58–73.
- Worsley, K. J., Poline, J. B., Friston, K. J., & Evans, A. C. (1997). Characterizing the response of PET and fMRI data using multivariate linear models. *Neuroimage*, *6*, 305–319.
- Zarahn, E., Rakitin, B., Abela, D., Flynn, J., & Stern, Y. (1997). Age-related changes in brain activation during a delayed item recognition task. *Neurobiology of Aging*, *28*, 784–798.