

# Extensive stimulus repetition leads older adults to show delayed functional magnetic resonance imaging adaptation

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**Abstract** We investigated whether extensive repetition can diminish age-related differences between younger and older adults in functional magnetic resonance adaptation (fMR-A). Datasets were obtained from 26 younger and 24 older healthy adults presented with two scenes that repeated 20 times amongst other novel scenes during fMRI scanning. The average cortical responses to the first eight (Repetitions 1-7) and the last eight (Repetitions 12-19) presentations out of 20 were compared within each group. Younger adults showed similar levels of fMR-A in both repetition sets.

Conversely, older adults did not show reliable fMR-A in Repetitions 1-7, but they did in Repetitions 12-19; subtracting the latter from the former revealed a significant effect within left inferior occipital, left lingual, and the posterior part of fusiform gyrus. We concluded that cortical responsiveness in older adults are compromised, but extensive repetition can lead older adults to show a delayed but closer level of fMR-A compared to younger adults.

**Keywords** Aging · fMRI · Adaptation · Repetition suppression · Scene recognition · Parahippocampus

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Functional brain imaging studies have clarified changing patterns in cortical activation (e.g. Park and Reuter-Lorenz 2009) as well as neural responsiveness during the course of aging. Brain activity is by nature transient, and evaluating its responsiveness in the temporal domain is necessary to better understand the aging brain. This has been done by measuring functional magnetic resonance adaptation (fMR-A), which indicates reduction in the magnitude of neural activity as a result of repeated stimulus presentation within functionally relevant cortical areas (Grill-Spector et al. 1999; Grill-Spector et al. 2006; Grill-Spector and Malach 2001; see also Desimone 1996; Wiggs and Martin 1998; but see Sawamura et al. 2006). Current studies shows that fMR-A changes with age; for example, older adults consistently show reduced fMR-A to repeated foreground objects during passive viewing tasks (Chee et al. 2006; Goh et al. 2007). Older adults showed reduced fMR-A compared to younger adults for repeatedly presented background scenes at least in Westerners (Goh et al. 2007) and faces (Lee et al. 2011). Similar age-related differences in fMR-A between younger and older adults also occur during auditory tasks (Grady et al. 2011). Together, these findings suggest that fMR-A is reduced with

age in simple tasks such as passive visual/audio recognition or making judgments based on perceptual aspects of stimuli. On the other hand, when a cognitive task engages more complicated processes, such as face identity judgments, fMR-A could increase with age because of decreased neural selectivity within the higher order visual area, as shown in Goh et al. (2010) in which an age-related increase in fMR-A was observed due to reduced neural selectivity when a target face is primed with a similar but not identical face. Deficits in age-related fMR-A are also observed for inhibitory attentional control with older adults showing increased fMRI-A in response to task-irrelevant visual information (Schmitz et al. 2010). Together, these findings suggest that fMR-A changes with age because of various kinds of cognitive decline. Simple perceptual tasks are associated with reduced fMR-A compared to younger adults, whereas reduced neural selectivity and inhibitory control deficits are associated with increased fMR-A.

There is evidence that fMR-A correlates with cognitive performance. For example, self-reported navigational competence was correlated with the magnitude of fMR-A within the parahippocampal gyrus to repeatedly presented pictures of a house (Epstein et al. 2005). In an auditory task, greater fMR-A within auditory cortex was associated with task performance in older adults (Grady et al. 2008). In the repetition priming task, greater fMR-A within the right prefrontal cortex was correlated with better performance in semantic processing in older adults (Bergerbest et al. 2009). These findings suggest that fMR-A is associated with better behavioral performance, which seems to indicate a connection with age-related fMR-A reduction. Possible reasons for reduced fMR-A with age could be bottom-up, physiological changes such as cellular and vascular alteration. However, it is also known that top-down attentional control modulates fMR-A; it was reported that fMR-A was recovered when older adults were explicitly instructed to attend to a task-relevant aspect of the stimuli (Chee et al. 2006). It was also shown that older adults show fMR-A to task-irrelevant stimulus features, which indicates inappropriate allocation of attentional resources (Schmitz et al. 2010). Therefore, two possible mechanisms explain fMR-A changes with age: bottom-up, physiological changes and top-down, attentional control deficits.

A possible reason for age-related differences in fMR-A in a simple visual task between younger and older adults is a lowered fMR-A plateau level. However, another possibility is a slow fMR-A with a relatively unchanged plateau level. If the second possibility is the case, then extensive repetition would increase fMR-A in older adults to a level similar to that seen in younger adults. This is in line with the fact that when older adults experience more repetition, their behavioral performance is closer to that of younger adults. From this, we hypothesized that older adults evince less responsive neural

processing compared to younger adults, and extensive repetition may help older adults achieve fMR-A comparable to younger adults. However, this possibility has not been explicitly addressed, as it is a common idea that fMR-A reaches a plateau after six to eight repetitions (Grill-Spector et al. 2006). Nonetheless, fMR-A continues to change beyond that point. Grill-Spector et al. (2008) demonstrated that fMR-A magnitude increased up to 32 presentations when the same pictures were presented 0, 4, 8, 16, and 32 times within each 32-s block (see also Grill-Spector et al. 2006). We speculated that six to eight repetitions may not be sufficient for older adults to effect full fMR-A, and that extensive repetition (more than eight) should induce fMR-A in older adults that is compared to fMR-A in younger adults.

The purpose of the present study was to examine whether extensive stimulus repetition would lead to fMR-A in older adults that are comparable to those found in younger adults with fewer stimulus repetitions. We analyzed datasets that included cortical responses to the repetitive presentation of visual stimuli: an indoor and an outdoor scene, 20 times each. Data during the first 1–8 presentations (Repetitions 1–7) were compared to those during the last 13–20 presentations (Repetitions 12–19) within each group. We expected that older adults would show a greater fMR-A during Repetitions 12–19, while younger adults would show significant fMR-A during early repetition that is maintained with extensive stimulus repetition. The results from other contrasts, including age-related changes in relational processes represented by Novel Pictures task minus Novel Scrambled task (Binder et al. 2005) are outside the scope of the present study and will be presented elsewhere.

## Materials and methods

### Ethics statement

The experiment was approved by the ethics committee of the National Center for Geriatrics and Gerontology, Japan. All experimental procedures were performed in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants.

### Participants

The young participants were 26 healthy adults (14 female, 1 left-handed, mean age 21.6, SD=1.6) with a mean minimal state exam (MMSE; Folstein et al. 1975) score of 29.1 (SD=0.9, range 27–30). The study began with 26 older adults, but datasets from the two participants were excluded because they both scored 23 on the MMSE. Data from the remaining 24 healthy older adults (12 female, 2 left-handed, mean age 66.4, SD=3.0, mean MMSE score 28.7, SD=1.1,

range 26–30) were analyzed. Handedness was determined using the Edinburgh Inventory (Oldfield 1971).

### Task

The participants performed an incidental-encoding task (Binder et al. 2005; Golby et al. 2001) adapted to the local population. The Novel Pictures and Repeating Pictures tasks required participants to discriminate indoor from outdoor scenes. The stimuli were selected from digital color pictures taken by the authors. Each image was resized to  $600 \times 600$  pixels and subtended  $22.5^\circ$  of horizontal and vertical visual angle in the scanner. These pictures did not contain words or people. A total of 40 unique pictures were presented during the Novel Pictures task, while two unique pictures were repeatedly presented 20 times each during the Repeating Pictures task. The Novel Scrambled task required participants to decide whether the left and right halves of scrambled nonsense images were identical. These stimuli were created by randomly rearranging 20-pixel square segments

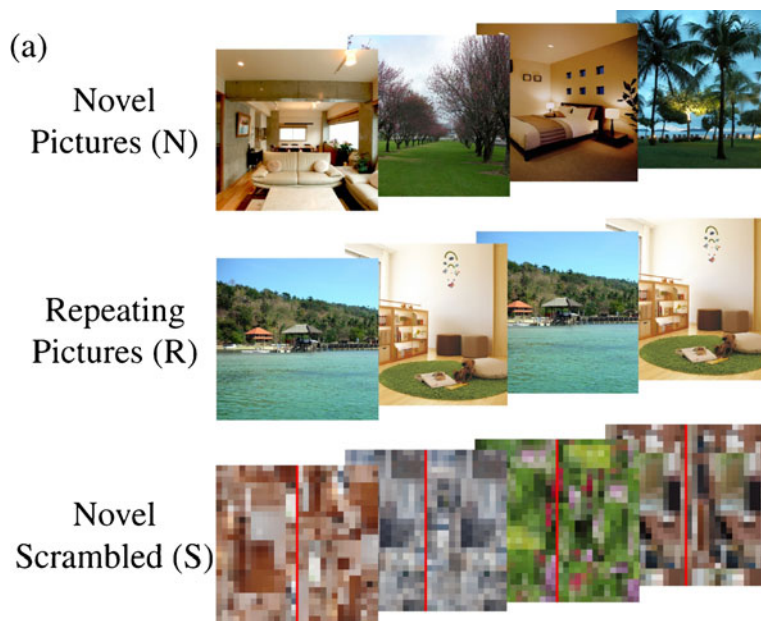
of the indoor and outdoor pictures. The halves of these scrambled images ( $600 \times 300$  pixels) were either combined with another retiling of the same picture to create mismatched halves or were duplicated to produce matched halves (targets). A red line bisected each stimulus to define the medial border of the hemifields. A total of 40 unique scrambled images were presented during the Novel Scrambled task. Examples of experimental stimuli are shown in Fig. 1a.

The stimuli were presented on a black background for 2500 ms and were separated by 500 ms blank interstimulus intervals. The stimuli were blocked by task into epochs lasting 24 s, with eight trials of a given task in each epoch. Each epoch included an equal number of stimulus types (indoor/outdoor, identical/not identical halves). Five epochs were administered for each task for a total of 15 epochs. The order of the three epochs was fixed (Novel Pictures task, Repeating Pictures task, and Novel Scrambled task), and the set of three epochs was repeated five times. Participants were instructed to press a button with the index finger when

**Fig. 1** Stimuli and contrast design used in the present study. **a** Example stimulus categories and presentation sequences.

Novel Pictures (N) was composed of 40 unique indoor and outdoor scenes. Repeating Pictures (R) consisted of an indoor and an outdoor scene that were presented 20 times each. Novel Scrambled (S) was composed of 40 unique images of pixelated and randomly scrambled scene images (note this condition is not examined in the present study). **b**

Schematic illustration of within-subject fMRI contrast. The factorial design was  $2 \times 2$ ; Group (Younger, Older) minus Repetition (1–7, 12–19)



(b)

Younger Adults	Epoch1 $N_1R_1S_1$ $(N_1+N_2)-(R_1+R_2)$ Repetition 1-7	Epoch2 $N_2R_2S_2$	Epoch3 $N_3R_3S_3$	Epoch4 $N_4R_4S_4$ $(N_4+N_5)-(R_4+R_5)$ Repetition 12-19	Epoch5 $N_5R_5S_5$
Older Adults	Epoch1 $N_1R_1S_1$ $(N_1+N_2)-(R_1+R_2)$ Repetition 1-7	Epoch2 $N_2R_2S_2$	Epoch3 $N_3R_3S_3$	Epoch4 $N_4R_4S_4$ $(N_4+N_5)-(R_4+R_5)$ Repetition 12-19	Epoch5 $N_5R_5S_5$

viewing an indoor scene and to press another button with the middle finger for an outdoor scene during the Novel Pictures and Repeating Pictures tasks. The participants' task during the Novel Scrambled task was to press a button assigned to the index finger when the left and right halves of the scrambled nonsense images were not identical and to press a button assigned to the middle finger when the bisected halves were identical.

#### Image acquisition and preprocesses

Imaging was performed with a 3.0-Tesla MRI scanner (MAGNETOM Trio, Siemens, Erlangen, Germany). Functional imaging of the entire brain was conducted using a gradient-echo echo-planar sequence (TE, 24 ms; TR, 2000 ms; FOV, 192 mm; matrix, 64×64; slice thickness, 3 mm; gap between slices, 0.75 mm). A series of 180 consecutive image volumes was acquired during functional scans. An additional set of high-resolution, T1-weighted anatomic reference images was obtained for localization purposes. The visual stimuli were presented with VisuaStimDigital for MRI (Resonance Technology Inc., CA, United States).

Image processing and analyses were performed with statistical parametric mapping (Friston et al., 1995) implemented in SPM8 (The FIL Methods Group, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL) running under MATLAB 7.9 (The MathWorks, MA, United States). Anatomical locations were identified with SPM toolbox WFU PickAtlas 2.4 (Lancaster et al. 1997, 2000; Maldjian et al. 2003; Maldjian et al. 2004; Tzourio-Mazoyer et al. 2002). The signal time-courses of regions of interest (ROIs) were calculated with MarsBaR 0.42 (Brett et al. 2002). The functional images were preprocessed with realignment, slice-timing correction, coregistration to the individual structural image, normalization to the template-matched segmented individual gray matter images with 2×2×2 mm resampling, and smoothing with the Gaussian kernel of 8 mm full width half maximum (FWHM). The Montreal Neurological Institute (MNI) coordinate system (ON, Canada) was used. Individual contrast maps were obtained using the General Linear Model.

#### Task validation

The experimental design of the current study was adopted from Binder et al. (2005) and Golby et al. (2001); thus, we first validated our experimental design by comparing the results from younger adults in this study to those from Binder et al. (2005). The results compared were of the Novel Pictures task minus Repeating Pictures task, the Novel Pictures task minus Novel Scrambled task, and the peak voxel

locations within bilateral hippocampi. Details of these comparison will be published elsewhere.

#### Designs for statistical tests

For behavioral data analyses, reaction times and response accuracies were tested with 2×2 mixed design ANOVA (Group vs. Repetitions); the factorial design was Group (Younger, Older) vs. Repetitions (1-7, 12-19). Greenhouse-Geisser correction was used wherever necessary. Uncorrected degrees of freedom with corrected p-values are reported. Post-hoc multiple comparisons were performed when the interaction was significant, and multiple comparison correction was performed with LSD method.

Functional MR-adaptation was examined with a block-design, which has demonstrated better sensitivity in measuring fMR-A compared with an event-related design (Grill-Spector et al. 1999; Grill-Spector et al. 2006). The Novel Pictures task served as a baseline to which fMR-A during the Repeating Pictures task was compared. The schematic illustration of data processing is shown in Fig. 1b. In creating a design matrix for the subject level, each epoch (comprised of 8 trials, resulting in 24 s length) was specified as a unit of block, resulting in 15 blocks in total. For each subject, Novel Pictures task minus Repeating Pictures task was calculated for the first and last two epochs, and the results were submitted to the subsequent group-level analysis. Random effects analyses were conducted on the group level with the factorial design Group (Younger, Older) vs. Repetitions (1-7, 12-19). First, a mixed design analysis of variance (ANOVA) was performed to test the 2×2 interaction. Two within-group comparisons of the first eight repetitions (Repetitions 1-7) minus the last eight repetitions (Repetitions 12-19) were conducted separately. A significance level was set to  $P<0.05$  for cluster-level correction with False Discovery Rate (FDR). Subsequently, the significant cluster obtained in the above subtraction served as an ROI to calculate epoch-by-epoch changes in fMR-A magnitude.

## Results

#### Behavioral data

The mean RT of the younger adults was 712.9 ms (SD=24.0) for Repetitions 1-7 and 702.8 ms (SD=29.0) for Repetitions 12-19. Those of the older adults were 913.7 ms (SE=27.8) and 859.0 ms (SE=33.6), respectively. A mixed design ANOVA revealed that the Age by Repetition interaction was marginally significant,  $F(1, 48)=2.97$ ,  $P=0.09$ , and main effects of Age and Repetition were significant,  $F(1, 48)=27.0$ ,  $P<0.001$  and  $F(1, 48)=6.30$ ,  $P<$



0.05, respectively. We performed a priori multiple comparisons for examining the direction of the interaction, and found that older adults had significantly shorter RTs during Repetitions 12–19 than during Repetitions 1–7 ( $P < 0.005$ ). None of the other comparisons reached the level of significance. The same analyses were performed for response accuracy. Younger adults showed a mean accuracy of 99.2% (SD=2.3) during Repetitions 1–7 and a mean accuracy of 99.6% (SD=1.4) during Repetitions 12–19. Older adults showed a mean accuracy of 99.2% (SD=1.9) and a mean accuracy of 99.0% (SD=0.3), respectively. Neither the ANOVA nor the multiple comparisons produced significant results in response accuracy.

#### Validation of the current task with imaging data

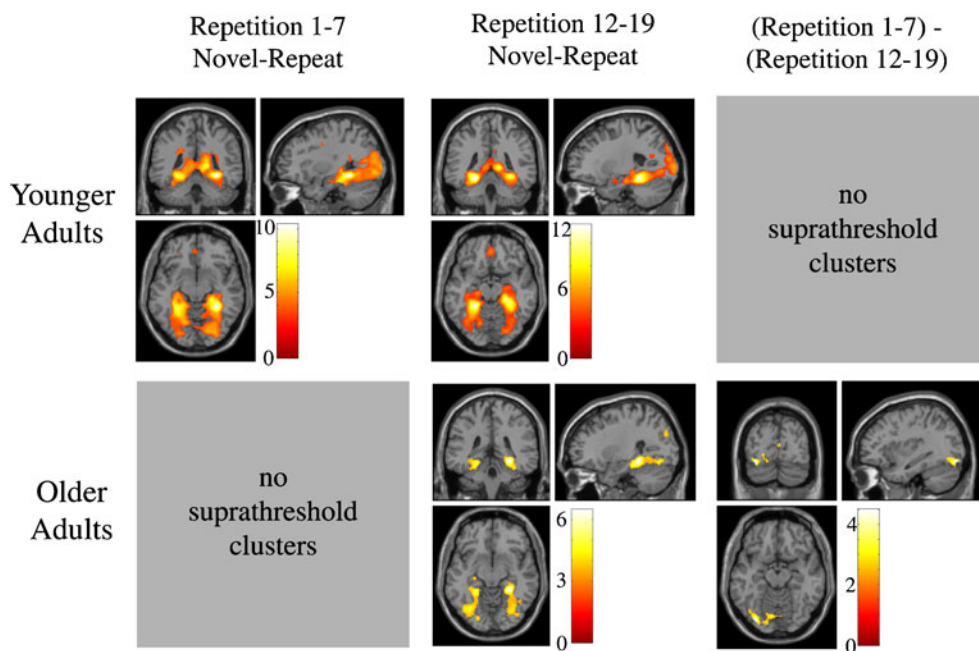
For the fMRI data analysis, task validation was first performed by comparing the current results of younger adults with Binder et al. (2005), from which the experimental design was adapted. We will briefly present results for replication purposes, and details will be reported elsewhere. The contrast Novel Pictures task minus Repeating Pictures task produced activations in fusiform, anterior cingulate, right postcentral, and left medial superior frontal. The contrast Novel Pictures task minus Novel Scrambled task produced activations in parahippocampi, angular, middle orbitofrontal, superior temporal, superior temporal poles, left middle frontal, and precentral. These patterns were consistent with Binder et al. (2005). Furthermore, an ROI analysis of the bilateral hippocampi based on Binder et al. (2005) revealed that peak voxels within the hippocampi were more posterior with the Novel Pictures task minus Repeating Pictures task than that of the Novel Pictures task minus Novel

Scrambled task, which also replicated the previous findings. The current task was thus validated by the successful replication of previous findings in younger adult data.

#### The effect of extensive repetition on older adults

First, a mixed design ANOVA analyzing group (Younger adults vs. Older adults) and Repetitions (Repetitions 1–7 vs. Repetitions 12–19) was performed. However, no clusters survived the statistical threshold in the interaction or main effects test. Next, a within-group comparison of Repetitions 1–7 minus Repetitions 12–19 was performed separately for younger and older adults. The results are shown in Fig. 2 and Table 1. Younger adults showed clear fMR-A during Repetitions 1–7 in areas including fusiform, parahippocampal, calcarine, median cingulate, paracingulate, and supplementary motor. During Repetitions 12–19, significant clusters were found in areas including fusiform, precuneus, and orbital part of superior frontal. Then, to test the effect of extensive repetition, the results from Repetitions 12–19 were subtracted from that of Repetitions 1–7. This did not yield a significant cluster for younger adults, suggesting that extensive repetition was not effective for them to further develop fMR-A. Older adults showed a different pattern; testing fMR-A during Repetitions 1–7 did not produce a significant cluster, which suggests a diminished fMR-A magnitude in older adults up to seven repetitions. During Repetitions 12–19, the results showed significant clusters in areas including parahippocampal, fusiform, and middle occipital. Then, Repetitions 12–19 were subtracted from Repetitions 1–7. This showed a significant cluster that includes left inferior occipital, left lingual, and a posterior part of the left

**Fig. 2** The results of fMR-A represented by Novel pictures task-Repeating pictures task from younger adults (*top row*) and older adults (*bottom row*) for Repetitions 1–7 (*left column*), Repetitions 12–19 (*middle column*), and subtraction of Repetitions 1–7 – Repetitions 12–19 (*right column*). Statistical thresholds used were  $P < 0.05$  for a cluster-level with FDR correction



**Table 1** Results for Repetitions 1–7, Repetitions 12–19, and within-group comparison for repetitions 1–7 minus Repetitions 12–19. ( $P < 0.05$  for a cluster-level with FDR correction).

Structure	Brodmann area	Cluster size (P-value)	t-value (Z-score)	MNI coordinate x y z
Younger adults, Repetitions 1-7				
Fusiform gyrus	19	18867 (0.001)	10.34 (7.46)	32 -44 -10
Median cingulate and paracingulate gyri	24	520 (0.001)	5.29 (4.67)	-4 -14 36
Older adults, Repetitions 1-7 (no suprathreshold clusters)				
Younger adults, Repetitions 12-19				
Fusiform gyrus	36	14242 (0.001)	11.68 (>7.62)	-24 -42 -14
Anterior cingulate and paracingulate gyri	32	634 (0.001)	5.96 (5.13)	-10 34 -4
Older adults, Repetitions 12-19				
Parahippocampal gyrus	19	1112 (0.001)	6.48 (5.47)	28 -38 -10
Fusiform gyrus	36	1094 (0.001)	5.30 (4.68)	-24 -42 -12
Middle occipital gyrus	19	257 (0.007)	3.98 (3.68)	42 -76 20
Younger adults, 1-7 minus 12-19 (no suprathreshold clusters)				
Older adults, 1-7 minus 12-19				
Fusiform gyrus	18	839 (0.030)	4.49 (4.08)	-34 -82 -14

fusiform. Together, the results suggest that the extensive repetition effects comparable fMR-A magnitudes in older adults compared to younger adults.

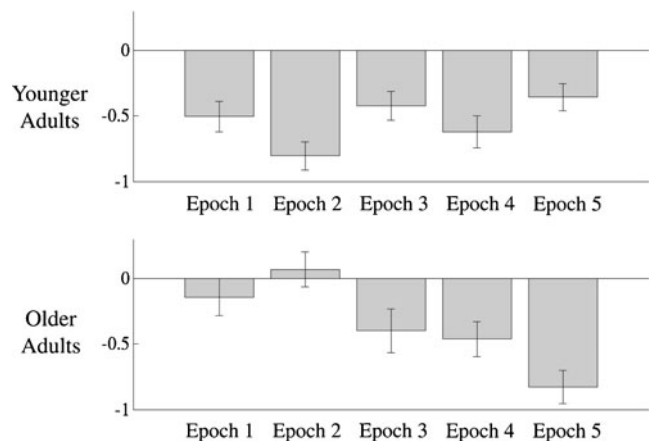
To further examine the effect of extensive repetition in older adults, we calculated epoch-by-epoch changes in a contrast estimate from an ROI that was defined as the area that showed significant difference in the contrast Repetitions 1-7 minus Repetitions 12-19 in the older adults (the activation map shown in the bottom-right in the Fig. 2). For the purpose of comparison, the same ROI was also applied to younger adults. The results are shown in Fig. 3. Comparing bar graphs between younger and older adults, we observed that older adults showed increased fMR-A magnitude as the repetition number increases, while younger adults did not. To examine the difference in the pattern, two-way mixed design ANOVAs (2 groups x 5 epochs) were performed. This revealed a significant interaction,  $F(4, 192) = 2.46$ ,  $P < 0.05$ , and multiple post-hoc comparisons with LSD corrections revealed a significant difference in the second epoch during which fMR-A of the younger adults was significantly increased than that of older adults ( $P < 0.05$ ). The ROI analysis thus indicated that fMR-A of older adults was slow, and extensive repetition led to fMR-A increases.

## Discussion

The results from the present study demonstrated that extensive repetition of simple visual stimuli increased fMR-A in older adults that is otherwise reduced in normal aging. The cortical areas that showed this effect include left inferior

occipital, left lingual, and the posterior portion of the left fusiforms gyrus. In contrast, extensive repetition did not significantly change fMR-A in younger adults. Some details of our findings are noteworthy of further discussion.

In our results, the left lingual gyrus of older adults showed continued fMR-A increase due to extensive stimulus repetition. Although the functional role of the lingual gyrus in scene recognition is not clearly defined, it is



**Fig. 3** Epoch-by-epoch changes in contrast estimates for younger adults (*top*) and older adults (*bottom*). The contrast estimates were calculated from an ROI that was defined to be the area that showed significant difference in the contrast Older adults Repetitions 1-7 minus Older adults Repetitions 12-19 (the activation map shown in the bottom-right in the Fig. 2). Mean values with 1 standard error are shown. Note the same ROI obtained from the older adults was also applied to younger adult data for the purpose of comparison. Two-way mixed design ANOVAs on groups vs. epochs revealed a significant interaction ( $P < 0.05$ )

reported in previous studies with younger adults that lingual and parahippocampal gyri show fMR-A to a repeatedly presented background scene (Chee et al. 2006; Goh et al. 2007). Functional MR-A in parahippocampal, which is primarily involved in scene recognition (Epstein and Kanwisher 1998; Chee et al. 2006), was not found in the present results, suggesting differential effects of extensive repetition on parahippocampal and lingual gyri. This may suggest that extensive repetition recruits relevant, but not functionally dedicated, regions. Other cortical regions that were found to show age-related effects for extensive repetition are left inferior occipital and the posterior part of the fusiform gyrus. In previous studies, these areas showed fMR-A to foreground objects but not to background scenes (Chee et al. 2006), and, intriguingly, neither region is known to be primarily involved in scene recognition. Our collective results suggest that extensive repetition in older adults recruited cortical regions that were related but not primarily dedicated to scene recognition, which may be related to compensatory mechanisms (Grady 2008).

There is a debate regarding whether age-related fMR-A is due to age-related deficits in physiological integrity or attentional control. A growing body of evidence suggests that older adults have deficits in inhibitory control of attention. For example, older adults have difficulty ignoring distracting information, particularly when it is meaningfully related to the target text (Connelly et al. 1991). It was suggested that hippocampal function is preserved in normal aging and that repetition-based memory enhancement engages attentional networks in the prefrontal cortex (Rand-Giovannetti et al. 2006). Supporting evidence for this view continues to emerge (Dale Stevens et al. 2008; Healey et al. 2008; Park and Reuter-Lorenz 2009; Sperling 2007). It is known that the control of attention changes neural activity (Murray and Wojciulik 2004; Yi and Chun 2005), and verbal instruction to attend to task-relevant visual objects help older adults recruit the functionally relevant cortical areas as younger adults did (Chee et al. 2006). However, this interpretation does not seem to be applicable to the present study because participants were instructed to perform a cognitive task, and their attentional states should have been equally controlled during the repetitive presentation. This is in contrast to previous studies that used passive viewing tasks in which participants were not clearly goal-oriented and their attentional states were less controlled (Chee et al. 2006; Goh et al. 2007). Given that a verbal instruction to internally control attention was sufficient to change cortical activation patterns, a goal-directed cognitive task that requires rapid, accurate judgment should engage more attention. This seems to suggest that at least a part of reduction in age-related fMR-A was triggered by bottom-up, physiological causes, rather than age-related attentional deficits. The literature suggests an altered cellular functionality due to  $\text{Ca}^{2+}$

homeostasis changes in pyramidal cells (Burke and Barnes 2006), synaptic changes that affect the formation of long-term potentiation (Rosenzweig et al. 1997), and vascular changes such as blood vessel stiffening (D'Esposito et al. 2003) as possible physiological reasons for reduced fMR-A in normal aging. Other supportive evidence includes findings that the onset of neural fMR-A measured by single-unit recording from area IT is approximately 150 ms after stimulus, which is considered to be too early for top-down influences (Xiang and Brown 1998). Similarly, the effect of visual repetition at occipitotemporal sites begins from 170 to 180 ms in human EEG studies (Begleiter et al. 1993; Schweinberger et al. 1995), which agrees with findings from animal studies. All of these reports suggest bottom-up, physiological mechanisms for reduced fMR-A in older adults. It should be also considered that in the current study, the cognitive demand could have been different between younger and older groups since we used the same task for both groups without controlling for task demand. Because of this, it is possible that the younger adults could have had more attentional resources at the early stage of the task, which can be associated with fMR-A, but the older adults may have had little attentional resources available at the early stage. If this was the case, it suggests the possibility that group differences were based on the relative difference in attentional resources between the two groups, which undermines the explanation by bottom-up, physiological causes. Taken together, our interpretation is that our results may be partly due to less attentional resources in older adults, as suggested by Chee et al. (2006) and Goh et al. (2007), and partly due to age-related changes in bottom-up mechanisms.

The current study is not without limitations. The stimuli presented in the study depicted scenes. It is unknown whether our findings can be generalized to other types of visual objects that are known to be processed in other specific cortical regions, such as faces and letters. It would be informative to clarify the stimulus type dependency of reduced fMR-A. Another issue is that the link between fMR-A and behavioral performance is not clear because the experimental design was not dedicated to that purpose. Additional evidence is required to strengthen the link between neural adaptation and behavioral performance.

## Conclusions

The present study demonstrated that extensive stimulus repetition (more than eight repetitions) helps older adults to further increase fMR-A within left inferior occipital, left lingual, and the posterior part of the fusiform, which is usually reduced during normal aging. These recruited regions are relevant, but not primarily dedicated, to scene

recognition in younger adults, suggesting that extensive repetition may involve functionally related areas. Cortical responsiveness in older adults are compromised, but extensive repetition can lead older adults to show a delayed but closer level of fMR-A compared to younger adults.

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## References

- Begleiter, H., Porjesz, B., & Wang, W. (1993). A neurophysiologic correlate of visual short-term memory in humans. *Electroencephalography and Clinical Neurophysiology*, 87, 46–53.
- Bergerbest, D., Gabrieli, J. D. E., Whitfield-Gabrieli, S., Kim, H., Stebbins, G. T., Bennett, D. A., & Fleishman, D. A. (2009). Age-associated reduction of asymmetry in prefrontal function and preservation of conceptual repetition priming. *Neuroimage*, 45, 237–246.
- Binder, J. R., Bellgowan, P. S. F., Hammeke, T. A., Possing, E. T., & Frost, J. A. (2005). A comparison of two fMRI protocols for eliciting hippocampal activation. *Epilepsia*, 46, 1061–1070.
- Brett, M., Anton, J.-L., Valabregue, R., Poline, J.-B. (2002). Region of interest analysis using an SPM toolbox [abstract] Presented at the 8th International Conference on Functional Mapping of the Human Brain, June 2–6, 2002, Sendai, Japan. *NeuroImage* 16, 2.
- Burke, S. N., & Barnes, C. A. (2006). Neural plasticity in the ageing brain. *Nature Reviews Neuroscience*, 7, 30–40.
- Chee, M. W. L., Goh, J. O. S., Venkatraman, V., Tan, J. C., Gutchess, A., Sutton, B., Hebrank, A., Leshikar, E., & Park, D. (2006). Age-related changes in object processing and contextual binding revealed using fMR adaptation. *Journal of Cognitive Neuroscience*, 18, 495–507.
- Connelly, S. L., Hasher, L., & Zacks, R. T. (1991). Age and reading: the impact of distraction. *Psychology and Aging*, 6, 533–541.
- D'Esposito, M., Deouell, L., & Gazzaley, A. (2003). Alterations in the BOLD fMRI signal with ageing and disease: a challenge for neuroimaging. *Nature Reviews Neuroscience*, 4, 1–10.
- Dale Stevens, W., Hasher, L., Chiew, K. S., & Grady, C. L. (2008). A neural mechanism underlying memory failure in older adults. *Journal of Neuroscience*, 26, 12820–12824.
- Desimone, R. (1996). Neural mechanisms for visual memory and their role in attention. *Proceedings of the National Academy of Sciences of the United States of America*, 93, 13494–13499.
- 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.
- Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state. A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, 12, 189–198.
- Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. P., Frith, C. D., & Frackowiak, R. S. J. (1995). Statistical parametric maps in functional imaging: a general linear approach. *Human Brain Mapping*, 2, 189–210.
- Goh, J. O., Chee, M. W., Tan, J. C., Venkatraman, V., Hebrank, A., Leshikar, E. D., Jenkins, L., Sutton, P. B., Gutchess, A. H., & Park, D. C. (2007). Age and culture modulate object processing and object-scene binding in the ventral visual area. *Cognitive, Affective, and Behavioral Neuroscience*, 7, 44–52.
- Goh, J. O., Suzuki, A., & Park, D. C. (2010). Reduced neural selectivity increases fMRI adaptation with age during face discrimination. *NeuroImage*, 51, 336–344.
- Golby, A. J., Poldrack, R. A., Brewer, J. B., Spencer, D., Desmond, J. E., Aron, A. P., & Gabrieli, J. D. E. (2001). Material-specific lateralization in the medial temporal lobe and prefrontal cortex during memory encoding. *Brain*, 124, 1841–1854.
- Grady, C. L. (2008). Cognitive neuroscience of aging. *Annals of the New York Academy of Sciences*, 1124, 127–144.
- Grady, C. L., Yu, H., & Alain, C. (2008). Age-related differences in brain activity underlying working memory for spatial and non-spatial auditory information. *Cerebral Cortex*, 18, 189–199.
- Grady, C. L., Charlton, R., He, Y., & Alain, C. (2011). Age differences in fMRI adaptation for sound identity and location. *Frontiers in Human Neuroscience*, 5, 1–12.
- Grill-Spector, K., & Malach, R. (2001). fMR-adaptation: a tool for studying the functional properties of human cortical neurons. *Acta Psychologica*, 107, 293–321.
- 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 cortex. *Neuron*, 24, 187–203.
- Grill-Spector, K., Henson, R., & Martin, A. (2006). Repetition and the brain: neural models of stimulus-specific effects. *Trends in Cognitive Sciences*, 10, 14–23.
- Grill-Spector, K., Golarai, G., & Gabrieli, J. (2008). Developmental neuroimaging of the human ventral visual cortex. *Trends in Cognitive Sciences*, 12, 152–162.
- Healey, M. K., Campbell, K. L., & Hasher, L. (2008). Cognitive aging and increased distractibility: costs and potential benefits. *Progress in Brain Research*, 169, 353–363.
- Lancaster, J. L., Summerlin, J. L., Rainey, L., Freitas, C. S., & Fox, P. T. (1997). The Talairach Daemon, a database server for Talairach Atlas Labels. *NeuroImage*, 5, S633.
- Lancaster, J. L., Woldorff, M. G., Parsons, L. M., Liotti, M., Freitas, C. S., Rainey, L., Kochunov, P. B., Nickerson, D., Mikiten, S. A., & Fox, P. T. (2000). Automated Talairach atlas labels for functional brain mapping. *Human Brain Mapping*, 10, 120–131.
- Lee, Y., Grady, C. L., Habak, C., Wilson, H. R., & Moscovitch, M. (2011). Face processing changes in normal aging revealed by fMRI adaptation. *Journal of Cognitive Neuroscience*, 23, 3433–3447.
- Maldjian, J. A., Laurienti, P. J., Burdette, J. B., & Kraft, R. A. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *NeuroImage*, 19, 1233–1239.
- Maldjian, J. A., Laurienti, P. J., & Burdette, J. B. (2004). Precentral gyrus discrepancy in electronic versions of the Talairach Atlas. *Neuroimage*, 21, 450–455.
- Murray, S. O., & Wojciulik, E. (2004). Attention increases neural selectivity in the human lateral occipital complex. *Nature Neuroscience*, 7, 70–74.
- Oldfield, R. C. (1971). The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia*, 9, 97–113.
- Park, D. C., & Reuter-Lorenz, P. (2009). The adaptive brain: aging and neurocognitive scaffolding. *Annual Review of Psychology*, 60, 173–96.
- Rand-Giovannetti, E. R., Chua, E. F., Driscoll, A. E., Schacter, D. L., Albert, M. S., & Sperling, R. A. (2006). Hippocampal and neocortical activation during repetitive encoding in older persons. *Neurobiology of Aging*, 27, 173–182.



- Rosenzweig, E. S., Rao, G., McNaughton, B. L., & Barnes, C. A. (1997). Role of temporal summation in age-related long-term potentiation-induced deficits. *Hippocampus*, 7, 549–558.
- Sawamura, H., Orban, G. A., & Vogels, R. (2006). Selectivity of neuronal adaptation does not match response selectivity: a single-cell study of the fMRI adaptation paradigm. *Neuron*, 49, 307–318.
- Schmitz, T. W., Cheng, F. H., & De Rosa, E. (2010). Failing to ignore: paradoxical neural effects of perceptual load on early attentional selection in normal aging. *The Journal of Neuroscience*, 30, 14750–14758.
- Schweinberger, S. R., Pfütze, E.-M., & Sommer, W. (1995). Repetition priming and associative priming of face recognition: evidence from event-related potentials. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 21, 722–736.
- Sperling, R. (2007). Functional MRI studies of associative encoding in normal aging, mild cognitive impairment, and Alzheimer's disease. *Annals of New York Academy of Sciences*, 1097, 146–155.
- Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., Mazoyer, B., & Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage*, 15, 273–289.
- Wiggs, C. L., & Martin, A. (1998). Properties and mechanisms of perceptual priming. *Current Opinion in Neurobiology*, 8, 227–233.
- Xiang, J. Z., & Brown, M. W. (1998). Differential neuronal encoding of novelty, familiarity and recency in regions of the anterior temporal lobe. *Neuropharmacology*, 37, 657–676.
- Yi, D.-J., & Chun, M. M. (2005). Attentional modulation of learning-related repetition attenuation effects in human parahippocampal cortex. *The Journal of Neuroscience*, 25, 3593–3600.