Learning Shapes the Representation of Visual Categories in the Aging Human Brain

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Abstract

■ The ability to make categorical decisions and interpret sensory experiences is critical for survival and interactions across the lifespan. However, little is known about the human brain mechanisms that mediate the learning and representation of visual categories in aging. Here we combine behavioral measurements and fMRI measurements to investigate the neural processes that mediate flexible category learning in the aging human brain. Our findings show that training changes the decision criterion (i.e., categorical boundary) that young and older observers use for making categorical judgments. Comparing the behavioral choices of human observers with those of a pattern classifier based upon multivoxel fMRI signals, we demonstrate learning-dependent changes in similar cortical areas for young and older adults. In particular, we show that neural signals in occipito-temporal and posterior parietal regions change through learning to reflect the perceived visual categories. Information in these areas about the perceived visual categories is preserved in aging, whereas information content is compromised in more anterior parietal and frontal circuits. Thus, these findings provide novel evidence for flexible category learning in aging that shapes the neural representations of visual categories to reflect the observers' behavioral judgments. ■

INTRODUCTION

The ability to group sensory events into meaningful categories is a cognitive skill critical for adaptive behavior and survival in complex environments (Miller & Cohen, 2001). Previous psychophysical work has shown that the brain meets this challenge by taking into account knowledge from previous experience to achieve flexible learning of visual categories. In particular, learning has been shown to shift the internal criterion that observers use for categorization (i.e., perceptual boundary between categories) and alter the behavioral relevance of stimulus features on which observers rely for making categorical decisions (Palmeri & Gauthier, 2004; Smith, Gosselin, & Schyns, 2004; Sigala, Gabbiani, & Logothetis, 2002; Goldstone, Lippa, & Shiffrin, 2001; Schyns, Goldstone, & Thibaut, 1998; Nosofsky, 1986). Further, recent neurophysiological (Miller & D'Esposito, 2005; Duncan, 2001; Miller, 2000) and brain imaging work (for reviews, see Ashby & Maddox, 2005; Keri, 2003) has identified the brain circuits involved in category learning. In particular, frontal brain circuits have been suggested to be involved in flexible categorical decisions and may modulate the processing of behaviorally relevant stimulus features for visual categorization in higher occipito-temporal areas. Despite this recent interest in understanding brain processes mediating category learning in young adults, relatively little is known about category learning in aging and the age-related changes that occur

in brain circuits involved in the representation of visual categories.

Here we combine behavioral and fMRI measurements to investigate the neural processes that mediate flexible category learning in the human aging brain. We used a categorization task in which young and older observers were presented with stimuli from a morphing space generated by varying the spiral angle between radial and concentric patterns (Figure 1A). Observers were asked to decide whether the viewed stimulus pattern was either radial or concentric. This task required observers to compare the sensory input (i.e., the stimulus on each trial) to an internal criterion defining the categorical boundary in the stimulus space. Behavioral performance showed that before training, both young and older observers placed the categorical boundary near the 45° spiral angle stimulus, reflecting the middle of the stimulus space on the basis of physical stimulus properties. However, by training observers with feedback, we were able to shift the categorical boundary (to 30° or 60° spiral angle), thereby dissociating the physical stimuli from their categorical interpretation. Interestingly, we observed similar behavioral learning effects for both young and older observers, suggesting that flexible category learning is maintained in aging.

Using fMRI, we investigated which cortical regions carry the neural signature of these learning-dependent changes in the categorical judgments of young and older observers. We reasoned that such regions would show learning-dependent changes in the neural representation of visual

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Figure 1. Stimulus and behavioral data. (A) Stimuli: Four example Glass pattern stimuli (100% signal) at spiral angles of 0°, 30°, 60°, and 90° are shown. The three boundaries (category boundary 45°, 30°, 60°) and spiral angles tested are shown by color bars (dark gray: stimuli that resemble radial, light gray: stimuli that resemble concentric) that indicate the categorical membership of the stimuli for each boundary. (B) Behavioral data collected in the laboratory are shown for each boundary session for both young adult and older adult observers. Solid lines indicate the cumulative Gaussian fits of the behavioral data for each boundary session (dotted gray: boundary 45°; thick black: boundary 30°; dashed gray: boundary 60°). Error bars indicate the 95% confidence interval at 50% concentric threshold following a bootstrap procedure.
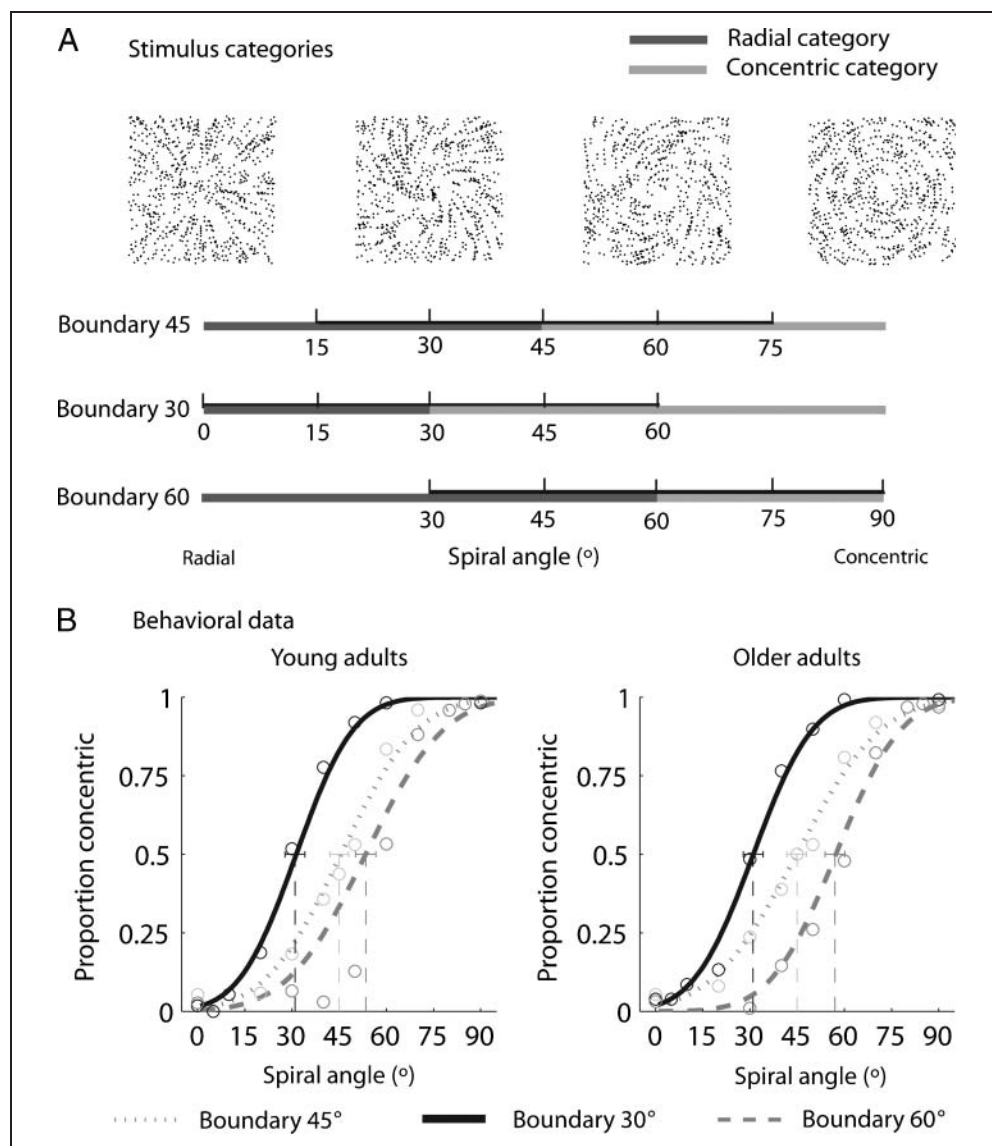
categories (concentric vs. radial patterns) that correspond to the behavioral judgments of the observers and reflect the shift in the category boundary. Previous neuroimaging studies of cognitive aging have shown differential activity in the same regions for young and older adults or recruitment of different regions in older adults even when task performance is matched (Cabeza & Nyberg, 2000; Grady, 2000). We therefore tested whether the cortical circuits that show learning-dependent changes in the neural representation of visual categories and support the ability for flexible category learning differ in young and older adults.

Isolating neural representations for different visual categories in the human brain is limited at the typical fMRI resolution that does not allow us to discern selectivity for stimulus features represented by overlapping neural populations. To overcome this limitation, we used advanced fMRI analysis methods (multivoxel pattern analysis [MVPA]) that are sensitive to neural information encoded at a finer-scale than the standard resolution of fMRI measurements (Haynes & Rees, 2006; Norman, Polyn, Detre, & Haxby,

2006; Cox & Savoy, 2003). Our results show that for both young and older observers, higher occipito-temporal areas (KO/LOS, LO) and areas along the occipital-parietal (cuneus, precuneus) and intraparietal sulcus (VIPs) contain information that allows the discrimination of stimulus categories from fMRI signals. More importantly, fMRI signals in these regions change with learning to reflect the perceived categories and the categorical boundary as shaped by training. These findings provide novel evidence for flexible category learning in both young and older adults that shapes the neural representations of visual categories to reflect the observers' behavioral judgments in occipito-temporal and posterior parietal regions.

METHODS

Observers

Two groups of 14 observers (young adult group: 7 men, 7 women, mean age = 24 ± 2.8 years; older adult group:

4 men, 10 women, mean age = 74 ± 4.1 years) participated in the experiment. Two observers from each group were excluded from the data analysis due to excessive head movement during scanning. Two additional observers from both groups were excluded due to the absence of a breath-hold fMRI scan, poor task performance during scanning, or low functional signal-to-noise (SNR) ratio (Supplementary material). All observers had normal or corrected-to-normal vision (older adults scored 20/20 on a visual acuity test) and gave written informed consent. All observers in the older adult group completed a minimental test with scores within the range of normal cognitive ability (mean = 28.3 (max score 30) ± 1.8). The study was approved by the local ethics committee.

Stimuli

We used Glass pattern stimuli (Seu & Ferrera, 2001; Glass & Perez, 1973; Glass, 1969) defined by white dot pairs (dipoles) displayed within a square aperture ($7.7° \times 7.7°$) on a black background (100% contrast). The dot density was 3% and the Glass shift (i.e., the distance between two dots in a dipole) was 16.2 arc min. The size of each dot was 2.3×2.3 arc min^2. These parameters were chosen on the basis of pilot psychophysical studies and in accordance with previous work (e.g., Wilson & Wilkinson, 1998) showing that coherent form patterns are reliably perceived for these parameters. We generated concentric and radial Glass patterns by placing dipoles tangentially (concentric stimuli) or orthogonally (radial stimuli) to the circumference of a circle centered on the fixation dot. Further, we generated intermediate patterns between these two Glass pattern types by parametrically varying the spiral angle of the pattern from 0° (radial pattern) to 90° (concentric pattern) (Figure 1A). For each dot dipole, the spiral angle was defined as the angle between the dot dipole orientation and the radius from the center of the dipole to the center of the stimulus aperture. Half of the observers were presented with clockwise spiral patterns (0° to 90° spiral angle) and half with anticlockwise spiral patterns (0° to −90° spiral angle). A new pattern was generated for each stimulus presented in a trial, resulting in stimuli that were locally jittered in their position.

To control for stimulus-specific training effects and ensure generalization of learning, we trained the observers with 80% signal stimuli but presented 75% signal stimuli during psychophysics testing (pre- and posttraining test) and fMRI scanning. This procedure ensured that learning could not be due to similar local cues between the stimuli used for training, tests, and scanning but rather global features used by the observers for stimulus categorization.

Design

All young adult and older adult observers participated in two fMRI sessions. Each session was preceded by psychophysical training outside the scanner, and the observers'

behavioral performance was matched before the two fMRI sessions (85% correct performance).

Psychophysical Training

First, all observers were familiarized with the task and stimuli in a short practice session. Observers were shown Glass patterns at 100% signal and were instructed to categorize each stimulus into one of two categories: similar to a radial Glass pattern (0° spiral angle) versus similar to a concentric Glass pattern (90° spiral angle). Then, during the pretraining test session (categorical boundary at 45°), observers were presented with Glass patterns (75% signal level) at 0°, 20°, 30°, 40°, 45°, 50°, 60°, 70°, and 90° spiral angle and instructed to perform the same categorization task. Data were collected from 64 trials per spiral angle (576 trials in total). Each stimulus was presented for 300 msec followed by a 500-msec interstimulus interval. Observers were instructed to categorize the stimuli into one of two categories: similar to a radial Glass pattern (0° spiral angle) versus similar to a concentric Glass pattern (90° spiral angle). No feedback was given to the observers during this session, allowing us to determine the categorical boundary per observer before training.

Following the pretraining test, observers were divided into two subgroups and trained to shift their categorization responses to a different boundary. Half the observers were trained with categories defined by a boundary at 30° spiral angle and the other half with categories defined by a boundary at 60° spiral angle. Observers were trained with audio error feedback to categorize the stimuli on the basis of the predefined boundary (boundary at either 30° or 60°). The stimuli presented were at 80% signal and the spiral angles used for the 30° boundary session were 0°, 5°, 20°, 25°, 35°, 40°, 55°, and 90°, whereas for 60° boundary session were 0°, 35°, 50°, 55°, 65°, 70°, 85°, and 90°. Each stimulus was presented for 300 msec, and observers were instructed to respond as fast as possible, indicating which category the stimulus belonged to by pressing one of two keys. Observers were trained (12 trials per spiral angle, 96 trials per run) until they reached a stable criterion performance (80% correct). Each training session comprised multiple runs (ranging from two to five runs). After training, observers performed the same task without feedback in a posttraining session (144 trials). Stimuli were at 75% signal level and presented for 300 msec each. For the 30° boundary group, observers were tested with stimuli 0°, 5°, 10°, 20°, 30°, 40°, 50°, 60°, and 90° of spiral angle, whereas for the 60° boundary group, observers were tested with stimuli 0°, 30°, 40°, 50°, 60°, 70°, 80°, 85°, and 90° of spiral angle.

fMRI Measurements

All observers participated in two fMRI sessions. In the first scanning session (after initial testing on the 45° boundary), observers were presented with stimuli at 15°, 30°, 45°, 60°,

and 75° spiral angles. In the second scanning session, observers trained on the 30° boundary space were presented with stimuli at 0°, 15°, 30°, 45°, and 60° spiral angles, whereas observers trained on the 60° boundary space were presented with stimuli at 30°, 45°, 60°, 75°, and 90°. Observers were instructed to perform a target detection task; that is, they pressed a button to indicate the presence of a square stimulus composed of dot dipoles similar to the radial and concentric stimuli. This target stimulus appeared equally frequently (two times per block) across conditions.

For each observer, we collected data from six to eight block-design runs in each session. Each run comprised of 15 blocks of stimuli (each 18-sec duration), with 10-sec duration fixation blocks at the beginning and at the end. Each block comprised of stimuli from one of the five spiral angles and was repeated three times in each run. The order of the blocks was randomized within each run, and different block orders were used for each run and observer. Each block consisted of 12 individual trials, comprised of 10 Glass pattern stimuli and 2 target stimuli presented in a randomized order. Within each trial, the stimulus was presented for 300 msec followed by the presentation of a fixation cross for 1200 msec (1.5 sec total trial length). Glass pattern stimuli were presented at 75% signal level and were redrawn on each trial. Further, to control for local adaptation due to stimulus repetition within a block, we generated different stimulus exemplars by varying the Glass shift (i.e., distance between the two dots in a pair was 15 or 17.4 arc min), dot density (2.5%, 3%, or 3.5%), and spiral angle jitter ($-2°$, $-1°$, $0°$, $1°$, or $2°$ relative to the spiral angle for each condition).

Data from two additional fMRI scans were acquired to measure the BOLD hemodynamic response function (HRF) and to estimate vascular reactivity. To measure the HRF, a radial black and white flickering (8 Hz) checkerboard stimulus was presented against a gray background for 500 msec. The stimulus was repeated 20 times in total at intervals of 18 sec. Observers fixated on a white cross in the center of the screen throughout the duration of the scan. To obtain an estimate of vascular reactivity, observers performed a hypercapnic breath-holding task. Observers fixated on a large black dot in the center of a gray background, and the color of the dot changed between black and white every 10 sec. Observers were instructed to hold their breath while the dot was white and to breathe normally while the dot was black. The depth of subjects breathing was monitored using pneumatic respiratory bellows to ensure the task was performed correctly.

fMRI Data Acquisition

All experiments were conducted at the Birmingham University Imaging Centre (3T Achieva scanner; Philips, Eindhoven, The Netherlands). EPI and T1-weighted anatomical (1 × 1 × 1 mm) data were collected with an eight channel SENSE head coil. For all fMRI measurements, gradient-echo EPI data were acquired from 32 slices (whole brain coverage,

repetition time = 2000 msec, echo time = 35 msec, flip angle = 80°, 2.5 × 2.5 × 3 mm resolution).

fMRI Data Analysis

fMRI data were processed using Brain Voyager QX (Brain Innovations, Maastricht, The Netherlands). Anatomical data was used for 3D cortex reconstruction, inflation, and flattening. Preprocessing of functional data included slice-scan time correction, head movement correction, temporal high-pass filtering (three cycles), and removal of linear trends. Within each block, individual trials with head motion larger than 1 mm of translation or 1° of rotation were excluded from the analysis. Spatial smoothing (Gaussian filter; full-width at half maximum, 6 mm) was performed only for group random effect analysis but not for data used for the multivoxel pattern classification analysis. The functional images were aligned to anatomical data, and the complete data were transformed into Talairach space. For each observer, the functional imaging data between the two fMRI sessions were co-aligned by registering all volumes to the first functional volume of the first run acquired during the first session. To avoid confounds from any remaining registration errors, we compared fMRI signals between stimulus conditions within each session rather than across sessions. A gray-matter mask was generated for each observer in Talairach space from the anatomical data and used to select only gray-matter voxels for further analyses.

Multivariate Brain Mapping Based on Stimulus Category

For each observer, we identified cortical regions whose activations correlated with stimulus category by performing a multivoxel searchlight analysis (Kriegeskorte, Goebel, & Bandettini, 2006) on data from each scanning session. In particular, we defined a spherical aperture with radius of 9 mm and moved this aperture voxel by voxel across the whole brain (only gray-matter voxels were included). For voxels within the aperture (98 voxels per aperture, on average), we used a linear support vector machine ([SVM] Vapnik, 1995) pattern classifier to classify fMRI signals on the basis of stimulus category (radial vs. concentric). That is, we trained the classifier to associate the fMRI signal from each stimulus block with a label (radial vs. concentric) that was determined by the category of the stimulus condition as defined by the boundary in each session (Supplementary material).

We averaged the volumes from each stimulus block (block duration = 18 sec, repetition time = 2 sec) to generate one training pattern per block. To account for the hemodynamic delay, we shifted the fMRI time series by two volumes (4 sec). To ensure generalization of the classification, we used a leave-one-run-out cross-validation procedure. For each cross validation, one run was left out as an independent test data set and the data from the rest of

the runs were used as the training set. The classification accuracy for each aperture was obtained by averaging the prediction accuracy across cross validations. The accuracy value for each voxel was obtained by averaging the accuracy values from all apertures in which this voxel was included. To identify voxels with accuracy significantly higher than chance across observers and boundaries, we conducted a second level statistical analysis (t test, $p < .05$, cluster threshold estimation 5 mm^2).

RESULTS

Psychophysical Data

We tested the observers' ability to categorize global form patterns into one of two categories (radial vs. concentric). Initial testing showed that both young adults and older adults set the boundary (50% concentric threshold) between categories at $44.4 \pm 1.1°$ (group mean $\pm$ *SE*) and $43.4 \pm 1.2°$ spiral angle, respectively. These values for the categorical boundary correspond closely to the mean of the physical stimulus space (45° spiral angle). We then trained observers using auditory feedback on incorrect trials to assign the same stimuli into different categories on the basis of a categorical boundary either at 30° or 60° of spiral angle. In particular, we trained half of the observers on the 30° and the rest on the 60° boundary. Figure 1 shows that training successfully shifted the perceptual boundary in both young and older adults. Testing the observers without feedback after training showed that training shifted the observers' criterion for categorization close to 30° (young adults, mean $\pm$ *SE* $= 31.5° \pm 1.6°$; older adults, mean $\pm$ *SE* $= 31.6° \pm 0.5°$) for the 30° boundary group and close to 60° (young adults, mean $\pm$ *SE* $= 56.7° \pm 0.6°$; older adults, mean $\pm$ *SE* $= 58.2° \pm 0.9°$) for the 60° boundary group (Figure 1B). Fitting the group behavioral data with a cumulative Gaussian function (Supplementary material) showed a significant shift in the boundary (i.e., 45° vs. 30°; 45° vs. 60°) for both young and older adults as indicated by the nonoverlapping error bars for 95% confidence intervals estimated on the basis of a bootstrap procedure. Further, to control for the possibility that this training-dependent shift in behavioral performance was due to the stimulus choice for the post-training test (i.e., different spiral angle conditions were tested for the observers trained on 30° and 60° boundary), we conducted a control experiment in which both groups of observers were tested on the same stimuli (i.e., spiral angle conditions) before and after training. A significant shift (bootstrapped 95% confidence intervals) in the threshold of the psychometric function after training relative to the pretraining performance was observed for both subject groups (Figure S1). These results suggest that the learning-dependent changes observed in behavioral performance represent a shift in the observers' internal criterion for categorization and are not simply due to stimulus choice for the posttraining test.

Finally, we fitted individual subject psychophysical data with a cumulative Gaussian function and calculated the 50% concentric thresholds for each group of observers. Two-way ANOVAs (Greenhouse–Geisser corrected) on Age Group (young adults, older adults) and Session showed significant differences in 50% threshold between sessions, 30° vs. 45° boundary, $F(1, 8) = 51$, $p < .001$; 45° vs. 60° boundary, $F(1, 8) = 24.2$, $p < .001$; 30° vs. 60° boundary, $F(1, 16) = 92$, $p < .001$), supporting the training-dependent performance shift of the boundary. The lack of significant interactions between Age Group and Session, 30° vs. 45° boundary, $F(1, 8) < 1$, $p = .96$; 45° vs. 60° boundary, $F(1, 8) = 1.21$, $p = .3$; 30° vs. 60° boundary, $F(1, 16) < 1$, $p = .43$), suggests similar learning effects between age groups.

fMRI Data: Pattern Classification across the Whole Brain

To investigate which cortical areas contain information that allows us to discriminate between stimulus categories (radial vs. concentric), we performed a multivoxel searchlight analysis (Kriegeskorte et al., 2006). We used a linear SVM to test for cortical areas that showed significantly higher accuracies for the stimuli at the extreme spiral angle for each boundary session (i.e., 45° boundary: 15° vs. 75°; 30° boundary: 0° vs. 60°; 60° boundary: 30° vs. 90°).

We performed this classification across the whole brain by defining a searchlight (aperture of 9 mm radius) that was moved serially throughout the entire cortex to evaluate the information content of voxel patterns across brain regions. Figure 2 shows group activation patterns averaged across sessions ($p < .05$, cluster threshold estimation 5 mm^2) for young (Figure 2A) and older (Figure 2B) adults. For the young adults, classification accuracy was significantly higher than chance in occipito-temporal areas (KO/LOS, LO), cuneus and precuneus regions, parietal regions along the intraparietal sulcus (VIPs, POIPs, DIPs), and frontal regions (PMd, SEF, ventral IFG). For the older adults, classification accuracy was significantly higher than chance in occipito-temporal areas (KO/LOS, LO), cuneus, precuneus, and VIPs. Similar activation patterns were observed, when we performed the multivoxel searchlight analysis using all stimuli within each category as defined by the boundary in each session. That is, for the 45° boundary, we trained the classifier to discriminate between stimuli at 15° and 30° versus 60° and 75° spiral angle; for the 30° boundary between stimuli at 0° and 15° versus 45° and 60° spiral angle; and for the 60° boundary between stimuli at 30° and 45° versus 75° and 90° spiral angle. These analyses show that in both young and older adults, occipito-temporal and posterior parietal regions contain information that allows us to discriminate between stimulus categories. However, informative activation patterns in dorsal parietal and frontal regions were predominantly evident in young rather than older adults.

In contrast, a standard univariate GLM analysis contrasting the BOLD responses to extreme concentric stimuli against
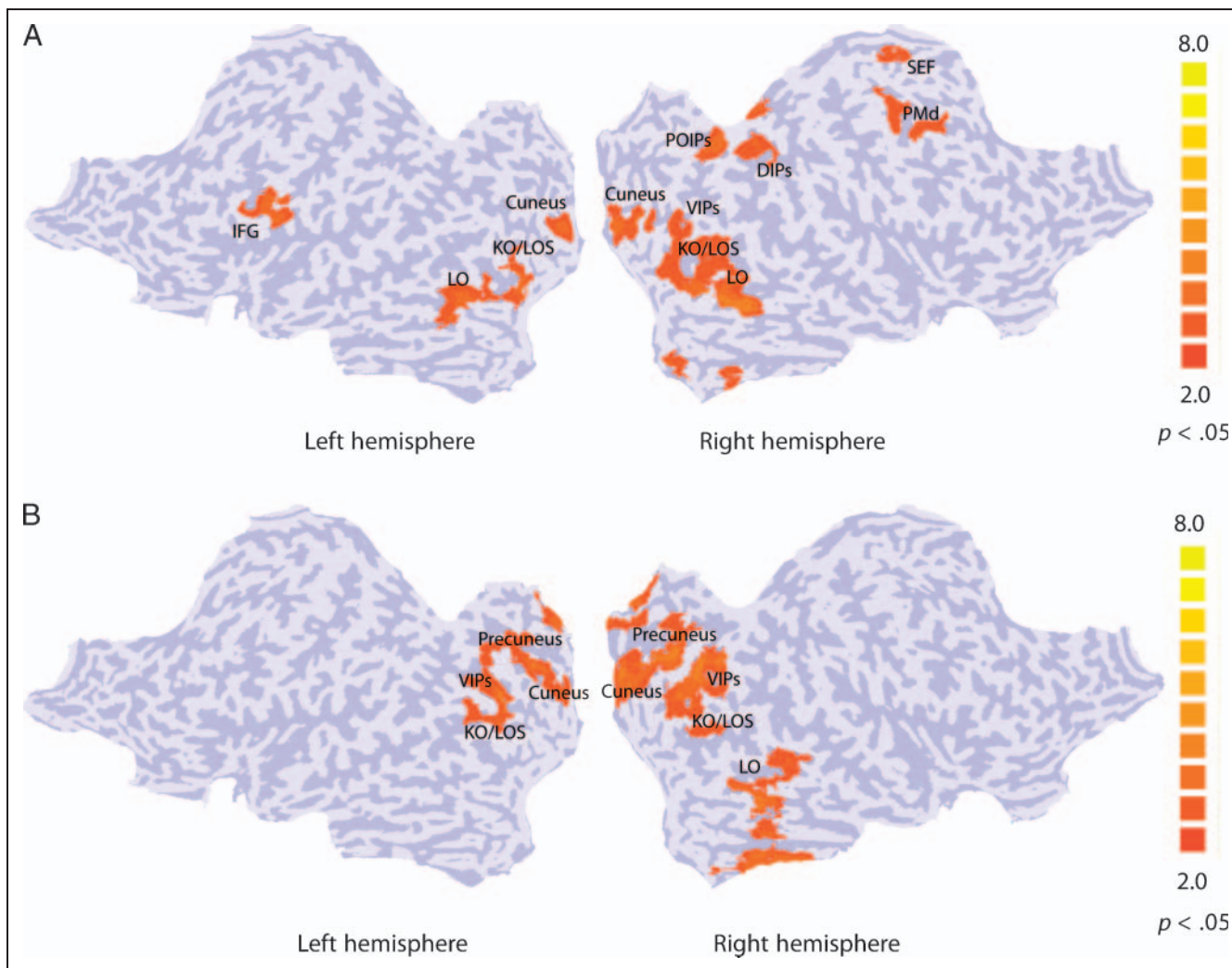
Figure 2. Searchlight classification based on stimulus category. Searchlight maps for (A) young and (B) older observers (data grouped across observers and boundaries) showing areas with significantly higher accuracy than chance (50% correct) ($p < .05$, cluster threshold estimation 5 mm^2) for the classification of fMRI signals based on stimulus category. The t value maps are superimposed on flattened cortical surfaces of both hemispheres. See Supplementary Table 1 for ROI definition and Talairach coordinates.

the responses to extreme radial stimuli from all sessions did not show any significant activations (random effects, $p < .05$; cluster threshold estimation 5 mm^2). This finding is consistent with the higher sensitivity of multivariate methods in detecting neural preferences for stimulus categories encoded at a finer spatial resolution than that of typical fMRI measurements by pooling weak activation biases across voxel patterns.

fMR-Metric Functions: Predicting Behavior from fMRI Data

The searchlight multivariate analysis identified occipitotemporal, parietal, and frontal regions containing information that allows to discriminate between visual categories (Figure 2). We then investigated which of these cortical regions show changes in fMRI activation patterns that relate to the behavioral learning effect, that is, changes in the observers' decision criterion after training as shown by the

shift in the observers' psychometric functions (Figure 1B). That is, we tested whether we could reliably predict differences in fMRI signals related to the perceived categories as shaped by training on the three different boundaries (45°, 30°, or 60° boundary).

For each observer, we identified ROIs on the basis of activation patterns from the searchlight analysis (Table S1 for Talairach coordinates). For young adults, ROIs comprised of activation patterns in extrastriate visual areas (KO/LOS, LO), regions along the OPS (cuneus and precuneus), regions along the IPS (ventral, VIPs; dorsal, DIPs), and frontal regions (PMd, SEF, IFG). For older adults, ROIs comprised of activation patterns in extrastriate visual areas (KO/LOS, LO), regions along the OPS: cuneus and precuneus and ventral IPS (VIPs). Further, using standard retinotopic mapping procedures in each individual observer, we identified V1 and V2 as control visual areas that are known to be engaged in the processing of basic visual features (e.g., orientation) and texture, respectively.

We trained a linear SVM to classify fMRI signals from these ROIs related to the extreme stimulus conditions in each category as determined by the boundary (i.e., 45° boundary: 15° vs. 75°; 30° boundary: 0° vs. 60°; 60° boundary: 30° vs. 90°). We then tested the accuracy of the SVM in predicting the stimulus category of intermediate stimuli between the extreme conditions from an independent data set. For each observer and region, we calculated the mean performance of the classifier (defined as the proportion of patterns classified as concentric for each stimulus condition) across cross validations. We calculated the mean classifier performance across observers for each condition and plotted the data after linear scaling (i.e., for each fMR-metric function, we scaled each prediction by subtracting the minimum value across conditions and dividing by the difference between maximum and minimum prediction values) to allow comparison between cortical areas. We fitted the classifier predictions (Figures 3 and 4: scaled data; Figure S2: nonscaled data) using the same procedure as for the behavioral data (Supplementary data). We refer to these functions as fMR-metric functions as their estimation resembles closely that of the psychometric functions (Li, Mayhew, & Kourtzi, 2009).

Figure 3A shows that for young adults the classifier's predictions were fitted significantly ($p < .05$) using a cumulative Gaussian function (bootstrap estimate of the 95% confidence interval) for V1, V2, KO/LOS, LO, VIPs, and PMd (see Table S2 for significance of the data fitting for each ROI). More importantly, in agreement with the observed changes in psychophysical performance due to training, fMR-metric functions in occipito-temporal (KO/LOS, LO), intraparietal (VIPs, DIPs), and PMd regions showed significant shifts (nonoverlapping bootstrapped confidence intervals) that matched learning-induced changes in the 30° and 60° categorization boundaries. We quantified these learning-induced changes using the 50% thresholds of individual participants' fMR-metric functions, obtained from all boundary sessions (30°, 45°, and 60°). Figure 3B indicates the difference between the 50% fMR-metric threshold of the 45° boundary session and the 50% fMR-metric threshold of the 30° and 60° boundary sessions, respectively. We calculated this threshold index for ROIs with significantly fitted fMR-metric functions. Significant differences in the 50% fMR-metric thresholds between 30° and 60° boundary sessions were observed in KO/LOS, $F(1, 8) = 17, p < .01$, LO, $F(1, 8) = 44, p < .001$, VIPs, $F(1, 8) = 18, p < .01$, and PMd, $F(1, 8) = 9, p < .01$. In contrast, no significant differences were observed in V1, $F(1, 8) = 0.3, p = .6$, or V2, $F(1, 8) = 0.1, p = .8$, and the 50% threshold remained close to 45° for both the 30° and the 60° boundary, suggesting that signals in these areas reflect the stimulus space rather than the category space as shaped by learning.

For the older adult group, we focused on extrastriate visual areas (KO/LOS, LO), regions along the OPS, and ventral IPS as these areas were shown by the searchlight analysis to contain information about stimulus categories (Figure 2B). Figure 4A shows that for older adults the classifier's predic-

tions were fitted significantly using a cumulative Gaussian function for KO/LOS, LO, and VIPs. Consistent with the behavioral learning effects, fMR-metric functions in these areas showed significant threshold shifts between the 30° and the 60° boundary sessions (Figure 4B). In particular, we observed significant differences in the 50% fMR-metric thresholds between 30° and 60° boundary sessions for KO/LOS, $F(1, 8) = 49, p < .001$, LO, $F(1, 8) = 7, p < .05$, and VIPs, $F(1, 8) = 19, p < .01$, but not in V1, $F(1, 8) = 0.6, p = .5$, or V2, $F(1, 8) = 0.9, p = .4$.

These results suggest that information about visual shape categories in occipito-temporal (KO/LOS) and ventral intraparietal regions is shaped by learning and reflects behavioral performance in categorization tasks. Importantly, information in these regions allows us to reliably decode the observer's categorical assignment of the stimuli on the basis of learned categorization criteria even when the observers do not engage in the categorization task. This finding suggests changes in the neural representations of the perceptual categories rather than simply task-related modulations. This result holds for both young and older observers as supported by the lack of significant interactions between Age Group and Session in these regions, KO/LOS, $F(1, 16) = 0.01, p = .9$; LO, $F(1, 16) = 2, p = .15$; VIPs, $F(1, 16) = 0.2, p = .7$. However, in young but not older adults, dorsal parietal (DIPs) and premotor (PMd) regions appear to contain information about the perceived visual categories as shaped by learning. Finally, in both young and older adults, fMR-metric functions in V1 and V2 were not shifted significantly between boundary sessions, suggesting that training did not change the stimulus representation in either primary or secondary visual cortex. This result in early visual areas is consistent with previous work (Wilson & Wilkinson, 1998), showing that the processing of global form patterns involves later rather than early visual areas that are known to be engaged in orientation (i.e., V1) and texture (i.e., V2) processing.

Control Analyses

Our results show that higher occipito-temporal and parietal regions in both young and older adults contain information about the perceived shape categories and change their processing with learning to reflect the observers' criterion (i.e., categorical boundary) in making categorical judgments. We further conducted additional analyses to rule out a number of less likely interpretations of our results.

First, to control for the possibility that these results are due to random correlations in the data, we computed the fMR-metric functions from randomly permuted fMRI patterns (i.e., we randomized the correspondence between fMRI data and stimulus labels and estimated the classifier prediction for each stimulus condition). The lack of significant fits (Figure S3) suggests that the MVPA predictions could not be simply accounted for by random variations in the data but rather reflect a link between task-relevant behavioral performance and activation patterns.

Figure 3. fMR-metric curves for young observers. (A) fMR-metric curves for each boundary session (30° and 60° boundary) and ROI. Average classifier prediction data across observers were scaled and fitted with cumulative Gaussian functions (solid lines). Error bars indicate the 95% confidence interval at 50% concentric threshold using a bootstrap procedure. (B) Fifty percent threshold index (difference between the 50% fMR-metric threshold of the 45° boundary session and the 50% fMR-metric threshold of the 30° and 60° boundary sessions, respectively) for ROIs with significantly fitted data (see Table S2). Error bars indicate the 95% confidence interval at 50% concentric threshold using a bootstrap procedure.
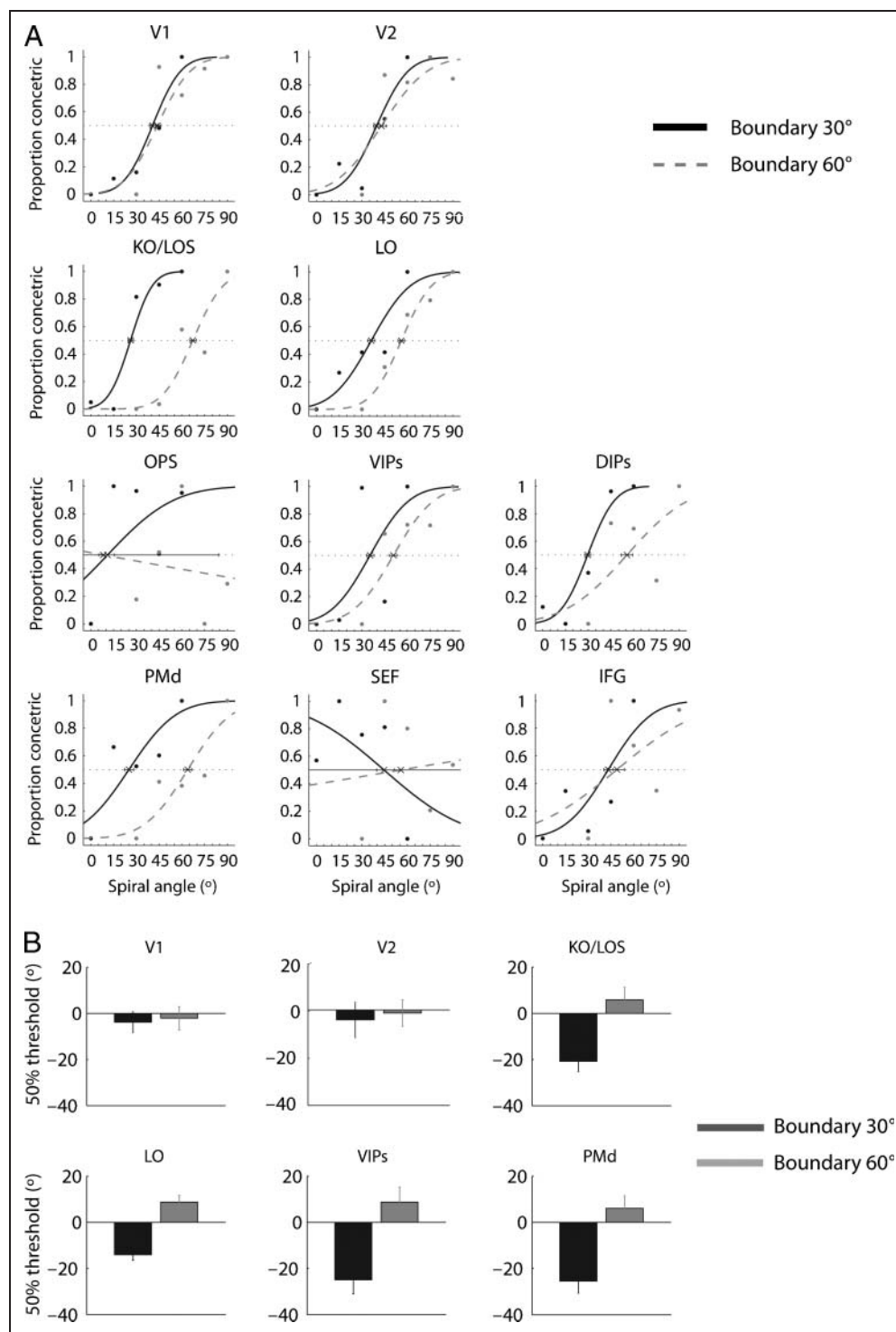
Second, our design ensured that the observers were not biased in their interpretation of stimulus categories by equating the number of conditions and stimuli across categories. As a result, the stimulus set tested in the two sessions could not remain identical when the category boundary changed across sessions. However, our design allowed us to directly compare between stimulus conditions (45°, 30°, 60°) that were common across different boundary sessions. Analysis of the univariate fMRI signals

(Figure S4) showed similar fMRI responses across stimulus conditions (i.e., when the stimuli were interpreted as the category boundary or not), suggesting that differences in the MVPA performance reflect the observers' perceived categories rather than differences in the stimulus statistics across conditions.

Third, to ensure that any performance differences in the categorization task between young and older adults did not confound the fMRI analyses, we asked all observers

to perform the same target detection task during scanning. Performance in this task for young adults ranged from 59.2% to 86.6% correct for response times (RT) between 854 msec (mean response time) and 1000 msec from stimulus onset, whereas for older adults from 62.7% to 88.6% correct for response times between 875 msec (mean response time) and 1000 msec from stimulus onset. These results show that both young and observers engaged fully in the task and that performance did not differ significantly either between boundary sessions—accuracy, $F(1, 18) =$

1.3, $p = .26$; RT, $F(1, 16) = 0.1$, $p = .8$—or between age group—accuracy, $F(1, 18) = 1.8$, $p = .2$; RT, $F(1, 16) = 0.05$, $p = .8$. Thus, differences in MVPA results between young and old adults could not be due to differences in task difficulty across age groups or general slowing of processing in older adults (Porciatti, Fiorentini, Morrone, & Burr, 1999; Kosnik, Winslow, Kline, Rasinski, & Sekuler, 1988).

Fourth, the interpretation of differences in BOLD signal between young and old adults is complicated by changes in the vasculature that occur during aging. For instance,

Figure 4. fMR-metric curves for older observers. (A) fMR-metric curves for each boundary session (30° and 60° boundary) and ROI. Average classifier prediction data across observers were scaled and fitted with cumulative Gaussian functions (solid lines). Error bars indicate the 95% confidence interval at 50% concentric threshold using a bootstrap procedure. (B) Fifty percent threshold index (difference between the 50% fMR-metric threshold of the 45° boundary session and the 50% fMR-metric threshold of the 30° and 60° boundary sessions, respectively) for ROIs with significantly fitted data (Table S2). Error bars indicate the 95% confidence interval at 50% concentric threshold using a bootstrap procedure.
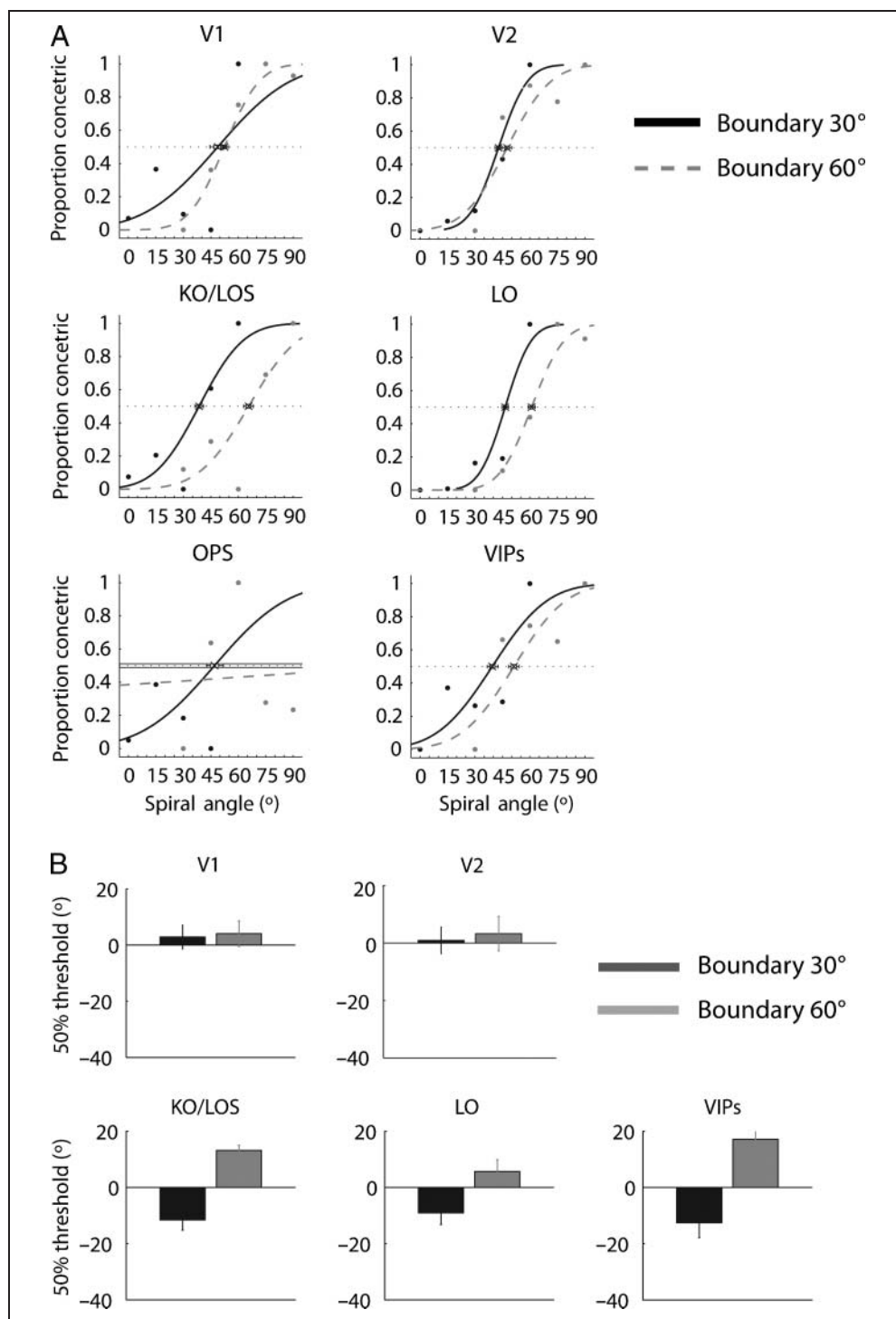
decreases in vessel wall compliance (Hajdu, Heistad, Siems, & Baumbach, 1990), hematocrit concentration (Levin et al., 2001), and alterations in CBF due to arterial disease (Hamzei, Knab, Weiller, & Rother, 2003; Pineiro, Pendlebury, Johansen-Berg, & Matthews, 2002) may alter the neurovascular coupling in older adults and cause differences in measured BOLD signal compared with young adults performing the same task (Restom, Bangen, Bondi, Perthen, & Liu, 2007; D'Esposito, Deouell, & Gazzaley, 2003; D'Esposito, Zarahn, Aguirre, & Rypma, 1999). To control for the possibility that differences in the activation patterns between young and old adults may occur due to differences in vascular reactivity, we collected fMRI data in both young and old adults during a breath-holding task that has been shown to result in vascular dilation induced by hypercapnia (Handwerker, Gazzaley, Inglis, & D'Esposito, 2007). We used the BOLD signal change induced by this task as an estimate of the vascular reactivity in each voxel. In particular, for each observer and ROI, we identified voxels that were significantly active in response to the breath-holding task (GLM regression analysis, threshold $p < .05$ uncorrected). Across ROIs, the mean proportion of voxels selected was $95 \pm 4\%$ in young adults and $94 \pm 5\%$ in older adults. For every selected voxel in each ROI, we calculated percent BOLD change related to the hypercapnic response across trials by subtracting the mean of two peak time points from the mean of the two prestimulus time points. Figure S5A shows that the percent BOLD signal in response to the breath-holding task was significantly, $F(2.1, 16.8) = 44.2, p < .001$, reduced in older compared with young adults across ROIs, consistent with previous studies (Handwerker et al., 2007). However, the lack of a significant effect of ROI, $F(2.1, 16.8) = 1.2$, $p = .3$, or interaction between ROI and Age Group, $F(1, 8) = 0.4, p = .7$, suggests that the differences in activation patterns revealed by the searchlight analysis between young and older adults (i.e., lack of significant patterns in DIPs and PMd for older adults) could not be simply accounted for by differences in vascular reactivity across age groups. Further, we used the BOLD response to the breath-holding task to normalize the stimulus evoked BOLD signal for each observer, as previously described (Handwerker et al., 2007). For each voxel, we divided the percent BOLD signal evoked by each stimulus block by the percent BOLD evoked by the hypercapnic breath-holding task. We then used the normalized signal time course for the multivoxel pattern classification and the fMR-metric functions (Figures 3 and 4; Figures S2 and S3).

Fifth, previous studies have shown differences in the peak latency of the HRF between young and older adults (Huettel, Singerman, & McCarthy, 2001; Taoka et al., 1998) and decreased spatial extent of activation in older adults related to either higher noise or lower signal magnitude (Huettel et al., 2001; Buckner, Snyder, Sanders, Raichle, & Morris, 2000; D'Esposito et al., 1999). To control for the possibility that differences in the activation patterns between age groups could result from differences in the HRF, we measured the HRF evoked by a reversing checkerboard

stimulus across ROIs for each observer. Figure S5B shows no significant difference in the peak HRF latency, $F(1.9, 15) = 0.2, p = .6$, between young and older adults. The lack of a significant interaction between ROI and Age Group, $F(1, 8) = 0.6, p = .5$, justified the choice of the same hemodynamic lag (4 sec) for the voxel time series used in the MVPA across ROIs for both young and older adults. Further, no significant differences were observed in BOLD amplitude, $F(1.9, 5) = 0.95, p = .5$, between young and older adults. This analysis was confirmed by estimation of the functional SNR for all voxels per ROI used for the MVPA (Figure S5C). This analysis did not show any significant difference in functional SNR across ROIs, $F(1.5, 12) = 2.1$, $p = .12$, age groups, $F(1.5, 12) = 0.42, p = .5$, or an interaction between ROI and Age Group, $F(1, 8) = 0.4, p = .65$. Thus, these analyses suggest that the differences in activation patterns revealed by the searchlight analysis between young and older adults (i.e., lack of significant patterns in DIPs and PMd for older adults) could not be simply accounted for by differences in HRF properties (peak latency or amplitude).

Finally, eye movement recordings conducted during scanning showed that there were no significant differences in the eye position, number, and amplitude of saccades across stimulus conditions and boundaries in either young or older adults (Figures S6 and S7). This analysis suggests that it is unlikely that the learning-dependent changes we observed were significantly confounded by eye movements.

DISCUSSION

Our findings provide novel evidence for flexible category learning in aging. We show that training changes the criterion (i.e., categorical boundary) that young and older observers use for making categorical judgments and results in changes in the neural representation of the perceived visual categories that reflect the observers' behavioral judgments. In particular, for both young and older adults, occipito-temporal and posterior parietal regions contain information that allows us to discriminate between stimulus categories. More importantly, the information content in these regions changes with learning to reflect the perceived categories and the categorical boundary as shaped by training. The fact that these changes were observed when observers performed the control (target detection) task during scanning rather than the categorization task suggests learning-dependent changes in the representation of the perceived categories rather than simply task-related modulations.

Interestingly, informative activation patterns in dorsal parietal and frontal regions were predominantly evident in young rather than older adults. These activation patterns in young adults are consistent with the role of fronto-parietal regions in categorization (Jiang et al., 2007; Freedman & Assad, 2006; Duncan, 2001; Freedman, Riesenhuber, Poggio, & Miller, 2001; Miller, 2000). It has previously been suggested that sensory information about visual categories is

combined with motor responses to form associations and representations of meaningful categories in frontal cortex (Muhammad, Wallis, & Miller, 2006; Toni, Rushworth, & Passingham, 2001). In turn, these category formation and decision processes may modulate selectivity for the perceived categories in occipito-temporal areas in a top–down manner (Op de Beeck, Torfs, & Wagemans, 2008; Mirabella et al., 2007; Op de Beeck, Baker, DiCarlo, & Kanwisher, 2006; Rotshtein, Henson, Treves, Driver, & Dolan, 2005; Smith et al., 2004; Freedman, Riesenhuber, Poggio, & Miller, 2003; Sigala & Logothetis, 2002).

Previous studies have shown informative activation patterns extending into prefrontal regions when observers are engaged in category learning tasks (Li et al., 2009). However, in our study, observers performed a control (target detection) task rather than the categorization task in the scanner. This may account for the reduced informative activation patterns we observed in frontal regions for young adults, consistent with task-dependent engagement of frontal circuits. Further, the reduction of informative activations in anterior parietal and frontal areas for older adults could not be attributed to differences in task difficulty between age groups, as performance of the control target detection task was similar for young and older observers. It is possible that the activation patterns observed in frontal regions for young but not older adults may mediate more complex category learning tasks (e.g., abstract rule learning) for which performance has been shown to decline with age (Schmitt-Eliassen, Ferstl, Wiesner, Deuschl, & Witt, 2007; Racine, Barch, Braver, & Noelle, 2006; Filoteo & Maddox, 2004; Ridderinkhof, Span, & van der Molen, 2002; Chasseigne, Mullet, & Stewart, 1997; Isingrini & Vazou, 1997; Kramer, Humphrey, Larish, Logan, & Strayer, 1994; Parkin & Lawrence, 1994; Axelrod & Henry, 1992).

These results are consistent with previous studies reporting complex alterations in brain activation patterns for older compared with young adults despite matched task difficulty and performance in cognitive tasks (Bennett, Sekuler, McIntosh, & Della-Maggiore, 2001; Grady, 2000; Madden et al., 1999; McIntosh et al., 1999; Cabeza et al., 1997). It is possible that the reduced informative signals in fronto-parietal cortical circuits for older adults relate to disruption in the coordination of large scale brain networks supporting interactions between sensory and frontal circuits (Andrews-Hanna et al., 2007), gray and white matter loss in frontal cortex (Bartzokis et al., 2004; Head et al., 2004; Madden et al., 2004; Salat et al., 2004; Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003), and functional underactivation of frontal circuits (Logan, Sanders, Snyder, Morris, & Buckner, 2002; Rypma, Prabhakaran, Desmond, & Gabrieli, 2001; Rypma & D'Esposito, 2000; Cabeza et al., 1997; West, 1996; Grady et al., 1995; Moscovitch & Winocur, 1995).

Taken together, our findings in young and older adults suggest that neural signals in occipito-temporal and posterior parietal regions preserve selective information about the perceived visual categories in aging, whereas this infor-

mation content may be compromised in more anterior parietal and frontal circuits. These findings advance our understanding of the neural processes that mediate learning and experience-dependent plasticity for categorical decisions in the human aging brain in three main respects. Previous studies have shown that performance declines with age for categorization tasks entailing learning of explicit abstract rules and cognitive strategies that guide visual attention to critical stimulus attributes (Schmitt-Eliassen et al., 2007; Racine et al., 2006; Filoteo & Maddox, 2004; Ridderinkhof et al., 2002; Chasseigne et al., 1997; Isingrini & Vazou, 1997; Kramer et al., 1994; Parkin & Lawrence, 1994; Axelrod & Henry, 1992). However, our findings show that both young and older adults can flexibly learn new decision criteria (i.e., categorical boundary) that determine the categorical membership of visual forms on the basis of stimulus–response associations. This is consistent with recent studies showing similar performance across age groups for probabilistic learning of categories on the basis of implicit stimulus–outcome associations (Fera et al., 2005; Davis, Klebe, Bever, & Spring, 1998) and with theoretical and psychophysical evidence that older adults can match the performance of younger adults given sufficient practice (Ratcliff, Thapar, & McKoon, 2006; Richards, Bennett, & Sekuler, 2006). Interestingly, age-related differences in perceptual learning have been reported for speech comprehension. In particular, similar levels of learning were observed for young and older adults for the initial task but older adults were unable to show transfer after training and adapt to differences in speech rate (Peelle & Wingfield, 2005).

Second, previous neuroimaging studies have identified a large network of cortical and subcortical areas involved in visual categorization (Ashby & Maddox, 2005; Keri, 2003) and have revealed a distributed pattern of activations for object categories in the temporal cortex (Williams, Dang, & Kanwisher, 2007; O'Toole, Jiang, Abdi, & Haxby, 2005; Hanson, Matsuka, & Haxby, 2004; Haxby et al., 2001). However, little is known about age-related changes in the neural substrates that mediate categorization processes in older adults. Recent studies show decreased activations in frontal and subcortical regions (Fera et al., 2005) and reduced neural specialization for visual categories in the temporal cortex (Park et al., 2004). Our study extends significantly beyond the localization of areas involved in categorization by combining behavioral and advanced MVPA of imaging measurements to characterize neural representations and learning-dependent plasticity for visual categories in the aging brain. In particular, we show that the patterns of activation in occipito-temporal and posterior parietal regions contain selective information for perceived visual categories that are shaped by training and may support flexible categorical judgments in aging.

Third, plasticity in the aging human brain has been demonstrated by numerous recent studies comparing the spatial extent of fMRI activations between young and older adults. These studies show age-related changes in cortical

organization that relate to underactivation (i.e., decreased activations in older adults) typically associated with cognitive decline or overactivation (i.e., increased activations and recruitment of different brain areas for older adults) that may reflect compensatory mechanisms or difficulty in recruiting specialized neural mechanisms (e.g., Grady, Springer, Hongwanishkul, McIntosh, & Winocur, 2006; Reuter-Lorenz & Lustig, 2005; Cabeza, Anderson, Locantore, & McIntosh, 2002; Reuter-Lorenz, 2002). Our work provides an alternate approach in the study of the aging brain by comparing the information content of brain areas engaged in the representation of visual categories between young and older participants rather than the amplitude of fMRI signals that could be confounded by age-related signal changes due to alterations in neurovascular coupling in aging. In particular, we take advantage of the higher sensitivity of multivariate methods in detecting neural preferences encoded at a finer spatial resolution than that of typical fMRI measurements. Using multivoxel pattern classification methods, we evaluate whether small biases across voxels related to the stimulus preference of the underlying neural populations are statistically reliable. Comparing fMR-metric functions that reflect the choices of an MVPA classifier to psychometric functions that reflect the observers' choices, we discern cortical areas that contain information about the perceived rather than the physical stimulus categories and shape their representations with learning according to the observers' behavior. Our findings provide novel evidence for learning-dependent plasticity in similar cortical areas for young and older adults; that is, higher occipito-temporal and posterior parietal regions show learning-dependent changes in the representation of visual categories.

However, cautious interpretation of these findings is necessary due to the complex nature of the BOLD signal. First, BOLD signals may differ across age groups due to age-related alterations in cerebrovascular dynamics. To control for this possibility, we used measurements of vascular reactivity and hemodynamics and normalized the BOLD signals used for MVPA for each of the observers (D'Esposito et al., 2003). Similar learning-dependent activation patterns observed for young and old adults in higher occipito-temporal and posterior parietal regions suggest that any remaining differences in neurovascular coupling between age groups could not significantly account for our findings. Second, MVPA on fMRI signals allows us to reliably extract information about the sensitivity of neural populations at a finer spatial resolution by pooling small biases across voxels, but it does not enable us to discern the nature of the signals that determine this sensitivity. The learning-dependent activity changes we observed may reflect changes in the selectivity of single neurons, correlations across local neural populations, or input from local or distant neural circuits. Future work using multivariate approaches for the analysis of both fMRI and electrophysiology signals would shed more light into the neural mechanisms that mediate learning-dependent plasticity across the lifespan.

REFERENCES

Andrews-Hanna, J. R., Snyder, A. Z., Vincent, J. L., Lustig, C., Head, D., Raichle, M. E., et al. (2007). Disruption of large-scale brain systems in advanced aging. *Neuron, 56,* 924–935.

Ashby, F. G., & Maddox, W. T. (2005). Human category learning. *Annual Review of Psychology, 56,* 149–178.

Axelrod, B. N., & Henry, R. R. (1992). Age-related performance on the Wisconsin card sorting, similarities, and controlled oral word association tests. *Clinical Neuropsychologist, 6,* 16–26.

Bartzokis, G., Sultzer, D., Lu, P. H., Nuechterlein, K. H., Mintz, J., & Cummings, J. L. (2004). Heterogeneous age-related breakdown of white matter structural integrity: Implications for cortical "disconnection" in aging and Alzheimer's disease. *Neurobiology of Aging, 25,* 843–851.

Bennett, P. J., Sekuler, A. B., McIntosh, A. R., & Della-Maggiore, V. (2001). The effects of aging on visual memory: Evidence for functional reorganization of cortical networks. *Acta Psychologica (Amsterdam), 107,* 249–273.

Buckner, R. L., Snyder, A. Z., Sanders, A. L., Raichle, M. E., & Morris, J. C. (2000). Functional brain imaging of young, nondemented, and demented older adults. *Journal of Cognitive Neuroscience, 12(Suppl. 2),* 24–34.

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., Grady, C. L., Nyberg, L., McIntosh, A. R., Tulving, E., Kapur, S., et al. (1997). Age-related differences in neural activity during memory encoding and retrieval: A positron emission tomography study. *Journal of Neuroscience, 17,* 391–400.

Cabeza, R., & Nyberg, L. (2000). Neural bases of learning and memory: Functional neuroimaging evidence. *Current Opinion in Neurology, 13,* 415–421.

Chasseigne, G., Mullet, E., & Stewart, T. R. (1997). Aging and multiple cue probability learning: The case of inverse relationships. *Acta Psychologica (Amsterdam), 97,* 235–252.

Cox, D. D., & Savoy, R. L. (2003). Functional magnetic resonance imaging (fMRI) "brain reading": Detecting and classifying distributed patterns of fMRI activity in human visual cortex. *Neuroimage, 19,* 261–270.

Davis, H. P., Klebe, K. J., Bever, B., & Spring, A. (1998). The effect of age on the learning of a nondeclarative category classification task. *Experimental Aging Research, 24,* 273–287.

D'Esposito, M., Deouell, L. Y., & Gazzaley, A. (2003). Alterations in the BOLD fMRI signal with ageing and disease: A challenge for neuroimaging. *Nature Reviews Neuroscience, 4,* 863–872.

D'Esposito, M., Zarahn, E., Aguirre, G. K., & Rypma, B. (1999). The effect of normal aging on the coupling of neural activity to the bold hemodynamic response. *Neuroimage, 10,* 6–14.

Duncan, J. (2001). An adaptive coding model of neural function in prefrontal cortex. *Nature Reviews Neuroscience, 2,* 820–829.

Fera, F., Weickert, T. W., Goldberg, T. E., Tessitore, A., Hariri, A., Das, S., et al. (2005). Neural mechanisms underlying probabilistic category learning in normal aging. *Journal of Neuroscience, 25,* 11340–11348.

Filoteo, J. V., & Maddox, W. T. (2004). A quantitative model-based approach to examining aging effects on information-integration category learning. *Psychology and Aging, 19,* 171–182.

Freedman, D. J., & Assad, J. A. (2006). Experience-dependent representation of visual categories in parietal cortex. *Nature, 443,* 85–88.

Freedman, D. J., Riesenhuber, M., Poggio, T., & Miller, E. K. (2001). Categorical representation of visual stimuli in the primate prefrontal cortex. *Science, 291,* 312–316.

Freedman, D. J., Riesenhuber, M., Poggio, T., & Miller, E. K. (2003). A comparison of primate prefrontal and inferior temporal cortices during visual categorization. *Journal of Neuroscience, 23,* 5235–5246.

Glass, L. (1969). Moire effect from random dots. *Nature, 223,* 578–580.

Glass, L., & Perez, R. (1973). Perception of random dot interference patterns. *Nature, 246,* 360–362.

Goldstone, R. L., Lippa, Y., & Shiffrin, R. M. (2001). Altering object representations through category learning. *Cognition, 78,* 27–43.

Grady, C. L. (2000). Functional brain imaging and age-related changes in cognition. *Biological Psychology, 54,* 259–281.

Grady, C. L., McIntosh, A. R., Horwitz, B., Maisog, J. M., Ungerleider, L. G., Mentis, M. J., et al. (1995). Age-related reductions in human recognition memory due to impaired encoding. *Science, 269,* 218–221.

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.

Hajdu, M. A., Heistad, D. D., Siems, J. E., & Baumbach, G. L. (1990). Effects of aging on mechanics and composition of cerebral arterioles in rats. *Circulation Research, 66,* 1747–1754.

Hamzei, F., Knab, R., Weiller, C., & Rother, J. (2003). The influence of extra- and intracranial artery disease on the BOLD signal in fMRI. *Neuroimage, 20,* 1393–1399.

Handwerker, D. A., Gazzaley, A., Inglis, B. A., & D'Esposito, M. (2007). Reducing vascular variability of fMRI data across aging populations using a breathholding task. *Human Brain Mapping, 28,* 846–859.

Hanson, S. J., Matsuka, T., & Haxby, J. V. (2004). Combinatorial codes in ventral temporal lobe for object recognition: Haxby (2001) revisited: Is there a "face" area? *Neuroimage, 23,* 156.

Haxby, J. V., Gobbini, M. I., Furey, M. L., Ishai, A., Schouten, J. L., & Pietrini, P. (2001). Distributed and overlapping representations of faces and objects in ventral temporal cortex. *Science, 293,* 2425–2430.

Haynes, J. D., & Rees, G. (2006). Decoding mental states from brain activity in humans. *Nature Reviews Neuroscience, 7,* 523–534.

Head, D., Buckner, R. L., Shimony, J. S., Williams, L. E., Akbudak, E., Conturo, T. E., et al. (2004). Differential vulnerability of anterior white matter in nondemented aging with minimal acceleration in dementia of the Alzheimer type: Evidence from diffusion tensor imaging. *Cerebral Cortex, 14,* 410–423.

Huettel, S. A., Singerman, J. D., & McCarthy, G. (2001). The effects of aging upon the hemodynamic response measured by functional MRI. *Neuroimage, 13,* 161–175.

Isingrini, M., & Vazou, F. (1997). Relation between fluid intelligence and frontal lobe functioning in older adults.

International Journal of Aging & Human Development, 45, 99–109.

Jiang, X., Bradley, E., Rini, R. A., Zeffiro, T., Vanmeter, J., & Riesenhuber, M. (2007). Categorization training results in shape- and category-selective human neural plasticity. *Neuron, 53,* 891–903.

Keri, S. (2003). The cognitive neuroscience of category learning. *Brain Research, Brain Research Reviews, 43,* 85–109.

Kosnik, W., Winslow, L., Kline, D., Rasinski, K., & Sekuler, R. (1988). Visual changes in daily life throughout adulthood. *Journal of Gerontology, 43,* P63–P70.

Kramer, A. F., Humphrey, D. G., Larish, J. F., Logan, G. D., & Strayer, D. L. (1994). Aging and inhibition: Beyond a unitary view of inhibitory processing in attention. *Psychology and Aging, 9,* 491–512.

Kriegeskorte, N., Goebel, R., & Bandettini, P. (2006). Information-based functional brain mapping. *Proceedings of the National Academy of Sciences, U.S.A., 103,* 3863–3868.

Levin, J. M., Frederick Bde, B., Ross, M. H., Fox, J. F., von Rosenberg, H. L., Kaufman, M. J., et al. (2001). Influence of baseline hematocrit and hemodilution on BOLD fMRI activation. *Magnetic Resonance Imaging, 19,* 1055–1062.

Li, S., Mayhew, S. D., & Kourtzi, Z. K. (2009). Learning shapes the representation of behavioral choice in the human brain. *Neuron, 62,* 441–452.

Logan, J. M., Sanders, A. L., Snyder, A. Z., Morris, J. C., & Buckner, R. L. (2002). Under-recruitment and nonselective recruitment: Dissociable neural mechanisms associated with aging. *Neuron, 33,* 827–840.

Madden, D. J., Turkington, T. G., Provenzale, J. M., Denny, L. L., Hawk, T. C., Gottlob, L. R., et al. (1999). Adult age differences in the functional neuroanatomy of verbal recognition memory. *Human Brain Mapping, 7,* 115–135.

Madden, D. J., Whiting, W. L., Huettel, S. A., White, L. E., MacFall, J. R., & Provenzale, J. M. (2004). Diffusion tensor imaging of adult age differences in cerebral white matter: Relation to response time. *Neuroimage, 21,* 1174–1181.

McIntosh, A. R., Sekuler, A. B., Penpeci, C., Rajah, M. N., Grady, C. L., Sekuler, R., et al. (1999). Recruitment of unique neural systems to support visual memory in normal aging. *Current Biology, 9,* 1275–1278.

Miller, E. K. (2000). The prefrontal cortex and cognitive control. *Nature Reviews Neuroscience, 1,* 59–65.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24,* 167–202.

Miller, B. T., & D'Esposito, M. (2005). Searching for "the top" in top–down control. *Neuron, 48,* 535–538.

Mirabella, G., Bertini, G., Samengo, I., Kilavik, B. E., Frilli, D., Della Libera, C., et al. (2007). Neurons in area V4 of the macaque translate attended visual features into behaviorally relevant categories. *Neuron, 54,* 303–318.

Moscovitch, M., & Winocur, G. (1995). Frontal lobes, memory, and aging. *Annals of the New York Academy of Sciences, 769,* 119–150.

Muhammad, R., Wallis, J. D., & Miller, E. K. (2006). A comparison of abstract rules in the prefrontal cortex, premotor cortex, inferior temporal cortex, and striatum. *Journal of Cognitive Neuroscience, 18,* 974.

Norman, K. A., Polyn, S. M., Detre, G. J., & Haxby, J. V. (2006). Beyond mind-reading: Multi-voxel pattern analysis of fMRI data. *Trends in Cognitive Sciences, 10,* 424–430.

Nosofsky, R. M. (1986). Attention, similarity, and the identification-categorization relationship. *Journal of Experimental Psychology: General, 115,* 39–61.

Op de Beeck, H. P., Baker, C. I., DiCarlo, J. J., & Kanwisher, N. G. (2006). Discrimination training alters object

representations in human extrastriate cortex. *Journal of Neuroscience, 26,* 13025–13036.

Op de Beeck, H. P., Torfs, K., & Wagemans, J. (2008). Perceived shape similarity among unfamiliar objects and the organization of the human object vision pathway. *Journal of Neuroscience, 28,* 10111–10123.

O'Toole, A. J., Jiang, F., Abdi, H., & Haxby, J. V. (2005). Partially distributed representations of objects and faces in ventral temporal cortex. *Journal of Cognitive Neuroscience, 17,* 580–590.

Palmeri, T. J., & Gauthier, I. (2004). Visual object understanding. *Nature Reviews Neuroscience, 5,* 291.

Park, D. C., Polk, T. A., Park, R., Minear, M., Savage, A., & Smith, M. R. (2004). Aging reduces neural specialization in ventral visual cortex. *Proceedings of the National Academy of Sciences, U.S.A., 101,* 13091–13095.

Parkin, A. J., & Lawrence, A. (1994). A dissociation in the relation between memory tasks and frontal lobe tests in the normal elderly. *Neuropsychologia, 32,* 1523–1532.

Peelle, J. E., & Wingfield, A. (2005). Dissociations in perceptual learning revealed by adult age differences in adaptation to time-compressed speech. *Journal of Experimental Psychology: Human Perception and Performance, 31,* 1315–1330.

Pineiro, R., Pendlebury, S., Johansen-Berg, H., & Matthews, P. M. (2002). Altered hemodynamic responses in patients after subcortical stroke measured by functional MRI. *Stroke, 33,* 103–109.

Porciatti, V., Fiorentini, A., Morrone, M. C., & Burr, D. C. (1999). The effects of ageing on reaction times to motion onset. *Vision Research, 39,* 2157–2164.

Racine, C. A., Barch, D. M., Braver, T. S., & Noelle, D. C. (2006). The effect of age on rule-based category learning. *Neuropsychology, Development, and Cognition, Section B, Aging, Neuropsychology and Cognition, 13,* 411–434.

Ratcliff, R., Thapar, A., & McKoon, G. (2006). Aging, practice, and perceptual tasks: A diffusion model analysis. *Psychology and Aging, 21,* 353–371.

Resnick, S. M., Pham, D. L., Kraut, M. A., Zonderman, A. B., & Davatzikos, C. (2003). Longitudinal magnetic resonance imaging studies of older adults: A shrinking brain. *Journal of Neuroscience, 23,* 3295–3301.

Restom, K., Bangen, K. J., Bondi, M. W., Perthen, J. E., & Liu, T. T. (2007). Cerebral blood flow and BOLD responses to a memory encoding task: A comparison between healthy young and elderly adults. *Neuroimage, 37,* 430–439.

Reuter-Lorenz, P. (2002). New visions of the aging mind and brain. *Trends in Cognitive Sciences, 6,* 394.

Reuter-Lorenz, P. A., & Lustig, C. (2005). Brain aging: Reorganizing discoveries about the aging mind. *Current Opinion in Neurobiology, 15,* 245–251.

Richards, E., Bennett, P. J., & Sekuler, A. B. (2006). Age related differences in learning with the useful field of view. *Vision Research, 46,* 4217–4231.

Ridderinkhof, K. R., Span, M. M., & van der Molen, M. W. (2002). Perseverative behavior and adaptive control in older adults: Performance monitoring, rule induction, and set shifting. *Brain and Cognition, 49,* 382–401.

Rotshtein, P., Henson, R. N., Treves, A., Driver, J., & Dolan, R. J. (2005). Morphing Marilyn into Maggie dissociates physical and identity face representations in the brain. *Nature Neuroscience, 8,* 107.

Rypma, B., & D'Esposito, M. (2000). Isolating the neural mechanisms of age-related changes in human working memory. *Nature Neuroscience, 3,* 509–515.

Rypma, B., Prabhakaran, V., Desmond, J. E., & Gabrieli, J. D. (2001). Age differences in prefrontal cortical activity in working memory. *Psychology and Aging, 16,* 371–384.

Salat, D. H., Buckner, R. L., Snyder, A. Z., Greve, D. N., Desikan, R. S., Busa, E., et al. (2004). Thinning of the cerebral cortex in aging. *Cerebral Cortex, 14,* 721–730.

Schmitt-Eliassen, J., Ferstl, R., Wiesner, C., Deuschl, G., & Witt, K. (2007). Feedback-based versus observational classification learning in healthy aging and Parkinson's disease. *Brain Research, 1142,* 178–188.

Schyns, P. G., Goldstone, R. L., & Thibaut, J. P. (1998). The development of features in object concepts. *Behavioral and Brain Sciences, 21,* 1–17; discussion 17–54.

Seu, L., & Ferrera, V. P. (2001). Detection thresholds for spiral Glass patterns. *Vision Research, 41,* 3785–3790.

Sigala, N., Gabbiani, F., & Logothetis, N. K. (2002). Visual categorization and object representation in monkeys and humans. *Journal of Cognitive Neuroscience, 14,* 187–198.

Sigala, N., & Logothetis, N. K. (2002). Visual categorization shapes feature selectivity in the primate temporal cortex. *Nature, 415,* 318–320.

Smith, M. L., Gosselin, F., & Schyns, P. G. (2004). Receptive fields for flexible face categorizations. *Psychological Science, 15,* 753–761.

Taoka, T., Iwasaki, S., Uchida, H., Fukusumi, A., Nakagawa, H., Kichikawa, K., et al. (1998). Age correlation of the time lag in signal change on EPI-fMRI. *Journal of Computer Assisted Tomography, 22,* 514–517.

Toni, I., Rushworth, M. F., & Passingham, R. E. (2001). Neural correlates of visuomotor associations. Spatial rules compared with arbitrary rules. *Experimental Brain Research, 141,* 359–369.

Vapnik, V. N. (1995). *The nature of statistical learning theory.* Springer.

West, R. L. (1996). An application of prefrontal cortex function theory to cognitive aging. *Psychological Bulletin, 120,* 272–292.

Williams, M. A., Dang, S., & Kanwisher, N. G. (2007). Only some spatial patterns of fMRI response are read out in task performance. *Nature Neuroscience, 10,* 685–686.

Wilson, H. R., & Wilkinson, F. (1998). Detection of global structure in Glass patterns: Implications for form vision. *Vision Research, 38,* 2933–2947.