

Where color rests: Spontaneous brain activity of bilateral fusiform and lingual regions predicts object color knowledge performance

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ARTICLE INFO

Article history:

Accepted 4 March 2013

Available online 19 March 2013

Keywords:

Resting-state activity
Object color knowledge
Functional connectivity
Network
fMRI

ABSTRACT

Knowledge of the physical attributes of objects is commonly assumed to be distributed near their respective modality-specific brain regions. The exact neural correlates for such knowledge, especially how it is maintained in the resting state, are largely unknown. In the current study, we explored the intrinsic neural basis related to a specific type of object knowledge – color – by investigating the relationship between spontaneous brain activity and color knowledge behavioral performance. We correlated the regional amplitude of spontaneous low-frequency fluctuations (ALFF, a resting-state fMRI parameter) with healthy participants' performance on two object color knowledge tasks (object color verification and color attribute judgment). We found that ALFF in bilateral lingual and fusiform gyri and right inferior occipital gyrus reliably predicted participants' color knowledge performance (correlation coefficients = 0.55–0.70), and that calcarine cortex showed a similar trend, although less stable. Furthermore, the ALFF-behavior correlations for other types of object knowledge (i.e. form, motion and sound) in these regions were minimal and significantly lower than those for color knowledge, suggesting that the effects in the observed regions were not merely due to general object processing. Furthermore, we showed that functional connectivity strengths of the lingual/fusiform and inferior occipital regions are significantly associated with color knowledge performance, indicating that they work as a network to support color knowledge processing or the acquisition of such knowledge. Our findings show the critical role of ventral medial occipito-temporal regions in processing or acquiring color knowledge and highlight the behavioral significance of spontaneous brain activity in the resting state.

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Introduction

We come to know the world through the various senses. We see red roses and tall buildings. We see birds fly and hear them serenade. When these objects come to mind, their physical (e.g., color, form, motion and sound) and functional properties are activated. It is commonly assumed that knowledge about the various physical properties of objects might be distributed in or near (e.g., anterior to) cortical areas that are involved in processing the corresponding sensory or motor features (e.g., Allport, 1985; Barsalou, 1999; Buxbaum and Saffran, 2002; Goldberg et al., 2006; Kellenbach et al., 2001; Kiefer et al., 2008; Martin et al., 1995; Miceli et al., 2001; Noppeney et al., 2005; Saygin, 2007; Thompson-Schill, 2003; Thompson-Schill et al., 1999; Warrington and Shallice, 1984; see Binder and Desai, 2011 for a review).

Here we focus on object color. Unlike other types of object knowledge such as form or motion, color knowledge relies almost exclusively on the visual modality and can rarely be deduced from other object features. One of the most compelling sources of evidence for the independence of modality-specific representations comes from a patient showing selective deficit of object color knowledge (Miceli et al., 2001). The patient, I.O.C., had difficulty with tasks involving object color knowledge retrieval but had normal performance on color perception and in tasks that probed other object feature knowledge (e.g., form and function). I.O.C.'s lesion was restricted to occipital and ventral temporal cortex in the left hemisphere, including the calcarine cortex, the lingual gyrus, the parahippocampal gyrus and the rostro-medial portion of the fusiform gyrus, suggesting that at least part of these regions are highly specific to the processing of object color knowledge, even relative to other types of visual properties (e.g., form). Other neurological cases have been reported showing color knowledge deficits with lesions involving (but not restricted to) left temporal regions, although the deficits were not specific to color processing (Farah et al., 1988; Luzzatti and Davidoff, 1994). Results from neuroimaging studies with healthy participants converge in ascribing to regions in occipital and ventral medial temporal cortex

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an important role in processing object color knowledge. These studies have found that occipital and ventral medial regions are more strongly activated by object color knowledge tasks in comparison to rest or to other knowledge types (e.g., action, sound, touch), although other brain regions including the inferior/superior parietal lobe and the medial/inferior frontal lobe have also been implicated (Chao and Martin, 1999; Hsu et al., 2011, 2012; Kellenbach et al., 2001; Martin et al., 1995; Oliver and Thompson-Schill, 2003; Simmons et al., 2007; Ueno et al., 2007). It remains unknown, however, whether and how color knowledge is maintained by spontaneous brain activity without explicit, task-directed behavior.

In the research reported here we take advantage of a resting-state functional magnetic resonance imaging (rs-fMRI) measure to elucidate the intrinsic neural basis related to object color knowledge representation, focusing on the low-frequency fluctuations (LFFs, 0.01–0.10 Hz), which are related to spontaneous neuronal activities (Biswal et al., 1995; Logothetis et al., 2001; Raichle, 2006). At least two different aspects of LFFs – the regional amplitude of low-frequency fluctuations (ALFF) and the resting-state functional connectivity (RSFC) measured by degree of synchronization – have been shown to reflect neuronal signals and are behaviorally relevant (Biswal et al., 1995; Zang et al., 2007; see Fox and Raichle, 2007 for a review). Both aspects have been shown to be able to identify populations with various types of neurological and psychiatric disorders such as Alzheimer's disease (He et al., 2007; Wang et al., 2011), mild cognitive impairment (Wang et al., 2011; Yi et al., 2012; Zhao et al., 2012), major depressive disorder (Zhang et al., 2011), ADHD (Zang et al., 2007) and schizophrenia (Hoptman et al., 2010). Significantly, several recent studies showed that in healthy populations the individual variations of ALFF and RSFC patterns associate with behavioral performances such as visual discrimination (Baldassarre et al., 2012; Lewis et al., 2009), attention (Mennes et al., 2011), reading ability (Hampson et al., 2006; Koyama et al., 2010; Wang et al., 2012), face processing (Zhu et al., 2011) and conceptual processing (Wei et al., 2012). The ALFF has also been reported to be associated with the magnitude of task-evoked brain activity during attention task (Mennes et al., 2011) and working memory task (Zou et al., *in press*) and be able to distinguish eyes-open from eyes-closed states (Yang et al., 2007). These findings indicate the potentials of ALFF and RSFC to reflect underlying neural mechanisms for cognition.

Here we explored the intrinsic neural correlates associated with object color knowledge by investigating whether regional ALFF patterns can predict variation in color knowledge performance in a group of healthy participants. After identifying the brain regions whose resting-state regional activity correlated with color knowledge performance, we further examined whether the association is indeed for object color knowledge as opposed to just any object property. We did this by comparing effects of color knowledge with those of other types of knowledge including visual form, motion, and sound. Finally, we explored how the color-specific regions work together by testing how the functional connectivity strengths between these regions and other regions relate to participants' object color knowledge performance. Complementing the task-based fMRI studies which explore the brain regions being activated during the performance of color knowledge tasks, the approach of associating resting-state activity patterns with behavior uncovers the brain regions and networks that are related to off-line color knowledge processing, such as those playing a role in the acquisition and integration of color knowledge.

Methods

Participants

Forty-eight healthy adults (22 female, 46 right-handed, 2 ambidextrous) with a wide range of age (49.7 ± 10.9 years old, range: 26–72 years old) and education levels (13.1 ± 3.9 years, range: 6–22 years), with normal or corrected to normal vision, completed

both behavioral tests and imaging scans. None had any history of psychiatric or neurological disease. All participants provided written informed consent and received monetary compensation for their participation. The study was approved by the institutional review board of the National Key Laboratory of Cognitive Neuroscience and Learning, Beijing Normal University.

Behavioral tests

For all behavioral tests, DMDX program (Forster and Forster, 2003) was used to present stimuli and record responses. Participants were asked to respond as accurately as possible without time pressure by pressing the correct response on a touch screen.

Tests of object color knowledge

Three color-processing tasks were administered, including a color perception test, an object color verification task and an object color attribute judgment task. The latter two tasks assess object color knowledge through pictorial and verbal inputs, respectively. Performance on these two tasks was combined to produce an object color knowledge index. The color perception task was carried out to exclude peripheral color perceptual deficits.

A color blindness test – “the color vision examination plates” (Yu et al., 1996) – that is widely used in clinical settings in China to diagnose acquired and congenital color vision deficiencies (protanopia, deuteranopia, protanomalopia, deuteranomalopia and monochromatism) was adopted as the color perception task. The test is similar to the Ishihara tests for color blindness (Ishihara, 1983) and contained 20 trials, including 10 digit and 10 geometric forms composed of color dots. According to the diagnosis manual, people with protanopia and deuteranopia can at most read correctly one item; people with protanomalopia and deuteranomalopia can read correctly nine to fifteen items; people with acquired color blindness or monochromatism are not able to read correctly any of the items. Participants with accuracy below 90% on this task were excluded from the study.

In the object color verification task (CV), a color patch and a gray-scale picture of an object were vertically aligned at the center of the touch screen, with a “Yes” on the bottom left and a “No” on the bottom right. Participants were asked to verify whether the color is typical for the object, and to press “Yes” or “No” on the screen accordingly (e.g., a red patch and an apple). The CV task included 20 common objects with prototypical colors (10 animals, 10 fruits/vegetables). Each item appeared twice, once with the congruent color patch and once with the incongruent one, creating 40 trials organized into two sets. Semantic categories and yes/no responses of the trials were counterbalanced across the two sets. One point was given if the participant responded correctly to an item on both sets (i.e., a correct “yes” and a correct “no” response), resulting in a total score of 20 points and a chance level of 25% accuracy in this verification task.

In the object color attribute judgment task (CAJ), a question concerning object color features (e.g., The brownish one is?) was presented on the touch screen with two items from the same object category (Lion/Penguin) horizontally aligned below the question. Participants were asked to press the best answer on the touch screen. The CAJ task had 30 questions (15 concerning animals and 15 concerning fruits/vegetables). Chance level accuracy was 50%.

Tests of other feature knowledge of objects

To verify whether any brain region found to correlate with object color knowledge performance was selective for such knowledge, other knowledge features, including visual form, visual motion and sound, were also tested. As for color knowledge, each of these feature types was assessed with a property verification and an attribute judgment task. Each verification task had two sets, with equal numbers of matching and non-matching trials. One point was given if the participant responded correctly to an item on both the matching and

non-matching trials resulting in a chance level of 25% accuracy in this task.

In the form verification task, two gray-scale pictures of object parts were vertically aligned at the center of the touch screen, with a “Yes” on the bottom left and “No” on the bottom right. Participants were asked to verify whether the two parts were from the same object or different objects and press “Yes” or “No” on the screen accordingly. The objects included animals, fruit and vegetables and manmade artifacts.

In the motion verification task, a clip of a moving-dot video and a gray-scale picture concerning human actions, tools or animals were vertically aligned at the center of the touch screen, with a “Yes” on the bottom left and “No” on the bottom right. Participants were asked to verify whether the motion pattern of the moving dots was consistent with the classic motion pattern of the objects or action in the picture and press “Yes” or “No” on the screen accordingly.

In the sound verification task, participants listened to a sound through headphones and at the same time watched a color photograph of an animal or a manmade object displayed at the center of the touch screen, with a “Yes” on the left and a “No” on the right. Participants were asked to verify whether the objects in the photograph could produce a sound like the one presented over the headphone, and press “Yes” or “No” on the screen accordingly.

All object attribute judgment tasks had identical test structures to the color attribute judgment task except for the number and categories of items involved. The chance level of the attribute judgment tasks was 50% in all cases.

Image acquisition

Image data were collected using a 1.5 T whole body MRI scanner (Signa Twinspeed 1.5 T, GE Healthcare, US) in the imaging department of China Rehabilitation Research Center. The participants lay supine with the head snugly fixed with straps and foam pads to minimize head movement. Two identical sequences of resting-state fMRI (rs-fMRI) scans were obtained consecutively, using an echo-planar imaging (EPI) sequence along AC–PC line with the following parameters: 28 axial slices, slice thickness = 4 mm, gap = 1 mm, time repetition (TR) = 2000 ms, time echo (TE) = 40 ms, flip angle (FA) = 90°, field of view (FOV) = 210 mm × 210 mm. During the rs-fMRI scans, participants were instructed to close their eyes, keep still, stay awake and not to think about anything in particular. At the same slice locations as the functional images, T1 anatomical images (28 axial slices, slice thickness = 5 mm, gap = 0, FOV = 250 mm × 250 mm, matrix = 256 × 256, TR = 3071 ms, TE = 9.6 ms, TI = 2000 ms, FA = 90°) were acquired to co-register the functional images onto the high-resolution anatomical three-dimensional magnetization-prepared rapid gradient echo (MPRAGE) sagittal images (248 slices, TR = 12.264 ms, TE = 4.2 ms, inversion time (TI) = 400 ms, slice thickness = 1.4 mm, slice spacing = 0.70 mm, voxel size after interpolated by scanner was 0.70 × 0.488 × 0.488 mm³, FA = 15°, FOV = 250 mm × 250 mm, in-plane resolution = 256 × 256). Two identical sequences of the high-resolution MPRAGE T1 images were collected. The order of the behavioral tests and the imaging acquisition varied across participants depending on participants' convenience. For the majority of the participants (38/48), the whole battery of behavioral tests was administered at least one day before the imaging session. For two participants, the imaging session preceded all behavioral tests. For eight participants, the color tests (and other tests) were conducted before the imaging session on the same day. We further analyzed our data excluding these latter eight participants whose resting state scans were most likely to be “contaminated” by the behavioral tests.

Data preprocessing

Preprocessing was performed using Statistical Parametric Mapping software (SPM5; <http://www.fil.ion.ucl.ac.uk/spm>) and Data Processing

Assistant for Resting-state fMRI (DPARSF, Yan and Zang, 2010). For the resting-state fMRI data sequence, the first 10 volumes of images were discarded for signal equilibrium. Slice timing and motion correction were performed and a mean functional image was acquired for each participant. No participant exhibited head motion >2.5 mm maximum translation or 2.5° rotation. A mean structural image was also obtained for each participant by averaging the two MPRAGE T1 image sequences after a linear co-registration. To normalize the functional images, each participant's mean structural brain image was first co-registered to the mean functional image using the 28 slices axial T1 images as intermediary and was subsequently segmented using the unified segmentation VBM module (Ashburner and Friston, 2005) implemented in DPARSFA. The parameters obtained in segmentation were used to normalize each participant's functional image onto the Montreal Neurological Institute (MNI) space. The functional images were then re-sampled to 3 mm isotropic voxels followed by spatial smoothing with a 6-mm full width at half maximum (FWHM) Gaussian kernel. Finally, linear trends were removed and the images were 0.01–0.1 Hz band-pass filtered to reduce the effects of low-frequency drifts and high-frequency noise (Zuo et al., 2010). The two functional sequences were preprocessed separately following the same protocol. Two participants whose images were not successfully segmented in the preprocessing stage were excluded from further analysis.

Calculation of ALFF

Because we were only concerned about the neuronal signals in gray matter (Biswal et al., 1995), further analysis was conducted with a gray matter mask. We included voxels with a probability higher than 0.4 in the SPM5 template onto the gray matter mask and excluded the cerebellar regions (91[#]–116[#]) in the Automated Anatomical Labeling (AAL) template (Tzourio-Mazoyer et al., 2002). In total, there were 36,272 voxels (979,344 mm³) in the gray matter mask.

The ALFF value of each voxel in the brain was extracted as the sum of amplitudes within the low-frequency range (0.01–0.1 Hz) (Zuo et al., 2010). For standardization purposes, the ALFF of each voxel was divided by the mean ALFF value within the gray matter mask for every participant. We calculate the voxel-wise ALFF values of the two functional sequences separately.

Data analysis

Eight participants were excluded from the formal analysis: two whose images were not successfully segmented in the preprocessing stage (see above in the Data preprocessing section), five had color perception accuracies below 90%, and one had an extremely low color verification score (40%, three standard deviations lower than the group average).

Behavioral scores

For each object feature task, participants' accuracies on verification and attribute judgment tasks were transformed to z-scores and averaged to form a composite score as a comprehensive index of the object feature knowledge.¹ Because color knowledge tasks included only living things while other knowledge tasks included nonliving items, we considered only living items in all tasks to avoid undesired category effects (see Table 1 for detailed information).

Although task instructions stressed that participants were to consider the typical color of an object, the answers were not as consistent as we had anticipated, especially when concerning animals. For instance, for the color of a monkey, both gray and brown were accepted as possible colors by some participants. We used two scoring methods in order to deal with this variability. One scoring method used the standard answer chosen by the experimenters as the correct response (scoring method 1), the other was to use the response given by the

¹ Five participants did not take the sound attribute judgment test. We replaced these missing values with the mean accuracy on this task.

Table 1

Stimulus types and behavioral data distribution of different object knowledge tasks. fv = fruits and vegetables; Veri = object verification task; Judge = object attribute judgment task; and S.M. = scoring method. The mean accuracy and standard deviations reported here represents only the living items (collapsing animal and fv) in each task, and are presented separately for verification and judgment tasks.

		Color		Form		Motion		Sound	
		Veri	Judge	Veri	Judge	Veri	Judge	Veri	Judge
Num. of items	Animal	10	15	12	15	15	15	17	15
	fv	10	15	12	15	–	–	–	–
S.M. 1	Mean	78.6	94.5	88.6	93.1	65.3	97.8	85.0	87.4
Acc. (%)	SD	10.7	4.5	8.1	4.6	20.4	4.4	10.1	13.2
S.M. 2	Mean	79.9	94.5	88.6	93.1	65.3	97.8	85.0	87.4
Acc. (%)	SD	11.5	4.5	8.1	4.6	20.3	4.4	10.1	13.2

majority of the participants as the correct answer (scoring method 2). We calculated the accuracy of each participant using both methods to obtain two color verification scores.

ALFF-behavior correlation analysis

Color knowledge-related brain regions. To explore the brain regions whose ALFF values predicted color knowledge performance, we carried out a whole-brain correlation analysis using the Resting-state fMRI Data Analysis Toolkit (REST, by Song et al., 2011, <http://resting-fmri.sourceforge.net>). The ALFF images of the two functional sequences of the rs-fMRI data (Session 1 and Session 2) were analyzed separately. Partial correlations between ALFF and color composite scores were calculated across the whole brain with age, gender and years of education removed as confounding factors. Results were corrected for multiple-comparisons using AlphaSim implemented in REST. A threshold of corrected cluster $p < 0.05$ (single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$) was set.

Functional specificity analysis: color knowledge relative to other types of object knowledge. In this section we examined the extent to which a region(s) showing association between its ALFF and color knowledge scores was specific to color knowledge. We tackled the issue of specificity from two inter-related angles: a) whether an area was related to color knowledge performance even when the contribution of other types of object knowledge was removed, i.e., whether the regional ALFF had a unique relationship with color knowledge processing beyond its relationship with object knowledge in general and b) whether the ALFF of the selected regions of interest (ROIs) correlated with color knowledge scores more strongly than with other types of knowledge.

Whole-brain functional specificity analysis. Here we attempted to explore regions showing “selective” effects of color knowledge processing by removing the contribution of participants’ performance on form, motion and sound tasks when calculating the partial correlation between ALFF and color knowledge performance. Participants’ age, gender and years of education were also removed as confounding factors. The whole-brain functional specificity analysis was performed using Session 1 and Session 2 ALFF images separately. Results were corrected for multiple-comparisons using AlphaSim implemented in REST. A threshold of corrected cluster $p < 0.05$ (single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$) was set.

Note that the full item sets in each knowledge tasks varied, with color knowledge tasks containing fruit/vegetables and animals, which were not fully included in sound and motion tasks (as fruit/vegetables did not have motion or sound properties). Only the form knowledge tasks included the full set of items used in the color knowledge tasks. We therefore further calculated the partial correlation between ALFF and the color composite score with participants’ age, gender, years of education and the composite scores on only the form knowledge tasks removed. Results were corrected for multiple-comparisons using

AlphaSim implemented in REST. A threshold of corrected cluster $p < 0.05$ (single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$) was set.

The ROI functional specificity analysis. Besides having unique effects that could not be explained by non-color knowledge, a further aspect of selectivity of color knowledge processing requires that it has stronger effects than other knowledge types. To examine this possibility, we treated the brain region(s) obtained in the whole-brain functional specificity analysis above as ROI(s) and compared the effects of color knowledge tasks (ALFF-color composite score correlation) with the effects of other knowledge tasks. Specifically, we defined the ROI(s) using the first functional sequence of rs-fMRI data (Session 1) and carried out the ROI comparisons on the second sequence (Session 2) to avoid the problem of circularity (double dipping). The ROI masks were drawn in regions showing significant correlations in the ALFF-behavior whole-brain functional specificity analysis on Session 1. Then the ALFF values of Session 2 in the ROI(s) were extracted. We examined whether there was significant correlation between ALFF values and the composite scores of other object feature knowledge, with the contribution of age, gender and years of education removed. To statistically compare the correlation between ALFF and color knowledge to correlations between ALFF and other types of object knowledge, we used the Hotelling’s t-test (the FZT computator, cgarbin@unl.edu, <http://psych.unl.edu/psyrcs/statpage/regression.html>).

Functional connectivity analysis and connectivity-behavior correlation analysis

To explore whether the key region(s) we found in the ALFF-behavior analysis interact with other brain regions or among themselves to form a functional network for object color knowledge, we used the region(s) significantly correlated with color knowledge performance in the whole-brain functional specificity analysis as seed ROI(s) and computed the resting-state functional connectivity between the seed ROI(s) and all other voxels in the gray matter mask mentioned above. We then examined the network’s functional relevance for color knowledge by correlating the RSFC strength with color knowledge performance. Before the RSFC analysis, six head motion parameters, global mean signal, white matter signal, and cerebrospinal fluid signal were regressed out from BOLD signals in DPARSF. The RSFC analysis was performed in REST. To avoid the potential circularity, we defined the significant color knowledge specific region(s) observed in the ALFF-behavior correlation analysis of Session 1 data as seed ROI(s). Then we computed the RSFC using the Session 2 data. For each participant, mean time series of the seed ROI(s) was calculated and then correlated with time series of all other voxels in the gray matter mask. The correlation coefficients were transformed to Fisher z-scores to form a z-functional connectivity (zFC) map for each participant for further statistical analysis. One-sample t-tests were performed on the zFC maps across participants to identify regions showing significant positive functional connectivity ($zFC > 0$) with the seed ROI(s). The threshold of significance was set at single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$ using AlphaSim correction. We then defined the significant regions as a mask and performed the zFC-behavior partial correlation analysis in it, with the contribution of participants’ age, gender, years of education and performances on other object knowledge removed. The threshold of significance was determined by running AlphaSim in the corresponding masks. We also performed the reverse analysis using identical procedures by defining the significant region(s) from Session 2 data as seed ROI(s) and computing the RSFC using the Session 1 data.

Results

Behavioral results

Forty participants were entered in the formal analysis. The behavioral results of the color verification task using the two scoring methods (see Methods section) were highly correlated ($R = 0.94$) and therefore

in the analysis below we used the results from scoring method 2. The mean accuracies and standard deviations of color verification and color judgment tasks for both scoring methods are presented in Table 1. The correlations between the composite scores of color knowledge performance and the composite scores of form/motion/sound knowledge performances were 0.56 ($p < 0.001$), 0.25 ($p = 0.12$) and 0.28 ($p = 0.08$) respectively. The partial correlations between them after removing the contribution of age, years of education and gender were 0.27 (color-form, $p = 0.09$), -0.20 (color-motion, $p = 0.22$) and 0.06 (color-sound, $p = 0.71$), respectively.

Color knowledge related brain regions

To explore the relationship between the brain's regional spontaneous functional activity and color knowledge behavior, we correlated the color composite scores and the ALFF value of each voxel in the whole brain resting-state analysis. As shown in Fig. 1 (see also Table 2), the overall pattern of results of the two scanning sessions were largely consistent. We discovered a set of regions showing positive correlations between ALFF values and color composite scores (after removing the contribution of age, gender and years of education). The effects of right lingual and fusiform gyri (right LG/FG) were significant in both sessions (Session 1: 1107 mm³, Session 2: 3024 mm³, overlapping volume: 837 mm³). The effects of the following brain regions passed the height threshold (single voxel $p < 0.01$) but did not pass the extent threshold in both sessions: left LG/FG (Session 1: 540 mm³; Session 2: 2025 mm³; overlapping volumes: 351 mm³), left middle temporal gyrus (left MTG, Session 1: 675 mm³; Session 2: 540 mm³; overlapping volumes: 243 mm³) and right inferior occipital gyrus (right IOG, Session 1: 486 mm³; Session 2: 864 mm³; overlapping volumes: 351 mm³). Furthermore, analyses using Session 1 data also revealed a cluster in right angular gyrus showing significant ALFF-color performance correlations, while analyses of Session 2 data found a significant cluster in right calcarine cortex (see Fig. 1 and Table 2 for detailed information). Weaker trends in the corresponding regions in the other data sessions (single voxel $p < 0.01$, cluster size < 135 mm³) were also observed. Finally, we performed additional analyses excluding the eight participants who took the behavioral tests before the resting-state scans on the same day. This was done to reduce the potential contamination effects of behavioral tests on the resting-state imaging data. The results with the remaining 32 participants were similar to those reported in the main text, with the ALFF of bilateral LG/FG regions significantly correlated with the color knowledge performances after controlling for the effects of participants' age, years of education and gender (left LG/FG, $[-24 -75 -9]$, peak $R = 0.66$, 1107 mm³; right LG/FG, $[30 -63 -9]$, peak $R = 0.71$, 1026 mm³).

Color knowledge-specific brain regions

The whole-brain functional specificity analysis

The results of the whole-brain functional specificity analysis are shown in Fig. 2 and Table 2. After removing the effects of form, motion and sound knowledge performance, we still observed significant positive correlations between ALFF values and color composite scores in the LG/FG regions in both Session 1 and Session 2 data. Additionally, ALFF values in right IOG also showed significant correlation with color composite scores in both Sessions. There were 486 mm³, 999 mm³ and 1215 mm³ overlapping voxels in left lingual/fusiform, right lingual/fusiform and right inferior occipital gyrus, respectively. ALFF values in one cluster (2322 mm³) in the right calcarine cortex showed significant correlation with color composite scores in the Session 2 data with weaker similar effects observed in the Session 1 data (single voxel $p < 0.01$, cluster size = 486 mm³).

We also ran the whole-brain partial correlation analysis again on the items overlapping between color tasks and the control tasks, i.e., with

only the composite scores on form knowledge of fruit/vegetables and animals removed. In this analysis, too, the ALFF in bilateral LG/FG regions were found to be significantly related to color composite scores in both sessions (the left LG/FG regions showed significance of corrected $p < 0.025$, under the threshold combination of single voxel $p < 0.05$, cluster size ≥ 2997 mm³, and a trend toward significance of corrected $p < 0.072$, under the threshold combination of single voxel $p < 0.01$, cluster size ≥ 783 mm³); the right IOG showed significant correlation with color scores in Session 2 but for Session 1 data (cluster size: 459 mm³; corrected $p < 0.46$) only passed the height threshold (single voxel $p < 0.01$). See Supplementary material (Supplementary Fig. 1 and Table 1) for detailed information.

The ROI functional specificity analysis

For the regions showing association with color knowledge obtained using Session 1 data in the whole-brain functional specificity analysis, we extracted their average ALFF value for Session 2 data and correlated them with participants' color, form, motion and sound composite scores. We then compared the ALFF-behavior correlation on color knowledge to those on form, motion and sound knowledge. This ROI-based functional specificity analysis showed that there was no significant correlation between the ALFF in the bilateral LG/FG and right IOG ROIs and participants' performance on form, motion and sound knowledge tasks (the max R value: $R_{\text{rightIOG_form}} = 0.06$, $p = 0.716$). T-test showed that the differences between R_{color} and R_{form} , R_{motion} and R_{sound} were all significant in both clusters (minimum t value $t = 2.65$, $p = 0.012$). See Fig. 2 for details. We also carried out the reverse analyses – defining ROIs using the significant regions of Session 2 data and extracted the average ALFF value of the Session 1 data. Similar pattern of results was obtained (see Supplementary Fig. 2, where results of the analyses with ROIs defined within each scanning session were also presented).

Functional network specific to object color knowledge

To explore whether the observed bilateral LG/FG and right IOG regions worked in concert among themselves or with other brain regions as an object color-knowledge network, for resting state imaging data in Session 2 we computed the functional connectivity between each of these color-knowledge-specific seed ROIs (defined using the ALFF-behavior results in Session 1) and all other voxels in the gray matter mentioned above. As shown in Fig. 3, large cortical areas, mainly the ventral posterior occipito-temporo-parietal cortices, showed significant positive RSFC with the bilateral LG/FG and right IOG clusters. Fig. 4 and Table 3 display the regions whose RSFCs with seed ROIs are specifically related to object color knowledge within these RSFC masks: for the left LG/FG seed ROI, the strengths of its RSFCs with the right lingual/fusiform gyrus, the right middle and superior occipital gyrus, cuneus and neighboring superior parietal regions were significantly positively correlated with participants' color knowledge performances; for the right LG/FG seed ROI, the strengths of its RSFCs with the contralateral lingual and fusiform gyrus, bilateral superior occipital/parietal and cuneus regions, and right anterior fusiform regions showed significant positive correlation with color knowledge performance; for the right IOG seed ROI, the strengths of its RSFCs with left fusiform gyrus/inferior temporal gyrus showed significant positive correlation with color knowledge performance. In other words, the strengths of RSFCs among the core color specific regions observed in the ALFF-behavior analyses (bilateral lingual/fusiform and right IOG clusters), as well as between these regions and adjacent occipito-temporo-parietal regions, predicted color knowledge performance, indicating an intrinsic color-knowledge specific network.

We also carried out the reverse analyses – using the regions showing significant ALFF-behavior correlation from Session 2 as seed ROIs (the right calcarine cluster was not included for consistency with the analysis above) and computing the RSFC using the Session 1 data. A similar pattern of results was obtained (Supplementary Fig. 3 and Table 2).

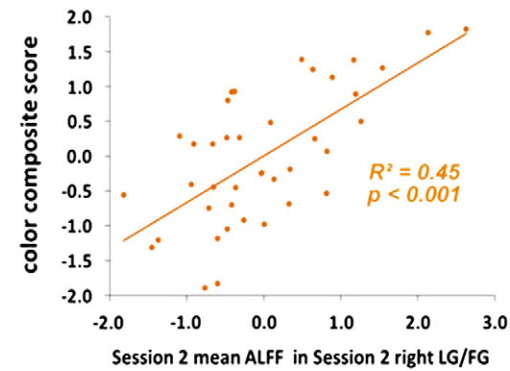
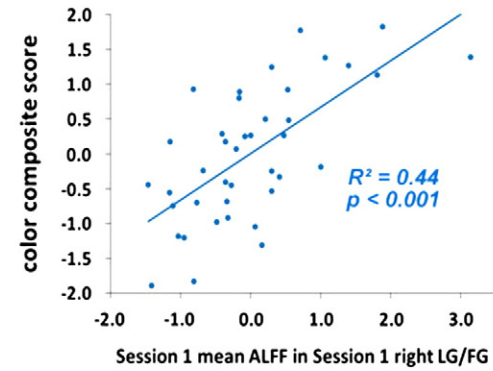
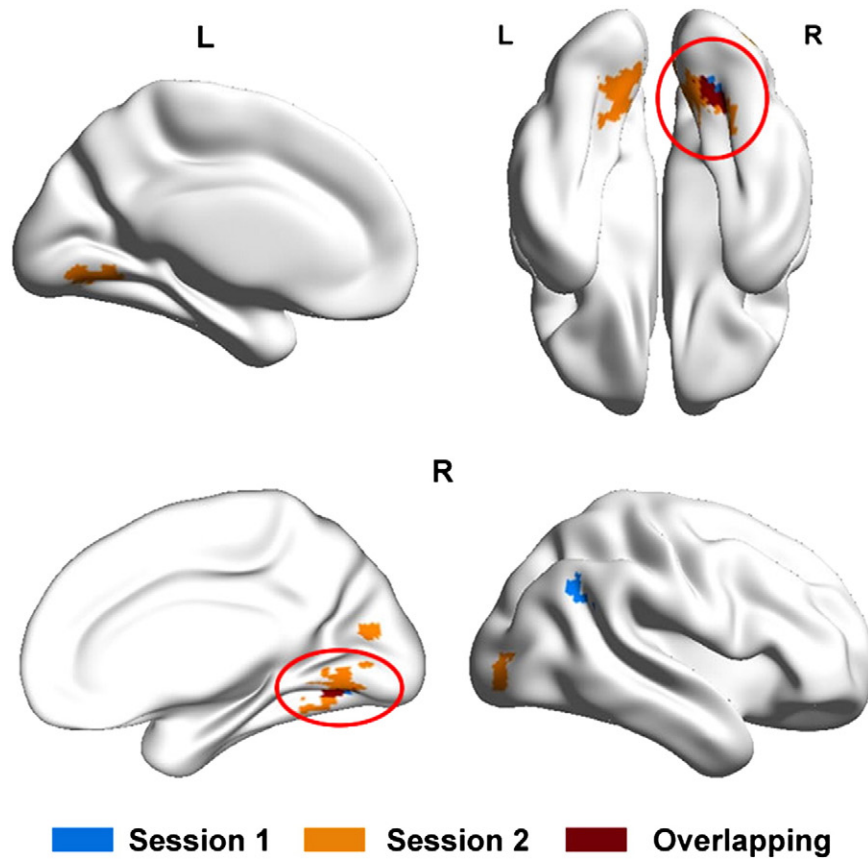


Fig. 1. Regions showing significantly positive partial correlation between ALFF and object color knowledge in Session 1 and Session 2. The significance threshold was set to the AlphaSim corrected cluster $p < 0.05$ (single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$). Blue patches indicate significant regions from the Session 1 data and orange patches indicate those from the Session 2 data. Overlapping regions, indicating consistency across sessions, are shown in dark red, which locate in the right lingual/fusiform (highlighted by a circle). Scatter plots show correlations between the color composite scores and average ALFF in each of the two sessions in their respective right lingual/fusiform cluster. The effects of age, gender and years of education were removed. Each dot represents data from one participant.

Table 2
Regions whose ALFF significantly or specifically related to object color knowledge performance in the whole-brain analysis.

Brain regions	BA	Peak MNI coordinates			Peak R	Cluster size	Cluster p
		x	y	z			
<i>Color knowledge related regions</i>							
Session 1							
R lingual gyrus/fusiform gyrus	18/19	30	−63	−9	0.64	1107	0.004
R angular gyrus	40	51	−57	33	0.54	837	0.021
Session 2							
R calcarine	18/23/30/31	3	−78	6	0.62	1620	0.001
L lingual gyrus/fusiform gyrus	18/19	−15	−63	−6	0.61	2025	0.001
R lingual gyrus/fusiform gyrus	18/19	18	−69	−6	0.59	3024	0.001
R inferior occipital gyrus	18/19	39	−90	−3	0.59	864	0.019
<i>Color knowledge specific regions</i>							
Session 1							
R lingual gyrus/fusiform gyrus	18/19	30	−63	−9	0.70	1431	0.001
R inferior occipital gyrus	18/19	36	−93	−6	0.61	837	0.021
L lingual gyrus/fusiform gyrus	18/19	−15	−66	−9	0.55	999	0.008
Session 2							
L lingual gyrus/fusiform gyrus	18/19/29/30	−15	−63	−6	0.69	2322	0.001
R calcarine	18/23/30/31	3	−75	6	0.65	2322	0.001
R lingual gyrus/fusiform gyrus	18/19/37	18	−69	−6	0.59	3078	0.001
R inferior occipital gyrus	18/19	39	−90	−3	0.59	891	0.018

BA = Brodmann area; R = right; and L = left.

Note that we employed a further approach where the overlapping regions in the two Sessions ALFF-behavioral results were used as seeds to optimize the reliability of the seed regions, and the results were overall consistent with the results above (see Supplementary results).

Combining the regional and connectivity features

To assess how much of the behavioral variance might be predicted from the resting-state fMRI patterns, we performed a multiple regression analysis to combine the joint contribution of the regional ALFF activity and RSFC pattern of the bilateral LG/FG and right IOG regions. In the regression model, the dependent variable was participants' color knowledge composite scores after regressing out the contribution of other types of object property knowledge and participants' age, years of education and gender. The independent variables included the ALFF values of the bilateral LG/FG and the right IOG, and the strength of the color knowledge relevant RSFCs. Here the purpose is to quantify the potential predictive power with just one resting state scan. We carried out this analysis using each of the two scanning sessions data separately, i.e., using the ALFF and RSFC information in the same session. For Session 1, the regression model explained 64.9% of the variation in participants' color knowledge performances ($R^2 = 0.65$; $F_{(10, 29)} = 5.36$, $p < 0.001$); and for Session 2, the regression model explained 64.7% of the variation in participants' color knowledge performances ($R^2 = 0.65$; $F_{(10, 29)} = 5.32$, $p < 0.001$).

Discussion

We observed that the spontaneous brain activity (ALFF) of regions in bilateral lingual/fusiform and right inferior occipital regions were significantly associated with object color knowledge behavioral performance in healthy individuals. These effects were not due to general object property processing as 1) the effects of color knowledge tasks remained significant after the effects of other types of property knowledge were removed; and 2) in these regions the correlations between their ALFFs and performance on other types of property knowledge (form, motion and sound) were minimal, and were significantly lower than the correlation between ALFF and color knowledge performance. We further observed that the degree of synchronization among these regions and adjacent occipito-temporo-parietal regions was strongly associated with participants' performance on object color knowledge, indicating that these regions work in concert with

each other as a network supporting processes that may predict color knowledge performance.

Our results corroborate previous findings with neuropsychological and task-based brain imaging approaches that the lingual and fusiform gyri are critical in object color processing. Patients showing color knowledge deficit have had lesions encompassing (but not restricted to) these two regions (Farah et al., 1988; Luzzatti and Davidoff, 1994; Miceli et al., 2001). In healthy participants color knowledge retrieval tasks induce activation in lingual and fusiform gyri (Chao and Martin, 1999; Hsu et al., 2011, 2012; Kellenbach et al., 2001; Martin et al., 1995; Ueno et al., 2007). Specifically, compared to other types of knowledge tasks, the activation by color knowledge tasks is stronger in bilateral fusiform gyrus, right parahippocampal gyrus and right superior orbital frontal lobe (color vs. action naming: Martin et al., 1995), left fusiform gyrus (color vs. motor property verification: Simmons et al., 2007), left posterior inferior temporal gyrus (color vs. sound and visual size attribute judgment tasks, Kellenbach et al., 2001); and left middle temporal gyrus and superior parietal lobe (color vs. sound, touch and taste property verification, Goldberg et al., 2006). It is worth noting that most of these studies compared object color knowledge to knowledge of non-visual modalities, and, therefore, such results may be related to visual properties in general rather than specific to color processing. We are aware of only two studies that compared object color knowledge to knowledge of other visual object properties. Kellenbach et al. (2001) did not find any color-knowledge specific regions in a whole-brain analysis when they compared object color to object size knowledge; they did, however, find a color knowledge effect in a ROI analysis in left posterior inferior temporal cortex. Oliver and Thompson-Schill (2003) failed to observe significantly stronger activation for object color knowledge compared to visual size and visual shape object knowledge in the fusiform regions of interest. Our finding that the spontaneous activity of lingual/fusiform regions associated with color knowledge performance and not with performance on other visual knowledge tasks suggests that these regions may indeed be more strongly related to object color processing than to general (visual) cognitive processing about objects.

We further observed that the bilateral lingual and fusiform gyrus and right inferior occipital gyrus work in concert with each other and adjacent occipito-temporo-parietal regions as a network involved in object color processing. The left fusiform/inferior temporal regions that showed high connectivity to right inferior occipital gyrus were more posterior than those temporal clusters frequently reported to be activated by object color knowledge retrieval (Chao and Martin,

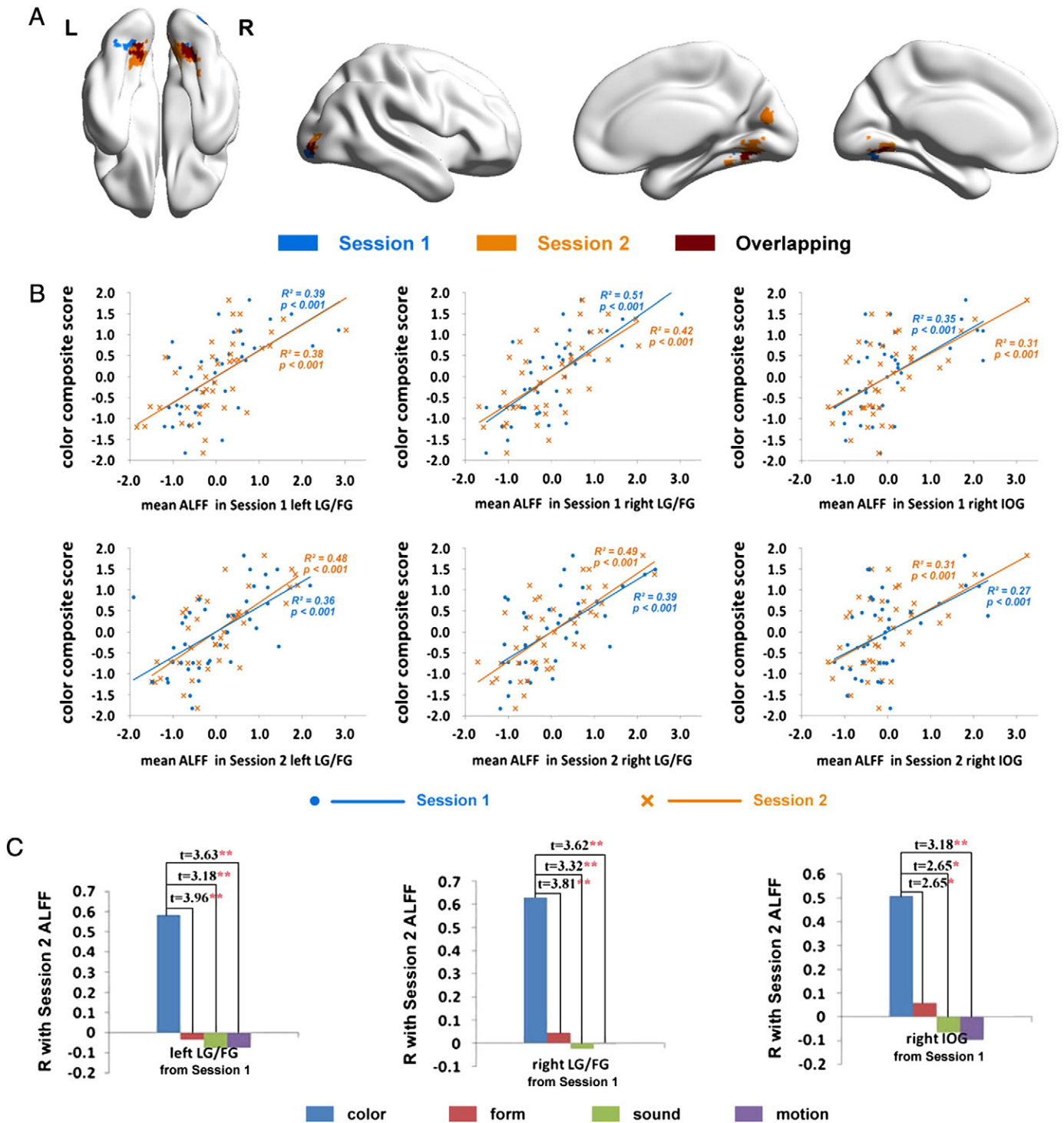


Fig. 2. A) Regions showing significant association with object color knowledge with the effects of other types of knowledge and participants' age, years of education and gender removed in Session 1 and Session 2. The significance threshold was set to the AlphaSim corrected cluster $p < 0.05$ (single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$). Blue patches indicate significant regions from the Session 1 data and orange patches indicate those from the Session 2 data. Overlapping regions across sessions are represented by dark red patches. B) Scatter plots show correlations between the color composite scores and average ALFF in each region found to be significant in Session 1 (top row) and Session 2 (bottom row) respectively. Each dot represents data from one participant. The blue dots represent data from Session 1 and orange dots represent data from Session 2. The effects of all other object knowledge, age, gender and years of education were removed. C) Bar maps show the effects of different types of knowledge (color, form, motion, sound) in each region in the ROI analysis. The significant regions in Session 1 were defined as ROIs and these regions' ALFF values in Session 2 were extracted to carry out the ALFF-behavior correlation. The height of the bar represents the correlation strength (Pearson R) between ALFF and composite scores of each type of object property knowledge. * $p < 0.05$ and ** $p < 0.01$.

1999; Goldberg et al., 2006; Hsu et al., 2011; Kellenbach et al., 2001; Martin et al., 1995; Simmons et al., 2007). The middle/superior occipital and neighboring parietal regions that showed connectivity to bilateral lingual/fusiform gyrus have been reported to be activated by tasks requiring color information retrieval, although not consistently:

Chao and Martin (1999) observed activation in the superior parietal lobule in color perception and object color naming tasks; Goldberg et al. (2006) observed superior parietal cortex activation when participants performed object color verification; Hsu et al. (2011) reported right cuneus and bilateral superior parietal activation in their auditory

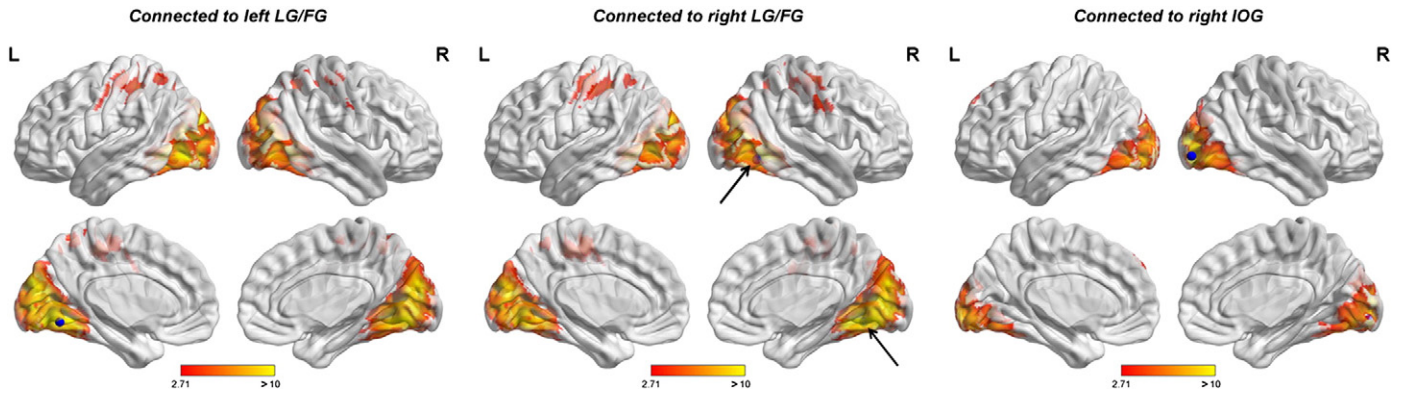


Fig. 3. Statistical maps of brain regions showing significant positive functional connectivity with the seed ROIs in bilateral LG/FG and right IOG. The significance threshold was set to the AlphaSim corrected cluster $p < 0.05$ (single voxel $p < 0.01$, cluster size $\geq 783 \text{ mm}^3$). The blue dots in the map indicate the approximate location of the seed ROIs. The color bar indicates the t value. The blue dot of the middle map is more medial and is pointed to by a black arrow.

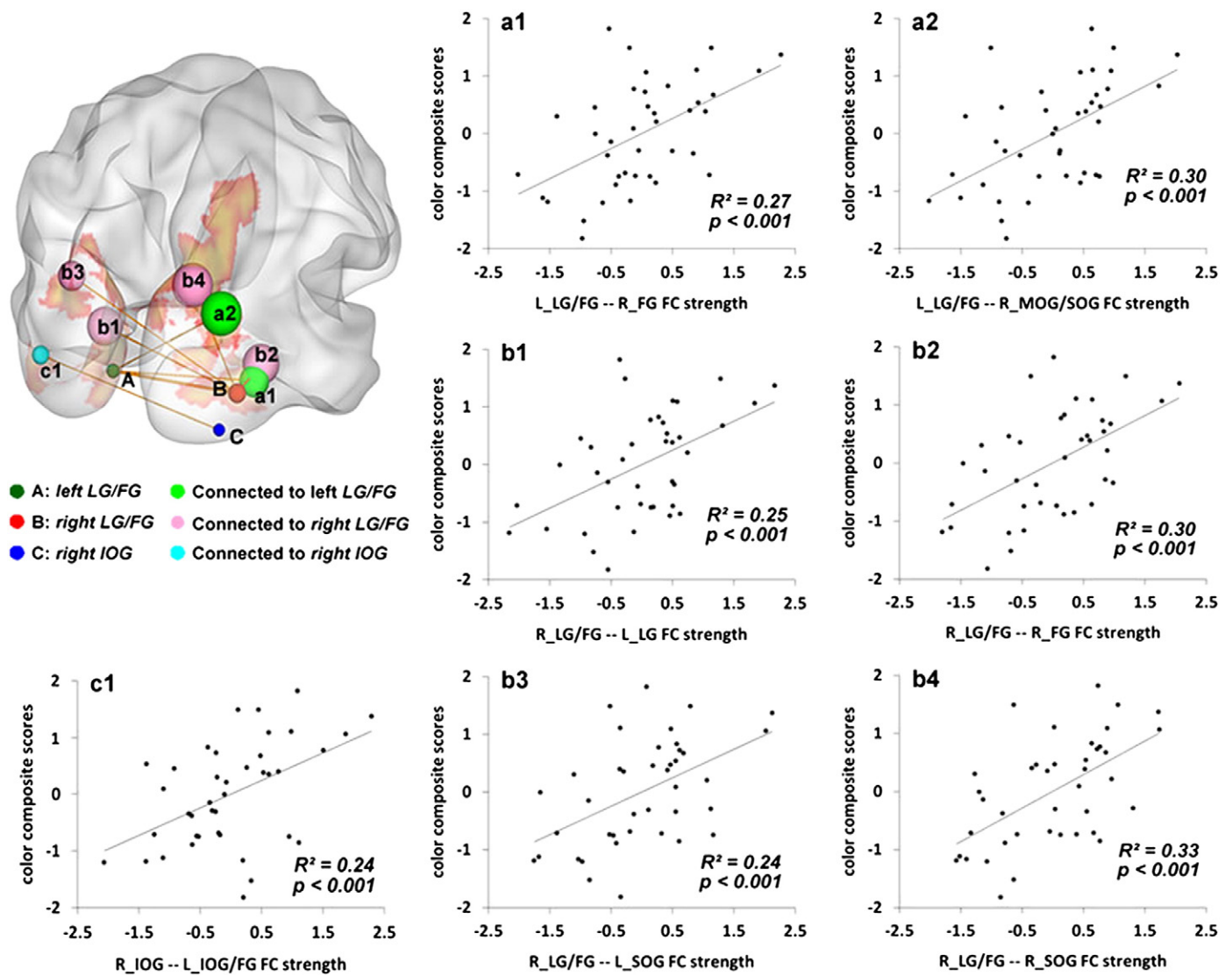


Fig. 4. The schematic view of the functional network of object color knowledge derived from RSFC data of Session 2. The orange patches indicate the actual areas of the significant clusters found in the RSFC-behavior analysis. For display simplicity, the darker red, green and blue points indicate the bilateral lingual/fusiform gyrus and right inferior occipital gyrus seed ROIs (defined using Session 1 data), respectively. Lighter color dots indicate clusters whose RSFC with the seed regions of corresponding color significantly correlated with color knowledge performance. The sizes of the points indicate the relative size of the clusters. The rods indicate significant correlations and thicker rods indicate greater correlation coefficients. Scatter plots show the positive partial correlations between participants' object color knowledge performance and the functional connectivity between each seed ROI and brain regions connected to them. The contribution of participants' age, gender, years of education and performance on other types of object knowledge was removed. Each dot represents data from one participant. The brain is viewed from right posterior.

Table 3

Brain regions whose functional connectivity with color-knowledge-specific seed ROIs are significantly positively related to object color knowledge performance. For the bilateral LG/FG masks, the threshold was set as the combination of single voxel $p < 0.05$, cluster size $\geq 1620 \text{ mm}^3$, corrected cluster $p < 0.05$; and for the right IOG mask, the threshold was the combination of single voxel $p < 0.05$, cluster size $\geq 1215 \text{ mm}^3$, corrected cluster $p < 0.05$.

Brain regions	BA	Peak MNI coordinates			Peak R	Cluster size	Cluster p
		x	y	z			
<i>Connected to left LG/FG</i>							
R fusiform gyrus/lingual gyrus	18/19/36/37	30	−48	−12	0.55	3159	<0.001
R middle/superior occipital gyrus/cuneus/superior parietal lobule	7/19/31/40	33	−84	30	0.56	5373	<0.001
<i>Connected to right LG/FG</i>							
R fusiform gyrus/lingual gyrus/parahippocampal gyrus/calcarine	18/19/30/36/37	30	−42	−9	0.51	4482	<0.001
L lingual gyrus/fusiform gyrus	18/19/30/37	−27	−45	−6	0.50	4185	<0.001
L superior occipital gyrus/cuneus	7/18/19	−24	−81	30	0.51	2673	<0.004
R superior occipital gyrus/cuneus/superior parietal lobule	7/19/31/39/40	21	−81	36	0.58	5427	<0.001
<i>Connected to right IOG</i>							
L fusiform gyrus/inferior temporal gyrus	19/37	−42	−66	−9	0.53	1377	<0.05

R = right and L = left.

version of object color similarity judgment task, but only observed superior parietal activation in the visual version; Kellenbach et al. (2001) did not find any parietal clusters using the object color judgment task; and, in Simmons et al. (2007), no cluster was reported to be activated by object color verification in comparison to motor verification. Our results suggest that the middle/superior occipital/parietal regions that are functionally connected to color related areas may participate in object color processing by interacting with the core regions in the lingual and fusiform gyri, and thus may not show effects as strong as the core regions in task-based fMRI studies. Their exact function in processing object color awaits further exploration.

A long-standing issue in object processing is the relationship between color knowledge and color perception processes (Allport, 1985; Barsalou et al., 2003; Martin and Chao, 2001; Thompson-Schill, 2003). In task-based neuroimaging studies, color knowledge sensitive regions have been found to overlap to some extent with (Hsu et al., 2011, 2012; Simmons et al., 2007) or be close to (Chao and Martin, 1999) regions reported to be involved in color perception. Chao and Martin (1999) reported that the coordinates of peak activation related to color knowledge retrieval were 2 cm lateral to the peak coordinates of color perception. One of the color-specific regions in our study, the right lingual/fusiform cluster (peak Talairach coordinates: Session 1: 27, −60, −9; Session 2: 16, −66, −7), lies between the color-knowledge region (peak Talairach coordinates: 38, −64, −16) and the color-perception region (peak Talairach coordinates: 4, −86, 0) in Chao and Martin's study. Another color-specific region to emerge from our study, the right IOG, has been associated with color perception, but not exclusively. It has been found to be activated when participants pay attention to color properties of nonsense objects (Cant and Goodale, 2007) or when participants learn and retrieve color information of random shapes (Ueno et al., 2007).

We have described our findings mainly in terms of the representation and retrieval of color knowledge as opposed to perceptual processes because we tested participants on object color knowledge, including a purely verbal color attribute judgment task without any color perception requirement. Furthermore, when we consider the results for the latter task, we obtained highly similar results to the picture task,² suggesting that a common element in these tasks may be object color knowledge processing and not perceptual color processing per se. However, the results could also be discussed from the perspective of the perceptual (and cognitive) processes that are involved

in acquiring and using object color knowledge. The measure used in this study – the correlation of resting state activity patterns with color knowledge performance – reflects an offline relationship between brain and behavior. The network observed with this measure may reflect the effects of early color perception processes needed for discriminating different colors, later processes needed to associate the discriminated colors to specific objects, and still later processes involved in generalizing these color–object relationships to object types and their names. All of these processes are needed to create stable object color-knowledge representations that could serve as the basis for performing the types of color knowledge tasks used in this study, such as the verbal color attribute judgment task. And, since individual differences in performance ultimately reflect not only the steady state of object color knowledge but also the developmental processes that resulted in that steady state, it is plausible to assume that resting state activity patterns are related both to object color knowledge and to the perceptual processes involved in acquiring that knowledge. In other words, the network we report here may be important both for color perception and color knowledge performance. More discriminating color perception tasks are needed to investigate more specifically whether the spontaneous activities in bilateral lingual and fusiform gyri and right inferior occipital gyrus are the neural basis for color knowledge or color perception, or both.

Finally, our study also has methodological implications. Although the neurophysiological mechanisms underlying ALFF and RSFC remains to be elucidated, they have shown to be correlated with electrophysiological recordings of neuronal firing (Nir et al., 2008), slow cortical potentials, and the band-limited power of fast electrical activity (Zhang and Raichle, 2010), and is affected by training (Lewis et al., 2009). A recent study demonstrated the significant spatial correlation between resting state functional connectivity strength and regional cerebral blood flow (Liang et al., 2013). We observed similar effects using two scanning sequences of resting-state functional data. The consistency of results across scanning sessions not only strengthens our findings but also provides evidence for the reliability of resting-state activities (Shehzad et al., 2009; Zuo et al., 2010). Furthermore, our results add to the cohort of findings showing that resting-state activity patterns are related to behavior in both pathological and healthy populations (Baldassarre et al., 2012; Hampson et al., 2006; Lui et al., 2009; Mennes et al., 2011; Wei et al., 2012; Zang et al., 2007; Zhu et al., 2011). Our study specifically highlights the potential value of studying spontaneous activity to reveal the neural mechanisms underlying the representation and acquisition of knowledge. Wei et al. (2012), using a methodology similar to the one used here, observed that the ALFF of left posterior middle temporal lobe was highly correlated with performance on object semantic tasks (measured by picture naming, picture associative matching and sound naming). In

² ALFF of voxels in right LG and neighboring FG (corrected $p < 0.05$) was found to be significantly related to object color attribute judgment scores whether or not compared to other object knowledge. These voxels overlapped with regions we found in the main analysis, with a relatively more medial and posterior peak coordinate (18, −72, −6).

our study here, the ALFF of left posterior middle temporal gyrus (pMTG) showed trends of correlation with color knowledge tasks, but the effect disappeared when the contribution of other knowledge tasks (i.e., form, motion, sound) was removed. This pattern of results is consistent with Wei et al.'s finding that left pMTG is relevant to more general conceptual tasks, while knowledge about more specific aspects of an object may also recruit regions/networks related to more specific modalities of processing. Such convergence highlights the relevance of the brain's intrinsic activity for highly specific cognitive representations. A methodological caveat of our study is that the timing of the imaging scanning sessions relative to the behavioral testing varied across participants reflecting their availability. It has been shown that rs-fMRI activity may be influenced by prior behavioral tasks (Lewis et al., 2009; Ma et al., 2011). We think it is unlikely that our results are fully driven by this variable because 1) For the majority of the participants (30/40), the whole battery of behavioral tests was administered at least one day before the imaging session, with the color tests and other object knowledge tests having potentially similar chance of affecting the resting-state activities; and 2) When we further analyzed our data excluding the eight participants whose resting-state scans were most likely to be "contaminated" by the behavioral tests, i.e., the color knowledge tests (and other tests) were conducted before the imaging session on the same day, and the results with the remaining participants were highly similar to those of the whole cohort. Nonetheless, this timing issue should be kept in mind when interpreting our results.

To conclude, we found that the spontaneous activity (ALFF) pattern in bilateral lingual and fusiform gyri and right inferior occipital gyrus and the degree of synchronization (RSFC) among these areas were significantly associated with color knowledge ability in healthy participants. These findings reveal a new type of neural mechanism for the participation of bilateral lingual/fusiform gyri and right inferior occipital gyrus in object color processing, and demonstrate the significance of spontaneous brain activity in the resting-state as a window into the neural basis of behavior.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2013.03.010>.

Funding

This study was funded by 973 Program (2013CB837300), Major Project of National Social Science Foundation (11&ZD186), NSFC (31171073; 31222024; 31271115; 81030028; 31221003), the National Science Fund for Distinguished Young Scholars (grant no. 81225012, YH) and the Fundamental Research Funds for the Central Universities. AC was supported by the Fondazione Cassa di Risparmio di Trento e Rovereto.

Acknowledgments

We thank Xueming Lu for help with data analyses and BNU-CN Lab members for help in data collection.

Conflict of interest statement

No author has any conflict of interest with respect to this article.

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