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## Research Report

# Distinct human face representations in the perirhinal cortex and fusiform gyrus

Tetsuya Iidaka<sup>a,\*</sup>, Tokiko Harada<sup>a</sup>, Satoshi Eifuku<sup>b</sup>, Ryuzaburo Nakata<sup>b</sup>, Norihiro Sadato<sup>c</sup><sup>a</sup>Department of Psychiatry, Nagoya University, Graduate School of Medicine, Nagoya, Japan<sup>b</sup>Department of Integrative Neuroscience, University of Toyama, Graduate School of Medicine and Pharmaceutical Sciences, Toyama, Japan<sup>c</sup>Division of Cerebral Integration, National Institute for Physiological Sciences, Okazaki, Japan

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## ABSTRACT

Face representation, which is believed to be processed in the temporal visual pathway, has been extensively investigated in humans and monkeys through neuroimaging and electroneurophysiology. Lesion studies in monkeys indicate that simple facial features are processed in the caudal regions, and that the combined and integrated features of the face are stored in the perirhinal cortex (PRC). However, this hypothesis still lacks experimental evidence in normal human subjects; therefore, we conducted 2 functional magnetic resonance imaging experiments to investigate whether the function of the PRC differs from that of conventional face-related areas during face recognition tests. In experiment 1, normal subjects learned 6 facial identity–figure associations before scanning, and their brain activity was measured during recognition testing of correct and incorrect face–figure pairs in 3 different angles. The degree of activation in the PRC differed among the facial angles, and activation in response to frontal views was greater than that to other views. In experiment 2, where face angle, but not identity, was paired with an abstract figure, activation was significantly greater in response to the frontal view than that to other views. In contrast, the degree of activation in conventional face-related areas, i.e., the fusiform gyrus, did not differ among viewing angles in both experiments. The results indicate that the function of face representation in the PRC differs from that in the conventional face-related areas, and that a frontal view of the face plays a role in the activation of face representation stored in the PRC.

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## 1. Introduction

The face has a variety of features that serve to distinguish one identity from another, such as parts, hairs, configuration, and outline. In everyday situations, the viewing angle of a face is a critical factor in recognizing personal identity. The ability to

recognize a person's identity from different viewing angles indicates the existence of face representation that is not specific to a particular view or angle but has a general property that associates a variety of facial features with personal memories. The distributed brain regions in the fusiform face area (FFA), superior temporal sulcus (STS), and amygdala have been asso-

\* Corresponding author at: Nagoya University, Department of Psychiatry, Graduate School of Medicine, 65 Tsurumai, Showa, Nagoya, Aichi, 466-8550, Japan. Fax: +81 52 744 2293.

E-mail address: [iidaka@med.nagoya-u.ac.jp](mailto:iidaka@med.nagoya-u.ac.jp) (T. Iidaka).

ciated with face processing (Haxby et al., 2000). However, it remains unclear how functionally different these regions might be when faces are presented from different viewing angles.

Neurophysiological studies in monkeys by using different facial viewing angles postulated that neurons in the STS and inferior temporal cortex might represent facial identity and viewpoint, respectively (Eifuku et al., 2004). The majority of face-responsive cells in the STS, which are sensitive to viewpoint, were reported to have preference for the frontal and profile views of the face (Perrett et al., 1991). In functional imaging studies of human subjects, the simple presentation of an unfamiliar face at different viewing angles did not elicit differential responses in the FFA (Fang et al., 2007; Tong et al., 2000) or the STS (Fang et al., 2007), whereas a view-dependent activity pattern in the FFA was observed when different angles were repetitively presented with brief intervals (Fang et al., 2007; Pourtois et al., 2005).

Another line of evidence with regard to visual object representation has suggested that the caudal regions of the temporal lobe, such as the FFA, process simple facial features and that these features are further integrated in the rostral regions, such as the perirhinal cortex (PRC). This is based on lesion studies in monkeys showing that bilateral ablations of the PRC selectively impaired perceptual discrimination of an odd individual's face from another individual's face presented at several different viewing angles (Buckley et al., 2001; Bussey and Saksida, 2002, 2005). Behavioral studies in humans with damage to the PRC showed similar findings (Lee et al., 2005, 2006).

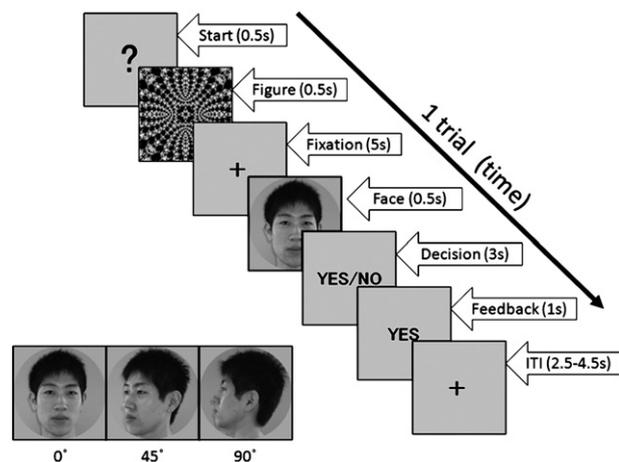
Functional neuroimaging studies in normal humans also showed that the PRC was significantly more activated when the subjects discriminated one identity from another identity presented at 4 different viewing angles than when they judged the differences in sizes of squares (Barense et al., 2007). The effect of face viewing angles on PRC activity was significant when the condition with different angles was contrasted with the condition consisting of only frontal faces (Barense et al., 2010). The effect of the viewing angle on PRC activity was stronger for familiar faces than for unfamiliar faces, indicating the combined effects of perception and memory on neural activity in the PRC (Barense et al., 2011). Furthermore, another neuroimaging study using face stimuli showed that the PRC was almost equally activated when the subject was engaged in perceptual and recognition judgments (O'Neil et al., 2009).

These studies suggest that the PRC plays a role in integrating multiple features of objects into a more abstract, object-level representation (Barense et al., 2010; Devlin and Price, 2007; Lee et al., 2008), indicating that representation in the PRC is crucial for visual discrimination (Buckley and Gaffan, 1998; Buckley et al., 2001; Bussey and Saksida, 2002, 2005; Bussey et al., 2002) as well as for memory (O'Neil et al., 2009) whenever a complex conjunction of features is processed (Buckley and Gaffan, 2006; Murray et al., 2007). This is particularly evident in objects with multiple viewpoints, but not exclusively in the case of the face. On the other hand, the caudal regions, such as the FFA, which process simple facial features, may have little relevance to the integration of multiple features into an object-level representation.

In the present study, we used functional magnetic resonance imaging (fMRI) and a paired recognition test of a face

and an abstract figure to investigate whether neural responses associated with different viewing angles of the face would differ between conventional face-related areas (e.g., FFA, STS, and amygdala) and the PRC. Previous neuroimaging studies have used simple visual judgment tasks involving different viewing angles of faces, objects, and scenes (Barense et al., 2010; Devlin and Price, 2007; Lee et al., 2008); however, no study has used a paired recognition task in which memory performance for both face and figure was required. We hypothesized that a well-learned face may form its representation in the temporal lobe, and this should be active when a cued abstract figure is shown and the subject is required to perform a recognition test for the probe face.

To test our hypothesis, 2 fMRI experiments were conducted in 2 different groups of subjects. In experiment 1, normal subjects studied 6 figure–face associations before fMRI scanning; fMRI was then used to measure the brain activity of these subjects during a recognition test for correct and incorrect pairs of figures and faces depicted using 3 different viewing angles (0°, 45°, and 90°; Fig. 1). The fMRI data for the entire brain was analyzed, with a particular focus on activity in the PRC and conventional face-related processing areas. In addition, we extracted signals from a predefined PRC region and tested whether the signal differed among the 3 viewing angles. We predicted that as the caudal regions process simple facial features and the majority of neurons prefer frontal and profile facial views (Perrett et al., 1991), these regions would be equally activated by these views. On the other hand, in the rostral region, which stores integrated features in relation to memory, the PRC would show different activity



**Fig. 1 – Schematic illustration of the experimental procedure during the test phase.** Each trial started with the presentation of a question mark for 0.5 s (the question mark was shown in red in the actual experiment), and then an abstract figure was shown for 0.5 s. After a 5-s fixation period, a facial picture was presented to the subject for 0.5 s. The subject judged whether the face was correctly paired with the figure and responded by pressing a button when the YES/NO panel was displayed on the screen. After pressing the button, feedback (YES or NO) was provided to the subject. The left lower panel shows an example of 3 facial angles (0°, 45°, and 90°) from 1 identity used in the test phase.

patterns among the facial viewing angles, with the strongest activity in particular toward the frontal view, which contains rich information about the identity of the face.

In experiment 1, however, the differences in PRC activation might be due to an implicit strategy of the subject during learning; that is, the subject might have particularly given attention to the frontal facial view more than to the other angles. Therefore, in experiment 2, 3 abstract figures were individually paired with 3 face angles (0°, 45°, and 90°) of a single identity to investigate whether the PRC becomes more activated in response to a frontal viewing angle than to the other angles. The subjects studied 3 figure–angle associations involving a single identity before fMRI scanning; fMRI was then conducted to measure the subjects' brain activity during the recognition test for correct and incorrect pairs of figures and angles. In this experiment, the subject must pay equal attention to each of the 3 viewing angles during the task to achieve a high performance level. Therefore, a critical difference between the 2 experiments was that the abstract figure was associated with identity in experiment 1 and with viewing angle in experiment 2. In both cases, we predicted that PRC activity would differ between the face angles and would be greater for the frontal viewing angle than for the other angles.

## 2. Results

### 2.1. Experiment 1

#### 2.1.1. Behavioral data

The results of the behavioral data are shown in Table 1. The subjective response rate and reaction time (RT) were entered into a 2-way analysis of variance (ANOVA) by using facial angles (0°, 45°, and 90°) and conditions (correct responses to correct pair: Hit condition; correct responses to incorrect pair: correct rejection, CR condition) as factors. A 2-way ANOVA conducted on the proportion of correct responses showed that the main effect of condition (Hit vs. CR,  $F(1, 19)=9.41$ ,  $p=0.006$ ) was significant but that the main effect of angle (0° vs. 45° vs. 90°,  $F(2, 38)=0.49$ ,  $p=0.49$ ) and their interaction effects ( $F(2, 38)=0.05$ ,  $p=0.81$ ) were not. A 2-way ANOVA of the RT data showed that the main effect of angle was significant ( $F(2, 38)=21.7$ ,  $p=0.001$ ) but that of condition ( $F(1, 19)=0.17$ ,  $p=0.68$ ) or their interaction effects ( $F(2, 38)=0.05$ ,  $p=0.82$ ) was not. Post hoc *t*-tests with the Bonferroni correction revealed a significant difference in RT between the 0° and 90° viewing

angles ( $p=0.01$ ), and between the 45° and 90° viewing angles ( $p=0.05$ ). These results indicate that the subjects' responses were slower when the faces were shown at 90° than at 0° and 45°.

#### 2.1.2. fMRI data

A full-factorial ANOVA design with facial angle as a factor was conducted on the contrast images that corresponded to each angle with the identity collapsed. ANOVA was conducted separately for the Hit and CR conditions with a binary mask, which constrained the analysis to the face-related regions (see [Experimental procedures](#)). The effect of facial angle on neural activity was significant in several brain regions. Under the Hit condition, the significant clusters were located in the left and right PRC, left middle temporal gyrus, lingual gyrus, subcortical structures, posterior cingulate cortex, and parietal lobe (Table 2, Fig. 2). Under the CR condition, there were significant clusters in the PRC and in the frontal and occipital lobes (Table 3, Supplementary Fig. 1). Particularly under the Hit condition, significant clusters were found in the temporal pole regions located in the left and right PRC (Fig. 3). Under the CR condition, there was a significant cluster in the right PRC that was adjacent to the cluster found under the Hit condition. As shown in the top panel of Fig. 4, the signals extracted from these clusters in the PRC were greater at 0° than at the other angles. Finally, under the Hit minus CR condition, there were significant clusters in the posterior and middle part of the cingulate gyrus and in the superior occipital gyrus (Table 4). The activity in the cingulate gyrus was lower at 45° than at the other angles.

We investigated the effect of the facial angle on neural activity in conventional face-related brain regions such as the FFA, amygdala, and STS. Face-related regions were identified in the FFA (right,  $x, y, z=48, -44, -24$ ; left,  $x, y, z=-46, -50, -24$ ), amygdala (right,  $x, y, z=16, -2, -12$ ; left,  $x, y, z=-18, 4, -16$ ), and STS (right,  $x, y, z=54, -18, -16$ ; see [Experimental procedures](#) and Supplementary Fig. 2). In contrast to PRC results, facial angle has no significant effect on neural activity in the face-related regions

**Table 1 – Behavioral results: experiment 1.**

	Correct response (%)	Reaction time (ms)
Correct pair (Hit)		
0°	95 (7)	912 (128)
45°	94 (8)	930 (153)
90°	95 (7)	968 (145)
Incorrect pair (CR)		
0°	97 (5)	905 (111)
45°	97 (6)	928 (156)
90°	97 (5)	956 (142)

Numerical values are mean and S.D. in parentheses.

**Table 2 – Brain regions in which significant main effect of face angle was observed under the Hit condition (experiment 1).**

L/R	Region name	BA	F-value	x, y, z	Size
L	Lingual gyrus (E)	19	17.71	-10, -90, -2	158
L	Perirhinal cortex (B)	36	14.6	-26, 0, -30	46
L	Middle temporal gyrus (C)	21	13.51	-54, -24, -8	13
R	Lingual gyrus (H)	18	11.68	16, -86, 8	80
R	Thalamus (F)		10.89	14, -24, 2	18
R	Putamen (D)		10.32	32, 6, -4	13
R	Perirhinal cortex (A)	36	9.63	30, 4, -32	25
R	Putamen (G)		9.52	30, -18, 6	10
L	Posterior cingulate cortex (I)	31	9.35	-2, -32, 34	36
L	Inferior parietal lobule	40	8.93	-42, -26, 24	10

Statistical threshold:  $p=0.001$ ,  $k=10$  voxels, L/R: left/right hemisphere, BA: Brodmann's area, alphabetical character in each region name indicates location of cluster shown in Fig. 2.

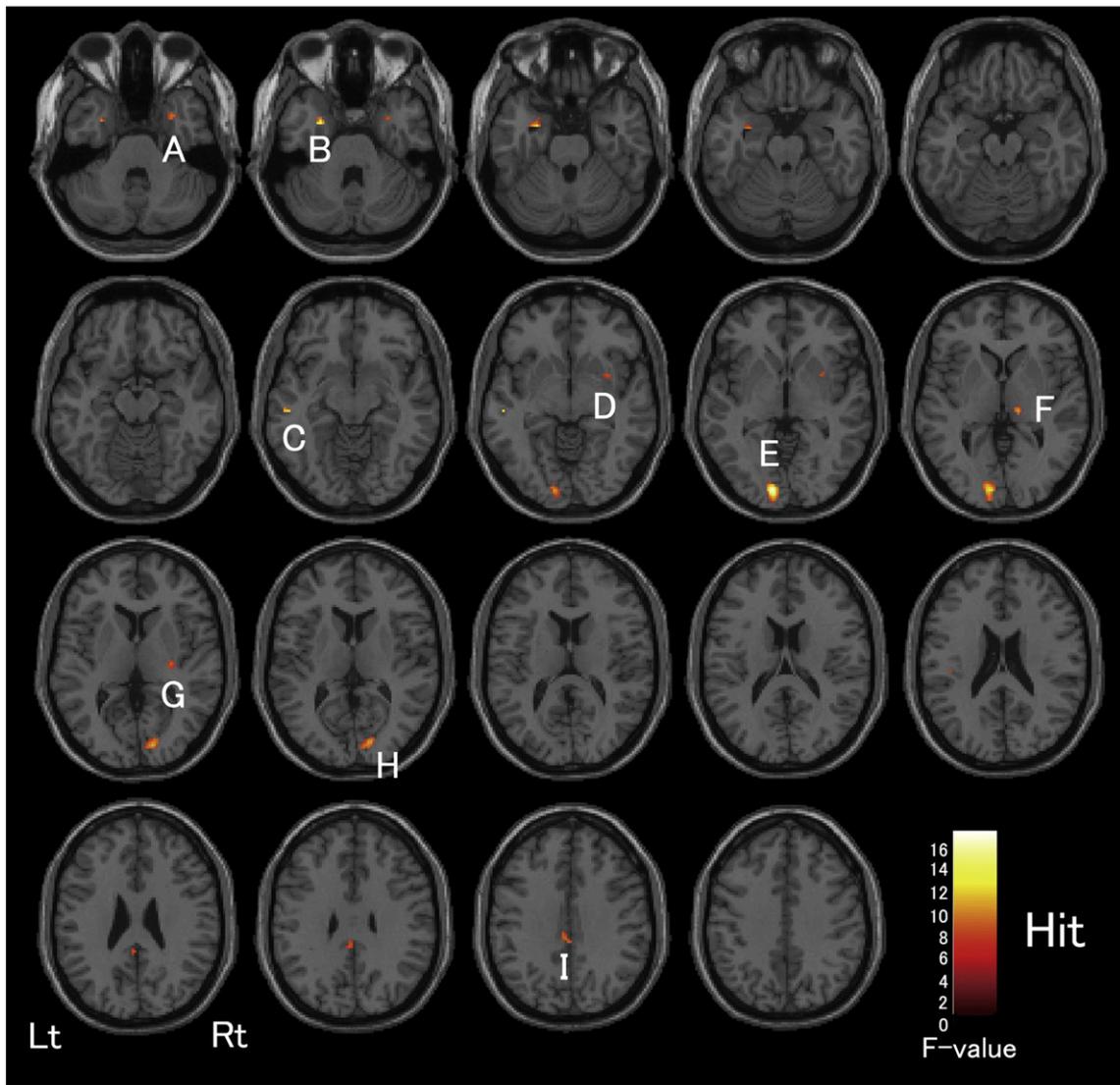


Fig. 2 – The results of ANOVA on the fMRI data obtained under the Hit condition with facial angle as a factor are shown on the canonical T1 template image. The images range from the z=−34 mm level (top left) to the z=+38 mm level (bottom right) with 4-mm increments. Detailed information for each cluster, as indicated by the alphabetical characters, is shown in Table 2.

(Fig. 4, bottom panel). The signals in these clusters did not significantly differ between the facial angles under the CR condition.

Finally, the results obtained from the predefined PRC regions (80% probability mask image; see Experimental procedures)

indicated that the activation was greater at 0° than at 90° (similar to that obtained from the whole brain analysis) and that the activity at 45° was intermediate between them under both the Hit and CR conditions (Fig. 5). However, the results of repeated-measures ANOVA showed that there was a significant difference in right PRC activation among the facial angles under the Hit condition ( $F(2, 38)=4.28, p=0.02$ ). Post hoc t-tests revealed that the difference between the 0° and 90° viewing angles survived Bonferroni correction at  $p=0.05$ . Although other ANOVAs failed to reach significance, the results for the left PRC under the Hit condition ( $F(2, 38)=3.03, p=0.06$ ) and for the right PRC under the CR condition ( $F(2, 38)=2.84, p=0.07$ ) were marginally significant.

**Table 3 – Brain regions in which significant main effect of face angle was observed under the correct rejection (CR) condition (experiment 1).**

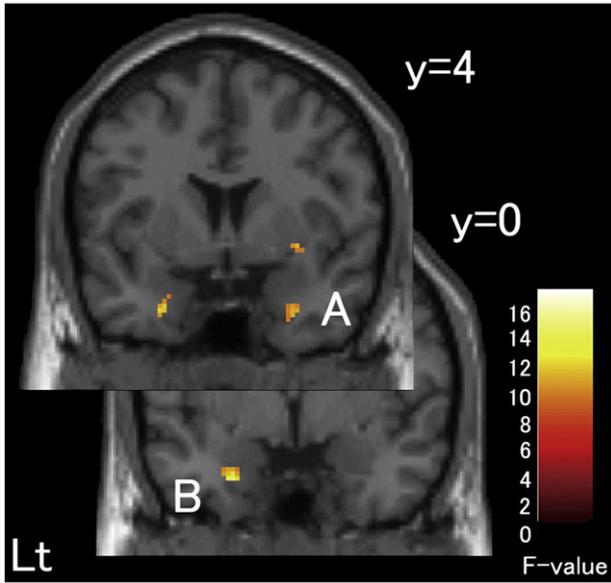
L/R	Region name	BA	F value	x, y, z	Size
L	Lingual gyrus (L)	18	12.63	−8, −88, −4	309
R	Perirhinal cortex (J)	36	11.38	34, 4, −28	18
R	Middle occipital gyrus (K)	19	10.4	52, −72, −8	12
L	Inferior frontal gyrus (M)	44	10.22	−50, 14, 8	30
L	Lingual gyrus	19	8.94	−10, −64, 2	15

Statistical threshold:  $p=0.001, k=10$  voxels, L/R: left/right hemisphere, BA: Brodmann’s area, alphabetical character in each region name indicates location of cluster shown in Supplementary Fig. 1.

## 2.2. Experiment 2

### 2.2.1. Behavioral data

The results of behavioral data are shown in Table 5. The mean of the correct responses did not significantly differ between



**Fig. 3** – The perirhinal regions where activation significantly differed among the facial angles under the Hit condition are superimposed on the canonical T1 template image ( $y=0$  and  $4$  mm). The alphabetical characters in the figure are as indicated in Table 2.

the viewing angles (Hit,  $F(2, 33)=1.91, p=0.16$ ; CR,  $F(2, 33)=0.69, p=0.51$ ). The results for RT did not significantly differ between the viewing angles for the Hit ( $F(2, 33)=1.33, p=0.27$ ) and CR ( $F(2, 33)=0.13, p=0.87$ ) conditions.

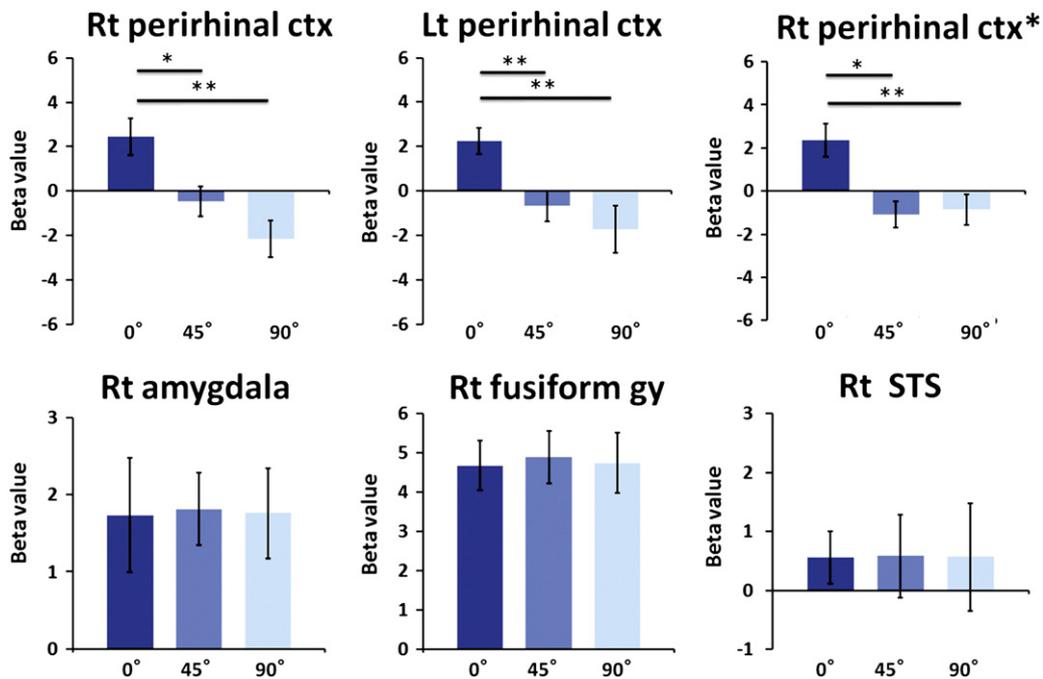
**Table 4** – Brain regions in which significant main effect of face angle was observed under the Hit minus correct rejection (CR) condition (experiment 1).

L/R	Region name	BA	F value	x, y, z	Size
	Cingulate gyrus	31	18.00	0, -34, 34	101
R	Cingulate gyrus	24	12.46	2, -16, 34	56
R	Superior occipital gyrus	19	9.91	26, -70, 26	11

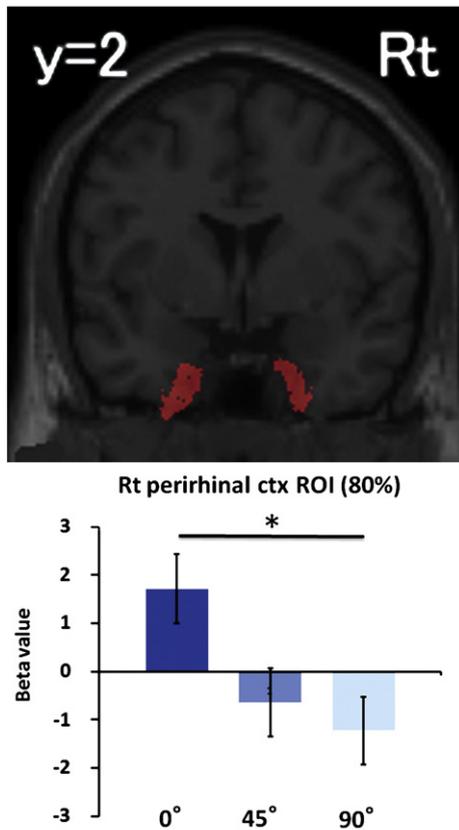
Statistical threshold:  $p=0.001, k=10$  voxels, L/R: left/right hemisphere, BA: Brodmann's area.

2.2.2. fMRI data

A full-factorial ANOVA design with facial angle as a factor was conducted on the contrast images that corresponded to each angle. The ANOVA was conducted separately for the Hit and CR conditions with a binary mask, which constrained the analysis to the PRC regions. In 2 PRC clusters, the effect of facial angle on neural activity was significant under the Hit condition but not under the CR condition. The significant clusters were located in the left and right PRC regions (Table 6 and Fig. 6). The PRC regions that were significant in the experiment 2 located in the anterior and superior part of the PRC that was found in the experiment 1. As shown in the bottom panel of Fig. 6, the signals extracted from these clusters in the PRC were significantly greater at  $0^\circ$  than at other angles. During the CR condition, the PRC was not significantly active and did not show an effect of the viewing angle. Finally, in the signals extracted from the right FFA ( $x, y, z=48, -44, -24$ ), there was no significant difference in activity between viewing angles for the Hit and CR conditions.



**Fig. 4** – The mean and 1 s.e. of the signal extracted from the spherical regions of interest ( $r=8$  mm) at peak voxel using the VOI function in SPM8 are shown. Each bar represents the mean for each facial angle. The peaks were selected from the clusters where the signal significantly differed among the angles (top panel) and where the signal was significantly greater for the face than for the figure (bottom panel). In the top panel, signals in the right and left PRC under the Hit condition and in the right PRC under the CR condition (indicated by an asterisk) are shown. In the bottom panel, signals in the amygdala, FFA, and STS are shown. The results of post hoc t-tests after the Bonferroni correction are indicated by asterisks ( $*p<0.05, **p<0.01$ ). ctx, cortex; gy, gyrus.



**Fig. 5 – Top: the predefined PRC regions with 80% probability in the left and right hemispheres are shown in red. The regions are superimposed on a canonical template of SPM8 in a coronal position. Bottom: the mean and 1 s.e. of the signal extracted from the right PRC under the Hit condition are plotted. An asterisk indicates a significance of  $p < 0.05$  after Bonferroni correction.**

### 3. Discussion

In experiment 1, activation differences were observed in the PRC among the facial angles when subjects performed recognition judgments of faces that were paired with abstract figures; however, no such activation differences were observed

in conventional face-related areas (e.g., the FFA, STS, and amygdala). The signal extracted from the PRC mask image also showed that activity in response to the frontal face was significantly greater than that to the profile face. In experiment 2, where an abstract figure was paired with a face angle but not with a face identity as in experiment 1, correct recognition of the frontal face again elicited the greatest activity in the PRC. The location of PRC region slightly differed between the experiment 1 and experiment 2; however, this may be due to the difference in task paradigm between the experiments. These results suggest that in the PRC, where multiple viewing angles are integrated and a single facial representation is stored, the signal was greater in response to the frontal face than to the other viewing angles. This indicates that neuronal response in the PRC may be more sensitive to the frontal face because facial information can be efficiently retrieved at this viewing angle. On the other hand, in the conventional face-related areas, separate templates of faces matched with 3 facial viewing angles elicited neural responses of equal strength among all viewing angles (Fang et al., 2007; Tong et al., 2000).

The PRC receives major cortical input from the unimodal TE and TEO visual areas (Webster et al., 1991) and the polymodal area of the parahippocampal gyrus, as well as from the STS, insula, and orbitofrontal cortex (Suzuki and Amaral, 1994a). The PRC is considered to be an interface between the hippocampal memory system and the ventral visual pathway in the temporal cortex (Suzuki and Amaral, 1994b). Lesion studies in monkeys revealed that ablation of the PRC impaired visual recognition when objects were presented at different viewing angles (Buckley and Gaffan, 1998; Buckley et al., 2001), indicating a role for this region in processing stimuli at an abstract level, such as object representation. In another study, the behavioral performance of monkeys with PRC lesions significantly worsened when several features overlapped between the stimuli (Bussey and Saksida, 2002). This suggests that representations of simple object features are processed in the caudal regions of the ventral visual stream (e.g., the FFA), and representations of the conjunction of these features are stored in the rostral regions (e.g., the PRC) (Bussey and Saksida, 2002; Bussey et al., 2002; Murray and Bussey, 1999).

In humans, lesions in both the hippocampus and PRC have been shown to impair the recognition of faces or objects from different viewpoints more than do lesions only in the hippocampus (Barense et al., 2007; Lee et al., 2005; Taylor et al., 2007). Subjects with semantic dementia whose neuropathological findings were observed in the temporal pole and the PRC had impaired recognition performance in tasks involving

**Table 5 – Behavioral results: experiment 2.**

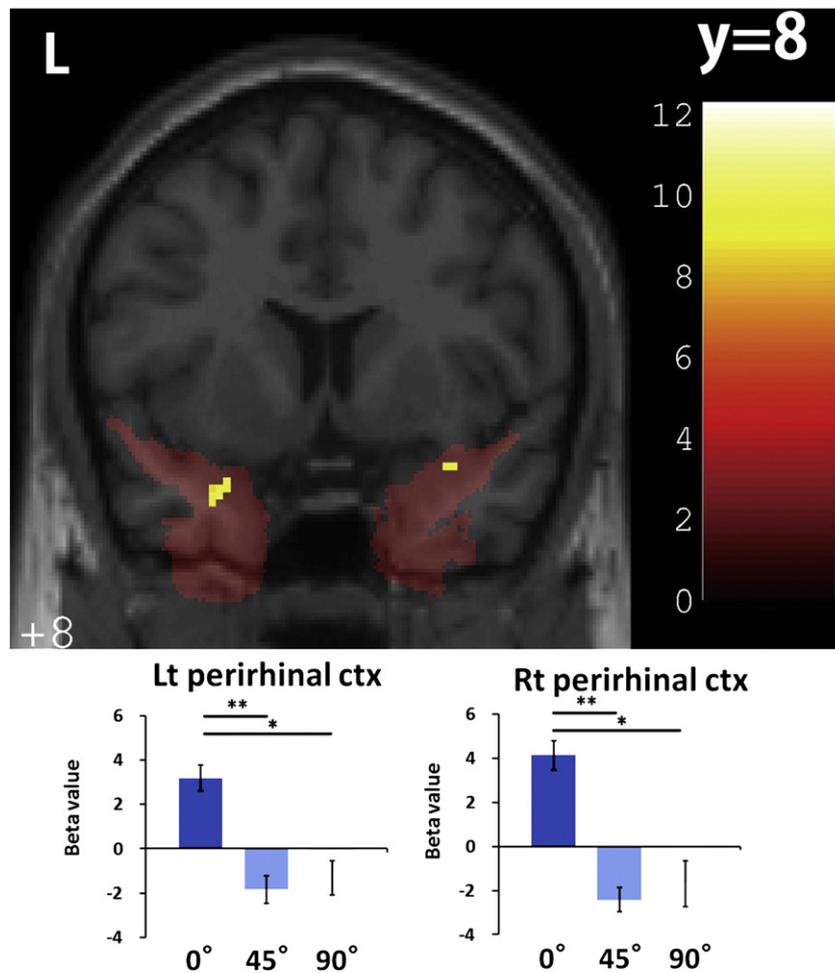
	Correct response (%)	Reaction time (ms)
Correct pair (Hit)		
0°	99 (2)	846 (109)
45°	97 (3)	889 (103)
90°	95 (7)	919 (118)
Incorrect pair (CR)		
0°	98 (3)	884 (78)
45°	99 (3)	904 (85)
90°	99 (1)	899 (130)

Numerical values are mean and S.D. in parentheses.

**Table 6 – Perirhinal regions in which significant main effect of face angle was observed under the Hit condition (experiment 2).**

L/R	Region name	BA	F-value	x, y, z	Size
R	Perirhinal cortex	36	13.02	34, 10, -20	17
L	Perirhinal cortex	36	10.23	-26, 8, -24	17

Statistical threshold:  $p = 0.001$ ,  $k = 10$  voxels, L/R: left/right hemisphere, BA: Brodmann's area.



**Fig. 6** – The perirhinal clusters (yellow) where activation significantly differed among the facial angles under the Hit condition are superimposed on the canonical T1 template image ( $y=8$  mm). The opaquely red areas are those covered by the PRC mask image (100% probability). At the bottom, the parameter estimates extracted from the left and right PRC peak voxels under the Hit condition are plotted for each viewing angle. Column indicates the mean and bar indicates 1 s.e. The results of post hoc t-tests after the Bonferroni correction are indicated by asterisks (\* $p < 0.05$ , \*\* $p < 0.01$ ).

different facial viewing angles as compared with Alzheimer's dementia patients whose pathological findings did not involve the PRC (Lee et al., 2006). Subjects with lesions in the PRC showed impairment in discriminating familiar and novel objects with highly overlapping stimulus features (Barense et al., 2005, 2007). These results suggest that visual representations in the PRC were integrated for both mnemonic and perceptual processing of complex conjunctions of features.

In a previous functional neuroimaging study of human subjects, the PRC was significantly more active when the task involved judgments at different facial viewing angles than when it involved judgments of different scenes (Lee et al., 2008). In another study, comparisons of faces presented at different viewing angles elicited greater activation in the PRC than when the views were at the same facial angle (Barense et al., 2010). In that study, a significant effect of viewpoint was also observed when using objects as stimuli, but not when scenes were used. Furthermore, the PRC was

significantly active under conditions in which 4 different viewing angles of animals or artificial objects (e.g., a cup or gun) were presented and subjects were told to discriminate one from another (Devlin and Price, 2007). These results indicate that the viewpoint effect is not specific to the face, but is a general property for stimuli such as animals and objects, all of which have multiple object-centered viewpoints.

The results of previous studies investigating neural responses to various facial angles seem to contradict the results of the present study showing view-variant activation in the PRC. The first explanation for the inconsistency is that the number of facial features associated with abstract figures was larger at 0° than at 45° and 90° because the frontal view contains rich information about identity. These features should be integrated into a higher-level representation to achieve the task. This prominent feature of the frontal face stimuli might elicit greater activation in the PRC in a similar way as in the previous studies where several different features at different angles were shown simultaneously in each

trial (Barense et al., 2010; Lee et al., 2008). Another explanation is that the present study used well-learned stimuli that were highly familiar to the subjects because the previous study showed that activation in the PRC during a face discrimination task was greater when the faces were familiar than when they were not (Barense et al., 2011). In addition, correct responses to the previously learned stimuli elicited greater activity in the PRC than incorrect responses to those stimuli during the face memory task (O'Neil et al., 2009). Finally, we used a sequential presentation of abstract figures and faces for the recognition test, whereas in previous studies different viewing angles were presented simultaneously in each trial (Barense et al., 2010; Devlin and Price, 2007; Lee et al., 2008). Therefore, activation of face representation in the PRC, recalled by a cued abstract figure, was significantly greater when the frontal face was presented rather than the face at other viewing angles because the frontal view contains rich information about identity.

A single unit recordings from the patients with epilepsy have shown that neurons in the hippocampus and related regions responded to different pictures of given individuals or landmarks (Quiroga et al., 2005). The results are inconsistent with those of the present study and indicate invariant representation of identity by single neuron in the medial temporal lobe. There are several explanations for the inconsistency. First is the methodological difference between fMRI and single cell recordings. Second, a study by Quiroga et al. did not measure neural responses in the perirhinal cortex. Third, in the present study unfamiliar faces were used as stimuli while Quiroga et al. used pictures of famous person and buildings as stimuli. A future study is needed to reconcile these differences between the experiments.

The FFA, STS, and amygdala are known to be involved in facial recognition and emotional processing in humans (Haxby et al., 2000; Kanwisher and Yovel, 2006). In particular, the FFA has been implicated in processing invariant aspects of faces, such as a person's identity, whereas the STS is implicated in processing the changeable aspects of faces, such as eye gaze and lip movements (Haxby et al., 2000). The simple presentation of an unfamiliar face at different viewing angles did not elicit differential responses in the FFA (Fang et al., 2007; Tong et al., 2000) or the STS (Fang et al., 2007), in agreement with the results of the present study. A view-dependent activity pattern in the FFA was observed only in studies that used an adaptation method in which different facial angles were repetitively presented with brief inter-stimulus intervals (Fang et al., 2007; Pourtois et al., 2005). Thus, in the FFA and STS which play critical roles in detecting faces the activity patterns do not significantly differ among the angles.

In conclusion, our analyses of 2 independent sets of fMRI data indicate that internal face representation in the PRC differs from face representation in conventional face-related areas, which include the FFA, STS, and amygdala. Conventional face-related areas responded similarly to multiple viewing angles, while the PRC responded more favorably to a frontal viewing angle than to the other angles when the subjects performed recognition tests for figure–face and figure–angle associations. Thus, conjunctive representation in rostral temporal areas such as the PRC may respond more to a stimulus that contains maximal facial information, as is found in the frontal view.

## 4. Experimental procedures

### 4.1. Experiment 1

#### 4.1.1. Subjects

Twenty healthy volunteers (12 males and 8 females, all right handed, mean age  $\pm$  S.D. = 21.1  $\pm$  1.7 years) with normal or corrected-to-normal vision were recruited for the fMRI study. The subjects provided written informed consent for the procedure. An experimenter carefully checked their physical and mental conditions according to our institution's standard protocol. This study was approved by the ethics committee of the National Institute for Physiological Sciences.

#### 4.1.2. Experimental stimuli

The facial pictures were selected from the Japanese Face Database provided by the Softpia Japan Foundation (<http://www.softpia.or.jp>; Ogaki, Japan). Three male and 3 female monochromatic faces with neutral expressions were used as the experimental stimuli. Each face was photographed from 7 different angles ranging from a frontal view to the left-side profile at intervals of 15° (i.e., 0°, 15°, 30°, 45°, 60°, 75°, and 90°). Thus, the facial stimulus set consisted of 42 facial pictures (6 facial identities  $\times$  7 viewing angles). Six monochromatic abstract figures were prepared and paired with each identity.

#### 4.1.3. Study phase (not scanned by fMRI)

Each subject was shown 6 printed sheets, each of which contained 7 different viewing angles of 1 identity as well as 1 abstract figure. The subject was instructed to view the sheets and to learn the 6 figure–face associations at their own pace. After an appropriate learning period, the subject was presented with the figures and faces separately and was told to correctly match the figure with the corresponding face. We used a set of 6 sheets, on each of which a single abstract figure was printed, and another set of 6 sheets, on each of which a single facial identity photographed from 7 angles was printed. This procedure (learning and then matching the associations) was repeated until the subject correctly matched all figure–face associations in 3 consecutive sessions. The study phase was conducted outside the fMRI scanner room and lasted for ~20 min, depending on the subject's learning speed.

#### 4.1.4. Test phase (scanned by fMRI)

During the test phase, 6 abstract figures and facial pictures taken at 0°, 45°, and 90° angles for each of the 6 identities were used as stimuli because of the limitation on scanning time (Fig. 1). We created correct and incorrect figure–face pairs with these stimuli. To make correct pairs, each figure was coupled with each of the 3 facial angles from the identity learned during the study phase. To make incorrect pairs, each figure was paired with each of the 3 facial angles from another identity. The identity used for the incorrect pair was randomly selected from the remaining 5 identities that were not paired with the figure during the study phase. Thus, we created 18 correct pairs (6 identities  $\times$  3 angles) and 18 incorrect pairs (6 identities  $\times$  3 angles) to present to the subjects during the test phase. The assignment of figure–face pairs was balanced across the subjects.

In each scanning run, each of the 36 pairs was randomly shown twice, and the subjects made a 2-alternative forced-choice judgment for each of the 72 figure–face pairs (i.e., 72 trials in each run). The run was repeated 4 times by randomly intermixing the presentation order of the pairs. Across the 4 runs, 48 trials for each of the 6 conditions (correct and incorrect pair conditions  $\times$  3 angles) were performed. A trial consisted of the presentation of a question mark (0.5 s), indicating the start of the trial, followed by an abstract figure (0.5 s), fixation (5 s), a face (0.5 s), a “YES/NO” judgment prompt (up to 3 s, depending on the subject’s response speed), and feedback (1 s) (Fig. 1). The YES/NO panel disappeared upon the subject’s response, and feedback for a correct response (YES or NO) was shown immediately. The length of the intertrial interval was randomized, ranging from 2.5 to 4.5 s. The subject judged whether the face correctly matched the figure (YES) or not (NO), and responded by pressing the corresponding button as quickly as possible. The stimuli were projected onto a transparent screen, which was hung from the bore of the MRI magnet, at a distance of 75 cm from the subject’s eyes. The subjects viewed the stimuli through a tilted mirror attached to the head coil of the scanner. The response was measured using a magnet-compatible button box that the subject held on the right hand. The subjective response rate and RT were entered into a 2-way ANOVA by using the facial angle (0°, 45°, and 90°) and condition (correct pair and incorrect pair) as factors.

#### 4.1.5. Image acquisition and preprocessing

Functional images of the brain were obtained in an axial-oblique position by using a 3-T MRI scanner (Allegra; Siemens, Erlangen, Germany) equipped with single-shot echo planar imaging (EPI; TR=2.3 s, TE=30 ms, flip angle=80°, 64 $\times$ 64 matrix and 36 slices, voxel size=3 $\times$ 3 $\times$ 3 mm) that was sensitive to blood oxygen level-dependent contrast. As the present study focused on neural activity in the ventral visual pathway of the temporal lobe, the top of the brain (superior part of the parietal lobe) was outside the field of view. The number of images obtained in each run was ~366 and varied depending on the subject’s response speed. After discarding the first 4 images, the successive images in each run were analyzed. A high-resolution anatomical T1-weighted image was also acquired (MPRAGE; TR=2.5 s, TE=4.38 ms, flip angle=8°, 256 $\times$ 256 matrix and 192 slices, voxel size=0.75 $\times$ 0.75 $\times$ 1 mm) for each subject. The data were analyzed using SPM8 (Wellcome Department of Imaging Neuroscience, London, UK). First, the signal in each slice was realigned temporally to that obtained in the middle slice by sinc interpolation, and all volumes were realigned spatially to the mean volume. The resliced volumes were then normalized to the standard Montreal Neurological Institute (MNI) space by using a transformation matrix obtained from the process normalizing the mean EPI image for each subject to the EPI template image. The normalized images were spatially smoothed with an 8-mm Gaussian kernel.

#### 4.1.6. First-level analysis

**4.1.6.1. Effects of facial angle on brain activation.** Following preprocessing, the data obtained from each subject were analyzed with a general linear model. At the first level (a fixed-effects model), each event was modeled as a hemodynamic response function. High-pass-frequency filters (128 s) were applied to the time series data. An autoregressive AR(1)

model was used to estimate the temporal autocorrelation. The images were scaled to a grand mean of 100 over all voxels and all scans within a session. In the subsequent analysis, the following conditions were modeled separately as regressors: 1, correct pair: 0°; 2, correct pair: 45°; 3, correct pair: 90°; 4, incorrect pair: 0°; 5, incorrect pair: 45°; 6, incorrect pair: 90°; and 7, abstract figure. As the mean accuracy of the task was high (96%), the missed and inaccurate responses were grouped as a regressor. In addition, the 6 movement parameters obtained during the realignment were entered as regressors. The parameter estimates for each condition and for the differences among the conditions were computed from the least mean square fit of the model to the time series data. Images of the parameter estimates representing event-related activity at each voxel were created for each condition and subject.

**4.1.6.2. Delineation of face-related regions.** We also investigated the effect of facial angle on neural activity in conventional face-related brain regions such as the FFA, amygdala, and STS. To delineate these regions, all facial events related to the 3 facial angles combined and all events related to the abstract figure were separately modeled as regressors (i.e., 2 conditions) in each subject, with the correct and incorrect conditions collapsed. One contrast image, which corresponded to a face-minus-figure subtraction, was computed in the same manner as in the previous section (i.e., high-pass frequency filter, autoregressive model, and inclusion of movement parameters).

#### 4.1.7. Second-level analysis

**4.1.7.1. Effects of facial angle on brain activation.** At the second level, the results from each subject were entered into a group analysis (a random-effects model). A full-factorial ANOVA design with facial angle as a factor was conducted on the contrast images that corresponded to each angle with the identity collapsed. ANOVA was conducted separately for Hit (correct pair), CR (incorrect pair), and Hit minus CR conditions with a binary mask, which constrained the analysis to the face-related regions. The binary mask image was created by contrasting all facial events and all figure events in each individual subject’s first-level analysis, and the resultant contrast images were entered into a 1-sample *t*-test at the second-level analysis with the statistical threshold set at  $p=0.1$ , uncorrected for multiple comparisons.

These analyses identified the brain regions where neural activity significantly differed among the facial angles for each Hit, CR, and Hit minus CR condition. The statistical significance threshold was set at  $p=0.001$ , uncorrected for multiple comparisons for height, and at  $k=10$  voxels for spatial extent, because we predicted that the PRC would show a differential activation pattern for each facial angle. The ANOVA results for the Hit and CR conditions are listed in Tables 2 and 3, respectively. With regard to these 2 conditions in particular, we believe that the brain responses to the Hit condition would be more informative than those to the CR condition because the face representation recalled by the abstract figure was matched with the probe face under the Hit condition. In addition, a previous fMRI study for the retrieval success of episodic memory showed that the Hit condition involved greater activation in several brain regions than the CR

condition did (Spaniol et al., 2009). The ANOVA results for the Hit minus CR condition are listed in Table 4.

Significant clusters are superimposed on the T1 template image in Fig. 2 for the Hit condition and in Supplementary Fig. 1 for the CR condition. The PRC clusters under the Hit condition are superimposed on the coronal view of the T1 template image in Fig. 3. Signals extracted from the PRC clusters for each facial angle by using the volume of interest (VOI) function of SPM8 ( $r=8$ -mm sphere) are shown in the top panel of Fig. 4. The VOI function of SPM extracts the eigenvariate values in a region, rather than the mean values, as the former is more robust to the heterogeneity of responses within a cluster. The mean value can be considered a special case of the eigenvariate if the corresponding eigenvector equally weights all voxels in a cluster. The eigenvariate provides a weighted mean where atypical voxels are down-weighted (<http://www.fil.ion.ucl.ac.uk/spm/>). Post hoc paired *t*-tests on the signal were conducted in each cluster to test the differences among the angles (threshold at  $p=0.05$ , after the Bonferroni correction for multiple comparisons).

**4.1.7.2. Delineation of face-related regions.** The contrast images resulting from the face-minus-figure subtraction conditions were entered into a 1-sample *t*-test at the second-level analysis to identify significant activation peaks associated with facial processing, using a statistical threshold set at  $p=0.001$  with  $k=10$  voxels (see Supplementary Fig. 2). The signals in response to each facial angle and in each region were extracted from the results of ANOVA with the facial angles as a factor (VOI function,  $r=8$  mm at peak voxels). These results are plotted in the lower panel of Fig. 4.

**4.1.7.3. Predefined ROI analysis in the PRC.** In the previous ANOVAs, we searched the whole brain for regions where the signal significantly differed between the facial angles; however, in the next analysis, we focused on an a priori region of interest (ROI) in the PRC. For this purpose, a probabilistic mask image of the PRC in the MNI standard space was created. The original image by Devlin and Price (2007) was developed by computing the probability of voxels being in the PRC, using high-resolution anatomical scans obtained from 11 participants. The image was thresholded at 80% probability, and the resultant image was converted to binary mask images separately for the left and right PRC. The volumes of the left and right PRC mask images were 1682 and 1525 mm<sup>3</sup>, respectively (Fig. 5). These mask images were applied to an ANOVA involving 3 facial angles to extract a mean parameter estimate of the left and right PRC regions in each subject by using the VOI function of SPM8. The extracted signals were further averaged across 20 subjects separately for the Hit and CR conditions. The mean and 1 s.e. of the signal are plotted in Fig. 5. Then, repeated-measures ANOVAs and post hoc paired *t*-tests with Bonferroni correction were conducted on these data.

## 4.2. Experiment 2

### 4.2.1. Subjects

Twelve healthy volunteers (6 males and 6 females, all right handed, mean age  $\pm$  S.D. = 22.3  $\pm$  1.8 years) with normal or

corrected-to-normal vision were recruited for the fMRI study. The subjects provided written informed consent for the procedure. An experimenter carefully checked their physical and mental conditions according to our institution's standard protocol. This study was approved by the ethics committee of the National Institute for Physiological Sciences.

### 4.2.2. Experimental stimuli

The same set of monochromatic faces used during the test phase of experiment 1 (0°, 45°, and 90° angles) and 3 monochromatic abstract figures served as stimuli. Here, to make correct pairs, the 0°, 45°, and 90° face angles of each identity were each paired with each of the 3 abstract figures in a one-to-one correspondence. In addition, we created incorrect figure–angle pairs with these stimuli by matching each figure with another angle of the same identity. The angle used for the incorrect pair was randomly selected from the remaining 2 angles. Thus, we created 3 correct and 3 incorrect pairs for each of the 6 identities for experiment 2. Each subject was assigned to a single identity in a random manner and viewed the same identity with 3 different angles paired with different figures.

### 4.2.3. Study and test phases

Each subject was shown printed sheets that contained 3 viewing angles of 1 identity as well as 3 abstract figures. The subject was instructed to view the sheets and learn the 3 figure–angle associations at their own pace in the same manner as in experiment 1. This procedure (learning and then matching the associations) was repeated until the subject correctly matched all figure–angle associations in 3 consecutive sessions. During the test phase and in a scanning run, the 6 pairs (3 correct and 3 incorrect pairs) were randomly shown 10 times each, and the subject made a 2-alternative forced-choice judgment for each of the 60 figure–angle pairs (i.e., 60 trials in each run). The run was repeated twice by randomly intermixing the presentation order of the pairs. Across the 2 runs, 20 trials were done for each of the 6 conditions. The time sequences of the trial and response pattern were the same as in experiment 1 (see Fig. 1).

### 4.2.4. Image acquisition and preprocessing

The MRI scanner, parameters of image acquisition, and methods for preprocessing of the image data were the same as those used for experiment 1.

### 4.2.5. First- and second-level analyses

Following preprocessing, the data obtained from each subject were analyzed with a general linear model at the first level (a fixed-effects model) and at the second level (a random-effects model) in the same way as in experiment 1. The following conditions were modeled separately as regressors: 1, correct pair: 0°; 2, correct pair: 45°; 3, correct pair: 90°; 4, incorrect pair: 0°; 5, incorrect pair: 45°; 6, incorrect pair: 90°; and 7, abstract figure. Images of the parameter estimates representing an event-related activity at each voxel were created for each condition and subject. A full-factorial ANOVA design with facial angle as a factor was conducted on the contrast images that corresponded to each angle. ANOVA was conducted separately for correct-pair (Hit) and incorrect-pair (CR) conditions with a binary mask, which constrained the analysis to the PRC regions (Devlin and Price, 2007). The

statistical significance threshold was set at  $p=0.001$ , uncorrected for multiple comparisons for height, and at  $k=10$  voxels for spatial extent.

Significant clusters within the PRC mask image are superimposed on the T1 template image in Fig. 6 for the Hit condition. The detail information of these clusters is shown in Table 6. Signals extracted from the peak voxel in the PRC for each facial angle by using the VOI function of SPM8 ( $r=8$ -mm sphere) are shown in Fig. 6. Post hoc paired  $t$ -tests on the signal were conducted in each cluster to test the differences among the angles (threshold at  $p=0.05$ , after the Bonferroni correction for multiple comparisons).

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## REFERENCES

- Barense, M.D., Bussey, T.J., Lee, A.C., Rogers, T.T., Davies, R.R., Saksida, L.M., Murray, E.A., Graham, K.S., 2005. Functional specialization in the human medial temporal lobe. *J. Neurosci.* 25, 10239–10246.
- Barense, M.D., Gaffan, D., Graham, K.S., 2007. The human medial temporal lobe processes online representations of complex objects. *Neuropsychologia* 45, 2963–2974.
- Barense, M.D., Henson, R.N.A., Lee, A.C.H., Graham, K.S., 2010. Medial temporal lobe activity during complex discrimination of faces, objects, and scenes: effects of viewpoint. *Hippocampus* 20, 389–401.
- Barense, M.D., Henson, R.N., Graham, K.S., 2011. Perception and conception: temporal lobe activity during complex discriminations of familiar and novel faces and objects. *J. Cogn. Neurosci.* 23, 3052–3067.
- Buckley, M.J., Gaffan, D., 1998. Perirhinal cortex ablation impairs visual object identification. *J. Neurosci.* 18, 2268–2275.
- Buckley, M.J., Booth, M.C., Rolls, E.T., Gaffan, D., 2001. Selective perceptual impairments after perirhinal cortex ablation. *J. Neurosci.* 21, 9824–9836.
- Buckley, M.J., Gaffan, D., 2006. Perirhinal cortical contributions to object perception. *Trends Cogn. Sci.* 10, 100–107.
- Bussey, T.J., Saksida, L.M., 2002. The organization of visual object representations: a connectionist model of effects of lesions in perirhinal cortex. *Eur. J. Neurosci.* 15, 355–364.
- Bussey, T.J., Saksida, L.M., Murray, E.A., 2002. Perirhinal cortex resolves feature ambiguity in complex visual discriminations. *Eur. J. Neurosci.* 15, 365–374.
- Bussey, T.J., Saksida, L.M., 2005. Object memory and perception in the medial temporal lobe: an alternative approach. *Curr. Opin. Neurobiol.* 15, 730–737.
- Devlin, J.T., Price, C.J., 2007. Perirhinal contributions to human visual perception. *Curr. Biol.* 17, 1484–1488.
- Eifuku, S., De Souza, W.C., Tamura, R., Nishijo, H., Ono, T., 2004. Neuronal correlates of face identification in the monkey anterior temporal cortical areas. *J. Neurophysiol.* 91, 358–371.
- Fang, F., Murray, S.O., He, S., 2007. Duration-dependent fMRI adaptation and distributed viewer-centered face representation in human visual cortex. *Cereb. Cortex* 17, 1402–1411.
- Haxby, J., Hoffman, E., Gobbini, M., 2000. The distributed human neural system for face perception. *Trends Cogn. Sci.* 4, 223–233.
- Kanwisher, N., Yovel, G., 2006. The fusiform face area: a cortical region specialized for the perception of faces. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 361, 2109–2128.
- Lee, A.C.H., Buckley, M.J., Pegman, S.J., Spiers, H., Scahill, V.L., Gaffan, D., Bussey, T.J., Davies, R.R., Kapur, N., Hodges, J.R., Graham, K.S., 2005. Specialization in the medial temporal lobe for processing of objects and scenes. *Hippocampus* 15, 782–797.
- Lee, A.C.H., Buckley, M.J., Gaffan, D., Emery, T., Hodges, J.R., Graham, K.S., 2006. Differentiating the roles of the hippocampus and perirhinal cortex in processes beyond long-term declarative memory: a double dissociation in dementia. *J. Neurosci.* 26, 5198–5203.
- Lee, A.C.H., Scahill, V.L., Graham, K.S., 2008. Activating the medial temporal lobe during oddity judgment for faces and scenes. *Cereb. Cortex* 18, 683–696.
- Murray, E.A., Bussey, T.J., 1999. Perceptual–mnemonic functions of the perirhinal cortex. *Trends Cogn. Sci.* 3, 142–151.
- Murray, E.A., Bussey, T.J., Saksida, L.M., 2007. Visual perception and memory: a new view of medial temporal lobe function in primates and rodents. *Annu. Rev. Neurosci.* 30, 99–122.
- O’Neil, E.B., Cate, A.D., Kohler, S., 2009. Perirhinal cortex contributes to accuracy in recognition memory and perceptual discriminations. *J. Neurosci.* 29, 8329–8334.
- Perrett, D.I., Oram, M.W., Harries, M.H., Bevan, R., Hietanen, J.K., Benson, P.J., Thomas, S., 1991. Viewer-centred and object-centred coding of heads in the macaque temporal cortex. *Exp. Brain Res.* 86, 159–173.
- Pourtois, G., Schwartz, S., Seghier, M.L., Lazeyras, F., Vuilleumier, P., 2005. Portraits or people? Distinct representations of face identity in the human visual cortex. *J. Cogn. Neurosci.* 17, 1043–1057.
- Quiroga, R.Q., Reddy, L., Kreiman, G., Koch, C., Fried, I., 2005. Invariant visual representation by single neurons in the human brain. *Nature* 435, 1102–1107.
- Spaniol, J., Davidson, P.S., Kim, A.S., Han, H., Moscovitch, M., Grady, C.L., 2009. Event-related fMRI studies of episodic encoding and retrieval: meta-analyses using activation likelihood estimation. *Neuropsychologia* 47, 1765–1779.
- Suzuki, W., Amaral, D., 1994a. Perirhinal and parahippocampal cortices of the macaque monkey: cortical afferents. *J. Comp. Neurol.* 350, 497–533.
- Suzuki, W.A., Amaral, D.G., 1994b. Topographic organization of the reciprocal connections between the monkey entorhinal cortex and the perirhinal and parahippocampal cortices. *J. Neurosci.* 14, 1856–1877.
- Taylor, K.J., Henson, R.N.A., Graham, K.S., 2007. Recognition memory for faces and scenes in amnesia: dissociable roles of medial temporal lobe structures. *Neuropsychologia* 45, 2428–2438.
- Tong, F., Nakayama, K., Moscovitch, M., Weinrib, O., Kanwisher, N., 2000. Response properties of the human fusiform face area. *Cogn. Neuropsychol.* 17, 257–280.
- Webster, M.J., Ungerleider, L.G., Bachevalier, J., 1991. Connections of inferior temporal areas TE and TEO with medial temporal-lobe structures in infant and adult monkeys. *J. Neurosci.* 11, 1095–1116.