Activation Reduction in Anterior Temporal Cortices during Repeated Recognition of Faces of Personal Acquaintances

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Repeated recognition of the face of a familiar individual is known to show semantic repetition priming effect. In this study, normal subjects were repeatedly presented faces of their colleagues, and the effect of repetition on the regional cerebral blood flow change was measured using positron emission tomography. They repeated a set of three tasks: the familiar-face detection (F) task, the facial direction discrimination (D) task, and the perceptual control (C) task. During five repetitions of the F task, familiar faces were presented six times from different views in a pseudorandom order. Activation reduction through the repetition of the F tasks was observed in the bilateral anterior (anterolateral to the polar region) temporal cortices which are suggested to be involved in the access to the long-term memory concerning people. The bilateral amygdala, the hypothalamus, and the medial frontal cortices, were constantly activated during the F tasks, and considered to be associated with the behavioral significance of the presented familiar faces. Constant activation was also observed in the bilateral occipitotemporal regions and fusiform gyri and the right medial temporal regions during perception of the faces, and in the left medial temporal regions during the facial familiarity detection task, which are consistent with the results of previous functional brain imaging studies. The results have provided further information about the functional segregation of the anterior temporal regions in face recognition and long-term memory. © 2001 Academic Press

INTRODUCTION

Recognition of the face of a familiar individual usually involves the retrieval of semantic or episodic memory concerning the individual. This semantic or episodic information is particularly rich in personal acquaintances, such as family members, friends, and colleagues, compared with famous people. Most of this semantic information may be dispensable for the execution of tasks in various face-recognition experiments including familiarity decision task. However, retrieval of these semantic information is so tightly connected with recognition of facial identity that it is difficult to be suppressed once it has been arisen (Bruce and Young, 1986; Damasio et al., 1990), and may be relevant for appropriate behavior in the real social life. It is known that repeated recognition of a famous face requires a shorter reaction time than the recognition of the same face at first time even if the presented pictures were different (Bruce and Valentine, 1985; Ellis et al., 1987). This kind of accelerated performance during repeated presentation of the same or similar stimuli, which is referred as "repetition priming," has been extensively studied in behavioral studies and considered to be a result of efficient information processing for repeated cognitive processes (see Buckner and Koutstaal, 1998; Schacter and Buckner, 1998a,b; Gabrieli, 1998, for review). One of the recent issues in functional brain imaging of the human brain is that activation decreases in specific activated regions but not in other activated regions during repeated processing of the same or similar visual stimuli. Visual recognition tasks involve perceptual processing as well as cognitive processing, such as memory retrieval, encoding, and semantic processing. When the stimuli are repeated, and the perceptual processing demands are the same or similar (perceptual priming), reduced activation may be observed in regions in the extrastriate cortex (Squire *et al.*, 1992; Buckner et al., 1995, 1998, 2000; Schacter et al., 1996; Grill-Spector et al., 1999). When stimuli that require the same or similar semantic processing, but in different forms or with different sensory modalities, are repeated (semantic priming), reduced activation may be observed in the inferior temporal cor-



tex or the left prefrontal cortex (Demb *et al.*, 1995; Wagner *et al.*, 1997; Buckner *et al.*, 1998). Repeated recognition of faces of familiar people causes an accelerated or efficient access to semantic information concerning these people, and this phenomenon should be regarded as semantic priming (Bruce and Valentine, 1985; Ellis *et al.*, 1987).

Neural correlates of the long-term memory about people are discussed in various fields in neuroscience. Neuropsychological studies have suggested that lesions in the anterior temporal cortices cause an impaired access to the semantic or conceptual knowledge of people (Ellis et al., 1989; Kapur et al., 1992, 1994; Markowitsch et al., 1993; Damasio et al., 1996; Tranel et al., 1997). The selective response of neurons to faces has been observed in the monkey anterior temporal cortices, such as the inferior temporal cortices (IT) and cortices in the superior temporal sulcus (STS) (Perret et al., 1984; Rolls, 1984; Baylis et al., 1985; Hasselmo et al., 1989). In functional brain imaging studies, various facial identity recognition tasks and control tasks were compared, and most studies have suggested activations in the temporal cortices including the lateral, medial, and polar regions (Sergent et al., 1992, 1994; Damasio et al., 1996; Gorno Tempini et al., 1998; Leveroni et al., 2000; Nakamura et al., 2000). However, the activation change during repeated presentation of familiar faces or that caused by semantic priming has not been studied yet.

In this study, we studied the locus of activation reduction for recognition associated with the repeated presentation of familiar faces. Colleagues of the authors participated in the experiment as subjects, and pictures of faces of other colleagues in the same institutes were acquired as visual stimuli. Thus, the presented familiar faces were those of the immediate colleagues of each subject. Recognition of a familiar face involves perception of a face, and access to the semantic memory about the individual. The subjects performed a task which requires recognition of familiar faces and two baseline tasks, each repeated five times. First, subtraction analysis was performed to extract brain regions where activation was relatively constant through the repeated task execution. Then, regression analysis was performed to extract brain regions where the regional cerebral blood flow (rCBF) decreases through repetition of the tasks involving recognition of a set of familiar faces. In all tasks, a response was required to confirm attention and analyze performance of the subjects, and these responses were comparable among the tasks. To avoid the confounding effect of perceptual priming, we presented pictures of a face from various views for both familiar and unfamiliar faces.

METHODS

Subjects

Seven right-handed normal male volunteers (aged 23 to 28 years) participated in this study. Four were colleagues of the authors in IDAC, Tohoku University, and three were colleagues of the authors in the Primate Research Institute, Kyoto University. Handedness was assessed based on the Edinburgh Handedness Inventory (Oldfield, 1971). None of the subjects had any signs or history of psychoneurological disease. Written informed consent was obtained from each subject in accordance with the guidelines approved by the National Institute for Longevity Science and the Helsinki Declaration of Human Rights, 1975.

Visual Stimuli

Digitized color square pictures were presented as visual stimuli during the tasks. Visual stimuli subtended a visual angle of 10° in both horizontal and vertical axes. Pictures of faces were collected from some of the colleagues of the authors in IDAC, Tohoku University and the Primate Research Institute, Kyoto University. Twenty familiar and 120 unfamiliar individuals were selected for each subject. Individuals who were possibly acquainted with the subject, or resembled famous social figures or personal acquaintances of the subject (as far as the authors knew) were excluded from the unfamiliar-individual candidates. The face of each individual as it appears in daily life in the institute was photographed, less than three months before PET measurements. Some individuals wore glasses or had a beard. All pictures were taken using a digital video camera while the individual was moving his/her head horizontally. Still pictures of the face directed leftward and rightward and from the frontal view were obtained from video recordings, and the neck, clothes, and background were masked out in gray.

Tasks

Each subject performed three tasks: control (C) task, face direction discrimination (D) task, and familiarface detection (F) task. In all three tasks, 48 visual stimuli were presented with 1-s presentation and 1-s interstimulus interval during each scan. Before execution of each task, the target stimuli were specified, and each subject was instructed to respond by clicking the computer mouse when the target stimuli were presented. One-half of the presented stimuli were target stimuli in each scan and the target and nontarget stimuli were presented at random. In the C task, scrambled pictures of a face with a red dot at one of the four corners (Fig. 1a) were presented and the targets were those with the dot on the left (or the right) corner (regardless of being in the upper or lower side). In both



FIG. 1. Examples of visual stimuli. (a) Example of a scrambled picture of a face presented in the C task. (b) Example of a picture of a face presented in the D and F tasks. Actual pictures are digitized color images. A dot located on the upper right corner of the sample pictures is actually colored red and can be located at any of the four corners.

the D and F tasks, pictures of faces directed leftward or rightward, or from the frontal view (Fig. 1b), were presented. There was also a red dot at one of the four corners in each picture, irrespective of the task. In the D task, all presented faces were unfamiliar to the subject and the targets were pictures with the face directed leftward (or rightward) (i.e., when the targets were faces directed leftward, half of the presented unfamiliar faces were directed leftward, and the rest (nontarget) involved faces directed rightward or from the frontal view). In the F task, 24 pictures of unfamiliar faces and 24 pictures of familiar faces were presented, and the targets were pictures of familiar faces. The assumed cognitive processes involved in these three tasks are summarized in Table 1. The three tasks constitute one session, and each subject repeated the sessions five times (e.g., CDFCDFCDFCDFCDF). The task order in the session was counterbalanced among the subjects. We pseudorandomized the order of presentation of familiar faces in the F task throughout the five sessions, rather than repeatedly presenting a specific set of familiar faces in every scan. In each F task scan, the face of a single individual never appeared or appeared once, twice, or three times, and the total number of presented familiar faces was 24 in each scan. This psudorandomization prevents the possible confounding effect of subjects' expectation that this face will appear next. The face of each familiar individual (including faces in the three directions altogether) appeared six times throughout the five sessions. Each picture of the familiar face (a face of a certain familiar individual in a certain direction) was presented twice and the second presentation never preceded the first presentation of the pictures of the same familiar face in other directions. The pictures of an unfamiliar face were used only once (i.e., the picture of the face of each unfamiliar individual appeared three times in different direction) throughout the D and F tasks.

Data Acquisition

Each subject was placed comfortably in a supine position in a PET scanner (Siemens/CTI ECAT EXACT HR) (Wienhard *et al.*, 1994). Transmission data for attenuation correction were acquired using three external 68Ge/68Ga sources. After a bolus injection of approximately 15 mCi (555MBq) of H₂¹⁵O, emission data were collected in the three-dimensional (3-D) mode immediately after radioactivity increase was detected, which lasted 90 s. Reconstruction and filtering gave a final image resolution of $4.0 \times 4.0 \times 3.4$ mm³. During the emission scans, task performances, including reaction times and accuracy, were recorded. A high-resolution T1-weighted magnetic resonance image (MRI) of the brain was acquired for each subject on separate occasion.

Performance Data Analyses

Each response (or no-response) in the C and D tasks can be objectively determined to correct or error, but that in the F task cannot, because familiarity is a subjective matter. Some pictures of faces may not be recognized as familiar at first look, but may be recognized as familiar at next appearance. What is important is not whether the presented face was that of a familiar individual or not, but whether the subjects recognized the presented face as familiar or not. Therefore, we regarded the face as unfamiliar while the subjects did not respond at early presentations, and once the subject responded, the face was considered as familiar regardless of the direction of the face in the following presentations. This correction caused the differences in the number of presentation of familiar faces in the F task among sessions and subjects. These differences in the number of presentation of familiar faces among sessions were tested for significance using the two-way analysis of variance (ANOVA), and compared using the Student's t test (Tukey-type correction for

TABLE 1

Cognitive Processes Involved in the Execution of Each Task

		Tasks			
Cognitive process	С	D	F		
Visual input (color and contrast)	+	+	+		
Perception of a face Discrimination of the location of the dot	- +	+	+		
Facial direction discrimination	—	+	_		
Access to long-term memory concerning a person	_	_	+		
Motor output	+	+	+		

Note. + and - indicate that the cognitive process is required and is not required in the task execution, respectively.



FIG. 2. (a) Mean number of familiar faces presented during each F task in five sessions after correction according to the subject's performance (see text). Error bars indicate standard deviation (SD). Each bar is partitoned with different patterns to show the mean number of presented faces for each "number of repeated presentations" (see text) (1, first presentation; 2, second presentation, and so on, as shown in the legend in the right side of the figure). * The mean numbers of presented familiar faces were significantly (P < 0.05) less than those in the rest of the sessions (sessions 2, 3, 4, and 5). (b) Mean reaction times (msec) for three tasks in five sessions. White, gray, and black bars indicate C, D, and F tasks, respectively. Error bars indicate SD. † The mean response times in the sessions 1 and 2 were significantly (P < 0.05) longer than those in sessions 3, 4, and 5 in the F task. (c) The mean reaction times (msec) for familiar faces at each "number of repeated presentations" (see text) (1, first presentation; 2, second presentation, and so on). Error bars indicate SD. [‡] The mean reaction times in the first presentation were significantly (P < 0.05) longer than those in the third, fourth, fifth, and sixth presentations. § The mean reaction times in the second presentation were significantly (P < 0.05) longer than those in the fourth, fifth, and sixth presentations.

multiple comparisons, P < 0.05) (Fig. 2a). Due to pseudorandomization of the order of familiar-face presentation and the above-mentioned correction, the famil-

iar faces were presented for various numbers of times in each F task scan. Some faces can be at first presentation and other faces can be at second presentation, or more. This "number of repeated presentations" for each face is essential for this study. The mean number of presented familiar faces is shown for each "number of repeated presentations" for each session in Fig. 2a. Differences in the percentages of the correct responses and the mean reaction times among sessions were tested for significance and compared (two-way ANOVA and Student's *t* test (Tukey-type correction for multiple comparisons, P < 0.05)) for each task (Table 2 and Fig. 2b). Because the effect of the repeated presentation could be more accurately evaluated when the reaction times were compared among "number of repeated presentations" rather than sessions, the mean reaction times for familiar faces were calculated for each "number of repeated presentations." The decrease in reaction times was also analyzed using the two-way ANOVA and post hoc comparisons with the Tukey-type correction for multiple comparisons (P < 0.05) (Fig. 2c).

PET Data Analyses

Processing of all PET images, unless otherwise specified, was performed using the Statistical Parametric Mapping (SPM) 96 software (Wellcome Department of Cognitive Neurology, London, UK) (Friston et al., 1995) implemented on MATLAB (Mathworks Inc., Sherborn, MA) on Sun workstations (Sun Microsystems, Mountain View, CA). For each subject, all PET images were realigned into the image of the first scan and coregistered onto the T1-weighted brain MRI with translation and rotation. For spatial normalization of PET images, parameters calculated in the transformation of each subject's MRI into the standard brain MRI of the Human Brain Atlas (HBA) system (Roland et al., 1994) were used. The transformation parameters consisted of linear parameters and a nonlinear deformation field, which were calculated using the Automated Image Registration (AIR) (Woods et al., 1998) and the Elastic transformation software (Shormann et al., 1995), respectively. Before carrying out statistical analysis, all PET images were smoothed with a 3-D Gaussian filter with 16 mm full-width at half maximum (FWHM) to improve the signal-to-noise ratio. To extract brain regions which show task-related steady rCBF changes and those which show an rCBF decrease through the repeated tasks, a voxel-by-voxel two-way ANOVA with repeated measurements and multivariate regression analysis were integrated using the general linear model. The multivariate analysis of covariance was performed implementing covariates of interest, modeling a constant task effect (one for all sessions) and a linearly decreasing effect (2, 1, 0, -1, and -2 for sessions 1, 2, 3, 4, and 5, respectively) for each task (C, D, and F: constant task effect; and rC, rD, and rF: linearly

TABLE 2

Performance	Data
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		(a) Percentage of	the correct response (%)		
	Session No.					
Task	1	2	3	4	5	
С	$\textbf{98.8} \pm \textbf{1.9}$	$\textbf{98.8} \pm \textbf{1.9}$	$\textbf{98.8} \pm \textbf{1.9}$	99.6 ± 0.9	98.3 ± 1.7	
D	97.1 ± 2.4	98.3 ± 1.7	95.8 ± 2.6	97.9 ± 2.1	99.2 ± 1.1	
F	$\textbf{98.8} \pm \textbf{2.8}$	98.3 ± 1.7	97.5 ± 3.4	$\textbf{98.8} \pm \textbf{1.9}$	97.5 ± 1.7	
		(b) Mean re	sponse times (ms)			
			Session No.			
Task	1	2	3	4	5	
С	478 ± 91	428 ± 45	457 ± 45	458 ± 87	460 ± 82	
D	544 ± 130	524 ± 82	503 ± 64	478 ± 73	480 ± 75	
F	728 ± 119	695 ± 83	573 ± 45	572 ± 73	577 ± 68	

Note. (a) The percentage of the correct responses during each task in each session. Values are means \pm standard deviation (SD) (%) of the percentage of correct response of all subjects. (b) The mean reaction times of the response (the delays between the presentation of the visual stimulus and the button press in the trials with correct response) during each task in each session. Values are means \pm SD (ms) of the mean reaction times of all subjects.

decreasing effect), and the five subject conditions and the global CBF as covariates of no interest. The voxel values in each image were adjusted to make global CBF into 50 ml/min/100 ml. Then, simple subtractions, F-C, D-C, and F-D, tests for significance of the linear rCBF decrease, rC, rD, and rF, and tests for significance of the difference in the regression slopes, rF-rC, rD-rC, and rF-rD, were performed. Simple subtractions and tests for significance of the linear rCBF decrease were thresholded at Z < 3.09 (P < 0.001, uncorrected for multiple comparisons), and the Talairach coordinates and the Z score of the voxel with a peak Zscore in each region are listed in Tables 3 and 4. In the tests for significance of the linear rCBF decrease, the significance (P < 0.05) of the difference in the regression slopes, rF-rC, rD-rC, and rF-rD is also indicated. Anatomical inferences on activated regions and regions showing a significant linear rCBF decrease were made by superimposing them onto the mean normalized MRIs of all subjects. To avoid pseudo-activation due to deactivation in a subtracted image and to eliminate the effect of different task requirement, as much as possible, interpretations were made for regions which show activation commonly in two subtractions. Commonly activated areas in F-C and D-C, and in F-C and F-D (Z < 3.09, P < 0.001 for both subtractions), are shown in Figs. 3a and 3b. To reveal brain regions where activation decreases specifically through the repetition of the F task, brain regions showing a decrease in rCBF through repetition of the F task were extracted from the brain regions which had a higher mean rCBF in the F task than those in the C and D tasks through the

sessions. In addition, we wanted to eliminate regions showing an rCBF decrease during the C or D task comparable to that during the F task, because we want to eliminate the regions which show an rCBF decrease solely caused by habituation for experimental environment, such as noise and the posture, and for experimental procedures, such as viewing stimuli, pressing button. To achieve these, rF (Z < 3.09, P < 0.001) were masked with F-C, F-D, rF-rC, and rF-rD (Z < 1.68, P <0.05) (Table 5 and Figs. 3c and 4). To profile the activations and their changes associated with repetition of the tasks, the means and standard deviations of adjusted rCBFs were plotted and the regression line was superimposed for each task for each peak voxel (Fig. 5). For all image statistics, voxels which survived correction for multiple comparisons based on the search volume and the estimated smoothness of the images (P <0.05), were also indicated.

RESULTS

Among the seven subjects, two subjects could not complete the PET experiment for physical reason or due to problems in equipment. The data of the five subjects who completed all the tasks were used for further analyses.

Behavioral Performance

Figure 2a shows the mean number of presented familiar faces (both total and separately for each "number of repeated presentations") in the F task for each

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TABLE 3

Significant Activations in the Simple Subtractions

Structure	F-C	D-C	F-D
R. inferior occipitotemporal region	-43, -69, -19 (6.41)*	-41, -72, -16 (6.75)*	
L. inferior occipitotemporal region	$43, -72, -14$ $(6.62)^*$	44, -72, -11 (6.98)*	
R. fusiform gyrus	-40, -39, -20 (6.78)*	-40, -39, -19 (6.83)*	
L. fusiform gyrus	32, -32, -18 (6.35)*	$34, -32, -19 (5.04)^*$	
L. lingual gyrus	Ť		17, -38, -7 (3.29)
R. parahippocampal gyrus	-31, -6, -29 (4.76)*	-31, -9, -30 (4.18)	, , , , ,
L. parahippocampal gyrus	‡		24, -4, -16 (3.22)
R. amygdala	-19, -1, -19 (4.56)*	-20, -3, -13 (3.63)	
L. amygdala	$23, -1, -14 (5.47)^*$		23, 4, -9 (3.38)
R. temporal pole	$-40, 22, -21 (5.92)^*$	-40, 20, -22 (4.06)	
L. temporal pole	44, 22, -16 (4.09)		39, 26, -20 (3.40)
R. anterior middle temporal gyrus	-52, 0, -19 (3.31)*		
L. anterior middle temporal gyrus	55, 0, -9 (4.88)*		
R. posterior middle temporal gyrus		-64, -42, -12 (3.19)	
R. hypothalamus	$-10, 0, -5 (4.79)^*$		-7, 0, -4 (3.74)
R. subcallosal anterior cingulate gyrus	$-10, 32, 0 (4.38)^*$		$-10, 36, 1 (4.62)^*$
R. superior rostral sulcus	-6, 46, -1 (4.12)		
R. anterior cingulate gyrus			-12, 40, 20 (3.54)
L. frontal pole	6, 62, 21 (5.42)*		6, 61, 21 (3.69)
R. medial frontal gyrus	-3, 51, 34 (4.15)		
L. posterior cingulate gyrus	2, -53, 16 (6.75)*	4, -53, 18 (5.28)*	
R. cerebellum	$-24, -81, -27 (4.96)^*$		
L. cerebellum	15, -79, -36 (4.80)*	14, -79, -35 (3.64)	

Note. Talairach coordinates and *Z* scores (in the parentheses) for peak voxels of significantly (Z > 3.09, P < 0.001, uncorrected for multiple comparisons) activated regions are given for three simple subtractions, F-C, D-C, and F-D. * Survived correction for multiple comparisons based on the search volume and the estimated smoothness of the images (P < 0.05). † Involved in the activated cluster with the peak at the left fusiform gyrus. ‡ Involved in the activated cluster with the peak at the left amygdala. R, right; L, left.

sessions. The numbers of presented familiar faces in the F task varied significantly among sessions after correction according to the subjects' response (F(4,16) = 11.18, P < 0.05). The number of presented pictures of familiar faces was significantly less (Student's *t* test with Tukey-type correction for multiple comparisons, P < 0.05) in the first session than in the subsequent four sessions. All the subjects responded correctly in almost all the trials in all the tasks in all the sessions (Table 2a), and differences in the percentages of correct responses were not significant among sessions in any of the tasks. The mean reaction times of all the subjects are shown for all the sessions for the three tasks as shown in Table 2b and Fig. 2b. Only in the F task was the session effect significant (F(4, 16) = 13.98, P < 0.05), and the reaction times in the first two sessions were significantly longer than those in the last three sessions (Student's t test with the Tukey-type correction for multiple comparisons, P < 0.05). All the subjects could name almost all the presented familiar faces after each F task was completed. When the reaction times for familiar faces in the F task were compared among "numbers of repeated presentations," the effect of the "numbers of repeated presentations" was significant (F(5, 20) = 22.02, P < 0.05) and the decrease in the mean reaction time was observed in the first four presentations. The reaction times in the first

presentation were significantly longer than those in the last four presentations and those in the second presentation were significantly longer than those in the last three presentations (Student's *t* test with the Tukey-type correction for multiple comparisons, P < 0.05).

Subtraction Analysis

The activations in the subtractions, the C task from the F task (F-C), the C task from the D task (D-C) and the D task from the F task (F-D), are shown in Table 3. The *Z* score threshold was set at Z < 3.09 (P < 0.001, uncorrected for multiple comparison), and anatomical inferences were made by superimposing the activations onto the mean normalized T1-weighted MRIs of all subjects. The Talairach coordinate (Talairach and Tournoux, 1988) and the Z score of each peak voxel are shown in the table. It is also indicated whether each peak activation survives the higher threshold which is corrected for multiple comparisons with the search volume (1,564,389 mm³) and the estimated smoothness of the images (P < 0.05). Brain regions commonly activated in F-C and D-C, which are assumed to be specifically involved in the perception of faces, and those commonly activated in F-C and F-D, which are assumed to be specifically involved in both the judgement

TABLE 4

Regions	Where the rCBF	Showed Significant	Decrease through	the	Sessions fo	or Each '	Гask
()		0					

Structure	rC	rD	rF
R. superior occipital gyrus		$-40, -72, 18 \ (4.65)^{*\dagger}$	
L. superior occipital gyrus			$46, -72, 15 (4.84)^{*^{\dagger \ddagger}}$
R. fusiform gyrus	-33, -30, -20 (3.57)	-43, -23, -15 (3.60)	
L. fusiform gyrus		25, -33, -20 (3.16)	30, -27, -20 (3.16)
L. parahippocampal gyrus		23, -12 , -27 $(4.53)^{*^{\dagger}}$	21, -19, -16 (3.32)
R. posterior superior temporal sulcus	-64, -46, 22 (3.23)		$-59, -59, 12 (4.02)^{\dagger\dagger}$
L. posterior superior temporal sulcus		45, -65, 23 (3.67)	
R. angular gyrus	-59, -52, 34 (3.83)		
L. angular gyrus	48, -51, 28 (3.63)		
L. posterior inferior parietal lobule		$32, -79, 39 (3.58)^{\dagger}$	
R. posterior inferior temporal gyrus		-52, -64, -13 (3.76)	
L. posterior inferior temporal gyrus		56, -45, -11 (3.88)	
R. posterior middle temporal gyrus		-64, -46, -4 (3.81)	
R. middle temporal gyrus			-66, -35, -6 (3.30)
L. middle temporal gyrus		52, -17, -7 (3.19)	$65, -29, 1 (3.83)^{\dagger}$
R. anterior inferior temporal gyrus	-47, -17, -35 (4.39)*		
L. anterior inferior temporal gyrus			$45, -12, -23 (3.32)^{\dagger}$
R. anterior middle temporal gyrus			$-45, 0, -26 (4.58)^{*}$
R. anterior superior temporal sulcus			$-55, -7, -12$ $(3.75)^{*^{\dagger}}$
L. anterior superior temporal sulcus			$52, -7, -7$ $(4.41)^{*^{\dagger}}$
R. temporal pole			$-31, 17, -29 (4.54)^{*^{\dagger \ddagger}}$
L. temporal pole			44, 17, -18 (3.99) ^{†‡}
R. inferior frontal gyrus	-42, 19, -8 (3.64)		
R. middle frontal gyrus	-31, 22, 55 (3.53)		
L. middle frontal gyrus		25, 22, 63 (3.79)	
L. anterior precuneus	13, -40, 39 (3.23)		
R. cerebellum	-21, -64, -22 (3.20)		
	-20, -56, -34 (3.19)		
L. cerebellum	· · · · · ·	14, -72, -30 (3.43)	13, -71, -40 (3.66)

Note. Talairach coordinates and *Z* scores (in the parentheses) for peak voxels of regions where the rCBF showed significant (Z > 3.09, P < 0.001) negative regression with the session numbers are given for each task (rC, rD, and rF correspond to the tasks C, D, and F, respectively). * Survived correction for multiple comparisons based on the search volume and the estimated smoothness of the images (P < 0.05). [†] Slope of the regression line is significantly (P < 0.05) negatively steeper than that of rC. [‡] Slope of the regression line is significantly (P < 0.05) negatively steeper than that of rD. R, right, L, left.

of familiar/unfamiliar or access to long-term memory, are superimposed onto the mean normalized T1-weighted MRIs of all subjects (Figs. 3a and 3b, respectively).

Brain regions commonly activated in F-C and D-C are the bilateral inferior occipitotemporal regions, the bilateral fusiform gyri, the right parahippocampal gyrus, the right amygdala, the right temporal pole, and the left cerebellum. Brain regions commonly activated in F-C and F-D are the left parahippocampal gyrus, the left amygdala, the left temporal pole, the right hypothalamus, the right subcallosal anterior cingulate gyrus, the left frontal pole, and the left posterior cingulate gyrus.

Regions where Activation in the F Task Significantly Decreased through Sessions					
Coordinate (Z)	F-C	D-C	F-D	rC	rD
-45, 0, -26 (4.58)*	2.72	ns	1.96	2.30	1.86
54, -6, -6 (4.35)*	3.30	1.67	1.77	ns	2.26
-29, 20, -27 (4.00)	3.94	2.51	1.66	ns	ns
44, 17, -18 (3.99)	3.33	ns	2.27	ns	ns
	Coordinate (Z) -45, 0, -26 (4.58)* 54, -6, -6 (4.35)* -29, 20, -27 (4.00) 44, 17, -18 (3.99)	Coordinate (Z) F-C -45, 0, -26 (4.58)* 2.72 54, -6, -6 (4.35)* 3.30 -29, 20, -27 (4.00) 3.94 44, 17, -18 (3.99) 3.33	Coordinate (Z) F-C D-C -45, 0, -26 (4.58)* 2.72 ns 54, -6, -6 (4.35)* 3.30 1.67 -29, 20, -27 (4.00) 3.94 2.51 44, 17, -18 (3.99) 3.33 ns	Coordinate (Z)F-CD-CF-D $-45, 0, -26 (4.58)^*$ 2.72 ns 1.96 $54, -6, -6 (4.35)^*$ 3.30 1.67 1.77 $-29, 20, -27 (4.00)$ 3.94 2.51 1.66 $44, 17, -18 (3.99)$ 3.33 ns 2.27	Coordinate (Z)F-CD-CF-DrC $-45, 0, -26 (4.58)^*$ 2.72 ns 1.96 2.30 $54, -6, -6 (4.35)^*$ 3.30 1.67 1.77 ns $-29, 20, -27 (4.00)$ 3.94 2.51 1.66 ns $44, 17, -18 (3.99)$ 3.33 ns 2.27 ns

TABLE 5Regions Where Activation in the ETask Significantly Decreased through Sessions

Note. Talairach coordinates and *Z* scores (in the parentheses) for peak voxels of regions where the rCBF showed significant (Z > 3.09, P < 0.001) negative regression with the session numbers in the F task (masked with F-C, F-D, rF-rC, and rF-rD (P < 0.05)) are given. *Z* scores for three simple subtractions (F-C, D-C, and F-D) and the tests for rCBF decrease in the other tasks (rC and rD) at the same voxels are also given. * Survived correction for multiple comparisons based on the search volume (whole brain) and the estimated smoothness of the images (P < 0.05). ns, nonsignificant ($Z \le 1.68$, $P \ge 0.05$). R, right; L, left.



FIG. 3. (a) Commonly activated regions in both F-C and D-C (P < 0.001). (b) Commonly activated regions in both F-C and F-D (P < 0.001). (c) Areas where rCBF showed significant (P < 0.001) decrease in activation in the F task (i.e., significant (P < 0.001) negative effect of session numbers masked with significant (P < 0.05) activation in F-C and F-D and significantly (P < 0.05) steeper negative regression slope in rF than those in rC and rD). Statistically significant areas are colored as indicated at the bottom of the figure and superimposed onto the mean normalized T1-weighted MRIs of all five subjects. Transaxial planes -30, -25, -20, -15, -10, 0, and 15 mm above the AC-PC plane (see ref.) are shown. The right side of the brain is shown on the left side of the figure.

Regression Analysis

Brain regions where the rCBF showed a significant decrease through sessions for each task (rC, rD, and rF correspond to the tasks C, D, and F, respectively) are shown in Table 4. Statistics and anatomical inferences were the same as those for conventional subtractions. Regions where the negative regression slope was significantly (P < 0.05) steeper in the F task than in the C task (rF-rC), in the D task than in the C task (rF-rC), and in the F task than in the D task (rF-rD) are also indicated. Brain regions where activation decreases specifically through the repetition of the F task (rF,

P < 0.001, masked with F-C, F-D, rF-rC, and rF-rD, P < 0.05) are listed in Table 5. Other details were the same as those for conventional subtractions. Because significant regions were searched in the commonly activated areas in both F-C and F-D (P < 0.05), the searched volume was reduced more than tenfold (110,004 mm³), but this was not reflected in the correction for multiple comparisons due to methodological difficulty (Worsley *et al.*, 1996). Figure 3c shows the activations superimposed onto the mean normalized T1-weighted MRIs of all the subjects. Figure 4 shows the activations rendered on the surface of the standard



FIG. 4. Areas where rCBF showed significant (P < 0.001) decrease in activation in the F task (see text and figure legend to Fig. 3c) are rendered onto the 3-D surface of the standard brain of HBA. The right side, frontal, and left side views are shown in the figure from left to right.



FIG. 5. RCBFs in three tasks in five sessions are shown for the voxel with a peak statistical value in each area where rCBF showed a significant (P < 0.001) decrease in activation in the F task (see text and figure legend to Fig. 3c). The vertical axes are the adjusted rCBFs (ml/dl/min). Error bars indicate SD. Regression lines are shown for the three tasks; dashed, thin solid, and thick solid lines correspond to C, D, and F tasks, respectively.

brain of HBA. The activated regions include the right anterior middle temporal gyrus, the left anterior superior temporal sulcus and the bilateral temporal poles. For each region, rCBF changes and regression lines for the three tasks are given in Fig. 5.

DISCUSSION

Activation reduction was observed in the bilateral anterior temporal cortices (anterolateral to the polar region) through the repetition of the F tasks, in which the subjects repeatedly recognized the faces of their personal acquaintances. To our knowledge, activation reduction associated with repeated cognitive processes in these regions has never been reported in previous functional brain imaging studies. The reaction times for familiar face detection in the F task were shorter in later sessions or at presentation with more "number of repeated presentations" for each face. The bilateral ventral occipitotemporal regions and the right medial temporal region including the amygdala were constantly activated in both the F and D tasks compared with the C task, and the left medial temporal region including the amygdala, as well as the hypothalamus, medial frontal cortices, and posterior cingulate cortex, were constantly activated in the F task compared with the D and C tasks, through the five sessions. Activation in the amygdala during face perception or familiarity decision with neutral faces has also been rarely reported.

Identity Repetition Priming and Activation Reduction

Recognition of the face of personal acquaintances usually involves access to semantic memory or associated information about the individual. Repeated access to semantic or associated information results in accelerated performance in accessing the same information when a related sensory stimulus was perceived (see Tulving and Schacter, 1990; Squire *et al.*, 1993; Buckner and Koutstaal, 1998; Schacter and Buckner, 1998a,b; Gabrieli, 1998 for review), which is sometimes referred to as "semantic (or conceptual) repetition priming." Neural correlates of the semantic repetition priming effect have been studied in many functional brain imaging studies using words or pictures of objects, and activation reduction was observed in the inferior temporal cortex and the left prefrontal cortex (Demb et al., 1995; Wagner et al., 1997; Buckner et al., 1998). The semantic (or conceptual) repetition priming effect has also been studied using famous faces in previous behavioral studies (Bruce and Valentine, 1985; Ellis et al., 1987), and reduced reaction times in familiarity decision tasks for repeated presentation of faces of famous people have been shown even with different pictures. Neural correlates of this "identity priming" effect have not yet been investigated in functional brain imaging studies. In this study, the reaction times for familiar face detection in the F task were shorter in later sessions or in presentations with more "numbers of repeated presentations" for each face. It may be reasonable to assume that the shorter reaction times for repeatedly presented familiar faces and observed activation reduction in the anterior temporal cortices are associated with the identity or semantic repetition priming effect.

Anterior Temporal Cortex and Long-Term Memory for People

Patients with circumscribed lesions in the anterior temporal cortex are quite rare, but some cases have been reported (Ellis *et al.*, 1989; Kapur *et al.*, 1992, 1994; Markowitsch *et al.*, 1993). These patients had lesions in the right or bilateral temporal poles, but the extent of the resected or damaged areas and clinical manifestations varied among patients. The common manifestation of these patients were loss of memory concerning people. All patients showed impaired performance in the famous face and name tests. Perfortion, including matching of faces, short-term memory, general long-term memory, were not at all impaired, or impared in various degree. Damasio et al. (1996) studied 127 patients with focal brain lesions, and showed that impairment in naming famous faces is correlated with damage in the left temporal pole. Similarly, Tranel et al. (1997) studied 116 patients with focal brain lesions, and showed that loss of conceptual knowledge for the presented faces is associated with the right temporal polar region. These neuropsychological studies suggest that anterior temporal cortices play an important role in access to the information about people. Recording studies showed that neurons in the STS and IT of monkeys selectively respond to the face of an individual (Perret et al., 1984; Rolls, 1984; Baylis et al., 1985; Hasselmo et al., 1989), and the anterior temporal cortices respond for recognition of familiar, but not for unfamiliar, faces in presurgical patients with epilepsy (Seeck et al., 1993, 1995; Puce et al., 1999). Puce et al. (1999) addressed the issue of semantic (identity) priming on intracranial event-related potential (ERP) study. In their study, reduced responses to famous faces primed with their names compared with those to nonprimed famous faces were observed in the ventral occipitotemporal regions and in the right anterior ventral temporal region. Response reduction in the right anterior ventral temporal region may correspond to the observed activation reduction in this study. In previous functional brain imaging studies on familiar face recognition tasks, some studies have showed activation in the anterior temporal cortex (Sergent et al., 1992; Damasio et al., 1996; Gorno Tempini et al., 1998; Leveroni et al., 2000; Nakamura et al., 2000). Gorno Tempini et al. (1998) reported that regions in the left anterior lateral temporal cortex were activated in both famous-face and famous-name tasks compared with the control nonfamous tasks, and argued that these regions are specialized to famous stimuli. Nakamura et al. (2000) observed activations in both familiar face detection task and familiar scene detection task in the right temporal pole and argued that this region is involved in the recognition of familiar objects. The results of the above two studies, as well as those of neuropsychological studies by Damasio et al. (1996) and Tranel et al. (1997), suggest a possible dichotomy, that is, the left temporal pole for verbal and the right temporal pole for nonverbal information on people. Activation reduction in the bilateral anterior temporal cortices observed in this study suggests that the recognition of the face of a personal acquaintance involves access to both verbal and nonverbal information about the individual.

mance on the tests evaluating other aspects of cogni-

While the neurobiological explanation for activation reductions in repeated cognitive processing is still unclear, studies of the inferior temporal cortex in monkeys have revealed that responses of some cells steadily decline either as novel stimuli become familiar (Baylis and Rolls, 1987; Riches et al., 1991; Miller et al., 1991) or as familiar stimuli are presented repeatedly over time (Rolls et al., 1989). The overall reduction in the number of highly activated cells presumably explains the reduced activation found in imaging studies. As the critical features of a new object are learned through experience, cells coding noncritical features drop out of the pool of activated cells, making the remaining population smaller but more selective (Li et al., 1993; Ungerleider, 1995). The first encounter with the face of a familiar person may activate various memory traces associated with the person, including visual, other modal or multimodal, semantic or episodic memories, most of which are not essential for the judgement of familiar/unfamiliar (Bruce and Young, 1986; Damasio et al., 1990). However, in the subsequent encounters of the face of the same person, activated memory traces may become more selective to the more essential ones for task execution. During the interview after completion of all the scanning sessions, one subject reported that "[in the F tasks,] when a picture of a familiar face was initially presented, the name of the person and several events associated with the person appeared in the mind. This was strongest at the first presentation, and became weaker as pictures of each familiar person were repeatedly presented." Other subjects also reported similar impressions. These subjective reports are consistent with the proposed mechanism of activation reduction in the cortical regions involved in long-term memory.

Some previous functional brain imaging studies involving familiar face recognition tasks failed to show activation in the anterior temporal cortices (Sergent *et al.*, 1994; Kapur *et al.*, 1995; Sugiura *et al.*, 2000). Sugiura *et al.* (2000) repeatedly presented the subject's own face. Sergent *et al.* (1994) chose familiar famous figures using a list of famous names before the PET experiment, and only mentally imaginable figures were used for the familiar face recognition (professional categorization) task. The failure to activate the anterior temporal cortex in these studies was possibly due to the repeated presentation of the face of the same individual or due to a recent access to long-term memory which may reduce the activation of these cortical regions.

Amygdala and Behavioral Significance

The amygdala was activated bilaterally in the F task compared with the C task. The right amygdala was also activated in the D task compared with the C task. As far as we know, activation associated with perception of unfamiliar faces or recognition of familiar faces has never been reported in functional brain imaging studies, although activation in the adjacent anteromedial temporal cortices has been occasionally reported

(Sergent et al., 1992, 1994; Kapur et al., 1995; Nakamura et al., 2000; Leveroni et al., 2000). In ERP studies of presurgical epileptic patients, Seeck et al. (1993, 1995) reported the response of the right amygdala during recognition of the faces of family members or friends. It is possible that recognition of the faces of personal acquaintances activates the amygdala but that of famous faces does not. If this is the case, amygdala activation should be associated with something beyond the identification of the face per se. One case study of a patient with damage in the bilateral amygdala has suggested that the amygdala is essential for recognition of facial expressions but not for recognition of identity (Adolphs et al., 1994). Bilateral amygdala damage is also known to cause an impaired ability to judge approachability and trustworthiness of unfamiliar faces (Adolphs et al., 1998). In primate studies, lesion studies indicate the relationship between amygdala lesions and impairment in a wide range of social behaviors (Weiskrantz, 1956; Kling and Steklis, 1976), and electrophysiological studies have shown that neurons in the amygdala respond to various social aspects in the presented visual stimuli as well as identity of conspecifics (Brothers et al., 1990; Brothers and Ring, 1993). Rolls and his colleagues compared response of face-selective neurons in STS and IT, and those in the amygdala, and suggested that while neurons selective to facial identity are seen in both populations, neurons in the amygdala play a role in connecting faces to emotional responses (Sanghera et al., 1979; Rolls, 1984; Leonard *et al.*, 1985). In functional brain imaging studies, activation of the amygdala for unfamiliar faces with fearful expressions has been reported both during conscious perception (Morris et al., 1996) and during presentation with backward masking (Whalen et al., 1998). The right amygdala is suggested to be associated with formation of long-term memory associated with emotionally arousing events (Cahill et al., 1996). In the eye-gaze direction judgement task, the left amygdala was sensitive to the task requirement, and the right amygdala was sensitive to eye-gaze directed to oneself (Kawashima *et al.*, 1998). Morris *et al.* (1998) presented conditioned visual stimuli and showed that the right and left amygdalae were responsive to masked (unconscious) and unmasked (conscious) conditioned stimuli, respectively. These findings indicate that the amygdala is sensitive to the behavioral significance of visual stimuli, and the right and left amygdalae may have functional differentiation, presumably in terms of unconscious/conscious aspects. We consider that the left or bilateral amygdala activation in our study is associated with the behavioral significance of a recognized acquaintance's face. The right amygdala was also activated in the D task compared with the C task, and this activation may be associated with some behavioral significance of presented unfamiliar faces or task settings. The fact that all the subjects were colleagues of the experimenters had possibly influenced the result. The subjects may be aware that presented faces were familiar to the experimenters, or that they were spontaneously searching for the familiar faces even in the D task.

The hypothalamus, as well as the medial frontal cortices, was activated in the F task compared with the C and D tasks. These brain structures, as well as the amygdala, are considered to comprise a system for emotional processing and decision making (Bechara *et al.*, 2000). The macaque IT projects to the amygdala, and it projects to the hypothalamus which is associated with emotional response (Sanghera *et al.*, 1979). The hypothalamus and the medial frontal cortices were activated during recognition of one's own face (Sugiura *et al.*, 2000). We consider that activation in these regions is also associated with the behavioral significance of the recognized acquaintances' faces.

Activation in the right parahippocampal gyrus and the right temporal pole during perception of faces is also a rare finding. Only Kapur *et al.* (1995) have reported the right parahippocampal activation during the gender classification task using unfamiliar faces. The possible explanation for the right amygdala activation during the D task compared with the C task may be also applicable to the right temporal pole and the right parahippocampal gyrus activation because these regions have tight reciprocal connections and functional associations (Nakamura and Kubota, 1996).

Posterior Ventral Occipitotemporal Cortex

In the posterior ventral occipitotemporal cortex in each hemisphere, two activation foci were observed during both the D and F tasks compared with the C task. The posterior focus is located at the inferior occipitotemporal junction or at the posterior part of the fusiform gyrus. The anterior focus is located at the anterior part of the fusiform gyrus. Activation of these posterior ventral occipitotemporal regions in facial perception tasks is frequently reported in recent functional brain imaging studies (Haxby *et al.*, 1991, 1994; Kapur et al., 1995; Puce et al., 1996; Gorno Tempini et al., 1998; Nakamura et al., 2000). The posterior focus corresponds to the region termed LO and is suggested to be involved in the visual recognition of objects (Malach et al., 1995; Kanwisher et al., 1997b, but see Allison et al., 1994; Sugiura et al., 2000). The anterior focus is suggested to be involved in the perception of faces specifically, and sometimes referred to as the fusiform face area (FFA) (Kanwisher et al., 1997a; McCarthy et al., 1997). The LO is assumed to correspond to one of the areas consisting the macaque ventral visual pathway, such as V4, TEO, and TE (Haxby et al., 1991; Malach et al., 1995; Tootell et al., 1996), along which object recognition is achieved (Tanaka, 1993). Grill-Spector et al. (1999) reported activation reduction in

the LO during repeated presentation of objects, including faces, from various views. The FFA is considered to be a homologue of the macaque IT (more specifically TE) (Kanwisher *et al.*, 1997a) where face-selective neurons are observed (see Desimone, 1991; Perrett *et al.*, 1992; Rolls, 1992, for review).

Methodological Consideration

All possible volunteers in the two institutes who met the criteria participated as subjects. However, the number of subjects whose data were actually used for statistical analysis was quite small. Thus, the results may be affected by intersubject variance.

We employed a simple linear decrease model in the regression analysis to show activation reduction. However, this simple linear decrease model may be inaccurate. The decrease in the activity of neurons selective to a specific face in the STS or IT of monkeys is reported to be larger between the first presentation and the second presentation than between any later two successive presentations (Rolls *et al.*, 1989; Li *et al.*, 1993). Nevertheless, at present, we consider the use of this simple linear decrease model as the best choice to acquire statistical sensitivity without a groundless hypothesis, using a limited number of subjects and scans.

The number of presented "familiar" faces was significantly less in the F task in the first session than in subsequent sessions. This may cause a reduced statistical power in the regression analysis using the linear decrease model, rather than an increased possibility of obtaining a false positive.

We argue that activation reduction in the anterior temporal cortices and shortening of the reaction times are associated with repeated access to the long-term memory about the individual. However, the present results per se do not exclude other possibilities, such as repeated perception of similar stimuli (various views of the same face can be more perceptually similar than that of different faces) or repeated performance of familiarity decision which is independent of the identity of the faces. The former alternative interpretation is unlikely when the results of Grill-Spector et al. (1999), that activation reduction was observed in the LO during repeated presentation of faces from various views, are considered. Their results also exclude the possibility that our result can be explained by the fact that same picture (the face in the same direction) was presented twice. However, the possibility of the latter alternative interpretation is quite difficult to exclude, although no previous findings support the notion that the anterior temporal cortex plays such a manipulative role.

The current results should be confirmed using more subjects, more refined models such as the nonlinear decrease model, and improved task designs in future studies.

Summary

Activation reduction associated with repeated recognition of familiar faces was observed in the bilateral anterior temporal cortices which are suggested to be involved in the access to long-term memory concerning people. This is considered to be associated with the identity or semantic repetition priming effect. The bilateral amygdala, the hypothalamus, and the medial frontal cortices were constantly activated during the recognition of acquaintances' faces. This activation is considered to be associated with the behavioral significance of the presented acquaintances' faces. Activation in the bilateral occipitotemporal regions and fusiform gyri during the perception of faces, and that in the bilateral parahippocampal gyri and temporal pole during the facial familiarity decision are consistent with previous findings of functional imaging studies.

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