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Critical Period for Cross-Modal Plasticity in Blind Humans: A Functional MRI Study

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The primary visual cortex (V1) in congenitally blind humans has been shown to be involved in tactile discrimination tasks, indicating that there is a shift in function of this area of cortex, but the age dependency of the reorganization is not fully known. To investigate the reorganized network, we measured the change of regional cerebral blood flow using 3.0 Tesla functional MRI during passive tactile tasks performed by 15 blind and 8 sighted subjects. There was increased activity in the postcentral gyrus to posterior parietal cortex and decreased activity in the secondary somatosensory area in blind compared with sighted subjects during a tactile discrimination task. This suggests that there is a greater demand for shape discrimination processing in blind subjects. Blind subjects, irrespective of the age at onset of blindness, exhibited higher activity in the visual association cortex than did sighted subjects. V1 was activated in blind subjects who lost their sight before 16 years of age, whereas it was suppressed in blind subjects who lost their sight after 16 years of age during a tactile discrimination task. This suggests that the first 16 years of life represent a critical period for a functional shift of V1 from processing visual stimuli to processing tactile stimuli. Because of the age-dependency, V1 is unlikely to be the "entry node" of the cortex for the redirection of tactile signals into visual cortices after blinding. Instead, the visual association cortex may mediate the circuitry by which V1 is activated during tactile stimulation.

INTRODUCTION

Braille reading requires converting simple tactile information into meaningful patterns that have lexical and semantic properties (Sadato *et al.*, 1998). Whereas visual letter identification is routinely accomplished within the visual system, the perceptual processing of Braille may be mediated by the somatosensory system. Electrophysiological and neuroimaging studies have indicated that, in blind subjects, the visual system is used for tasks other than processing visual information. Tactile imagery or Braille reading in blind subjects causes task-related activation in the occipital leads of the electroencephalogram (EEG; Uhl *et al.*, 1991), which suggests that somatosensory input is redirected into the occipital area. It is known that the primary visual cortex (V1) is activated when subjects with congenital and early-onset blindness (<13 years old) read Braille and carry out other tactile discrimination tasks (Sadato *et al.*, 1996, 1998; Lanzenberger *et al.*, 2001). Transcranial magnetic stimulation (TMS) induces transient disruption of cortical function during identification of Braille letters in early-onset blind subjects (<10 years old) but not in sighted subjects reading embossed Roman letters (Cohen *et al.*, 1997), demonstrating the functionality of the visual cortex of blind subjects. A woman blind from birth who was a proficient Braille reader sustained bilateral occipital damage from an ischemic stroke (Hamilton *et al.*, 2000). Following the stroke, she was not able to read Braille, yet her somatosensory perception appeared to be otherwise unchanged. This case supports emerging evidence of the recruitment of striate and prestriate cortex for Braille reading in early-onset blind subjects. Different neural networks representing different modalities are activated during the performance of tactile discrimination tasks by blind and sighted subjects: the tactile processing pathways generally linked to the secondary somatosensory area (SII) are rerouted in blind subjects to the ventral occipital cortical regions generally reserved for visual shape discrimination (Sadato *et al.*, 1998). These findings suggest a remarkable plasticity of the brain, potentially permitting additional processing of tactile information in the visual cortical areas.

Reorganization of brain function may differ in early-onset and late-onset blind subjects (Kujala *et al.*, 2000). There is evidence of a critical period for involvement of the visual cortex: Braille reading activates V1 in early-onset but not late-onset blind subjects. Stimulation of the visual cortex using TMS causes errors in Braille reading only in early-onset blind subjects (Cohen *et al.*,

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TABLE 1

Characteristics of the Subjects

Subject no.	Age (year)	Sex	Cause of blindness	Age at onset of blindness (year)	Visual acuity[a] (L/R)	Age at start of Braille reading (year)	Training (h/day)	Reading hand
			Early-onset blind subjects (<16 years of age)					
1	58	F	Microphthalmos	<1	0/0	7	3 1/2	L/R
2	39	F	Microphthalmos	<1	0/HM	6	1/2	L
3	55	M	Microphthalmos	<1	0/0	6	1	L
4	56	M	Eye infection	2	0/0	6	1/4	L
5	48	F	Glaucoma (postmeasles)	3	LP/0	7	1/2	L
6	51	M	Glaucoma (postmeasles)	9	0/0	6	1/4	L
7	39	M	Optic nerve atrophy	10	0/0	6	1/4	L
8	21	M	Retinitis pigmentosa	12	HM/HM	19	6	L
9	25	M	Retinitis pigmentosa	15	LP/LP	7	3	L/R
			Late-onset blind subjects (>16 years of age)					
10	30	M	Retrolental fibroplasia	20	HM/HM	20	6	L
11	41	M	Glaucoma	24	0/0	24	1/6	R
12	42	F	Atrophy of retina and choroid plexus	27	HM/LP	14	1/2	L
13	39	M	Retinitis pigmentosa	37	ND/ND	36	1/4	R
14	52	M	Retinitis pigmentosa	40	LP/LP	33	3	L
15	63	M	Retinitis pigmentosa	51	LP/LP	45	1	L

[a] Visual acuity categories: the subject had no remaining vision (0), could see only hand movements (HM), had only light perception (LP), or could only see digit (finger) number at 1 meter (ND). L, left; R, right.

1999), although some authors report activation of V1 in late-onset but not congenitally blind subjects (Büchel *et al.*, 1998). Thus, the effect of the age at onset of blindness on plasticity in neural substrates for tactile discrimination is not fully known.

To clarify the critical period of the plastic change due to visual deprivation, we used functional MRI and passive tactile tasks with and without discrimination components. Discrimination task with Braille characters was adopted instead of Braille words (Sadato *et al.*, 1996, 1998; Büchel *et al.*, 1998) because Braille word reading may induce recall of visual features of the objects indicated by the words, which in turn may activate V1 in late-onset blind subjects whereas not in early or congenital blind. Blind subjects with various ages at onset of blindness and sighted subjects were included. Sighted subjects exhibited parietal and frontal cortical involvement without activation of the occipital cortex. V1 was active in early-onset blind (<16 years old), but not late-onset blind (>16 years old) subjects during a tactile discrimination task. On the other hand, the visual association cortex was activated irrespective of the age at onset of blindness.

SUBJECTS AND METHODS

We studied 15 blind subjects, 4 women and 11 men, aged 43.9 ± 12.3 years (mean ± SD). Nine of them lost their sight before the age of 16 years, and the others after age 16 years. All blind subjects were blind due to dysfunction at the level of the eye or early optic nerve. Their clinical characteristics are summarized in Table 1. Control subjects were 8 sighted volunteers, 5 women and 3 men, aged 29.0 ± 4.5 years. The subjects were all right-handed according to the Edinburgh handedness inventory (Oldfield 1971). There was no history of neurological or psychiatric illness in any of the subjects, and except for the blindness, none had any neurological deficits. The protocol was approved by the ethical committee of Fukui Medical University, and all subjects gave their written informed consent for the study.

MRI

A time-course series of 126 vol was acquired using T2*-weighted, gradient echo, echo planar imaging (EPI) sequences with a 3.0 tesla MR imager (VP, General Electric, Milwaukee, WI). The raw data were transferred to a parallel supercomputer (ORIGIN2000, SGI, Mountain View, CA) for reconstruction of the consecutive two-dimensional images using a two-dimensional fast Fourier transform (General Electric). Each volume consisted of 36 slices, with a slice thickness of 3.5 mm and a 0.5-mm gap, to include the entire cerebral and cerebellar cortex. The time-interval between two successive acquisitions of the same image was 3000 ms, and echo time was 30 ms. The field of view (FOV) was 22 cm. The in-plane matrix size was 64 × 64 pixels with a pixel dimension of 3.44 × 3.44 mm. The magnetic shim was optimized such that a

true in-plane resolution of 3.44 × 3.44 mm was realized. Tight but comfortable foam padding was placed around the subject's head to minimize head movement.

For anatomical reference, T2-weighted fast spin echo images were obtained from each subject with location variables identical to those of the EPIs. In addition, high-resolution whole-brain MRIs were obtained with a conventional T2-weighted, fast spin echo sequence. A total of 112 transaxial images were obtained. The in-plane matrix size was 256 × 256, and slice thickness was 1.5 mm, and pixel size was 0.859 × 0.859 mm.

Tactile Tasks

Braille tactile discrimination task. A session consisted of six task and six rest periods, each 30 s in duration, alternating task and rest periods. Braille stimuli were presented passively using a plastic rail on which different pairs of two-dot standard Braille characters (center-to-center distance, 5 mm) were printed. The rail was 1.7 m long. The skid (1 m in length), through which the rail was moved manually by an examiner from the outside of the MRI gantry, was fixed on the left side of the subject's body. The subject placed their right arm across their chest, rested their thumb and four fingers at a fixed position on the skid, and placed their right index finger with the finger pad on the rail (Fig. 1). The position of the rail was first set so that the subject's right index finger was located between two consecutive pairs of Braille characters. The subject's left hand was placed on a button box connected to a microcomputer for recording the response.

For sighted subjects, a pacemaking cue was projected onto a semitransparent screen hung approximately 1.5 m from the subject's eyes. For this, an LCD projector (Epson ELP-7200L, Tokyo, Japan) was connected to a personal computer (Toshiba Dynabook with Windows95, Tokyo, Japan) in which in-house software was used to generate a visual cue which is a small filled circle. To fix the eye position, the subject were requested to gaze the cue circle throughout the session. This was to control eye movement, because saccadic eye movement is known to suppress the activity of the striate cortex even in the darkness (Paus *et al.*, 1995). For 18 s before a session, a yellow cue was presented to allow the subject time to position both hands. Then, during the tactile discrimination task, red and green cues, each 3 s in duration, were given alternately for 30 s. When the red cue was on, the examiner slowly moved the rail to present passively a pair of two-dot Braille characters to the subject's finger pad. The rail was moved three times in 3 s: 30 mm in the head-to-foot direction in 1 s, 30 mm in the foot-to-head direction in the next second, and 30 mm again in the head-to-foot direction in 1 s. The speed of presentation was approximately 30 mm/s. The rail moved quietly without making any task-related sound. The examiner also confirmed that the subject did not move the right index finger for exploration. When the green cue was on, the rail stopped moving, and the subject responded by pushing a button with their left index finger if the pair-wise characters were the same, or with their mid-

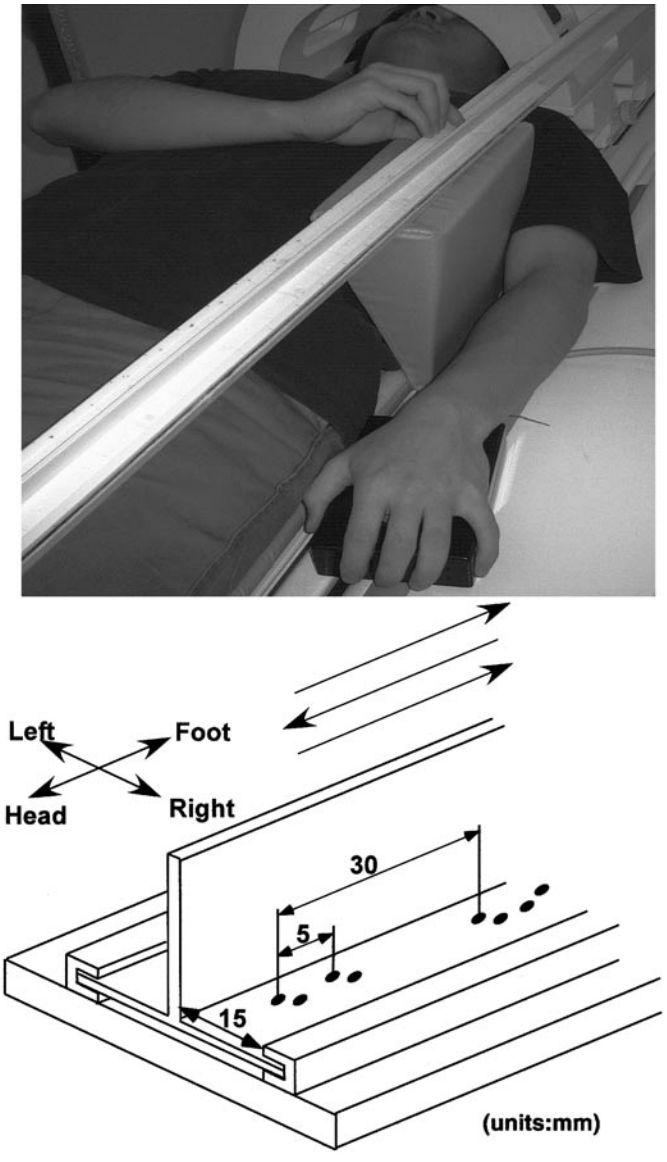


FIG. 1. Experimental setup. (Top) During each session, with their heads positioned in the MRI magnet, subjects placed their right arm across their chest, rested their thumb and four fingers at a fixed position on a skid, and placed their right index finger with the finger pad on a plastic rail on which Braille characters were printed. The subject's left hand was placed on a button box connected to a microcomputer for recording the response. The skid (1 m in length), through which the rail was moved manually by an examiner from outside the MRI gantry, was fixed on the left side of the subject's body. The rail was 1.7 m long. (Bottom) Details of the rail and skid. The upper part of the skid was open, allowing access with the index finger to the flat portion of the plastic rail on which different pairs of two-dot standard Braille characters (center-to-center distance, 5 mm) were printed. Pair-to-pair distance was 30 mm.

dle finger if the characters were different. Reaction times were not measured. A 30-s rest condition followed, in which red and green cues were given alternately, as in the task condition. When the red cue was on, no tactile stimulus was presented. When the green cue was on, the subject pushed buttons with their left index and middle finger alternately. The comparison of images collected during the discrimination task versus those during rest periods enable correction for the effects of the cue and response movement.

For blind subjects, the cue for a response was a touch to the subject's left toe given every 6 s by the examiner. A total of 30 pairs of Braille characters were presented, half of which were different and half of which were the same.

Braille tactile nondiscrimination task. In the tactile nondiscrimination task, which was used to control for sensorimotor effects, six-dot, instead of two-dot, Braille characters were presented when the red cue was given. When the green cue was on for sighted subjects or the touch cue was given for blind subjects, the subject pushed buttons with the left index and middle finger alternately. Other variables were identical to those in the Braille tactile discrimination task. Each subject underwent two different sessions (discrimination and nondiscrimination).

Data Analysis

The first 6 vol of each fMRI session were discarded due to unsteady magnetization, and the remaining 120 vol per each session, 240 vol per each subject were used for analysis. The data were analyzed using statistical parametric mapping (SPM99, Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks, Sherborn, MA; Friston *et al.*, 1994, 1995a,b). Following realignment, all images were coregistered to the high-resolution, 3-dimensional, T2-weighted MRI, with use of the anatomical MRI with T2-weighted spin echo sequences from locations identical to those of the fMRI images. The parameters for affine and nonlinear transformation into a template of T2-weighted images that was already fit for a standard stereotaxic space (MNI template; Evans *et al.*, 1994) were estimated using the high-resolution, 3-dimensional, T2-weighted MRI using least squares means (Friston *et al.*, 1995b). The parameters were applied to the coregistered fMRI data. The anatomically normalized fMRI data were filtered using a Gaussian kernel of 10 mm (full-width at half-maximum) in the *x*, *y*, and *z* axes.

Statistical analysis. Statistical analysis was conducted at two levels. First, individual task-related activation was evaluated. Second, so that inferences could be made at a population level, individual data were summarized and incorporated into a random effect model (Friston *et al.*, 1999).

Individual analysis. The signal was proportionally scaled by setting the whole-brain mean value to 100 arbitrary units. The signal time-course of each subject, with 240 time points, was modeled with two box-car functions convolved with a hemodynamic response function, high-pass filtering (120 s), and session effect. To test hypotheses about regionally specific condition effects, the estimates for each condition were compared by means of linear contrasts of (1) discrimination task versus rest period and (2) nondiscrimination task versus rest period. The resulting set of voxel values for each comparison constituted a statistical parametric map (SPM) of the *t* statistic (SPM{*t*}). The SPM{*t*} was transformed to the unit normal distribution (SPM{*Z*}). The threshold for the SPM{*Z*} of individual analyses was set at $P < 0.05$ with a correction for multiple comparisons at the voxel level for the entire brain (Friston *et al.*, 1996).

To test for the dependency of V1 activation on age at onset of blindness, as suggested by Cohen *et al.*, (1999), the percentage of change in the MR signal (percentage signal change) measured in V1, relative to the global mean signal, was measured on a region-of-interest basis. In each subject's SPM{*Z*}, comparing discrimination task versus rest period, a spherical volume of interest with a diameter of 20 mm was placed with the center (0, −90, 0) based on Talairach's atlas. Within this sphere, we searched for a local maximum (increase) or local minimum (decrease) of signal change related to the tactile discrimination task compared with the rest condition. The statistical threshold was $P < 0.05$ corrected for multiple comparisons within the search volume (Friston, 1997). The percent signal change evoked during the tactile discrimination task compared with the rest condition relative to the global mean signal (=100) was calculated with the regressor (the box-car function for the discrimination session convolved with the hemodynamic input function) and the estimated parameters, and were plotted against age at onset of blindness (Fig. 2). Because the percent signal change reversed from positive to negative as the age at onset of blindness increased past 16 years of age, we categorized the 9 subjects who lost their sight before age 16 as "early-onset blind subjects" and the other 6 who lost their sight after age 16 as "late-onset blind subjects."

Group analysis with random effect model. The weighted sum of the parameter estimates in the individual analysis constituted "contrast" images, which were used for the group analysis (Friston *et al.*, 1999). The contrast images obtained by individual analysis represent the normalized task-related increment of the MR signal of each subject, that is, discrimination task versus rest period and nondiscrimination task versus rest period. To examine the effect of the tactile discrimination task by each group (early-onset blind, late-onset blind, and sighted) and the task × group interaction, the contrast images of the early-onset blind,

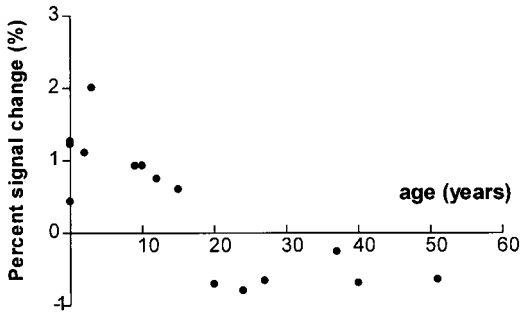


FIG. 2. Adjusted MR signal change recorded in V1 in 15 blind subjects plotted against the age at onset of blindness. V1 was more active during a tactile discrimination task in early-onset blind subjects (<16 years of age) but was less active in late-onset blind subjects (>16 years of age). For each subject, a spherical volume of interest, with a diameter of 20 mm and a center of (0, −90, 0), was selected based on the atlas of Talairach. The local maximum (increase) or local minimum (decrease) signal change related to tactile discrimination was measured in the volume within the sphere. The statistical threshold was $P < 0.05$, corrected for multiple comparisons within the spherical volume.

late-onset blind, and sighted groups were entered into a random effect model. Significant signal changes for each contrast were assessed by means of *t* statistics on a voxel-by-voxel basis (Friston *et al.*, 1995a). The resulting set of voxel values for each contrast constituted a statistical parametric map (SPM) of the *t* statistic (SPM{*t*}). The SPM{*t*} was transformed to the unit normal distribution (SPM{*Z*}). The threshold for the SPM{*Z*} was set at $Z > 3.09$ and $P < 0.05$ with a correction for multiple comparisons at the cluster level for the entire brain (Friston *et al.*, 1996).

RESULTS

Task Performance

Task performance (percentage correct response) of the early-onset blind group (80.7 ± 12.4%) was significantly better than that of the late-onset blind (57.8 ± 14.9%) and sighted (59.2 ± 12.6%) groups ($P = 0.0002$, one-way ANOVA).

Individual Analysis

Individual SPM{*z*} showed that during the discrimination task, compared with the rest period, V1 in early-onset blind subjects was activated, whereas it was inhibited in late-onset blind subjects (Fig. 2). The location of the local maximum (increase) in the early-onset blind group was $x = -2.2 \pm 5.6$ mm, $y = -91.8 \pm 6.4$ mm, and $z = -1.3 \pm 3.5$ mm ($n = 9$), overlapping with the local minimum (decrease) in the late-onset blind group, $x = 2.0 \pm 4.9$ mm, $y = -87.7 \pm 5.3$ mm, and $z = 2.1 \pm 2.0$ mm ($n = 6$). Task performance significantly positively correlated with the activity of V1 ($y = 21.2x + 68.3$, $r^2 = 0.3902$, $F_{1,13} = 8.319$, $P = 0.0128$; Fig. 3). Figure 4 shows representative examples from each group.

Group Analysis with the Random Effect Model

Tactile discrimination task. The bilateral inferior and superior parietal lobules, superior and inferior occipital gyri, fusiform gyri, cerebellum, and prefrontal areas; the left primary sensorimotor area and postcentral gyrus; and the right dorsal premotor area (PMd) and supplementary motor area (SMA) were activated in both early-onset and late-onset blind subjects (Fig. 5). In sighted subjects, the bilateral inferior and superior parietal lobules, postcentral gyri, and PMd; the left ventral premotor cortex, thalamus, and inferior prefrontal regions; and the right dorsolateral prefrontal area were active during the tactile discrimination task (Fig. 5). Activation of V1 during the tactile discrimination task was more prominent in early-onset than in late-onset blind or sighted subjects (Fig. 6). The bilateral dorsal to ventral visual cortices; and the left inferior frontal gyrus, postcentral gyrus, and superior parietal lobule were more active during the tactile discrimination task in blind subjects compared with sighted subjects, regardless of the age at onset of blindness (Table 2 and Fig. 7). The bilateral anterior parietal operculum and secondary somatosensory cortex (SII) were more active during the tactile discrimination task in sighted subjects compared with blind subjects (Table 2 and Fig. 7).

Tactile nondiscrimination task. The bilateral inferior frontal gyrus; the left primary sensorimotor area (extending anteriorly to the PMd and SMA and posteriorly to the postcentral gyrus and superior parietal lobule); and the right inferior and superior parietal lobule, PMd, and cerebellum were active in both early-onset and late-onset blind subjects during the tactile

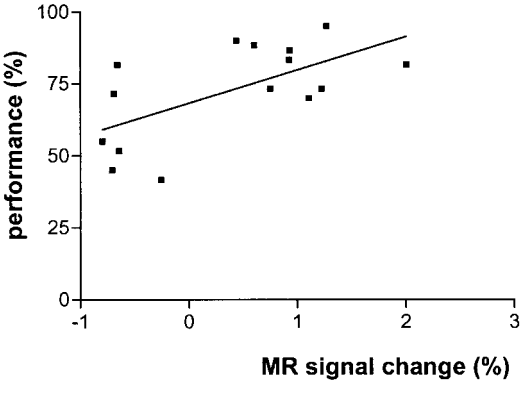
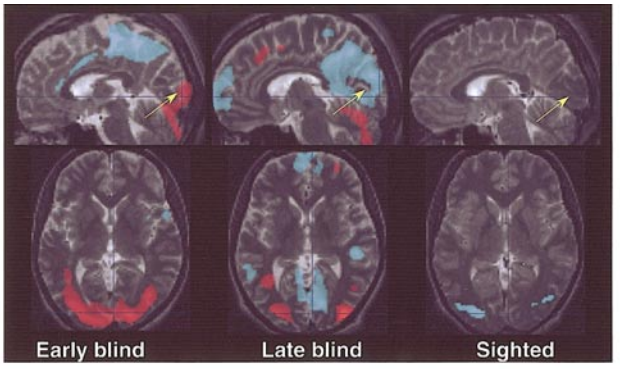


FIG. 3. Task performance (percentage correct) plotted against percent MR signal change in V1 during a tactile discrimination task. There was a significantly positive correlation between task performance and activity in V1 ($y = 21.2x + 68.3$, $r^2 = 0.3902$, $F_{1,13} = 8.319$, $P = 0.0128$).



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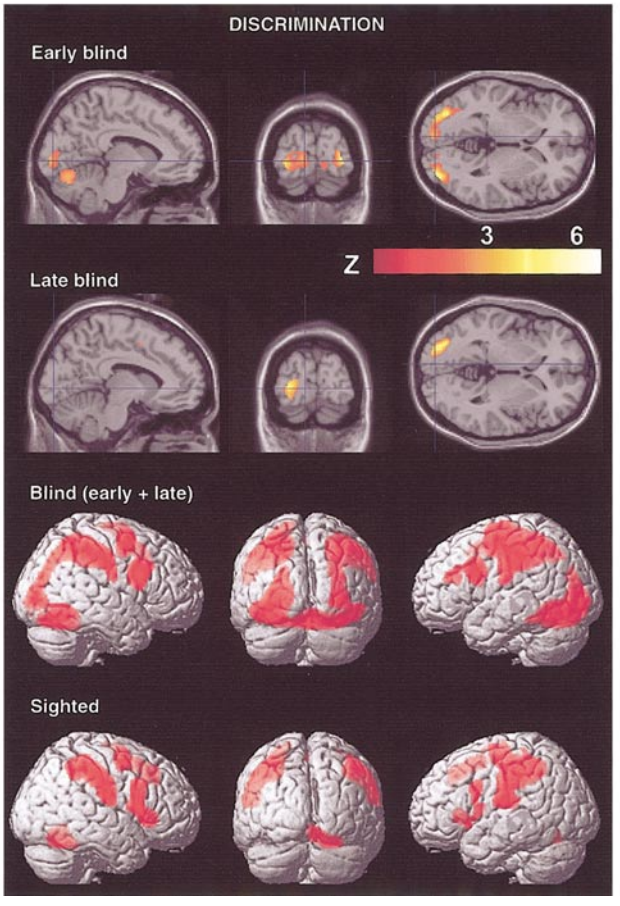

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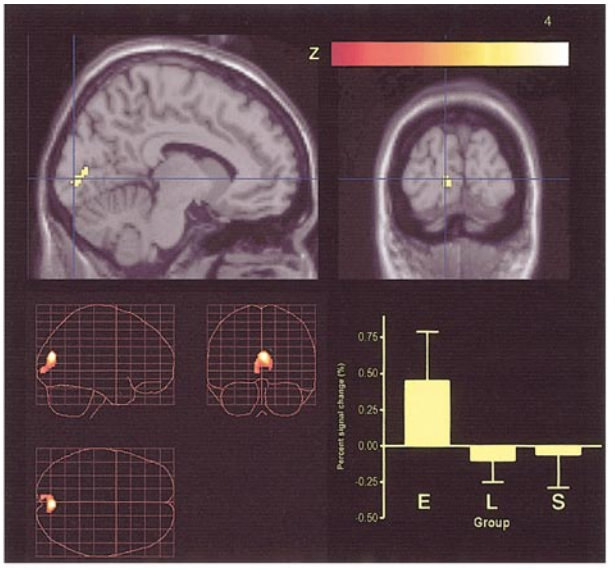

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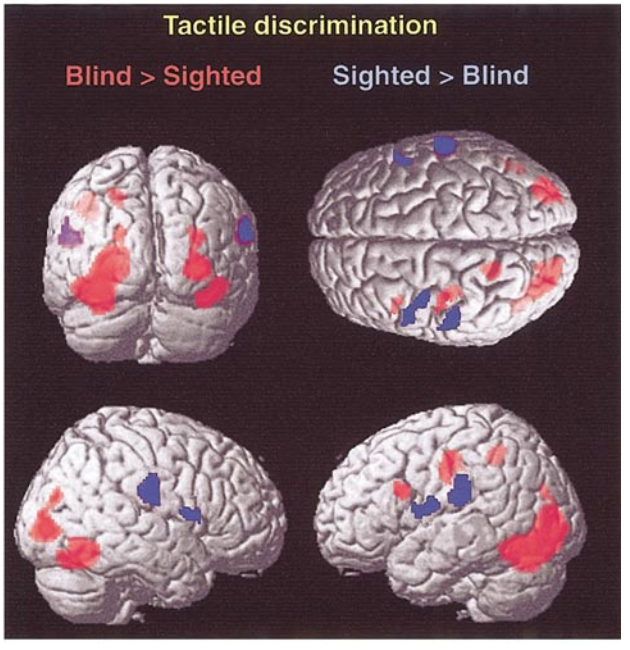

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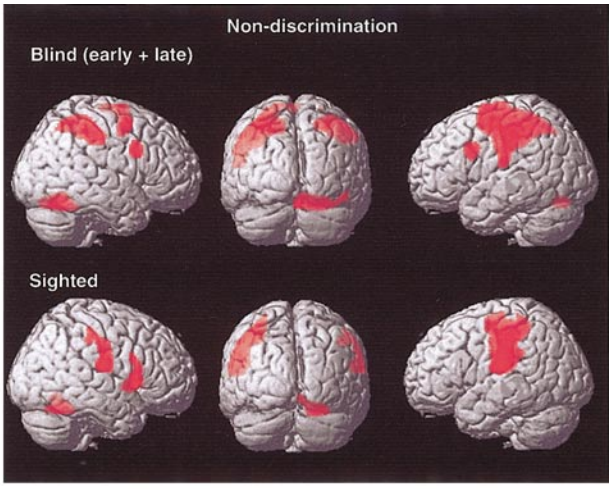
FIG. 4. Statistical parametric maps of individual analysis of neural activity in early-onset blind (left), late-onset blind (middle), and sighted (right) subjects during the Braille discrimination task compared with that during the rest period. A representative case is shown for each group. The task-related increase in MR signal (activation; shown in red) and the task-related decrease (inhibition; shown in light blue) were superimposed on sagittal (upper row) and transaxial sections of the T2-weighted high-resolution MRI of each individual. Only pixel areas that were significantly ($P < 0.05$) different between conditions, with a correction for multiple comparisons at the voxel level, are shown. fMRI data were normalized into the stereotaxic space. The blue lines indicate the projections of each section that cross in the center of V1. The Talairach coordinates are: $x = 4$ mm, $y = -90$, and $z = 0$. The yellow arrows indicate the calcarine fissure.

FIG. 5. Statistical parametric maps of average neural activity within each group during the Braille discrimination task compared with that during the rest period. In early-onset blind (top) and late-onset blind (second row) subjects, task-related increases in MR signal (activation) were superimposed on three orthogonal sections of T1-weighted high-resolution MRIs unrelated to the subjects of the present study. fMRI data were normalized into the stereotaxic space. The blue lines indicate the projections of each section that cross in the center of V1. The Talairach coordinates are: $x = -8$ mm, $y = -90$, and $z = 0$. Z score is as indicated by the color bar; statistical significance increasing as red proceeds to white. Statistical parametric maps of average neural activity combining early-onset and late-onset blind subjects (third row) and that of sighted subjects (bottom) were superimposed on surface-rendered, high-resolution MRIs unrelated to the subjects of the present study. The statistical threshold was $P < 0.05$ with a correction for multiple comparisons at the cluster level.

FIG. 6. There was more prominent activation in early-onset than in late-onset blind subjects during the tactile discrimination task. Upper row, focus of activation in pseudocolor functional MRIs superimposed on high-resolution anatomical MRIs in sagittal and coronal planes, as indicated by the blue lines that cross at (−8, −92, 2). The statistical threshold was $P < 0.05$, corrected for multiple comparisons at the cluster level. Z score is as indicated by the color bar; statistical significance increasing as red proceeds to white. Lower left, statistical parametric maps are shown in standard anatomical space. The 3-dimensional information was collapsed into 2-dimensional sagittal, coronal, and transverse images (i.e., maximum intensity projections viewed from the right, back, and top of the brain). Lower right, the percent signal change in V1 (−8, −92, 2) in early-onset blind (E), late-onset blind (L), and sighted (S) groups. In this group analysis, the increase in signal change was smaller than that in the individual analysis of local maximum and local minimum foci (see Fig. 2).



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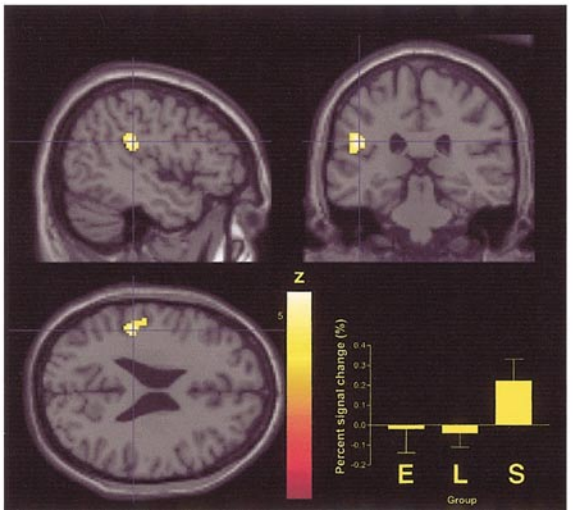

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FIG. 8. Statistical parametric maps of average neural activity within each group during the nondiscrimination task compared with that during the rest period. A combined statistical parametric map of all blind subjects (top) and one of all sighted subjects (bottom) were superimposed on surface rendered high-resolution MRIs unrelated to the subjects of the present study viewed from the right, back, and left. The statistical threshold was $P < 0.05$ with a correction for multiple comparisons at the cluster level.

FIG. 9. There was more prominent activation in SII in sighted subjects than in early-onset or late-onset blind subjects during the tactile nondiscrimination task. Focus of activation on a pseudocolor functional MRI superimposed on a high-resolution anatomical MRI in the sagittal (upper left), coronal (upper right), and transaxial (lower left) planes, as indicated by the blue lines that cross at (−46, −30, 24) corresponding to SII. Activity level is as indicated by the color bar; activity increasing as red proceeds to white. The statistical threshold was $P < 0.05$, corrected for multiple comparisons at the cluster level. Lower right, the percent signal change in the SII (−46, −30, 24) in early-onset blind (E), late-onset blind (L), and sighted (S) groups.

nondiscrimination task. The bilateral postcentral gyrus and SII; the left SM1; and the right inferior frontal gyrus and cerebellum were active in sighted subjects during the tactile nondiscrimination task (Fig. 8).

The left SII of sighted subjects was more prominently active during the nondiscrimination task compared with blind subjects (Table 2, Fig. 9).

DISCUSSION

The results of the present study using fMRI show that there is a critical period from birth to approximately 16 years of age for reorganization of the V1 to function during tactile discrimination tasks. People who lost their sight before age 16 years exhibited increased activity in the V1 during a tactile discrimination task. In contrast, people who lost their sight after age 16 years and sighted controls exhibited decreased activity in the visual cortex during the same tactile task.

Task Design

Previous studies (Sadato *et al.*, 1996, 1998; Cohen *et al.*, 1999) utilized tactile discrimination tasks that involve active exploration, which include inherent variability that cannot be completely controlled for using subtraction paradigms (Sadato *et al.*, 2000). It is difficult, therefore, to determine whether the task-related activity measured during these tasks is sensory or motor, or both (Kujala *et al.*, 2000), especially because enhanced movement-related potentials have been observed in blind subjects, compared with sighted subjects (Lehtokoski *et al.*, 1998). To exclude the effect of motor control, the present study eliminated active finger movement for both the discrimination and nondiscrimination tasks. The results of the present study are consistent with those of previous studies that utilized active exploratory tasks (Sadato *et al.*, 1996, 1998; Cohen *et al.*, 1999), confirming that posterior activation in blind subjects is due to sensory rather than motor processes.

Performance Differences

Performance on the Braille tactile discrimination task was significantly better in the early-onset than in the late-onset blind and sighted groups. Performance of the last two groups did not differ significantly. Because performance of the discrimination task involving exploratory movement is experience dependent (Heller, 1989), the elimination of the exploratory move-

FIG. 7. Areas more prominently activated during the tactile discrimination task in all blind subjects compared with sighted subjects (red) and in sighted subjects compared with blind subjects (blue). The areas are superimposed on surface-rendered high-resolution MRIs viewed from the back, top, right, and left. All blind subjects exhibited activation of the bilateral occipital cortex (middle and inferior occipital gyri and fugiform gyrus), left inferior frontal gyrus, postcentral gyrus, and superior parietal lobule, more prominent than sighted subjects. The SII and parietal operculum was suppressed bilaterally in blind subjects. Statistical threshold is $P < 0.05$, corrected for multiple comparisons at cluster level, $Z > 3.09$.

TABLE 2

Cortical Areas Differentially Activated during a Passive Tactile Discrimination Task and a Nondiscrimination Task in Blind (Both Early-Onset and Late-Onset, $n = 15$) Subjects and Sighted ($n = 8$) Subjects

Cluster level		Voxel level						Location	
P	size	*P*	*t*	*Z*	*x* (mm)	*y* (mm)	*z* (mm)	Side	Area
				Tactile discrimination: Blind > Sighted					
<0.001	323	<0.001	8.92	5.68	32	−88	2	R	GOm (19)
<0.001	1761	0.002	6.92	4.94	−34	−78	−4	L	GOi (18)
		0.005	6.41	4.72	−42	−64	−16	L	GF (37)
<0.001	384	0.006	6.31	4.67	48	−60	−14	R	GF (37)
0.002	95	0.034	5.4	4.23	−46	14	24	L	GFi (44)
<0.001	261	0.043	5.27	4.16	−44	−18	32	L	GPoC
0.003	89	0.135	4.64	3.81	−20	−46	48	L	LPs (7)
				Tactile discrimination: Sighted < Blind					
<0.001	184	0.004	6.14	4.59	64	−16	30	R	SII
<0.001	94	0.009	5.70	4.38	−42	−4	18	L	Parietal operculum
0.002	49	0.020	5.29	4.17	52	6	10	R	Parietal operculum
<0.001	128	0.028	5.11	4.07	−58	−22	28	L	SII
				Tactile nondiscrimination: Blind < Sighted					
0.026	250	0.18	5.40	4.19	−46	−30	24	L	SII

Note. Abbreviations: GF, fusiform gyrus; GFi, inferior frontal gyrus; GOi, inferior occipital gyrus; GOm, middle occipital gyrus; GPoC, postcentral gyrus; GTi, inferior temporal gyrus; LPs, superior parietal lobule; SII, secondary somatosensory cortex. Numbers in parentheses are Brodmann's areas. All *P* values are corrected for multiple comparisons. Height threshold, $Z = 3.09$, $P = 0.001$. L, left; R, right.

ment aspect in the present study makes it likely that performance differences are related to the perceptual component. The absence of performance differences in sighted and late-onset blind subjects is consistent with a recent study showing that early-onset (<5 years old) but not late-onset (>5 years old) blind Braille readers can detect a significantly finer offset in the alignment of a row of three embossed dots, compared with sighted subjects (Grant *et al.*, 2000). This result illustrates the impact of the age that visual deprivation begins and its relation to a critical period for tactual acuity, at least for discrimination of passively presented Braille characters.

Age Dependency of V1 Activation

The results of the present study support the idea that involvement of V1 during tactile discrimination depends on the age at onset of visual deprivation. The MRI signal increased in early-onset blind subjects and decreased in late-onset blind subjects, reversing at approximately 16 years of age, which is consistent with results of TMS and PET studies (Cohen *et al.*, 1999). Although task performance was positively correlated to the activity of V1, two late blind subjects who showed equivalent performance to the early blind did reveal negative response in the V1. And hence the divergent findings of V1 are difficult to be explained by performance alone. Evidence of the functional relevance of the visual cortex, including the V1, to tactile discrimination in early-onset blind subjects was first shown using TMS (Cohen *et al.*, 1997), and later confirmed by a case report of infarction of the occipital artery area (Hamilton *et al.*, 2000). Taken together, it is concluded that the V1 of early-onset blind subjects is functionally relevant.

There is a previous report that a Braille reading task activated both striate and extrastriate visual cortex in late-onset blind subjects, but only the extrastriate visual cortex in congenitally blind subjects (Büchel *et al.*, 1998). The authors speculated that activation of V1 in late-onset blind subjects may be due to visual imagery in subjects with early visual experience. These seemingly contradictory results have at least two possible explanations. First, there may be a difference in the control conditions used in the studies. In the present study, we utilized a rest period as a control, rather than an auditory discrimination task, as used in their study, because there is evidence that auditory stimuli activates visual areas in blind subjects. Roder *et al.* (1999) found that blind subjects showed sound localization abilities that were superior to those of sighted controls at far lateral locations. Electrophysiological recordings obtained at the same time suggested posterior shift of the early spatial attention mechanisms in the blind subjects. Results from a study using magnetoencephalography, showed that the visual association

cortices of early-onset blind subjects are activated during auditory discrimination tasks (Kujala *et al.*, 1995), indicating that these subjects exhibit auditory-to-visual cross-modal plasticity (i.e., the occipital association areas, generally involved in dorsal-stream visual processing, are active during auditory localization tasks). This cross-modal plasticity appears to be independent of the age at onset of blindness, because recordings of event-related-potentials also indicate that posterior brain areas are involved in active sound-change detection in both early-onset and late-onset blind subjects (Kujala *et al.*, 1997). In totally blind subjects, auditory stimulation activates the occipital area, which suggests that deafferented posterior visual areas are recruited to carry out auditory functions (Leclerc *et al.*, 2000). Finally, a PET study showed that the occipital cortex is involved during sound localization tasks in congenitally blind subjects (Weeks *et al.*, 2000). Taken together, these results indicate that V1 in early-onset blind subjects (Büchel *et al.*, 1998) may be active during both tactile tasks and auditory tasks, but in different ways, so if auditory-related activity is subtracted from activity evoked during a Braille tactile task, the results may be skewed. In the present study, on the other hand, the rail moved quietly without any task-related auditory stimulation. And hence the results clearly indicate the effect of tactile shape discrimination alone: V1 was active during the tactile discrimination task only in early-onset blind subjects, not in late-onset blind subjects.

The second explanation of the seemingly contradictory findings is related to the characteristics of the tactile task condition. Heller (1989) studied the contribution of visual experience to tactile perception in congenitally blind, late-onset blind, and sighted subjects. Late-onset blind subjects were far better than the congenitally blind or sighted subjects at tactile picture identification. The author concluded that the superiority of late-onset blind subjects is due to visual exposure to drawings and the rules of pictorial representation, which may be helpful in tactile picture identification when combined with tactual experience. Performance in tactile matching accuracy was similar for sighted subjects and both groups of blind subjects, however, indicating that visual experience is clearly not necessary for efficient tactile form perception (Heller, 1989). This is consistent with the findings of the present study, as it utilized a sort of tactual form matching task in which performance of late-onset blind subjects was not better than that of early-onset blind subjects, and V1 was not activated. Büchel *et al.* (1998), however, utilized Braille word reading, which may induce recall of visual features of the objects indicated by the words, which in turn may activate V1 in late-onset blind subjects. We conclude that the difference between the results of the present study and those of Büchel *et al.* (1998) is due to differences in task and control conditions.

Different Neural Activity Recorded from Blind and Sighted Subjects during Tactile Discrimination

Parietal cortex. Compared with sighted subjects, blind subjects, irrespective of age at onset of blindness, exhibited more prominent activation of the left postcentral gyrus, bilateral posterior parietal cortex, and association visual cortices during the tactile discrimination task. The sighted subjects, however, exhibited more prominent activation of the bilateral SII.

The most prominent activation of the left postcentral gyrus in the present study was close to the postcentral sulcus presumably corresponding to Brodmann's area (BA) 2. In macaque monkeys, lesions of BA 1 affected only texture discrimination, and of BA 2, only size or shape tasks, but removal of BA 3b, severely affected all tasks (Randolph and Semmes, 1974; Carlson, 1981). As sensory information is transferred from S1 to BA 5, transformation of that information begins in BA 1 and BA 2 (Pearson and Powell, 1985; Shanks *et al.*, 1985).

The superior parietal lobule (LPs) is designated as BA 7, and area 7 of macaque monkeys is said to be homologous to BA 7 of humans (Haxby *et al.*, 1991). Neuronal populations in the LPs posterior to the postcentral sulcus in monkeys are responsive to somaesthetic stimuli from both the skin and joints (Sakata *et al.*, 1973; Hyvärinen and Poranen, 1974; Mountcastle *et al.*, 1975; Robinson and Burton, 1980). Neurons in this cortical area encode the kinematics (e.g., position, direction, and displacement) of the upper limbs (Kalaska *et al.*, 1990). In an activation study using PET, a passive tactile stimulus on the right fingertip activated the left LPs (Burton *et al.*, 1997).

Another PET study (Roland *et al.*, 1998) showed that somatosensory perception of form (length and shape) is related to activation of the anterior part of the intraparietal sulcus, and that perception of roughness is related to activation of the SII, which suggests the existence of separate neuronal circuitry for processing the different somatosensory submodalities of microgeometry and macrogeometry. Other neuroimaging studies showed that the contralateral postcentral gyrus, LPs, and the cortex lining the anterior part of the intraparietal sulcus were activated specifically during haptic processing of shape and length of objects (Roland and Larsen, 1976; Seitz *et al.*, 1991; O'Sullivan *et al.*, 1994; Hadjikhani and Roland, 1998) or during non-Braille tactile shape discrimination (Sadato *et al.*, 1998, 2000). The fact that there was more prominent activation of the postcentral gyrus to posterior parietal cortex and less activation of the SII in blind subjects than in sighted subjects in the present study, suggests that there is greater demand for shape discrimination processing in blind subjects.

Occipital cortex. The results of the present study confirmed that the visual association cortex is involved in tactile discrimination in blind subjects irrespective of the age at onset of visual deprivation. This observation suggests that the dynamics of the reorganization of brain functions due to visual deprivation may be mediated by the visual association cortex. Maunsell *et al.* (1991) have reported that in V4, a visual area, neuronal activity can be affected by haptic information of orientation utilized to perform a visual orientation-matching task. They suggested that the information encoded in neuronal activity represents general orientation regardless of the sensory modality through which the information arrives. Human neuroimaging studies combined with TMS also support the idea that the visual association cortex is affected by nonvisual sensory information. Disrupting function of the occipital cortex in sighted subjects by means of focal TMS interferes with tactile discrimination of grating orientation (Zangaladze *et al.*, 1999). The activated area is located in the extrastriate cortex near the parieto-occipital sulcus. The authors speculated that involvement of the visual cortex may be beneficial in the discrimination of macrogeometric features such as orientation and shape, because processing of orientation and shape discrimination generally involves vision. Performance of a tactile object recognition task by sighted subjects may involve a network of cortical regions subserving somatosensory, motor, visual, and, at times, lexical processing (Deibert *et al.*, 1999). The authors stressed that the visual cortices may be involved in topographic spatial processing of tactile object recognition. Amedi *et al.* (2001) found that both tactile and visual object recognition tasks activated the ventral visual pathway. They speculated that this bimodal activation in the occipitotemporal regions reflects stored object-related visual information that can be accessed via cues from the somatosensory modality. This is consistent with the present finding that there was no occipital activation in sighted subjects because the task was tactile discrimination without object recognition, which primarily relies on vision (Amedi *et al.*, 2001).

Involvement of the visual association cortex during performance of tactile tasks by blind subjects is consistent with the concept of amodal processing of spatial information (Heller, 1989). The present study included subjects with a relatively large variety of visual disturbances. All but one blind subject had lost pattern vision. Several others had defective light or motion perception, or both. One subject with pigmentary degeneration of the retina had digit (finger) number perception at a distance of 1 m. Nevertheless, activation of the visual association cortex during the tactile discrimination task was consistently observed in all blind subjects. This finding suggests that light perception specifically may not be critical for the activation, but a decline in the higher processing of vision is. Furthermore, involvement of the visual association cortex is more prominent during the discrimination task than during the nondiscrimination task. This indicates that cross-modal recruitment of the visual cortex is enhanced by the discrimination process. Thus, the visual association cortex may be related to the shape discrimination process in a modality-independent manner.

Involvement of V1. In the present study, tactual activation of V1 depended on age at onset of blindness, but activation of the visual association cortex did not. Thus, V1 is unlikely to be the "entry node" of the cortex for tactile signals redirected into visual cortices after visual deprivation.

V1 is a topographically organized low-level cortex (i.e., early in the visual processing sequence) that receives high resolution information during bottom-up perception, enabling effective edge-detection and region-organizing processes (Felleman and Van Essen, 1991). A visual imagery task that requires one to visualize patterns that depict information such as length, width, orientation, and the amount of space between bars, activated V1 in a functionally relevant way (Kosslyn *et al.*, 1999). This finding suggests that stored information can evoke visual patterns in relatively low-level visual areas during imagery, promoting shape processing. Because the majority of visual areas in the macaque monkey have reciprocal connections to other visual areas, receiving information from the areas to which they send information (Felleman and Van Essen, 1991), it is possible that the top-down processing during visual imagery is mediated by the visual association cortex.

Considering that both tactile and visual processes are represented in the visual association cortex, visual and tactile processing may be competitively balanced in the association cortices where the inputs adjoin (Rauschecker, 1995). Therefore, visual deafferentation causes less demand on the bottom-up processing of vision, which may in turn introduce opportunity for expansion of the tactile representation in the visual association cortex.

Taken together, the results of the present study may be interpreted as follows. In blind subjects, whose bottom-up visual processing is interrupted, tactile shape discrimination processing expands into the visual association cortex. In early-onset, but not late-onset blind subjects, V1 is also recruited in a functionally relevant way, as in top-down processing during visual imagery, resulting in better performance on shape discrimination in early-onset blind subjects.

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