

Cortical activity during tactile exploration of objects in blind and sighted humans

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Abstract. *Purpose:* Recent studies show evidence of multisensory representation in the functionally normal visual cortex, but this idea remains controversial. Occipital cortex activation is often claimed to be a reflection of mental visual imagery processes triggered by other modalities. However, if the occipital cortex is genuinely active during touch, this might be the basis for the massive cross-modal plasticity observed in the congenitally blind.

Methods: To address these issues, we used fMRI to compare patterns of activation evoked by a tactile object recognition (TOR) task (right or left hand) in 8 sighted and 8 congenitally blind subjects, with several other control tasks.

Results: TOR robustly activated object selective regions in the lateral occipital complex (LOC/LOtv) in the blind (similar to the patterns of activation found in the sighted), indicating that object identification per se (i.e. in the absence of visual imagery) is sufficient to evoke responses in the LOC/LOtv. Importantly, there was negligible occipital activation for hand movements (imitating object palpations) in the occipital cortex, in both groups. Moreover, in both groups, TOR activation in the LOC/LOtv was bilateral, regardless of the palpating hand (similar to the lack of strong visual field preference in the LOC/LOtv for viewed objects). Finally, the most prominent enhancement in TOR activation in the congenitally blind (compared to their sighted peers) was found in the posterior occipital cortex.

Conclusions: These findings suggest that visual imagery is not an obligatory condition for object activation in visual cortex. It also demonstrates the massive plasticity in visual cortex of the blind for tactile object recognition that involves both the ventral and dorsal occipital areas, probably to support the high demand for this function in the blind.

Keywords: Crossmodal plasticity, multisensory processing, neuroimaging, tactile object recognition, visual imagery

1. Introduction

We experience our environment through several sensory modalities at the same time. The information provided by these sensory systems is synthesized in our brains to create a coherent and unified experience of

perception (Stein and Meredith 1993). The multisensory nature of our perceptions has several behavioral advantages including more rapid response and improved recognition in noisy environments (i.e. a low signal to noise ratio).

In recent years, the advent of non-invasive functional neuro-imaging techniques has made it possible to investigate the neural basis of cross-modal processes (such as the judgment of the geometric dimensions of an object, (Hadjikhani and Roland 1998) in humans. For instance, several groups ((Amedi et al., 2001; Amedi et al., 2002; James et al., 2002; Zhang et al. 2004; Beauchamp 2005; Macaluso 2006; Lacey et al., 2007),

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for a review see (Lacey et al., 2009)) have found evidence for visuo-tactile convergence of object-related information in the LOTv, (Amedi et al., 2001; Amedi et al., 2002), a sub-region within the human lateral occipital complex (LOC, (Malach et al., 1995)). The defining features of this region are that it is robustly activated during both visual and tactile object recognition; it shows a preference for objects compared to scrambled objects (or textures) in both modalities, and it is not activated by accompanying motor or naming aspects of a object recognition task. Pietrini and colleagues (Pietrini et al., 2004) further demonstrated that a similar category specific pattern of activation can be seen in the occipito-temporal cortex when the objects are recognized by either vision or by touch. For example, regions showing greater fMRI activation when viewing faces than when viewing shoes showed the same preference when the objects were recognized only by touch. This suggests that a common representation of 3D objects is activated by both modalities.

Nevertheless, one of the major issues still under debate is to what extent this activation is the result of evoked visual imagery rather than the processing of tactile input per se (Zhang et al., 2004; Sathian 2005). While we have previously shown that visual imagery of objects activates LOTv significantly less than palpating the same objects (Amedi et al., 2001), it might still be argued that the visual imagery of an object is inherently more effective when palpating an object than when a participant is requested to imagine it without sensory aid. In fact, a recent study (Zhang et al., 2004) reported a correlation between the degree of tactile object activation in the right LOTv and visual imagery abilities in the sighted (using the vividness of visual imagery questionnaire).

One way to circumvent the effects of visual imagery is to investigate the pattern of responses evoked by tactile object recognition in the congenitally blind. Since congenitally blind people have never had any visual experience, they probably lack the capability for *visual* imagery. If one can observe occipito-temporal activation in the congenitally blind similar to that found in sighted peers, this would strongly indicate that the visual cortex has the built-in machinery to process *tactile* objects per se, or at least that visual imagery is not necessary to create tactile responses in ventral visual areas (but see also discussion).

The issue of plasticity of tactile object recognition in the posterior occipital, early ("retinotopic" in sighted) areas in congenitally blind subjects has been studied extensively with Braille-like stimuli (Sadato et al.

1996; Cohen et al., 1997; Hamilton and Pascual-Leone 1998; Burton et al., 2002; Sadato et al., 2002; Amedi et al., 2003; Burton 2003) or other simple tactile stimuli (e.g. flutter vibration in (Burton et al., 2004)), but to a very limited extent using natural objects (Pietrini et al., 2004). Braille and Braille-like stimuli are fundamentally different from natural objects, and it might well be that the neural structures that support them are different to some extent.

Another advantage of the use of tactile object recognition is that unlike Braille reading, both blind and sighted subjects can perform the task, and do it well with either hand. This allows us to compare the activation evoked by tactile processing within and between the two groups and to assess the degree to which tactile responses in the occipital cortex are specific to the contralateral hand exploring the objects, another topic that has been neglected in research on both sighted and blind human subjects. Typically, early sensory areas show a clear contralateral preference while higher areas have much more bilateral responses. Specifically, V1 is activated almost exclusively by a visual stimulus in the contralateral visual field while this bias is much more subtle in LOC. Would a similar pattern of bilateral activation be observed in LOC for tactile objects when using the right or the left hand? Would this pattern be similar in blind and sighted subjects?

To date, no study has addressed lateralization in the LOC for *tactile* objects, while only one study (Pietrini et al., 2004) has examined tactile object recognition of natural objects in both congenitally blind and sighted subjects. This study was pioneering in showing visual cortex activity in the blind during natural tactile object recognition. However, the minimal number of early blind subjects ($n = 2$) in that study did not allow for a quantitative comparison of the level of activation in regions of interest between the two groups, or a detailed anatomical comparison between the activation patterns among the groups or within and between group comparisons that could be generalized to the population level. In addition, as no mapping of visual areas (combined with surface reconstruction) was conducted, it is difficult to assess precisely which putative visual areas were specifically recruited in the blind. This issue was studied extensively with Braille stimuli of words, letters and different symbols and patterns (Sadato et al., 1996; Cohen et al., 1997; Hamilton and Pascual-Leone 1998; Burton et al., 2002; Sadato et al., 2002; Amedi et al., 2003; Burton, 2003; Burton et al., 2004) but not using natural objects (e.g. tools). The activation pattern for natural three-dimensional objects might be different from the essentially two dimensional Braille pattern.

Table 1
Characteristics of the blind subjects

Subject	Age and sex	Cause of blindness	Light perception	Handedness	Preferred hand for Braille reading	Braille reading since (age)
# 1	20 F	Microphthalmia	None (prosthesis)	Right	Right	5
# 2	45 M	Retinopathy of prematurity	None	Right	Right	7
# 3	51 F	Leber's congenital amaurosis	None	Right	Right	6
# 4	32 M	Retinopathy of prematurity	Faint	Right	Right	6
# 5	30 F	Rubella	None	Right	Left	6
# 6	31 M	Retinopathy of prematurity	None	Right	Left	6
# 7	28 M	Retinopathy of prematurity	None (prosthesis)	Right	Left	6
# 8	19 F	Retinopathy of prematurity	None	Right	Left	5

To examine these questions, we studied a group of 8 congenitally blind (without any light perception) participants and a matched group of 8 sighted subjects, both performing the same tactile object recognition without any visual guidance. This experimental setting, combined with the use of full cortical 3D reconstruction and unfolding techniques, allowed for a relatively reliable comparison within and between the two groups.

2. Materials and methods

2.1. Subjects

8 blind and 8 sighted native Hebrew speakers participated in the experiment. The Tel-Aviv Sourasky Medical Center Ethics Committee approved the experimental procedure. Written informed consent was obtained from each subject. An expert ophthalmologist examined the blind subjects to assess the cause of blindness and tested for the presence of any light perception. All 8 subjects were congenitally blind, had major retinal damage, and their blindness was not due to a progressive neurological disease. Seven of the subjects did not have any form of light perception (See Table 1). The last subject (#4) could only report the presence of a strong light, but could not localize it or recognize any pattern. Handedness of subjects was assessed using the adapted version of the Edinburgh test. Both blind (mean = 73.12; SD = 13.94) and sighted (mean = 84.37; SD = 11.18) subjects were right handed. Sighted controls were 4 women and 4 men, matched for age, gender and handedness. Sighted subjects were blindfolded throughout the scan.

2.2. MRI acquisition

The BOLD fMRI measurements were performed in a whole-body 1.5-T, Signa Horizon, LX8.25 General Electric scanner. The functional MRI protocols were based on multi-slice gradient echo-planar imaging using a standard head coil. The functional data were obtained under the optimal timing parameters: TR = 3 sec, TE = 55 ms, flip angle = 90°, imaging matrix = 80 × 80, FOV = 24 cm. The 17 slices with a slice thickness of 4 mm and a 1 mm gap were oriented in the axial or oblique position, for optimal coverage of the occipital cortex. The scan covered the whole brain except the most dorsal tip and/or the most ventral tip of the brain (depending on the brain size of each individual, location and angle of the slices).

2.3. Experimental setup

During the entire experiment the subjects had both of their hands on a custom made table, and kept their hands still during the non-tactile conditions, palpating the objects with the instructed hand in the tactile conditions and moving the right hand in the air during the motor control.

2.4. Stimuli and experimental paradigms

Five different experimental conditions were used in a block design paradigm. These were: tactile object recognition (TOR) with either the right or the left hand (rTOR and lTOR, respectively); a sensory-motor control with the right hand only (SMC); a verbal memory task of the object's names (VM); and a rest baseline period. All epochs lasted 12 seconds followed by 9 seconds of rest period. Each epoch was repeated five

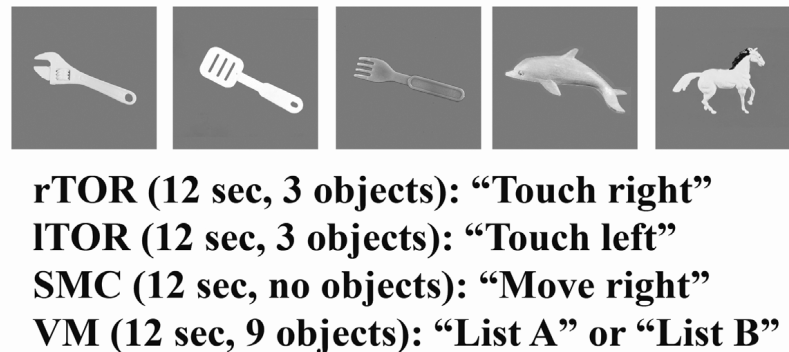


Fig. 1. Experimental design. Five different experimental conditions were used in a block design paradigm. These were: tactile object recognition (TOR) with the right or the left hand (rTOR and lTOR, respectively), a sensory-motor control using the right hand (SMC), a verbal memory task (VM), and a rest baseline period. All epochs lasted 12 seconds followed by 9 seconds of rest period. Each epoch was repeated five times using different stimuli (exemplars are depicted in the figure). A short (~ 1 sec) auditory instruction was given before the beginning of each epoch (the exact instruction is reproduced in the figure).

times using different stimuli. A short (~ 1 sec) auditory instruction was given before the beginning and at the end of all epochs. For TOR we used a set of 30 objects, 15 for rTOR and 15 for lTOR. The objects were 3D solid objects in a convenient size to grasp with one hand (Fig. 1). The touched objects were presented to the subjects by the experimenter every 4 seconds to the right or left hand (depending on the condition). The subjects were required to covertly name the objects. The subjects received a short auditory cue (lasting ~ 1 sec) at the beginning and the end of each tactile object recognition block to make sure they only touched the objects during the blocks and with the appropriate hand. Scans started only when all subjects could recognize at least 87.5% of the objects by touch in the scanner (tested inside the scanner before and after data acquisition but not during the acquisition itself). In the sensory-motor (SMC) task the subjects made hand movements using their right hand, imitating the grasping and exploration of objects. Unlike our previous studies on sighted subjects (Amedi et al., 2001; Amedi et al. 2002), we did not use tactile textures as the corresponding control stimuli (to tactile objects), as our pilot neuroimaging results showed that tactile textures generate a very different profile of activation in the blind compared to the sighted. The SMC however yielded a relatively similar pattern of activation (e.g. See Fig. 3b). Since our main focus was to compare the magnitude of activation to object palpation at different levels (blind versus sighted; left hemisphere versus right, left hand versus right hand etc.), a tactile texture condition did not seem relevant to the questions we defined. On the other hand, including a motor imitation condition (SMC) enabled us to test the potential role of motor hand movement in

the fMRI activation of occipital cortex in the blind. We also had a verbal memory condition (VM), in which subjects had to recall words from one of two lists that were learned in advance (one week before the scan). Each list contained nine words. The words in the list were of objects, a subset of the same objects that the subjects needed to recognize by touch in the TOR conditions. Before scanning, we verified that all subjects (blind and sighted) could recall inside the magnet at least eight out of the nine words from each list during the epoch period. This condition also served as a control for object naming. Finally, in the rest condition, subjects placed both hands on the table and were requested to wait without hand movement until the next instruction.

2.5. Data analysis

Data analysis was performed using the Brain Voyager QX 1.10 software package (Brain Innovation, Maastricht, the Netherlands). Before statistical analysis, head motion correction, linear trend removal and a standard high pass temporal filtering of 3 cycles per experiment scan time were performed. To better align data across subjects within and between groups we also used standard spatial smoothing of the data (using a Gaussian kernel of 8.0 mm FWHM). A general linear model (GLM; (Friston et al., 1995)) was used to generate statistical parametric maps. Across – subject statistical parametric maps were calculated using hierarchical random – effects model (RFX) analysis (Friston et al., 1999) and RFX 2 way ANOVA (see below). This was done after the voxel activation time courses of all subjects were transformed into Talairach space

(Talairach and Tournoux 1988), Z – normalized and concatenated. We used a statistical threshold criterion of $p < 0.05$ corrected for multiple comparisons using a cluster-size threshold adjustment, based on a Monte Carlo simulation approach extended to 3D data sets using the threshold size plug-in BrainVoyager QX ((Forman et al., 1995); for more details on implementation see (Amedi et al., 2005; Amedi et al., 2007)). This cluster threshold estimator takes input regarding the functional voxel size (3 mm^3 for 3D BrainVoyager QX data), the total number of significant voxels within a map, and the estimated smoothness of a map and runs Monte Carlo simulations (1,000 iterations) to estimate the probability of clusters of a given size arising purely by chance. Because the minimum cluster size for a corrected P value (0.05) is estimated separately for each map, the cluster sizes can differ for different comparisons.

The retinotopic borders displayed on the Talairach normalized brain of the blind were estimated using the rotating wedge technique (Engel et al., 1997), on one of the sighted subjects. The Talairach normalized volumetric time course of activation of a sighted subject was superimposed on a blind subject's Talairach normalized brain. Then the approximate retinotopic borders were assessed using the phase information (see also (Amedi et al., 2003)).

The average percent signal change and the averaged activation time course of individual subjects was obtained, pooling across all statistically significant clusters using a fixed model GLM approach corrected for multiple comparisons as described above or for the peak voxel in a smoothed volume (after applying spatial smoothing with a Gaussian kernel of 8 mm Full Width Half Maximum) in each region of interest. Then, the average time course of a given ROI was calculated by averaging the time course across all subjects. The left and right LOC/LOtv ROIs were defined according to a specific localizer mapping (see results for the various contrasts used to double check the pattern of activation in this ROIs). Significant cluster selection in the left and right S1/M1 ROIs was based on anatomical markers (i.e. for the peak significant voxel falling within any bank of the central sulcus).

The statistical analysis of variance (ANOVA) of the BOLD signal within and across groups was based on the application of multiple regression analysis to time series of task-related functional activation (Friston et al., 1995). We used a 2-way factorial random effect analysis of variance (RFX-ANOVA). Factors (or levels) were group (blind, sighted) and condition type (rTOR,

SMC) as implemented in the respective Brainvoyager QX tool. Activation maps are presented for each corresponding contrast on a full Talairach – normalized (Talairach and Tournoux 1988) unfolded brain (for orientation we present also the inflated brain for the first presented contrast. The F values of the ANOVA were corrected for multiple comparisons and converted to p-values using the same cluster-size Monte-Carlo simulation as described above.

3. Results

We investigated the patterns of cortical activation in 8 congenitally blind subjects and 8 matched sighted subjects under five different experimental conditions (Fig. 1). These included (1) Tactile recognition of objects, using the right hand, termed rTOR; (2) a corresponding sensory-motor control condition (SMC), in which subjects imitated the motor movements of object palpation with the right hand; (3) a tactile object recognition task with the left hand (lTOR); and (4) a verbal memory task (VM), in which subjects covertly recalled lists of previously learned words of these objects; (5) a rest condition, which served as the hemodynamic baseline condition. We focus here primarily on the issue of the representation of tactile objects in the visual cortex of the blind and sighted participants. The results of the VM task, (which to a large extent verified previously published results, apart from the fact that the retrieved words here were of objects rather than abstract words), are not discussed here.

Data were analyzed on several levels. We first present the group analysis of the cortical activation in the blind and sighted populations (Fig. 2c and 2b respectively), as well as the different activation patterns when contrasting the blind vs. sighted groups (Figs 2a and Fig. 3). The two-way (group and condition type) random effect analysis of variance (RFX-ANOVA) results are presented in Fig. 2. Group results for the direct rTOR vs. SMC (object palpation in the right hand versus sensory motor control in the right hand) in the sighted and blind are presented in Fig. 2b and 2c respectively. Additionally, a table of Talairach coordinates of the peaks of all active clusters for each of these 3 maps is presented in Tables 2–4, corresponding to Fig. 2a–c. Finally, we focus on a specific region of interest in the lateral occipital cortex (LOC/LOtv), and analyze the time course and magnitude of the activation in this ROI on a subject-by-subject basis in the blind and sighted groups. We

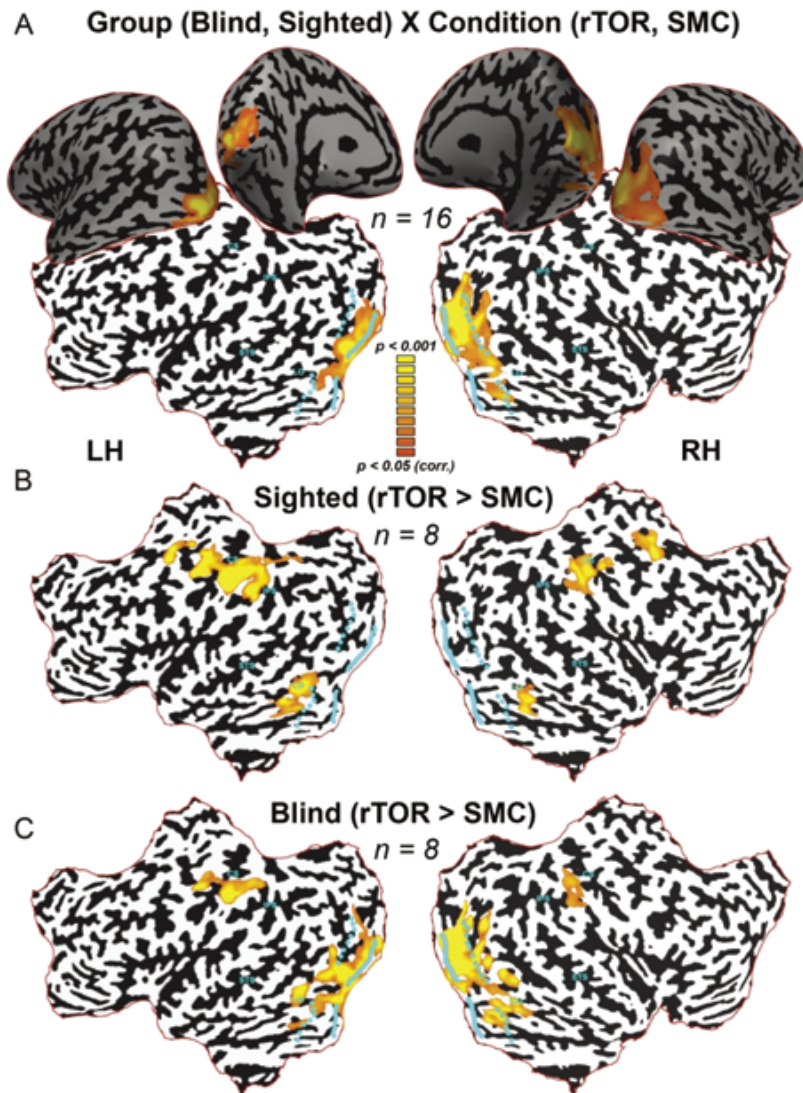


Fig. 2. The commonalities and differences in patterns of activation during tactile object recognition versus motor control in blind and sighted subjects. Statistical parametric maps of tactile object recognition (TOR) activation versus motor control movements (SMC) in sighted (b; $n = 8$), congenitally blind (c; $n = 8$) subjects and the difference between them (a) using a random effect ANOVA analysis. The data are presented on a full Talairach – normalized inflated and unfolded brain of the left and right hemispheres. (a) Interaction effect between group and task showing plasticity in the visual cortex of the blind for TOR (See also the direct contrast between the blind and sighted presented in Fig. 3. (b) rTOR > SMC in sighted (c) rTOR > SMC in blind. STS – Superior Temporal Sulcus; IPS – Intraparietal Sulcus; CS – Central Sulcus.

also compare the LOC/LOtv activation to the activation profile in the primary sensory-motor cortex (Fig. 4).

In the first step we present the pattern of activation in the sighted and blind in detail during tactile object recognition using the right hand (rTOR), contrasted with the right hand sensory-motor control (SMC) condition (Fig. 2b and 2c respectively). In the sighted, TOR using the right hand activated somatosensory regions in the parietal cortex, showing the typical contralateral preference (S1, S2, and anterior IPS). In addition,

activation was found in the lateral occipital complex (LOC) bilaterally, as reported previously (Amedi et al., 2001; Amedi et al., 2002; James et al., 2002; Stoesz et al., 2003; Pietrini et al., 2004). (For a recent review see (Lacey et al., 2009)).

In the blind, fMRI activation was found in similar brain regions. The most conspicuous difference between the two groups was the robust posterior occipital activation, apparent in the blind but not in the sighted. This additional occipital activation was most evident

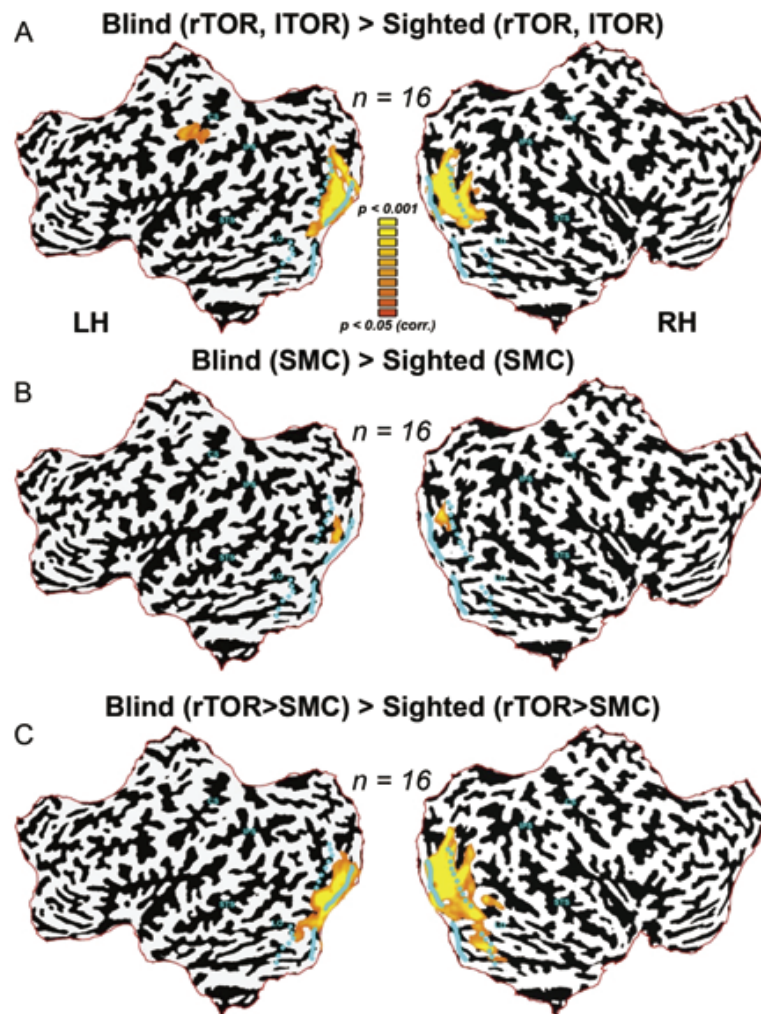


Fig. 3. Cortical plasticity in the blind is specific to TOR rather than to motor hand movements. Statistical parametric maps of the direct comparison between the blind and sighted groups using random effect analysis. The data are presented on a full Talairach – normalized unfolded brain of the left and right hemispheres. (a) Contrasting blind and sighted maps for TOR in either of the hand versus SMC (balanced) (b) test for the difference between right hand movements (SMC) (c) TOR > SMC in blind versus sighted suggests most of the interaction effect seen in visual areas in Fig. 2a is due to higher activation in the blind in the rTOR (rather than the SMC) condition.

in the dorsal and central (“foveal”) regions of the left hemisphere, and in both ventral and dorsal posterior occipital regions of the right hemisphere. A similar pattern of activation was observed during tactile object recognition using the left hand (ITOR), apart from the opposite laterality in primary somatosensory areas (not shown here but see Figs 3a and 4).

In order to investigate the differential contribution of the TOR condition in contrast to the SMC condition between the blind and sighted groups directly we used a 2-way factorial RFX ANOVA. Beside a small cluster in the left sensory-motor cortex around the central sulcus all areas showing a group \times task interaction (Fig. 2a)

were found in posterior occipital areas. This was also further verified using a direct contrast that showed a very similar pattern of posterior occipital specific higher activation in the blind for the rTOR vs. SMC contrast (Fig. 3c).

Theoretically, the extra activation reported during TOR could have resulted from the sensory-motor rather than the tactile components of the task. To further test for potential stronger activation in the blind for sensory-motor control we directly contrasted the two groups for the SMC condition (Fig. 3b). Much weaker plasticity for this condition was found in the occipital lobe (aside from small bilateral clusters in the dorsal

Table 2
Blind vs. sighted interaction contrast presented in TAL coordinates

		B-S interaction		
	Cortical region	TAL coordinates		
		X	Y	Z
Left Hemisphere	Post. Occ.	-16	-88	9
Right Hemisphere	Post. Occ.	17	-89	17

Table 3
Sighted peak activation presented in TAL coordinates for TOR-MC contrast

		Sighted (Peak activation) TOR-MC		
	Cortical region	TAL coordinates		
		X	Y	Z
Left Hemisphere	LOtv	-41	-62	-6
	IPS	-39	-36	43
	postCG	44	-23	45
	SFS/preCS	20	-7	61
Right Hemisphere	LOtv	43	-54	-9
	IPS	38	-35	45
	postCG	-38	-28	44
	SFS/preCS	-22	-14	62

stream). Thus, we suggest that the widespread occipital activation during TOR in the blind is not due to the motor (or proprioceptive) components of the object recognition task. Rather, it is a genuine result of the tactile object recognition process involved in this task.

To further test this directly using the various conditions employed in the experiment (and to assess the significance of each difference between the two groups directly), we generated a map showing the difference between the blind and sighted patterns of activation (Fig. 3). We looked for regions that were significantly more active in the blind than in the sighted (after applying a correction for multiple comparisons), by applying three different contrasts: (1) searching for voxels that were significantly more active in the blind during TOR regardless of the palpating hand compared to sighted (rTOR and lTOR; Fig. 3a); (2) voxels that were significantly more active in the blind group during SMC, when contrasted with the sighted group for the same condition (Fig. 3b); and (3) voxels that were more active in the rTOR > SMC contrast in the blind than in the sighted group for the same contrast (Fig. 3c). The results basically confirmed the differences discussed above. The areas showing significantly more activation during TOR but not during SMC in the blind group compared to the sighted group were the right hemisphere posterior occipital areas (both ventral and dorsal areas) and

Table 4
Blind peak activation presented in TAL coordinates for TOR-MC contrast

		Blind (Peak activation) TOR-MC		
	Cortical region	TAL coordinates		
		X	Y	Z
Left Hemisphere	LOtv	-51	-62	1
	IPS	-44	-29	41
	Post CG	-44	-26	45
	post occ.	-30	-90	7
Right Hemisphere	LOtv	41	-63	-1
	IPS	49	-24	40
	Post CG	46	-33	56
	post occ.	14	-91	13

the left dorsal and central occipital areas. The extra activation seen in the blind was most pronounced in the posterior occipital areas and did not expand to higher order areas in the occipito-temporal or occipito-parietal cortex. The motor control condition elicited similar activation patterns in the two groups (not shown) aside from a small cluster in dorsal occipital area bilaterally (appearing in the blind vs. sighted SMC contrast, Fig. 3b), which might be related to the expansion in the blind of motor action plans to the dorsal posterior occipital areas which are involved in visually guided motion action (Goodale and Milner 1992; Shmuelof and Zohary 2005). This, coupled with the fact that cortical activation is observed in the blind during Braille reading, suggests that the occipital activation found in the blind when using tactile stimuli is probably associated with tactile processing (object or Braille letter recognition or even vibro-tactile stimulation (Burton et al., 2004)) but not with the motor components of the tasks.

Finally, in order to quantitatively compare the magnitude of activation in LOC/LOtv specifically in both the sighted and the blind groups during tactile object recognition, we calculated the average percent signal change in LOC/LOtv and in early sensory-motor regions (S1/M1) during tactile object recognition using the right hand (rTOR), left hand (lTOR), and during the sensory-motor control condition (using the right hand, SMC). This was done by assessing the average magnitude of activation (across subjects) in the voxel showing the greatest signal (i.e. peak voxel in smooth volume, thus reflecting the activation in a Gaussian window around the peak, see also methods) for (lTOR > rest) and (rTOR > rest), separately for each test and each individual. The resulting average percent signal change for each condition (lTOR, rTOR and SMC) in the two groups is shown in Fig. 4. As expected, the ac-

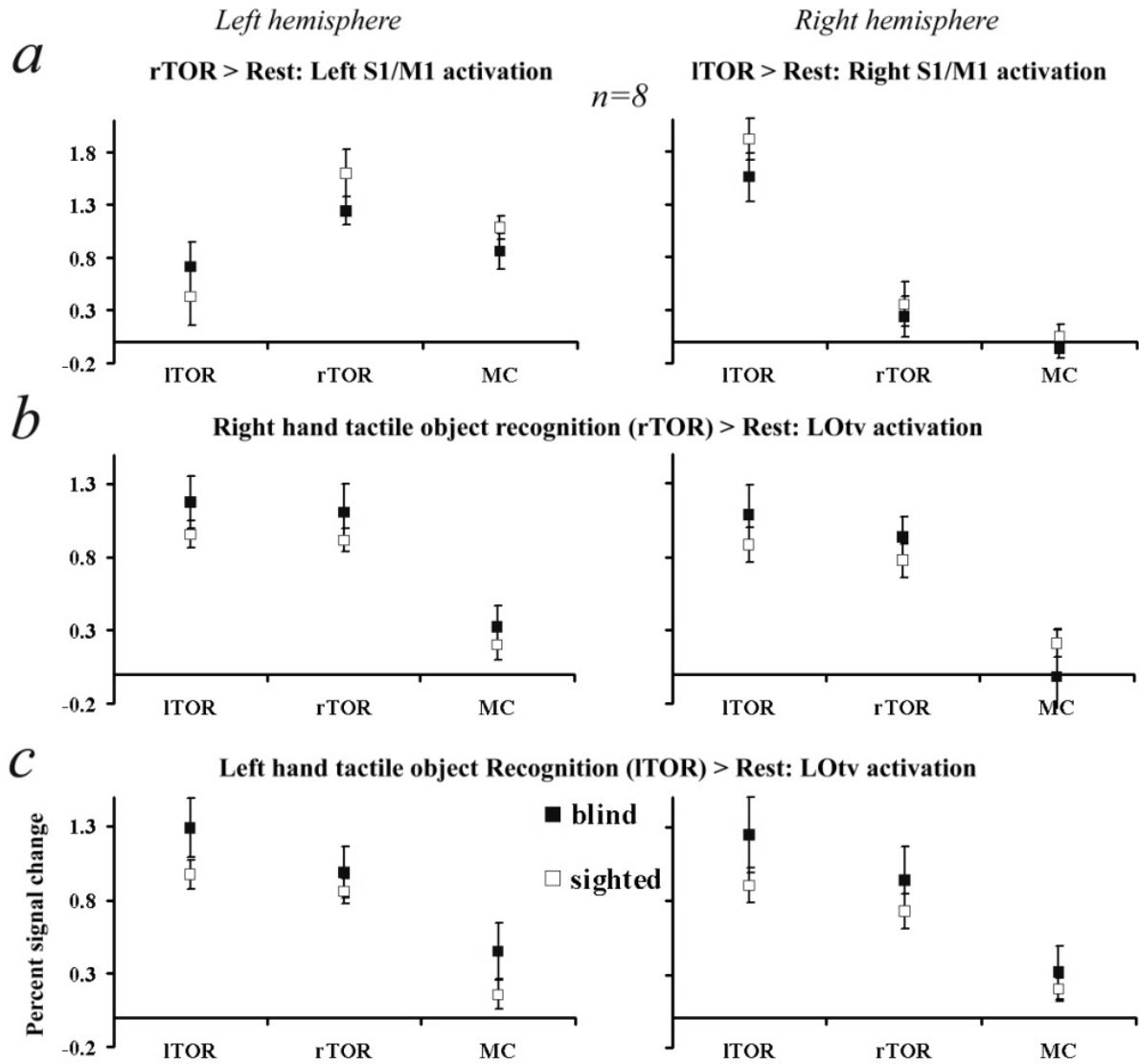


Fig. 4. The average percent signal change for ITOR, rTOR and SMC in LOTv of the blind and the sighted. Quantitative comparison of the magnitude of activation in LOTv in the blind and in the sighted groups with the right hand (rTOR), left hand (ITOR) and during right hand motor control (SMC). Average percent signal change in S1 and LOTv peak voxels for ITOR and rTOR separately for each participant and for each group. (a) Activation in primary sensory-motor cortex showed robust contralateral activation and weak ipsilateral activation for TOR in each hand in both groups. SMC activated only the contralateral (left) hemisphere. (b) Peak voxels selected by right hand TOR were also activated by left hand TOR to a similar extent in both the left and right hemisphere and in both blind and sighted subjects. Greater activation was found to ITOR in relation to the SMC even though both conditions were not part of the statistical test used to define the ROI (i.e. there was no a priori bias to any of them). (c) Peak voxels selected by left hand TOR vs. rest show a similar pattern.

tivation in sensory-motor (S1/M1) cortex in both blind and sighted subjects showed a clear preference for the contralateral hand. Thus, the rTOR and SMC conditions (which both require using the right hand) generated greater activation in the left S1/M1, while ITOR led to greater activation in the right S1/M1. This was the case in both groups (Fig. 4a) with no clear difference

between them. On the other hand, in LOTv, the activation was bilateral, irrespective of whether the peak voxels were selected according to their activation when using the right hand (Fig. 4b) or the left hand (Fig. 4c). In both groups LOTv activation during the *unselected* tactile condition (ITOR in Fig. 4b and rTOR in Fig. 4c) was greater than during the motor control, indicating

the relevance of this region for tactile object processing.

The average LOTv Talairach coordinates, as calculated from the location of the peak voxel across subjects, was highly consistent between the two groups: (Left hemisphere. Blind: $X = -44 \pm 5$ S.D. $Y = -60 \pm 5$ $Z = -5 \pm 5$. Sighted: $X = -44 \pm 5$, $Y = -62 \pm 5$ $Z = -5 \pm 5$; Right hemisphere. Blind: $X = 42 \pm 5$ S.D. $Y = -63 \pm 6$ $Z = -3 \pm 5$. Sighted: $X = 44 \pm 6$, $Y = -56 \pm 6$ $Z = -2 \pm 3$). This is highly consistent with previous studies in sighted subjects (Amedi et al., 2001; Amedi et al., 2002; Pietrini et al., 2004). These results suggest that the tactile representation in LOTv is bilateral, selective to the tactile rather than to the motor (or proprioceptive) components, and is observable in a situation where no visual experience or visual memory is possible (due to the congenital nature of the blindness).

4. Discussion

4.1. Summary of results

The main novel findings we report are:

- (1) Tactile object recognition is characterized (in addition to activation of parieto-frontal networks) by robust LOC/LOTv activation in the congenitally blind, as in sighted controls. The pattern of fMRI activation during tactile exploration of objects in LOC/LOTv is bilateral in both blind and sighted, regardless of the palpating hand. The magnitude of this activity is similar in blind and sighted controls. These results indicate that visual imagery is *not* an obligatory condition for *tactile* object-related activation in LOC/LOTv, since such imagery is lacking in the congenitally blind.
- (2) As a group, the congenitally blind showed additional preferential activation in posterior occipital areas during TOR, when compared to their sighted peers (Figs 2–4). The results corroborate and extend previous studies that showed massive occipital activation on a variety of other tactile tasks (such as Braille reading, simple vibro-tactile stimulation, etc., for a review see Pascual-Leone et al., 2005)).
- (3) The most prominent occipital activation during tactile object recognition was observed in the dorsal and central retinotopic areas bilaterally, unlike during Braille reading, verb-generation or verbal memory, which typically show greater

activation in the left ventral stream (Amedi et al., 2003; Raz et al., 2005). This is congruent with early studies in the blind that suggested an expansion of tactile responsiveness from the early somatosensory cortex via the posterior parietal cortex (corresponding to areas 7a and 7b in primates) to the dorsal posterior occipital cortex (see Pons, 1996; Sadato et al., 1996)). We elaborate in the next sections on each of these main findings in light of previous works, and possible confounding factors.

4.2. The role of visual imagery in tactile activity in the occipital ('visual') cortex

Some previous studies have suggested that visual imagery might be responsible for the tactile activation seen in areas generally considered visual (for example, activation of the parieto-occipital cortex during tactile discrimination of grating orientation; (Sathian et al., 1997; Zangaladze et al., 1999; Zhang et al., 2004)). This raises the issue of whether the fMRI activation in LOTv during tactile object recognition could be attributed to visual imagery alone. Previously we showed that only negligible activation exists in LOTv during object recognition based on characteristic auditory cues (Amedi et al., 2002), although it resulted in reliable object recognition. Nevertheless it could still be claimed that object palpation may induce better visual imagery because it is intrinsically related to the three-dimensional shape of an object, whereas recognition of objects through their typical sounds may not. In this study we showed that *congenitally blind* people who have never had any visual experience (and thus are unlikely to have any visual imagery capabilities) still show robust LOTv activation during TOR (as well as for Braille reading; (Amedi et al., 2003)), similar in magnitude to that found in the sighted. Thus, although visual imagery might accompany and aid tactile object recognition in some cases via top-down mechanisms (for a review see Lacey et al., 2009), clear tactile-based activation can be found in LOTv in its absence. The LOTv activation in the blind and the sighted might still stem from different mechanisms; namely visual imagery enhanced by tactile exploration in the sighted and pure tactile responses following cross-modal plasticity in the blind. While this is a valid, though somewhat less likely alternative explanation for the present results, further studies are needed to fully clarify this issue.

4.3. *The nature of object representation in the ventral visual pathway*

We found robust bilateral tactile activation in LOTv during TOR, irrespective of the palpating hand. This was the case in both the blind and the sighted groups. Interestingly, unlike the strict contralateral responses found in both primary somatosensory areas (and retinotopic visual areas for vision), activation in LOC during *visual* object recognition (in the sighted) was also often bilateral, irrespective of whether the object was presented in the contralateral or the ipsilateral hemifield. These findings lend weight to the argument that representation in LOC is probably more related to object geometric shape than to the specific circumstances in which it was recognized (i.e. which side of the visual field it appeared in or which hand made contact with it). This is consistent with size, translation and rotation invariance found in LOC for visual objects. This hypothesis needs to be further studied in other experimental conditions. For instance, our recent finding of LOTv responses in sighted and two blind individuals reconstructing shape by a visual-to-auditory sensory substitution (Amedi et al. 2007) but a lack of such activation for general arbitrary associations between object sounds and identity is in line with this reasoning.

This hypothesis is also supported by the category-related specialization for faces, objects, and scenes that has been observed in ventral temporal cortex for *visually* presented objects (but see an alternative explanation below). A similar category-related division has been found (within LOTv) when objects are recognized by touch (Amedi et al., 2002; Pietrini et al., 2004). These category-related responses are correlated across touch and vision, suggesting that a common representation of 3D objects is activated by both these modalities. Finally, this hypothesis is also congruent with the James and colleague results (James et al., 2002), who showed fMRI activation in occipital areas during haptic exploration of novel abstract objects. They reported that the magnitude of tactile-to-visual priming was similar to the magnitude of visual-to-visual priming, suggesting that vision and touch share common representations in LOTv (see also (Easton et al., 1997a; Easton et al., 1997b; Reales and Ballesteros 1999)).

Finally, Sathian and colleagues (Stoesz et al., 2003; Prather et al., 2004) showed that both IPS and LOTv are preferentially activated by macrospatial shape recognition (of imprinted symbol identity) but not during a microspatial task (gap detection or orientation judgment). This demonstrates that LOTv activation is maintained

even in the absence of active exploration, thus excluding a contribution from the motor system and in line with the current results in the sighted subjects showing negligible activation to the sensory-motor control (Fig. 4) and very little plasticity to this component in the blind (Fig. 3b).

The same group (Lacey et al., 2009) presented a conceptual model for the representation of object form in vision and touch that reconciles top-down (e.g. visual imagery) and bottom-up multisensory convergence approaches. In this model, LOTv contains a representation of object form that can be flexibly addressed either bottom-up or top-down, depending on object familiarity, but independent of the modality of sensory input. Haptic perception of unfamiliar shape relies more on a bottom-up pathway from the PCS (part of S1) to the LOTv with support from spatial imagery processes. Since the global shape of an unfamiliar object can only be computed by exploring it in its entirety, the model predicts a heavy somatosensory drive of the LOTv, with associated involvement of the IPS in processing the relative spatial locations of object parts in order to compute global shape. Haptic perception of familiar shape depends more on object imagery involving top-down paths from prefrontal and parietal areas into the LOTv. For familiar objects, while spatial imagery remains available (perhaps in support of view-independent recognition), the use of object imagery is online (perhaps as a kind of representational shorthand sufficient for much cross-modal processing of familiar objects), served by top-down pathways from prefrontal areas into the LOTv. It would be interesting in future studies to further test this model's predictions, for instance, for a larger bottom-up drive in the congenitally blind who lack the top-down visual imagery component, for instance using effective connectivity approaches.

4.4. *Functional relevance of the ventral visuo-tactile object representation*

What is the functional relevance of the reported LOTv activation in both the sighted and the blind? Does it reflect a genuine contribution to tactile perception per se? Cross-modal integration? Is it just an epiphenomenon? One (indirect) way to assess these questions is to study the effect of brain lesions. Some evidence suggests that patients with visual agnosia also suffer from tactile agnosia (e.g. (Morin et al., 1984; Feinberg et al., 1986; Ohtake et al., 2001)). Interestingly, Kilgour and Lederman have recently reported evidence of an individual

with haptic prosopagnosia (i.e. a deficit in recognizing familiar faces by touch), in addition to visual prosopagnosia following lesions to the occipital, temporal and prefrontal regions (Kilgour et al., 2004). In an experimental setting, TMS can be used to create “virtual lesions” in normal individuals (Pascual-Leone 2000). The advantage of using this method over the classic lesion approach is that the TMS is applied in a ‘clean’ experimental setting. Thus, it is not prone to confounding factors such as possible (compensatory) plasticity (over a long period of time following the lesion), the widespread nature of most lesions, and individual differences in lesion location across cases. Zangaladze et al. (Zangaladze et al., 1999) used this technique to show interference with a tactile orientation task during TMS delivered to area PO, while Merabet et al. (Merabet et al., 2004) showed that inhibitory repetitive TMS (at 1 Hz) to the occipital cortex reduced performance in tactile distance judgments but not in roughness judgments, suggesting an involvement of the occipital cortex in tactile distance judgments. Both studies support the view that the occipital cortex is engaged in tactile tasks requiring fine tactile spatial discrimination. Based on the present results, our prediction is that TMS over LOTv will hamper performance in tasks requiring fine discrimination of tactile geometric shape.

4.5. *The nature of object representation in the blind*

In the blind, additional regions with TOR preference were located in the dorsal and central retinotopic regions bilaterally and in addition in the right ventral retinotopic regions. These occipital regions showed negligible activation during the motor control condition, suggesting that in the blind they are also higher-tier regions in the *tactile* hierarchy. Based on the present (as well as previous) results, we hypothesize that TMS in both the LOTv and retinotopic areas of the blind (especially in the right hemisphere) will have an effect on tasks requiring tactile object recognition.

Consistent with this position, previous rTMS studies showed that in the blind, TMS trains to occipital and occipito-temporal regions resulted in increased error rates in recognizing Braille and embossed letters (Cohen et al. 1997), but did not interfere with the detection of tactile stimulation. In fact, there is some evidence that even when visual input is suppressed for only a week, occipital activation during Braille reading and tactile object recognition can be seen in blindfolded patients (Pascual-Leone and Hamilton 2001; Pascual-

Leone et al., 2005), and TMS disrupts Braille letter identification in these subjects.

An alternative, not necessarily contradictory possibility is that top-down attention mechanisms, such as spatial attention, may be more robustly activated in the blind (see above a general framework integrating bottom-up and top-down components in TOR). Such mechanisms have previously been shown to exert powerful modulation on early visual areas. This alternative assumes that spatial attention mechanisms still function in the occipital cortex of the blind, which is an intriguing unresolved issue on its own. Nevertheless, spatial attention typically enhances the specific retinotopic area corresponding to the attended location in space. Thus the pattern of activation in the blind should be dependent on *where* attention is directed. The fact that hand identity had no effect in our experiment argues against this notion, since the left hand is on our left side of the visual space & vice versa.

4.6. *Development of the occipito-parietal sensory-motor pathways is also independent of sight*

Consistent with the results presented here which demonstrate the independence of tactile responses in ventral occipital cortex of visual experience, several recent findings have shown that the dorsal occipital cortex also develop sensory-motor, action related activation in congenitally blind. Findings such as those reported by Fiehler and colleagues (Fiehler et al., 2008; Fiehler et al., 2009) show that the sensory-motor aspects of dorsal stream activation arise without developmental dependence on visual input. Thus, the action representation system of the dorsodorsal and ventrodorsal stream is utilized not only for visual but also for kinesthetic action control. This is generally in line with the model put forward by Dirckman and de Haan (Dirckman and de Haan 2007) suggesting that somatosensory information is also processed in two pathways subserving action and perception. These findings taken together suggest that both the dorsal and ventral visual pathways and functions can develop even in the absence of vision in congenitally blind individuals. Therefore, they favor the idea of general metamodal operators (Pascual-Leone and Hamilton 2001) which perform computations regardless of the sensory input modality, in both the ventral and dorsal “visual” streams.

4.7. Summary and conclusions

Our main finding is that robust tactile responses in 'visual' object-related areas (i.e. the LOTv) are similar in magnitude in both blind and sighted subjects and in both the left and right hemispheres. This suggests that visual imagery is not necessary for evoking tactile responses in visual object-related areas. Furthermore, the tactile responses in LOTv show a similar lack of hemispheric laterality as the region's visual response to objects. This supports the idea that both senses are involved in a relatively abstract and generalized representation of objects. The expansion of tactile object related activation to the posterior occipital cortex (in the congenitally blind) supports previous evidence for such effects during other tactile tasks (Braille reading or vibro-tactile flutter discrimination) and suggests that ventral-occipital back-projections may play a role in its establishment. However, the enhanced activity in the blind in dorsal occipital-posterior areas during tactile object recognition (areas that are often involved in planning motor action on visual objects) may indicate that the development of tactile responses in the primary visual cortex of the blind could also be mediated by a strengthening of existing parieto-occipital connections rather than those arising from ventral stream areas. Further research, possibly using diffusion tensor imaging (DTI) or effective connectivity approaches, may be able to provide an answer to this question.

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