Brain Topogr
DOI 10.1007/s10548-009-0075-8

ORIGINAL PAPER

Reorganisation of the Right Occipito-Parietal Stream for Auditory Spatial Processing in Early Blind Humans. A Transcranial Magnetic Stimulation Study

O. Collignon · M. Davare · E. Olivier · A. G. De Volder

Received: 16 December 2008 / Accepted: 16 January 2009

Abstract It is well known that, following an early visual deprivation, the neural network involved in processing auditory spatial information undergoes a profound reorganization. In particular, several studies have demonstrated an extensive activation of occipital brain areas, usually regarded as essentially "visual", when early blind subjects (EB) performed a task that requires spatial processing of sounds. However, little is known about the possible consequences of the activation of occipitals area on the function of the large cortical network known, in sighted subjects, to be involved in the processing of auditory spatial information. To address this issue, we used event-related transcranial magnetic stimulation (TMS) to induce virtual lesions of either the right intra-parietal sulcus (rIPS) or the right dorsal extrastriate occipital cortex (rOC) at different delays in EB subjects performing a sound lateralization task. Surprisingly, TMS applied over rIPS, a region critically involved in the spatial processing of sound in sighted subjects, had no influence on the task performance in EB. In contrast, TMS applied over rOC 50 ms after sound onset, disrupted the spatial processing of sounds originating from the contralateral hemifield. The present study shed new lights on the reorganisation of the cortical network dedicated to the spatial processing of sounds in EB by showing an early contribution of rOC and a lesser involvement of rIPS.

Keywords Blindness · Plasticity · Spatial hearing · Occipital cortex · Intraparietal sulcus

This article is published as part of the Special Issue on Multisensory Integration.

Electronic supplementary material The online version of this article (doi:10.1007/s10548-009-0075-8) contains supplementary material, which is available to authorized users.

O. Collignon · A. G. De Volder
Neural Rehabilitation Engineering Laboratory, Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium

M. Davare · E. Olivier
Laboratory of Neurophysiology, Institute of Neuroscience, Université Catholique de Louvain, Brussels, Belgium

O. Collignon (✉)
Département de Psychologie, Centre de Recherche en Neuropsychologie et Cognition (CERNEC), Université de Montréal, 90 Vincent d'Indy, Succ. Centre-Ville, Montréal (Québec), CP 6128H3C 3J7, Canada
e-mail: olivier.collignon@uclouvain.be

Introduction

Vision plays a crucial role in analysing spatial information (Spence and Driver 2004) and it has long been debated whether early visual deprivation will either hamper the processing of non-visual spatial information or improve the performance of preserved sensory systems. Recent behavioural studies clearly demonstrated that vision is not a prerequisite for the calibration of auditory localization cues and that early blind people (EB) may even show supranormal abilities in some auditory localisation tasks [see (Collignon et al. 2008b) for a recent review on that topic]. In line with these behavioural studies, functional neuroimaging experiments showed a profound reorganisation of the brain network dedicated to the processing of the spatial attributes of sounds in blind subjects. In particular, several positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have demonstrated an increased activation in occipital areas during auditory spatial processing in EB (Arno et al. 2001; De Volder et al. 1999; Gougoux et al. 2005; Leclerc et al. 2000; Poirier et al. 2006;

Voss et al. 2008). Moreover, it has been suggested that the recruitment of these visual areas deprived of their normal inputs may explain the exceptional abilities of EB in performing auditory spatial tasks (Gougoux et al. 2005).

In sighted subjects, the spatial attributes of sounds are thought to be mainly processed within a dorso-lateral "where" stream, including the caudal superior temporal cortex, the posterior parietal cortex (PPC), and the dorso-lateral prefrontal cortex. This circuit is anatomically distinct from a ventrolateral "what" stream involved in the processing of non-spatial features of sounds, such as pitch or vocalization (Rauschecker 1998; Romanski et al. 1999; Rauschecker and Tian 2000). This organisation is somewhat comparable to the functional subdivision of the visual system into an occipito-parietal and an occipito-temporal stream involved, respectively, in processing spatial and object information (Haxby et al. 1991). As far as the processing of spatial information is concerned, auditory and visual "where" streams seem to overlap, at least partly, in the intraparietal sulcus (IPS) where multisensory representations of the external space are known to exist, particularly in the ventral region of IPS (VIP) (Avillac et al. 2005; Bremmer et al. 2001; Mullette-Gillman et al. 2005; Schlack et al. 2005; Stricanne et al. 1996). Moreover, recent studies in both animals and humans have shown that some visual areas, usually regarded as exclusively "visual", e.g. the extrastriate occipital cortex, may also play a role in the spatial processing of sound (Allman et al. 2008; Collignon et al. 2008a; Fishman and Michael 1973; Lewald et al. 2004a; Morrell 1972; Poirier et al. 2005; Zimmer et al. 2004).

Transcranial Magnetic Stimulation (TMS) has proven useful to interfere transiently and reversibly with the function of a given cortical area in order to determine both the causal role of this particular region in the task at hand and the timing of its contribution (O'Shea et al. 2008; Walsh and Cowey 2000). In a recent study, we demonstrated that, in healthy participants, TMS could be used to disclose the time-course of the spatial processing of sounds in the dorso-lateral "where" stream (Collignon et al. 2008a). In particular, we found that a virtual lesion of the right dorsal extrastriate occipital cortex (rOC), occurring 50 ms after the stimulus presentation, impairs the lateralization of sounds presented bilaterally whereas a virtual lesion of the right intra-parietal sulcus (rIPS) induced 100–150 ms after the stimulus onset led to a rightward bias for sounds originating either from the centre or from the left side. This result points to a distinct role of the rOC and rIPS in the spatial processing of sounds and also provides compelling evidence, in sighted subjects, for an earlier contribution of the rOC to the processing of non-visual spatial information when compared with the rIPS.

As already mentioned, a major functional reorganisation of the brain circuit dedicated to the spatial processing of sounds is thought to occur in EB. For example, in a recent PET study, Gougoux et al. (2005) found a significant correlation between occipital activation level and auditory spatial performance in EB subjects who disclosed enhanced auditory spatial abilities, whereas such a correlation was not found for parietal regions. Interestingly, in a similar experiment performed in sighted subjects, Zatorre et al. (2002) reported opposite results namely, a positive correlation between neural activity in the right PPC and auditory spatial performance and an absence of correlation in occipital regions. These results thus suggest major changes between SC and EB in the brain circuitry underlying the spatial processing of sounds.

The goal of the present study was therefore to investigate the possible changes in the rOC and rIPS contribution to auditory spatial processing in EB. As in our previous study (Collignon et al. 2008a), we applied TMS over rIPS and rOC at different delays in EB subjects performing a sound lateralization task. By comparing the results obtained in EB with those found in sighted subjects in our previous study (Collignon et al. 2008a), we aimed to provide further insights into the early role of vision in shaping the functional properties of these two brain areas involved in spatial hearing.

Materials and Methods

Subjects

Six congenitally blind subjects with no residual light perception participated in this experiment (1 female; range 22–55 years, mean ± SD: 32 ± 14; Table 1). None of the participants had neurological, psychiatric, or other medical problems or had any contraindication for TMS according to safety guidelines for magnetic stimulation (Belmaker et al. 2003; Wasserman et al. 2000). None of the subjects was taking psychotropic medication at the time of testing. Participants were naive to the purpose of the study, and information about the experimental hypothesis was provided only after the tests were completed. The experiment was undertaken with the understanding and written consent of each subject. The experimental procedures were approved by the local Ethics committee of the Université Catholique de Louvain and the study conforms with The Code of Ethics of the World Medical Association (Declaration of Helsinki), printed in the British Medical Journal (18 July 1964).

Transcranial Magnetic Stimulation (TMS)

TMS was performed by using two Magstim Model 200 connected to a Bistim module (Magstim Company,

Table 1 Characteristics of the blind subjects

Subjects	Age	Sex	Handedness	Residual vision	Blindness onset	Cause of blindness
1	22	M	R	No	Congenital	Bilateral Retinoblastoma
2	22	M	L	No	Congenital	Retinopathy of prematurity
3	23	F	A	No	Congenital	Prenatal infection with Cytomegalovirus
4	30	M	R	No	Congenital	Genetic*
5	42	M	R	No	Congenital	Retinopathy of prematurity
6	55	M	R	No	Congenital	Bilateral retinoblastoma

Note: *M* male, *F* female, *R* right handed, *L* left handed, *A* ambidextrous

* No additional details available

Whitland, UK), in order to apply paired-pulse TMS (interval 5 ms) through a 70 mm outer diameter figure-of-eight stimulation coil. The use of short interval paired-pulse maximises the disruptive capacity of TMS when compared with single-pulse, while preserving the high temporal resolution of this technique (Collignon et al. 2008a; Davare et al. 2006). The coil was held tangential to the skull with the handle pointing towards the midline. TMS intensity was set for all subjects at 50% of maximum Bistim stimulator output.

Before each experiment, the coil position was precisely determined for each subject by means of an on-line co-registration of the stimulation sites onto individual anatomical high-resolution T1-weighted magnetic resonance images (MRIs) (Noirhomme et al. 2004). On the basis of anatomical landmarks, the coil was positioned over the right intraparietal sulcus (rIPS), the right dorsal occipital cortex (rOC) and the right primary somatosensory cortex (rS1). S1 was used as a control stimulation site in order to control for non-specific effects of TMS. This site was targeted by positioning the coil over the superior portion of the right postcentral gyrus, 20 mm laterally with respect to the midline (Brodmann's areas 3, 1, 2). The rIPS stimulation site was located in front of the junction between the supramarginalis and angularis gyri (overlapping Brodmann's areas 7, 40). The rOC stimulation site was located on the dorsal part of the right lateral occipital gyri, posterior to the transverse occipital sulcus (extrastriate occipital cortex corresponding to Brodmann's areas 18, 19). As in previous TMS studies (Collignon et al. 2008a; Collignon et al. 2007; Lewald et al. 2004a, 2004b), we focused our investigation on the right hemisphere because of the large body of evidence indicating a right-hemispheric dominance for auditory spatial processing both in blind (Gougoux et al. 2005; Weeks et al. 2000) and sighted subjects (Griffiths et al. 1998; Lewald et al. 2002; Weeks et al. 1999; Zatorre et al. 2002). The software used for co-registration was further used to normalize individual coordinates of the TMS sites with respect to the Montreal Neurological Institute (MNI) brain atlas. In the present study, the mean normalized MNI coordinates ($x,y,z \pm$ SD, $n = 6$) of the stimulation sites were respectively 22 ± 6, -15 ± 5, 77 ± 2 mm for S1, 41 ± 9, -55 ± 9, 55 ± 5 mm for rIPS, and 24 ± 5, -92 ± 1, 29 ± 4 mm for rOC (Fig. 1). These coordinates are very close to those of the stimulation sites investigated in sighted subjects in our previous study (Collignon et al. 2008a). TMS was well tolerated and none of the subjects reported having experienced either phosphenes or any hints of tactile or auditory sensations following TMS.

Stimuli and Procedure

During the whole experiment, participants sat in a silent room with their head restrained by forehead and chin rest in a straight-ahead position. Their eyes were kept closed by applying a blindfolding mask with cotton to exert a little pressure on the eyelids. They were instructed to fix virtually a target situated in front of them during the whole experiment.

Stimuli consisted of short band-pass noise bursts (bandwidth of four octaves with a centre frequency of 2 kHz, plateau time 40 ms, rise/fall time 5 ms) and were delivered via insert earphones (Philips HJ030). Intensity of the sound was set at 75 dB SPL in the "best" ear. Subjects were then asked to adjust the tone's loudness in the other ear until they perceived the same sound intensity as in the "best" ear, so that the sound was perceived as coming from the centre when delivered in both ears. The rationale for this normalization procedure was that subjects usually exhibit asymmetries in the sensitivity of the ears inducing left or right deviation for central sounds.

Interaural level difference (ILD) and Interaural time difference (ITD), two critical cues for sound localization in azimuth, were then adjusted to yield five distinct intracranial sound locations with position L2 (more eccentric left position), position L1 (less eccentric left position), position C (Central sound), position R1 (less eccentric right position), position R2 (more eccentric right position). ILD and ITD adjustment of auditory stimuli produce intracranial

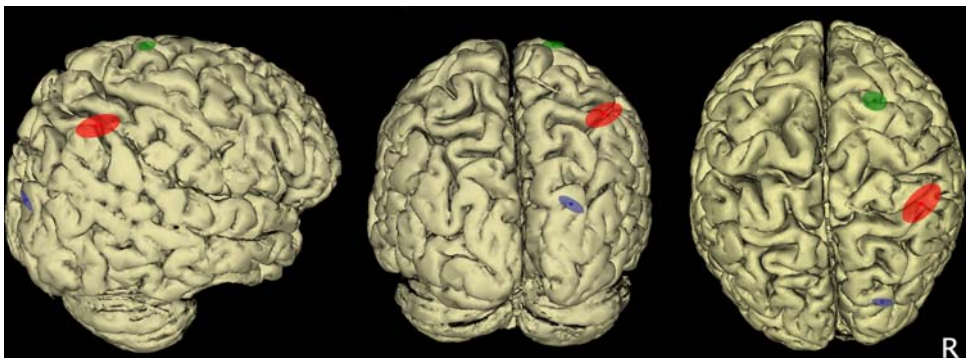

Fig. 1 Location of the TMS sites. Brain locations of the TMS coil positions to induce virtual lesion of the primary somatosensory cortex (rS1 *green*), the intra-parietal sulcus (rIPS *red*), and the dorsal extrastriate occipital cortex (rOC *blue*) in the right hemisphere. These regions were targeted for each subject by means of a neuronavigational system (Noirhomme et al. 2004). The mean normalized MNI coordinates (x,y,$z \pm$ SD; $n = 6$) of the stimulation sites were, respectively, 22 ± 6, -15 ± 5, 77 ± 2 mm for rS1; 41 ± 9, -55 ± 9, 55 ± 5 mm for rIPS; and 24 ± 5, -92 ± 1, 29 ± 4 mm for rOC. The stimulated sites are projected on a sagittal, coronal and horizontal view of a 3D-reconstruction of the MNI normalized brain. Each ellipse was centred on the mean MNI coordinates of rS1, rIPS and rOC stimulation points and their surface shows the 95% confidence interval of the normalized coordinates calculated for each subject

sound positions (Blauert 1997), thus when using the term "spatial processing of sound" in this experiment we refer to the ability to lateralize intracranial sounds perceived along a line joining the two ears relative to an auditory median plane inside the head.

In order to determine the percentage of errors and standardize the performance of participants, we used a staircase method to adjust individually ITDs and ILDs. Steps of 2% ILD were always paired with steps of 24 μs ITD and were adjusted to induce approximately 80% of correct responses in the less eccentric right or left position (L1 and R1) and approximately 90% of correct responses in the more eccentric right or left position (L2 and R2). This adjustment was performed before each experimental session. Across subjects, ILD differences were 4 ± 3% and 6 ± 3% for the first (L1–R1) and second (L2–R2) location levels respectively combined with ITD differences of 46 ± 30 μs and 74 ± 30 μs for the first and second location levels respectively. These values obtained in EB did not differ from the ones we found in sighted subjects (Collignon et al. 2008a). This absence of difference between both populations may suggest that supra-normal abilities in EB are more susceptible to emerge in higher-order cognitive tasks rather than in basic sensory measurements (Collignon et al. 2006).

We used a two alternatives forced choice paradigm in which subjects were instructed to categorise the perceived intracranial position of the sounds as either "left" or "right" with respect to the median plane of the head (Blauert 1997) by pressing the appropriate response key using, respectively, the left or right index finger. If subjects failed to respond within 1.5 s, the same trial was immediately presented. Subjects were explicitly instructed to favour response accuracy rather than response speed.

In order to determine the time-course of rIPS and rOC contributions to auditory spatial processing, paired-pulse TMS was delivered at six different delays after the stimulus presentation. The stimulus-pulse onset asynchronies (SOAs) varied from 50 to 300 ms, by increments of 50 ms. TMS trials were randomly intermixed with trials with no TMS in order to determine a baseline in the auditory spatial task. Testing was divided into two experimental sessions, both lasting approximately 2 hours. Each session consisted of 12 blocks (4 blocks for each of the three stimulation sites: rS1, rIPS, rOC). Block order was counterbalanced across subjects. In two successive blocks, TMS was never applied over the same stimulation site and for the overall experiment, each site was preceded by the same number of blocks gathered for the two other stimulation sites. During each block, the 5 auditory stimuli (L2, L1, C, R1, R2) were presented in a pseudo-random order either without TMS ($n = 5$) or with TMS applied at one of the six SOAs ($n = 30$). Each trial was separated by 6 s. Stimuli presentation and TMS were triggered by custom-made software created with Labview (National Instruments, Austin, TX).

During the course of the whole experiment, participants wore a high-quality hearing protector (Peltor optime 3 H540B; attenuation value 35 dB) on top of the headphones in order to minimise auditory interferences produced by the TMS coil while discharging. This hearing protector had a neckband system to allow the free positioning of the TMS coil over the scalp.

Data Analysis

Task performance was quantified by measuring the percentage of right-sided responses following the presentation

of sounds either to the left, the centre or the right side. Data were analysed separately for each TMS delay (50, 100, 150, 200, 250 and 300 ms) by means of two ways 4X5 ANOVAs with sites (BASELINE, rS1, rIPS and rOC) and sound origins (L2, L1, C, R1, R2) as within-subject factors. BASELINE performance was obtained by merging together scores obtained in the "no TMS" trials gathered for the three stimulation sites. Based on significant *F*-values, Fisher post-hoc analyses were performed when appropriate. Significance level for all statistics was fixed at $P < 0.05$. Raw data are provided in a supporting table as electronic supplementary material.

Results

The effect of the TMS-induced virtual lesions on sound localization performance in EB is illustrated in Fig. 2. For all TMS delays, statistical analyses revealed a significant main effect of sound origins ($F(4/20)$ from 50.7 to 92.5, all $P < 10E\text{-}5$). As expected, these results demonstrated that the proportion of right-sided responses increased gradually as the target was progressively shifted from L2 to R2.

When TMS was delivered 50 ms after the stimulus presentation (Fig. 2a), no significant main effect of the factors sites ($F(3/15) = 0.5$; $P = 0.69$) but a significant interaction between the sites and sound origins factors ($F(12/60) = 2.3$; $P = 0.02$) was found. Post-hoc analyses showed that the percentage of right-sided responses was significantly higher when TMS was delivered over rOC than over rS1 for L1 sounds ($P = 0.01$); no significant differences were found for the others sound positions. In contrast, virtual lesion of rIPS induced at the same delay did not induce a significant change in subject's performance when compared to the rS1 control site. This finding demonstrates that a virtual lesion of rOC performed 50 ms after the stimulus presentation impaired the ability to locate sounds originating from the left hemi-space. The finding that this deficit was present only for sounds close to the midline (L1) may be explained by the fact that they were more difficult to locate than the eccentric ones (L2), and thus more susceptible to the effect of TMS.

No significant main effect of the factors sites and no significant interaction between the factors sites and sound origins were found for the other TMS delays. These results indicate that virtual lesions of the three stimulation sites

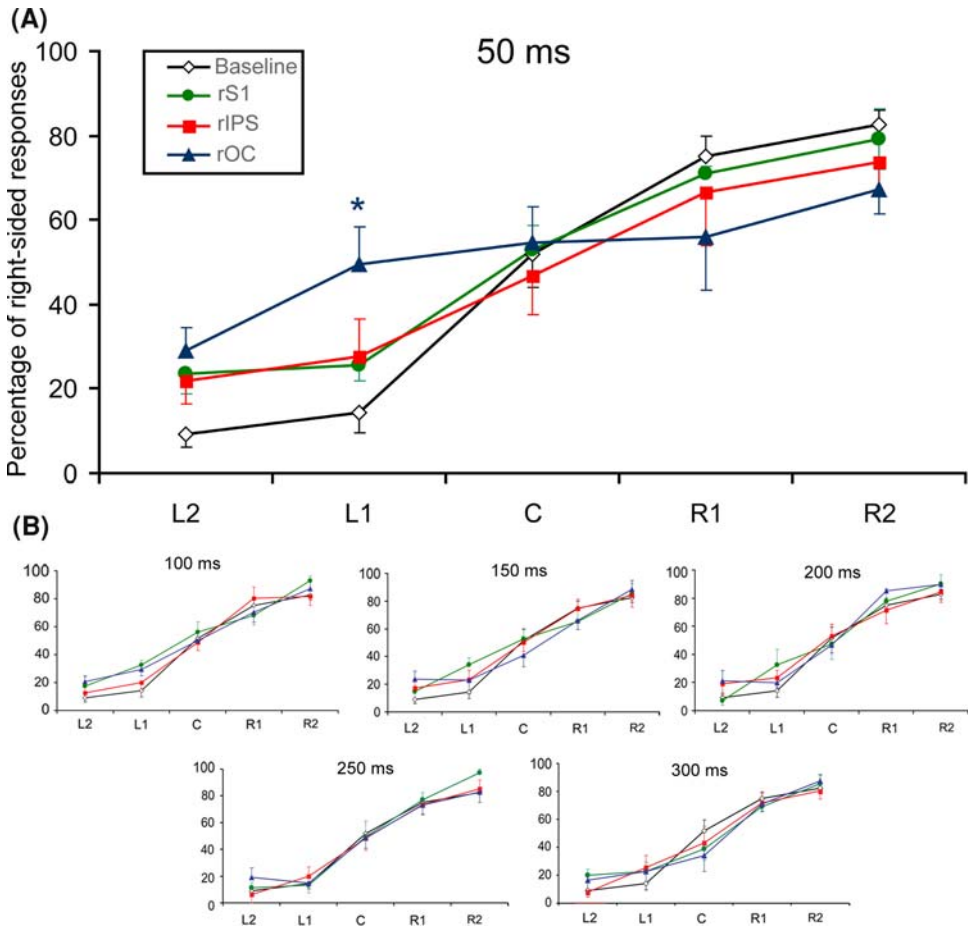

Fig. 2 Effects of virtual lesion on perceived location of sound. The figure represents the perceived location of sounds in baseline condition (*black* line; all panels) and when TMS was delivered at 50 ms (panel **a**) and at delays between 100 and 300 ms (panel **b**) after sound onset over the primary somatosensory control site (rS1 *green dots*), over the right dorsal extrastriate occipital cortex (rOC *blue triangles*) and over the right posterior parietal cortex (rIPS *red squares*). Sound location performance is expressed as the rate of right-sided responses depending on sound origin. Error bars denote standard errors. When compared to baseline as well as to the rS1 control site, a virtual lesion of the rOC 50 ms after sound onset led to a significant increase of erroneous right-sided responses for sound coming from the first left level (L1 see panel **a**). No significant changes in performance were found for TMS-to-sound asynchronies 100, 150, 200, 250 and 300 ms (panel **b**) (*$P < 0.05$)

had no significant influence on the performance after 50 ms.

In order to gain further insights into the functional reorganization of rOC and rIPS for the spatial processing of sounds following early visual deprivation, we compared the performance obtained in the present experiment with data gathered in sighted subjects in a previous experiment using the same paradigm (Collignon et al. 2008a). Data were analysed separately for each delay (50, 100, 150, 200, 250 and 300 ms) by means of three ways 2X4X5 ANOVAs with populations (Blind and Sighted) as the between-subject factor and sites (BASELINE, rS1, rIPS and rOC) and sound origins (L2, L1, C, R1, R2) as within-subject factors. For 50 ms delay, we only found a significant interaction between the factors sites and sound origins ($F(12/132) = 4.8$; $P < 10E\text{-}5$). Post-hoc analyses showed that a virtual lesion of rOC, when compared to rS1, yielded to an impairment in the spatial processing of sounds in both populations, especially for sounds coming from the left side (for L2, $P = 0.004$; for L1, $P = 0.002$). When TMS was delivered 100 ms after sound presentation, we found a significant triple interaction between the factors populations, sites and sound origins ($F(12/132) = 2.1$; $P = 0.02$). Post hoc-analyses showed that a virtual lesion of rIPS, when compared to rS1, yielded to an impairment in the spatial processing of L2 ($P = 0.0003$), L1 ($P = 0.000007$) and Central ($P = 0.005$) sounds in sighted subjects only. For the 150 ms delay, we found a tendency for a triple interaction between the factors populations, sites and sound origins ($F(12/132) = 1.7$; $P = 0.08$). Again, this indicates an increased proportion of right-sided responses for sounds coming from the left side and the centre following virtual lesion of rIPS in sighted subjects. Except for the main effect of sound origins, no results were significant when TMS was applied at longer delays (200–300 ms). A summary of the main results described above are illustrated in Fig. 3.

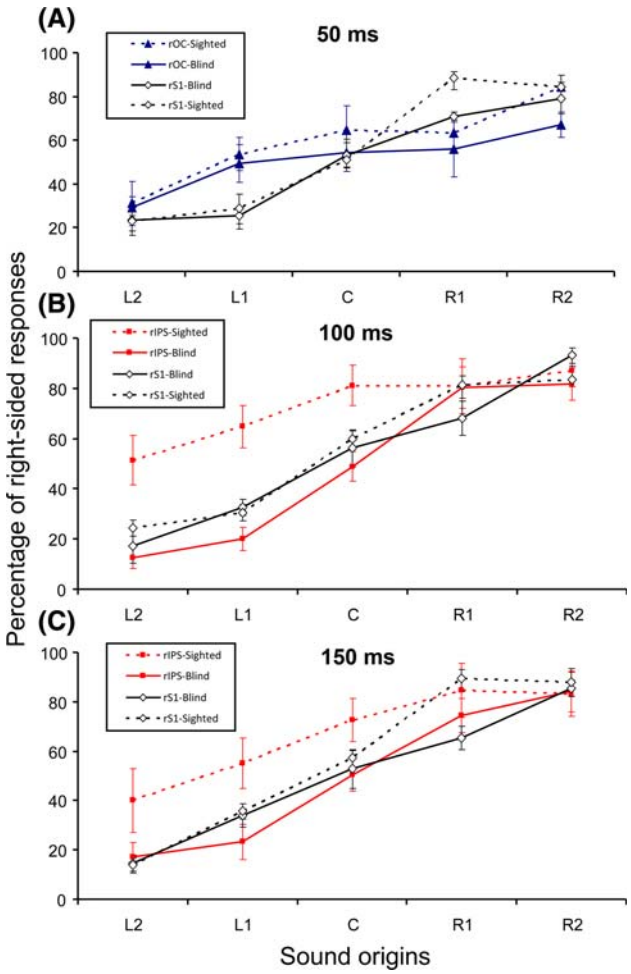

Fig. 3 Effects of the TMS in early blind compared to sighted subjects. This figure illustrates the influence of TMS on the performance obtained in the present experiment with EB when compared to the ones obtained previously in SS with the same paradigm (Collignon et al. 2008a). The effects of virtual lesions are illustrated only for delays where TMS proved to have a significant influence on the perceived location of sound either in the blind or in the sighted group. Sound location performance is expressed as the rate of right-sided responses depending on sound origin. Error bars denote standard errors. The figure represents the perceived location of sounds in the control condition where TMS was applied on rS1 (*black line*; all panels) and when TMS was delivered 50 ms after sound onset over rOC (panel **a**), when TMS was delivered 100 ms after sound onset over rIPS (panel **b**) and when TMS was delivered 150 ms after sound onset over rIPS (panel **c**). Continuous lines illustrate the performance of EB and dashed lines the performance of SS. When compared to the rS1 control site, a virtual lesion of the rOC 50 ms after sound onset led to a significant increase of erroneous right-sided responses for sounds coming from the left and a significant decrease of correct right-sided responses for sound coming from the right in both groups. However, TMS-induced virtual lesion of rIPS 100 and 150 ms after sound onset led to a significant disruption in the lateralization of the contralesional sounds in sighted subjects only, whereas TMS-induced virtual lesion of rIPS did not affect the sound lateralisation task in blind subjects

Discussion

The aim of the present study was to investigate further the role, and time-course, of rOC and rIPS involvement in a sound lateralization task in early blind subjects. To do so, we used TMS in order to interfere transiently and reversibly with the function of these two cortical areas. Combined with a precise quantification of the deficits resulting from such virtual lesions, this approach allowed us to investigate rIPS and rOC involvement in the spatial processing of sounds. In this study, rS1 was used as a control site to eliminate possible unspecific effects of TMS. Our results show that TMS applied over rIPS did not alter the spatial processing of auditory information in EB whereas a virtual lesion of rOC induced 50 ms after the stimulus presentation disrupted the spatial processing of sounds in the left hemispace.

Our observation that TMS over rIPS did not interfere with the spatial processing of sounds in EB at any delays contrasts with our previous findings in sighted subjects that a virtual lesion of rIPS affects the location of central and left-sided sounds when applied 100 and 150 ms after the stimulus onset (Collignon et al. 2008a) (Fig. 3b–c). Interestingly, in EB there are other examples of an absence of disruptive effect of TMS when applied over brain areas known to be involved, in sighted subjects, in a given process. For example, Cohen et al. (1997) found that TMS applied over the sensory-motor cortex significantly impaired the performance of sighted subjects during various tactile discrimination tasks whereas it had no effect in EB. Amedi et al. (2004) found that TMS applied over the inferior prefrontal cortex significantly decreased performance in a verb generation task in sighted subjects but not in an early blind group. It is worth noting that in the two aforementioned studies (Amedi et al. 2004; Cohen et al. 1997), as in the present one, the tasks investigated were systematically impaired following virtual lesion of the occipital regions, suggesting an extensive functional reorganization of the occipital cortex when deprived from visual inputs since birth (Bavelier and Neville 2002; Merabet et al. 2005).

In line with the present results, Zatorre et al. (2002) found that the right PPC activation observed in an auditory spatial task in sighted subjects was positively correlated with their performances. In contrast, Gougoux et al. (2005) failed to find such a correlation in EB though it was present for occipital regions. Altogether, these studies suggest that regions involved in specific cognitive abilities in sighted subjects may lose, at least partly, their functional specificity in blind subjects concomitantly with an increased contribution of occipital brain areas. In particular, the network normally dedicated to the processing of auditory spatial information may be more posteriorly distributed in EB. This hypothesis is consistent with previous studies showing that event-related potentials (ERPs) elicited by a change in the location of a repetitive sound are distributed on a more posterior portion of the scalp in EB than in sighted subjects (Kujala et al. 1992; Leclerc et al. 2000; Roder et al. 1999). Furthermore, in a PET study, Weeks et al. (2000) demonstrated elegantly that the neural network dedicated to auditory localization was shifted to posterior brain areas in EB when compared to sighted subjects, extending from the inferior parietal lobule (IPL) to dorsal occipital regions. Altogether, these results from the literature and those from the present study should not be regarded as evidence for a general lack of PPC involvement in auditory localization in EB, but probably for a lack of rIPS functional (causal) contribution to this process.

In sighted subjects, it is widely accepted that rIPS receives inputs from different sensory modalities and integrates space-related information gathered from these different modalities into a unique representation of the external space (Andersen 1997; Andersen and Buneo 2002; Eimer 2001; Grefkes and Fink 2005; Kennett et al. 2001; Mullette-Gillman et al. 2005; Schlack et al. 2005). Some authors have suggested that specific subregions of rIPS (the lateral or ventral intra-parietal regions) may code multisensory inputs in a predominantly eye-centered reference frame for action (Andersen and Buneo 2002; Avillac et al. 2005). Indeed, in sighted subjects, spatial sounds merge with other sensory inputs in the rIPS in order to remap multimodal information gathered in different reference frames in a common representation of external space, which is predominantly eye-centered because of the dominant role of vision in space processing. Hence, one may postulate that the absence of the visual input from early infancy would influence the neural responsiveness of the rIPS region to auditory space-related stimuli. Indeed, neurons in the Anterior Ectosylvian Sulcus (AES; possibly the cat's homolog of the primate PPC) in animals that have been dark reared do not show any evidence of multisensory integration capacities (supra-additive responses to bimodal events originating from the same spatial location) whereas these integrative properties are extensively present in sighted cats (Carriere et al. 2007). The present results obtained in EB suggest that this region may have lost its functional implication in the spatial processing of sounds, as a consequence of an early visual deprivation.

Another interesting finding of the present study is that, in EB, a virtual lesion of rOC induced disruption in the spatial processing of sounds, in particular those originating from the left hemispace. This is in agreement with previous neuroimaging studies showing an activation of this region during auditory spatial tasks in EB (Arno et al. 2001; De Volder et al. 1999; Leclerc et al. 2000; Poirier et al. 2006; Vanlierde et al. 2003; Weeks et al. 2000). The present TMS results thus provide further evidence that the right dorsal extrastriate occipital cortex is part of the brain network responsible for auditory spatial processing in EB (Collignon et al. 2007; Collignon et al. 2008b). We found here that virtual lesions of rOC affected the performance in the auditory lateralization task when applied 50 ms after sound onset. This early intervention of rOC in auditory spatial processing is in line with electrophysiological studies demonstrating that early auditory ERP component (the N1, beginning 80–100 ms after the onset of the stimulus) is enhanced in response to an auditory target during a spatial localization task on posterior electrodes in EB (Leclerc et al. 2000; Leclerc et al. 2005; Roder et al. 1999). Interestingly, it has been shown that TMS-induced virtual lesion

of the occipital cortex at a delay of 60 ms after stimulus presentation impaired the discrimination of tactile stimuli in EB (Pascual-Leone et al. 2005). Given the very short latency of the disruptive effect of TMS applied over rOC on auditory spatial processing and considering the absence of rIPS contribution to this function, we suggest that sounds may reach the occipital cortex in EB either via subcortical connections (Piche et al. 2007) or direct "feed-forward" afferences arising from the auditory cortex, as suggested by anatomical data gathered in monkeys (Falchier et al. 2002).

Surprisingly, no significant difference between early blind and sighted subjects was found when TMS was delivered over rOC whereas several studies have pointed to an enhanced activation of occipital regions during sound spatial processing in EB (Arno et al. 2001; De Volder et al. 1999; Gougoux et al. 2005; Leclerc et al. 2000; Poirier et al. 2006; Roder et al. 1999; Voss et al. 2008; Weeks et al. 2000). This observation reinforces the view that occipital involvement in auditory spatial processing is not a specific feature of EB and that, even in sighted subjects, occipital brain areas may be more involved in auditory processing than previously thought (Collignon et al. 2008a; Fishman and Michael 1973; Giard and Peronnet 1999; Lewald et al. 2004a; Molholm et al. 2002; Morrell 1972; Poirier et al. 2005; Zimmer et al. 2004). However, even if rOC participates in spatial hearing in blind and sighted subjects, we speculate that this region does not necessarily share similar principles of neuronal coding in both populations. In a previous study, we suggested that the disruption of auditory spatial tasks induced by rOC virtual lesions in sighted subjects may result from an alteration of the eye position signal or of the calibration of head-centred sound coordinates with respect to the position of the eyes in the orbit (Collignon et al. 2008a). These two mechanisms may not apply in EB because of the absence of vision since birth. Rather, the rOC contribution to auditory spatial processing in EB may be more related to sound processing per se. This view may be related to a recent PET study showing that the level of functional activation of this brain area was correlated with sound localization accuracy in EB but not in sighted subjects (Gougoux et al. 2005). Further studies are clearly needed to determine how crossmodal plasticity in congenitally blind people and multisensory processing in the occipital cortex of sighted people are linked.

Acknowledgements We wish to thank the blind volunteers for their participation. Thanks are also due to C. Veraart for discussions and to B. Gerard for technical help. This experiment was supported by an FRSM Grant #3.4505.04 (ADV). ADV is senior research associate and MD and OC are postdoctoral researchers at the National Funds for Scientific Research (NFSR; Belgium).

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