

Time-course of Posterior Parietal and Occipital Cortex Contribution to Sound Localization

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Abstract

■ It has been suggested that both the posterior parietal cortex (PPC) and the extrastriate occipital cortex (OC) participate in the spatial processing of sounds. However, the precise time-course of their contribution remains unknown, which is of particular interest, considering that it could give new insights into the mechanisms underlying auditory space perception. To address this issue, we have used event-related transcranial magnetic stimulation (TMS) to induce virtual lesions of either the right PPC or right OC at different delays in subjects performing a sound lateralization task. Our results confirmed that these two areas participate in the spatial processing of sounds.

More precisely, we found that TMS applied over the right OC 50 msec after the stimulus onset significantly impaired the localization of sounds presented either to the right or to the left side. Moreover, right PPC virtual lesions induced 100 and 150 msec after sound presentation led to a rightward bias for stimuli delivered on the center and on the left side, reproducing transiently the deficits commonly observed in hemineglect patients. The finding that the right OC is involved in sound processing before the right PPC suggests that the OC exerts a feedforward influence on the PPC during auditory spatial processing. ■

INTRODUCTION

It is now clearly established that many brain areas beyond the primary auditory cortex play a role in the spatial processing of sounds. Particularly, several functional neuroimaging and transcranial magnetic stimulation (TMS) studies have demonstrated the contribution of the posterior parietal cortex (PPC) to spatial hearing (Lewald, Foltys, & Topper, 2002; Maeder et al., 2001; Bushara et al., 1999; Griffiths et al., 1998). These findings have led to the conclusion that the PPC is part of an auditory “where” stream, projecting from the caudal superior temporal cortex to the dorsolateral prefrontal cortex (Warren & Griffiths, 2003; Zatorre, Bouffard, Ahad, & Belin, 2002; Rauschecker & Tian, 2000).

In addition, other brain areas, which are traditionally regarded as exclusively involved in visual information processing, seem to also play a role in auditory spatial processing. Indeed, several functional neuroimaging studies in humans and electrophysiological studies in animals have suggested a contribution of the extrastriate occipital areas (OC) to the spatial processing of sounds (Poirier et al., 2005; Zimmer, Lewald, Erb, Grodd, & Karnath, 2004; Maeder et al., 2001; Fishman & Michael, 1973; Morrell, 1972). Moreover, in a recent TMS study, Lewald, Meister, Weidemann, and Topper (2004) also evidenced the involvement of this area in spatial hearing in human

subjects. Taken together, these results challenge the classical view that the OC is exclusively dedicated to vision and suggest close interconnections between the neural representations of auditory and visual spaces.

However, two possible mechanisms may account for the contribution of the PPC and the OC in auditory spatial processing (Macaluso & Driver, 2005). The first hypothesis suggests a “feedforward” influence of the OC onto high-order multisensory regions such as the PPC, whereas the second one relies on “top-down” influences from the PPC on specialized areas such as the OC, via back-projections. New insight into the organization of the network responsible for spatial hearing could thus be gained by investigating the time-course of the PPC and the OC in the spatial processing of sounds. Recently, event-related potentials studies (Mishra, Martinez, Sejnowski, & Hillyard, 2007; Molholm et al., 2002; Giard & Peronnet, 1999) have shown that the latency of auditory-evoked activity in the occipital region can be as short as 50 msec. These results render unlikely the hypothesis that auditory input influences visual areas via feedback projections but rather favor the “feedforward” hypothesis (Foxye & Schroeder, 2005). If this latter hypothesis is correct, an earlier involvement of the OC compared to that of the PPC in a sound lateralization task should be observed.

TMS can be used to produce transient virtual lesions of a small brain region in healthy subjects. Combined with a precise quantification of the deficits resulting

from such virtual lesions, this approach permits to infer the contribution of the stimulated brain area to the task under investigation (Davare, Andres, Clerget, Thonnard, & Olivier, 2007; Davare, Andres, Cosnard, Thonnard, & Olivier, 2006; Walsh & Cowey, 2000). The aim of the present study was to determine the respective timing of the PPC and OC contribution to auditory spatial processing. To do so, TMS was applied over these cortical areas at different delays with respect to the stimulus presentation during an auditory lateralization task. TMS was also applied over the right primary somatosensory cortex (S1) to test for the specificity of the effects. As in previous TMS studies (Lewald, Meister, et al., 2004; Lewald, Wienemann, & Boroojerdi, 2004), we focused our investigation on the right hemisphere because of the large body of evidence indicating a right-hemispheric dominance for auditory spatial processing in humans (Lewald et al., 2002; Zatorre et al., 2002; Bushara et al., 1999; Weeks et al., 1999; Griffiths et al., 1998).

METHODS

Participants

Seven right-handed healthy participants (5 men; range = 23–31 years, mean \pm SD: 26 ± 3) participated in this study. Their vision was normal, or corrected-to-normal, and none of them had any neurological history. Subjects were screened for potential risk of adverse reactions to TMS by using the Transcranial Magnetic Stimulation Adult Safety Screen (TASS; Keel, Smith, & Wassermann, 2001). All experimental procedures were approved by the Ethics Committee of the Université catholique de Louvain, and all subjects gave their written informed consent.

Transcranial Magnetic Stimulation

We used two Magstim Model 200 single-pulse stimulators connected to a Bistim module (Magstim Company, Whitland, UK) to apply paired-pulse TMS (interval 5 msec) through a 70-mm outer diameter figure-of-eight stimulation coil. The use of short interval paired-pulse maximizes the disruptive capacities of TMS (compared to single-pulse TMS) while preserving the excellent temporal resolution of the technique (Davare et al., 2006). The coil was held tangential to the skull with the handle pointing leftward. 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 coregistration 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, TMS was applied over the right PPC, the right OC, and over the right primary somatosensory cortex (S1). S1 was used as a control stimulation site in order to eliminate nonspecific effects of TMS.

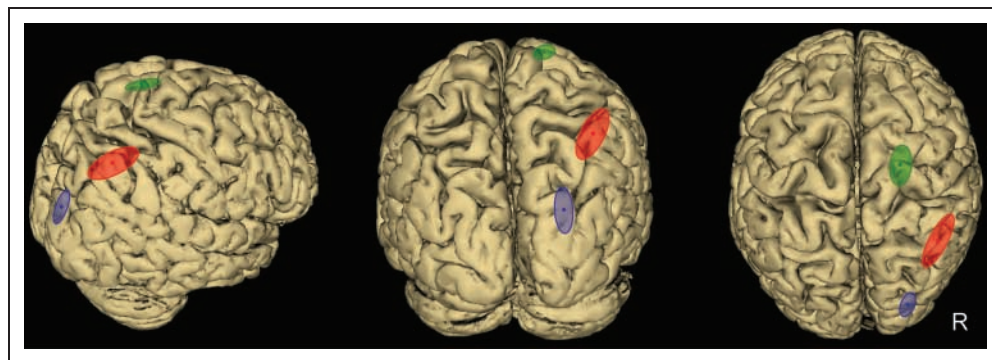
This site was targeted by positioning the coil over the superior portion of the right postcentral gyrus, roughly 20 mm laterally with respect to the interhemispheric fissure (Brodmann's areas 3, 1, 2). The PPC stimulation site was located over the right intraparietal sulcus (IPS), in front of the junction between the supramarginalis and angularis gyri (overlapping Brodmann's areas 7, 40), as determined on the basis of published results of a functional imaging study gathered during sound location tasks (Bushara et al., 1999). The OC stimulation site was located on the dorsal part of the right lateral occipital gyri (LOG), posterior to the transverse occipital sulcus (extrastriate occipital cortex corresponding to Brodmann's areas 18, 19). The software used for coregistration also allowed us 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 ($x,y,z \pm SD$, $n = 7$) of the stimulation sites were, respectively, 19 ± 5 , -34 ± 10 , 79 ± 2 mm for the S1 site; 39 ± 8 , -64 ± 13 , 50 ± 8 mm for the PPC site; and 25 ± 4 , -92 ± 6 , 28 ± 8 mm for the OC site (Figure 1). TMS was well tolerated and none of the subjects reported having experienced either phosphenes or any hints of tactile or auditory sensations following TMS.

Given that the coil was positioned more laterally for the PPC and OC conditions of stimulation, the contribution of additional spatial cues introduced by TMS may be greater than for the S1 control site. One may therefore wonder if part of the results we report in the present study may be due to indirect effects of TMS rather than to the actual contribution of the virtually lesioned cortical areas to sound localization. In order to rule out this possibility, an additional control experiment was performed on six subjects (3 men; range = 24–28 years, mean \pm SD = 26 ± 2) with the application of sham stimulation over the OC and PPC sites. Because our task required a manual response, we chose this method rather than a stimulation over S1 4 cm from the midline (like the PPC site) to avoid stimulation of the hand representation (Lotze et al., 2003). The mean normalized MNI coordinates ($x,y,z \pm SD$; $n = 7$) of the sham stimulation sites were, respectively, 40 ± 9 , -56 ± 16 , 50 ± 5 mm for the PPC and 24 ± 4 , -97 ± 5 , 20 ± 11 mm for the OC.

Stimuli and Procedure

Participants sat in a silent and darkened room and were asked to keep their eyes on a fixation point consisting of a 2° large white circle on a black background continuously displayed on the center of a computer screen. Participants were carefully positioned 60 cm from the computer screen, their heads exactly aligned with the screen's center and stabilized by restraints on both the chin and forehead.

Figure 1. Location of the TMS sites. Brain locations of the TMS coil positions to induce virtual lesion of the primary somatosensory cortex (S1; green), the posterior parietal cortex (PPC; red), and the dorsal extrastriate occipital cortex (OC; 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 ($x, y, z \pm SD$; $n = 7$) of the stimulation sites were, respectively, 19 ± 5 , -34 ± 10 , 79 ± 2 mm for S1; 39 ± 8 , -64 ± 13 , 50 ± 8 mm for the PPC; and 25 ± 4 , -92 ± 6 , 28 ± 8 mm for the OC. Each ellipse was centered on the mean MNI coordinates of S1, PPC, and OC stimulation points and their surface shows the 95% confidence interval of the normalized coordinates calculated for each subject.

Stimuli consisted of broad band-passed noise bursts (bandwidth of four octaves with a center frequency of 2 kHz, plateau time 40 msec, rise/fall time 5 msec) 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 center. The rationale for this normalization procedure was that subjects usually exhibited 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 primary cues for sound localization in azimuth, were then jointly adjusted to yield five distinct intracranial sound locations with position L2 (sound more clearly perceived at the left ear), position L1 (sound more slightly perceived at the left ear), position C (Central sound), position R1 (sound more slightly perceived at the right ear), position R2 (sound more clearly perceived at the right ear). ILD and ITD manipulation of auditory stimuli only produce intracranial sound images (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 participants’ performance, we used a staircase method to adjust individually ITDs and ILDs. Steps of 2% ILD were always paired with steps of 24 μ sec ITD and were adjusted to induce approximately 80% of correct responses in the less eccentric right or left position (L1 and R1) and 90% of correct responses in the more eccentric right or left position (L2 and R2). Across subjects, ILD differences were $4 \pm 1\%$ for R1 and L1 and $6 \pm 1\%$ for L2 and R2 and the ITD differences were, respectively, 46 ± 16 μ sec and 70 ± 16 μ sec. These sounds lead to a near-centered intracranial perceived location, roughly estimated to the foveal–parafoveal border if we

attempt to make a correspondence with 3-D sounds (Blauert, 1997). This adjustment was performed before each experimental session.

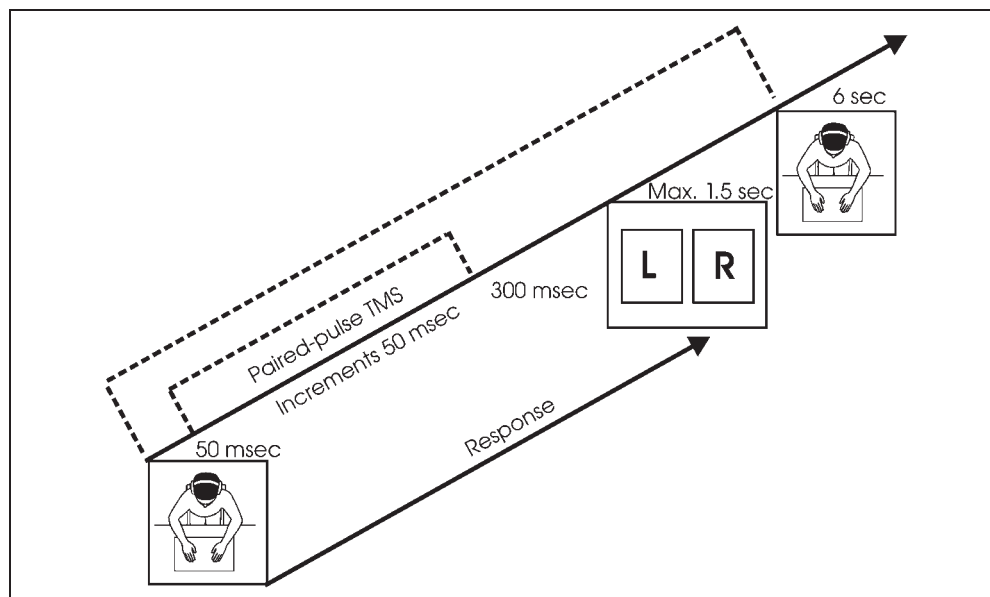
We used a two-alternative forced-choice task in which subjects were instructed to indicate the perceived intracranial position of the sound with respect to the median plane of the head (Blauert, 1997) by pressing a “left” or “right” key with the index finger of each hand. If subjects omitted to respond within 1.5 sec, the same trial was immediately presented again. Subjects were explicitly instructed to favor response accuracy rather than response speed.

In order to determine the time-course of PPC and OC 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 msec, by increments of 50 msec. TMS trials were randomly intermixed with trials with no TMS in order to determine a baseline in the auditory spatial task. Testing was divided across two experimental sessions, both lasting approximately 2 hr. Each session consisted of 12 experimental blocks, that is, 4 experimental blocks for each of the three stimulation sites. During each block, the five auditory stimuli were presented in a pseudorandom order either without TMS ($n = 5$) or with TMS applied at the six SOAs ($n = 30$), thus adding up to 35 trials per block. Block order was counter-balanced across subjects. In two successive blocks, TMS could never be applied over the same stimulation site and each site was preceded by the same number of blocks on the two other cortical locations.

Sounds were presented with an interstimuli interval of 6 sec (Figure 2). Stimuli presentation, TMS triggering, and randomization were controlled 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 minimize auditory interferences produced by the TMS coil while discharging. This hearing

Figure 2. Time-course of the task. Schematic representation of trial events. Virtual lesions induced by paired-pulse TMS (interval 5 msec) were delivered at six different delays after auditory spatial stimulus onset. Investigated sounds-to-TMS pulse onset asynchronies (SOAs) ranged from 50 to 300 msec, with increments of 50 msec. These TMS trials were randomly intermixed with trials without TMS to establish a baseline. Subjects determined the perceived location of the sound by pressing a left–right manual response key within 1.5 sec. Interval between two auditory spatial stimuli was 6 sec.



protector had a neckband system to allow the free positioning of the TMS coil over the scalp.

Statistical Analysis

Task performance was estimated by measuring the percentage of right-sided responses given following sounds

presented either to the left or right side, or at the center. Data were analyzed separately for each TMS delay (50, 100, 150, 200, 250, and 300 msec) by means of two-way 3×5 ANOVAs with sites (S1, PPC, and OC) and sound origins (L2, L1, C, R1, R2) as within-subject factors. Based on significant *F* values, Fisher post hoc analyses were performed when appropriate. Raw data are given in Table 1.

Table 1. Sound Location Performance

Sound Origin	TMS Sites	Baseline	50 msec	100 msec	150 msec	200 msec	250 msec	300 msec
L2	S1	9	23	24	14	6	22	14
	PPC	7	31	51	40	18	15	13
	OC	12	31	25	27	18	11	20
L1	S1	21	29	30	36	19	33	19
	PPC	23	44	65	55	37	29	22
	OC	18	54	28	35	20	24	28
C	S1	44	51	60	57	57	51	51
	PPC	51	63	81	73	66	47	65
	OC	49	64	57	60	55	55	54
R1	S1	82	88	81	89	82	79	87
	PPC	69	85	81	85	84	83	81
	OC	78	63	74	75	76	74	72
R2	S1	87	84	84	88	88	91	96
	PPC	89	89	87	83	87	83	88
	OC	82	85	80	88	81	80	83

Percentage of right-sided responses for both sound locations coming from the left side (L2: sound more clearly perceived at the left ear; L1: sound more slightly perceived at the left ear), for sounds coming from the center (C) and for both sound locations coming from the right side (R1: sound more slightly perceived at the right ear; R2: sound more clearly perceived at the right ear). Performance is illustrated according to TMS sites (S1, PPC, OC, sham PPC, and sham OC) and stimulus-to-TMS pulse onset asynchronies range from 50 to 300 msec and in baseline (no TMS).

RESULTS

The effect of the virtual lesions on sound localization is illustrated in Figure 3. For all delays, statistical analyses revealed a significant main effect of sound origins [$F(4/$

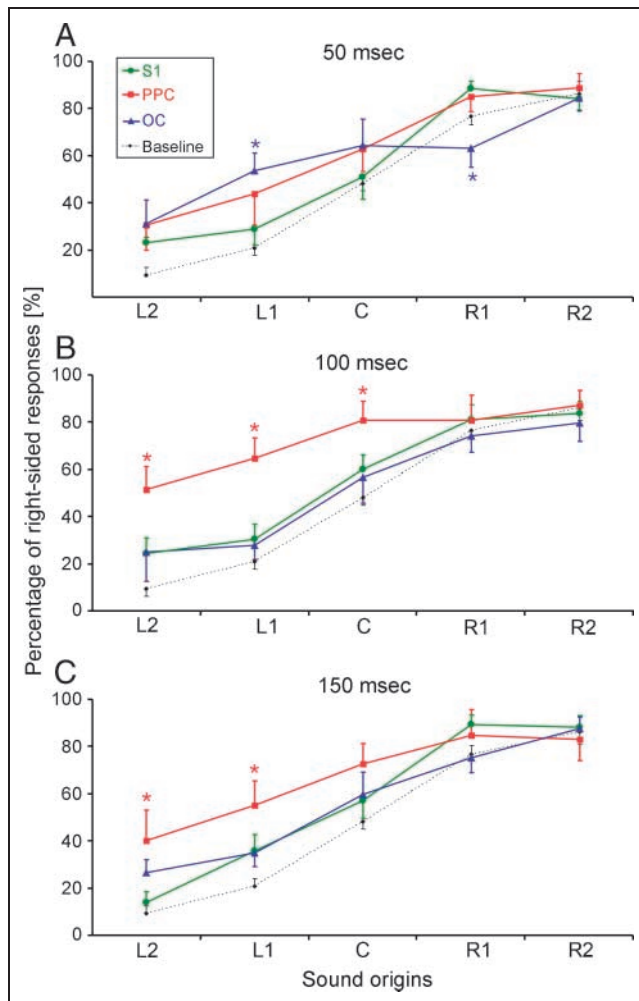


Figure 3. Effect of virtual lesions on perceived location of sound. The figure represents the perceived location of sounds in baseline condition (dashed line; all panels) and when TMS is delivered 50 msec (A), 100 msec (B), and 150 msec (C) after sound onset over the sensorimotor control site (S1; green dots), over the right dorsal extrastriate occipital cortex (OC; blue triangles), and over the right posterior parietal cortex (PPC; red squares). Sound location performance is expressed as the rate of right-sided responses depending on sound origin. Error bars denote standard errors. Compared to the S1 control site, virtual lesion of the OC led to a significant increase of erroneous right-sided responses for sound coming from the left (level L1) and a significant decrease of correct right-sided responses for sound coming from the right (level R1) when TMS was delivered 50 msec after sound onset. Moreover, virtual lesion of the PPC led to a significant increase of erroneous right-sided responses for sound coming from the left (level L1 and L2) when TMS was delivered 100 and 150 msec after sound onset and also an increase of right-sided responses for sound coming from the center (B) when TMS was delivered at 100 msec. Performance resulting from TMS-to-sound asynchronies 200, 250, and 300 msec are not illustrated because no significant effects were observed at these delays, whatever the sound origin. * $p < .05$.

24) from 19.6 to 91.17, all $p < .000001$]. As expected, these results showed that the proportion of right-sided responses increases progressively as we move from L2 to R2 (see Table 1).

When TMS was delivered 50 msec after the stimulus presentation (Figure 3A), we found a significant interaction effect between the sites and sound origins [$F(8/48) = 2.58, p = .02$]. Post hoc analyses showed that the percentage of right-sided responses was significantly higher when TMS was delivered over OC than over S1 ($p = .004$) for L1 sounds and significantly lower when TMS was delivered over OC than over S1 ($p = .004$) and PPC ($p = .012$) for R1 sounds. This indicates that a virtual lesion of OC induced 50 msec after the stimulus presentation impaired the ability to locate sounds bilaterally. The finding that this deficit was present only for sounds close to the midline may be explained by the fact that these sounds (L1 and R1) are more difficult to locate than the two eccentric ones (L2 and R2).

When TMS was delivered 100 msec after sound presentation (Figure 3B), we found a main effect of the sites [$F(2/12) = 5.52, p = .02$], indicating that the proportion of right-sided responses increased significantly following virtual lesion of the PPC when compared with S1 ($p = .02$) and OC ($p = .009$). Post hoc analysis revealed that this increase in right-sided responses consequent to right PPC lesions was only present for sounds originating from L2 ($p = .003$ compared to S1 and $p = .004$ compared to OC), L1 ($p = .0003$ compared to S1 and $p = .0001$ compared to OC) and C ($p = .02$ compared to S1 and $p = .007$ compared to OC). This indicates that, at this particular delay, a virtual lesion of the PPC induced a rightward bias for left and central sounds.

For the 150-msec delay (Figure 3C), we found a significant Sites \times Sound origins interaction [$F(8/48) = 2.51, p = .02$]. A post hoc analysis showed that the percentage of right-sided responses was significantly higher when TMS was applied over the PPC than over the S1 for sounds originating from L2 ($p = .0006$), L1 ($p = .009$), and C ($p = .04$). Moreover, the proportion of right-sided responses following PPC virtual lesion was also significantly higher than after OC lesion for L1 sounds ($p = .006$) and close to be significant for L2 ($p = .06$) and C ($p = .08$) sounds. This finding confirms that a virtual lesion of the right PPC induced 150 msec after sound onset yielded a rightward bias for left and central sounds, similar to that found for the 100-msec delay.

TMS applied at other delays had no effect. All statistical differences in TMS over the OC or the PPC compared to TMS over S1 were also significant when compared to baseline.

In order to control further for possible unspecific effects of TMS, we also applied sham stimulation over the OC and the PPC at delays for which TMS was found to affect sound localization (50, 100, and 150 msec). As previously, the percentage of right-sided responses were analyzed separately for the three delays by means of

two-way 3×5 ANOVAs with sites (S1, sham PPC, and sham OC) and sound origins (L2, L1, C, R1, R2) as within-subject factors. In contrast to what we found for actual TMS, the data gathered following sham TMS applied over either the OC or the PPC failed to reveal a main effect of the factor sites or an interaction effect between the factors sites and sound origins (F from 0.35 to 1.9, all $p > .2$). These results clearly favor the idea that interference in the spatial processing of sound resulted from a virtual lesion of the PPC and the OC rather than from nonspecific TMS effects.

DISCUSSION

The present study provides further evidence for the involvement of the PPC and the OC in auditory spatial processing. In addition, our results indicate that a virtual lesion of the right OC, occurring 50 msec after the stimulus onset, impairs the lateralization of sounds presented bilaterally, whereas a virtual lesion of the right PPC, induced 100–150 msec after the stimulus onset, leads to a rightward bias for sounds originating either from the center or from the left side. Therefore, the present study points to a distinct role of the right OC and the PPC in the spatial processing of sounds and also provides compelling evidence for an earlier contribution of the OC when compared with the PPC.

Contribution of the PPC in Spatial Sound Processing

Virtual lesion of the right PPC induced 100 and 150 msec after sound presentation induced a rightward bias for sound coming from the center and from the left side, confirming the functional role of this structure in spatial hearing. The lateralization of the effects is consistent with both electrophysiological studies in monkeys (Stricanne, Andersen, & Mazzoni, 1996) and neuroimaging studies in humans (Tiitinen et al., 2006; Palomaki, Tiitinen, Makinen, May, & Alku, 2005; Palomaki, Alku, Makinen, May, & Tiitinen, 2000), showing that the right PPC is preferentially tuned for sounds originating from the contralateral space. Moreover, we found that virtual lesions of the right PPC mimicked the rightward shift in perceived location of sounds classically observed in hemineglect patients with right parietal lesion (Pavani, Farne, & Ladavas, 2005; Tanaka, Hachisuka, & Ogata, 1999; Pinek, Duhamel, Cave, & Brouchon, 1989; Bisiach, Cornacchia, Sterzi, & Vallar, 1984). In fact, many neglect patients exhibit auditory as well as visual deficits, and the severity of these deficits seems to correlate (Pavani, Husain, Ladavas, & Driver, 2004; Pavani, Ladavas, & Driver, 2003). Consistently, it has been shown that, in healthy subjects, a TMS-induced virtual lesion of the right PPC led to a deficit in the spatial processing of visual (Thut, Nietzel, & Pascual-Leone, 2005; Bjoertomt,

Cowey, & Walsh, 2002; Fierro et al., 2000), auditory (Lewald et al., 2002), and tactile stimuli (Nager, Wolters, Munte, & Johannes, 2004).

The PPC receives extensive information from multiple sensory modalities (Lewis & Van Essen, 2000), and both electrophysiological studies in monkeys and neuroimaging studies in humans have shown that some regions in the IPS contain multisensory representations of external space (Avillac, Deneve, Olivier, Pouget, & Duhamel, 2005; Mullette-Gillman, Cohen, & Groh, 2005; Schlack, Sterbing-D'Angelo, Hartung, Hoffmann, & Bremmer, 2005; Bremmer et al., 2001; Stricanne et al., 1996). These findings have led to the view that some areas of the IPS are involved in the integration of different spatial reference frames built from distinct sensory modalities (e.g., vision is initially eye-centered, whereas audition is head-centered) in order to generate modality-invariant representations of the external space for actions (Mullette-Gillman et al., 2005; Schlack et al., 2005). Consequently, it can be assumed that, in the present study, TMS applied over the IPS actually interfered with a high-order region involved in multisensory spatial processing, resulting in an impairment in auditory spatial judgment.

Contribution of the OC in Spatial Sound Processing

The present study also showed that a virtual lesion of the OC interfered with a sound lateralization task. Such an involvement of early visual areas in auditory spatial processing may appear paradoxical from a classical perspective that rather predicts that these cortical areas process sensory-specific information. However, several animal and human studies have questioned this view by showing that auditory stimulation can drive (unisensory condition) or modulate (multisensory condition) some neural activity in the occipital areas (see Ghazanfar & Schroeder, 2006 for a review). In adult cats, Morrell (1972) has found that up to 41% of recorded neurons in extrastriate occipital areas could be driven by both visual and auditory stimuli and that the receptive fields of both responses typically spatially overlapped (Morrell, 1972; see also Fishman & Michael, 1973 for comparable results). This suggests a close interaction between these two modalities in occipital region for object localization. Recent studies in humans have also evidenced an occipital involvement in auditory spatial processing (Poirier et al., 2005; Renier et al., 2005; Lewald, Meister, et al., 2004; Zimmer et al., 2004). Moreover, cross-modal influence of auditory stimuli in the OC during spatial processing seems to depend on eye position in the orbit (Zimmer et al., 2004; see also Macaluso, Driver, Van Velzen, & Eimer, 2005; Macaluso, Frith, & Driver, 2002 for a role of eye position in tactile-induced visual activations). It seems therefore that a “remapping” across changes in posture to keep the different senses spatially aligned may not be an exclusive feature of high-order

multisensory brain areas such as the PPC but could even be present in the so-called unimodal brain region. The occipital cortex may thus be a primary relay involved in the calibration of head-centered sound coordinates with respect to the position of the eyes in the orbit. In the study of Zimmer et al. (2004), the finding that the right occipital region was identically activated for left and right sound presentation, in combination with eccentric eye position, coincides with our result that TMS disrupted sounds coming from both the left and right sides. This could be due to the fact that either left or right sounds (in head-centered reference frame) could arise in the left visual field depending on the eye position in the orbit. We thus speculate that TMS may have disrupted the neural process responsible for the remapping of sound location relative to the actual eye position (which was always straight ahead in the present study), inducing an alignment of near-centered auditory stimuli with the central eye fixation. For more eccentric sound locations, it is possible that the disruption in coordinate alignment caused by TMS was not sufficient to produce errors in location judgment. The present results may thus provide support to the recent hypothesis challenging the traditional “visually specific” view of the occipital cortex (Pascual-Leone & Hamilton, 2001) and suggest the presence of neural circuits processing auditory spatial information in this region, putatively to calibrate and integrate auditory and visual spatial frames of references.

The finding that TMS influenced auditory spatial processing earlier when applied on the OC (50 msec) than on the PPC (100–150 msec) strongly favors a “feedforward” influence of the occipital areas onto the parietal ones. Interestingly, the timing of occipital TMS interference on auditory processing found in the present study is remarkably consistent with previous electroencephalogram and magnetoencephalogram studies demonstrating early auditory influences (~50 msec after sound onset) on occipital regions (see Foxe & Schroeder, 2005 for a review). Along these lines, recent anatomical studies have provided evidence for direct projections from the auditory cortex to the visual cortex in monkeys (Clavagnier, Falchier, & Kennedy, 2004; Rockland & Ojima, 2003; Falchier, Clavagnier, Barone, & Kennedy, 2002). If we hypothesize that such connections exist in humans, auditory spatial information could be conveyed to the OC via this pathway and, in the present study, TMS may have interfered either with the transfer or the processing of this information to the OC, as early as 50 msec after sound presentation.

However, although we found that TMS applied over the OC impaired sound localization abilities, this may not necessarily point to a direct contribution of this area to auditory spatial processing per se. Firstly, one may argue that visual imagery account for the OC’s contribution to nonvisual processing (Sathian, Zangaladze, Hoffman, & Grafton, 1997). Nonetheless, the early TMS effect (50 msec) and the

relatively simple left–right judgment required in this task do not support this hypothesis. A second plausible explanation for the present results lies in the fact that virtual lesions of the OC could have altered an eye position signal, known to be present in the dorsal extrastriate occipital region (Rosenbluth & Allman, 2002; Trotter & Celebrini, 1999; Law, Svarer, Rostrup, & Paulson, 1998; Galletti, Battaglini, & Fattori, 1995) and further used in the processing of auditory spatial cues. We know from behavioral experiments that eye position influences the localization of sounds (Lewald, 1998; Lewald & Ehrenstein, 1996). It would therefore be possible that an incorrect eye position signal induced by OC virtual lesions could be relayed to multisensory cortical areas such as the PPC, wherein eye position is integrated into auditory coordinates, and thus, leads to a misallocation of auditory sources. Because right extrastriate occipital activity may be evoked by left or right eye position (Nakamura, Chung, Graziano, & Gross, 1999; Trotter & Celebrini, 1999; Galletti et al., 1995), our TMS may have induced a bilateral disruption of the neural coding of the actual central eye position, thus leading to an increase of the central perception of the near-centered sounds.

In contrast with the present study, we have previously observed that virtual lesion of the right dorsal occipital region by TMS disrupted auditory spatial performance in blind but not in sighted participants (Collignon, Lassonde, Lepore, Bastien, & Veraart, 2007). We postulated that the occipital contribution to auditory spatial processing could be less important in sighted participants because vision dominates the spatial representation in this area compared to blind participants, in whom this region is more extensively activated by auditory inputs, probably because of cross-modal reorganizations (Bavelier & Neville, 2002). The use of a different—and presumably more disruptive—TMS protocol (double pulse event-related TMS vs. 1-Hz off-line TMS in our previous study) and a more demanding auditory spatial task could explain, at least in part, the discrepancies between these two studies. Moreover, the present experiment required an absolute sound lateralization relative to the intracranial auditory median plane of the head, compared to our previous study where the participants were asked to judge the relative position of two external sounds. Moreover, another factor that differentiates both studies is that participants had to fixate a visual target throughout the experiment in the present study. One may wonder if the fact that subjects were fixating a visual stimulus had influenced the results, for example, by inducing a remapping of near-centered sounds to a straight-ahead position determined by the position of the eyes. Further studies, for example, in the dark or with eyes closed, are needed to clarify this point: They should investigate further the role of the OC in equivalently sensitive tasks requiring either absolute or relative judgments on sound positions as well as the influence of the presence (or absence) of a visual frame of reference during such tasks.

Conclusion

The present findings shed new light on the time-course of the contribution of the OC and the PPC to spatial hearing. Because previous electrophysiological experiments demonstrated that some neurons in the OC and the PPC have spatially overlapping auditory and visual receptive fields (Mullette-Gillman et al., 2005; Schlack et al., 2005; Fishman & Michael, 1973; Morrell, 1972), we speculate that TMS disruption of the OC and the PPC may have affected regions involved at different levels in the neural network dedicated to the alignment of auditory and visual spatial frames of references. The earlier intervention of the OC compared to that of the PPC in spatial sound processing might indicate that the OC represents a preliminary step in the remapping process, and thus, exerts a “feedforward” influence on the PPC in the production of a multisensory spatial percept for action. Another possible explanation is that OC virtual lesions yielded an incorrect eye position signal subsequently sent to multimodal cortical areas such as the PPC, where it is integrated to auditory coordinates and leading, therefore, to a sound misallocation. Further neurophysiologic investigations will be needed to address the precise and respective role of occipital and parietal regions in the spatial processing of auditory information, for example, by comparing directly the influence of head or eye position on auditory receptive fields in both regions.

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