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The effect of brain lesions on sound localization in complex acoustic environments

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Localizing sound sources of interest in cluttered acoustic environments—as in the 'cocktail-party' situation—is one of the most demanding challenges to the human auditory system in everyday life. In this study, stroke patients' ability to localize acoustic targets in a single-source and in a multi-source setup in the free sound field were directly compared. Subsequent voxel-based lesion-behaviour mapping analyses were computed to uncover the brain areas associated with a deficit in localization in the presence of multiple distracter sound sources rather than localization of individually presented sound sources. Analyses revealed a fundamental role of the right planum temporale in this task. The results from the left hemisphere were less straightforward, but suggested an involvement of inferior frontal and pre- and postcentral areas. These areas appear to be particularly involved in the spectrotemporal analyses crucial for effective segregation of multiple sound streams from various locations, beyond the currently known network for localization of isolated sound sources in otherwise silent surroundings.

Keywords: sound localization; auditory scene analysis; selective attention; stroke; human
Abbreviation: VLBM = voxel-based lesion-behaviour mapping

Introduction

Localizing and orienting to the source of a sound is often the first step when responding to an event in the environment. The subcortical and cortical mechanisms underlying this crucial process in human space perception have long been investigated using various methodological approaches. It is well known that auditory localization relies on the processing of interaural differences in level and time as well as monaural spectral cues (Middlebrooks and Green, 1991). Most of these basic neurocomputations for the generation of auditory space have been demonstrated in the subcortical auditory pathway, including brainstem, thalamus and midbrain, up to the primary auditory cortex. Beyond primary auditory areas, processing of sound location at the cortical level has been shown to take place in a network encompassing primarily dorsal areas, including posterior parts of superior temporal gyrus, inferior parietal lobule, and superior frontal sulcus, but also involving ventral areas, such as the anterior temporal lobe and inferior frontal lobe (Arnott *et al*., 2004; Lewald *et al*., 2008; Recanzone, 2011). Until now, almost all studies that have investigated the neural underpinnings of sound localization have implemented a single sound source presented in otherwise silent surroundings. Such an acoustic situation is extremely artificial, because in natural environments auditory events usually do not occur in isolation. Rather, a listener is typically faced with a multitude of simultaneously present sound sources at various locations. The extraction

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and localization of the event of interest in such a complex acoustic environment represents a substantially higher demand of auditory processing, as it requires the simultaneous analysis of non-spatial aspects, such as spectral content, in addition to genuine spatial cues.

Using functional MRI, MEG (magneto-encephalography), and EEG, several previous studies have focused on non-spatial aspects of the segregation of multiple sounds and have observed involvement of auditory cortex (Gutschalk *et al*., 2007; Schadwinkel and Gutschalk, 2010, 2011), inferior and middle frontal gyri, superior temporal gyrus, perirolandic cortex (Dykstra *et al*., 2011), and intraparietal sulcus (Cusack, 2005; Teki *et al*., 2011). However, the question of how the brain analyses and concentrates on the location of a sound of interest in the presence of multiple, spatially separated distracter sources—as in the so-called 'cocktail-party' situation (Cherry, 1953; Bregman, 1971)—to date has received only marginal attention. Using functional MRI in combination with presentation of multiple virtual sound sources in healthy participants, Zündorf *et al*. (2013) revealed widespread activity in posterior superior temporal gyrus, anterior insula, supplementary motor area, and a frontoparietal network during localization of a target sound in a 'cocktail-party' situation. Contrasts indicated a critical role of planum temporale and inferior frontal gyrus in extracting the sound of interest among the acoustical distracters, and of the precuneus in orienting spatial attention to the target location (Zündorf *et al*., 2013).

In the present study, naturally occurring stroke lesions are used to uncover the brain areas associated with a deficit in sound localization in cluttered auditory environments ('cocktail-party' situation) as compared to a preserved or only slightly disturbed single-source localization. Unlike functional MRI in healthy participants, lesion analyses allow us to identify those areas the integrity of which is necessary to successfully perform the respective task. Most previous studies with brain damaged individuals have focused on the localization of single stimuli (Clarke *et al*., 2000, 2002; Spierer *et al*., 2009). Only one study has investigated disturbances in sound lateralization in a quasi multi-source situation. Efron *et al*. (1983) presented patients with left or right anterior-temporal cortectomy with five environmental sounds through headphones that were distributed along the interaural axis by means of interaural level differences. They observed more errors in localization for target sounds to the contralesional (17%) than to the ipsilesional side (5%). However, with respect to the neural processing of sound location, these findings must be taken with caution as there is growing evidence that results obtained with interaural differences or even virtual sound sources (generated using head-related transfer functions) are less reliable than those obtained with actual free-field sound sources (see Getzmann and Lewald, 2010). Thus, the impact of focal brain lesions on auditory spatial functions under realistic conditions with multiple sources in the free soundfield has remained almost totally unknown.

The present voxel-based lesion-behaviour mapping (VLBM) study aimed to fill this gap. Stroke patients with chronic unilateral brain damage were tested for specific deficits in sound localization in a free-field multi-source environment. Target sounds were presented simultaneously with multiple auditory distracters and direct comparisons between processing of single versus multiple sound sources were conducted.

Materials and methods

Participants

Fifty neurological patients [mean age 61.9 years, standard deviation (SD) 10.8 years; age range 32–79 years; 30 male] suffering from first-ever, unilateral cerebral stroke with cortical involvement (23 left-sided, 27 right-sided) admitted to the Centre of Neurology at Tübingen University, participated in the experiment. Patients with diffuse lesions, tumours, further neurological or psychiatric disorders, severe comprehension/communication disabilities, or asymmetrical hearing loss (see below for details), as well as patients whose magnetic resonance or CT scan did not reveal any obvious lesion, were not considered. Patients with persistent aphasia were considered for participation based on a screening interview either with the patient directly or with a family member, assessing the patient's general ability to understand and communicate. Patients were behaviourally tested during the chronic phase of the stroke (mean time post-stroke 1033 days, SD 642). Clinical and demographic data are presented in Table 1. In addition, 20 healthy age-matched (mean age 58.8 years, SD 7.5; age range 50–72 years; 10 male) participants were investigated. All participants gave their written informed consent to participate in the study that was conducted in accordance with the ethical standards laid down in the Declaration of Helsinki and approved by the local Ethics Committee.

Clinical examination

All participants underwent standard audiometry and were tested for spatial neglect as well as for visual and auditory extinction during the same session as the experimental task.

Pure tone audiometry was conducted at frequencies of 0.25, 0.5, 1, 1.5, 2, 3, 4, 6 and 8 kHz. Participants were classified using the hearing impairment classification of the World Health Organization (WHO) guidelines (1991); mean hearing thresholds of $\leqslant 25$ dB Hearing Level (HL) across frequencies and both ears were considered normal (Table 1). Brain damaged patients, as a group, did not differ from healthy controls with respect to the proportion of hearing impairment classes (Fisher's exact test, $P = 0.056$). As there is growing evidence that performance in single- or multi-source localization is independent of hearing thresholds (Lewald and Hausmann, 2013), we refrained from excluding individuals with hearing impairments. On the other hand, a difference in mean hearing thresholds between both ears of >10 dB was considered asymmetrical and led to exclusion, as asymmetrical hearing loss is known to have an impact on sound localization performance (Blauert, 1997).

In right brain damaged patients, spatial neglect was assessed using three standard tests: Bells Test (Gauthier *et al*., 1989); Letter Cancelation Task (Weintraub and Mesulam, 1985); and Copying Task (Johannsen and Karnath, 2004). In left brain damaged patients, only the Bells Test was applied. The cancellation tasks were scored using the Centre of Cancellation measure and software (Rorden and Karnath, 2010). Centre of Cancellation scores >0.09 in the cancellation tasks and a score of >1 in the copying task (Johannsen and Karnath, 2004) indicated spatial neglect.

Visual extinction was tested by presenting geometric shapes (square, circle, rhomb, triangle; size 1.5° visual angle) for 180 ms on a PC

Table 1 Clinical and demographical data of participants

	Left brain damage	Right brain damage	Healthy controls
n	23	27	20
Sex (M/F)	16/7	14/13	10/10
Age (SD)	65.0 (7.9)	59.3 (12.3)	59.0 (7.5)
Hearing loss*			
% normal	52	59	90
% mild	26	37	10
% moderate	13	4	0
% severe	9	0	0
Spatial neglect			
% present	0	0	
CoC-score**	0	0	
Extinction			
% present visual	0	7.4	
% present auditory	0	11	
Aphasia, % present	17.4	0	
TSL and imaging days (SD)	2.8 (3.1)	2.6 (2.4)	
TSL and sound localization testing days (SD)	983.8 (431.7)	1088.7 (625.0)	
Lesion size, mean voxels (SD)	4700 (5369)	6554 (8788)	

*Hearing thresholds of $\leqslant 25$ dB [HL (hearing level)] were considered as normal, 26–40 dB HL as mild, 41–60 dB HL as moderate, 61–80 dB HL as severe, and $\geqslant 81$ dB HL as profound hearing loss (WHO, 1991).
**Averaged over Bells Test and Letter Cancellation Task.
CoC = Centre of Cancellation; TSL = time since lesion.

monitor at an eccentricity of 10° either to the left or to the right (10 trials each) or bilaterally (10 trials) of a central fixation cross in pseudorandom order. Ten points were counted for each missed contralesional stimulus, five when the contralesional stimulus was detected, but not identified. Auditory extinction was tested presenting white noise stimuli (duration 40 ms; rise/fall time 20 ms) either to the left or to the right (10 trials each) or binaurally (10 trials) through headphones (K 271 STUDIO, AKG) in pseudorandom order. Patients were classified as showing visual and/or auditory extinction when they correctly responded to at least 90% of the unilateral stimuli on each side, but failed to perceive the left stimulus during bilateral stimulation in >50% of the trials.

Sound localization task

Sound localization of individually presented sounds (single-source condition) as well as localization of a target sound with multiple auditory distracters (multi-source condition) was tested using the same experimental set-up, stimuli, and pointing procedure as in Zündorf *et al*. (2011). In brief, five environmental sounds (dog barking, baby crying, man laughing, cuckoo clock, telephone ringing) were selected from an online sound library (Marcell *et al*., 2000) based on their familiarity and recognizability. Verbal sounds were not included as such stimuli represent a potential confound in aphasic patients. All sounds lasted 2 s and were digitized at 44.1 kHz sampling rate and 16-bit resolution using Cool Edit 2000 software (Syntrillium Software Corporation). The experiment was conducted in a sound-proof room. The participant sat on a comfortable chair and was surrounded by a semicircle on the horizontal plane (1.5 m radius), supporting five broadband loudspeakers ($5 \times 9\,cm^2$; SC 5.9, Visaton). Speaker positions were at 90° and 45° to either side of the participant's median plane, and within the participant's median plane (0°), at ear level. Speakers were covered by acoustically transparent fabric.

For response a swivel hand pointer was mounted in front of the participant. The swivel pointer consisted of a metal rod that the participant could rotate in the horizontal plane (Lewald *et al*., 2000). The position of the pointer was recorded by a potentiometer. A key was mounted on the upper side of the rod. The position of the pointer was recorded when participants pressed this response key. Participants wore a blindfold and their head was fixed by stabilizing rests for forehead and occiput.

For the single-source condition, each target sound was presented five times (one presentation at each of the five speaker positions) in pseudorandom order, thus comprising 25 trials in total. This task was immediately followed by the multi-source condition, in which all five sounds were presented simultaneously, each sound coming from a different speaker position. Twenty combinations of the five sounds for the five positions were selected. Each combination was presented twice for each target sound, 10 times in total (200 trials in all). Trials were presented in five blocks, each consisting of 40 trials. During each block, the participants were instructed to sustain attention to one target sound. A fixed, pseudorandom order of combinations of sound positions was generated for each block, which was identical for all participants. The order of the trials was constrained such that successive repetitions of identical or similar auditory scenes were excluded, with balanced distribution of the location of the target sound. In breaks between blocks, participants were verbally instructed by the experimenter which sound was the target in the next block. Stimuli were presented with a fixed intertrial interval of 8 s. Participants were instructed to attentively listen to the sounds as long as they were present. Within 5 s after sound offset, the participants had to respond, and 6 s after sound offset the next trial began. The participants were instructed to point with the swivel pointer as accurately as possible toward the location of the target sound. The mean absolute error in pointing to the target (i.e. the unsigned deviation of the pointing direction with respect to the actual target location) was used as the

measure of localization performance in both conditions. We were specifically interested in the characterization of deficits in localization of a target sound in the presence of multiple auditory distracters rather than general sound localization deficits affecting also localization of individually presented sound sources.

For this purpose, in a first approach, we calculated the difference between the participants' mean absolute errors obtained in the multi-source and the single-source conditions and normalized this value with reference to the analogue difference obtained from the control sample. This measure served as the dependent, continuous variable for the first VLBM analysis. In a second approach, we implemented the revised Standardized Difference Test introduced by Crawford and Garthwaite (2005). With this single-case approach, the performances measured in both tasks were converted to *z*-scores, based on the data of the control sample. The difference between these two *z*-scores was divided by the standard deviation of the differences between the two *z*-scores, referred as Z-DCC (Crawford *et al*., 2010). Thus, for each patient a fully normalized value was computed, representing the magnitude of the difference in individual performance between the tasks by taking into account the performance of the control group in both tasks and their respective difference. This computation highlights those patients with large differences in the performance between the multi-source and the single-source condition tasks. We thus obtained (i) a group of subjects in whom the differences between both tasks were statistically significant in comparison with the performance of controls; and (ii) a group of subjects in whom this test did not reach significance. We used the effect size (Z-DCC) for the difference between single subject and controls as the dependent, continuous variable for the second VLBM analysis.

Lesion analysis

All patients included in the study had unilateral lesions as a result of haemorrhage or ischaemic stroke demonstrated by magnetic resonance or CT scans. Patients underwent imaging at admission and consecutive days until a conclusive diagnosis could be made. The mean time between stroke onset and imaging for all patients was 2.7 days (SD 2.7). For patients with magnetic resonance scans, we used diffusion-weighted imaging when imaging was conducted within the first 48 h post-stroke and T_2-weighted FLAIR sequences when the images were acquired at least 48 h after stroke onset.

Lesion borders were marked directly on the individual magnetic resonance or CT scans using MRIcroN software (www.mricro.com/mricron). Subsequently, both the anatomical scan and the lesion shape were mapped onto stereotaxic space using the 'Clinical Toolbox' for normalization (Rorden *et al*., 2012; http://www.mccauslandcenter.sc.edu/CRNL/clinical-toolbox) implemented in the SPM8 software package (Wellcome Department of Cognitive Neuroscience, University College London, UK; http://www.fil.ion.ucl.ac.uk). To investigate the relationship between lesion location and performance in sound localization with multiple sound sources, VLBM analyses were performed by using the *t*-test statistics of the NPM software (Rorden *et al*., 2007) provided by the MRIcroN software package. Separate analyses were computed for the patients with left brain damage and right brain damage, respectively. We conducted *t*-tests on voxels damaged in at least 15% of individuals of the sample ($n = 3$, left brain damage; $n = 4$, right brain damage), and thresholded with a 5% false discovery rate (FDR) to control for multiple comparisons. Coordinates [*x*, *y*, *z* (mm)] are in Montreal Neurological Institute (MNI) space. To relate the resulting statistical maps to cortical structures, we overlaid the maps on the Automated Anatomical Labelling atlas (Tzurio-Mazoyer *et al*., 2002) distributed with MRIcron.

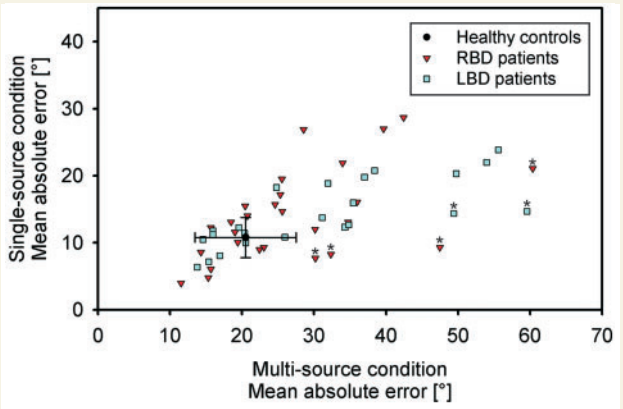

Figure 1 Sound localization performance of individual stroke patients and healthy controls in the single-source and multi-source conditions. Red triangles indicate data of patients with right brain damage (RBD), light blue squares represent data of patients with left brain damage (LBD). Patients with significant revised Standardized Difference Test are represented with an asterisk above the data point. The black circle indicates the group average of healthy controls. Error bars, standard deviations (in healthy subjects).

Results

Behavioural performance

Figure 1 shows the performances in sound localization for the single-source and multi-source conditions. In healthy participants, the mean absolute error was 10.8° (SD 3.0°) in the single-source condition, and 20.5° (SD 7.0°) in the multi-source condition. For patients with left and right brain damage, the mean absolute error in the single-source condition was 14.2° (SD 4.9°) and 14.1° (SD 6.8°), respectively. In the multi-source condition, the mean absolute error for patients with left and right brain damage was 31.2° (SD 14.5) and 27.1° (SD 11.4), respectively. To analyse the specific ability to localize a target sound in the presence of multiple auditory distracters we calculated the difference between the mean absolute errors in the multi-source minus the single-source conditions for each participant and normalized this value based on the analogue difference value obtained from the control sample. The mean of these difference values was 0.01° (SD 1.00°) in healthy participants, 1.07° (SD 1.69°) in patients with left brain damage, and 0.51° (SD 1.41°) in patients with right brain damage. A one-way ANOVA on this variable across the three subject groups did not reach significance [$F(2,67) = 3.049$, $P = 0.054$], although there was a numerical tendency towards a greater difference between single- and multi-source localization in the group with left brain damage than in the right brain damage and control groups. Based on the revised Standardized Difference Test, four (14.8%) patients with right brain damage and two (8.7%)

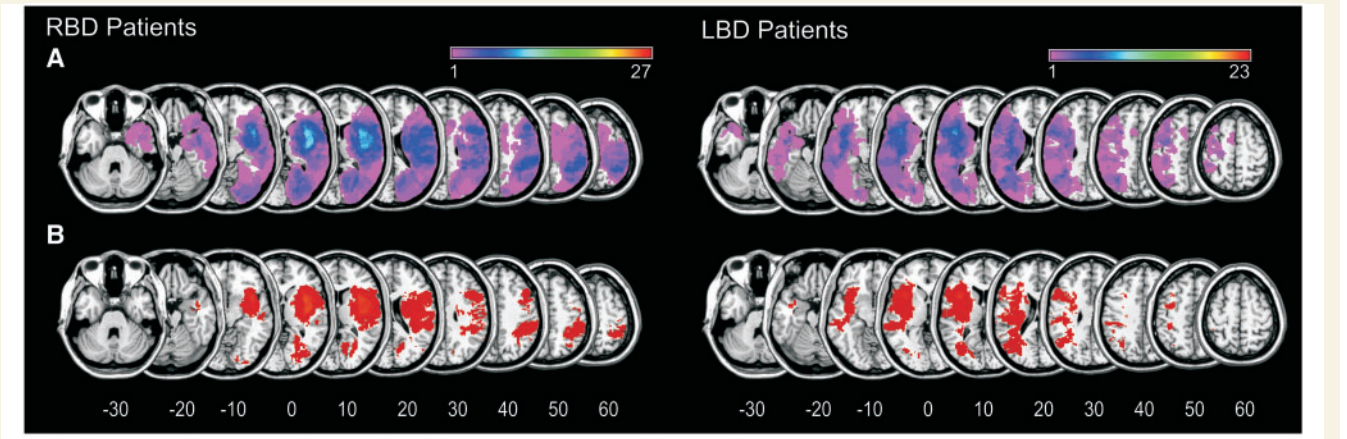

Figure 2 Overlap plots and voxels included in the statistical analyses. (**A**) Overlapping lesion plots for patients with right (RBD) and left (LBD) brain damage. The number of overlapping lesions is illustrated by different colours coding increasing frequencies from violet ($n = 1$) to red (n = maximum). (**B**) Voxels included in the statistical analysis, at least affected in 15% of the subjects. MNI z-coordinates (mm) of each transverse section are given.

patients with left brain damage were significantly worse in multi-source, as compared to single-source, localization.

Lesion analysis

Figure 2A shows the simple lesion overlays of all participants and Fig. 2B the voxels that were subject of the statistical VLBM analyses (i.e. those voxels there were affected in at least 15% of the subjects). We compared the size of the lesions in both groups to account for the potential impact of lesion size on the results of behavioural and lesion analyses. The mean size of the lesions was 4700 voxels (SD 5369) in the group with left brain damage and 6554 voxels (SD 8788) in the group with right brain damage, with no significant difference between groups [$t(48) = 1058$, $P = 0.30$].

The first VLBM analysis was based on each participant's difference between the mean absolute errors in the multi-source minus the single-source conditions, normalized on the difference obtained from the control sample. Patients with left and right brain damage were analysed separately (Fig. 3). In patients with right brain damage, the resulting lesion area ($t \geqslant 2.99$, $P < 0.05$, FDR corrected) overlapped mainly the superior temporal gyrus (86.2% of the lesion map; peak: $x = 52$, $y = -35$, $z = 8$) and to a lesser extent the supramarginal gyrus (3.8%; $x = 60$, $y = -35$, $z = 25$) and angular gyrus (1.8%). In patients with left brain damage, the lesion area ($t \geqslant 3.49$, $P < 0.05$, FDR corrected) overlapped the precentral gyrus (62.2%; $x = -49$, $y = -6$, $z = 22$), inferior frontal operculum (17.0%; $x = -40$, $y = 13$, $z = 18$), rolandic operculum (10.5%; $x = -49$, $y = -11$, $z = 20$) and to a lesser extent the postcentral gyrus (4.5%; $x = -52$, $y = -9$, $z = 20$).

The second VLBM analysis was based on the effect size (Z-DCC) obtained from the revised Standardized Difference Test (Crawford and Garthwaite, 2005; Crawford *et al.*, 2010). No voxels of the statistical maps resulting from this analysis survived the correction for multiple comparisons. We thus performed subtraction analyses (Rorden and Karnath, 2004) between patients with versus without statistically significant differences between multi-source and single-source sound localization, as obtained by the revised Standardized Difference Test (Fig. 4). This test revealed four patients with right brain damage and two patients with left brain damage showing significantly worse performance in multi-source, as compared to single-source, localization. Figure 4A shows simple lesion overlays for the patients with left and right brain damage with and without significant differences between single-source and multi-source sound localization, whereas Fig. 4B shows the subtraction plots resulting from the same data. In patients with right brain damage, the lesion area overlapped mainly the superior temporal gyrus (66.8% of the lesion map; peak: $x = 57$, $y = -24$, $z = 3$). Parts of the lesion area also overlapped the pallidum (6.6%; $x = 23$, $y = 3$, $z = -4$) and the putamen (3.7%; $x = 20$, $y = 11$, $z = -5$), and to a lesser extent the supramarginal gyrus (2.6%), amygdala (2.5%) and angular gyrus (1.3%). With respect to white matter, the lesion covered part of the anterior and posterior limbs of the internal capsule (3.0 and 1.2%, respectively), as well as the external capsule (1.9%). In patients with left brain damage, the lesion area overlapped mainly with a white matter bundle, namely the superior longitudinal fasciculus (48.0%; $x = -44$, $y = -13$, $z = 22$). With respect to grey matter, the lesion overlapped mainly the postcentral gyrus (27.1%; $x = -52$, $y = -9$, $z = 23$), rolandic operculum (18.6%; $x = -44$, $y = -13$, $z = 20$), insula (7.6%; $x = -37$, $y = -13$, $z = 20$) and to a lesser extent the precentral gyrus (0.9%).

Discussion

Our results document that sound localization under free-field conditions with multiple sources can selectively be disturbed after stroke, even when localization of single sound sources remains relatively preserved. We identified two cortical areas specifically associated with a sound localization deficit in such a 'cocktail-party' situation. In the right hemisphere, the two different VLBM analyses (based on two different measures) consistently

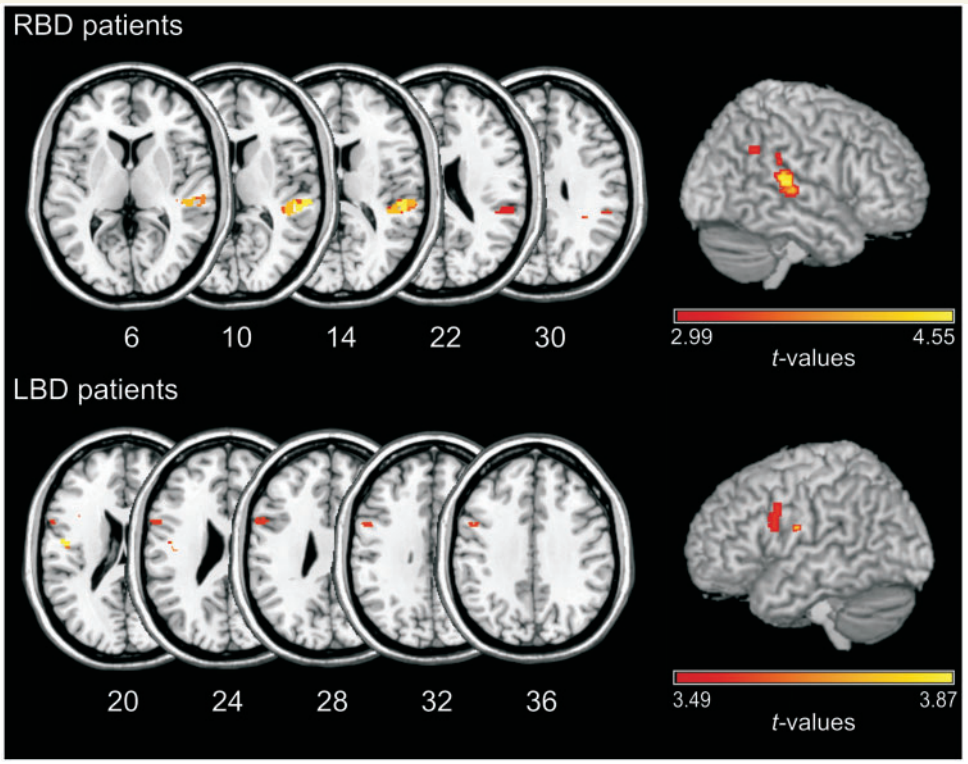

Figure 3 Statistical VLBM analysis (*t*-statistics) for the groups of patients with right (RBD) and left (LBD) brain damage, focusing on the difference between each patient's mean absolute errors in the multi-source minus the single-source conditions. Data were normalized with reference to the difference obtained from the control sample. Voxels displayed survived a correction for multiple comparisons using 5% discovery rate cut-off threshold. MNI *z*-coordinates (mm) of each transverse section are given.

revealed the critical lesion area overlapping mainly the posterior part of the superior temporal gyrus, including the planum temporale, and extending towards the angular and supramarginal gyri. In the left hemisphere, these two VLBM analyses revealed slightly different results, showing either a cluster mainly covering the precentral gyrus, extending to the inferior frontal gyrus, postcentral gyrus and rolandic operculum, or a lesion area overlapping mainly the superior longitudinal fasciculus. However, these areas actually were located very close to each other, with a more anterior position resulting from the first analysis and a more medio-posteriorly position resulting from the second analysis. There was even some degree of overlap between the results of both analyses at the level of the left rolandic operculum.

The auditory cortical system has been proposed to be organized in two (postero-dorsal and antero-ventral) processing streams, both originating in the primary auditory cortex (Recanzone and Cohen, 2010). Within each of these two largely segregated pathways, processing seems to be organized in a serial manner. In particular in the posterodorsal stream, which is known to be critically involved in auditory spatial functions, a hierarchical organization may exist, in which regions posterior to the primary auditory cortex, namely the planum temporale, may represent an initial stage of spatial processing (Krumbholz *et al*., 2005). When considering this, one may expect that a serious disturbance of spatial performance must occur with lesions around the planum temporale, as such lesions may not only disturb processing in this specific area, but also in all subsequent stages of serial processing within the postero-dorsal pathway. The latter view is in full accordance with the predictions of the model that the planum temporale acts as a 'computational hub' that segregates concurrent sounds by analysis of their spectrotemporal patterns and gates this information to higher-order auditory areas for further object recognition and spatial processing (Griffiths and Warren, 2002). In line with these views, the present lesion analysis in the group with right brain damage revealed a crucial role of the right planum temporale in sound localization in multi-source environments. This finding corresponds well with recent functional MRI results showing activation of this area when healthy participants performed the same 'cocktail party task' as used here (Zündorf *et al*., 2013).

For the group with left brain damage, the first VLBM analysis indicated a critical involvement of the left inferior frontal gyrus in multi-source sound localization. This region also corresponds with the functional MRI findings obtained in healthy participants with the same task as used here (Zündorf *et al*., 2013). The inferior frontal gyrus has traditionally been associated with the anteroventral auditory pathway, because of its well-known involvement in frequency and pitch processing (Zatorre *et al*., 1992; Linden *et al*., 1999; Alain *et al*., 2001; Kiehl *et al*., 2001; Müller *et al*., 2001), auditory working memory (Stevens *et al*., 1998), and sound identification (Tranel *et al*., 2003; Lewis *et al*., 2004). Beyond that, studies have suggested that the inferior frontal gyrus is part of a

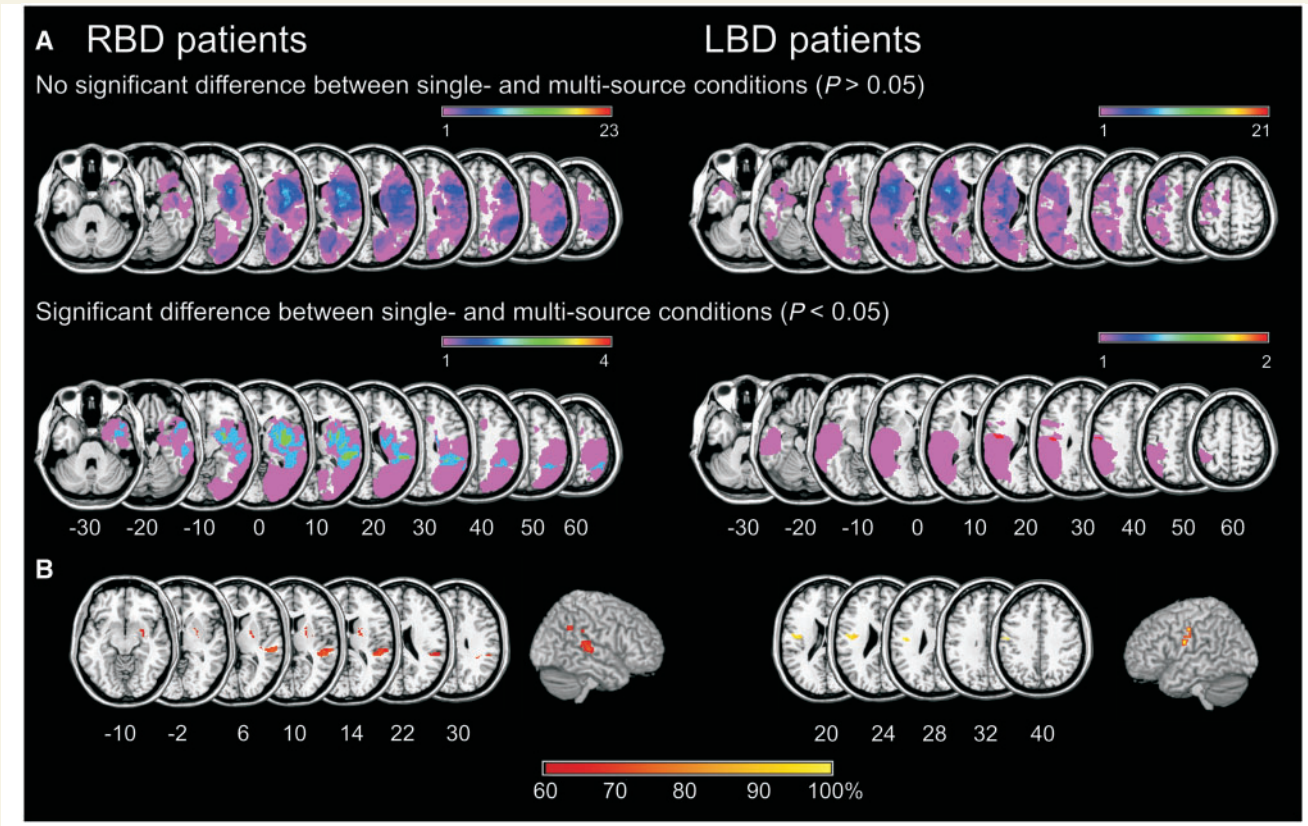

Figure 4 Subtraction analysis for patients with versus without statistically significant differences between single-source and multi-source sound localization, as obtained by the revised Standardized Difference Test. (**A**) Lesion overlays for the patients with left (LBD) and right (RBD) brain damage without significant differences between single-source and multi-source sound localization (upper row of sections) and for the patients showing such significant differences (next lower row of sections). (**B**) Subtraction plots of the patients with significant revised Standardized Difference Test differences minus the patients without significant differences. The voxels shown were at least 60% more frequently damaged in patients with a significant difference between single- and multi-source localization than in patients without such a significant difference between these two conditions. MNI *z*-coordinates (mm) of each transverse section are given.

shared spatial and non-spatial cortical auditory network, because of the consideration that complex spectrotemporal processing is not only vital for sound object identification, but also for spatial hearing based on spectral localization cues (Zatorre *et al*., 1999; Cohen *et al*., 2004; Lewald *et al*., 2008; Lewald and Getzmann, 2011). Functional imaging studies have revealed part of the inferior frontal gyrus—also referred as to inferior frontal junction—and precentral gyrus to be related to a variety of tasks involving higher attentional and cognitive demands. The coordinates of this area as defined in a meta-analysis by Derrfuss *et al*. (2005) correspond well with the present results. Thus, it cannot be ruled out that the observed behavioural pattern corresponds to a more general cognitive impairment rather than a specific auditory spatial deficit.

In our second VLBM analysis (based on Z-DCC), however, the inferior frontal gyrus was not revealed in the group with left brain damage. The lesion area rather covered mainly the left superior longitudinal fasciculus. This white matter bundle is a major pathway connecting parietal and frontal areas (Makris *et al*., 2005), and it is known to play an important role in spatial orienting and awareness as well as attentional control, not only in the visual domain (Doricchi and Tomaiuolo; 2003; Makris *et al*., 2005; Thiebaut de Schotten *et al*., 2005, 2008; Doricchi *et al*., 2008; Suchan *et al*., 2014), but also in the tactile modality and presumably across further sensory modalities (Chechlacz *et al*., 2013). Thus, it is plausible that damage in this area contributed to the auditory spatial deficits observed here in the multi-source condition. Nevertheless, given the small number of patients with left brain damage showing a significantly worse performance in multi-source than in single-source localization, the conclusions that can be drawn from the present findings on the role of left inferior frontal gyrus and left superior longitudinal fasciculus in this task are limited.

Although the role of the planum temporale in auditory stream segregation has been reported several times, it is still a matter of debate whether this function is subserved preferentially by the left planum temporale (Deike *et al*., 2004, 2010; Alain *et al*., 2005; Bidet-Caulet *et al*., 2007; Zündorf *et al*., 2013), the right planum temporale (Snyder *et al*., 2006), or the planum temporale bilaterally (Zatorre *et al*., 2002; Gutschalk *et al*., 2005). Although the left primary auditory areas showed a high temporal resolution for auditory processing, the right posterior superior temporal gyrus is rather specialized for analysis of spectral features (Zatorre and Belin, 2001; Poeppel, 2003). The present study clearly documented a crucial involvement of the right, but not left, planum temporale in multi-source localization. Do these findings argue

against an involvement of the left planum temporale in multi-source sound localization? If we define the planum temporale as a region of interest, we found for the right hemisphere three patients in whom this region of interest was entirely covered by their lesion (97.6–100%), two patients with a high degree (47.8 and 57.6%), and two further patients with a low degree (6.0 and 9.8%) of overlap. For the left hemisphere, we found only one patient fully covering this area (who in fact demonstrated a selective deficit in multi-source sound localization with normal single-source localization performance), and six further patients in whom this region was partially affected with a low degree of overlap (1.6–20.4%). A plausible reason for this low density of lesions around the left planum temporale is that patients with severe aphasia and comprehension difficulties—who commonly have lesions affecting the posterior superior temporal gyrus (Kreisler *et al*., 2000)—could not be systematically included in the present investigation due to their communication impairments. Thus, our results cannot be taken as an argument against any involvement of the left planum temporale in multi-source localization. Rather, we positively conclude that the integrity of the right planum temporale is a necessary prerequisite for adequate performance in a 'cocktail-party' situation.

In conclusion, the results from both VLBM analyses clearly demonstrate the crucial role of the right planum temporale for sound localization in complex acoustic environments with multiple distracters. This area may represent an essential component of the cortical network performing the segregation of various sound locations in a 'cocktail-party' situation. The results from the left brain damage group are less straightforward. They indicate the involvement of left inferior frontal areas and superior longitudinal fasciculus in multi-source sound localization, but caution should be taken, as the results from both analysis approaches differed slightly and only very few patients were identified in the left brain damage group to have a significant difference between single and multi-source localization performance. Notwithstanding, as the auditory system operates in a dual-serial fashion, it is unlikely that left inferior frontal areas and planum temporale process spectrotemporal information in the same manner. Each region might have a unique, but indispensable, functional significance in performing the task. Follow-up studies and a larger number of patients with left brain damage with this deficit are needed to elucidate the mechanisms subserved by these left hemisphere areas in further detail.

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