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ORIGINAL ARTICLE

Implicit representation of the auditory space: contribution of the left and right hemispheres

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Abstract

Spatial cues contribute to the ability to segregate sound sources and thus facilitate their detection and recognition. This implicit use of spatial cues can be preserved in cases of cortical spatial deafness, suggesting that partially distinct neural networks underlie the explicit sound localization and the implicit use of spatial cues. We addressed this issue by assessing 40 patients, 20 patients with left and 20 patients with right hemispheric damage, for their ability to use auditory spatial cues implicitly in a paradigm of spatial release from masking (SRM) and explicitly in sound localization. The anatomical correlates of their performance were determined with voxel-based lesion-symptom mapping (VLSM). During the SRM task, the target was always presented at the centre, whereas the masker was presented at the centre or at one of the two lateral positions on the right or left side. The SRM effect was absent in some but not all patients; the inability to perceive the target when the masker was at one of the lateral positions correlated with lesions of the left temporo-parieto-frontal cortex or of the right inferior parietal lobule and the underlying white matter. As previously reported, sound localization depended critically on the right parietal and opercular cortex. Thus, explicit and implicit use of spatial cues depends on at least partially distinct neural networks. Our results suggest that the implicit use may rely on the left-dominant position-linked representation of sound objects, which has been demonstrated in previous EEG and fMRI studies.

Keywords Lesion studies · Auditory spatial processing · Attention · Sound object segregation · Unilateral neglect

Abbreviations

SRM	Spatial release from masking task
LHD	Left hemispheric damage
RHD	Right hemispheric damage
ITD	Interaural time difference
VLSM	Voxel-based lesion-symptom mapping

Introduction

Spatial cues contribute to the ability to segregate sound sources and thus facilitate their detection and recognition (Bregman 1994) as demonstrated in experiments presenting stimuli in free-field conditions (Drennan et al. 2003) or with simulations by means of interaural intensity (Bronkhorst and Plomp 1988; Culling and Summerfield 1995) or interaural time differences (ITD; Culling and Summerfield 1995; Darwin 1997; Gockel and Carlyon 1998; Licklider 1948). The often used paradigm of spatial release from masking (SRM) represents an elegant way to assess the use of spatial cues for sound object segregation (Carhart et al. 1967; Culling et al. 2004; Hawley et al. 1999, 2004; Saupe et al. 2010; Thiran and Clarke 2003; Duffour-Nikolov et al. 2012). This paradigm involves a target sound and a masker that overlap in spectral content so that the target fails to be perceived when they are presented simultaneously at the same position. When the masker is presented at another position, the target tends to be detected and the rate of detection increases with spatial separation of the target and the masker. This performance increase related to the spatial separation of both sounds is referred to as the SRM effect. The SRM paradigm can be readily used in patient populations, where it has been demonstrated that the use of spatial cues can occur implicitly, i.e., without awareness of the actual position of the sound object (Thiran and Clarke 2003).

The explicit localization of sounds implies conscious perception of a sound position and is typically tested with tasks of discrimination or identification of sound positions,

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which are presented in free-field conditions (Haeske-Dewick et al. 1996; Poirier et al. 1994; Ruff et al. 1981) or simulated by ITD (Altman et al. 1979; Griffiths et al. 1996; Tanaka et al. 1999). Activation studies in normal subjects (Arnott et al. 2004; De Santis et al. 2007; Ducommun et al. 2002, 2004; Kaiser and Lutzenberger 2001; Lewald et al. 2002; Spierer et al. 2009) and behavioural studies in brain-damaged patients (Altman et al. 1979; Bisiach et al. 1984; Ruff et al. 1981; Spierer et al. 2009; Tanaka et al. 1999; Zatorre and Penhune 2001) have shown that sound localization involves the posterior part of the superior temporal gyrus, the inferior parietal lobule and the superior frontal gyrus. These regions are part of the dorsal auditory stream, as postulated by the dual-stream model of auditory processing (Rauschecker 1998; Rauschecker and Scott 2009). Explicit sound localization is mainly disturbed by RHD, illustrating right hemispheric dominance for auditory spatial representation (Spierer et al. 2009).

In cases of focal hemispheric lesions, deficits in implicit use of auditory spatial cues and in explicit sound localization cues can be impaired independently. An early study reported the case of a young woman who sustained a large right hemispheric stroke and did not consciously perceive any sound position; despite this profound spatial deafness, she used auditory spatial cues perfectly well for the segregation of sound objects (Thiran and Clarke 2003). In a subsequent study of 13 consecutive patients with a first hemispheric lesion, 5 were impaired in sound localization but not in the implicit use of auditory spatial cues, whereas 1 patient had the reversed profile, and 4 patients were deficient in both (Duffour-Nikolov et al. 2012). Further studies have demonstrated that the implicit use of auditory spatial cues can be preserved in auditory neglect, i.e., in a clinical condition in which the attention to the left hemispace is impaired following a right hemispheric lesion (Bellmann et al. 2001; Spierer et al. 2007). Because of the relatively small number of patients involved in each of the studies, none of them analysed the anatomical correlates of the implicit use of auditory spatial cues.

The above evidence suggests that distinct neural networks underlie the implicit use of spatial cues and the explicit sound localization, possibly with differentially weighted hemispheric dominance. This issue is of high conceptual interest, for addressing differences in conscious and unconscious processing. There is also, however, clinical relevance to it. Numerous patients who sustained hemispheric lesions but no damage to auditory periphery or brain stem complain of major difficulties when exposed to noisy surroundings (Efron et al. 1983; Litovsky et al. 2002; Zündorf et al. 2014); their problem is likely to be faulty auditory streaming, i.e., the segregation of different sound objects that constitute an auditory scene (Cherry 1953).

The dual-stream model of auditory processing (Rauschecker 1998; Rauschecker and Scott 2009) posits separate processing of sound meaning along the ventral stream and of sound position along the dorsal stream. It is supported by an impressive body of evidence from imaging studies. Identification of sounds has been shown to rely on the anterior temporal convexity and their localization on the parietal convexity (Ahveninen et al. 2006; Anourova et al. 2001; De Santis et al. 2007; Hart et al. 2004; Maeder et al. 2001; for a review; Arnott et al. 2004).

In addition to sound localization, spatial cues contribute to auditory streaming in complex auditory scenes (e.g., Eramudugolla et al. 2008; Middlebrooks and Onsan 2012). The segregation of sound objects in this context requires a combined encoding of the meaning and the position, i.e., a position-linked representation of sound objects. Such a representation has been recently demonstrated using a repetition priming EEG paradigm and was characterized by repetition enhancement when an object changed position and repetition suppression when it did not (Bourquin et al. 2013). Independently of whether the initial presentation was within the right or left space, the differential repetition priming effect occurred within the left hemisphere, at 20–39 ms post stimulus onset in the posterior part of the superior and middle temporal gyri and at 143–162 ms in the left inferior and middle frontal gyri. The position-linked encoding is partially present at the level of early-stage auditory areas on the supratemporal plane, as demonstrated recently in a 7 T fMRI study (Da Costa et al. 2018). This evidence suggests that a third, most likely left-dominant auditory pathway encodes sound objects in respect to their position (for review see Clarke and Geiser 2015).

We have investigated the anatomical substrate of the third auditory pathway in a new series of patients with a first unilateral hemispheric stroke. The implicit use of auditory spatial cues was assessed with an SRM paradigm. Two hypotheses were tested. First, we postulated that sound object segregation within the whole space relies on a left hemisphere network, indicating left hemispheric dominance for the implicit representation of the auditory space. Second, if sound segregation is supported by predominantly left hemispheric networks, we may expect sound object segregation to be often preserved in left unilateral neglect. In addition, the attentional bias in neglect may even attenuate the salience of the masker in the left space, thus yielding an asymmetric SRM effect. In addition, we have investigated in the same population the neural substrate of explicit sound localization, expecting to find, as previously reported, a right hemispheric dominance (e.g., Spierer et al. 2009).

Materials and methods

Participants

Forty patients with a first unilateral focal lesion were included in this study, 20 with left hemispheric damage (LHD; 12 males) and 20 with right hemispheric damage (RHD; 12 males). All patients but two (L10, L20) were right handed. Clinical and demographic data are provided in Table 1. The inclusion criteria were the following: (1) absence of history of prior neurological or psychiatric disorders; (2) normal hearing; (3) absence of major comprehension deficits; and (4) absence of major behavioural problems. An independent samples *t* test confirmed that both patient groups did not differ in lesion size (Fig. 1), [t (38) = 27.85, p = .351, LHD: M = 119,285 ml; RHD: M = 84,266 ml] or in age [t (38) = 35.61, p = .35, LHD: M = 51.35 years; RHD: M = 55.35 years]. In addition to the above patient population, 17 normal subjects without a history of neurological or psychiatric disorders and with normal hearing were tested to validate the SRM paradigm (8 males; mean age = 26.47 years, SD 3.64). All participants signed an informed consent form according to the procedures approved by the Ethics Committee of the Canton de Vaud, Switzerland. Patients were tested during the subacute or early chronic phases of stroke [on average 126.5 days after the brain lesion (SD 253.7), range (11, 1593)]. The range in delay post-stroke was close for both groups, LHD (25; 1066) and RHD (11; 1593). RHD patients were, however, tested slightly earlier than LHD patients [t (38) = 27.88, p = .03, LHD: M = 128.95 days; RHD: M = 47.1 days]; the testing of LHD patients had to be delayed in several cases because of initial severe comprehension deficits. As shown in previous studies, performance of patients in auditory spatial tests during the subacute and chronic stages of stroke is representative of damage to specialized networks. Whereas during the acute stage, sound localization deficits tend to occur independently of whether the dorsal auditory stream is damaged or not, while during the subacute stage they occur almost exclusively and during the early chronic stage only when it is damaged (Adriani et al. 2003; Rey et al. 2007).

Tasks

Spatial release from masking task

This test is a detection task that consists of two sound objects presented concurrently, one being masked by the second (Fig. 2a). The target, which is an 800 ms cry of a tawny owl (20–5000 Hz, centred between 350 and 900 Hz; "All Birds of Europe", Delachaux & Niestlé) is always presented at the same, central position (ITD = 0 µs). The masker consisted of a 2.5 s helicopter sound (20–5500 Hz, the frequency region containing the dominant sound energy was at approximately 700 Hz; Nathan Sound Loto) and was presented at five different positions (ITD = − 1000, − 300, 0, 300, 1000 µs, designated thereafter as positions LL, L, Ce, R and RR). The subject had to detect the target, the owl cry. The masker, i.e., the helicopter, was presented in 35 trials with the target and in 43 trials without it. To avoid the effect of expectation, the target was presented in eight catch trials with different timings (500 µs or 1500 µs after the onset of the masker); the catch trials were not included in the analysis. Performance was expressed as sensitivity d' (Macmillan and Creelman 2004). The current SRM paradigm has been elaborated on the basis of a previous version, which included nine masker positions and was validated in normal subjects and patient populations (Thiran and Clarke 2003; Duffour-Nikolov et al. 2012). On average, normal subjects detect the target less often when the masker is in central than in peripheral positions creating a U-shaped curve of performance (see Fig. 3 in Thiran and Clarke 2003). The SRM effect, corresponding to the gain in target detection due to the spatial separation between the target and the masker, is expressed here as the difference between d' at a given lateral position of the masker and d' at the central position (e.g., at the position LL: $\Delta d'_{LL} = d'_{LL} - d'_{Ce}$). $\Delta d'$ was used for VLSM analyses.

Auditory lateralization task

As described in previous studies (Clarke et al. 2000; Bellmann et al. 2001), this test consists of 60 sounds of a bumblebee, ranging from 20 to 10,000 Hz presented over 2 s including 100 ms rising and falling times. Five different azimuthal positions (12 sounds at each position) were simulated by varying the ITD creating one central (no ITD) and four lateral intra-cranial positions, two in each hemispace. For lateral positions, the ITD was 0.3 ms (intermediate lateralization) or 1 ms (extreme lateralization). The task consisted of precisely indicating the perceived position of the bumblebee on a graduated semi-circle affixed on the headphone (from 0° at the vertex to 90° at each ear) with the index finger of the ipsilesional hand and of the right hand for the control group. Performance at this task was measured by calculating a relative score, i.e., the Global score, based on the comparison of the relative positions attributed to two consecutive stimuli (Spierer et al. 2009). When a stimulus was correctly placed to the left or to the right of the previous stimulus in correspondence with the difference in ITD or within ± 10° of the previous location for identical stimuli,

Table 1 Patient characteristics

	Sex	Age (years)	Delay (days)	Regions involved in the lesion	Volume (mm^3)
L1	F	54.8	116	Pre- and postcentral gyri, IFG, MFG, insula, IPL, SMG, putamen	11,491
L2	F	63.9	1066	Pre- and postcentral gyri, insula, MTG, STG, IPL, SMG, SPL, middle occipital Precuneus, cuneus	212,322
L3	M	59.0	173	Pre- and postcentral gyri, IFG, MFG, insula, STG, temporal pole, IPL, SMG	120,586
L4	F	43.6	77	Hippocampus, parahippocampus, amygdala	5768
L5	F	57.0	455	Precentral gyrus, IFG, MFG, insula, STG, temporal pole, putamen, caudate	110,585
L6	M	46.7	275	Pre- and postcentral gyri, IFG, insula, STG, MTG, IPL, SMG	90,908
L7	M	67.4	96	Insula, STG, MTG, IPL, SMG, middle occipital, precuneus	116,536
L8	M	18.1	150	Pre- and postcentral gyri, IFG, MFG, SFG, insula, SMA, STG, MTG, precuneus, cingulate, calcarine, parahippocampus, cuneus, IPL, middle occipital	686,030
L9	M	57.0	59	Insula, MTG, STG, ITG, temporal pole, fusiform gyrus	59,600
L10	F	39.4	34	IFG, MFG, insula, putamen, caudate	39,308
L11	M	72.2	67	GP, putamen, thalamus	2049
L12	F	35.2	58	Pre- and postcentral gyri, IFG, MFG, insula, STG, IPL, putamen	175,608
L13	M	70.9	25	Putamen, claustrum	3667
L14	M	53.0	46	Insula, caudate	1622
L15	F	48.0	199	Pre- and postcentral gyri, IFG, MFG, insula, STG, MTG, IPL, SMG, putamen	185,755
L16	M	65.8	137	Pre- and postcentral gyri, IFG, MFG, insula, STG, MTG, putamen, caudate	146,120
L17	M	21.3	173	Postcentral gyrus, insula, STG, IPL, SMG	60,113
L18	M	49.6	96	IFG, MFG, insula, MTG, STG, temporal pole, putamen, caudate	120,671
L19	F	47.9	46	Pre- and postcentral gyri, IFG, MFG, insula, STG	98,284
L20	M	52.7	177	Pre- and postcentral gyri, IFG, MFG, SFG, insula, SMA, STG Temporal pole, cingulate, IPL, SMG	138,679
R1	M	46.8	33	Pre- and postcentral gyri, IFG, MFG, insula, STG, IPL, SMG, putamen	216,742
R2	F	53.0	136	Precentral gyrus, IFG, insula, putamen	56,934
R3	F	63.4	37	Pre- and postcentral gyri, IFG, MFG, insula, STG, temporal pole, IPL, SMG, putamen, caudate	187,341
R4	M	64.4	11	Putamen, caudate, GP	4146
R5	M	56.9	22	Fusiform gyrus, hippocampus, parahippocampus, precuneus, posterior cingulate Calcarine, cuneus, thalamus	108,636
R6	M	58.0	42	Lingual gyrus, cuneus, calcarine, inferior occipital, fusiform	52,896
R7	M	51.0	15	Precentral gyrus, IFG, Insula, STG, putamen	44,647
R8	M	54.5	105	STG, MTG, IPL, SMG, middle and superior occipital gyri, precuneus	68,839
R9	F	42.3	16	Thalamus, GP, putamen	4899
R10	F	41.8	16	Pre- and postcentral gyri, IFG, MFG, insula, STG, IPL, SMG, putamen, caudate	128,796
R11	F	50.4	40	Pre- and postcentral gyri, IFG, MFG, insula, STG	69,679
R12	M	61.7	27	Precentral gyrus, STG, IPL, thalamus, putamen	34,849
R13	M	69.0	29	Pre- and postcentral gyri, IFG, MFG, SFG, insula, STG, IPL, SMG, putamen	258,635
R14	F	66.1	44	Precentral gyrus, IFG, insula, STG, IPL, SMG, putamen, caudate	63,508
R15	F	52.1	24	Pre- and postcentral gyri, IFG, MFG, insula, MTG, STG, IPL, SMG	143,126
R16	F	69.4	16	ITG, middle and inferior occipital gyri, fusiform gyrus, lingual	29,452
R17	M	74.5	45	Pre- and postcentral gyri, MFG, IPL	4395
R18	M	58.2	1593	Putamen, insula, caudate	24,713
R19	M	49.1	214	Precentral gyrus, IFG, MFG, insula, ITG, STG, temporal pole, putamen, caudate	148,454
R20	M	26.1	17	Putamen, caudate, GP, thalamus	34,641

GP, globus pallidus; IFG, inferior frontal gyrus; IPL, inferior parietal lobule; MFG, middle frontal gyrus; MTG, middle temporal gyrus; SFG, superior frontal gyrus; SMA, supplementary motor area; SMG, supramarginal gyrus; SPL, superior parietal lobule; STG, superior temporal gyrus

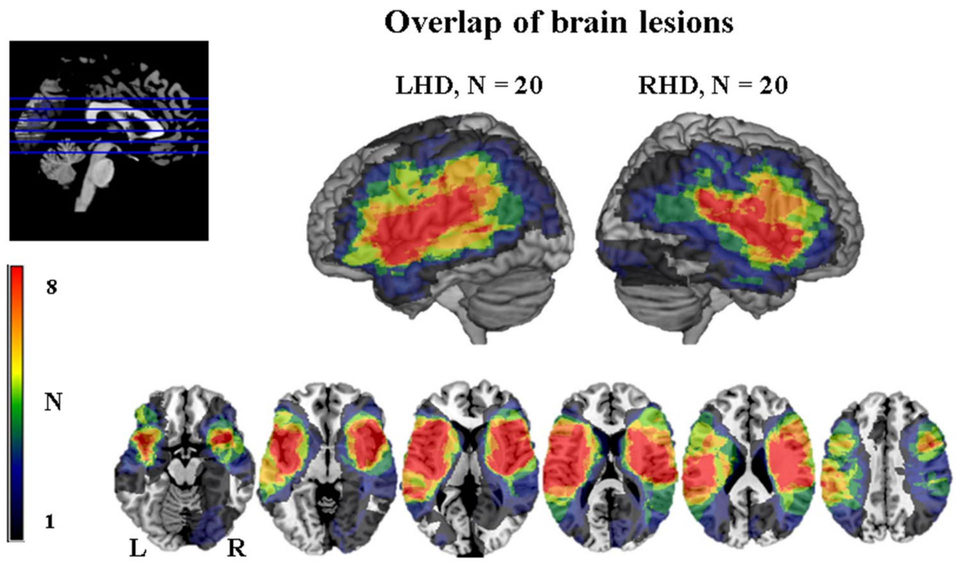

Fig. 1 Overlap of LHD ($n=20$) and RHD ($n=20$) included in this study on surface renderings and axial slices of an MRI template. The level of the slices is indicated in the inset

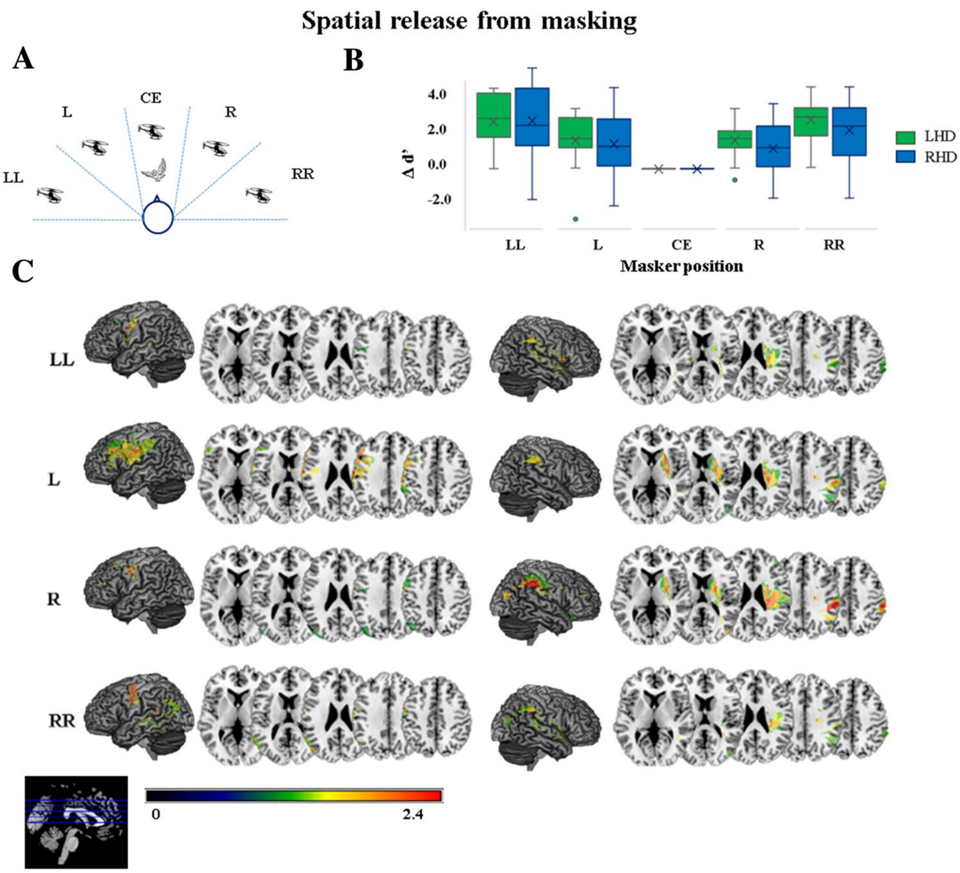

Fig. 2 SRM paradigm, behavioural performance and anatomical correlates. **a** The target, an owl cry, was always presented at the central position (CE) and the masker, a helicopter, at CE or at one of the lateral positions (LL, L, R, RR). **b** Behavioural performance is expressed as gain in d' ($\Delta d'$) with respect to CE. **c** The diminished SRM effect, i.e., the inability to benefit from the spatial separation of the target and the mask at LL, L, R and RR correlated with specific lesions in LHD and RHD

the response was counted as correct (maximal score 59, cut-off score 52).

Data analysis

Statistical analyses of behavioural and population data

For the SRM task, mixed-design ANOVA including the between-subjects factor Group (LHD, RHD) and the within-subject factor Masker position (LL, L, R, RR) were performed on the $\Delta d'$ using a specific hierarchy. The first ANOVA assessed the SRM effect by analysing the $\Delta d'$ performance at each masker position for both patient's groups. Two post hoc mixed-design ANOVAs were performed on $\Delta d'$ to investigate performance asymmetries in both patient groups. The first ANOVA included the extreme masker positions (LL, RR) as the within-subject factor, the second ANOVA included the intermediate masker positions (L, R), and both included the between-subjects factor Group (LHD, RHD).

For the auditory lateralization task, a one-way ANOVA with the factor Group (LHD, RHD) was performed on the Global score to investigate differences in performance between the two groups.

Analyses were processed using R (R Foundation for Statistical Computing, Vienna, Austria).

Voxel-based lesion-symptom mapping

Voxel-based lesion-symptom mapping (VLSM) was used to investigate the relationship between the anatomy of the brain lesions and the behavioural deficits observed following a first unilateral stroke. VLSM is a mass univariate analysis method allowing the testing of each voxel separately and determining its impact on a particular behaviour of interest when this voxel is damaged.

Lesions were drawn on MRI or CT scans of the 40 patients on axial slices using the MITK 3 M3 software and then normalized on the standard Montreal Neurological Institute's (MNI) brain template (Rorden and Brett 2000; Brett et al. 2001). Then, VLSM statistical analyses were performed on the normalized lesions with the non-parametric mapping toolbox (NPM) from MRICroN software package (Rorden et al. 2007). The minimal group size for analysis was set to 15% of patients, i.e., *t* tests were restricted to voxels lesioned in at least three patients in each group. The statistical test used was the Brunner–Munzel test, FDR corrected, with the tBM map intensity (0, 2.4).

To extract the brain regions affecting the implicit use of spatial cues, we used the following normalized behavioural measure (Table 2): we calculated an index coming from the difference between the accuracy for the central position and each of the four lateral positions (LL: $\Delta d'_{LL} = d'_{LL} - d'_{Ce}$; L: $\Delta d'_{L} = d'_{L} - d'_{Ce}$; R: $\Delta d'_{R} = d'_{R} - d'_{Ce}$; RR: $\Delta d'_{RR} = d'_{RR} - d'_{Ce}$). A small index indicates that the patient cannot benefit from the implicit spatial cues to improve his accuracy for the lateral position. VLSM analyses were performed on these normalized behavioural data.

In VLSM analyses, the continuous variables need to represent the range of performance between excellent and very poor. We used the index $\Delta d'$, the low scores of which represented lack of the SRM effect, i.e., deficient performance. Using VLSM we identified brain regions, associated with low $\Delta d'$, representing thus the anatomical substrate of SRM (Fig. 2). To identify with VLSM brain regions that are critical for the explicit use of spatial cues, we used the Global score of the auditory lateralization task (Table 2).

Results

Behavioural data

Spatial release from masking

The average detection scores (d') for the LHD group and for each masker position were LL: 3.52 ± 1.24 (mean ± SD); L: 2.47 ± 1.72; CE: 0.96 ± 1.39; R: 2.48 ± 1.32; and RR: 3.55 ± 1.33. The average detection scores (d') for the RHD group and for each masker position were LL: 2.99 ± 1.43 (mean ± SD); L: 1.71 ± 1.35; CE: 0.38 ± 1.17; R: 1.47 ± 1.2; and RR: 2.42 ± 1.64 (Table 2).

The SRM effect scores ($\Delta d'$) for the LHD group and for each masker position were LL: 2.6 ± 1.5 (mean ± SD); L: 1.5 ± 1.4; CE: 0 ± 0; R: 1.5 ± 0.9; and RR: 2.6 ± 1.3. The average detection scores (d') for the RHD group and for each masker position were LL: 2.6 ± 1.8 (mean ± SD); L: 1.3 ± 1.5; CE: 0 ± 0; R: 1.1 ± 1.3; and RR: 2 ± 1.7.

The SRM effect was analysed using a mixed-design ANOVA with the between-subjects factor Group (LHD, RHD) and the within-subject factor Masker position (LL, L, R, RR) on the $\Delta d'$ (Fig. 2b). There was a significant main effect of Masker position [$F(3,36) = 28.977$, $p < .001$], driven by a greater effect in the lateral (LL, RR) than medial (L, R) positions (Fig. 2b). The interaction between Group and Masker position [$F(3, 36) = 1.265$, $p = .29$] and the main effect of Group were not significant [$F(1,38) = 0.510$, $p = .479$].

To appreciate the putative asymmetry in performance, we compared the effect in the two lateral positions and the two medial positions separately. The SRM effect, analysed for the two lateral positions using a mixed-design ANOVA with the between-subjects factor Group (LHD, RHD) and the within-subject factor Masker side (LL, RR), yielded a significant interaction between Group and Masker side [$F(1, 38) = 4.498$, $p = .041$], driven by a greater asymmetry for RHD (LL: 2.6 ± 1.8; RR: 2 ± 1.7; mean ± SD) than for LHD (LL: 2.6 ± 1.5; RR: 2.6 ± 1.3). There was no significant main effect of Group [$F(1,38) = 0.305$, $p = .584$] or Masker side [$F(1, 38) = 3.64$, $p = .064$]. Post hoc *t* tests between the $\Delta d'$ for LL and RR revealed a significant asymmetry in the RHD group [$t\ (19) = 2.657$, $p = .016$] with greater SRM effect in LL than RR; there was no significant asymmetry in the LHD group [$t\ (19) = -0.163$, $p = .872$] for these positions. Thus, RHD tended to impair the SRM

Table 2 Performance in SRM and in auditory lateralization

Patient	SRM: d' for masker at					SRM: $\Delta d'$				SRM asymmetry		Auditory lateralization
	LL	L	CE	R	RR	LL	L	R	RR	LL–RR	L–R	Global score
L1	0.89	0	−1.12	0	1.63	2.01	1.12	1.12	2.75	−0.74	0	52
L2	2.01	0.74	−0.39	1.13	0	**2.4**	**1.13**	**1.52**	**0.39**	2.01	−0.43	**49**
L3	4.38	1.62	0	1.62	4.38	4.38	1.62	1.62	4.38	0	0	58
L4	4.38	4.38	4.38	4.38	4.38	**0**	**0**	**0**	**0**	0	0	58
L5	1.25	−1.62	1.12	0.5	3.26	0.13	−2.74	−0.62	2.14	**−2.01**	**−2.12**	59
L6	3.26	3.26	1.25	3.26	4.38	2.01	2.01	2.01	3.13	0	−1.12	59
L7	3.26	2.76	0	1.12	2.76	3.26	2.76	1.12	2.76	0.50	1.54	56
L8	4.38	2.76	0	2.76	4.38	4.38	2.76	2.76	4.38	0	0	57
L9	2.76	1.62	0	1.62	2.01	2.76	1.62	1.62	2.01	0.75	0	59
L10	4.38	4.38	2.76	4.38	4.38	1.62	1.62	1.62	1.62	0	0	57
L11	4.38	4.38	1.63	3.25	4.38	2.75	2.75	1.62	2.75	0	1.13	58
L12	4.38	3.26	1.12	3.26	4.38	3.26	2.14	2.14	3.26	0	0	58
L13	4.38	2.76	2.37	2.76	4.38	2.01	0.39	0.39	2.01	0	0	57
L14	4.38	3.26	0	2.01	4.38	4.38	3.26	2.01	4.38	0	1.25	57
L15	1.25	0	0	2.01	1.25	**1.25**	**0**	**2.01**	**1.25**	0	−2.01	54
L16	4.38	2.76	0	2.37	4.38	4.38	2.76	2.37	4.38	0	0.39	58
L17	4.38	3.25	1.62	2.75	4.38	2.76	1.63	1.13	2.76	0	0.50	54
L18	4.38	4.38	1.12	4.38	4.38	3.26	3.26	3.26	3.26	0	0	57
L19	3.26	4.38	3.26	4.38	4.38	**0**	**1.12**	**1.12**	**1.12**	−1.12	0	57
L20	4.38	1.12	0	1.62	3.26	4.38	1.12	1.62	3.26	1.12	−0.50	58
R1	1.62	0	0	0	1.12	1.62	0	0	1.12	0.50	0	**34**
R2	4.38	1.62	1.12	2.37	3.26	3.26	0.5	1.25	2.14	1.12	−0.75	57
R3	3.26	1.12	0	0.5	3.26	3.26	1.12	0.5	3.26	0	0.62	56
R4	4.38	4.38	2.76	3.26	4.38	1.62	1.62	0.5	1.62	0	1.12	56
R5	2.37	2.37	0	0.89	3.26	2.37	2.37	0.89	3.26	−0.89	1.48	55
R6	3.26	1.64	−1.12	1.62	2.76	4.38	2.76	2.75	3.88	0.50	0.02	56
R7	4.38	3.26	0	2.37	4.38	4.38	3.26	2.37	4.38	0	0.89	57
R8	2.75	2.01	1.12	1.12	1.63	1.63	0.89	0	0.51	1.12	0.89	51
R9	4.38	2.01	−0.89	1.25	1.13	5.27	2.9	2.14	2.02	**3.26**	**0.76**	55
R10	2.75	2.37	1.63	0.88	2.75	1.12	0.74	−0.75	1.12	0	1.49	**50**
R11	2.76	1.25	−1.62	0	1.13	4.38	2.87	1.62	2.75	**1.63**	**1.25**	59
R12	1.12	0	0	0	0	1.12	0	0	0	1.12	0	58
R13	4.38	3.26	−1.12	2.37	3.26	5.5	4.38	3.49	4.38	1.08	0.89	56
R14	2.75	1.24	1.62	0	1.24	1.13	−0.38	−1.62	−0.38	**1.51**	**1.24**	53
R15	0.75	1.13	−0.36	0.89	0	**1.11**	**1.49**	**1.25**	**0.36**	0.75	0.24	52
R16	−0.74	−1.13	0.89	1.25	−0.74	**−1.63**	**−2.02**	**0.36**	**−1.63**	0	−2.38	55
R17	4.38	3.26	2.01	4.38	4.38	2.37	1.25	2.37	2.37	0	−1.12	**50**
R18	3.26	0	0	1.12	2.37	3.26	0	1.12	2.37	−0.01	−1.12	54
R19	3.26	2.76	1.63	2.76	4.38	1.63	1.13	1.13	2.75	−1.12	0	57
R20	4.38	1.62	0	2.37	4.38	4.38	1.62	2.37	4.38	0	−0.75	58

The SRM effect was assessed as the abilility to detect the target (d') as a function of masker position at LL, L, CE, R or RR. The gain in target detection was calculated as $\Delta d'$ between a given masker position and CE; bold denotes cases with low $\Delta d'$ and/or $\Delta d'$ which is smaller for lateral than medial positions. In RHD, the SRM effect tended to be asymmetric, i.e., stronger when the masker was on the left than on the right (in particular R9, R11 and R14, in bold). Asymmetric SRM effect was rare in LHD (in L5 favouring the right space, in bold). Explicit auditory lateralization was assessed with the global score [maximum = 59, deficient performance in bold; Bellmann et al. (2001) and Spierer et al. (2009)]

effect less when the masker was contralesional, possibly by decreasing the saliency of the masker in a neglect-like fashion. The SRM effect, analysed for the two more medial positions using a mixed-design ANOVA with the between-subjects factor Group (LHD, RHD) and the within-subject factor Masker side (L, R), yielded no significant interaction

[$F(1,38) = 0.644$, $p = .427$] or significant main effect of factors Masker side [$F(1,38) = 0.580$, $p = .451$] or Group [$F(1,38) = 0.692$, $p = .411$].

Auditory lateralization task (explicit use of spatial cues)

The mean Global score was 56.6 (SD 2.5) for the LHD and 53.8 (SD 5.4) for the RHD group; one-way ANOVA with between-subjects factor Group (LHD, RHD) revealed a tendency [$F(1,40) = 3.97$, $p = .053$] for patients with LHD to perform better.

The discrimination of the two positions simulated by ITD of 0.3 ms versus 1.0 ms within either hemispace and the symmetry of their perception on the right and left side (Fig. 3) was assessed by comparing angular values in a group analysis with a two-way ANOVA with within-subject factors position (ITD 0.3 ms; 1.0 ms) and hemispace (left, right). The patient group with LHD presented a significant main effect of position [$F(1,79) = 12.096$, $p = .001$], but no significant main effect of hemispace [$F(1,79) = 0.605$, $p = .439$] nor a significant interaction between position and hemispace [$F(1,79) = 0.000$, $p = .989$]. Post hoc analysis confirmed a significant difference between L and LL (mean ± SD: − 34.67° ± 21.5° and − 56.33° ± 22.6°, respectively; $t = -5.281$, $p < .001$) and between R and RR (44.27° ± 20.9° and 59.44° ± 20.8°); $t = -5.508$, $p < .001$. Thus, as a group, patients with LHD tended to discriminate correctly the two positions within each hemispace. Patient group with RHD presented a significant main effect of position [$F(1,79) = 10.042$, $p = .002$] and hemispace [$F(1,79) = 4.567$, $p = .036$], but not a significant interaction [$F(1,79) = 0.023$, $p = .880$]. Post hoc analysis showed a significant difference between R and RR (56.53 ± 21.3 and 71.65 ± 16.8); $t = -4.438$, $p < .001$ but not between L and LL (− 45.33 ± 25.9 and − 54.44 ± 36); $t = -1.467$, $p = .159$. The main effect of hemispace was driven by greater angular values within the right than left space. Thus, as a group, patients with RHD failed to discriminate the two positions within the left hemispace and presented a rightward bias.

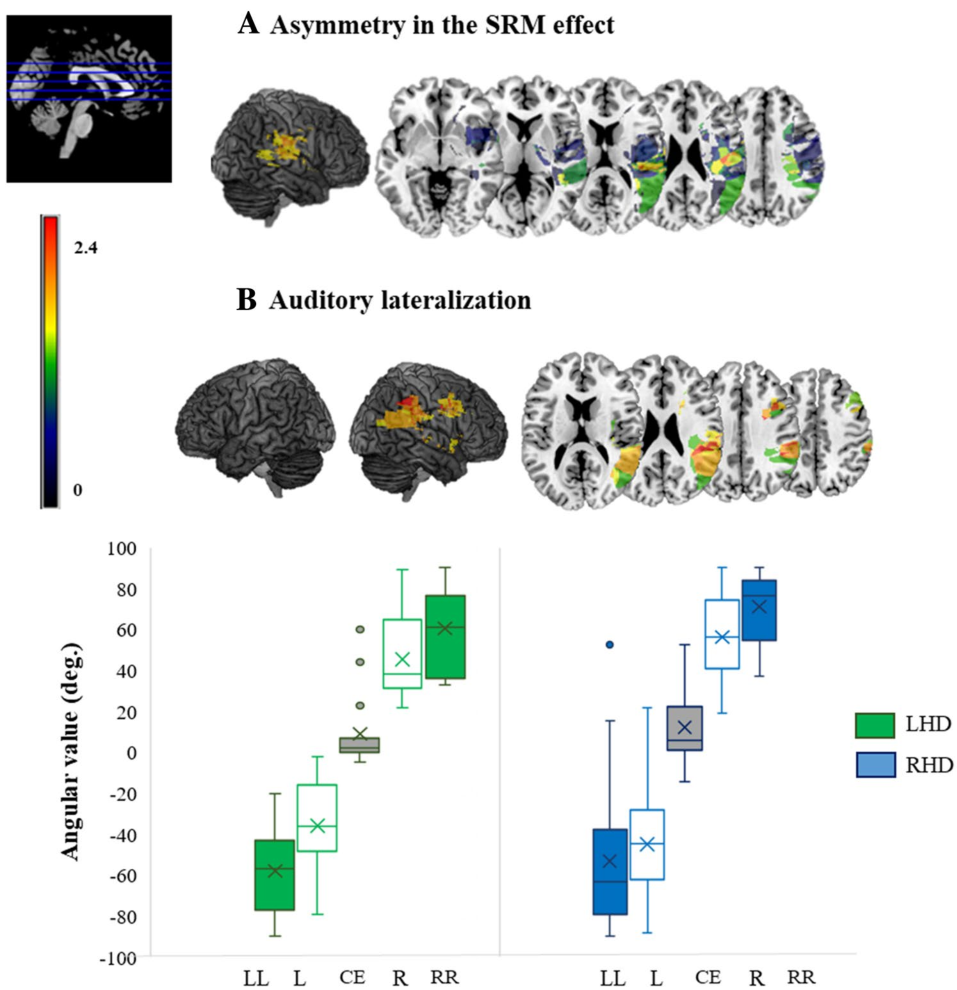

Fig. 3 **a** Anatomical correlates of asymmetrical performance in SRM with greater effect for masker positions at LL than RR in patients with RHD. **b** Performance and anatomical correlates of explicit sound localization. Positions attributed to ITD of 0.3 ms and 1.0 ms favouring the left (L, LL) and right side (R, RR) are shown in box plots for patients with LHD and RHD

Voxel-based lesion-symptom mapping

Spatial release from masking

An absence of the SRM effect, reflecting a failure to benefit from spatial separation between target and masker sounds, was associated with lesions of the left or right hemisphere (Fig. 2c). Within the left hemisphere, the regions critical for the SRM effect included the precentral gyrus for masker positions LL, R and RR and the posterior part of the middle frontal gyrus as well as the precentral and postcentral gyri for L. Within the right hemisphere, the regions critical for the SRM effect included the upper part of the inferior parietal lobule and the deep paraventricular white matter for LL and RR; the upper part of the inferior parietal lobule, the deep paraventricular white matter, the internal capsula and basal ganglia for L and R.

Behavioural results highlighted the asymmetric SRM effect associated with RHD, with a greater effect when the mask was at LL than RR. This asymmetry was associated with damage to the inferior part of the inferior parietal lobule and the posterior part of the superior temporal gyrus (Fig. 3a).

Auditory lateralization task (explicit use of spatial cues)

As indicated by the comparison of behavioural scores, the explicit auditory lateralization task tended to be more disturbed following right than left hemispheric lesions. Furthermore, impairment in auditory lateralization was associated with lesions of specific regions within the right hemisphere: the inferior part of the inferior parietal lobule, the operculum, the insula and the anterior part of the superior temporal gyrus (Fig. 3b). No specific regions were highlighted within the left hemisphere.

Dissociation between deficits in individual cases

Asymmetry or absence of the SRM effect occurred often without deficits in sound localization (L4, L5, L15, L19, R9, R11, R14, R15, R16; Table 2), rarely in association with it (L2). Conversely, deficits in sound localization in RHD occurred without SRM anomalies (R1, R10, R17). Isolated deficits were present in cases with small or large regions. Absent SRM effect without sound localization deficits was found in association with lesions of 5768 (L4) to 185,755 mm^3 (L15); asymmetrical SRM effect with 4899 (R9) to 69,679 mm^3 (R11); and isolated sound localization

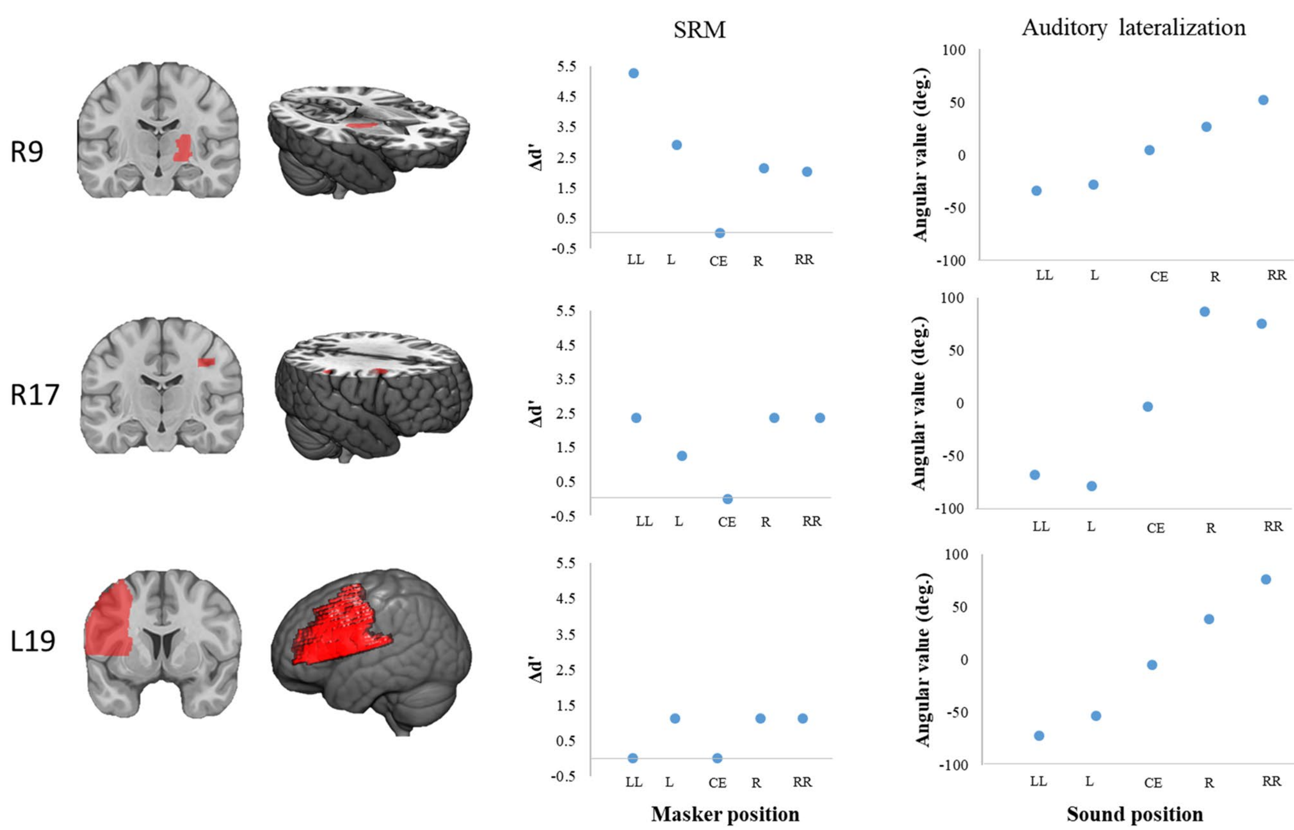

Fig. 4 Lesion location and performance in SRM and explicit localization tasks in selected patients

deficit with 4395 (R17) to 216,742 mm^3 (R1). This indicates that the location rather than the size of the lesion was determined. Three individual cases illustrate this (Fig. 4). R9 presented asymmetrical SRM effect without sound localization deficits in association with a small lesion of the basal ganglia and the lateral part of the thalamus. R17 had an isolated sound localization deficit and a small lesion involving the pre- and postcentral gyri, the posterior part of the middle frontal gyrus and the inferior part of the inferior parietal lobule. L19 presented an isolated SRM deficit; no sound localization deficit was present despite the relatively large lesion.

Discussion

Our results suggest that in addition to the well-established right-dominant auditory spatial representation, which is relevant for explicit sound localization, there is a second auditory spatial representation, which is involved in the implicit use of auditory spatial cues and relies predominantly on left hemispheric networks. This interpretation is further supported by the relationship between sound object segregation and auditory neglect. Sound object segregation is often preserved in neglect (Bellmann et al. 2001; Duffour-Nikolov et al. 2012; Spierer et al. 2007; Thiran and Clarke 2003); as shown here, it can be modulated by lateralized attentional bias.

Left hemispheric dominance for the implicit representation of the auditory space

The SRM effect was absent in some but not all patients, more often after LHD than RHD. In LHD, the inability to perceive the target when the masker was at one of the lateral positions correlated with lesions of the temporo-parieto-frontal cortex. This observation documents a critical role of the left hemisphere in auditory streaming by means of spatial cues and together with previous studies (Zundorf et al. 2013; Bourquin et al. 2013) which suggests that the left hemisphere comprises an implicit representation of the auditory space.

A series of activation and lesion studies analysed the implicit use of auditory spatial cues employing different paradigms and by exploring one hemispace at a time or the whole auditory space (Krumbholz 2004; Schadwinkel and Gutschalk 2010a, b; Zundorf et al. 2013). The streaming of complex harmonic tones by ITD cues was investigated in studies focusing on the perisylvian regions. They highlighted the role of the anterolateral part of Heschl's gyrus (Schadwinkel and Gutschalk 2010a) and of the planum temporale, where the magnitude of neural activity reflected spatial separation of sound sources (Schadwinkel and Gutschalk 2010a, b). They revealed a preference of the planum temporale for contralateral positions, as shown in earlier studies for simple stimuli (e.g., Krumbholz 2004). When more complex auditory surroundings were simulated and whole brain analysis was performed, localizing a meaningful sound among four other simultaneously presented sounds, compared to localizing a sound object presented on its own, activated the left planum temporale and the left precuneus (Zundorf et al. 2013).

A series of activation studies highlighted steps of the combined encoding of the identity of an object and its position and led to the identification of position-linked representation of sound objects, which was independent of the ventral and dorsal auditory streams (for a review, see: Clarke and Geiser 2015). These experimental paradigms involved sound objects presented one at a time at different spatial positions, with analyses concerning the whole auditory space or hemispace. Neuronal populations that specifically encode the identity of an object and track it across the whole space were identified within the left hemisphere (Bourquin et al. 2013). In this study, auditory evoked potentials were recorded while subjects listened to environmental sounds, which were lateralized to the right or to the left. In this sequence, an acoustically different sound of the same object was presented a second time, several items after the first presentation, either on the same or on the opposite side. The difference in priming effect was driven by repetition suppression for the same position and repetition enhancement for a change of position; this effect occurred at 20–39 ms post-stimulus onset within the posterior part of the left superior temporal gyrus and at 143–162 ms in the left inferior frontal gyrus. These results suggested a left hemispheric dominant encoding of sound objects in space. Two 7T fMRI studies investigated combined encoding of the meaning and the position of environmental sounds at the level of early-stage auditory areas, i.e., in the planum temporale. Within a set of lateral belt areas, the encoding of the meaning of the sound was modulated by their spatial position, favouring the encoding within the contralateral space (Da Costa et al. 2018; van der Zwaag et al. 2011).

Lesion studies corroborate the contribution of the left hemisphere to sound object segregation on the basis of spatial cues. The present study showed that the SRM effect depended critically on the integrity of the left frontal, parietal and temporal cortices. Damage to these regions annihilated the beneficial effect of the spatial separation between the target and masker, independently of whether the masker was located on the right or left side. In contrast, the critical regions within the right hemisphere stretch over the paraventricular white matter where temporo-parietal callosal fibres pass and includes only a small part of the inferior parietal cortex. Previously, two single cases of impaired SRM were reported in association with LHD; the lesions involved the temporo-parietal cortex and frontal cortex, respectively (Duffour-Nikolov et al. 2012).

An alternative way of appreciating the ability to use spatial cues for segregation of sound sources is dichotic and diotic listening. In these tests, two words are presented simultaneously, in dichotic listening, one word to each ear, and in diotic listening, one word on each side lateralized by means of ITDs (e.g., Bellmann et al. 2001). Primarily, these tests serve to evaluate auditory neglect, which is characterized by a unilateral extinction (Bellmann et al. 2001; Clarke and Thiran 2004; Jacquin-Courtois et al. 2013; Spierer et al. 2007). However, in some patients the extinction impacts both ears and/or both sides. Bilateral, symmetrical extinction in dichotic listening has been reported when lesions occurred in a large left fronto-parietal region or within a small region in the right parietal operculum. Bilateral, symmetrical extinction in diotic listening has been reported when lesions occurred in a large left fronto-parieto-temporal region or within a smaller right fronto-parietal region (Tissieres et al. 2018).

Thus, streaming of complex harmonic tones (Schadwinkel and Gutschalk 2010a, b) and position-linked representation of sound objects (Bourquin et al. 2013; Da Costa et al. 2018; van der Zwaag et al. 2011) appear to rely on two processing stages. The first stage preferentially involves the contralateral space and takes place in early-stage auditory areas; the second stage concerns the whole space and relies on predominantly left hemispheric networks. Lesion studies corroborate the critical involvement of the left hemisphere in sound object segregation on the basis of spatial cues (present study; Tissieres et al. 2018).

Right hemispheric contribution to spatial release from masking

Our results show that within the right hemisphere, the SRM effect relies on the upper part of the inferior parietal lobule, the basal ganglia and the deep white matter, hinting at similarities but also at differences in respect to the anatomical substrate of sound localization. Part of the inferior parietal lobule appears to be critical both for SRM and for explicit sound localization (see also Spierer et al. 2009; Zündorf et al. 2016), which offers an explanation for the previously reported co-occurrence of SRM and sound localization deficits (Duffour-Nikolov et al. 2012). In contrast, damage to basal ganglia, which we found here to interfere with the SRM effect, has been previously described as not causing sound localization deficits (Zündorf et al. 2016). According to our results, deep white matter lesions appear to be critical within the right but not left hemisphere. Their location makes them likely to interrupt the callosal pathways at its paraventricular trajectory and/or the superior longitudinal fasciculus. The contributions of these two tracts to SRM need to be addressed in further studies.

Right hemispheric dominance in sound localization

Our results confirm differential contribution of the right versus left hemisphere to sound localization. RHD tended to be associated with less good performance than LHD (Fig. 3b). VLSM analysis identified the critical region within the right hemisphere, namely the inferior parietal lobule, the operculum, the insula and the anterior part of the superior temporal gyrus (Fig. 3b). No specific regions were highlighted within the left hemisphere. Very similar results were reported in a previous study, which showed that sound localization deficits concerned predominantly the contralateral, right space in LHD and the whole space in RHD; VLSM analysis highlighted the predominant role of the right hemisphere and in particular the inferior parietal lobule, the operculum, the insula and the superior temporal gyrus (Spierer et al. 2009). Furthermore, these results corroborate previous studies, which described pervading sound localization deficits following right parietal lesions (Bisiach et al. 1984; Clarke et al. 2002; Ducommun et al. 2002; Pavani et al. 2005; Pinek et al. 1989; Tanaka et al. 1999).

In our RHD population, sound localization deficits never occurred in association with asymmetry or absence of the SRM. This observation is in agreement with the previously described dissociation (Duffour-Nikolov et al. 2012; Thiran and Clarke 2003).

Segregation of sound objects and unilateral neglect

Unilateral neglect was often found to have an auditory component (e.g., Pavani et al. 2003). Diagnosis of auditory neglect is based on the performance in three key tests: dichotic and diotic listening and sound localization tasks (Bellmann et al. 2001; Clarke and Thiran 2004). Deficits in these tests can occur independently of each other and thus define distinct types of auditory neglect. Left extinction on dichotic and/or diotic listening characterizes the attentional variant of auditory neglect and a rightward shift in auditory spatial representation, associated with alloacusis, the spatial variant (Bellmann et al. 2001; Clarke and Thiran 2004; Heilman and Valenstein 1972; Pavani et al. 2003; Renzi et al. 1984; Tissieres et al. 2017, 2018).

Two lines of evidence suggest that sound object segregation by means of auditory spatial cues and auditory spatial attention depend on distinct neural mechanisms but interact when it comes to awareness of individual sound objects. First, the left-sided extinction, which has been demonstrated with diotic listening paradims and which is characteristic of the attentional variant of auditory neglect (Bellmann et al. 2001; Spierer et al. 2007; Thiran and Clarke 2003), can only occur when the two simultaneously presented sound objects are successfully segregated (Tissieres et al. 2018). Second, our results, together with a previous study, demonstrate that auditory streaming can be modulated by neglect. Here behavioural measures revealed asymmetric SRM effects associated with RHD, with a greater release from masking when the mask was at LL than at RR. This asymmetry was associated with damage to the inferior part of the inferior parietal lobule and the posterior part of the superior temporal gyrus (Fig. 3), a region reported to be critical for neglect in the chronic stage of stroke (Karnath et al. 2012). The most likely explanation is that RHD decreased the saliency of the masker when presented on the left and enhanced thus the perception of the target. A previous study has shown that auditory stream segregation on the basis of non-spatial cues was impaired when stimuli were presented to the left but not to the right ear (Carlyon et al. 2001), probably due to decreased saliency of the stimuli.

The two-way interaction between auditory streaming on the basis of spatial cues and auditory neglect suggests that both depend on a common intermediate stage. The shared processing step may well be the previously reported position-linked representation of sound objects (Bourquin et al. 2013; Clarke and Geiser 2015).

Conclusions

Whereas the explicit localization of sounds depends on a right-dominant neural network (e.g., Spierer et al. 2009), two lines of evidence indicate that implicit use relies on a distinct left-dominant network. First, as demonstrated for the first time here, the SRM effect for both the right and left space depends critically on a left temporo-parieto-frontal network. In contrast, the role of the right hemisphere is more limited, with a part of the inferior parietal lobule being implicated. In addition, sound object segregation on the basis of spatial cues has often been preserved in neglect (Spierer et al. 2007; Thiran and Clarke 2003) and tends to be modulated by the rightward attentional bias. Second, as reported previously, the combined representation of the meaning and the position of sound objects is independent from the dorsal "Where" and ventral "What" auditory streams and involves a third, left-dominant auditory pathway (Bourquin et al. 2013; Clarke and Geiser 2015; Da Costa et al. 2018). This third auditory pathway is likely to play a key role in the segregation of sound objects on the basis of spatial cues.

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Compliance with ethical standards

Conflict of interest The authors reported no conflict of interest.

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