Deficit of auditory space perception in patients with visuospatial neglect

Francesco Pavani a,c,*, Francesca Meneghello b, Elisabetta Ládavas a

a Dipartimento di Psicologia, Università degli Studi di Bologna, Bologna, Italy
b ‘San Camillo’ Hospital, Alberoni, Italy
* ‘Fratincini’ INRCA Hospital, Firenze, Italy

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Abstract

There have been many studies of visuospatial neglect, but fewer studies of neglect in relation with other sensory modalities. In the present study we investigate the performance of six right brain damaged (RBD) patients with left visual neglect and six RBD patients without neglect in an auditory spatial task. Previous work on sound localisation in neglect patients adopted measure of sound localisation based on directional motor responses (e.g., pointing to sounds) or judgement of sound position with respect to the body midline (auditory midline task). However, these measures might be influenced by non-auditory biases related with motor and egocentric components. Here we adopted a perceptual measure of sound localisation, consisting in a verbal judgement of the relative position (same or different) of two sequentially presented sounds. This task was performed in a visual and in a blindfolded condition. The results revealed that sound localisation performance of visuospatial neglect patients was severely impaired with respect to that of RBD controls, especially when sounds originated in contralesional hemispace. In such condition, neglect patients were always unable to discriminate the relative position of the two sounds. No difference in performance emerged as a function of the visual condition in either group. These results demonstrate a perceptual deficit of sound localisation in patients with visuospatial neglect, suggesting that the spatial deficits of these patients can arise multimodally for the same portion of external space. © 2001 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The auditory system computes sound position through differences in intensity and time of arrival of sound at each ear, and through spectral changes introduced by the external ear on the sound wave [6]. The correspondence between these auditory inputs and the spatial positions in external space is to some extent systematic and predictable, and an accurate representation of auditory space can be achieved based on auditory inputs only. This has clearly been shown in behavioural and neurophysiological studies in animals raised without vision [37] and in psychophysical investi-

*Corresponding author. Present address: Institute of Cognitive Neuroscience, University College London, Alexandra House, 17 Queen Square, London WC1N 3AR, UK. Tel.: +44-20-76791125; fax: +44-20-78132835.
E-mail address: f.pavani@ucl.ac.uk (F. Pavani).
Evidence for deficits of auditory space perception in visuospatial neglect patients has been described in clinical reports. Neglect patients may sometimes respond to voices or sounds originating from the affected hemisphere as if they occurred in the ipsilesional side of space (a phenomenon described as ‘allocusis’ [13] or ‘allochiria’ [5]). Other forms of sound mislocalisation toward the ipsilesional side have been described in studies requiring a pointing response to the perceived sound position. In such motor tasks, patients with left neglect are typically asked to point manually to free-field sounds [25,33,34], or to indicate manually on the head-surface the perceived lateralisation of a sound presented dichotically over headphones [1,3]. These studies usually reveal systematic rightward errors in pointing to sounds, which are more severe in neglect patients than in right-brain damaged patients without neglect, or in left-brain damaged patients.

However, whenever a directional motor response to the sound is required, the observed directional errors might be the consequence of a systematic error at the level of the sensory-motor transformation involved in the response, rather than the direct consequence of an altered perception of sound location. For instance, as suggested by Bisiach and colleagues [3], the systematic underestimation of left sounds position in neglect patients, might be the consequence of a reduced exploration of the contralesional side of space (directional hypokinesia [4,29]). Another example of motor bias on sound localisation performance has recently been described in a patient with neglect, whose pointing to sounds was systematically biased toward the starting position of the hand in space [25].

To exclude a potential motor component in the sound localisation errors of neglect patients, Bisiach and colleagues [3] examined the performance of two neglect patients in a task that avoided any directional motor response to sounds. The task consisted in rotating a central knob to adjust the position of a sound presented dichotically through headphones, until the sound was perceived to be aligned with the subjective head/body midline. Such task, usually named auditory midline task, confirmed the existence of sound localisation errors in neglect patients, which emerge as a rightward shift of localisation responses (for similar results in group studies see [24,47,49]).

The measure of sound localisation in the auditory midline task relies crucially on the estimation of the head/body midline position. If such estimation is correct, the measure of sound localisation is reliable. However, if the subjective midline is biased laterally, the measure of sound localisation will be biased accordingly. In other words, a deviation of the subjective midline would inevitably result in a sound localisation error. This problem might be particularly true for patients with neglect, since several studies have shown that the head/body midline position can indeed be deviated in some of these patients ([23]; though see Ref. [16]). Therefore, when the auditory midline task is used in neglect patients, it remains unclear whether neglect alters the perception of sound position, the perception of the head/body midline, or both these aspects at the same time.

Given the uncertainty related with the interpretation of previous auditory studies, the present study examined auditory space perception in visuospatial neglect patients by using a perceptual task, in which the measure of sound localisation does not rely on a motor response or the estimation of the subjective head/body midline. Patients were asked to compare the relative position of two sequentially presented sounds and report verbally whether they originated from same or different locations (relative discrimination task [39]). By systematically varying the distance between the two acoustic stimuli it is possible to determine at which spatial separation the two sound sources are reliably discriminated, and thus measure the perceptual component of sound localisation accuracy.

If the poorer sound localisation performance of visuospatial neglect patients is the result of a genuine deficit of auditory space perception, neglect patients should be more impaired than right brain damaged (RBD) controls in this perceptual task. Specifically, neglect patients should find it more difficult to discriminate between same or different sound positions, particularly when the auditory stimuli originate in contralesional hemisphere. By contrast, if the poor auditory performance of neglect patients reported in previous studies is mainly the consequence of biased sensory-motor transformations or of erroneous estimation of the body midline, no difference between the two groups should emerge when sound localisation is measured using a perceptual task.

A further aspect considered in the present study was the effect of visual information on patients’ sound localisation performance, and particularly whether the presence of visual information can enhance auditory spatial deficits of patients with visuospatial neglect. To this aim all patients were asked to perform the auditory task either in vision or in no-vision condition. In the vision condition, the apparatus was visible, but vision of the loudspeakers was always prevented. In the no-vision condition, patients were blindfolded. As suggested by previous works [8,19,21,22,26,44], visuospatial neglect is more severe when vision is allowed as compared to when vision is precluded. Accordingly, if representation of auditory space is directly influenced by the representation of visual space, neglect patients performance in the auditory spatial task should be more impaired in the vision condition than in the no-vision condition.
2. Method

2.1. Patients

Twelve RBD patients gave their informed consent to participate in the study and were recruited from the ‘S.Camillo’ Hospital (Alberoni, Italy) and from the ‘Fraticini’ INRCA Hospital (Florence, Italy). All patients suffered unilateral ischemic lesions in the right hemisphere; side and site of the lesion were documented by CT scan. Patients were oriented in time and space, and their Mini Mental State Examination [17] score was within normal limits; age, sex, length of illness as well as clinical details are provided in Table 1. All patients presented a left hemiplegia and were right handed.

Patients were subdivided in two groups on the basis of the presence or absence of visuospatial neglect: a group of six patients with left neglect (N+) and a group of six patients without neglect (N−). The assessment of visuospatial neglect was based on their performance in a series of clinical tests including: a letter cancellation test [14], a bell cancellation test [18], a line bisection test, and two tests extracted from the RBIT [52]: figure description and menu list. As can be seen in Table 1, all neglect patients showed a marked left–right difference in the two cancellation tests, whereas such difference was absent in control patients. Control patients M.A. and C.E. presented a slight rightward advantage in the cancellation tests. For this reason they have been submitted to a more detailed examination which confirmed the absence of visuospatial neglect.

The two groups did not differ in age (mean N− = 59; mean N+ = 62), length of illness (mean N− = 11 months; mean N+ = 14 months) and years of schooling (mean N− = 10; mean N+ = 9). All comparisons between the two groups were not significant at t-test.

Patients were tested in a subjective audiometry for the sound frequency used during the experimental session (1.2 kHz tone) and were included in the study only if they showed a normal or near to normal hearing threshold and no difference between ears of more than 5 dB. According to this criterion two patients were excluded during the screening session. Importantlly, when tested for their ability to detect free-field sounds presented in different spatial positions, all patients reported the totality of auditory stimuli, thus showing no sign of auditory neglect for the stimuli used in the present study. Note however that some auditory neglect deficits may have emerged if more complex auditory tasks were adopted (e.g., a syllable identification task [44]). Finally, the two groups did not differ in their ability to discriminate verbally whether sounds originated from the left of the right hemispace. When sounds originated from the left hemispace mean error percentage was 5% for N− patients and 4% for N+ patients; when sounds originated from the right hemispace mean error percentage was 2% for N− patients and 3% for N+ patients (both comparisons were not significant at t-test).

2.2. Apparatus

The apparatus consisted of nine piezoelectric loudspeakers (0.4 W, 8 Ω), arranged horizontally at ear level. Loudspeakers were mounted on a vertical plastic net (height 30 cm, length 150 cm) supported by four wooden stands fixed to the table surface and arranged in semicircle. With respect to the centre of the apparatus, four loudspeakers were placed on the left side

<table>
<thead>
<tr>
<th>Patient</th>
<th>Group</th>
<th>Sex/age</th>
<th>Education (year)</th>
<th>Lesion site (CT scan)</th>
<th>Onset (month)</th>
<th>Bell cancellation test (% of accuracy)</th>
<th>Letter cancellation test (% of accuracy)</th>
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<td>Left</td>
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<tr>
<td>M.A.</td>
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<td>M, 33</td>
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<td>P T</td>
<td>4</td>
<td>71</td>
<td>88</td>
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<tr>
<td>M.L.</td>
<td>N−</td>
<td>M, 55</td>
<td>19</td>
<td>sc</td>
<td>4</td>
<td>100</td>
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<tr>
<td>M.M.M.</td>
<td>N−</td>
<td>F, 70</td>
<td>15</td>
<td>sc</td>
<td>11</td>
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<tr>
<td>C.E.</td>
<td>N−</td>
<td>M, 51</td>
<td>8</td>
<td>F P T sc</td>
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<td>M, 54</td>
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<tr>
<td>R.M.F.</td>
<td>N+</td>
<td>F, 52</td>
<td>8</td>
<td>F O T</td>
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<td>47</td>
<td>76</td>
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<tr>
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<td>N+</td>
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<td>24</td>
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<tr>
<td>S.S.</td>
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<td>M, 68</td>
<td>8</td>
<td>F P O T sc</td>
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<td>18</td>
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</tr>
<tr>
<td>Z.C.</td>
<td>N+</td>
<td>M, 66</td>
<td>15</td>
<td>F</td>
<td>2</td>
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<td>18</td>
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a F, frontal lobe; T, temporal lobe; P, parietal lobe; O, occipital lobe; sc, subcortical.
could either be presented from the same loudspeaker as S1, or from one of the remaining eight different loudspeakers. The time interval between S1 and S2 was 500 ms. Patients were required to give a verbal response about the relative position of the two sounds, responding ‘same’ when they thought that the two stimuli originated from the same position and ‘different’ when they thought that the two stimuli originated from different positions. The experimenter recorded patient’s response at the end of each trial.

All patients participated in two experimental sessions, run on consecutive days and lasting about 60 min each. The sound localisation task was divided in six experimental blocks, equally distributed in the two sessions. Ten practice trials preceded the first block. Each of the 32 experimental conditions in which S1 and S2 were presented from different loudspeakers (4 positions for S1 × 8 positions for S2) was composed of 12 trials, whereas each of the four experimental conditions in which S1 and S2 were presented in the same spatial position was composed of 24 trials. This results in a total of 480 trials overall. The order of experimental conditions in each block was randomised, and stimulus position was unpredictable in every trial. Patients performed half of the experimental blocks in a normal vision condition, and the other half in a blindfolded condition. The two visual conditions alternated between blocks, and their order was counterbalanced between patients.

3. Results

For each condition in which S1 and S2 were presented from different spatial positions, a measure of performance was calculated based on two values: (1) correct detection rate (or hit rate, \( H_r \)), i.e. the number of ‘different’ answers, divided by the number of valid trials in that condition; and (2) false alarm rate (\( FA_r \)), i.e. the number of ‘different’ answers produced when the two sounds were in fact presented in the same spatial position, divided by the number of valid trials in that condition. The false alarm rate was used to compute the safe rate (\( S_r \)) as \( 1 - FA_r \). The final performance measure (\( P \)) for a given condition was calculated as \( P = H_r + S_r \) [39]. Discrimination threshold (i.e. the value of performance above which discrimination was considered above chance) was fixed at 0.60. Overall, no bias to respond ‘same’ or ‘different’ was found in the pattern of patients’ responses.

Patients’ ability to discriminate between S1 and S2 when they occurred in different spatial positions was evaluated separately for each of the four spatial positions where S1 could be presented (i.e., −30°, −10°, +30° and +10°). Mean performances were analysed using mixed analyses of variance (ANOVA) with one
between-subjects factor (Group: N+ and N−), and two within-subjects factors (S2 Position: 8 positions; visual condition: normal vision or blindfolded). Newman–Keuls test was used for all post-hoc analysis.

3.1. S1 in position +30

Mean performances when S1 was presented in position +30 in the right hemispace are presented separately for N+ patients and N− patients in Fig. 2(A). Both psychometric functions show a typical trend: patients’ ability to discriminate between the two sound sources increases with the distance between S1 and S2 ([26] for normative data on neurologically healthy subjects). Safe rate for N+ patients was 0.87 whereas for N− patients was 0.85.

The ANOVA revealed a main effect of S2 Position \( [F(7,70) = 23.5, \ P = 0.0001] \). Mean performance was below discrimination threshold when S2 was presented 10° or 20° to the left of S1 \( (P = 0.42 \text{ and } 0.60, \ \text{respectively}) \) and when S2 was presented 10° to the right of S1 \( (P = 0.23) \). By contrast, mean performance increased significantly \( (P < 0.02) \) and was above threshold for all conditions in which the spatial separation between S1 and S2 was above 20°. No other main effect or interaction was significant; specifically, there was no significant effect of group or visual condition.

3.2. S1 in position +10

Mean performances when S1 was presented in position +10 in the right hemispace are presented in Fig. 2(B). Safe rate for N+ patients was 0.80 whereas for N− patients was 0.89. The ANOVA revealed a main effect of S2 Position \( [F(7,70) = 9.78, \ P = 0.0001] \). Mean performance was below discrimination threshold when S2 was presented 10° to the left of S1 \( (P = 0.47) \) and when S2 was presented 10° or 20° to the right of S1 \( (P = 0.31 \text{ and } 0.50, \ \text{respectively}) \). Mean performance increased significantly \( (P < 0.03) \) and was above threshold for all conditions in which the spatial separation between S1 and S2 was above 20°. No other main effect or interaction was significant.

Fig. 2. Mean performance of the two groups of patient as a function of S2 Position, when S1 was presented in position +30 (A), +10 (B), −10 (C) and −30 (D). Bold lines indicate N− patient, dotted lines indicate N+ patients. The measure of performance represents patients’ ability to discriminate between the position of S1 and S2. For clarity, all graphs also plot the position where S1 and S2 originate from the same spatial position; however, the performance value associated with this position is fixed to zero (see text for safe rates of each S1 position). Bars indicate the variability of performance across patients (standard error). Asterisks indicate significant differences between groups (*, \( P < 0.01 \)).
3.3. S1 in position – 10

Mean performances when S1 was presented in position – 10 in the left hemispace are presented in Fig. 2(C). Safe rate for N+ patients was 0.82 whereas for N− patients was 0.93. Unlike the analysis conducted for S1 in position + 30 and + 10, the ANOVA revealed a main effect of the group factor \( F(1,10) = 7.28, P = 0.02 \), caused by higher mean performance for N− patients (0.72) than N+ patients (0.53). The main effect of S2 Position was also significant \( F(7,70) = 14.8, P = 0.0001 \). On average, mean performance was below discrimination threshold when S2 was presented 10°, 20° or 30° to the left of S1 \( (P = 0.36, 0.45 \) and 0.52, respectively) and when S2 was presented 10° to the right of S1 \( (P = 0.48) \). Mean performance increased significantly \( (P < 0.02) \) and was above threshold only for conditions in which S2 appeared in the right hemifield and the spatial separation between S1 and S2 was above 20°.

However, mean performance was significantly lower for N+ patients with respect to N− patients when S2 was presented in position – 40 \( (0.28 \text{ vs. } 0.76; P < 0.0006) \), – 30 \( (0.27 \text{ vs. } 0.63; P < 0.01) \) and 0 \( (0.35 \text{ vs. } 0.61; P < 0.03) \). Thus, N+ patients were unable to discriminate the two sounds above threshold in all conditions in which S1 and S2 appeared in the left hemifield. By contrast, N− patients were below discrimination threshold only when the angular separation between the two stimuli was less than 20° (i.e. S2 in position – 20 and 0). This caused a significant interaction between group and S2 position \( F(7,70) = 2.57, P = 0.02 \). No other main effect or interaction was significant.

3.4. S1 in position – 30

Mean performances when S1 was presented in position – 30 in the left hemispace are presented in Fig. 2(D). Safe rate for N+ patients was 0.86 whereas for N− patients was 0.94. The ANOVA revealed a main effect of the group factor \( F(1,10) = 7.14, P = 0.02 \), caused by higher mean performance for N− patients (0.72) than N+ patients (0.59). The main effect of S2 Position was also significant \( F(7,70) = 34.1, P = 0.0001 \). In both groups performance was below discrimination threshold when S2 was presented 10° to the left of S1 \( (P = 0.16) \) or 10° to the right of S1 \( (P = 0.30) \), whereas performance increased significantly \( (P < 0.01) \) when the distance between S1 and S2 was above 20°.

However, performance in the two groups differed when S2 was presented 20° to the right of S1, in position – 10 within the left hemifield. In this condition, N+ patients showed a poor discrimination performance \( (P = 0.42) \), whereas N− patients showed a significantly higher performance \( (P = 0.81, P < 0.001) \). This resulted in a significant interaction between group and S2 position \( F(7,70) = 2.18, P = 0.05 \). No other main effect or interaction was significant.

4. Discussion

The present study investigated auditory space perception in patients with unilateral neglect by using a perceptual measure of sound localisation, based on discrimination of the relative position of two sequentially presented sounds. The results demonstrate that neglect patients are clearly more impaired at the relative discrimination task than RBD patients without neglect, but only when both sounds originate in the contraleisional hemispace. In the left hemispace, control patients reliably discriminate between same and different sound positions whenever the spatial separation between the two sounds was at least 20°. By contrast, neglect patients were unable to discriminate the relative spatial positions of two left sounds, even when their angular separation was above 20°.

In the right hemispace, the difference between the two groups disappeared and all patients discriminated between same and different sound positions when the spatial separation between the two sounds was at least 20°. This result is particularly important because it demonstrates that the deficit described in neglect patients does not depend on a general difficulty in performing the relative discrimination task [11]. Instead, it can be interpreted as a specific difficulty in discriminating the spatial position of sounds presented in contraleisional space. Interestingly, this difficulty was overcome when just one sound was presented in right hemispace and the other sound was presented in left hemispace. In this condition, neglect patients performance was comparable to that of RBD controls. This result might suggest some preserved coding of the hemispace of sound presentation, despite the severe impairment of sound localisation within the contraleisional hemifield.

These findings considerably extend previous neuropsychological evidence on sound localisation deficits of visuospatial neglect patients, by showing that an auditory spatial impairment exist in these patients independently of potential motor or egocentric biases. Unlike the results obtained when neglect patients were required to point manually to the perceived sound position [1,3,25,34], our findings cannot be attributed to any neglect-related directional motor deficit or other type of sensory-motor biases introduced by the motor response. Moreover, at variance with the results obtained when neglect patients were required to perform an auditory midline task [3,24,47,49], our findings cannot be explained as the consequence of an altered perception of the subjective head/body midline.
The difference between the measure of sound localisation adopted in the present study and those adopted in previous studies, becomes particularly evident when the effects of the presence or absence of visual information on sound localisation performance are considered. In the present study, the different visual conditions (vision vs. no-vision) did not produce any variation in the sound localisation performance of either group of patients. Specifically, the total absence of visual information did not result in a better auditory performance of neglect patients. This finding differs from the results obtained in the visual modality [8,19,21,22,26], in which neglect-related deficits typically improve when patients are blindfolded (though see Ref. [35,36] for negative results). Moreover, and more relevant to the aim of the present study, this finding differs from the results obtained in auditory tasks that required a manual pointing to free-field sounds, in which ipsilateral sound localisation errors are clearly more pronounced when vision is allowed as compared to when vision is precluded [25,32].

Such differential effect of vision in the auditory perceptual task and in auditory spatial tasks requiring manual pointing to sounds, suggest that different mechanisms may be activated by the two tasks. When hand-pointing response is required, the spatial coordinates of the sound might be partially remapped into eye-centred coordinates, due to hand-eye sensorymotor coordination [10,46]. Given the visual nature of the spatial deficit in neglect patients, such an eye-centred remapping would have a detrimental effect on sound localisation, producing a systematic rightward bias on hand-pointing to sounds. In this respect it is worthwhile to remember that eye-deviation towards the right has been often observed in visual neglect patients [27,50]. This effect would be more pronounced when vision is allowed as compared to when vision is precluded. In the present study, however, no motor response was required. Thus, patients could have performed the relative discrimination task within the initial head-centred coordinate system used to encode sound position, with no need of further coordinate transformation. This might explain why the perceptual task adopted in the present study was not affected by the modulation of the visual condition.

The presence of sound localisation deficits in our relative discrimination task suggests a derangement of auditory space perception in neglect patients. However, before concluding in favour of a predominantly perceptual deficit due to an impairment of auditory spatial maps, it is important to consider other possible explanations. In particular, the observed deficits might be conceived as an inability in retaining and comparing the spatial position of target sounds. According to this hypothesis, contralesional auditory deficit in neglect patients would not result from a perceptual deficit of sound localisation, but rather from a selective deficit of auditory spatial memory for positions in contralesional hemispace.

This hypothesis clearly predicts that neglect patients’ performance would vary as a function of whether the first stimulus was presented on left or right side. For instance, when the two sounds appeared in opposite hemifields (i.e., S1 on the left and S2 on the right, or viceversa), performance should have been worse when the left sound was presented first (S1) and the right sound was presented second (S2). Indeed, in such a case, the first stimulus had to be retained for 500 ms (interval between the two targets) before the second stimulus appeared and the perceptual match could be accomplished. This prediction was verified in a new analysis, in which performance in trials where S1 appeared on the left side and S2 on the right side were compared with trials where the two sounds had same spatial separation but opposite sequence. These comparisons revealed that performance did not vary as a function of the side of the first stimulus (for all comparisons \( P > 0.05 \) at \( t \)-test), suggesting that neglect patients’ discrimination ability was not influenced by a possible impairment in retaining left side stimuli.

This result argues against an explanation of the findings in terms of mere inability of remembering location of contralesional stimuli. Instead, the results of the present study are compatible with a contralesional deficit of auditory space perception in patients with visuospatial neglect.

Such interpretation is in agreement with the results of a recent electrophysiological study that revealed pathological early stages of auditory spatial input processing in patients with unilateral neglect [12]. Deouell and colleagues observed that the typical event-related brain potentials elicited in response to a change in sound spatial position (mismatch negativity [31]) was reduced in neglect patients when sounds were presented in the left hemispace relative to when sounds were presented in the right hemispace. Importantly, these findings were obtained in a passive listening situation, in which patients were not required to produce any stimulus-related response (i.e., patients were shown a silent movie and instructed to ignore any sound), clearly suggesting that the observed deficit might have arisen pre-attentively, at a purely perceptual stage.

The auditory spatial deficits revealed in the present study are particularly interesting in light of recent evidence that indicates the parietal lobe as a major area for the processing of auditory spatial information. Converging evidence in animals and humans suggests the existence of two separate neural pathways in the auditory system: one specialised for the processing of auditory patterns and the other specialised for the processing of auditory spatial information [9,38]. While the first pathway involves the superior temporal cortex,
the second pathway mainly involves the parietal areas. Such parietal involvement during sound localisation has also been confirmed by recent functional imaging studies, which revealed a predominantly parietal activation during auditory spatial tasks [7,20,51]. Given that unilateral neglect is typically associated with a lesion of the parietal areas [48], the severe impairment of auditory space perception observed in our patients might thus relate with the damage to this neural substrate.

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