Sound lateralisation in patients with left or right cerebral hemispheric lesions: relation with unilateral visuospatial neglect

Hirotaka Tanaka, Kenji Hachisuka, Hajime Ogata

Abstract

***Objectives*—To localise the brain lesion that causes disturbances of sound lateralisation and to examine the correlation between such deficit and unilateral visuospatial neglect.**

***Method*—There were 29 patients with right brain damage, 15 patients with left brain damage, and 22 healthy controls, who had normal auditory and binaural thresholds. A device was used that delivered sound to the left and right ears with an interaural time difference using headphones. The amplitude (an index of ability to detect sound image shifts from the centre) and midpoint (an index of deviation of the interaural time difference range perceived as the centre) parameters of interaural time difference were analysed in each subject using 10 consecutive stable saw toothed waves.**

***Results*—The amplitude of interaural time difference was significantly higher in patients with right brain damage than in controls. The midpoint of the interaural time difference was significantly more deviated in patients with right brain damage than in those with left brain damage and controls ($p<0.05$). Patients with right brain damage with lesions affecting both the parietal lobe and auditory pathway showed a significantly higher amplitude and deviated midpoint than the controls, whereas right brain damage with involvement of only the parietal lobe showed a midpoint significantly deviated from the controls ($p<0.05$). Abnormal sound lateralisation correlated with unilateral visuospatial neglect ($p<0.05$).**

***Conclusions*—The right parietal lobe plays an important part in sound lateralisation. Sound lateralisation is also influenced by lesions of the right auditory pathway, although the effect of such lesions is less than that of the right parietal lobe. Disturbances of sound lateralisation correlate with unilateral visuospatial neglect.**

(*J Neurol Neurosurg Psychiatry* 1999;**67**:481–486)

Keywords: sound lateralisation; auditory pathway; parietal lobe; unilateral visuo-spatial neglect

Department of Rehabilitation, Tokyo Rosai Hospital, 4-13-21 Ohmori-minami, Ohta-ku, Tokyo 143-0013, Japan
H Tanaka

Department of Rehabilitation Medicine, University of Occupational and Environmental Health, 1-1 Iseigaoka, Yahatanishi-ku, Kitakyushu, Fukuoka 807-8555, Japan
K Hachisuka
H Ogata

Correspondence to: Dr Hirotaka Tanaka, Department of Rehabilitation Medicine, Tokyo Rosai Hospital, 4-13-21 Ohmori-minami, Ohta-ku, Tokyo 143-0013, Japan. Telephone 0081 3 3742 7301; fax 0081 3 3744 9310.

Received 4 August 1998 and in final form 7 May 1999
Accepted 21 May 1999

Patients with unilateral spatial neglect show deficits in orienting towards, responding to, and reporting on stimuli located in the contralateral space of a cerebral hemispheric lesion. Although many researchers have described unilateral spatial neglect in visual modality,[1 2] directional hearing, auditory neglect, and auditory extinction remain to be investigated. Directional hearing is the ability to localise sound direction, and impairment of directional hearing is one of the aspects of unilateral spatial neglect in the auditory field, which also includes auditory neglect and extinction.[3] Bender and Diamond identified a relation between impairment of directional hearing and auditory extinction,[4] whereas Tanabe reported that the disturbance of directional hearing is different from auditory neglect or extinction.[5]

To evaluate directional hearing, the following three tests have been used. (1) Sound localisation in free field: to localise a sound source originating from loudspeakers.[6–10] (2) Sound localisation in virtual field: to localise spatial auditory information which is three dimensionally synthesised through headphones using digital filters constructed from head related transfer functions.[11] (3) Sound lateralisation: to determine the side of a sound signal presented through headphones while the interaural time difference and interaural intensity difference are changing.[12 13]

The relation between sound localisation and lateralised brain lesions has been previously examined. Several studies have reported that patients with supratentorial lesions exhibited impaired sound localisation in the contralateral auditory field, and showed no relation between impairment of sound localisation and laterality of the brain lesion.[6–8] On the other hand, Nordlund suggested that patients with brain lesions are able to locate sound from any direction unless the lower auditory pathways are affected.[14] Studies from our laboratory showed that patients with cerebral hemispheric lesions, including those affecting the auditory pathways, have a reduced capacity and anterior-posterior confusion of sound localisation in the anterior auditory space when tested in an anechoic chamber equipped with loudspeakers.[15] By contrast, patients with unilateral visuospatial neglect exhibited no left-right confusion, and their ability to localise the sound source in the left auditory space was similar to that of patients without unilateral visuospatial neglect.[15] Other studies have also shown that auditory neglect can be dissociated from visual neglect, but omissions of sounds are always more marked in the left ear of patients with a brain lesion on the right side.[16] Ruff *et al* indicated reduced capacity of sound localisation in patients with right brain lesions.[17] In this regard, Làdavas *et al* described a patient with a right temporal-parietal-occipital lobe lesion whose responses to left auditory stimuli were influenced by visual and proprioceptive spatial information.[9] The relation between visual and auditory systems in patients with brain lesions was also studied recently by Soroker *et al*, who reported that patients with damage to the right hemisphere associated with visual neglect failed to localise sounds on the left side and that blindfolding improved the localisation performance.[10]

There are still controversies as to whether patients with right cerebral hemispheric lesions have reduced capacity of directional hearing and whether the impairment of directional hearing correlates with unilateral visuospatial neglect. The reasons for the discrepancies may be due to differences in the sensitivity of the measuring instruments and accuracy of detecting brain lesions. In the present study, we examined the relation between sound lateralisation and unilateral visuospatial neglect. For this purpose, we compared sound lateralisation in patients with right brain damage (RBD) and patients with left brain damage (LBD) by using a method that discriminates interaural time differences. The site of brain lesion was confirmed by MRI.

Material and methods

SUBJECTS

Subjects for the sound lateralisation test were consecutive stroke outpatients who visited our clinic for routine follow up examination, and who fulfilled the following inclusion criteria. Each patient had a unilateral cerebral hemispheric lesion confirmed by MRI, had no severe or moderate aphasia, was able to understand and perform the sound lateralisation test, had an auditory threshold of 45 dB for pure tones of 500 Hz, and a binaural threshold difference of 10 dB, and voluntarily enrolled in the study with informed consent. A total of 44 patients (34 men and 10 women) fulfilled the above criteria and were enrolled as the test subjects in the present study The control subjects included 22 right handed healthy volunteers (five men and 17 women), who had no history of neurological or auditory diseases. The auditory threshold of the control subjects was 45 dB or less for pure tones of 500 Hz, and binaural threshold differences of 10 dB or less.

APPARATUS

Defects in sound lateralisation were examined using an automatic self recording device (TD-01, Rion Co, Tokyo, Japan) which generated an identical continuous narrow band sound of 500 Hz centre frequency and 75 Hz bandwidth through each headphone. The device generated an interaural time difference and interaural intensity difference, with a time difference range of 2 to 2048 μs.[12 13] The sound signal was digitised by an A/D converter and processed through two circuits. In the first, the signal was relayed to a variable delay circuit that created a time delay of 2 μs each step at a constant rate of 25 steps/s. In the other circuit, the signal was relayed to a fixed delay circuit. These processed signals were reconverted into analogue signals using separate D/A converters. The sound signals, which could be controlled by a changeover switch, were delivered to headphones through amplifiers. With the constant change in interaural time difference, the subject perceived the sound as moving from the centre to the right or left side in an imaginary field. A thermal printer connected to the self recording device showed a continuous pattern of saw toothed waves. The waves were positive when the signals from the right headphone preceded those from the left headphone, and negative when the signals from the right headphone lagged after those from the left headphone.

PROCEDURE

The sound lateralisation test was performed over a period of 10 minutes, in a quiet room. Sound was presented to each ear through headphones at 20 dB above the subject's auditory threshold. If the sound was not at the centre of the imaginary field, the output level from the right headphone was adjusted by 1 dB increments or decrements. The subject was instructed to press a lever to the right or left side as soon as possible when the sound image was perceived as having deviated towards the right or left side, respectively. Firstly, the sound of the right headphone began to precede gradually that from the left headphone, and after several seconds, the subject noticed that the sound had moved towards the right side in the imaginary field. When the subject pressed the lever to the right, the sound from the right headphone began to delay by 2 μs/step at 25 steps/s. At that stage, the sound from the right headphone lagged behind that from the left headphone, and was finally perceived as having deviated toward the left side. When the subject pressed the lever to the left, the sound from the right headphone began to precede again by 2 μs/step at 25 steps/s. The subject was asked to practice a few trials, and data acquisition began after it was confirmed that the subject was able to adequately handle the lever. The test was terminated after obtaining 10 consecutive stable saw toothed waves.

The amplitude of the interaural time difference was defined as the average amplitude of 10 consecutive stable saw toothed waves, and reflected the ability to detect a sound image shift from the centre—that is, an index of sound lateralisation. The midpoint of interaural time difference was defined as the average midpoint between the right and left peaks of 10 consecutive stable saw toothed waves, reflecting deviation of interaural time difference range perceived as a centre—that is, an index of deviation. If the midpoint deviates to negative, sound lateralisation is regarded as having deviated to the right side because more preceded signals from the left headphone are necessary to perceive the sound image as having moved to the left side.

For evaluating unilateral visuospatial neglect, Albert's line cancellation test,[18] copy figure test, and line bisection test were performed in advance. One or more omissions of crossing a line on the left side in the Albert's line

Table 1 Patient characteristics

	Control (n=22)	*Left brain damage (n=15)*	*Right brain damage (n=29)*
Age (y)	56.4 (11.4)	58.5 (10.9)	56.7 (12.3)
Sex (men/women)	5/17	11/4	23/6
Auditory threshold (dB):			
Right	32.3 (6.9)	33.3 (4.9)	33.8 (7.3)
Left	31.4 (8.2)	29.7 (6.9)	33.3 (7.0)
Causes of brain lesion:			
Haemorrhage	0	5	18
Infarction	0	9	9
Subarachnoid haemorrhage	0	1	2
Unilateral visuospatial neglect	0	0	10
Auditory extinction	0	0	2

Data on age and auditory threshold are presented as mean (SD).

Table 2 Amplitude and midpoint of interaural time difference in the groups

	Control (n=22)	*Left brain damage (n=15)*	*Right brain damage (n=29)*
Amplitude (μs)	559 (304)	750 (607)	1085 (558)*
Out of normal range‡	1	1	13
Midpoint (μs)	32 (97)	30 (14)†	–235 (392)*†
Out of normal range§	0	1	9

Data of amplitude and midpoint are presented as mean (SD). Amplitude is an index of ability to detect sound image shifts from the centre. Midpoint is an index of deviation of the interaural time difference range perceived as the centre.
* and †p<0.05 compared with the control and left brain damage groups, respectively; one way ANOVA followed by Scheffe's test.
‡Number of patients with an amplitude out of the normal range (<1167 μs).
§number of patients with a midpoint out of the normal range (from –162 to 227 μs).

cancellation test were defined as abnormal. The copy figure test consisted of reproducing two figures cited from the standardised test of higher motor function,[19] and one or more omissions of a line on the left side were defined as abnormal. The line bisection test was to make a mark at the midpoint of a line 20 cm long, printed on a sheet of B5 paper. A deviation of 1 cm or more from the midpoint to the right was defined as abnormal. Patients with one or more abnormal findings were diagnosed as having unilateral visuospatial neglect.

For evaluation of auditory extinction, the sound of snapping fingers was delivered to each ear. After it was confirmed that the subject was able to recognise the stimulus, the stimulus was delivered at random to the right ear, left ear, or both ears. Auditory extinction represented repeated neglect of bilaterally applied sound stimulus to one ear.

Brain MRI was performed using 1.5-tesla equipment (Toshiba MRI-200 FX III) to confirm the presence or absence of a brain lesion as well as its location. The involvement of the parietal lobe or auditory pathways was determined by a qualified neuroradiologist based on the atlas of Kretschmann and Weinrich.[20]

STATISTICAL ANALYSIS

All data were expressed as mean (SD). Statistical analysis was performed using a commercial software package (StatView, ver 4.01). One way analysis of variance (ANOVA) was applied to examine differences in age among the control, RBD, and LBD groups, and in amplitude and midpoint of the interaural time difference among the three groups and among the five subgroups (control, RBD with or without a parietal lobe lesion and with or without an auditory pathway lesion). When necessary, ANOVA was followed by Scheffe's test for multiple comparisons. Fisher's exact test was used to compare differences in disturbances of sound lateralisation and unilateral visuospatial neglect. A p value<0.05 denoted the presence of a statistically significant difference.

Results

PATIENTS' CHARACTERISTICS

We tested 29 patients with RBD and 15 with LBD. There were no significant differences in age among control subjects, and patients with RBD or LBD (table 1). The cause of brain lesion included cerebral haemorrhage, cerebral infarction, and subarachnoid haemorrhage (table 1). The mean interval between the onset of cerebrovascular accident and present study was 8.2 (SD 18.9) months. Ten patients with RBD had unilateral visuospatial neglect, and two patients had both auditory extinction and unilateral visuospatial neglect.

AMPLITUDE AND MIDPOINT OF INTERAURAL TIME DIFFERENCE

Twenty five patients with RBD were able to recognise a sound image shift toward the right and left auditory fields, exhibiting at least 10 consecutive stable saw toothed waves, but the other four patients failed. The negative peaks of the four patients with RBD were out of scale toward the negative side and the amplitude of the interaural time difference in these patients was more than the maximum measurable amplitude (2048 μs). Accordingly, the mean amplitude in these patients was set at 2048 μs. Furthermore, in the same patients, the midpoints of the interaural time difference were out of scale toward the negative side and were less than the minimum measurable midpoint (–1024 μs). Accordingly, the mean midpoint in these patients was set at –1024 μs. All patients with LBD and control subjects were able to recognise a sound image shift toward the right and left auditory fields, exhibiting at least 10 consecutive stable saw toothed waves.

The mean amplitude and midpoint of interaural time difference for each group are shown in table 2. The mean amplitude was significantly higher in patients with RBD than in controls (oneway ANOVA followed by Scheffe's test, p<0.05). The ability of patients with RBD to discriminate interaural time difference tended to be lower than controls. The amplitude recorded in 21 of 22 controls and 14 of 15 patients with LBD fell within the normal range (1167 μs, calculated as the mean of the control group (2 SD)). By contrast, the amplitude recorded in 13 of 29 patients with RBD did not.

The midpoint in patients with RBD was significantly more deviated toward the negative side than the controls and patients with LBD (one way ANOVA followed by Scheffe's test; p<0.05, p<0.05), and the range of interaural time difference perceived as being the centre was deviated to the right. The midpoint recorded in all control subjects and 14 of 15 patients with LBD fell within the normal range (representing the mean of the control group (2 SD); from –162 to 227 μs). By contrast, the midpoint recorded in nine of the 29 patients with RBD did not. Thus, the amplitude and

Table 3 Effects of lesions affecting the parietal lobe and/or auditory pathway on the amplitude and midpoint recorded in the patients with right brain damage

	Control	*Right brain damage*			
	(n=22)	*NP/NA (n=6)*	*NP/A (n=5)*	*P/NA (n=3)*	*P/A (n=15)*
Amplitude (μs)	559 (304)	666 (362)	894 (277)	1276 (955)	1283 (537)*
Midpoint (μs)	32 (97)	6 (76)	−59 (99)	−557 (529)*	−326 (443)*

Data represent the mean (SD). NP/NA=without lesions of the parietal lobe nor auditory pathway; NP/A=without parietal lobe involvement but with auditory pathway lesion; P/NA=with lesion of the parietal lobe but without auditory pathway involvement; P/A=with parietal lobe and auditory pathway involvement.
*p<0.05, compared with the control group; one way ANOVA followed by Scheffe's test.

midpoint of only three of the control subjects and patients with LBD were outside the normal range, whereas 14 of the 29 patients with RBD showed abnormal amplitude and midpoint. These results indicate that disturbances in sound lateralisation correlated with right cerebral hemispheric lesions.

EFFECT OF INVOLVEMENT OF RIGHT PARIETAL LOBE AND AUDITORY PATHWAYS ON AMPLITUDE AND MIDPOINT

We further analysed the effect of involvement of the right brain lesion and auditory pathways on the amplitude and midpoint parameters of interaural time difference. For this purpose, we subdivided the RBD group into four subgroups according to the presence or absence of lesions affecting the parietal lobe and/or auditory pathways, as confirmed by MRI. The NP/NA group consisted of six patients without involvement of the parietal lobe or auditory pathway. The NP/A group consisted of five patients without involvement of the parietal lobe but with involvement of the auditory pathway. The P/NA group consisted of three patients with parietal lobe involvement but without auditory pathway involvement. The P/A group consisted of 15 patients with involvement of both the parietal lobe and auditory pathway. The amplitude of the interaural time difference was higher in all RBD groups than the control group although this was significant in only the P/A group (one way ANOVA followed by Scheffe's test, $p<0.01$; table 3). Furthermore, the midpoints of interaural time difference deviated toward the negative side in all RBD groups relative to the control (table 3). Such deviation was significant in the P/NA and P/A groups relative to the control group (one way ANOVA followed by Scheffe's test, $p<0.05$, $p<0.05$; table 3).

RELATION BETWEEN UNILATERAL VISUOSPATIAL NEGLECT AND SOUND LATERALISATION

Finally, we analysed the relation between unilateral visuospatial neglect and sound lateralisation— that is, amplitude and midpoint of interaural time difference, in patients with RBD (table 4). A significantly higher proportion of patients with unilateral visuospatial neglect showed increases in amplitude of the interaural time difference and deviations of the midpoint compared with those without unilateral visuospatial neglect (Fisher's exact test, $p<0.05$, $p<0.05$). All six patients with both unilateral visuospatial neglect and abnormally deviated midpoint had also abnormally increased amplitude of the interaural time difference.

Table 4 Relation between interaural time difference and unilateral visuospatial neglect in patients with the right brain damage

	Unilateral visuospatial neglect		
Interaural time difference	*(+)*	*(−)*	*Total*
Amplitude:			
Abnormal*	8	5	13
Normal	2	14	16
Total	10	19	29
Midpoint:			
Abnormal†	6	3	9
Normal	4	16	20
Total	10	19	29

*Patients with amplitude of interaural time difference being out of the normal range.
†Patients with shift of midpoint of interaural time difference being out of the normal range.
Fisher's exact test for the 2×2 table, p<0.05.

We also examined the relation between unilateral visuospatial neglect and sound lateralisation according to the presence or absence of lesions of the right parietal lobe and auditory pathway, although the sample size was small in each subgroup. Seven of eight patients with unilateral visuospatial neglect and abnormally increased amplitude and all six patients with unilateral visuospatial neglect and abnormally deviated midpoint showed both parietal lobe and auditory pathway involvement. Patients with only one unilateral visuospatial neglect, abnormally increased amplitude, or deviated midpoint showed no definite relation with lesions of the right parietal lobe and auditory pathway. Most patients with RBD with normal sound lateralisation had no unilateral visuospatial neglect.

Discussion

Although we could not show any relation between sound localisation in a free field and laterality of brain lesion in our previous study,[15] the results of the present study indicated that sound lateralisation is related to lesions of the right cerebral hemisphere and correlates with unilateral visuospatial neglect. The discrepancy in the results of the two studies may be due to patient selection and the method used for the evaluation. For evaluating sound localisation in a free field, patients should be seated and maintain their body and head in a straight position surrounded by loudspeakers arranged in an anechoic chamber. As some patients with severe unilateral visuospatial neglect have their body and head twisted or tilted towards the right, these patients are not suitable for examination of sound localisation in free field. In the present study, there was no need to pay attention to the twist and tilt of the body and head because headphones were used instead of loudspeakers for examining sound lateralisation. Therefore, the subjects in this study included a few patients who showed severe unilateral visuospatial neglect and twisted and tilted their body and head, who might have been otherwise excluded from the previous study.

Sound lateralisation primarily depends on discrimination of interaural time difference and interaural intensity difference threshold. If identical sounds with any combination of interaural time difference or interaural intensity difference are simultaneously presented to both ears through headphones, the sound image is lateralised to the side causing the earlier or louder stimulus to be heard.[13] The apparatus used in our study is an automatic self recording device, which can synthesise sound with various interaural time difference and interaural intensity difference. However, we only examined the ability to discriminate interaural time difference in the present study as we found in a series of preliminary studies that the reproducibility of sound lateralisation by discriminating interaural intensity difference threshold was poor compared with that obtained by discriminating interaural time difference. Our decision was also based on the results reported by Sato *et al* indicating that some patients with postlabyrinth disorders showed no disturbances of directional hearing in interaural intensity difference but in interaural time difference.[12] Considering the results of our previous[15] and present studies, we think that the use of headphones to examine sound lateralisation to discriminate interaural time difference is more sensitive than that with loudspeakers in a free field.

Sanchez-Longo *et al* examined 50 patients for auditory localisation using loudspeakers.[7] They found that patients with temporal lobe lesions showed abnormal sound localisation in the contralateral auditory field. However, it was not clear whether this abnormality was caused by parietal lobe lesion and whether it correlated with unilateral visuospatial neglect. Ruff *et al* showed that the displacement error scores in patients with right posterior brain lesions in free field were consistently higher than those of the other groups studied,[17] although they did not specify whether the lesion involved the temporal and parietal lobes. Yamada *et al* examined sound lateralisation in patients with left temporal lobe lesions using a method similar to that employed in our study.[13] They showed that the discrimination threshold of interaural intensity difference was higher in patients with LBD than in healthy controls. However, they did not examine patients with right cerebral hemispheric lesions or the relation between sound lateralisation and unilateral visuospatial neglect. Our study examined the type of patients who showed sound lateralisation and the relation between sound lateralisation and unilateral visuospatial neglect using a method that examined discrimination of the interaural time difference.

In the present study, patients with RBD showed diminished ability to detect a sound image shift from the centre and deviation of the range perceived as the centre toward the right. Laterality of the cerebral hemispheric lesion is essential to induce a disturbance of sound lateralisation, as lesions of the right parietal lobe were associated with disturbance of sound lateralisation whereas patients with lesions of the left parietal lobe did not exhibit such abnormality. Based on our results of analysis of localisation of the brain lesion, the responsible compartment for sound lateralisation seems to be the right parietal lobe and auditory pathways. Patients with lesions affecting these areas are more likely to exhibit disturbances of sound lateralisation and unilateral visuospatial neglect. Furthermore, some patients with lesions involving only one of these areas may also show a disturbance of sound lateralisation. Because a significant deviation of sound image toward the right was detected in patients with lesions that affected only the parietal lobe but was not with lesions localised in the auditory pathway, the most important area for sound lateralisation seems to be the right parietal lobe, followed by the right auditory pathway.

Our results also showed a relation between unilateral visuospatial neglect and sound lateralisation. When both the parietal lobe and auditory pathway in the right cerebral hemisphere are involved, abnormal sound lateralisation toward the left was closely associated with unilateral visuospatial neglect. There was no relation between unilateral visuospatial neglect and sound lateralisation in subjects with lesions of the left parietal lobe. Interestingly, our results showed that the midpoint of the range perceived as the centre in the auditory field was deviated to the right in the same way as deviation of visual localisation in unilateral visuospatial neglect. If these phenomena are derived from a common supramodal system for spatial attention, a substantial degree of correlation should be expected between neglect manifestations in different sensory modalities.[10] We noticed failure of patients with RBD to recognise a sound image shift from the centre— that is, an increase in the threshold of discrimination of interaural time difference. An increase in threshold to stimuli has not been found in the visual modality, and may be one of the features in the auditory modality. Although the precise mechanism and relation between sound lateralisation and visuospatial neglect needs further examination, non-lateralised attentional defects, which may constitute an important component of the neglect phenomenon,[21] seem probably to cause an increase in the threshold of discrimination of interaural time difference.

In conclusion, our results showed that the right parietal lobe plays an important part in sound lateralisation whereas the right auditory pathway plays a lesser part in this process, as evaluated by discrimination of interaural time difference. We also showed that disturbances of sound lateralisation correlated with unilateral visuospatial neglect.

This work was supported by a grant from the Medical Research Council of Labour Welfare Corporation.

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