

Disturbed Sound Lateralization in Patients with Spatial Neglect

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Abstract

■ Previous studies on auditory space perception in patients with neglect have investigated localization of free-field-sound stimuli or lateralization of dichotic stimuli that are perceived intracranially. Since those studies in part revealed contradictory results, reporting either systematic errors to the left or systematic errors to the right, we reassessed the ability of auditory lateralization in patients with right hemispheric lesions with and without neglect. Unexpectedly, about half of the patients with neglect showed erratic judgments on sound position, that is, they were completely unable to lateralize sounds. The remaining neglect patients only showed a small deviation of the auditory median plane to the left side,

indicating that they perceived the sounds as slightly shifted to the right side. The comparison between both groups revealed higher severity of neglect in the group of neglect patients who were unable to perform the task, suggesting that the inability of sound lateralization was associated with the strength of clinical neglect. However, we also observed 1 out of 9 patients with left brain damage who was not able to lateralize spatial sounds. This patient did not show any symptoms of spatial neglect. Thus, it may be that a spatial auditory deficit, such as that observed here in right-brain-damaged patients, only co-occurs with spatial neglect if the right superior temporal cortex is lesioned. ■

INTRODUCTION

Spatial neglect is a disorder that is characterized by a deviation of the field of exploration to the side ipsilateral to the lesion leading to neglect of information located on the contralesional side of space (Karnath, Niemeier, & Dichgans, 1998; Karnath & Perenin, 1998). It has frequently been reported that the perception of subjective straight ahead (SSA) is also shifted to the ipsilesional side in such patients (Pisella, Rode, Farnè, Boisson, & Rossetti, 2002; Chokron & Bartolomeo, 2000; Richard, Honoré, & Rousseaux, 2000a, 2000b; Richard, Rousseaux, & Honoré, 2001; Ferber & Karnath, 1999; Farnè, Ponti, & Làdavas, 1998; Rossetti, Rode, & Pisella, 1998; Perenin, 1997; Chokron & Imbert, 1995; Karnath, 1994, 1997; Mark & Heilman, 1990; Heilman, Bowers, & Watson, 1983). Few studies had found individual neglect patients with either a normal position of the SSA or SSA shifts that were not correlated with scores of neglect tests (Bartolomeo & Chokron, 1999; Chokron & Bartolomeo, 1997, 1998; Hasselbach & Butter, 1997). Thus, it may be tentatively concluded that the majority of experiments on this issue is consistent with the assumption of an egocentric frame of spatial reference in patients with neglect that is shifted toward the ipsilesional side. The question arises

whether this view may be generalized to the perception of spatial position of auditory stimuli, that is, whether the auditory space of neglect patients is also shifted compared to healthy subjects.

Previous investigations on this issue were inconsistent. In a first type of experiments, auditory lateralization was tested by variation of interaural differences in time of arrival (ITD) or sound-pressure level (ILD) of dichotic stimuli presented via headphones. Since only one of the two main spatial cues for horizontal sound localization (either ITD or ILD) was present, subjects perceived these stimuli intracranially, that is, along the interaural line inside the head (see Blauert, 1997). Bisiach, Cornacchia, Sterzi, and Vallar (1984) investigated 15 right-brain-damaged patients who had both neglect and hemianopia in such an auditory lateralization task. Variable ILDs were presented in random order and patients indicated stimulus locations on their head by pointing with their nonparetic hand. The patients exhibited a leftward shift of their auditory median plane (AMP); that is, they perceived the auditory stimuli shifted to the right compared to healthy subjects. Tanaka, Hachisuka, and Ogata (1999) examined 12 right-brain-damaged patients with spatial neglect by using a different psychophysical method. The intracranial position of the sound image was changed by variation of ITDs stepwise from one side to the other until the subject indicated that the sound had passed the median plane of the head. The authors confirmed

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the observations of Bisiach et al. (1984) by showing a shift of the AMP toward the left side.

Beyond such auditory lateralization tasks, a second type of studies employed tasks in which sound sources had to be localized in extrapersonal space. For this purpose, stimuli were displayed either via loudspeakers or via headphones. In the latter case, stimuli were used that simulated ear-canal waveforms produced by free-field sources; such stimuli are perceived as being located outside the head (see Wightman & Kistler, 1989a, 1989b). By employing a pointing task, Pinek, Duhamel, Cave, and Brouchon (1989) demonstrated a systematic rightward error of azimuthal sound localization in three patients with spatial neglect (two of these had hemianopia in addition), which corresponded to a leftward shift of the AMP. Vallar, Guariglia, Nico, and Bisiach

(1995) investigated 11 right-brain-damaged patients with spatial neglect who indicated the moment at which a sound moving stepwise from one side to the other passed the median plane. Unlike Pinek et al. (1989), these authors found a rightward shift of the AMP. Using a similar method as Vallar et al. (1995), Kerkhoff, Artinger, and Ziegler (1999) also reported a rightward shift of the AMP in a single neglect patient.

Summing up, localization of externalized sound has been reported to be shifted either to the right (Pinek et al., 1989) or to the left (Kerkhoff et al., 1999; Vallar et al., 1995) in patients with spatial neglect, while lateralization of intracranial sound images was reported to be shifted to the right (Tanaka et al., 1999; Bisiach et al., 1984). In light of these inconsistent findings, here we made a renewed approach to this problem

Table 1. Demographic and Clinical Data of the Different Groups of Brain-Damaged Patients and Healthy Subjects

	<i>Neglect</i>		<i>RBD</i>		<i>HA</i>		<i>LBD</i>		<i>Healthy Subjects</i>	
Number	15		10		7		9		10	
Sex	8 f, 7 m		1 f, 9 m		1 f, 6 m		2 f, 7 m		2 f, 8 m	
Age, mean (SD)	60	(15.7)	52	(9.1)	65	(13.9)	62	(16.0)	62	(7.5)
Etiology										
Infarct	12		7		6		7			
Hemorrhage	3		3		1		2			
Lesion										
Cortical/subcortical	10		3		7		7			
Basal ganglia	3		4		–		2			
Thalamus	2		3		–		–			
Time since lesion Days, mean (SD)	10.8	(5.5)	8.5	(6.2)	8.2	(9.7)	7.6	(4.3)		
Visual field defect (% present)	0		0		100		0			
Letter Cancellation										
Left, mean (SD)	5.3	(6.4)	28.8	(1.9)	29.7	(0.5)	28.7	(0.9)		
Right, mean (SD)	20.9	(8.7)	29.7	(0.5)	29.3	(0.8)	28.0	(1.4)		
Bells Test										
Left, mean (SD)	3.4	(3.7)	14.7	(0.7)	14.3	(0.8)	13.9	(1.2)		
Right, mean (SD)	10.9	(5.3)	14.8	(0.6)	14.5	(0.8)	13.0	(0.7)		
Baking Tray task										
Left, mean (SD)	5.1	(3.5)	7.8	(0.9)	8.0		8.1	(0.2)		
Right, mean (SD)	10.9	(3.5)	8.2	(0.5)	8.0		7.9	(0.2)		
Copying % omitted, mean (SD)	58.2	(27.1)	1.3	(4.0)	0.0		3.2	(5.8)		

Neglect = right-brain-damaged patients with neglect; RBD = right-brain-damaged patients without neglect; HA = right-brain-damaged patients with hemianopia following an infarct in the territory of the posterior cerebral artery; LBD = left-brain-damaged patients without neglect or hemianopia; Sex: f = female, m = male. Visual field defects (hemianopia, quadrantanopia) were assessed by standard neurological examination and/or Tübingen perimetry.

employing a task of auditory lateralization in acute stroke patients. The main rationale for choosing the method of dichotic stimulation was that we were interested in genuine auditory disorders of space perception. As mentioned above, shifts of the SSA have been shown to occur with spatial neglect. Consequently, systematic errors with judgments on the location of sound sources in external space can be either due to (a) a shift of the egocentric reference frame while hearing is normal or to (b) a shifted auditory space with normal egocentric reference frame. The present method employed judgments on positions of intracranial percepts in relation to the median plane of the head. That is, we measured the ITD that evoked a percept located in the center of the head. Thus, factors involving shifts of the egocentric frames of reference affecting localization in external space may be excluded. Moreover, the patients in the present study had to indicate sound locations verbally so that possible influences of motor impairments on the behavioral responses were cancelled, which might have affected measures of sound position in the previous studies of Pinek et al. (1989) and Bisiach et al. (1984).

Auditory lateralization was examined in four groups of patients with acute unilateral brain damage, consecutively admitted to the Department of Neurology at the University of Tübingen 15 right-brain-damaged patients with neglect, 7 right-brain-damaged patients with hemianopia (HA) following infarcts in the territory of the posterior cerebral artery, 10 right-brain-damaged patients without neglect and hemianopia (RBD), and 9 left-brain-damaged patients without neglect and hemianopia (LBD). In addition, a group of 10 healthy subjects was tested. All subjects gave their informed consent to participate in the study that has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Table 1 gives an overview of all subjects included.

Dichotic stimuli were presented via headphones. The ITD of the sound stimulus was varied over a range from -400 (sound leading at the left ear) to $+400$ μsec (leading at the right ear). Immediately after stimulus presentation, subjects were required to indicate whether the perceived intracranial position of the sound was to the “left” or “right” of the median plane of the head.

RESULTS

Acuity of Sound Lateralization

For each subject, the frequency of the judgments “right” was plotted as a function of ITD. In 7 out of 15 neglect patients (46.7%), we found erratic distributions of left/right judgments on dichotic sound ($R^2 < .75$, $p > .05$), indicating a general inability of auditory lateralization (Figure 1A, open symbols). The remaining 8 neglect patients (Figure 1A, closed symbols) showed psychometric functions of sigmoidal shape ($R^2 > .75$, $p < .05$),

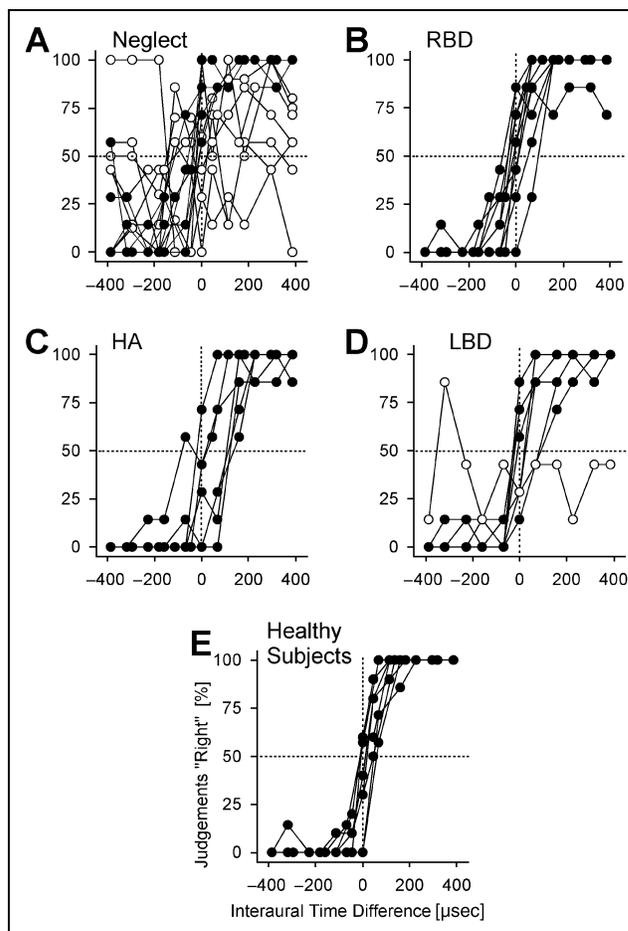


Figure 1. Individual psychometric functions for lateralization of dichotic sounds with variable ITDs in the four groups of brain-damaged patients (A–D) and healthy subjects (E). The percentage of judgments “right” is plotted as a function of the ITD. Each data point is averaged over seven trials. Closed symbols indicate a significant fit of the individual data to a sigmoid function ($R^2 > .75$, $p < .05$). Open symbols indicate a nonsignificant fit ($R^2 < .75$, $p > .05$) due to erratic left/right judgments on the auditory stimuli, which document a general inability of sound lateralization. Negative ITDs indicate stimuli leading in time on the left ear, positive ITDs indicate stimuli leading in time on the right ear. RBD = right-brain-damaged patients; HA = patients with hemianopia; LBD = left-brain-damaged patients.

indicating a significant ability to make left/right judgments on the sound stimuli presented. In the groups without neglect, that is, the RBD patients, HA patients, LBD patients, and healthy subjects (Figure 1B–E), only one LBD patient was not able to lateralize sound stimuli (Figure 1D, open symbols). The R^2 values were taken as a measure of the acuity of sound lateralization. The comparison between the five groups of subjects revealed a significant difference, $F(4,46) = 4.01$, $p = .007$. Post hoc testing with an adjusted α level of $p < .008$ revealed significantly lower R^2 values for the group of neglect patients compared to the groups of RBD patients, $t(14) = -3.22$, $p = .006$, HA patients, $t(14) = -3.24$, $p = .006$, and healthy subjects, $t(14) = -3.4$, $p = .004$. Since the LBD group included one patient with

an erratic psychometric function, no significant difference in the acuity of sound lateralization of the neglect and LBD groups could be demonstrated, $t(22) = -1.47$, $p = .17$. However, we found no significant differences when the LBD group was compared with the RBD group, $t(8) = -.91$, $p = .39$, or healthy subjects, $t(8) = 1.06$, $p = .32$.

Systematic Errors in Sound Lateralization

In all subjects who were able to lateralize auditory stimuli (i.e., who showed $R^2 > .75$), systematic shifts of the AMP were analyzed (Figure 2). The differences between the five groups of subjects were significant, $F(4,38) = 6.47$, $p < .001$. Post hoc testing using an adjusted α level of $p < .006$ revealed that the patients with neglect showed a significant deviation of the mean AMP to the left ($-41.0 \mu\text{sec}$) compared to the group of healthy subjects, $+19.3 \mu\text{sec}$, $t(15) = -3.69$, $p = .002$, and the HA patients, $+67.7 \mu\text{sec}$, $t(10) = 3.77$, $p = .004$. Thus, neglect patients perceived a dichotic sound with constant ITD farther to the right compared to HA patients or healthy subjects. No significant differences (see adjusted α level above) in the mean position of the AMP was obtained when the neglect group was compared with the RBD group, $-3.6 \mu\text{sec}$, $t(15) = -1.91$, $p = .076$, and the group of LBD patients, $+18.0 \mu\text{sec}$, $t(14) = -2.91$, $p = .012$.

In contrast, the mean AMPs measured in the three brain-damaged groups of patients without neglect did not significantly differ from that of healthy subjects, HA: $t(8) = 1.86$, $p = .102$, RBD: $t(18) = 1.49$, $p = .154$, LBD:

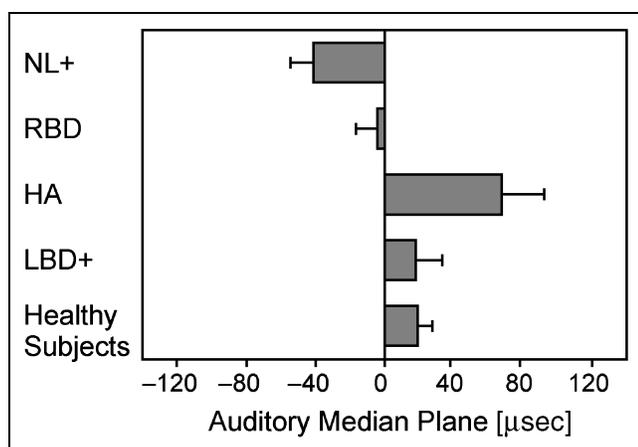


Figure 2. Mean deviation ($\pm\text{SEM}$) of the AMP in the brain-damaged patient groups and the healthy subjects. Only those subjects whose left/right judgments on auditory stimuli could be fitted to a sigmoidal equation were included ($R^2 > .75$, $p < .05$). Negative values indicate a deviation of the AMP to the left (or a shift of the auditory percept to the right), positive values indicate a deviation of the AMP to the right (or a shift of the auditory percept to the left). NL+ = subgroup of neglect patients with significant sound lateralization ability; RBD = right-brain-damaged patients; HA = patients with hemianopia; LBD+ = left-brain-damaged patients with significant sound lateralization ability.

$t(14) = -2.85$, $p = .78$. In addition, we found no significant difference between the patients with right hemispheric lesion with and without hemianopia, RBD versus HA: $t(9) = 2.58$, $p = .029$.

Relation between Clinical Data and the Ability of Sound Lateralization

To investigate possible factors that might determine the ability or inability to perform sound lateralization, we compared age, the time passed since lesion, volume and location of the lesion, and the severity of neglect between those neglect patients who were able to lateralize sound stimuli (NL+) and those who were not able to perform this task (NL-). We found no significant differences in age, $t(10) = -1.2$, $p = .26$, time since lesion, $t(12) = -.52$, $p = .61$, or lesion volume, $t(13) = -.63$, $p = .54$.

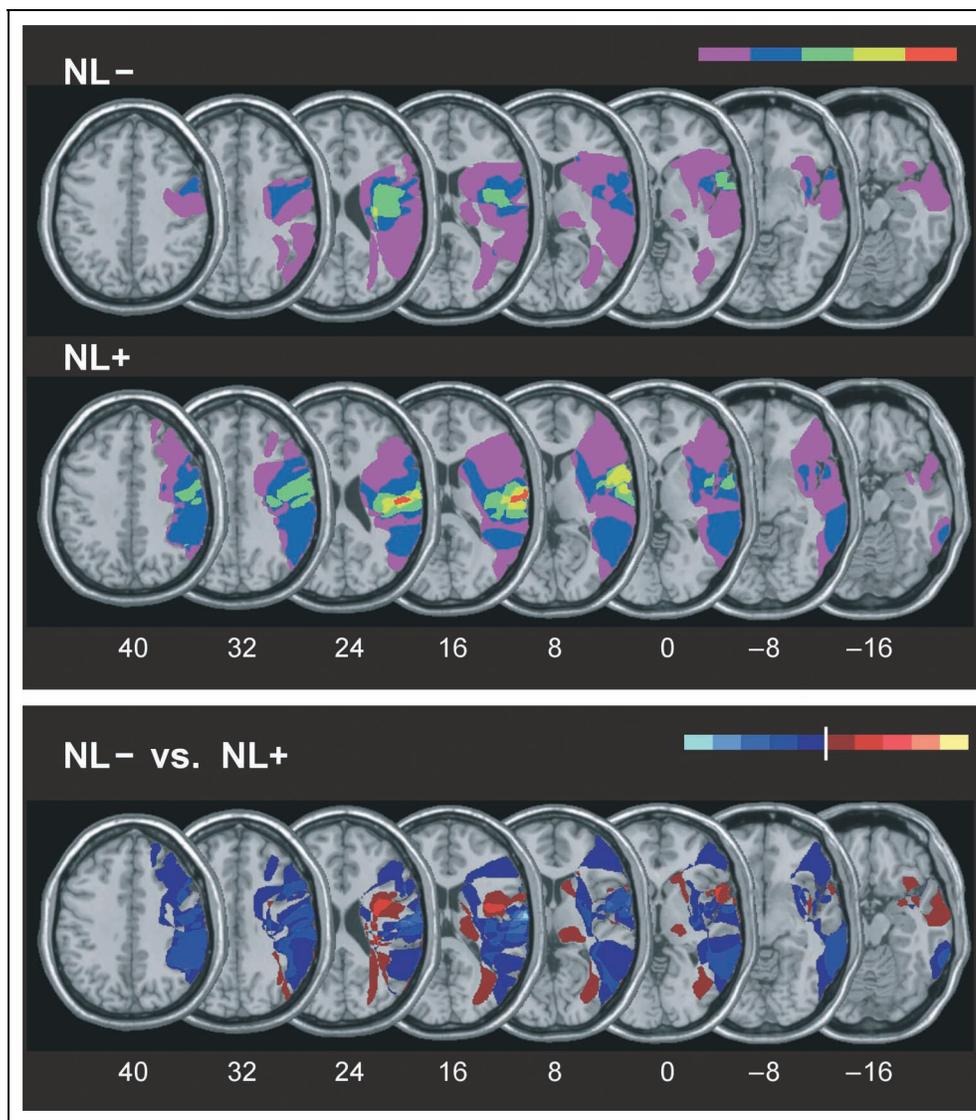
In 10 out of the 15 neglect patients, we found lesions that involved cortical areas. In the other 5 neglect patients, lesions were confined to subcortical structures, namely, the basal ganglia or the thalamus. These latter subjects were excluded from the following lesion analysis aiming to identify the cortical structures typically affected in the two groups of neglect patients. In both groups, we found a lesion overlap in the superior temporal gyrus (STG) and planum temporale that extended into the subcortical white matter and pre- and postcentral gyri (Figure 3). To directly compare lesion location between the two groups, we subtracted the superimposed lesions of the NL+ patients ($n = 5$) from those of the NL- patients ($n = 5$). The analysis did not reveal a specific area typically involved in the NL- patients (Figure 3).

In contrast, a significant relation was observed between sound lateralization and the severity of neglect symptoms (Figure 4). The subgroup of NL- patients showed significantly higher percentage omission scores than the NL+ patients in the Bells test, $t(12) = -2.27$, $p = .042$ and the copying task, $t(12) = -3.55$, $p = .004$. A numeric tendency for more severe neglect in NL- patients was also present in the Letter Cancellation and the Baking Tray tasks (Figure 4).

DISCUSSION

In the present study, patients with acute spatial neglect were examined for their ability of sound lateralization. Unlike all previous research on this topic (Bellmann, Meuli, & Clarke, 2001; Cusack, Carlyon, & Robertson, 2001; Kerkhoff et al., 1999; Tanaka et al., 1999; Vallar et al., 1995; Pinek & Brouchon, 1992; Pinek et al., 1989; Bisiach et al., 1984), we found about half of the consecutively admitted patients to be completely unable to perform this task (NL-); they showed erratic judgments on intracranial sound locations. The remaining patients with acute neglect (NL+) performed the

Figure 3. Top: Overlapping lesion location in 10 neglect patients who had lesions involving cortical structures (NL+ = subgroup of 5 neglect patients with significant sound lateralization ability; NL- = subgroup of 5 neglect patients who showed erratic left/right judgments in the sound lateralization task). The number of overlapping lesions is illustrated by different colors coding increasing frequencies from violet ($n = 1$) to red ($n = 5$). Talairach z coordinates (Talairach & Tournoux, 1988) of each transverse section are given. Bottom: The superimposed lesions of the NL+ patients ($n = 5$) were subtracted from the superimposed lesions of the NL- patients ($n = 5$). The number of overlapping lesions of the NL- group after subtraction of the NL+ group is illustrated by different colors coding increasing frequencies from dark red (difference +1) to yellow (difference +5). The different colors from dark blue (difference -1) to light blue (difference -5) indicate regions damaged more frequently in the NL+ group than in the NL- group.



lateralization task with similar accuracy as the control groups, with the exception of a small deviation of the subjective AMP to the left. These patients perceived intracranial sound locations with a slight, systematic error to the right, ipsilesional side.

The large proportion of patients who were unable to lateralize sound was unexpected and in seeming discrepancy to earlier investigations on auditory perception in neglect patients. Most likely, it may be due to the fact that previous investigators have examined patients at least 1 month or more poststroke, that is, almost in the postacute or in the chronic phase of the stroke (Bellmann et al., 2001; Cusack et al., 2001; Kerkhoff et al., 1999; Tanaka et al., 1999; Vallar et al., 1995; Pinek et al., 1989). In contrast, all neglect patients in the present study were tested in the acute phase, namely within the first 2 weeks after stroke onset. Comparison between NL+ and NL- patients revealed a significant difference in the severity of neglect symptoms. The NL- patients showed higher percentage omission scores in standard

neglect tests than the NL+ patients. Sound lateralization performance thus obviously is associated with the strength of clinical neglect.

A further difference to some of the previous investigations is that we concentrated on the physiologically relevant, central range of interaural differences. We cannot exclude the possibility that NL- patients were actually able to lateralize ITDs of more than ± 400 μ sec. But from a functional point of view, a potential detection threshold of such a magnitude would reflect a severe disturbance of auditory localization that has to be equated with a complete inability to hear clearly defined locations of sound sources in extrapersonal space.

The direction of AMP deviation to the left found in the present NL+ patients is in agreement with previous studies that have investigated lateralization of dichotic sound (Tanaka et al., 1999; Bisiach et al., 1984). Such a shift in auditory lateralization necessarily predicts a related shift in auditory azimuthal coordinates (Blauert, 1997). The shift of intracranial percepts to the right in

about half of the present neglect patients thus implies a shift of externalized auditory percepts to the same side. However, when the mean difference of the AMP of NL+ and healthy subjects (50 μ sec) is converted into an angular value by using the equation of Kuhn (1977), the resulting azimuthal deviation in free-field-sound localization by 3.5° is only marginal. Thus, although there was a statistically significant auditory shift in the acute NL+ patients with reference to healthy controls, its slight magnitude rather argues for the stability of the reference frame in spatial hearing than for substantial deviations from normal performance, as this can be observed in the visual modality (Pisella et al., 2002; Richard et al., 2000a, 2000b, 2001; Chokron & Bartolomeo, 2000; Ferber & Karnath, 1999; Farnè et al., 1998; Rossetti et al., 1998; Perenin, 1997; Chokron & Imbert, 1995; Karnath, 1994, 1997; Mark & Heilman, 1990; Heilman et al., 1983). The finding that there was no statistical difference between the NL+ patients and the right- or left-brain-damaged controls pointed in the same direction of interpretation.

In accordance with these (indirect) conclusions from our data, Pinek et al. (1989) have actually demonstrated such a systematic rightward error by few degrees in free-field-sound localization of neglect patients. On the other hand, Kerkhoff et al. (1999) and Vallar et al. (1995) reported an opposite, leftward deviation, which was considerably larger in magnitude (around 20°). This apparent contradiction may be due to substantial methodological differences. While Pinek et al. (1989) instructed their patients to point to sound locations, patients in the studies of Kerkhoff et al. (1999) and Vallar et al. (1995) had to judge sound positions with reference to their visual SSA. As has been shown in several studies, the perception of SSA is shifted to the

ipsilesional side in many patients with spatial neglect (Pisella et al., 2002; Richard et al., 2000a, 2000b, 2001; Chokron & Bartolomeo, 2000; Ferber & Karnath, 1999; Farnè et al., 1998; Rossetti et al., 1998; Perenin, 1997; Chokron & Imbert, 1995; Karnath, 1994, 1997; Mark & Heilman, 1990; Heilman et al., 1983). Therefore, it is likely that the patients' leftward tendency in localizatory judgments in the studies of Kerkhoff et al. (1999) and Vallar et al. (1995) merely reflects this rightward shift of the SSA, rather than a genuine shift in representation of auditory space.

Our results obtained in NL+ patients may also be compatible with a recent study on vertical sound localization of neglect patients (Pavani, Làdavas, & Driver, 2002). Although there was an obvious deficit of these patients, that was more pronounced when sounds were presented on the left, they were, nevertheless, still able to discriminate between different sound locations in the vertical dimension. It has, however, to be noted that vertical sound localization is based on mechanisms that are quite distinct from those for the azimuthal dimension (Blauert, 1997), so that the deficits found by Pavani et al. (2002) cannot directly be compared with the present data.

How can the present rightward shift of sound localization in NL+ patients be interpreted? The bias argues against the view that neglect is associated with a general, supramodal deviation of egocentric space representation towards the ipsilesional side. There are obvious differences regarding the way in which auditory and visual space perception are affected in neglect. Although an intraindividual comparison has not been carried out so far, the shift in visual localization not only seems to be much larger than the shift in sound localization, but also occurs in the opposite direction. While in neglect patients the visual SSA can be shifted towards the ipsilesional side, the present study revealed a small deviation of the AMP towards the contralesional side. Moreover, a "neglect" in the strict sense of the term, namely, a failure to react to stimuli located on the contralesional side (even when there is no concurrent stimulus on the ipsilesional side), as this is typically observed for visual events, does not seem to exist in the auditory modality. As in previous studies, each of the present patients with acute neglect responded to all auditory stimuli, independently of whether the sound was lateralized on the left or right side. The patients rather could not lateralize the sounds or lateralized them with a slight rightward shift. This makes it doubtful that a causal relationship exists between spatial neglect and the auditory deficits reported here. Especially, the complete inability to lateralize sound stimuli appears to only co-occur with genuine symptoms of neglect. This co-occurrence may possibly be due to a colocalization of distinct neural circuits processing visuospatial and audiospatial information within structures affected by the stroke.

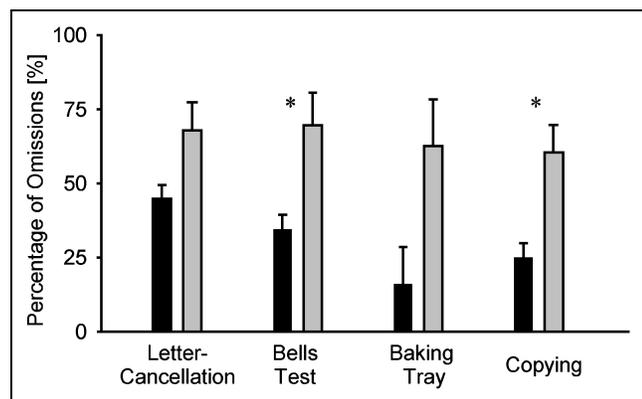


Figure 4. Mean percentage of omissions (\pm SEM) obtained in the four neglect tests (Letter Cancellation, Bells test, Baking Tray task, copying task) with those neglect patients who were able to lateralize auditory stimuli (NL+, $n = 8$, black bars) and those who showed erratic left/right judgments in the sound lateralization task (NL-, $n = 7$, gray-shaded bars). Higher percentage scores indicate more severe neglect. *Significant differences between the two subgroups of neglect patients ($p < .05$).

In both the NL+ and NL- groups, we found a lesion overlap in the STG and planum temporale that extended into the subcortical white matter and pre- and postcentral gyri. This corresponds to the recent observation that it is the planum temporale and STG rather than the inferior parietal lobule typically lesioned in neglect patients (Karnath, Ferber, & Himmelbach, 2001). The STG receives polysensory inputs from the dorsal and ventral pathways of visual information processing (Seitzer & Pandya, 1994; Bruce, Desimone, & Gross, 1981). It was also shown to be involved in auditory spatial processing. Woldorff et al. (1999) compared activation in the auditory cortex of left and right binaural sounds in a study employing functional magnetic resonance imaging (fMRI). Independently of sound direction, both the left and right STG were found to be activated to a similar degree. A further fMRI study by Maeder et al. (2001) revealed stronger activation of the posterior parts of the STG with a task requiring lateralization of ITDs than with a sound-recognition task. Alain, Arnott, Hevenor, Graham, and Grady (2001) and Weeks et al. (1999) suggested that, in addition to the left middle temporal gyrus (Brodmann's area, BA 37) and the right inferior temporal gyrus (BA 20), sound location is processed also in the STG (BA 22/42). Studies carried out in nonhuman primates (Tian, Reser, Durham, Kustov, & Rauschecker, 2001; Rauschecker & Tian, 2000; Recanzone, 2000) investigated the spatial tuning properties of neurons in the so-called lateral belt area that constitutes part of the dorsal aspect of the STG. In accordance with the fMRI data in humans, neurons in the caudal part of the lateral belt were found to respond preferentially to spatial sounds. It is thus at hand why a lesion in the STG causes not only visual but also auditory spatial deficits or distortions as observed in the present neglect patients.

However, there is evidence that disturbed sound lateralization or localization also occurs independently of spatial neglect. In the present study, 1 out of 9 patients with left brain damage was found who was not able to lateralize spatial sounds but did not show any symptoms of spatial neglect. The lesion of this subject was located in the putamen. As shown by Yeterian and Pandya (1998), the putamen has direct connections to the STG. In a group of four left hemispheric patients, Clarke, Bellman, Meuli, Assal, and Steck (2000) found two patients who had an auditory spatial deficit, but no signs of spatial neglect. The lesions of the patients included the STG, respectively, the planum temporale. In addition, Yamada, Kaga, Uno, and Shindo (1996) reported that patients with left temporal lobe lesions, partially including the STG, had a significant deficit in discrimination of ITDs. Zatorre and Penhune (2001) examined patients with varying amounts of resections from the STG. In their right-brain-damaged patients, excisions restricted to the rostral temporal cortex were sufficient to produce disturbed sound localization, without any associated disorder, such as spatial neglect.

These latter studies suggest that a spatial auditory deficit might only co-occur with spatial neglect if the right STG is lesioned. Thus, it would be interesting to find out whether or not lesions of the human left STG and/or planum temporale also are associated with auditory spatial deficits. However, since patients with such lesions usually have severe aphasia, development of new experimental designs that allow the study of spatial lateralization without necessitating speech competence is warranted. A further point that needs clarification is the tendency that sound lateralization was shifted in HA patients, however, opposite to the slight deviation found in NL+ patients. This suggests a significant role of primary visual cortical areas in sound localization.

In conclusion, the present study demonstrated that about half of consecutively admitted patients with acute neglect were unable to lateralize sounds. The data suggest that acute neglect is associated with severe general disturbance in processing of auditory spatial cues, rather than with a systematic shift in the internal representation of acoustic space. This deficit appears to only co-occur with genuine symptoms of neglect possibly due to co-localization of distinct neural circuits processing visuospatial and audiospatial information within superior temporal cortex.

METHODS

Assessment of Spatial Neglect

Patients were classified as having spatial neglect when they showed the typical clinical behavior, such as (a) a spontaneous deviation of the head and eyes toward the ipsilesional side, (b) orienting towards the ipsilesional side when addressed from the front or the left, and (c) ignoring of contralesionally located people or objects. In addition, patients (d) had to fulfill the criterion in at least two of the following four clinical neglect tests: the "Letter Cancellation" task (Weintraub & Mesulam, 1985), the "Bells test" (Gauthier, Dehaut, & Joannette, 1998), the "Baking Tray task" (Tham & Tegnér, 1996), and a copying task. For details concerning test analysis and criteria used for the diagnosis of spatial neglect, see Karnath, Himmelbach, and Rorden (2002).

Lesion Analysis

All patients had circumscribed unilateral brain lesions due to ischemic stroke or hemorrhage demonstrated by magnetic resonance imaging (MRI), including diffusion, T1- and T2-weighted MRI, or computed tomography (CT). Patients with diffuse or bilateral brain lesions, patients with tumors, as well as patients in whom MRI or CT scans revealed no obvious lesion were excluded. The lesions were mapped using MRIcro software (Rorden & Brett, 2000; www.mricro.com). The lesions were drawn manually on slices of a template MRI scan from the Montreal Neurological Institute (www.bic.mni.mcgill.ca/

cgi/icbm_view). This template is approximately oriented to match Talairach space (Talairach & Tournoux, 1988) and it is distributed with SPM99 (www.fil.ion.ucl.ac.uk/spm/spm99.html). The procedure allowed us to measure normalized lesion volume, superimpose lesions to find regions of mutual involvement, and conduct a lesion subtraction analysis. These techniques have been described elsewhere in detail (Karnath et al., 2002; Rorden & Brett, 2000).

Monaural Hearing Test

All subjects were tested for unilateral hearing loss. For this purpose, sound stimuli (band-pass-filtered noise, cutoff frequencies 0.6 and 5 kHz; duration 600 msec; rise and fall time 20 msec) were presented monaurally via headphones (HD580, Sennheiser, Wedemark, Germany). Stimulus sound-pressure level was varied following a quasi-random order from 0 to 80 dB re 20 μ Pa, in steps of 10 dB. Subjects were instructed to verbally indicate when they perceived a sound. The procedure consisted of 63 trials and was carried out separately for each ear. Individuals who exhibited differences of more than 10 dB in the sensitivities of the two ears were excluded from the main experiment.

Procedure

In the main experiment, the subject sat on a chair in a dark and sound-proof room. The head was stabilized in line with the trunk by a chin rest. Dichotic stimuli (band-pass-filtered noise, cutoff frequencies 0.6 and 5 kHz; duration 2 sec; rise and fall time 20 msec; 70 dB re 20 μ Pa) were presented via headphones (HD580, as above). The ITD of the sound stimulus was varied between trials following a quasi-random order over a range from -400 (sound leading at the left ear) to $+400$ μ sec (leading at the right ear), in steps of 80 μ sec. Immediately after stimulus presentation, subjects were required to indicate whether the perceived intracranial position of the sound was to the “left” or “right” of the median plane of the head. Sound stimuli were presented with intervals of 5 sec. In case the subject did not respond within this 5-sec interval, the respective trial was repeated at the end of the session. Each session was composed of 77 trials. All subjects gave verbal “left/right” judgments, with the exception of two aphasic patients who were trained to press one of two “left” or “right” keys mounted on a small box with their nonparetic hand. A continuously illuminated red light-emitting diode (LED), mounted in the median plane of the head at eye level (distance 100 cm), served as fixation target. This LED was in the center of an array of a horizontal and a vertical LED bar (length 7 cm each). To control fixation, the horizontal and vertical LED bars were subsequently illuminated for 1 sec (on average every 10th trial) and the subject had to indicate the

order (“first horizontal” or “first vertical”). To avoid interference with the auditory lateralization task, the fixation-control task was presented in the silent intervals following auditory stimulus presentations. If the subject failed to perform the fixation-control task correctly, judgments on the auditory stimuli were not registered until the next correct response to visual stimulation was given. Nonregistered trials were repeated at the end of the session.

Data Analysis

For each subject, the frequency of the judgments “right” was plotted as a function of ITD. Data were fitted to the sigmoid equation $f(\text{ITD}) = 100/(1 + e^{-k(\text{ITD} - \text{ITD}_{50\%})})$ where f is the frequency of judgments “right,” given as percentage, $\text{ITD}_{50\%}$ is the ITD where f is 50%, k is the slope of the function at $\text{ITD}_{50\%}$, and e is the base of the natural logarithm (cf. Lewald & Karnath, 2001). The ITD where the proportion of the subject’s judgments “left” or “right” was 50% ($\text{ITD}_{50\%}$) was defined as the AMP. The coefficient of determination (R^2) obtained from the fit was used as a measure for the subject’s acuity of sound lateralization, while the AMP indicated systematic shifts in lateralization. A value of $R^2 > .75$ ($p < .05$) was defined as the criterion for the subject’s general ability of sound lateralization. It has to be emphasized that this definition of the “ability of sound lateralization” refers to the range of ITDs of ± 400 μ sec since larger ITD detection thresholds, corresponding to more than 30° in azimuth (Kuhn, 1977), may be functionally insignificant. For further statistical analyses, we used analyses of variance and subsequent t tests with an adjusted α level for multiple testing.

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