NOTE

GAZE DIRECTION MODULATES AUDITORY SPATIAL DEFICITS IN STROKE PATIENTS WITH NEGLECT

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ABSTRACT

We investigated the effects of eye position on auditory spatial deficits in four patients with left neglect and right-hemisphere damage, using three blocked gaze directions (35 degrees to the right, central, or 35 degrees to the left), while preventing any head-movement to ensure that initial auditory inputs remained constant regardless of eye-in-orbit position. The auditory task required speeded discrimination of sound elevation, with patients moving a central lever up or down according to the vertical position of a peripheral target sound, regardless of its side (left or right). Replicating previous auditory research, the patients’ vertical discrimination performance was worse for auditory targets on the contralesional (left) versus the ipsilesional side, indicating neglect-related auditory deficits on this task. Critically, while this worse performance for left than right auditory targets was present (for both reaction times and errors) when gaze was directed centrally or rightwards, it was considerably reduced when gaze was directed leftwards. These results demonstrate that lateral gaze-direction can modulate neglect-related auditory spatial deficits, even though eye-position did not alter the initial auditory inputs. This outcome may relate to audio-visual links in spatial orienting and potentially some retinocentric influences on perceived sound location, although the latter alone could not explain all our results. Such findings might involve multisensory brain structures in which responses to sounds are modulated by eye-in-orbit position.

Key words: visual neglect, auditory neglect, auditory space perception, gaze direction, multisensory

INTRODUCTION

Stroke centred on the right perisylvian region, including inferior parietal cortex, superior temporal and/or inferior frontal cortex, can often result in the neuropsychological syndrome of unilateral spatial neglect (Vallar, 1993; Karnath, 2001; Husain and Kennard, 1996). Neglect patients typically behave as if contralesional space no longer existed, failing to report or orient appropriately to stimuli presented contralaterally to the damaged hemisphere, even in the absence of any primary sensory or motor loss (e.g., see Robertson and Marshall, 1993; Bisiach and Vallar, 2000; Karnath et al., 2002, for reviews). Although this neurological disorder has been predominantly studied within the visual modality, it is now well established that some forms of neglect can arise for other sensory modalities as well, including touch (e.g., De Renzi et al., 1970; Bisiach et al., 1985; Vallar, 1997) or hearing (e.g., Bisiach et al., 1984; Pavani et al., 2001, 2002a). Here we focus on auditory deficits in neglect.

Some neglect-related disturbances in the auditory domain have been documented both clinically (e.g., Bender and Diamond, 1965; Heilman and Valenstein, 1972) and experimentally (e.g, De Renzi et al., 1984; 1989; Bisiach et al., 1984; Tanaka et al., 1999; Bellmann et al., 2001; Pavani et al., 2001, 2002a; see Pavani et al., 2004, for review). Some patients with neglect may fail to detect or identify contralesional sounds under bilateral presentation (e.g., De Renzi et al., 1989; Bellmann et al., 2001). In addition, they may suffer sound localisation deficits, involving azimuthal as well as vertical position of contralesional auditory targets. For instance, they may show lateral biases in the ipsilesional direction when pointing to contralesional single sounds (Bisiach et al., 1984; Pinek et al., 1989; Pavani et al., 2003); manifest poor discrimination of the relative position of two sequential sounds at different contralesional azimuthal positions (Pavani et al., 2001; Tanaka et al., 1999); or show increased errors and/or delay when asked to discriminate the vertical position of contralesional sounds, as compared with ipsilesional sounds (Pavani et al., 2002a).

Several studies within the visual domain have shown that visual aspects of neglect can be affected by postural manipulations that change current trunk, head, or eye-in-orbit position. For instance, unlike primary sensory loss, some contralesional visual deficits in neglect patients can be modulated by trunk rotation (Karnath et al., 1991), head rotation (Karnath et al., 1991; Vuilleumier et al., 1999) or manipulations that produce illusory sensation regarding the current head and/or trunk position (e.g., neck muscle vibration, Karnath et al., 1993; plus caloric vestibular stimulation, Cappa et al., 1987; Rubens, 1985). In addition, contralesional visual deficits in some neglect patients have been shown to improve for a given retinal position when gaze is deviated towards the ipsilesional side (e.g., Koosstra and Heilman, 1989; Vuilleumier et al., 1999; Vuilleumier and Schwartz, 2001; but see...
Mattingley et al., 2000), so that the same retinal visual stimulus now falls further to the ipsilesional side relative to the head/body.

Although these results indicate that postural factors can modulate visual aspects of spatial neglect, the effects of such posture manipulations on non-visual manifestations of neglect have been less studied (but see Bisiach et al., 1985; Valler et al., 1993; Vuilleumier et al., 1999). The present study therefore investigated the effects of eye-in-orbit posture on auditory disturbances in neglect patients, using a recently introduced measure for neglect-related auditory deficits (Pavani et al., 2002a). Right-hemisphere stroke patients with left visual neglect were required to perform a speeded discrimination of sound elevation, by moving a central lever up or down according to the vertical position of a peripheral target sound, regardless of its side (left or right). In such a task, right-hemisphere neglect patients are typically slower and less accurate when discriminating the vertical position of left than right sounds (see Pavani et al., 2002a). The new manipulation in the present study was that, across blocks, gaze-direction (and thus eye-in-orbit posture) was either 35 degrees to the right, central, or 35 degrees to the left. Crucially, head and trunk position were held constant, thus ensuring that initial auditory inputs at the two ears, as well as the external positions of the auditory targets with respect to the body, actually remained unvaried throughout the experiment despite the manipulation of gaze direction. The experimental question was whether gaze direction could modulate neglect-related auditory deficits, despite not altering the auditory input itself.

**METHODS**

**Patients**

Four right brain-damaged patients gave informed written consent to participate. All had suffered unilateral ischemic lesions in the right hemisphere; side and site of the lesion were documented by CT scan. For three patients the lesion was reconstructed according to Damasio templates (Damasio and Damasio, 1989; see Figure 1 and Table I); for patient B.E. only the neuroradiologist’s lesion description was available (see legend to Figure 1 and Table I). All of the selected patients showed contralesional auditory neglect in the speeded vertical discrimination test with central gaze; patients C.T., D.B.M. and L.L. had also participated in our original study on auditory deficits in vertical discrimination of sound position (Pavani et al., 2002a). Visual neglect was assessed on admission using the Behavioural Inattentional Test (BIT, Wilson et al., 1987), and also at the subsequent time of the experiment using standard cancellation tests (i.e., bell cancellation, Gauthier et al., 1989; letter cancellation, Diller and Weinberg, 1977, star cancellation, Wilson et al., 1987). Clinical details for each patient are reported in Table I, together with the results for cancellation tests. As can be seen from Table I, all patients presented strong neglect on admission (BIT cut off 129/146), whereas by the time of experimental testing patients C.T. and B.E. now showed only mild visual neglect on bell and letter cancellation tests respectively (but note that all their missed visual targets were still located at the extreme left). All patients showed normal hearing or only mild hearing loss on pure-tone audiometry, with Hearing Level of 26dB or less (see Katz et al., 2001 for a scale of hearing impairment) and no difference between ears above 10dB. All patients were oriented in time and space, and their Mini-Mental State Examination score (Folstein et al., 1975) was within normal limits. They presented left hemiplegia and were right-handed.

**Apparatus**

Patients sat in a silent dimly lit room, with the apparatus approximately 70 cm in front of them. This comprised 4 loudspeakers (0.4W, 8 Ohm), mounted in two columns of 2 speakers each, on wooden supports (each 150 cm in height, 10 cm in width) fixed to the edge of a table (see Figure 2). On each support, one loudspeaker was mounted 50 cm above ear level and one 50 cm below. A strip of black fabric was stretched from the top to the bottom of each support to cover all loudspeakers, thus preventing any visual cues about their exact elevation. One support was placed 25 cm to the right of the patient’s midsagittal plane (+ 17.5 degrees), and the other 25 cm to the left (− 17.5 degrees). A polystyrene bar (150 × 5 cm) was suspended at eye-level horizontally (equidistant from upper and lower speakers). Three red LEDs were used as visual cues:

**TABLE I**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/Age</th>
<th>Education</th>
<th>Visual field</th>
<th>Lesion site</th>
<th>Onset (months)</th>
<th>Shaper cancellation test (% of accuracy) at time of testing*</th>
<th>Letter cancellation test (% of accuracy) at time of testing</th>
<th>BIT Conventional on admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>C.T.</td>
<td>F/41</td>
<td>8</td>
<td>Hemianopic</td>
<td>F, P</td>
<td>&gt; 24</td>
<td>88 (100)</td>
<td>90 (90)</td>
<td>65/146</td>
</tr>
<tr>
<td>D.B.M.</td>
<td>F/48</td>
<td>5</td>
<td>Hemianopic</td>
<td>T, P</td>
<td>13</td>
<td>12 (82)</td>
<td>30 (95)</td>
<td>124/146</td>
</tr>
<tr>
<td>L.L.</td>
<td>F/48</td>
<td>12</td>
<td>Normal</td>
<td>F, P</td>
<td>2</td>
<td>65 (94)</td>
<td>90 (95)</td>
<td>127/146</td>
</tr>
<tr>
<td>B.E.</td>
<td>M/39</td>
<td>8</td>
<td>Normal</td>
<td>T, P, O</td>
<td>5</td>
<td>96 (96)</td>
<td>95 (100)</td>
<td>15/146</td>
</tr>
</tbody>
</table>
Fig. 1 – Reconstruction of lesions for three patients according to Damasio and Damasio’s template scheme (Damasio and Damasio, 1989). For patient B.E. only the neuroradiologist’s lesion description was available, reporting an infarct in the territory of the right middle cerebral artery that resulted in a vast temporo-parietal-occipital hypodensity.

Fig. 2 – Schematic view of the experimental setup. Note that all loudspeakers (shown as dotted rectangles) were occluded from view behind a strip of black fabric. Fixation points are indicated with filled grey circles on the horizontal bar, at eye-level.
were poked through this to provide visual fixation markers at 3 different position in space: 50 cm to the left, centrally, or 50 cm to the right with respect to the patient’s midsagittal plane (−35, 0 and +35 degrees respectively).

Each acoustic stimulus consisted of a 220 ms train of 6 bursts of broad-band noise, each burst lasting 20 ms with 20 ms gaps. This type of auditory stimulus was chosen because broad-band stimuli with multiple onsets and offsets are known to facilitate sound localisation in the vertical plane, as required here (see also Pavani et al., 2002a). An acoustic stimulus could be presented from any one of the loudspeakers, at approximately 60 dB(A) of intensity as measured at the patient’s head. All loudspeakers were connected to an input/output electronic interface, controlled through a laptop computer using custom software (XGen Experimental Software, http://www.micro.com). Patients’ responses in the elevation (up/down) discrimination task were recorded by means of a digital joystick mounted on a 45-degree slanted surface, attached to the table and suspended centrally in front of the patient’s chest (see Figure 2).

**Procedure**

Patients were instructed to maintain fixation at the currently illuminated LED (left, central or right) while keeping their head and body straight throughout each trial. One experimenter sat in front of the patient, on the other side of the apparatus, to check eye position before starting every trial. Occasional trials in which gaze deviated from fixation were tagged on-line by the experimenter and excluded from subsequent analysis. A second experimenter stood behind the patient to hold his/her head in a straight position throughout.

On each trial, an acoustic stimulus was presented through any one of the four loudspeakers that were placed above or below ear level on either side. Patients were required a speeded discrimination about the vertical position of each acoustic target, regardless of its side, by moving the central joystick lever directly up for an upper sound, or directly down for a lower sound, with the right hand (see also Pavani et al., 2002a). Joystick movement was constrained to one dimension in a vertical slot. Gaze direction was either central (0 degrees), to the left

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**Fig. 3 – Bars indicate mean reaction times (A) and errors (B) across all patients as a function of gaze direction (leftwards, central, rightwards) and stimulus side (left, right). Individual performance is also indicated in each plot: for patient D.B.M. (squares), B.E. (downward triangles), C.T. (circles), and L.L. (upward triangles).**
(– 35 degrees) or to the right (+ 35 degrees). Note that this did not alter the auditory inputs or the position of the ears.

All patients participated in two experimental sessions, run on consecutive days and lasting about 60 minutes each. The order of blocked gaze-directions was counterbalanced across sessions and patients, and within each session followed an ABCCBA order. A total of 160 trials were presented for each condition of fixation, divided into 4 blocks of 40 trials (2 in each session), resulting in 480 trials overall (160 trials × 3 conditions of gaze). Ten practice trials preceded the first block, at the beginning of each session. For each blocked condition of gaze, the four possible sound-sources obtained by permutations of target side (left or right) and sound elevation (up or down) were equally likely in a randomly intermingled sequence.

RESULTS

Every patient was able to detect and respond to each sound. Trials on which an incorrect elevation-discrimination response occurred were discarded from the reaction time (RT) scores. Bars in Figure 3 show mean RTs after these exclusions (inset A) and mean errors (inset B), as a function of gaze direction (left, centre or right) and of auditory stimulation side (left or right).

RT data were analysed using repeated-measure ANOVA with two factors (gaze direction: left, centre or right; target side: left or right). Huynh-Feldt correction for sphericity violation was applied when necessary. This analysis showed a significant main effect of target side [F (1, 3) = 21.00, p < 0.02], caused by longer up-down discrimination RTs for auditory targets on the contralesional (left) than on the ipsilesional side (left targets: mean RT = 826 ms; right targets: mean RT = 776 ms). This result reveals auditory spatial deficits in the vertical dimension for contralesional targets in our neglect patients, in replication of Pavani et al. (2002a). The left/right difference in errors was numerically smaller during leftward (2%) than central (4%) or rightwards fixation (12%). While this pattern supports the RT results by showing that the smallest left/right difference in accuracy emerged during leftward fixation, it also suggest that fixating rightward can contribute to increase disadvantage for contralesional sounds (see Figure 3b).

DISCUSSION

The results of the present study demonstrate that neglect-related auditory spatial deficits for contralesional left sounds can be modulated by direction of gaze, even though this does not alter the auditory inputs. When gaze was directed rightwards or centrally, vertical discrimination performance was consistently worse for left than right auditory targets, indicating neglect-related auditory spatial deficits in this task (as in Pavani et al., 2002a). By contrast, when gaze was directed leftwards, this neglect-related difference between performance for left versus right sounds was eliminated for the same auditory inputs, and patients now performed with comparable efficiency regardless of target side. Crucially, these modulations emerged despite the sound sources’ locations with respect to the head and the trunk remaining constant throughout the experiment, thus ensuring that initial auditory inputs to the ears also remained constant across gaze directions.

As anticipated in the Introduction, effects of gaze-direction on neglect have previously been observed in the visual modality. However, unlike the present results, improvement of neglect-related disturbances in vision has typically been observed when gaze was directed rightwards. For instance, Kooistra and Heilman (1989) described one patient with left visual neglect and apparent hemianopia, whose visual performance for visual targets in the left retinal hemifield improved when his eyes were

\footnote{When Bonferroni correction is applied ($\alpha = 0.05/3 = 0.017$), significance for the t-test comparison on the left/right difference still emerges for the rightward gaze condition, even at a two-tail level. The same post-hoc comparison for the central gaze condition now reached statistical significance only when a one-tail assumption is accepted (i.e., worse performance for left than right targets; $p < 0.002/0.017 = 0.015$). We believe such an assumption is actually justified in this specific case, since it reflects the typical disadvantage for contralesional targets evident in neglect, and is in agreement with our previous finding using the present auditory elevation-discrimination task during central fixation with visual neglect patients (Pavani et al., 2002a).}
directed 30 degrees towards the right, but who did not show any improvement for leftward eye positions. Similarly, Vuilleumier and colleagues observed that pseudo-hemianopic visual impairments, line bisection errors or contralateral visual extinction could be significantly ameliorated for left retinal targets with rightward as compared with leftward eye-in-orbit positions (Vuilleumier et al., 1999; Vuilleumier and Schwartz, 2001).

This apparent discrepancy between previous visual results and our present auditory findings (i.e. in terms of exactly which gaze-direction is beneficial) may be resolved when one considers the fact that, unlike the present study, previous research on the effects of eye-position for visual neglect or extinction were logically unable to manipulate gaze-direction without conjointly manipulating the external location of a given retinal visual stimulus. In fact, in order to hold constant the retinal position of visual stimuli across different gaze conditions, the visual stimuli had to be moved laterally with respect to the head or the trunk according to the current gaze direction. Specifically, the same retinal visual stimuli were displaced to the right of the body midline when gaze was directed rightwards, but to the left of the body midline when gaze was directed leftwards (e.g., see Kooistra and Heilman, 1989; Vuilleumier et al., 1999; Vuilleumier and Schwartz, 2001). This itself may have influenced patients’ visual performance, as visual neglect typically improves when stimuli are positioned further towards the right of the body midline (whereas it can worsen for visual stimuli positioned to the left of the body: e.g. Heilman and Valenstein, 1979; Menneemeier et al., 1994). Similarly, Bisiach et al. (1985) observed that neglect-related disturbances of tactile exploration improved when the target stimulus (a board) was placed to the right of the body midline, with head and gaze held central. Note that in the present auditory study, gaze direction was not confounded with the external position of the auditory stimuli relative to head or trunk, as these were held constant throughout. Thus, while previous demonstrations of visual improvements with rightward gaze may have been due to a shift in the external location of the stimuli relative to the head/trunk, no such shift applied to the present auditory stimuli, where a benefit for leftward gaze was found instead.

Our findings demonstrates for the first time that effects of gaze direction on neglect-related deficits can extend to perception of auditory stimuli. This contrasts with the negative results of the only previous study (to our knowledge) of whether gaze direction can modulate auditory neglect. Specifically, Vuilleumier et al. (1999) examined two patients with auditory neglect on a dichotic listening task, and observed that patients’ ability to identify contralesional words was apparently not affected by changes in gaze direction. However, any modulations related to gaze direction in that study might in principle have been hidden by a floor effect in contralesional performance (especially for their patient G.Y.). Moreover, dichotic-listening tasks might show less influence of gaze direction, because stimuli are typically presented monaurally over headphones, rather than from external sound-sources that can be looked towards (see previous inconsistent results on the effects of gaze-direction on dichotic listening in healthy participants, e.g. Hynd et al., 1986; Asbjørnsen et al., 1990; Struthers et al., 1992). It would be interesting to examine whether auditory stimuli presented through headphones, but filtered according to listeners’ own head-related-transfer function in order to produce a sound percept externalised to a virtual location outside the listener’s head (e.g., see Wightman and Kistler, 1989; Pavani et al., 2002b), might be sensitive to gaze-direction manipulations, as for the present free-field sounds.

Some reliable modulations of gaze direction on auditory perception have been shown in healthy participants when auditory targets were presented in the free-field, as here. For instance, a classic study by Morais and colleagues (Morais et al., 1980) showed that gazing towards a sound source improved syllable identification performance at that location, presumably as a result of overt orienting of attention to that region of space (see also Spence et al., 2000; Spence and Driver, 1996 for evidence of audio-visual links in normal spatial attention). In addition, some small but consistent effects of static eye-position on auditory processing have been documented in normals using localisation rather than identification tasks. For instance, Lewald and Ehrenstein (Lewald, 1997, 1998; Lewald and Ehrenstein, 1996) showed that lateral gaze displacement can systematically bias perceived horizontal location of sounds in normals, with apparent sound location typically shifting a few degrees opposite to the current static gaze direction.

Although horizontal spatial biases during lateralised gaze posture might in principle have contributed to our finding to some extent (e.g., by apparently shifting auditory targets further to the intact right side when gaze was directed leftwards), this small spatial bias appears unlikely to be the only determinant of the very substantial effect of eye-position observed here, which arose for vertical discrimination rather than lateral judgements. Instead, the improvement in neglect-related auditory deficits observed here may be compatible with the above-mentioned audio-visual links in spatial attention (e.g., Morais et al., 1980; Spence et al., 2000; Spence and Driver, 1996), which typically lead to improved performance in normals (in both RT and errors, as here) for auditory locations in the portion of space towards which visual attention is directed. Although in the present study lateral gaze-direction was always more eccentric than sound source locations (i.e., speakers at ± 17.5 degrees,
lateral fixations at ± 35 degrees), it should be noted that while gaze (and thus overt visual attention) was not directed to exactly the same location as the auditory sources on the same side, deviated gaze was nevertheless still much further away from the sound sources on the other side. Our results suggest that auditory improvement for the region of space near overt visual attention may occur in neglect patients also, even when speakers are not directly visible or aligned with gaze, and in an auditory task for which vision was completely irrelevant throughout. It would be interesting to examine whether looking directly at the sound source could further enhance any effect of gaze direction in visuospatial neglect patients, and might do so even in complete darkness.

A further aspect to consider when discussing the effect of gaze-direction on auditory processing in neglect patients is that gaze shifts will change the retinotopic (or oculocentric) position of sound sources. In the present study, when gaze was directed leftwards, all sound sources now fell visually in the right (ipsilesional) visual field, with those speakers to the left of the body-midline now occupying a right visual-field position (although note that the exact position of the speakers, and in particular their elevation, was occluded; see Figure 2). In principle at least, this shift in the retinotopic location of sound-sources might contribute to the improved discrimination performance for contralesional sounds during leftward gaze. Similarly, when gaze was directed rightwards, all sound sources now fell visually in the left (contralesional) visual field, potentially leading to worse auditory discrimination performance with respect to central gaze. Increased disadvantage for contralesional sounds during rightward gaze was indeed observed in accuracy data (see Figure 3b). However, the retinotopic/oculocentric position of sound sources cannot be the sole factor behind all of our results, since performance did not depend only on the retinotopic location of each sound (e.g. performance for right sounds when gazing rightwards was not equivalent to that for left sounds when gazing centrally, despite their equivalent retinal positions under these conditions; not even for the two patients with hemianopia; see performance of C.T. and D.B.M. in Figure 3).

The overall pattern or results suggests that although retinotopic/oculocentric sound location could have played some role in modulating auditory performance for the visual neglect patients, it is not the sole factor affecting neglect patients’ performance across gaze directions. One issue for future research concerns the relative contribution of overt versus covert orienting mechanisms in the modulation effects observed here. In particular, it would be interesting to separate experimentally the direction of covert visual attention from the direction of gaze. This would help disentangle the relative contribution of any audio-visual link in covert attention from the role of retinotopic coding of sound sources in visual neglect patients. However, note that from a clinical perspective our findings already suggest a new strategy for temporary amelioration of neglect-related spatial disturbances for contralesional sounds, via direction of gaze.

This modulation of auditory processing as a function of gaze-direction might potentially relate to neurophysiological findings showing that some neural responses to sounds can be modulated by current eye-in-orbit position, in several brain areas. For instance, the superior colliculus of primates (Jay and Sparks, 1984) and cats (Hartline et al., 1995; Peck et al., 1995), as well as the lateral intraparietal cortex of primates (Stricanne et al., 1996) contains neurons whose auditory receptive fields are modulated when the eyes move, even when the head and ears remain stationary, as here. Moreover, recent neurophysiological evidence has revealed that eye-in-orbit position may modulate neural responses to sounds even in areas of the primate auditory pathway, such as the inferior colliculus (Groh et al., 2001) and primary auditory cortex (Werner-Reiss et al., 2003).

In conclusion, we have provided the first positive evidence that gaze direction can modulate neglect-related auditory deficits, even while the external location of the sounds, and the auditory inputs to the ears, are held constant. We suggest that this result may relate to audio-visual links in spatial attention as well as potential effects of sound localisation coding in retinotopic coordinates, enhancing auditory perception in the region of space towards which gaze is directed, even for unseen sound sources.

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