SPECIAL ISSUE

AUDITORY DEFICITS IN VISUOSPATIAL NEGLECT PATIENTS

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Abstract

Since the pioneering experimental work of Bisiach et al. (1984) on deficits in sound localisation associated with unilateral brain lesions and visual neglect, a number of systematic investigations have examined auditory processing in visuospatial neglect patients. Evidence from a variety of experimental paradigms has revealed some auditory deficits in detection and identification tasks, during bilateral stimulation; plus localisation deficits for single sounds. These deficits emerge predominantly for contra-lesional sounds, although some auditory disturbances applying to both contra- and ipsilesional sounds have also been documented. Here we review evidence suggesting that some of these auditory deficits arise in relatively high-level stages of spatial processing. In addition, we present new analyses showing that auditory deficits in identification and localisation tasks often correlate with clinical measures of visual neglect, across a variety of different studies and tasks. This empirical relation suggests that a disturbance of multisensory spatial processing may often account for the joint auditory and visual spatial deficits in neglect patients, although rarer dissociations between the modalities should also be considered.

Key words: hemispatial neglect, extinction, auditory perception

Visual neglect is a common deficit after unilateral brain injury, particularly following strokes centred on the right perisylvian region, including the inferior parietal, superior temporal and inferior frontal lobes (Vallar, 1993; Husain and Kennard, 1996; Karnath, 2001). Patients with visuospatial neglect typically fail to report or orient appropriately for visual stimuli presented contralaterally to the damaged hemisphere, often behaving as if contralesional visual space no longer existed (e.g., Robertson and Marshall, 1993; Bisiach and Vallar, 2000; Driver and Vuilleumier, 2001). In daily life, they may neglect food on the left part of their plate, fail to groom the left side of their body, ignore people standing on their left side, and so on. Remarkably, this pathological behaviour can emerge even in the absence of any primary sensory or motor loss; and even for mentally reconstructed visual images in some cases (Bisiach and Luzzatti, 1978; Bisiach et al., 1981). Such observations have led to proposals that the deficits may relate to impairments in mechanisms of spatial representation (Bisiach and Luzzatti, 1978; Rizzolatti and Berti, 1993) and/or spatial attention (Heilman and Watson, 1977; Kinsbourne, 1987; Posner and Driver, 1992; Mesulam, 1998).

In 1984, Bisiach, Cornacchia, Sterzi and Vallar pointed out that if neglect affects high-level processing of space, it may extend beyond the visual domain to affect other modalities also. In particular, these authors argued that it could emerge for auditory spatial processing as well. In a large group-study of 107 unilateral brain-damaged patients, Bisiach and colleagues (1984) observed that patients with right hemisphere lesions and visual neglect tended to show larger auditory localisation errors (characteristically showing errors that suggested mislocalization in an ipsilesional direction, i.e. sounds heard further to the right than their true location) compared to patients without visual neglect, particularly when pointing to contralesional sounds. This pioneering study was among the first to recognise the importance of extending investigations of unilateral neglect to other sensory modalities (see also Heilman and Valenstein, 1972; De Renzi et al., 1970), and of investigating the relation between manifestations of neglect across different senses. In recent years, issues concerning multimodal representation of space have also been studied in other domains of cognitive neuroscience (such as neurophysiology and neuroimaging, e.g., Andersen et al., 1997; Macaluso and Driver, 2004), with data indicating that parietal cortex and other brain structures commonly associated with neglect (e.g., superior temporal lobe, Karnath, 2001; premotor and frontal cortex, Husain and Kennard, 1996) may play a fundamental role in multisensory processing of space.

The pioneering auditory study of Bisiach et al. (1984) took an experimental approach, going beyond previous anecdotal evidence from the clinic for auditory localisation deficits in visual neglect patients. For instance, Denny-Brown et al. (1952) had described the case of patient that could hear a sound in either ear (monaurally), but “always reported that the direction of the sound was from the right” (see also Bender and Diamond, 1965; Diamond and Bender, 1965). This phenomenon has been described as ‘alloacusis’ (Bender and Diamond, 1965) or ‘allochiria’ (Bisiach and Vallar, 2000). Other disturbances of auditory processing in visual neglect patients, as observed anecdotally in clinical practice, suggested possible impairments even in detection of contralesional sounds. For instance, Heilman and Valenstein (1972) noted that visual neglect patients may sometimes fail to respond when verbally addressed from the contralesional space (see also Battersby et al., 1956), suggesting that contralesional detection deficits might emerge for hearing as well as vision.

Since these early clinical studies, many systematic investigations of auditory processing in visual neglect patients have now been carried out. This new body of evidence has consistently shown that visual neglect patients can manifest contralesional deficits in a variety of auditory tasks (detection, identification and localisation). In addition some evidence for non-spatial auditory deficits (i.e. applying to central and ipsilesional sounds, as well as contralesional sounds) is also emerging, apparently in agreement with recent findings that visual neglect patients may suffer some non-spatial disturbances in the visual modality also (e.g., Husain et al., 1997; Duncan et al., 1999; Battelli et al., 2001; for reviews see Robertson, 2001; Husain and Rorden, 2003). Here we review the literature on auditory deficits in visual neglect patients, seeking in particular to establish whether any empirical relation can be found between visual and auditory disturbances in these patients.

Initial evidence from auditory detection studies was equivocal about whether deficits in neglect patients reflected suppression of auditory input from the contralesional ear, or higher-level spatial deficits (e.g., see Beaton and McCarthy 1993, 1995; Bellmann et al., 2001). As will be described, more recent contributions clearly suggest that left ear-suppression alone is unlikely to be the sole determinant of all contralesional auditory deficits in visual neglect patients. Instead, a role for higher-level spatial factors in some of these auditory deficits is becoming increasingly evident. We shall also present evidence from new correlation analyses, that reveal a consistent relation between the severity of auditory deficits and of visual neglect across patients, for several different experimental paradigms and dependent variables.

The theoretical and clinical implications of this reliable correlation will be discussed with respect to recent findings on multisensory spatial processing, from other domains of cognitive neuroscience.

Detection of Suprathreshold Sounds on Left versus Right: Contralesional Ear Suppression or Impairment of High-Level Spatial Representations?

A characteristic clinical feature of patients with visual neglect is that they often fail to detect contralesional visual targets, as in visual search or cancellation tasks. By contrast, in the auditory domain, apparently preserved detection of free-field suprathreshold left unilateral sounds is usually observed with bedside confrontation techniques (e.g., Bender and Diamond, 1965) or in more systematic experimental investigations (e.g., Bisiach et al., 1984; Pinek et al., 1989; Pavani et al., 2001, 2002a). Note that most studies of auditory perception in visual neglect patients used strong suprathreshold auditory stimuli, while any relation between different hearing thresholds at the two ears and degree of auditory and visuospatial neglect has remained largely overlooked (but see Pavani et al., submitted). However, visual neglect patients do not necessarily suffer any disadvantage for left sound detection when unilateral auditory stimuli are presented monaurally near hearing threshold, during pure-tone audiometric tests. For instance, Bisiach and colleagues (1984) noted that, unlike visual neglect, the interaural intensity difference of any hearing loss in 43 unilateral brain-damaged patients did not differ as a function of lesion side (left or right), or of the presence/absence of visual defects.

Thus, no simple correspondence between the presence of neglect symptoms in vision, and the co-occurrence of auditory deficits, seems to emerge when simple detection of unilateral free-field sounds is tested. De Renzi and colleagues (1989) suggested that preserved detection of suprathreshold unilateral auditory targets in neglect patients might conceivably relate to the fact that free-field sounds will reach both ears, and so project bilaterally to auditory cortices. Consequently, even when one hemisphere is damaged, the other hemisphere might remain able to process a sound coming from either side of space (De Renzi et al., 1989). Accordingly, they studied 45 brain damaged-patients with right or left hemisphere lesions in an auditory detection task, but now using unilateral stimulation restricted to a single ear alone (over headphones). With such a monaural method, somewhat stronger lateralisation may be obtained at the cortical level (see Woldorf et al., 1999 for recent fMRI evidence of predominantly contralateral auditory activations during monaural dichotic-listening in normals), although auditory pathways from each ear do not project only to contralateral cortex, but also ipsilaterally to some lesser extent.

In their study, De Renzi et al. (1989) presented a 4-minute long pure-tone, occasionally interrupted by brief 300 ms silent gaps, and asked patients to respond to each silent gap by pressing a key. Target side was either predictable (i.e., silent gaps presented to either just the left or right ear throughout an experimental block) or unpredictable (silent gaps randomly presented to either left or right ears during each experimental block). Detection deficits for left unilateral targets were observed in 7 right brain-damaged patients regardless of target-side predictability; and in 2 further right brain-damaged patients only when target side was unpredictable. Among these 9 patients, 7 also showed severe visual neglect (in a pointing task and a sentence reading test). Thus, it appears that some detection deficits for left auditory targets can be observed in visual neglect patients when unilateral stimulation is restricted to one ear alone (but note that this particular deficit might in principle result from poor processing at the contralesional ear, rather than some higher-level disturbance in auditory processing, as will be discussed later).

One striking difference between many clinical tests for visual neglect (e.g., cancellation) versus typical auditory tasks (e.g., detecting a single auditory event in free-field, or over headphones) concerns the presence or absence of concurrent competing stimuli. Thus, cancellation sheets typically display many visual stimuli together, often among distractors; whereas auditory tasks often present a single sound against silence. This alone might explain why auditory deficits are often not so immediately apparent. When even a minimal version of concurrent competing auditory stimulation has been examined, by presenting two simultaneous sounds rather than a single sound, a consistent failure to detect contralesional targets has typically been observed for free-field sounds (e.g., Bender and Diamond, 1965, Heilman and Valenstein, 1972) as well as for stimuli presented dichotically over headphones (e.g., De Renzi et al., 1984, 1989).

The similarity between this auditory phenomenon and visual extinction (in which a contralesional target goes undetected only when presented simultaneously with an ipsilesional one; Bender, 1952), has naturally led several authors to describe auditory deficits under bilateral simultaneous stimulation as ‘auditory extinction’ (De Renzi et al., 1984, 1989), while others have occasionally termed it ‘auditory neglect’ (Heilman and Valenstein, 1972; Hugdahl et al., 1991). Such terminology might imply that these auditory deficits result from the same type of impairment (e.g., attentional and/or representational) that underlies visual extinction or visual neglect. However, several further considerations raised initial doubts about any such conclusion. First, the incidence of extinction of the contralesional ear (over headphones) seems comparable in left and right brain-damaged patients, which stands in apparent contradiction to the predominance of visual neglect and visual extinction following right-hemisphere lesions in particular (e.g., Stone et al., 1991, 1993; although note that lesions to either hemisphere can sometimes result in contralesional visual neglect or visual extinction, with this just tending to be more common after right-hemisphere damage). For instance, De Renzi and colleagues (1984) described contralateral ear extinction in 40% of their brain-damaged patients, with no prevalence of the deficit for right versus left brain-damaged patients (although it should be noted that contralateral auditory extinction did tend to last longer for patients with right-hemisphere lesions in this study, as is also the case for visual neglect; Stone et al., 1991). Second, a failure to report contralesional stimuli under simultaneous dichotic stimulation has been observed following a wide range of brain lesions, in brain areas that are not usually associated with visual neglect, such as auditory areas in the temporal lobe (Kimura, 1967; Sparks et al., 1970) or corpus callosum (Milner et al., 1968; Sparks and Geschwind, 1968). Third, some evidence has been taken to suggest that the contralesional detection deficits apparent in dichotic (headphone) tests of auditory extinction may not be consistently associated with either visual extinction or visual neglect (although see later). For instance, De Renzi et al. (1984) reported 17 patients with auditory extinction but apparently no visual extinction (as measured by confrontation); and 4 patients with visual extinction but apparently no auditory extinction. Similarly, they described 4 out of 24 patients showing strong visual neglect (in a pointing task and a sentence reading test), but no apparent sign of auditory extinction (note however that in the remaining 20 cases auditory extinction and visual neglect were associated).

This set of evidence led some authors (e.g., Beaton and McCarthy 1993, 1995; Bellmann et al., 2001) to raise the issue of whether poor detection of sounds at the contralesional ear, during concurrent bilateral dichotic stimulation, could be related to neglect of contralesional auditory space; or instead should perhaps be interpreted as mere suppression of the auditory information entering the contralesional ear. Indeed, the existence of contralateral ear-suppression was first suggested in the 1960’s, within the literature on dichotic listening and hemispheric specialisation in normals (e.g., Kimura, 1967; Sparks and Geshwind, 1968). As mentioned above, when auditory inputs are confined to one ear alone they will initially project predominantly (though not exclusively) to the contralateral cortical hemisphere. Such contralateral projections appear to be particularly dominant (e.g., Woldorff et al., 1999) when simultaneous auditory input is presented to the other ear (i.e., in dichotic conditions).

This could potentially be due to inhibition of the ipsilateral auditory pathway when competition between the two ears occurs (Kimura, 1967; Milner et al., 1968; Sparks and Geshwind, 1968). In such a context, a unilateral lesion might prevent processing of input to the contralesional ear during dichotic stimulation, leading to poor detection for stimuli presented at that ear. As we will show later, while this interpretation may be plausible for some cases and some tasks, more recent evidence shows that ear suppression is unlikely to be the sole determinant of contralesional auditory deficits in patients with visual neglect.

To summarise, impaired detection of suprathreshold contralesional sounds in neglect patients has been commonly observed only when auditory targets are presented together with other competing sounds (i.e., during double bilateral presentation; but see De Renzi et al., 1989). In such situations, contralesional auditory deficits have been observed for some free-field sounds, but particularly for sounds presented dichotically over headphones. This raises the issue of whether the contralesional auditory deficits should be considered a direct outcome of the spatial origin of the sound, or instead as the consequence of poor processing of auditory input at the contralateral ear. As we shall see in the following section, several lines of evidence from the recent literature on auditory disturbances in identification tasks now suggest that an explanation of contralesional auditory deficits in terms of mere left-ear suppression is not adequate for all neglect patients.

Identification Tasks for Sounds on Left versus Right Suggest a Role for some Higher-Level Spatial Factors

Another way to examine auditory deficits in visual neglect patients is to require identification or discrimination of auditory stimuli, instead of their simple detection. This approach has typically made use of verbal material (e.g., consonant-vowel pairs, Soroker et al., 1995a; or words, Bellmann et al., 2001), although discrimination for non-verbal stimuli has sometimes also been studied (e.g., pitch discrimination, Pavani et al., 2002a).

As with simple detection tasks, identification of unilateral auditory stimuli has not always revealed consistent deficits for contralesional stimuli in neglect patients. No significant difference between left versus right identification performance emerged for monaural consonant-vowel pairings (Hugdahl et al., 1991) or bisyllabic words (Bellman et al., 2001; Pavani et al., submitted).

Similarly, using a paradigm in which neglect patients were asked to identify consonant-vowel syllables presented in the auditory free-field, 60 degrees to either the left or the right of the subject, Deouell and Soroker (2000) did not observe any difference in the identification rate for left versus right stimuli. However, using a similar free-field paradigm but with more lateralised speakers (now 90 degrees on either side), Soroker and colleagues (1995a) found that neglect patients could be less accurate than healthy controls in identifying contralesional targets (for similar results see also Soroker et al., 1995b, Calamaro et al., 1995). Interestingly, this disadvantage in reporting far-left auditory syllables correlated with the degree of visual neglect [r (4) = .77; Soroker et al., 1995a], as measured by the Behavioural Inattentional Test (BIT, Wilson et al., 1987), in the 6 patients studied.

Systematic auditory deficits in identification tasks for neglect patients have more often been observed under bilateral simultaneous stimulation, with competition thus arising between different concurrent auditory targets. With such a method, deficits for contralesional sounds have emerged for both free-field stimulation (e.g., Soroker et al., 1995b; Calamaro et al., 1995; Soroker et al., 1997; Deouell and Soroker, 2000) and dichotic presentation over headphones (e.g., Hugdal et al., 1991; Bellmann et al., 2001; Pavani et al., submitted). These auditory deficits were typically more pronounced in visual neglect patients than in healthy controls. More importantly, some studies have observed worse performance for identification of left sounds, during bilateral stimulation, when comparing visual neglect patients to right brain-damaged patients without neglect (e.g., Calamaro et al., 1995; Pavani et al., submitted; but see Soroker et al., 1997).

The argument (e.g., Beaton and McCarthy 1993, 1995) that such auditory deficits might result from 'left ear suppression', rather than a disturbance in contralesional spatial processing, could in principle also apply for these identification studies, just as for the detection studies described earlier. Moreover, it should be noted that even some 'free-field' identification studies might be subject to this interpretation, since very strong lateralisation of external speakers (e.g., at 90 degrees on either side, Soroker et al., 1995b) should also result in large intensity differences at the two ears. However, converging evidence from different experimental paradigms using auditory identification tasks now suggests that an explanation of all the observed auditory deficits in terms of mere 'left ear suppression' may be inadequate.

The first piece of evidence suggesting a role for the perceived external spatial origin of the sound is that auditory deficits for stimuli presented from the left side can apparently be ameliorated when these sounds are made to appear as if they originate from the right side instead. In one study, this change in perceived sound position was achieved by administering auditory stimuli on the far left in the presence of a fictitious visible sound source (a 'dummy' loudspeaker) on the right (Soroker et al., 1995a; Calamaro et al., 1995; see also Soroker et al., 1995b). Thus, despite left stimuli presumably reaching predominantly the contralesional ear (in terms of stronger intensity), their identification was apparently modulated by their perceived spatial location, as manipulated by vision of the dummy speaker.

A study that directly addressed the role of stimulated-ear versus perceived sound-position in producing auditory deficits in identification tasks was recently conducted by Bellmann and colleagues (2001). These authors studied the performance of four right brain-damaged patients in identification tasks for bilateral simultaneous words. In separate blocks, word lateralisation was either achieved dichotically (each word presented to one ear only) or diotically (each word presented binaurally, but with interaural time difference at the two ears now serving as the only localisation cue; see Morais and Bertelson, 1975). In the latter situation, because both ears receive the same acoustic stimuli at the same intensity level, a selective failure to identify 'left' stimuli could not be accounted for in terms of contralateral ear suppression alone. The results suggested a clear-cut dissociation among the four patients. Two patients were impaired in reporting left words regardless of the adopted lateralisation method (i.e., similar results for dichotic and diotic stimuli), suggesting an identification deficit for sounds perceived as originating from contralesional space. The other two patients showed poorer performance for left than right words on dichotic but not diotic presentation, consistent with a deficit for sounds at the contralesional ear.

This study suggests that, in some right brain-damaged patients, contralesional auditory deficits may depend crucially on the ear of entry of each stimulus; whereas in other cases, the deficits may be driven by higher-level spatial factors. However, it remains unclear how these distinct types of deficits (and particularly those described as reflecting a 'genuine attentional spatial deficit'; Bellmann et al., 2001, p.683) relate to visual neglect, or to any impairment of space perception, for several reasons. First, the two patients showing clinical signs of visual neglect at the time of testing (cases JCN and AJ), dissociated in terms of their performance on the auditory tasks (i.e., one showed contralesional deficits in both auditory tasks, whereas the other was impaired only in the dichotic task). Second, the two patients whose behaviour was compatible with higher-level deficits of auditory space processing had right subcortical lesions (mainly involving basal ganglia and the insula) lying deep to the inferior frontal region associated with neglect (Husain and Kennard, 1996). Although, lesions to these subcortical structures can produce hemineglect symptoms, it has sometimes been suggested that these symptoms may be associated more with intentional (i.e., motoric) rather than attentional disturbances (e.g., Ferro et al., 1987; Ferro and Kertesz, 1984). Moreover, there is currently a lack of clear evidence for any role of basal ganglia and insula in auditory spatial processing based on neurophysiology or functional imaging.

Using similar methods to Bellmann et al. (2001), we have recently explored further the issue of how auditory deficits in identifying dichotic or diotic verbal materials may relate to visuospatial neglect (Pavani et al., submitted). In 11 right brain-damaged patients, selected for showing some degree of visual neglect on clinical testing at the time of the experiment or previously, we observed contralesional deficits in the dichotic task, which correlated significantly with the degree of visual neglect on cancellation tests. Thus, although some contralesional deficits in dichotic-listening tasks may depend to some extent on suppression of auditory input at the contralesional ear (as suggested by some of Bellmann et al.'s results), these deficits can nevertheless still have some relation to visual neglect (as suggested by the correlation between contralesional auditory deficits for dichotic sounds, and visuospatial neglect, that we recently found). This correlation appears to favour a high-level rather than low-level (i.e. ear-of-entry only) explanation. Interestingly, when presented with bilateral diotic materials, the patients in our study showed a non-spatial auditory deficit, that equally disrupted identification for left and right words (as compared with unilateral diotic stimulation). This deficit also correlated with the degree of visual neglect, and will be discussed later in the section about non-spatial auditory deficits.

Finally, a recent study by Carlyon et al. (2002) provides evidence that, in visual neglect patients, less attentional resources may be available for left auditory stimuli than right, during dichotic presentation over headphones. They asked patients to perform an auditory streaming task (van Noorden, 1975), in which a pair of tones with different frequencies (A or B) is presented in the sequence 'ABA-ABA-ABA'. In healthy subjects, this sequence is initially heard as a 'galloping' rhythm corresponding to the repeating triplets; but after several seconds the percept of a galloping rhythm is lost, with the A and B tones now splitting into two separate streams (auditory streaming effect). Crucially, the degree of attention devoted to the auditory sequence appears to be an important factor for this build-up of auditory streaming, in normals (Carlyon et al., 2002). When applying this paradigm to visual neglect patients, Carlyon et al. found that such patients show less stream segregation for left than right tone sequences. Streaming for right auditory stimuli (but not left) was similar to that observed for stimuli presented to either ear of healthy controls or brain-damaged patients without neglect, who showed no lateralised asymmetry.

To summarise, as in the detection studies reviewed in the previous section, auditory identification or discrimination studies have reliably revealed contralesional deficits of auditory processing under conditions of double simultaneous stimulation (i.e., bilateral concurrent stimuli). Some of the novel experimental approaches adopted with such auditory identification studies (e.g., inducing illusory changes in perceived sound position; controlled use of auditory cues to lateralisation via headphones; or auditory streaming) have begun to shed new light on these contralesional auditory deficits and their relation to neglect-related spatial disturbances. In particular, many of the recent studies suggest a role for higher-level spatial factors (e.g., perceived external position, spatial attention, relation to visual neglect) in the contralesional auditory deficits observed for neglect patients. Even auditory studies that presented stimuli dichotically may reveal deficits that are not solely due to ear of entry.

Localisation for Left versus Right Sounds; Pointing Tasks and the Role of Vision

As mentioned in the introduction, one deficit of auditory processing that has often been reported anecdotally in clinical studies of right brain-damaged patients concerns the ability to localise sounds in space. Denny-Brown and colleagues (Denny-Brown et al., 1952) described clinically the case of a patient with preserved detection for unilateral sounds, but apparent mislocalisation of left sounds to the right side of space. Similarly, Bender and Diamond (1965; see also Diamond and Bender, 1965) observed that in brain-damaged patients with ‘hemispatial disorientation’ and contralesional auditory deficits, left stimuli were sometimes reported to originate from the opposite side or towards the midline. Altman and colleagues (1979) noted that psychiatric patients treated with electrical stimulation of the right hemisphere showed transient impairment of sound localisation, with systematic directional errors towards the right side. Interestingly, they reported concurrent visual neglect symptoms during stimulation in some of the patients and proposed that auditory and visuospatial disorders may be related manifestations of multimodal unilateral neglect (Altman et al., 1979).

As mentioned earlier, one of the first studies to directly address the question of whether sound-localisation deficits in right brain-damaged patients may relate to visual neglect was conducted by Bisiach and colleagues in 1984. 107 patients with right- or left-hemispheric lesions (plus a group of healthy participants) were studied in manual ‘pointing’ to a pure-tone sound delivered through headphones. Sound lateralisation was achieved using intensity difference at the two ears, and participants were instructed to indicate with their ipsilesional forefinger the perceived lateral location of the sound on their skull (note that for stimuli such as those used in the Bisiach et al. (1984) study – i.e., pure tones played dichotically over headphones – the sounds will actually be heard as if coming from a source ‘inside’ the head, because such stimuli lack the pinna and ‘head-related transfer’ spectral cues that lead sounds to be heard as coming from an external source). Brain-damaged patients were subdivided into four groups, according to lesion side (left or right) and presence or absence of any visual defects detected on confrontation. The results showed that the 25 right brain-damaged patients with visual defects showed the largest systematic directional errors in pointing to the sounds, apparently displacing perceived sound location towards the ipsilesional right side of their head. Within this group, 15 patients showed visual neglect on cancellation tests, and localisation errors were therefore examined as a function of presence versus absence of visual neglect. Although this comparison did not reach statistical significance ($F < 1$), directional errors in the sound-localisation task were numerically larger in the visual neglect patients than in patients without neglect.

Other studies of manual pointing to sounds in brain-damaged patients (often using external sound-sources in free-field, rather than headphone stimulation) have also observed sound-localisation errors in right-hemisphere patients (e.g., Ruff et al., 1981; Pinek et al., 1989; Pinek and Brouchon, 1992; Ládavas and Pavani, 1998; Pavani and Ládavas, 1999; Pavani, 2000; Pavani et al., 2003). But the relation between these localisation deficits and visual neglect has appeared to be controversial. Ruff and colleagues (1981) reported that posterior lesions to the right hemisphere produced large localisation errors (with no systematic directional error) for both contralesional and ipsilesional sounds; but they did not find any reliable association between these auditory localisation deficits and neglect in the visual or auditory modality (measured only by confrontation techniques). Similarly, Pinek and colleagues (1989) studied three patients with lesions centred on the right parietal lobe and visual neglect, observing systematic localisation errors in pointing towards the right for contralesional sounds in only two of their cases (the third showing systematic rightward errors only for ipsilesional sounds). By contrast, in a group study with 22 right-brain damaged patients, Pavani and colleagues (Pavani and Ládavas, 1999; Pavani et al., 2003) observed larger localisation errors (ipsilesional shifts in pointing) for left and central free-field sounds than for right sounds, in neglect patients versus right-hemisphere control patients.

A possible reason for the apparent discrepancies between different studies was initially proposed by Bisiach and colleagues (1984), while discussing the statistically non-significant effect of visual neglect on sound localisation in their study. They noted that auditory and visual tasks might often have different sensitivities, with perhaps the “auditory lateralisation task being a more sensitive tool to detect neglect than the visual cancellation task” (Bisiach et al., 1984, p.50). This raises the general issue of whether it is always appropriate to compare neglect-related disturbances in vision and audition using cut-off methods (e.g., assigning patients to

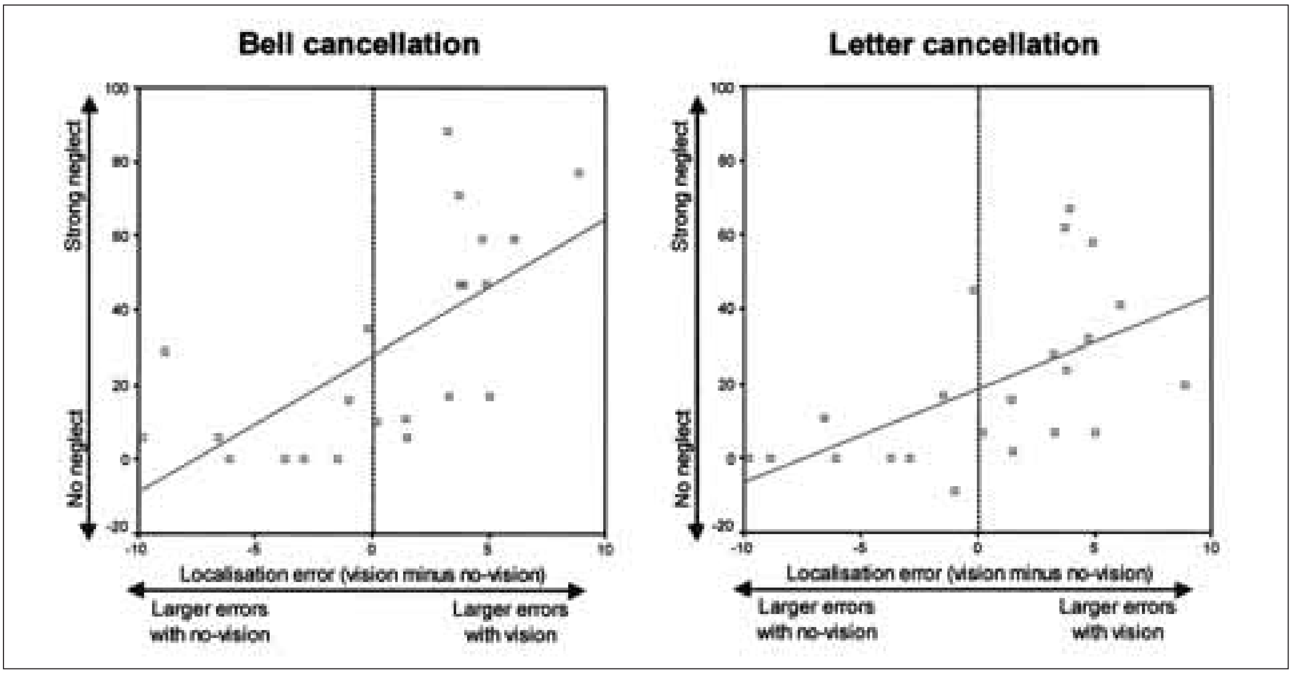

Fig. 1 – *Patient-by-patient correlation plots for the difference in auditory localisation errors in the vision minus no-vision conditions (from Pavani et al., 2003), against the score on cancellation tests (bell cancellation and letter cancellation). Data points falling to the right of the vertical dotted line in each plot correspond to larger localisation errors in presence of vision; data points falling to the left of the vertical dotted line correspond to larger localisation errors in absence of vision.*

either a neglect or noneglect group based on a cut-off score for a cancellation task); or whether alternative methods for comparing auditory and visual deficits along a more continuous scale might be more appropriate (e.g., correlation analyses). This methodological point may be of considerable importance when trying to establish any empirical relation between disturbances of space perception across different sensory modalities, as will be discussed further later.

Another possible interpretation of the discrepancies observed in previous manual pointing studies (concerning whether auditory mislocalisation does or does not relate to the presence of visual neglect), might involve the possible role of vision during some auditory tasks. The presence or absence of ambient vision is known to affect manual pointing to sounds in normal subjects, even in the absence of any task-relevant visual information, with more accurate localisation responses typically being observed with eyes open than when blindfolded (Warren, 1970; Platt and Warren, 1972), even when the sound-sources themselves cannot be seen. This phenomenon (termed ‘visual facilitation’) has been attributed to better eye-hand coordination in presence of vision (Platt and Warren, 1972; see also Cohen and Andersen, 2002 for one possible neural explanation of this phenomenon). In the auditory pointing study conducted by Pavani and Ládavas (1999; see also Pavani, 2000; Pavani et al., 2003), sound sources were always occluded from view, as was the responding hand; but pointing to sounds was nevertheless studied both with eyes open and with a blindfold. A similar pattern of performance to normal ‘visual facilitation’ (i.e. more accurate pointing with eyes open, even though neither the sound-sources nor the responding hand were visible) was observed for right-brain damaged patients without neglect (Pavani and Ládavas, 1999). By contrast, neglect patients were clearly more impaired (i.e. showed a greater tendency to point erroneously in a direction that was ipsilesional to the actual sound-source) when pointing to sounds with eyes open, versus when blindfolded (Pavani and Ládavas, 1999; Pavani et al., 2003; see also Soroker et al., 1997).

Moreover, as can be seen in Figure 1, the severity of visuospatial neglect for different patients on the bell-cancellation test (Gauthier et al., 1989; Figure 1A) and on the letter-cancellation test (Diller and Weinberg, 1977; Figure 1B) correlated significantly with this difference between localisation errors in auditory pointing for the vision minus no-vision conditions [r (20) = 0.66, $p < 0.001$; r (20) = 0.56, $p < 0.007$, respectively; analysis of data for 22 patients taken from Pavani et al., 2003]. Larger auditory pointing errors in the presence of vision correlated with high neglect scores (top right side of the plot); whereas larger auditory pointing errors in absence of vision correlated with lower neglect scores (bottom left side of the plot).

This suggests that while right-hemisphere control patients (and normals) can benefit from the presence of ambient vision (even when it is task-irrelevant; c.f. Platt and Warren, 1972; Warren, 1970) in auditory pointing tasks, patients with marked visual neglect show an opposite pattern, such that they are particularly hindered by the presence of vision. Note that this finding of worse rather than better performance in the presence of ambient vision for neglect patients argues against the eyes-open condition simply producing more alertness than the blindfolded condition (cf., Robertson et al., 1997). In fact, it appears that the mere presence of vision can exacerbate pointing errors to sounds in neglect patients, perhaps by attracting manual pointing responses (even for an unseen hand) further towards ipsilesional visual space.

This new finding could offer a possible explanation for the apparent discrepancies observed in the previous studies of manual pointing to sounds, which were in fact conducted under diverse visual conditions. For instance, it may be noteworthy that some of those studies which failed to show consistent localisation deficits for contralesional sounds in neglect patients actually used blindfolded conditions throughout the experiment (e.g., Pinek et al., 1989; Ruff et al., 1981). As shown in Figure 1, errors in pointing to sounds may be more apparent in a visible environment (even when vision provides no task-relevant information).

These results of Pavani and colleagues (1999; Pavani et al., 2003; see also Ládavas and Pavani, 1998; Pavani, 2000) indicate a role for vision (and thus possibly for eye-hand coordination) when pointing to sounds, and in doing so they emphasise a possible confound in using manual pointing as a measure for auditory space processing in patients. Whenever a directional motor response to a sound (e.g., pointing) is required, the observed directional errors might in principle be the consequence of some systematic error at the level of the motor response involved in the task, rather than the direct consequence of an altered perception of sound location. This potential confound becomes particularly relevant when considering localisation by neglect patients, as it is well-known that some patients with neglect can present with motor deficits in initiating or directing actions towards contralesional space (e.g., 'directional hypokinesia', Heilman et al., 1985; 'melokinetic neglect'; Bisiach et al., 1990; 1995; see also Husain et al., 2000), in addition to any perceptual, attentional or representational deficits. Moreover, it has previously been shown that some visual measures of neglect can also be modulated by the hand or manual starting position adopted for the motor response (e.g., Halligan et al., 1991).

This potential problem of motor influences was once again anticipated by Bisiach et al. (1984) in their pioneering auditory study. They commented that the systematic underestimation of left sound eccentrity by neglect patients, in a pointing task, might in principle have been the consequence of reduced motor exploration of the contralesional side of space, rather than a genuine auditory spatial deficit. To exclude such a potential motor confound, they devised a new task, as described in the next section.

Auditory Midline Tasks; Shift of Auditory Localization or Shift of Subjective Head/Body Midline?

In the new auditory task introduced by Bisiach et al. (1984), in order to circumvent spatial motor factors, the patients now had to rotate a central knob to adjust the perceived position of a single sound presented dichotically through headphones (by changing the relative intensity at the two ears), until the sound was perceived subjectively to be coming from the middle of the head. This task was performed by two neglect patients, revealing shifts in sound localisation for this task towards the ipsilesional side. That is, both patients systematically gave a greater intensity to the left-ear channel, indicating that sounds had to be lateralised further to the left to be perceived at the middle (compatible with a rightward shift in perceived sound-position; see Figure 2A, in which the bold concentric circle indicates actual sound position, while the dashed concentric circle indicates hypothetically perceived sound position). Note that this mislocalization result might be attributed to ear of entry, or to perceived spatial source; but the important point for present purposes is that it cannot be attributed to any motor bias.

This initial result was subsequently replicated and extended by Tanaka et al. (Tanaka et al., 1999) in a group-study of 44 patients with left or right-hemisphere lesions (plus 22 healthy controls), using interaural time difference (i.e. purely diotic rather than dichotic cues) as the lateralisation method over headphones (instead of interaural intensity difference as used by Bisiach et al., 1984; but note that with the purely diotic cues, sounds over the headphones should again be heard as coming from 'inside' the head). Tanaka et al. observed that right brain-damaged patients, unlike left brain-damaged patients and healthy controls, systematically perceived the sound as being aligned with their head/body midline when the interaural time difference favoured the left ear (i.e., with stimulation at the left ear slightly leading in time). As for Bisiach et al.'s study, this finding is compatible with a rightward shift of perceived sound position (see Figure 2A). Importantly, this result emerged in a significantly higher proportion of patient with visuospatial neglect than in right brain-damaged controls.

Two further studies have also used auditory-midline tasks, but now for sounds perceived as originating from external space, rather than being heard as originating from 'inside' the head, due either to presentation of external sounds in the free-

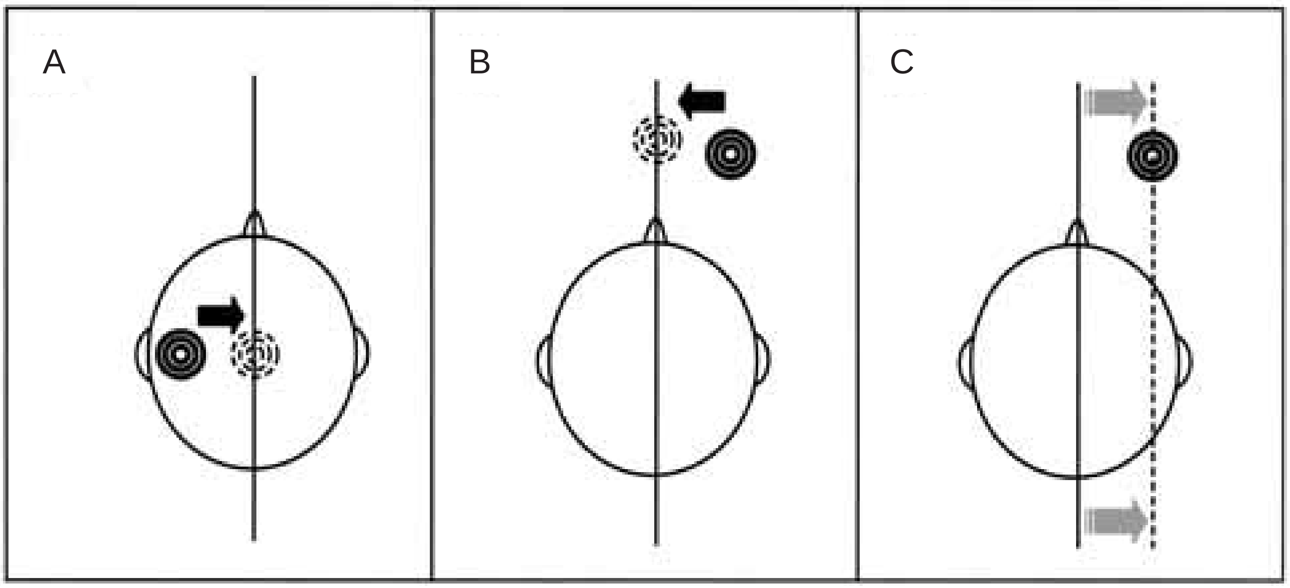

Fig. 2 – *Schematic description for the results of studies using an auditorymidline task. The actual sound position when patients perceived the sound as central or as aligned with their head/body midline is indicated schematically by bold concentric circles (within the head for A, as in Bisiach et al., 1984 and Tanaka et al., 1999; on the right, outside the head for B and C, as in Vallar et al., 1995 and Kerkhoff et al., 1999). Veridical head/body midline is indicated by a bold line, passing through the centre of the head. Insets A and B depict how various results might be interpreted if one assumes no pathological shift of the subjective head/body midline; the hypothetical perceived sound position is indicated by dashed concentric circles. Inset C depicts how the results might be interpreted if one assumed a pathological rightward shift of the perceived head/body midline instead; the possible shifted midline is indicated by a dashed line (translated midline shown; but a similar argument would apply, at least for sounds in front of the head, for a pathologically rotated subjective midline).*

field (Vallar et al., 1995) or within virtual auditory space by using head-related transfer functions over headphones (Kerkhoff et al., 1999). These two studies observed that, unlike right brain-damaged controls and healthy participants, patients with left neglect reported the head/body midline to be aligned with sounds that were actually displaced to the right (this is the opposite result to neglect patients' choice of leftward sounds as phenomenally central in Bisiach et al., 1984; Tanaka et al., 1999). As shown in Figure 2B, if one assumed that perception of the head/body midline remains accurate in neglect patients (i.e., passing through the objective centre of the head/body; see bold vertical line illustrating this schematically in Figure 2B), then choice of a rightward sound as appearing to be central would imply a shift in perceived sound position towards the left (leading to opposite conclusions than Bisiach et al.,1984 and Tanaka et al., 1999).

However, an alternative explanation might resolve these apparent discrepancies. As noted earlier, the sounds should be heard as originating from 'inside' the head in the studies of Bisiach et al., (1984), and Tanaka et al. (1999); but as originating from external auditory space in Vallar et al. (1995) and Kerkhoff et al. (1999), due to the different types of auditory information that were available. Moreover, when subjects are asked to compare an external sound to their head/body midline (as in Vallar et al., 1995; Kerkhoff et al., 1999), is should be noted that this task must rely not only on auditory processing, but also on how the subject perceives their head/body midline to be oriented with respect to the outside world. Thus, when sounds are adjusted to yield a setting that is shifted laterally relative to the true head/body midline, it can remain ambiguous whether this abnormality reflects perceptual mislocation of sounds, or instead mislocalisation of the head/body midline itself (or some combination). To illustrate this argument, Figure 2C shows hypothetical 'translation' (Vallar et al., 1995) of the perceived head/body midline (shown by the dashed vertical line), which would be compatible with misjudging a rightward sound as centrally aligned with the subjective midline. Note also that this potential problem in interpreting auditorymidline tasks (i.e. equivocality over whether it is auditory location that has shifted, or instead perception of where the head/body midline lies) may particularly apply for neglect patients, since several non-auditory studies have shown that unilateral neglect patients can indeed present an altered perception of their subjective head/body midline with respect to external space (e.g., Karnath, 1997; Ferber and Karnath, 1999; but see Farné et al., 1998). Thus, when an auditory-midline measure is used, it can remain unclear whether neglect alters the perception of sound position, the perception of the head/body midline, or both these aspects at the same time. (Note also that any pathological misperception of how the head/body is oriented with respect to external space may have been less of a problem in Bisiach et al., 1984, and Tanaka et al., 1999, as in those studies the particular types of sounds used (over headphones, without pinna or head-related transfer cues) should have been heard as arising from 'inside' the head, not from an external spatial source).

Auditory Localization Tasks that Avoid both Spatial Motor Responses and any Midline Comparisons still Reveal Deficits in Localization for Neglect Patients

An alternative type of auditory localisation task, which does not rely on any directional motor response, nor on any comparison between sound position and the head/body midline, has recently been applied to neglect patients by Pavani et al. (2001). Patients were required to judge verbally the relative position of two brief tones, presented in close temporal succession (separated by 500 ms), from nine possible free-field locations (see Figure 3). The task was performed either with eyes open or blindfolded, but vision of the loudspeakers was occluded throughout. On each trial, the two sounds originated from either the same or different spatial locations (actually 20% same locations, and 80% different locations, though subjects were not informed of these probabilities). The patients were instructed to report verbally whether the position of the two successive sounds was 'same' or 'different'. In this task, right-brain damaged patients without neglect reliably discriminated between different sound positions whenever the spatial separation between the two sounds was at least 20 degrees, regardless of whether these appeared in left or right hemispace. A similar performance emerged also in neglect patients, but only when at least one of the two sounds originated from the right hemispace. By contrast, when both sounds were presented within the left visually-neglected field, patients were unable to discriminate different sound positions even when the spatial separation between the stimuli exceeded 30 degrees. Interestingly, although this task was performed both with eyes open and blindfolded, no effect from the presence of ambient vision was found. This contrasts with the pointing results of Ládavas and Pavani (1998), and Pavani et al. (1999; Pavani, 2000; Pavani et al., 2003; see also Figure 1), as described earlier, thus suggesting that the effect of ambient vision in those studies may relate to their use of a pointing task, and thus to the involvement of eye-hand coordination.

Pavani et al.'s (2001) results from the same/different successive-discrimination task appear to demonstrate a genuine deficit of auditory localization for contralesional space processing in visual neglect patients, which cannot be attributed to response-related motor errors (since no directional motor response was required, unlike the pointing studies); nor to any biases in judging the perceived position of the subjective head/body midline. The findings thus support and extend other evidence of pathologically increased thresholds for detecting changes in sound position in visual neglect patients, as previously found when sounds were lateralised over headphones using interaural time differences (Tanaka et al., 1999; Cusack et al., 2000). These results are also compatible with recent electrophysiological evidence showing that the typical event-related brain potential elicited in response to a sudden change in sound properties (i.e., the auditory mismatch negativity response; Naatanen and Alho, 1995) is reduced for contralesional sounds in neglect patients, particularly when the change involves the sound's spatial position (Deouell et al., 2000).

A final aspect which has been recently considered for localisation tasks (Pavani et al., 2002a) is whether any auditory spatial deficits in neglect relate to just the horizontal dimension, or may instead extend to vertical auditory space perception as well. This issue is relevant to understanding whether sound-localisation deficits should just be interpreted as the result of horizontal localisation biases (as the manual pointing studies and the 'auditory midline' studies described earlier appeared to suggest); or should instead be considered as reflecting an increased uncertainty for contralesional sound locations (with increased uncertainty then leading to increased response biases in pointing tasks, etc). The existence of vertical auditory deficits in neglect patients would support an account in terms of increased uncertainty (or greater variability) in auditory localisation, as purely horizontal shifts or biases should not affect processing for the elevation of the stimuli.

To address this issue we studied two groups of right-brain damaged patients (with versus without visual neglect), in a task requiring vertical discrimination of sound position (Pavani et al., 2002a). Such vertical spatial discrimination is predominantly based on spectrotemporal analysis of the sound waveform at each ear (Blauert, 1983), for cues that relate to the spectral effects of the pinna and the head-related transfer function. On each trial in Pavani et al.'s study, one brief broad-band sound was presented either at an upper or lower free-field location, in left or right hemispace. Patients were required to perform a speeded discrimination of vertical sound position, by moving a central joystick according to the perceived elevation of the sound (i.e., up or down), regardless of sound side (see schematic of the experimental set-up in Figure 4). In this task, any spatial uncertainty (i.e. localization difficulty) for left sounds should be revealed by an impairment in vertical spatial discrimination performance for left versus right hemispace. The task was always performed with eyes open, but speakers were occluded throughout. Unlike non-neglect patients, patients with visuospatial neglect showed a clear disadvantage for left versus right stimuli (as

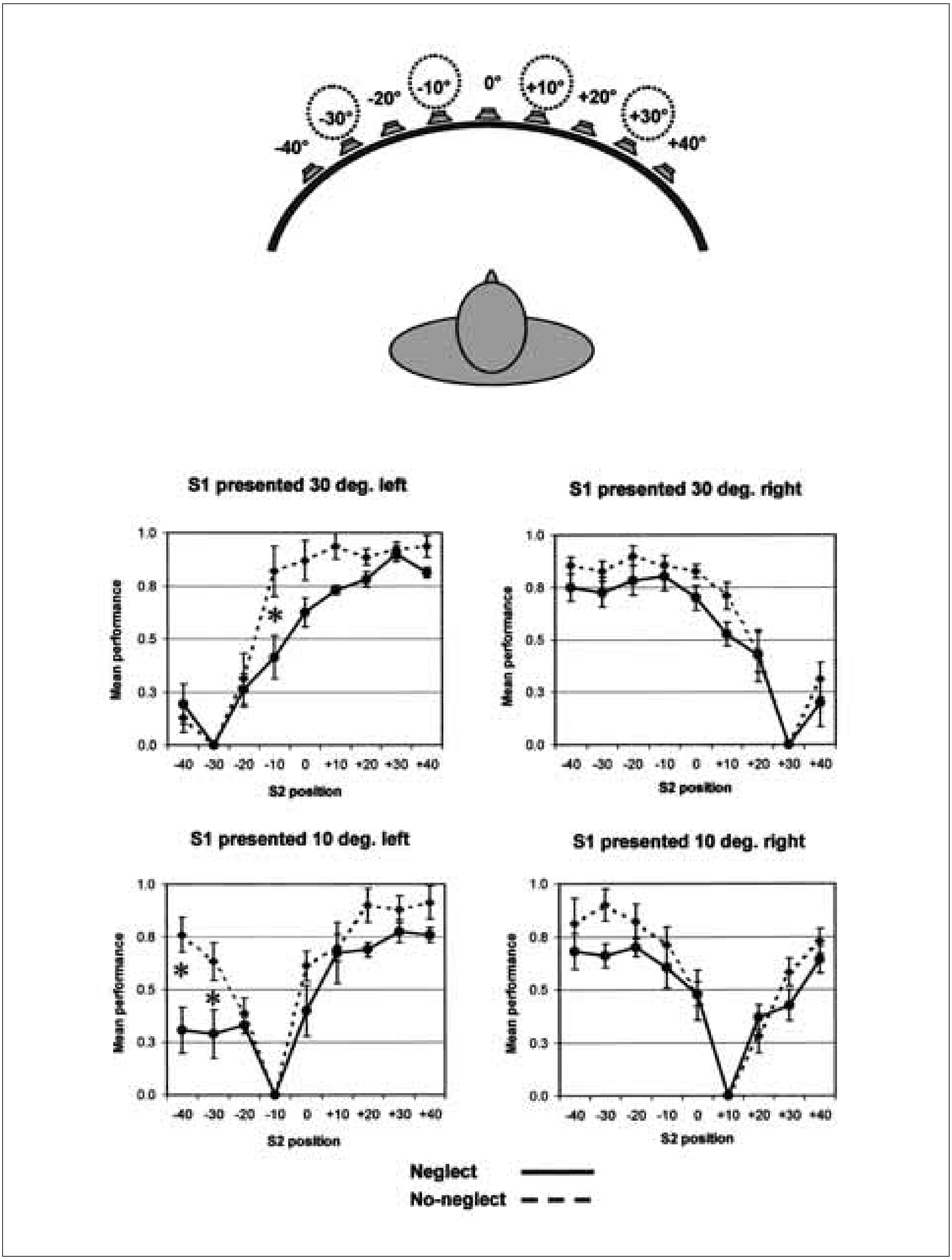

Fig. 3 – *Top: Birds-eye schematic view of the experimental setup used by Pavani et al., 2001. Angular positions of sound sources are indicated near each cartooned loudspeaker. Circled numbers indicate positions where the first stimulus (S1) of the two successive sounds could be presented (i.e., – 30, – 10, + 10, + 30 degrees). The second sound (S2) could be presented from any of the nine locations. Note that all loudspeakers were occluded behind a sound-transparent panel. Bottom: Mean performance (calculated as correct detection of sound-position change multiplied by the correct detection of no-change) of the two groups as a function of S1 position (shown in separate graphs) and S2 position (bars indicate the standard error). Bold lines indicate visual neglect patients, dotted lines indicate control patients. Asterisks indicate statistical differences between the two patients groups. Neglect patients were significantly more impaired than right brain-damaged controls when both sounds (S1 and S2) appeared on the left side.*

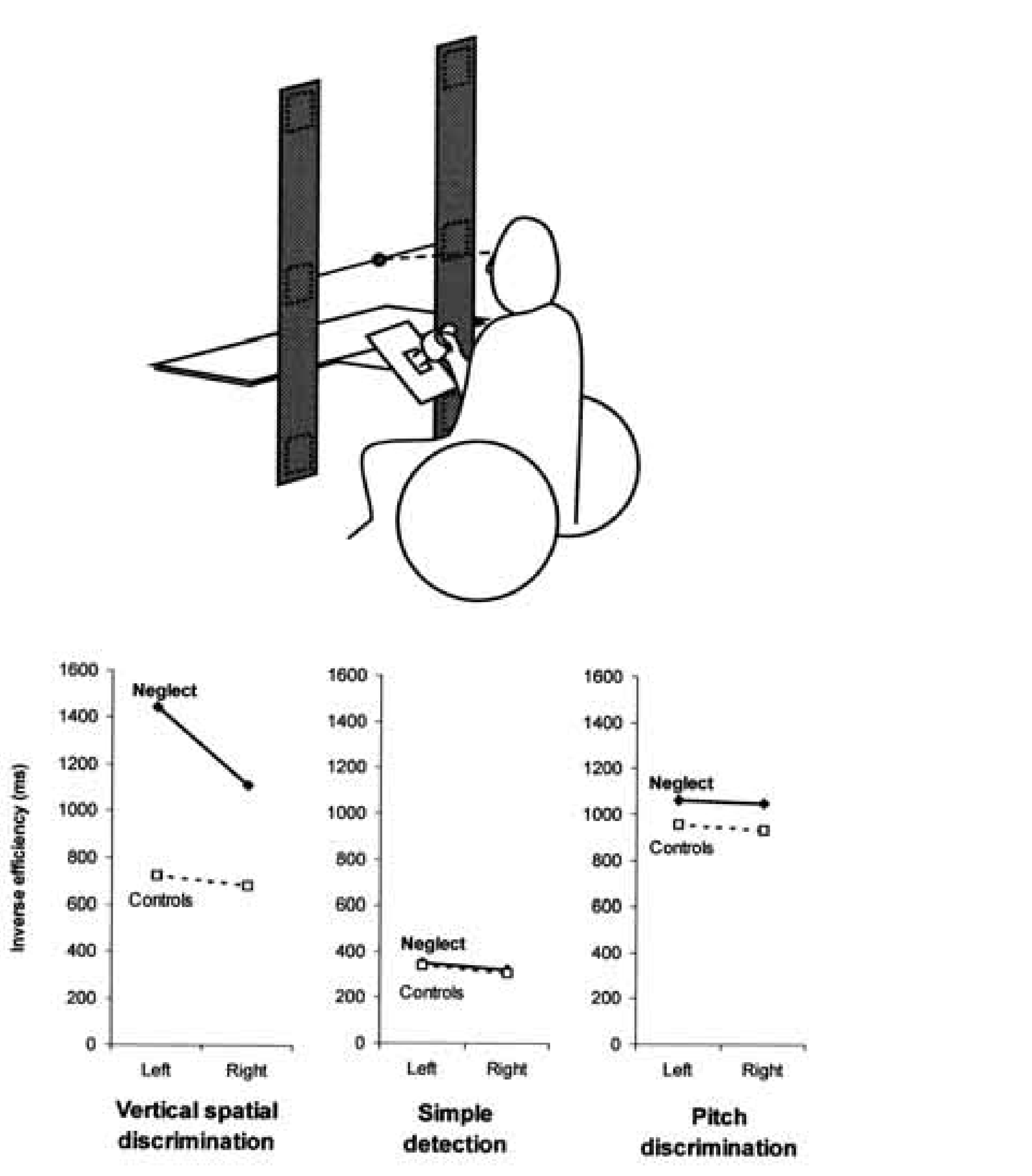

Fig. 4 – *Top: Schematic view of the experimental setup used by Pavani et al., 2002a. Note that all loudspeakers (shown as dotted rectangles) were hidden behind a strip of black fabric. Bottom: Mean inverse efficiency scores (i.e., combined measure of reaction time and accuracy scores used in the study, calculated as the mean reaction time divided by the proportion of correct trials in a given condition) as a function of acoustic task (vertical spatial discrimination, simple detection, or pitch discrimination) and stimulation side (left versus right). Higher scores indicate less efficient performance. Bold lines indicate visual neglect patients, dashed lines indicate control patients. A significant difference between the two groups emerged only in the vertical spatial-discrimination task, particularly for left sounds. By contrast no group difference emerged for simple detection or pitch discrimination tasks.*

revealed by longer reaction times and more localisation errors; see Figure 4). Interestingly, such a contralesional deficit emerged for the vertical spatial task, but not when the neglect patients had to perform a simple detection or a pitch discrimination task for unilateral stimuli at comparable lateral positions in left or right space.

To summarise the above sections on localisation tasks, there now appears to be converging evidence for spatial auditory deficits in neglect patients, across several different sound-localisation paradigms (i.e. pointing to sounds, auditory midline, same-different tasks, perceptual thresholds, and vertical discriminations); and across different stimulation methods (free-field sounds; or headphone stimuli lateralised using intensity or interaural time differences, or head-related transfer functions).

These deficits appear to reflect increased uncertainty about sound location towards the contralesional side, as recently revealed by the existence of similar disturbances for both horizontal and vertical space perception (Pavani et al., 2001, 2002a). However, they are also characterised by horizontal ipsilesional biases (i.e. systematic shifts in reported position, towards the ipsilesional side) when motor responses are involved (as in pointing tasks) or when sound position is compared with the head/body midline (although here it may sometimes be that the subjective head/body midline has shifted pathologically, rather than localization of the sound itself). Although the exact nature of the horizontal biases remains to be ascertained, some of these could reflect pathological visual influences on localization responses (consistent with some of the results found when comparing eyes-open versus blindfolded conditions), particularly when a manual pointing response is involved.

Non-Spatial Auditory Deficits Suggest Multimodal Capacity Limitations in Neglect

All of the studies discussed so far focused on spatially-specific auditory deficits in visual neglect patients. The detection and identification studies examined patients' performance as a function of the spatial location of the auditory targets (e.g., left versus right), whereas localisation studies examined the patients' auditory spatial processing directly, at different locations. However, a growing body of evidence now suggests that visuospatial neglect patients may also suffer some non-spatial deficits, in visual tasks (e.g., Husain et al., 1997; Duncan et al., 1999; Battelli et al., 2001; Robertson, 2001; Husain and Rorden, 2003). More recently, non-spatial deficits have also been demonstrated using auditory stimuli, in patients with visual neglect (e.g., Robertson et al., 1997; Cusack et al., 2000; Pavani et al., submitted).

Robertson and colleagues (1997) were the first to report non-spatial auditory deficits, using an auditory test of sustained attention (Wilkins et al., 1987). Patients were presented with central tone-sequences of variable length and were simply required to count how many target tones occurred in each series. In this task, right brain-damaged patients with neglect were significantly more impaired than non-neglect patients, perhaps reflecting a difficulty in sustaining attention or maintaining arousal. Moreover, performance in the sustained auditory task correlated significantly with several measures of visual neglect (star cancellation, line bisection, BIT scores, comb and razor tests).

More recently, Cusack and colleagues (2000) asked a group of right brain-damaged patients with visual neglect to listen to a rapid sequence of auditory stimuli presented over headphones, in order to detect which of the stimuli differed from the others. In agreement with the results of the localisation studies described in the previous section, neglect patients' performance was pathological (with respect to age-matched controls) when the feature-change concerned sound position (cf., Tanaka et al., 1999; Deouell et al., 2000; Pavani et al., 2001). More interestingly, a 'non-spatial' deficit emerged when auditory stimuli were always presented centrally, with the task now consisting of detecting which of the sounds in the rapid sequence had a higher pitch. This deficit could not be attributed to an inability to perceive any change in sound frequency, as shown by a control experiment in which neglect patients were as accurate as controls in perceiving frequency modulations for a single tone presented alone. Thus, the authors suggested that this result could represent a non-spatial problem with comparisons between brief successive sounds, possibly due to attentional limits.

Finally, Pavani and colleagues (Pavani et al., submitted) have recently observed a non-spatial auditory deficit in neglect patients for bilateral words presented diotically (i.e., each stimulus presented binaurally, but with interaural time difference at the two ears as the localisation cue). In this test, each word reaches both ears and hemispheres, so should not suffer from any suppression of auditory input from the contralesional ear, potentially leading to better performance (c.f. Bellmann et al., 2000). However, bilateral words with diotic cues in fact proved more difficult for our patients with strong visual neglect than for controls, but with this deficit affecting 'left' and 'right' sounds equally on double stimulation, as compared with presentation of a single word diotically to either side. This result is not likely to reflect a difficulty in making comparisons between auditory objects (cf., Cusack et al., 2000) because no such comparison was required on this task. Instead, as has previously been suggested for vision (Husain et al., 1997; Robertson, 2001), such a deficit might in principle reflect general capacity-limitations in neglect patients, in addition to their spatial biases.

Is there an Empirical Relation between Visuospatial Neglect and Auditory Deficits?

The evidence presented so far demonstrates that patients with visuospatial neglect can show pathological performance in a variety of auditory tasks. Auditory deficits have been predominantly described for contralesional auditory targets in detection and identification tasks (primarily with bilateral stimulation); and also in localisation tasks (even with single unilateral stimulation). In addition, some recent evidence suggests that some non-spatial auditory deficits may also be observed. But it remains unclear so far whether any relation between these auditory deficits and the presence of visual neglect can be consistently established. Across different type of auditory tasks, several authors have observed that auditory deficits can be more pronounced in visual neglect patients than in right-brain damaged controls without neglect (e.g., Calamaro et al., 1995; Bisiach et al., 1984; Vallar et al., 1995; Pavani et al., 2001, 2002a; Pavani et al., submitted; Tanaka et al., 1999). However, some apparent dissociations between auditory deficits and visual neglect (or visual extinction) in individual cases have also been reported (e.g., De Renzi et al., 1984).

As mentioned earlier, Bisiach and colleagues (1984) suggested that such apparent dissociations might reflect, to some extent, the different sensitivity of the tests adopted for measuring auditory and visual deficits. Indeed, while the degree of auditory deficits in those studies which have focused on this particular modality is typically measured using complex auditory tests (e.g., difficult dichotic listening tasks, discrimination of sound position, or speeded responses to sound positions), any visual disturbances in the same patients are often examined only with standard pen-and- paper clinical measures (e.g., cancellation tests for visual neglect), or with clinical confrontation tests for visual extinction. In such contexts, it is possible that the auditory measures might be less subject to potential floor or ceiling effects than standard clinical measures. Ideally, one would wish to adopt equally sensitive measures for both auditory and visual performance, but note that it may not always be obvious which variables (e.g., accuracy, speed, stimulus intelligibility) should be considered when trying to equate task-difficulty across different sensory modalities.

Whatever measures of visual and auditory performance are used, the relation between any auditory deficits and visual neglect may also be difficult to establish firmly when simply comparing two dichotomised patient groups (i.e. ‘neglect’ vs. ‘no-neglect’), created on the basis of cut-off scores for different clinical tests. This seems particularly problematic given that a patient diagnosed with neglect at one point in time may later be reclassified as non-neglect (i.e. when showing ‘recovery’ on some particular clinical measure) under a dichotomous approach. An alternative approach could be to examine the correlation between auditory deficits and degree of visual neglect, using more continuous measures. In principle, this could directly address the empirical question of whether stronger visual neglect is often associated with more pronounced auditory disturbances. Such correlational analyses have been adopted in only a few of the reviewed studies to date (Soroker et al., 1995, Robertson et al., 1997; Pavani et al., submitted), but may prove useful in confirming any empirical relation between visual and auditory disturbances.

Accordingly, we re-analysed all of our own previous data-sets (Pavani and Làdavas, 1999; Pavani et al., 2001, 2002a; Pavani et al., submitted) using such a correlational approach, to test for any consistent relation between severity of visual neglect (on clinical measures), and severity of auditory deficit (on all the different experimental measures used). In all studies, the patients presented unilateral right-hemisphere lesion, showed no major cognitive impairment on clinical assessment (e.g., on the Mini-Mental test), other than visual neglect in some cases, and showed normal hearing or only mild hearing loss, with no difference between the two ears above 15dB. Table I shows Pearson’s correlation coefficient ‘*r*’ (together with its one-tail statistical significance and the number of subjects in each analysis) between the severity of visual neglect and each of the dependent auditory variables used in each study. Correlations passing conventional levels of significance are indicated with bold fonts. For each cancellation test (bells, letters, Mesulam and star cancellation), we expressed each patient’s performance with a single score (right minus left performance, divided by right plus left). Line bisection errors (in centimetres) were entered directly for the correlation analyses. Figure 5 shows the scatter plots for each of the assessed correlations.

As can be seen from Table I, the striking outcome of these new analyses was that performance in clinical tests of visual neglect correlated significantly with the auditory dependent measures on 10 of the 14 correlations assessed. Moreover the correlations closely approached significance for 2 of the 4 remaining analyses; while the two least significant correlations both concerned line-bisection rather than cancellation as the measure of neglect, which may be sensitive to different aspects of syndrome (e.g., Halligan and Marshall, 1998). Although correlation results must always be interpreted with some caution (as they do not necessarily indicate a direct causal relationship between the two variable of interest, but could in principle arise due to intervening variables), the consistent findings strongly suggests an empirical relation between the severity of visual neglect on cancellation, and the auditory deficits observed in our experimental studies (which were predominantly contralesional deficits; but note that performance for bilateral diotic words regardless of side also correlated with the Mesulam cancellation test).

This empirical relation appears consistent with the notion that several of the areas typically

TABLE I

Pearson's Correlation Coefficient 'r' (together with its one-tail significance and the number of subjects in each analysis) between Clinical Tests of Visual Neglect and the Dependent Auditory Variable in each Study. Significant Correlations are Indicated with Bold Fonts. Scatterplots for each Correlation Analysis are shown in Figure 5; insets in that Figure are coded with letters as Referred to in the Table, below each Significance Value

Study	Auditory task	Dependent variable	Bell cancellation[1]	Letter cancellation[2]	Mesulam cancellation[3]	Star cancellation[4]	Line bisection[4]
Pavani and Ládavas (1999)	Manual pointing to free-field sounds	Mean localisation error (with eyes open)	***r* = 0.72 p < 0.0001 N = 22 Fig. 3A**	***r* = 0.74 p < 0.0001 N = 22 Fig. 3E**	n/a	n/a	n/a
		Mean localisation error (blindfolded)	*r* = 0.32 p < 0.08 N = 22 Fig. 3B	***r* = 0.38 p < 0.04 N = 22 Fig. 3F**	n/a	n/a	n/a
Pavani, Meneghello and Ládavas (2001)	Discrimination of relative position for two sucessive (same vs. different)	Mean performance when both sounds are contralesional	***r* = 0.57 p < 0.03 N = 12 Fig. 3C**	***r* = 0.60 p < 0.02 N = 12 Fig. 3G**	n/a	n/a	n/a
Pavani, Ládavas and Driver (2002)	Vertical discrimination of (up vs. down)	Percent errors for contralesional sounds	***r* = 0.77 p < 0.01 N = 8 Fig. 3D**	***r* = 0.70 p < 0.03 N = 8 Fig. 3H**	n/a	n/a	n/a
Pavani, Husain, Malhotra and Driver (submitted)	Identification of bilaterally presented words	Percent errors for contralesional dichotic words (spatial deficit)	n/a	n/a	***r* = 0.77 p < 0.003 N = 11 Fig. 3I**	***r* = 0.72 p < 0.006 N = 11 Fig. 3K**	*r* = 0.34 p = 0.2 N = 11 Fig. 3M
		Percent errors for diotic words regarless of side (non-spatial deficit)	n/a	n/a	***r* = 0.55 p < 0.04 N = 11 Fig. 3J**	*r* = 0.50 p = 0.06 N = 11 Fig. 3L	*r* = 0.25 p = 0.2 N = 11 Fig. 3N

[1] Gauthier et al., 1989; [2] Diller and Weinberg, 1977; [3] Mesualm, 1985; [4] Wilson et al., 1985.

damaged in neglect patients (e.g., inferior and superior parietal regions, superior temporal, premotor and frontal areas) may be crucial brain areas for processing of multisensory space. Such brain areas could provide a common multimodal substrate for the related auditory and visual deficits that we have now observed in neglect patients. Some evidence that is broadly consistent with this multisensory notion has emerged from neurophysiological studies in animals.

Multisensory neurons, that can respond to stimulation in more than one modality (e.g., vision and audition), and that typically have related spatial selectivity (e.g., respond for visual or auditory stimuli occurring in a similar region of space), have been found cortically in parietal, superior temporal and premotor areas (e.g., Mazzoni et al., 1996; Stricanne et al., 1996; Andersen et al., 1997; Duhamel et al., 1998; Graziano and Gross, 1998); and also at the subcortical level (e.g., superior colliculus, Stein and Meredith, 1993; basal ganglia, Hikosaka et al., 1989). In recent years, neuroimaging studies have also shown multisensory responses in similar brain areas for neurologically normal humans (see Macaluso and Driver, in press, for review). For instance, Bushara and collegues (1999) have observed that visual and auditory localisation tasks activate areas bilaterally in the superior and inferior parietal lobule, as well as right medial frontal cortex. Similarly, Bremmer and colleagues (2001) have found multimodal activation in intraparietal sulcus, inferior parietal lobule and ventral premotor cortex, in response to visual, auditory and tactile moving stimuli (see Macaluso and Driver, 2004, for review).

Giving such findings of multimodal brain structures involved in spatial representation, the existence of multisensory deficits in neglect patients appears to be expected. However, it is important to note also that neuroimaging results have also suggested that some modality-specific (i.e., unimodal) brain areas may exist quite close to those regions representing multisensory space (e.g., Bushara et al., 1999; Bremmer et al., 2001). For instance, Bushara and colleagues (1999) observed some modality-specific visual or auditory activations during localisation tasks, within the superior parietal lobule and in the middle frontal gyrus bilaterally; auditory-specific localisation areas were also described in the right inferior temporal gyrus and in left inferior frontal gyrus. Similarly, Bremmer and colleagues (2001) noted a preferentially visual activation in the more posterior areas of the superior parietal lobe (see also Downar et al., 2000).

Associated auditory and visual spatial deficits, as demonstrated by the correlations we find, could in principle arise following either damage to multisensory spatial representations, or coincident damage to separable but neighbouring unimodal spatial representations for each of the two modalities. It may be difficult to separate these two possible explanation for associations based on

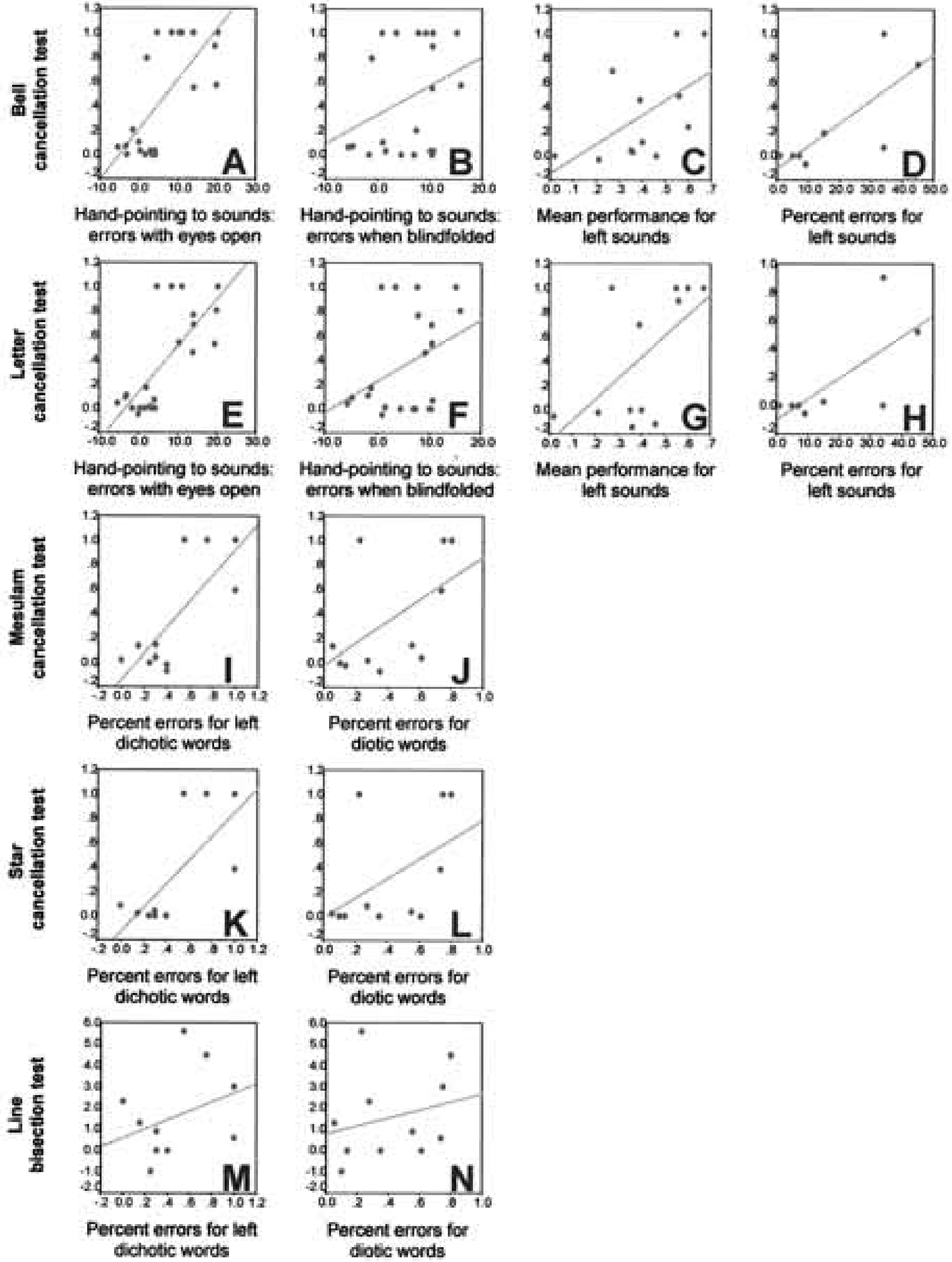

Fig. 5 – *Scatterplots of the correlation analyses presented in Table I. Note that there is a reliable correlation between the severity of visual neglect (Y-axis) and the auditory deficit on experimental measures (X-axis) for most plots.*

behavioural evidence alone. Traditional neuropsychology tends to emphasize dissociations as more revealing than associations (e.g., see Shallice, 1988, for such arguments). Thus, any single case within the scatter plots of Figure 5 that does not fit the overall correlative pattern (i.e. showing strong visual neglect without auditory deficits, or vice-versa) might be considered from this perspective as providing the most telling evidence, indicating that auditory and visual spatial representations can be separable. However, while double-dissociations in rare cases may show that some auditory and visual components may indeed be separable, this still begs an explanation for the overall associative (correlative) pattern that is observed. Moreover, such double dissociations need not entail that there are no common multisensory components that can produce associated deficits when damaged. It may be that rather than showing complete separability of all auditory and all visual spatial representations, the rare dissociative cases with only a visual or only an auditory deficit may instead serve to provide important information for delimiting the high-level multimodal brain structures. With the advent of high-resolution structural and functional neuroimaging, it may now be possible to test whether the lesions of cases with dissociated auditory or visual deficits differ systematically from those patients with associated deficits; and to relate this to whether the implicated structures are unimodal or multisensory, as revealed by functional imaging in normals

Conclusions

Although the body of work on auditory processing in neglect patients is still relatively small when compared with the extensive research on visual disturbances in neglect, many of the issues initially raised by the pioneering work of Edoardo Bisiach and colleagues (e.g., Bisiach et al., 1984; see also Heilman et al., 1979; De Renzi et al., 1984, 1989) have now been addressed, and some new conclusions can be drawn.

First, the existence of auditory deficits in many visual neglect patients appears now to be unequivocally established. Converging evidence from different experimental paradigms, and from diverse auditory measures, has revealed consistent spatial disturbances of auditory processing in visual neglect patients. Auditory deficits have been predominantly described for contralesional auditory targets in detection and identification tasks when bilateral stimulation is used; whereas sound-localisation tasks have revealed predominantly contralesional deficits even for single unilateral stimuli. In addition, some non-spatial auditory disturbances have also been shown.

Second, some of the novel experimental approaches adopted in recent identification studies (e.g., visually-induced illusory changes in perceived sound position; controlled use of auditory cues for localisation over headphones; attentional manipulations; or auditory streaming) have demonstrated that no explanation in terms of mere left-ear suppression can explain all the deficits observed. Higher-level spatial factors are also implicated.

Third, the presence of task-irrelevant visual information appears to play a role in some auditory deficits in visual neglect patients (as revealed by some of the results with eyes open versus blindfolded conditions), particularly when pointing to sounds is involved.

Finally, it is for the first time now clear (see Figure 5) that various auditory deficits, as revealed by experimental testing, correlate consistently with the severity of visual neglect, as measured by clinical tests (particularly cancellation tests). This suggests a relation between auditory and visual deficits, which appears broadly compatible with the multimodal spatial nature of many of the brain areas that are typically lesioned in neglect patients.

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