Pavani and colleagues (2005, this issue) present the first evidence that gaze direction can influence the auditory symptoms of unilateral neglect. In their experiment, patients undertook a speeded auditory localization task in either their left or right hemifield, while gaze was maintained either centrally or laterally. Consistent with the expected symptoms of auditory neglect following right brain damage, patients were slower and more error prone in discriminating the elevation of left sounds than right sounds when gaze was directed centrally or to the right. However, when patients directed their gaze to the left, symptoms of auditory neglect virtually disappeared. These novel findings suggest that crossmodal links in spatial attention may be relatively preserved in some neglect patients, possibly through the recruitment of surviving subcortical networks. Furthermore, the results have potential implications for the role of coordinate transformations in the parietal cortex and the targeting of rehabilitation strategies that encourage the spatial representation of target stimuli in relatively preserved frames of reference.

**MULTIMODAL ATTENTION AND COORDINATE TRANSFORMATION IN UNILATERAL NEGLECT**

A critical aspect of Pavani and colleagues’ interpretation is that attentional processing in the neglected hemifield of brain-damaged patients is partially preserved. There is already substantial evidence that neglected stimuli are processed pre-attentively, and can influence behaviour despite being reported by patients as absent (Mattingley et al., 1997). For instance, stimuli that are either neglected or extinguished may nevertheless elicit flanker interference effects (Cohen et al., 1995), act as visual primes for meaning or form (Berti and Rizzolatti, 1992; McGlinchey-Berroth et al., 1993), and even induce Stroop effects (Berti et al., 1994; see Driver and Vuilleumier, 2001 for review). Within the context of spatial attention, Bartolemeo et al. (2001) reported modest performance costs in neglect patients when a peripheral spatial cue in the neglected hemifield preceded a target on the ipsilesional side. D’Erme et al. (1992) reported a similar but larger invalidity cost for cues presented in contralesional space. Overall, these results suggest that neglected stimuli are processed sufficiently to serve as attentional cues (see also Vuilleumier, 2002).

Attentional mechanisms within sensory modalities may be partially preserved in neglect, but what of attentional links between modalities? Despite a large body of evidence indicating the existing of multimodal attentional mechanisms (Spence and Driver, 1996, 1997; Spence et al., 1998; Driver and Spence, 1998), relatively few studies have examined whether such links are preserved within contralesional space for neglect patients. A recent study by di Pellegrino and Frassinetti (2000; see also Carey, 2000) showed that the visual symptoms of bilateral extinction were significantly reduced when patients placed their hands in proximity to visual targets, compared to when their hands were either (a) placed proximally but covered from view, (b) placed further away, or (c) placed further away but with visual cues depicting hands presented adjacent to the visual targets. These results indicate that both placing and
seeing the hands near the visual stimuli was required for extinction to be diminished. One interpretation of this observation is that the recruitment of brain regions involved in visuo-somatosensory integration increased the salience of visual events in the contralesional hemifield. A similar interpretation may apply to the results of Pavani and colleagues, which show for the first time that the directing of gaze toward neglected space can reduce the symptoms of auditory neglect. In both cases, the activation of multimodal neurons with receptive fields in the neglected hemifield may increase the salience of events in the target modality (see Figure 1). Many neural regions may be involved in such benefits, including subcortical structures such as the inferior and superior colliculi (Groh et al., 2001; Stein and Meredith, 1993), and surviving cellular networks in the ipsilesional parietal cortex (Andersen et al., 1997).

An important future step in understanding the cause of the perceptual improvements shown by Pavani and colleagues (2005, this issue) will involve functional neuroimaging of patients while performing the same task. If the salience of the target events is enhanced by multimodal interactions, then increased activity might be expected in neural areas that represent salience, such as the posterior parietal Cortex (PPC) and intraparietal area (Bisley and Goldberg, 2003). This question could also be examined by temporarily disrupting the parietal cortex in healthy subjects using transcranial magnetic stimulation (TMS) (Chambers et al., 2004; Stewart et al., 2001). If the recruitment of crossmodal attentional mechanisms increases the gain of auditory signals in the PPC, then healthy participants should be more resistant to interference of parietal activity when gaze is directed toward the location of an auditory target.

How might the representation of a stimulus within a multimodal network influence salience? Pouget et al. (2002) argue compellingly that the most efficient form of multimodal processing is undertaken by transforming the spatial coordinates of auditory, visual and tactile signals into a single frame of reference. These transformations might result in an auditory target being encoded in eye-centered, head-centered, body-centered or world-centered coordinates. Combined with evidence that the PPC plays a critical role in coordinate transformations (Cohen and Andersen, 2002), the results of Pavani and colleagues (2005, this issue) could reflect the protection of auditory stimulus information by being recoded within a reference frame that has been left relatively intact within the damaged parietal lobe. Since neglect is a disorder that operates within multiple frames of reference.
(Salinas and Sejnowski, 2001; Halligan et al., 2003), it will be important in future research to chart the relationship between the frame of reference affected in individual neglect patients and the combinations of crossmodal interactions that are most effective in reducing symptoms. If the benefits shown by Pavani and colleagues arise from multimodal coordinate transformation, then the reduction in neglect symptoms should be greatest when the target modality is encoded in the frame of reference least affected by neglect.

**Potential Caveats**

Notwithstanding the importance of the findings presented by Pavani and colleagues (2005, this issue), there are two outstanding issues that only future studies may be able to resolve. First, their findings are potentially inconsistent with those of Soroker et al. (1997), who showed that blindfolding patients improved the symptoms of auditory neglect to a similar level obtained in a control group. The authors attributed the beneficial effect of blindfolding to a reduction in distraction resulting from simultaneous multimodal inputs. This finding is difficult to reconcile with the benefits of gaze direction shown by Pavani and colleagues, and suggests that multimodal processing may either enhance or impair neglect depending on the attentional capacity of the patient. As the authors point out, a useful extension of their paradigm would involve the direction of gaze while patients are either blindfolded or in complete darkness. Furthermore, without measuring the full range of neglect symptoms within eye-, head-, body- and world-centered coordinates, it is difficult to compare the effects of manipulations that may alter the frame of reference in which a target stimulus is represented.

A second caveat with Pavani and colleagues’ interpretation is that during conditions of left gaze deviation, both left and right sounds fell within the right (preserved) visual field. This situation arose because patients directed their gaze laterally to spatial locations that were 17.5° more eccentric than the positions of the speakers. Could the encoding of auditory location in ipsilesional retinotopic space have contributed to the observed benefits? Pavani and colleagues suggest that if retinotopic coding of auditory location was the sole contributor to their results then performance should have been identical between conditions of gazing rightwards while discriminating right auditory targets and gazing centrally while responding to left auditory targets. In both these conditions, the retinotopic positions of the sounds immediately to the left of fixation were identical, and only the eye-in-orbit position differed. Since performance varied between these two conditions, Pavani and colleagues argue that retinotopic influences can be excluded as the sole determinant of the results. Although this point is true for sounds to the immediate left of fixation, it does not exclude the possibility that retinotopic encoding of the opposite sound may have influenced the benefits of contralesional gaze direction. Note, for instance, that when gazing rightwards, the left-most speaker was located 52.5° left of fixation, but when gazing centrally, the right-most speaker was located 17.5° to the right of fixation. Directing gaze thus altered the expected location of one auditory target in retinotopic coordinates, leaving open the possibility that encoding of the auditory targets in ipsilesional retinotopic space contributed significantly to the observed benefits of leftward gaze direction.

Finally, the benefits of encoding auditory location in ipsilesional retinotopic space might also be modulated by eye-in-orbit position. This explanation is by no means incompatible with the multimodal facilitation hypothesis proposed by Pavani and colleagues (2005, this issue) and is known to be a key component in the recoding of auditory stimulus information in an eye-centered reference frame (Stricanne et al., 1996; Cohen and Andersen, 2000).

**Rehabilitation Strategies and Conclusions**

Whatever their underlying cause, Pavani and colleagues’ (2005, this issue) findings provide new insights into potential rehabilitation strategies for neglect patients. Perhaps the most obvious benefit may result from lasting cortical plasticity, in which the salience of contralesional auditory stimuli is enhanced. Could long-term participation in a gaze direction paradigm achieve this goal? Might such a regime encourage the learning of gaze direction strategies in patients that countermand the usual rightward attentional bias observed in neglect (Bartolomeo and Chokron, 2002)? Robertson et al. (1995) showed that a rehabilitation program emphasizing visual scanning was effective in reducing the symptoms of visuospatial neglect 5-12 days after training ceased. If Pavani and colleagues’ results reflect the benefits of multimodal coordinate transformations then successful rehabilitation will require strategies that target intact reference frames. Consider, for instance, a patient who experiences neglect primarily in head-centered space but to a lesser extent in eye-centered space. This patient might be expected to show long-term improvements in auditory perception following a treatment regime that encourages the recoding of contralesional auditory locations in eye-centered coordinates. A similar mechanism may underlie the benefits of caloric stimulation in neglect, during which iced water is injected in the contralesional ear (Rubens, 1985). As pointed out by Driver and Vuilleumier (2001), caloric stimulation may activate visuo-vestibular neurons in the PPC, encouraging the recoding of visual stimuli in a world-centered reference frame (Snyder et al., 1998).
In summary, the findings of Pavani and colleagues (2005, this issue) are consistent with the emerging view that unilateral neglect is singularly neither a disorder of spatial attention nor spatial representation, but rather one of coordinate transformation resulting from depletion of neurons in the temporal and parietal cortex (Pouget and Driver, 2000). Further studies extending Pavani and colleagues’ findings in patients, and in normal populations using TMS, will provide further insights into the mechanisms underlying coordinate transformations in humans. To determine the usefulness of multimodal strategies as rehabilitation tools, comprehensive measurements of neglect are required within multiple reference frames. Treatments that encourage the recoding of spatial information in relatively preserved frames of reference may provide a promising avenue for managing unilateral neglect.

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References


