Much to our regret we recognise, that our recently published data and considerations based on these facts were substantially misunderstood in the present comment of John Marshall and colleagues (this volume). First, we must reject the assumption, that our work “confirms that unilateral visuo-spatial neglect can result from lesions of right temporal cortex and from lesion of right parietal cortex”. In fact, we published an analysis of the cortical anatomy of 25 patients with spatial neglect demonstrating a significant area of lesion overlap, that was located in the middle part of the superior temporal gyrus and not in the parietal cortex or the temporo-parieto-occipital (TPO) junction area (Karnath et al., 2001). This outcome is fundamentally different from the hitherto known findings of previous studies on the same topic, recently reviewed by Vallar (2001).

Second, and even more important, we never intended to distinguish between several subgroups of neglect patients. A differentiation between “pure spatial neglect” on the one hand and “impure spatial neglect” on the other hand representing two different types of neglect, as put forward here by John Marshall and his colleagues (this volume), is misleading and does not exist in our conclusions and considerations. The term “pure” spatial neglect, that we used in our recent article (Karnath et al., 2001), simply referred to the fact, that patients with neglect included in that study did not suffer from hemianopia, a neurological symptom that is frequently observed in association with hemispatial neglect. Our work was motivated by the fact, that preceding studies on the same topic included a considerable proportion of neglect patients with additional hemianopia. Although hemianopia and hemispatial neglect frequently co-occur, hemianopia obviously represents an unique disorder and cannot be regarded as an integral part of the neglect syndrome.

Following an infarct in the vascular territory of the middle cerebral artery (MCA), hemianopia results from damage to the optic radiation. Including a considerable number of neglect patients with additional hemianopia in anatomical studies thus will bias the region of overlap to those areas associated with the occurrence of hemianopia, i.e. the subcortical and cortical neural tissue supplied by the posterior branch territory of the MCA. (The cortical tissue that mortifies with such lesions is located in the inferior parietal lobe and the TPO junction area as can be taken, for example, from our recent study that illustrated the lesion overlap in four patients with “pure” hemianopia, i.e. who had only hemianopia after a right MCA infarct without additional spatial neglect.)

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To make this methodological problem more lucid, let us assume, that we are interested to identify the typical site of lesion location in patients with Wernicke’s aphasia after left hemisphere brain damage. If we would include not only patients with “pure” Wernicke’s aphasia but also a significant proportion of patients with Wernicke’s aphasia who have hemianopia in addition (due to the lesion in the vascular territory of the posterior branch territory of the left MCA), we reasonably expect, that this analysis will not show the same outcome compared to an analysis of patients with Wernicke’s aphasia only.

By eliminating an important confounding variable in previous anatomical analyses, we found a region of cortical lesion overlap (Karnath et al., 2001), that was fundamentally different from those cortical lesion sites originally described by Heilman et al. (1983) and later also by Vallar and Perani (1986). Thus, we strongly suggest, that future work on the anatomy of hemispatial neglect (but, of course, also on other neuropsychological disorders) should take care of the co-occurrence of symptoms other than the symptom of research interest. One way to do this is the exclusion of patients showing the confounding symptom from the experimental and the control groups (cf. Karnath et al., 2001). An alternative strategy is to directly contrast (e.g. by subtraction) the lesion overlap in a sample of patients who show a certain symptom (e.g. spatial neglect) with the lesion overlap of a control sample that is comparable with respect to relevant demographic and clinical variables (such as age, frequency of additional neurological symptoms etc.) but do not show the symptom of research interest.

A recent study combined both these strategies to identify the structures within the basal ganglia and within the thalamus that are typically associated with human spatial neglect (Karnath et al., 2002). The comparison of lesion location in patients with and without neglect was carried out by using a free software package (MRIcro [Rorden and Brett, 2001]) which allows a direct subtraction of lesion overlap of one group of subjects from another group. The crucial difference of lesion overlap between both groups thus can be plotted in only one set of standard slices. A similar technique has been used previously for anatomical comparison between patient groups (e.g., Weiller et al., 1990, 1993; Adolphs et al., 2000). We think that this procedure supplements and may be even more informative than the illustration of lesion location with two separate figures of superimposed plots (one highlighting lesion locus for the patients, who show the symptom of research interest, and the other indicating the regions impaired in the control group).

To conclude, new tools are now available that allow a more precise lesion localization than ever before. The entire lesioned area of each individual subject can be used for a high resolution analysis in Talairach space (Talairach and Tournoux, 1988). Automatic three-dimensional rendering of the lesion data derived from the transversal MRI or CT slices became possible without the uncertainty brought in by the paper-and-pencil procedures used in previous anatomical studies (e.g. Heilman et al., 1983; Vallar and Perani, 1986; Perenin, 1997). Such lesion analyses in 3D Talairach space thus have a strong degree of correspondence to the published literature from functional imaging studies. Precise comparisons between lesioned areas in patients and activated areas in
healthy subjects become possible. Neuroscientists should take advantage of these new potentialities to gain new insights into the functional anatomy of the human brain.

REFERENCES


