First publ. in: Neuroscience Letters 201 (1995), pp. 262-264

Cortical reorganization in human amputees and mislocalization of painful stimuli to the phantom limb

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Abstract

In human arm amputees, a significant relationship was found between the amount of reorganization in the primary somato-sensory cortex, and the amount of body surface from which painful stimuli evoked sensations that were perceived to be emanating from the now missing extremity, i.e. the phantom limb. This mislocalization could be evoked almost equally from stimulation of either side of the body. Based on these findings obtained by magnetic source imaging and psychophysical testing in eight amputees, it is concluded that the extent of the generally known cortical reorganization contralateral to the amputation is an indicator of more widespread plastic changes in the brain involving bilateral pathways.

Keywords: Amputation; Cortex; Mislocalization; Phantom limb

Cortical reorganization has received considerable attention because of its potential relevance to functional outcome following central nervous system injury [1–4]. Research with monkeys showed that, following removal of input from a portion of the primary somatosensory cortex by either amputation [1] or dorsal rhizotomy [2], there is a topographically systematic 'invasion' of the affected cortical zone by neighbouring cortical areas whose innervation has remained intact. In addition, it was observed that after arm amputation in humans, tactile stimulation of either the trunk or the face ipsilateral to the amputation stump can lead to a point-to-point somatotopic referral of stimuli applied to specific locations on the skin to specific locations on the phantom limb. This phenomenon, termed 'remapping', has been claimed to be the perceptual correlate of cortical reorganization reported in the primate studies [5]. However, in contrast we had previously demonstrated cortical reorganization with magnetic source imaging that was independent of somatotopic remapping after amputation [7].

In the present study, we systematically investigated the relation of the amount of cortical reorganization and the amount, rather than the pattern, of mislocalization to the phantom limb. We had earlier found a nearly perfect correlation between cortical reorganization and phantom limb pain, indicating the importance of the nociceptive system for cortical reorganization [6]. In this study, we employed painful stimulation (pinprick) as well as stimulation in three other somesthetic modalities (touch by a cotton applicator, vibration by a tuning fork and heat by a 40°C thermode), in order to compare the capacity of the different modalities to produce mislocalization to the phantom limb. Since pinprick and thermode application also activate touch receptors, sites where the pin or thermode evoked the same referred sensation as the cotton applicator were not considered pain or heat points, respectively. Each of the four different types of stimuli was applied to 30 standard sites bilaterally on the body (ten on

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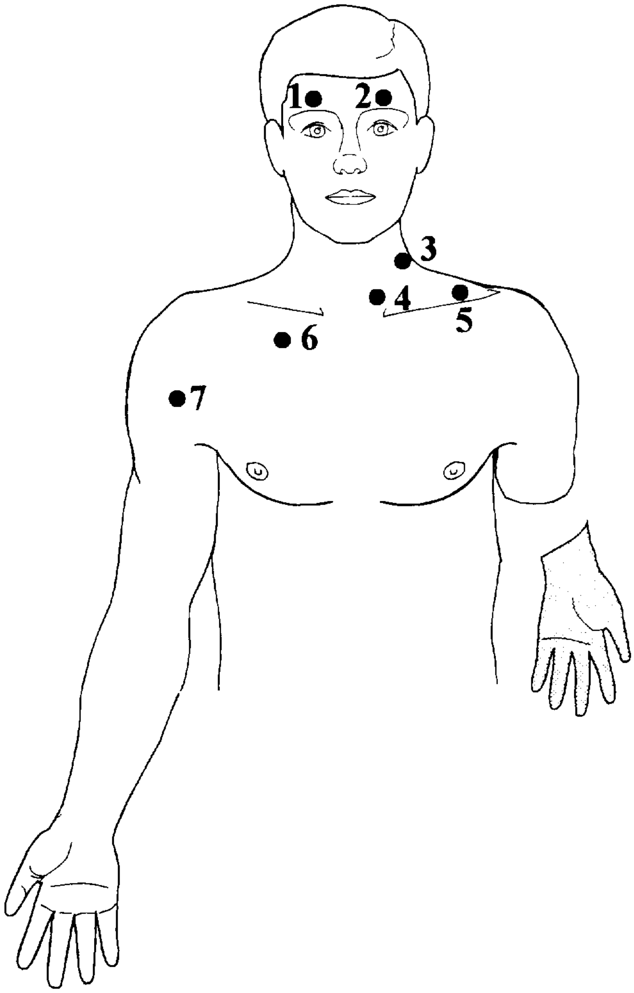

Fig. 1. Illustration of the localization in one amputee of sites from which painful stimuli elicited sensations which were perceived to be emanating from the phantom hand. An intense sensation in the whole phantom was evoked from all sites.

the face, ten on the ventral trunk and ten on the back and legs).

The subjects were eight human upper extremity amputees with phantom sensation. All but one, who was operated for an osteosarcoma, had been amputated because of accidents. The mean age of was 54 years (range 24–70 years) and the mean interval since amputation 22 years. Cortical reorganization was assessed with magnetic source imaging by a method described previously [6,7]. Briefly, it was based on the source localization of the cortical representation of the lip on the amputated side. The Euclidian distance (in cm) was calculated between the localization that would have resulted from simply mirroring the cortical representation of the lip on the intact side and the actual representation of the lip on the amputated side. The latter source was generally found relatively more cranial and medial, i.e. in a localization corresponding to the former hand representation.

Mislocalization was elicited by tactile, vibratory, thermal and painful stimulation. At some stimulation sites it

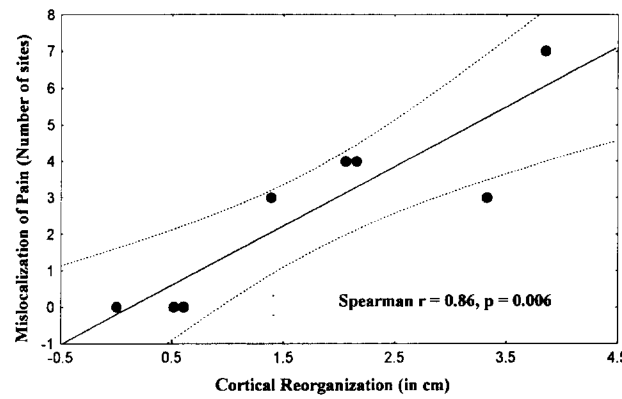

Fig. 2. Amount of cortical reorganization (in cm) for each subject plotted against the total number of sites (ipsi- and contralateral to the amputation) from which painful stimuli evoked sensations mislocalized to the phantom limb. The amount of cortical reorganization is based on the shift of the lip representation towards the former hand representation (for details see text and [7]).

was evoked by only one modality, at other sites by several. The referral pattern was almost never somatotopic. The sites were distributed across subjects at various different locations on the face and ventral trunk. Of particular interest was the fact that mislocalization in all modalities could be elicited not only from sites ipsilateral to the amputation, but contralateral to it as well (approximately 40%). An example is given in Fig. 1. Moreover, for painful stimulation, the number of body locations from which mislocalization to the phantom limb could be elicited was strongly correlated (Spearman $r = 0.86$, $P = 0.006$) with the amount of cortical reorganization. Fig. 2 presents a scatter plot of the data. This relationship was not significant for non-painful stimuli.

To date, in most experiments concerning cortical reorganization after amputation or dorsal rhizotomy [1,2,5,6, 8], only unilateral effects in the primary somatosensory cortex contralateral to the lesion were studied. The bilaterality of the sites eliciting mislocalization in this study, however, cannot be explained solely on the basis of the generally known invasion of cortical projections from neighbouring areas into the 'amputation' zone. The perceptual results here suggest instead that the underlying morphological changes go beyond the contralateral primary somatosensory cortex, and probably involve bilateral cerebral structures. The cortical reorganization that was observed here with magnetic source imaging, and was found to be strongly correlated with the number of bilateral sites eliciting mislocalization, seems to be an indicator of these more general plastic changes.

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