

Commentary

'Pseudo-neglect' in CRPS is closer to 'anti-neglect' than to classical hemi-neglect?

Attention can exert a powerful effect on the perception of pain sensations, so much so that distraction can have an analgesic effect on acute pain equal to that of opiates [21]. Spatial attention can modulate heat pain detection and discrimination, as demonstrated by studies in which a pain stimulus is presented following a cue, which is located either on the same side as the stimulus or on the opposite side. The cue on the opposite side leads to increased error rates and response latencies for heat pain stimuli [2,8]. In turn, a lateralized visual discrimination task is performed more rapidly when it is preceded by a painful stimulus on the same side as the visual stimulus than on the opposite side. Similarly, eye orientation to the side of the painful stimulus leads to higher pain ratings [18]. These results suggest that visual stimuli and painful stimuli can interact by shifting spatial attention to one or the other side of the body.

In this issue of PAIN, Reinersmann et al. report that the shift of the visual subjective body midline (vSM) towards the left side was greater in patients with complex regional pain syndrome (CRPS) than in patients with other types of chronic pain, or in healthy controls [20]. This leftward bias is referred to as 'pseudo-neglect' and is interpreted to be the result of right hemispheric dominance in spatial perception, including perceptual representation of one's own body (body schema). This observation may be related to the finding that vSM deviates to the affected side in patients with CRPS and that this effect can be reversed by nerve blockades with local anesthetic or ischemia [23]. Other body schema abnormalities in patients with CRPS include the finding that such patients take longer to recognize the laterality of a hand in a picture when the pictured hand corresponds to the laterality of the affected hand [17].

This study adds interesting detail to the concept of CRPS, which has evolved from a "sympathetically-maintained pain" to a syndrome of sensory-motor-autonomic dysfunctions [1]. Reinersmann et al. demonstrated that the shift in visual subjective midline was specific to CRPS vs. other upper limb pain syndromes. However, the relationship of the term 'pseudo-neglect' as used in this paper to the classical hemi-neglect is uncertain.

Hemi-neglect is failure of a subject 'to report, respond, or orient to meaningful stimuli contralateral to the brain lesion' [10]. Visual spatial hemi-neglect is most commonly observed after lesions of the right parietal cortex, but can also occur after right sided lesions of the prefrontal cortex, the superior temporal gyrus, the frontal operculum, or the thalamus [12,25]. The phenomenon of extinction is considered to be a subtle form of neglect [10,11], which is measured by a dual simultaneous stimulation (DSS) protocol. Extinction is the failure to report stimuli on the affected (left) side of the body when an identical simultaneous stimulus occurs on the

opposite (right) side, but not when the stimulus is presented on the affected side alone (DSS protocol) [10].

There is now evidence for thermal pain extinction following right hemisphere strokes. In some subjects with visual spatial hemi-neglect, thermal stimuli presented bilaterally were extinguished on the left side when presented in a DSS protocol [15]. In subjects with visual spatial hemi-neglect and without thermal pain extinction, the sensation of the thermal pain stimulus on the affected (left) side was not extinguished but was often mislocalized to the unaffected (right) side, and the submodality of the stimulus (cold or hot) was often misidentified. The proportion of subjects with thermal pain extinction, mislocalization and misidentification was significantly higher in subjects with visual spatial neglect than in healthy controls, and in controls with stroke but without hemi-neglect.

These findings suggest that hemi-neglect due to loss of function in the right hemisphere influences spatial discrimination and intensity of perception of painful stimuli. In contrast, the vSM shift ('pseudo-neglect') is suggested to be due to increased activity in the right hemisphere. The bloodflow response to painful stimuli on either side of the body is lateralized to the right side of many structures in the brain, including the inferior parietal cortex and dorsolateral prefrontal cortex [4]. Ipsilateral intensity-dependent activation by painful stimuli has also been found and can also be consistent with pain-related neglect [5,19].

Ipsilateral projections of pain pathways have also been demonstrated for monkey thalamic [3,26], and parietal cortical neurons by bilateral receptive fields to painful stimuli [7,13]. Some of these neurons are multimodal and respond to the presentation of a nociceptive stimulus when it is located in extra-personal space close to the nociceptive receptive field of the neuron [6]. It is unclear to what extent these responses to acute nociception-related stimuli are relevant to the present study of chronic pain, but peripheral pain generators in CRPS may lead to the activation of neurons in the right parietal lobe [22].

Performance of a task requiring identification of the mid-sagittal plane leads to activation of the posterior parietal cortex bilaterally, which is greater in the right hemisphere [9,24]. Thus, one may speculate that pain-related activation of the right parietal lobe may increase a leftward bias of spatial attention. This seems to be contrary to a study in which stimulation of right parietal cortex was carried out in patients with implanted grids for seizure monitoring. This stimulation produced transient hemi-neglect of the left side, and not the leftward bias which might be predicted by the phenomenon of 'pseudo-neglect' [14]. It may be that stimulation facilitates simple behaviors but disrupts complex behaviors such as spatial attention [16].

In summary, the data presented by Reinersmann and colleagues add interesting detail to our understanding of the changes in body representation in the brain of patients with CRPS. The term 'pseudo-neglect', however, may be slightly misleading since it suggests a similarity to classical hemi-neglect, a perspective that we do not believe is supported by the currently available data. We suggest using the framework of spatial attention instead, which will place these phenomena in the context of the cognitive-evaluative component of pain perception.

Conflict of interest statement

None of the authors has a conflict of interest with respect to this commentary.

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