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Are movement disturbances in complex regional pain syndrome intentional?

In this issue of European Journal of Pain you will find a paper by Bank and colleagues (Bank *et al.*, 2015) entitled *Intended and unintended (sensori-)motor coupling between the affected and unaffected upper limb in complex regional pain syndrome* (CRPS). Bank et al. measured intentional and unintentional coupling of limb movements in 20 patients with upper-limb CRPS and 40 healthy controls in an attempt to differentiate impairments in voluntary and automatic sensorimotor processes in CRPS patients. The participants performed wrist flexion-extension movements in tasks known to engage intentional inter-limb coupling: active bimanual movements, requiring in-phase or anti-phase patterns with the two hands; kinesthetic tracking, requiring active unimanual movements to consciously track automated (passive) movements of the opposite limb; and unintentional inter-limb coupling (active unimanual movements timed to a metronome while ignoring automated, passive movements of the opposite limb). Two results stand out: (1) performance was impaired in CRPS patients in tasks engaging intentional but not unintentional coupling of limb movements; (2) variability in performance of all movement tasks was significantly greater in CRPS patients than in healthy controls. Interestingly, motor impairment and variability were greatest when the affected limb was the voluntarily active limb.

Many forms of chronic pain are characterised by sensitization to nociceptive input driven, in part, by active facilitation of nociceptive signals and failure of inhibitory pain controls. In CRPS, this appears to be accompanied by bilateral disinhibition of the primary motor cortex (Di Pietro *et al.*, 2013). Well-documented motor disturbances in CRPS include tremor, muscular weakness, joint stiffness and dystonia. It is worth noting here that in the study of Bank et al. (2015), severely dystonic patients with CRPS were excluded and, consequently, the generalizability of the current findings to these patients is unknown. Even though most patients had only mild or moderate CRPS, generating repetitive wrist movements during the tasks was so aversive that one patient withdrew and most others reported intense pain. Furthermore, severe pain during performance of the tasks was associated with greater variability in movements of the affected limb. While this shows that sensorimotor impairments are directly related to the level of pain, the question remains: what processes mediate sensorimotor disturbances during intentional movements of the painful limb in CRPS?

Under normal conditions, acute noxious stimuli evoke reflexive withdrawal responses, a protective reduction in movements of painful body parts and compensatory adjustments by other body parts (Bank *et al.*, 2013). However, more complex psychobiological processes may underlie movement disturbances in CRPS. While observations of psychological symptoms, such as anxiety and depression, and ‘negative’ results from pharmacological studies examining the effect of alpha-1 adrenoceptor agonists and antagonists led to claims of a psychogenic cause of CRPS (Verdugo & Ochoa, 1994; Ochoa, 1999), more recent research provides strong evidence of a neurological contribution to motor disturbances in these patients (Di Pietro *et al.*, 2013). Bank et al. (2015) propose that impairment in intentional but not unintentional inter-limb coupling does not necessarily point to a psychogenic or factitious cause of movement disturbances but, rather, suggests that altered function in higher-order motor areas of the brain plays a role. Psychogenic and neurological causes of movement disturbances are not necessarily independent as psychogenic factors, over time, may alter function in motor areas of the brain. Given the known relationships between chronic pain and anxiety, it seems plausible that injury or pain encourages fear of movement, which results in reduced use of the affected limb and, in turn, alters neurological and motor function. Indeed, in healthy adults, limb disuse has been shown to produce symptoms similar to those of CRPS, such as pain on movement, cold hyperalgesia, mechanical hyperalgesia to skinfold pressure, decreases in tactile acuity, shrinkage and reduced activation of involved areas in the primary somatosensory cortex, and disinhibition of the primary motor cortex (Zanette *et al.*, 2004; Terkelsen *et al.*, 2008; Lissek *et al.*, 2009). Therefore, restrictive movement of the affected limb in CRPS could lead to altered cortical function, which then increases the variability of movements both during intentional and unintentional coupling of limb movements. Finally, the association between limb disuse and cortical change might be influenced by the neurological and psychological effects of chronic pain acting somewhat in opposition: disinhibition in cortical motor areas prompts a hyperexcitable primary motor cortex to facilitate movement of the limb away from noxious stimuli whereas anxiety and fear promote protective restriction of movements that do, or potentially could, induce pain. The positive correlations between movement variability and pain during tasks involving active movements of the affected limb suggest that these opposing neurological and psychological influences become stronger as pain increases.

It is worth commenting on the therapeutic implications of inter-limb coupling training. As suggested by Bank et al., training protocols that require the affected limb to synchronise movements with the unaffected limb (either active or passive) might be effective in improving function of the affected limb. Given the similarities in motor disturbances in CRPS and following stroke, it is not surprising that interventions that aim to alter brain function to improve motor function following stroke, such as motor imagery and mirror therapy, have been used in CRPS. Indeed, graded motor imagery, which involves limb laterality training, motor imagery, and mirror therapy in sequence, has been shown to reduce pain and improve motor function (Moseley, 2006). It seems plausible that adding inter-limb coupling training to the graded motor imagery intervention could initiate training-induced changes in the motor cortex, which might act to normalise the hyperexcitable motor cortex and, as a result, lead to greater improvements in motor function in CRPS. Similarly, incorporation of cognitive-behavioural strategies that target movement-related fear could augment treatment outcomes by addressing the volitional component of movement disturbances in CRPS.

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