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Topical review

Neglect-like symptoms in complex regional pain syndrome: Learned nonuse by another name?

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1. Introduction

The use of the term 'neglect-like' to characterise symptoms displayed by patients with complex regional pain syndrome (CRPS) [15] has proved to be provocative. It has provided the stimulus for an ever-increasing number of studies exploring spatial perception in affected patients, with calls for further related studies [20]. Although this work would undoubtedly be of interest, there are perhaps 2 important factors to consider if such studies are undertaken. Firstly, studies that have relied on standard *clinical* tests typically used to identify spatial neglect after stroke have not confirmed the presence of a related deficit in CRPS [13,18,29]. Some deviations from normal have emerged using *laboratory-based* measures [25,33], but it is important to acknowledge that the extent of any deficit in spatial perception after CRPS is not comparable with that seen commonly after stroke. Second, it is worth remembering that the clinical observations that first gave rise to the term 'neglect-like' with regard to CRPS were dominated by observations relating to *movement* rather than to *perceptual* difficulties [15]. It is noteworthy that since these initial observations were made, there has been relatively little attention paid in experimental studies to these interesting motor aspects of behaviour. In contrast to the recent review in *Pain* [20], here we consider the primary observation of 'motor underuse' in CRPS, looking at comparisons with 'motor neglect' [19] and more generally with movement difficulties in patients following stroke.

2. Basis for 'neglect-like symptoms' in patients with CRPS

When describing the apparent 'neglect-like' symptoms in CRPS, Galer et al. [15], p. 390 included a clear qualifying statement: 'We do not suggest that the symptoms and signs seen in our patients are analogous to the classic hemispatial neglect that develops following stroke'. Nevertheless, the term has endured, along with a succession of studies and related correspondence drawing attention to similarities between these 'neglect-like symptoms' and neglect after stroke. Analysis of the work of Galer et al. [15] on 'neglect-like symptoms' reveals abnormalities to be largely confined to difficulties with movement. Of the 11 cases presented, a common theme was a sense of disconnection from the affected limb and a need to focus specifically on the limb to move it. When movement did occur, it was slow to be initiated (hypokinetic), slow in execution (bradykinetic) and lacked normal amplitude (hypometric). However, when patients were strongly encouraged to move, there was a dramatic improvement affecting all of the above motor parameters. There was no sense that patients lacked awareness of these difficulties; rather, the patients were particularly mindful of the problems and eloquent in describing them. In cases in which intervention led to pain being alleviated, motor difficulties remained. Subsequent questionnaire studies exploring patients' perceptions of neglect-like symptoms confirmed their presence (at least to some extent) in the vast majority of respondents with CRPS [14,16]. Similar features were also evident in patients with limb pain but who were not classified as having CRPS, although these were not as common or as severe.

Despite occasional suggestions of neglect-like symptoms affecting sensory perception in patients with CRPS [25,33] the balance of data appear to point towards a tendency for neglect-like symptoms to mainly affect movement (Table 1). This is in contrast to the literature on neglect after stroke, which tends to focus on implications for visual perception.

3. CRPS and motor neglect

A lack of spontaneous movement in the affected limb of patients with CRPS, and the contrasting dramatic improvement in motor performance when they are strongly encouraged to move [15], are evocative of descriptions of motor neglect after stroke [19]. Motor neglect may be defined as "an underutilisation of one side, without defects of strength, reflexes or sensibility" [19], p. 152. To highlight the independent problem of motor neglect, published accounts normally select cases in which visual or other sensory aspects of neglect, as well as hemiparesis, are either minimal or absent. However, it is accepted that, in many cases, these occur concurrently [6,19,28]. Recognition of this has led to a more recent definition: "the underuse or underutilization of a contralesional limb that cannot be explained by primary sensori-motor deficits" [27], p. 864.

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Table 1
Studies exploring 'neglect-like' symptoms in patients with CRPS.

References	CRPS Sample	Assessment	Results	Comments
[15]	11	Case Reports	Observations primarily of 'motor' aspects of neglect, but also other 'neglect' of affected side	Authors do not claim that 'neglect-like symptoms' are analogous to neglect
[16]	242	Survey of CRPS patients	84% confirmed at least one (motor) 'neglect-like' symptom	Patient recognition of difficulties in stark contrast to neglect following brain injury
[30]	24	Sensory impairments and motor disturbance	50% showed sensory impairment extending beyond the affected limb (quadrant or hemi-sensory); more frequent for left-sided symptoms (77%). These signs related to greater motor disturbance	Only study to show a strong asymmetry for symptoms based on side affected
[13]	114	Neurological examination, questioned regarding feelings of foreignness of limb; subgroups tested on line bisection and sensory extinction	54% expressed feelings of foreignness; no indication of sensory neglect on testing	No measurement of motor components of neglect
[14]	123	Questionnaire based on previous version [16]	90% confirmed at least one (motor) 'neglect-like' symptom	Non-CRPS pain patients also reported 'neglect-like' symptoms (80%) but CRPS more severe
[33]	36	Visual subjective body midline	Deviation towards affected side when tested in dark conditions	Intervention that reduced pain 'normalised' performance in a tested subgroup; performance deteriorated as pain returned
[25]	10	Tactile Temporal Order Judgment task	Impaired limb had to be stimulated at least 25ms before the unimpaired limb for stimuli to be considered simultaneous (indicative of extinction)	Further analysis exploring the effect of 'crossed hands' showed that prioritisation of stimuli was 'space-based' rather than 'arm-based'
[18]	20	Questionnaire based on previous version [14]; Battery of neglect tasks exploring visuo-spatial functioning	No evidence of sensory neglect on battery of tasks	Evidence of 'neglect-like' symptoms from questionnaire but indistinguishable from 'non-CRPS' pain controls
[29]	24	Visual subjective body midline and line bisection	No neglect on line bisection. Visual subjective body midline deviated towards left side (regardless of affected side)	CRPS patients had a greater motor impairment than the pain control group despite comparable pain scores

A clinical diagnosis, made on the basis of a mismatch between the spontaneous movement observed in a patient's affected limb and that when they are strongly encouraged to move during examination, may be prone to inaccuracy. In the neurological literature, this encouragement has taken the form of patients being "actively encouraged" [22], p. 69, being "asked with insistence" [9], p. 147 and being "strongly prodded" (*sic*) [5], p. 1758. Although these may seem unsatisfactory assessment methods, they compare with accounts from the CRPS literature of patients being "verbally exhorted" [15], p. 388 to move, and being "told to look at the hand and repeatedly told to move" [15], p. 389.

As the presence of sensory problems or weakness (ie, hemiparesis) also makes objective measurement of motor neglect problematic, investigators have tested for the related problem of motor extinction. The approach here is to compare movement of the affected limb when moving in isolation (ie, unilaterally) with the same movement when conducted simultaneously with the unaffected side (ie, bilaterally). The selective deficit that becomes apparent in the affected limb when the patient moves bilaterally is indicative of motor extinction and has been measured objectively in a number of studies exploring motor neglect [10,17,24,28,38]. The deficit is analogous to the more familiar problem of sensory or perceptual extinction whereby a patient becomes unaware of a stimulus on the side of space opposite a brain lesion only when it is presented simultaneously with another identical stimulus on the same side of space as the brain lesion [11]. Anecdotally, it has been observed that patients with CRPS can display signs of motor extinction also [23]. When asked to make bilateral movements during visual feedback therapy (while the affected limb is obscured by a mirror), McCabe states "some. . .patients are convinced that they are performing these movements although the hidden limb remains static or only moves for a brief period before stopping" [23], p. 172–173.

Despite these similarities, there are also key differences. Motor neglect is the consequence of a brain lesion, typically a stroke on the side opposite the deficit [27]. Motor neglect becomes apparent immediately after stroke, and motor performance often improves over the first few days and weeks [39]. The profile for patients with CRPS is very different. They rarely have a brain lesion and, where they do, this is not considered to be the cause of their neglect-like symptoms. Also, the symptoms become apparent much later, and the length of time since injury is often suggested to be significant in the development of problems [13]. Observation of patients' behaviour in relation to their limb also differs. Patients with motor neglect tend to take poor care of their limb, their apparent indifference to it suggested by their allowing it to assume uncomfortable postures [28] with no automatic 'placing' [19]. In contrast, patients with CRPS appear highly aware of their limb, 'protecting' it by holding it in a flexed posture close to the chest [15]. Lack of awareness of their deficit is often cited as a central problem in stroke rehabilitation, as patients may not effectively engage with treatment which often demands insight into their difficulties [3]; for severe cases, such 'anosognosia' may even result in explicit denial of the problem [4,39]. Clearly, pain is considered critical in the development of neglect-like symptoms in patients with CRPS, but is rarely a consideration in patients with motor neglect. Also, in patients with motor neglect, the 'underuse' tends to apply to one side of the whole body, but is normally limb specific in patients with CRPS.

4. Underuse of a limb in CRPS as a learned behaviour

We would agree with others that 'neglect' is not the optimal term to characterise the underuse of an affected limb demonstrated by many patients with CRPS [13,21]. However, it seems likely that patients with CRPS share mechanistic similarities with a problem described in the stroke rehabilitation literature as 'learned nonuse' [36]. Learned nonuse "is characterised by a motor deficit that is greater than appears to be warranted by the organic status of the individual" [34], p. 291. Furthermore, Taub et al. [36] consider "an index of learned nonuse would be the difference between a measure of what a person can do in the laboratory when

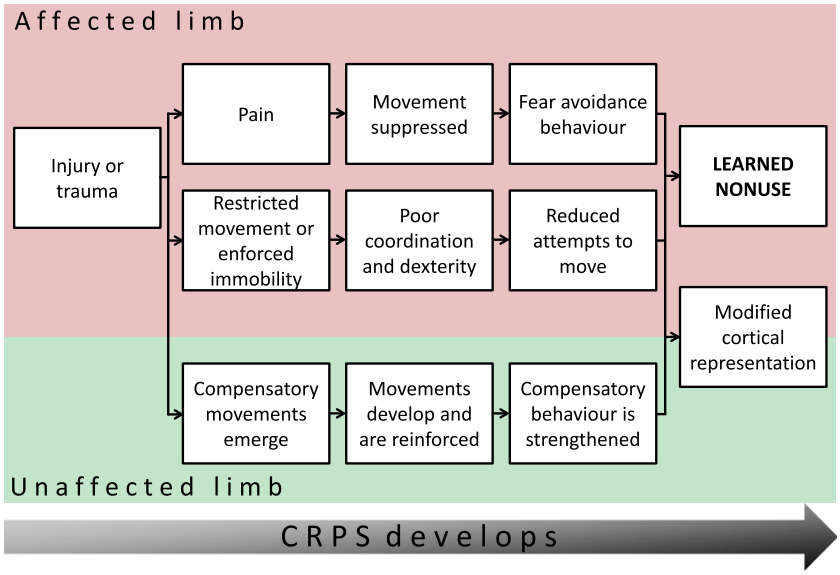

Fig. 1. Proposed model for the development of learned nonuse in patients with complex regional pain syndrome (CRPS). Adapted from previous models proposed for the development of learned nonuse in patients following brain injury [34–36].

requested to do the best he can and a measure of what a person actually does do spontaneously" [p. 244]. Given this characterisation, it is difficult to differentiate the resulting behaviour from that of motor neglect (see earlier here).

The pathway to developing learned nonuse after stroke is based on *operant conditioning* and has been clearly defined by Taub et al. [34–36]. A patient has a stroke leading to a dramatic loss of movement and generalised depression of that patient's central nervous system. Subsequent attempts to move either are unsuccessful or require much greater effort; and compensatory strategies develop (eg, use of the unaffected limb). This failure of movement leads to a decline in attempts to move, and this pattern of behaviour is strengthened and reinforced alongside the use of compensatory activity. As learned nonuse subsequently becomes established with a corresponding shrinkage in the cortical representation of the affected limb, any returning potential to move is not exploited, as no attempt is now made. Therefore, at least some of the motor deficit that we see in patients after stroke is considered to result from this learned suppression of movement [32,36].

We suggest that the underuse of an affected limb in CRPS arises from a very similar mechanism. Indeed, the often enforced immobility as a result of the predisposing trauma (eg, fracture), the added presence of pain and the movement-related phenomenon of fear avoidance [31] may strengthen the pathway to nonuse (Fig. 1).

5. Implications for rehabilitation

After stroke, recognition of learned nonuse has led to the development of 'Constraint-Induced Movement Therapy' (CIMT) and variants of this approach [26,40]. The basic idea with CIMT is to constrain movement of the unaffected limb (using a mitt or splint) and 'force' use in the affected limb by engaging patients in a course of relatively intensive progressive exercise (often termed 'shaping'). Interestingly, patients with excessive pain in a hemiparetic limb are routinely excluded from CIMT studies, presumably due to the perceived negative impact that this may have on their participation [2,26,40]. However, for those patients who do participate in CIMT and who have some degree of pain, there is evidence that the functional gains made occur without any increase in their pain symptoms [37]. The application of CIMT in patients with CRPS may be worth considering. The recent emergence of graded exposure therapy for patients with CRPS draws parallels with the use of CIMT after stroke and has shown encouraging results [8,12]. The approach draws primarily on addressing fear avoidance and perceived harmfulness [7], but the described interventions may also address learned nonuse. Although there is no physical constraint of the unaffected limb in exposure therapy, interventions referring to the encouragement of patients to "engage in activities, movements and situations they have been avoiding for a long time" [8], p. 266 and the use of active functional exercise to gain "a rapid and functional use of the affected extremity as quickly as possible" [12], p. 1061 resonate with descriptions of CIMT. The emphasis on education and reassurance in exposure therapy is clearly considered critical. Whether CIMT for stroke would benefit from developing these areas would be of interest, as would the impact of introducing an element of 'constraint' to exposure therapy.

6. Future directions

As others have noted, clearly there is value in exploring deficits that exist across different conditions (eg, CRPS and stroke), both to achieve a clearer understanding of their underlying mechanisms and to share potentially fruitful interventions [1]. Here, we have argued that mechanisms underpinning 'motor neglect' and 'learned nonuse' are distinct, although the behaviours clearly share numerous characteristics. We suggest that underuse of an affected limb in patients with CRPS corresponds with the latter, and could benefit from further investigation and explicit comparison with underuse that follows stroke.

Conflict of interest statement

The authors report no conflict of interest.

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