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Clinical Note

Dysynchiria is not a common feature of neuropathic pain

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Abstract

Patients with chronic neuropathic pain (non-CRPS) and brush-evoked allodynia watched a reflected image of their corresponding but opposite skin region being brushed in a mirror. Unlike complex regional pain syndrome Type 1, this process did not evoke any sensation at the affected area ('dysynchiria'). We conclude that central nociceptive sensitisation alone is not sufficient to cause dysynchiria in neuropathic pain. The results imply a difference in cortical pain processing between complex regional pain syndrome and other chronic neuropathic pain.

Keywords: Dysynchiria; CRPS; Neuropathic pain

1. Introduction

Neuropathic pain shows various symptoms including brush-evoked allodynia, which means that normally non-painful touch is experienced as painful. In Complex Regional Pain Syndrome type 1 (CRPS), brush-evoked allodynia is common (Birklein, 2005), as is a related phenomenon, called 'dysynchiria', whereby stimulation of the intact limb elicits pain (brush-evoked allodynia) or paresthesia at the corresponding site on the affected limb, if the patient watches the stimulation in a mirror (Acerra and Moseley, 2005). The term 'dysynchiria' derives from 'synchiria', which describes a phenomenon, first reported in amputees (Jones, 1907), whereby the patient watches the reflected image of the intact limb being stimulated and experiences the sensation at corresponding sites on both limbs. The mechanisms underpinning dysynchiria and synchiria are not known. However, that visual input of the skin area being touched activates the cortical pain matrix, implies (i) that bimodal visual-tactile neurons are involved (Spence, 2002), and (ii) that the central nervous system networks associated with pain are activated more easily than normal. This is important because it raises the possibility that dysynchiria may offer a clinical method to detect such facilitation of pain networks. However, because CRPS is associated with multiple changes in central representations (Janig and Baron, 2003), it is important to demonstrate dysynchiria in a population that is characterised by central sensitisation but not by the other multiple representations. This study investigated whether dysynchiria was present in 12 patients with chronic neuropathic pain and associated brush-evoked allodynia.

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Table 1
Subject characteristics

Subject: sex/age	Anatomic location of allodynia	Diagnosis	Sensory findings	Duration of symptoms (year)	Allodynia derived pain on VAS
M/66	2nd and 3rd digit of left hand	Radiculopathy C7	AD, HA, SP	18	4
F/82	Th 1–4 ventral	Postherpetic neuralgia	AD, HA, SP	3	3.5
M/72	C6 left hand	Radiculopathy–myelopathy after cervical spinal stenosis	AD, HA, PT, SP	1	5
F/63	Left hand	Arm plexopathy after tumor surgery	AD, SP	12	3
F/86	Th 10–12 right and ventral	Postherpetic neuralgia	AD, HA, SP, PT	4	7.5
M/61	Right and ventral thoracic pain	Neuropathy of intercostals nerves after lobectomy	AD, SP, PT	3	4
M/40	Left knee	Posttraumatic neuralgia of the infrapatellar nerve	AD, SP	5	7.5
F/26	Ventral and lateral side of the left thigh	Pelvic plexopathy with affection of N. cutaneus lateralis	AD, SP	2	7.5
M/27	C7 right hand	Traumatic lesion of arm plexus	AD, HA, SP	1	7
F/42	Ulnar side of the left forearm	Postraumaic neurologia of the ulnar nerve	AD, SP, PT	4	5
F/44	Left hand (pronounced C7)	Syringomyelia C5–Th1	AD, SP, HT	33	10
M/31	C8 right hand	Syringomyelia C7–C8	AD, SP	5	3

The table shows the clinical characteristics of our patients. The location, diagnosis and rating of brush-evoked allodynia (on an visual analogue scale, VAS) as well as other signs of pain are presented in detail.
AD, allodynia; HA, hyperalgesia; PT, paraesthesia; SP, spontaneous pain.

2. Patients and methods

Our study was approved by the local ethics committee. In an ongoing study 121 patients with CPRS 1 were tested and 71 of them showed the phenomenon of dysynchiria (Moseley, 2005, unpublished data). In order to uphold the hypothesis that dysynchiria does not occur in our chosen population, with an alpha level of 5%, 80% power and no dropouts, we would require 10 subjects. Therefore, we examined 12 patients (6 women, 6 men, mean age 53 ± 6 (SEM) years). All patients showed signs of central sensitisation, which was confirmed by the presence of brush-evoked allodynia (Woolf et al., 1994) (Table 1). We excluded patients with CRPS, bilateral neuropathic pain and bush-evoked allodynia on a body site, where placing the mirror was not possible. After providing informed consent, the patients described their symptoms. The area of brush-evoked allodynia was mapped performing soft brush stroking (stimulation force 0.8 N; movement speed 2 cm/s) with a one inch wide (2.5 cm) soft water-colour brush and was marked with a waterproof pen. Soft brush stimulation was applied five times in every condition on the respective skin areas. The stimulation force was 0.8 N and the movement speed approximately 2 cm/s and the intervals between each brush stroking were 3 s long. The following three tests were performed in randomised order: (1) the patient watched the allodynic area being brushed; (2) a mirror was placed between the painful area and the corresponding site on the opposite side of the body, so that the allodynic area was hidden from view. This time, the corresponding site on the opposite side of the body was brushed while the patient watched it *in the mirror*, so that it looked like they were watching the allodynic area being brushed; (3) without the mirror in place, the patient watched the corresponding skin on the opposite side being brushed. During all tests, the patients were asked to report the location and type of evoked sensation and to rate the intensity of the sensation on a visual analogue scale (VAS) ranging from 0 to 10 and anchored with 'no pain' on the left and 'most painful imaginable experience' on the right.

3. Results

Statistic analyses were undertaken using SPSS (SPSS 10.1 for Windows, Chicago, IL, USA). All further values are given as mean ± SEM. Statistical significance was considered at $p < 0.05$. During condition one, light brushing evoked pain in all patients (mean VAS rating: 5.6 ± 0.6). When the corresponding site on the opposite side was brushed, it evoked the sensation of light touch at the stimulated site (mean VAS 0 ± 0, Wilcoxon, $p < 0.001$) but no sensation at the allodynic site, regardless of whether the patient was watching the reflected image in the mirror (condition two), or the actual site being touched (condition three) (mean VAS +/+0, Wilcoxon, $p < 0.001$). That is, neither synchiria nor dysynchiria were present. For detailed presentation of results see Table 1.

4. Discussion

In this study, we could not reproduce the phenomenon dysynchiria, which was described in CRPS I (Acerra

and Moseley, 2005), in non-CRPS patients with brush-evoked pain. Therefore, we conclude that dysynchiria is not simply a consequence of sensitisation of central pain networks. This position is based on the presumption that our patient group was likely to have developed sensitisation of nociception (Woolf, 1983; Chen and Huang, 1992; Woolf et al., 1994). In recent years we made progress to understand that neuropathic pain is not defined by its cause but the mechanism underlying it. Divergent mechanisms of allodynia are discussed. One mechanism might be central sensitization maintained by ongoing peripheral nociceptive input (Klede, Handwerker et al., 2003) or in case of neuropathic pain by altered processing of sensory stimuli (Woolf et al., 1994; Maihofner and Handwerker, 2005). Psychogenic factors might also contribute to brush-evoked pain (Verdugo et al., 2004). However, psychogenic involvement has a neuronal correlate either. Because, our patient group had brush-evoked allodynia that was more or less restricted to the skin in the vicinity of the inciting pain focus or nerve lesion, we conclude that they indeed had sensitised central pain networks. That we could not demonstrate dysynchiria here – but have previously in CRPS (Acerra and Moseley, 2005) – implies that it may be consequent to other aspects of CRPS pathophysiology. There is mounting evidence that CRPS is associated with many central and peripheral changes (Janig and Baron, 2003), which offer potential mechanisms for dysynchiria. For example, bilateral cortical disinhibition in CRPS (Schwenkreis et al., 2005) raises the possibility that impaired normal inhibitory controls on visual-tactile interaction might be impaired. Alternatively, enhanced bilateral activation of sensory cortex in response to unilateral touch (Forss et al., 2005) raises the possibility that a direct intercortical facilitation could be involved (Schwenkreis et al., 2005). It would be interesting to know whether subjects with more extensive bilateral cortex activation after sensory stimulation are predisposed to CRPS. Finally, perhaps it is the incongruence between visual input that the skin is being touched and the absence of corroborative tactile input that evokes pain in people with CRPS. That would be broadly consistent with the incongruence theory that is central to the cortical model of pathological pain (Harris, 1999), although that model is open to debate (Moseley, 2006).

If neither dysynchiria nor synchiria is present in neuropathic pain, why then might synchiria be evident in amputees (Jones, 1907)? Relevant here is the observation that phantom limb pain shares similarities with CRPS that have not been documented for neuropathic pain of the type studied in the present work. For example, similar changes in the organisation of primary somatosensory (Flor et al., 1995) or motor cortices (Pleger et al., 2004). Furthermore, clinical phenomena such as distorted body schema (Forderreuther et al., 2004; Moseley, 2005) and sensory referral according to S1 somatotopy (Ramachandran and Rogers-Ramachandran, 2000; McCabe et al., 2003) have been reported in phantom limb pain and CRPS. It seems unlikely that one of these mechanisms is alone sufficient, but it is possible that a combination of them could underpin dysynchira.

In summary, dysynchiria could not be evoked in patients with chronic neuropathic pain associated with brush-evoked pain (allodynia). Even though speculative at this time, dysynchira might be useful as a clinical sign to differentiate CRPS from neuropathic pains of the type studied here.

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