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Original article

Distinguishing between nociceptive and neuropathic components in chronic low back pain using behavioural evaluation and sensory examination

N. Spahr [a, b, *], D. Hodkinson [a], K. Jolly [a], S. Williams [a], M. Howard [a, 1], M. Thacker [a, b, c, 1]

[a] Dept. of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK
[b] Dept. of Physiotherapy, Guy's & St Thomas' NHS Foundation Trust, London, UK
[c] Centre of Human & Aerospace Physiological Sciences, King's College London, UK

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ABSTRACT

Background: Diagnosis of chronic low back pain (CLBP) is traditionally predicated on identifying underlying pathological or anatomical causes, with treatment outcomes modest at best. Alternately, it is suggested that identification of underlying pain mechanisms with treatments targeted towards specific pain phenotypes may yield more success. Differentiation between nociceptive and neuropathic components of CLBP is problematic; evidence suggests that clinicians fail to identify a significant neuropathic component in many CLBP patients. The painDETECT questionnaire (PDQ) was specifically developed to identify occult but significant neuropathic components in individuals thought to have predominantly nociceptive pain.
Methods: Using the PDQ, we classified 50 CLBP patients into two distinct groups; those with predominantly nociceptive pain (Group 1) and those with a significant neuropathic component (Group 2). We characterised these two distinct CLBP sub-groups using a) questionnaire-based behavioural evaluation measuring pain-related function and quality of life, pain intensity and psychological well-being and b) sensory examination, using two-point and tactile threshold discrimination.
Objective: We sought to determine if differences in the pain phenotype of each CLBP sub-group would be reflected in sensory and behavioural group profiles.
Results: We report that Group 1 and Group 2 sub-groups demonstrate unique clinical profiles with significant differences in sensory tactile discrimination thresholds and in a wide range of behavioural domains measuring pain intensity, disability and psychological well-being.
Conclusion: We have demonstrated distinct clinical profiles for CLBP patient sub-groups classified by PDQ. Our results give diagnostic confidence in using the PDQ to characterise two distinct pain phenotypes in a heterogeneous CLBP population.

1. Introduction

Heterogeneity in the clinical presentation of Chronic Low Back Pain (CLBP) makes diagnosis and treatment challenging. CLBP treatment pathways are traditionally predicated on identifying pathophysiological causes, which are not possible to identify in 90% of patients (Koes et al., 2006). Attention has focused on identifying sub-groups within the heterogeneous CLBP population, in order to more effectively target treatments (Delitto, 2005; Foster et al., 2011; Huijnen et al., 2015; O'Sullivan, 2005; Stanton et al., 2011; Turk, 2005). These subgroups may be variously defined by physiological or psychological determinants. Alternately, it has been suggested that identification of underlying pain mechanisms and treatments targeted towards specific pain phenotypes may yield more successful outcomes (Woolf, 2004). Clinically, this is important, as patients with neuropathic pain (NeuP) demonstrate poorer outcomes and greater comorbidities than patients with nociceptive pain (Smith and Torrance (2012); Smith et al. (2007) Jensen et al., 2007).

The definition and diagnosis of NeuP and its differentiation from nociceptive pain remains controversial. Current IASP guidelines stipulate that a demonstrable lesion or disease of the somatosensory nervous system is necessary in order to arrive at a definitive

* Corresponding author. Dept. of Neuroimaging, Institute of Psychiatry, Psychology and Neuroscience, PO89, De Crespigny Park, London SE5 8AF, UK.
E-mail address: nicolas.1.spahr@kcl.ac.uk (N. Spahr).
[1] Authors were equally responsible for the supervision of the published work.

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neuropathic classification (International Association for the Study of Pain, 2016) For a full up to date description of the issues underlying the diagnosis and definition of neuropathic pain see Finnerup et al. (2016). Using the current IASP guidelines, only a small percentage of CLBP patients can be classified as 'neuropathic' yet, in routine clinical practice, many patients with low back pain present with symptoms that are indicative of a significant neuropathic component (i.e spread of pain, paroxysmal pain, dysaesthesia, allodynia). However, these patients may either present with no history or confirmatory evidence of a lesion or disease process, with equivocal examination findings and with pain that is not in a 'neuroanotomically plausible' distribution. Recent work suggests that clinicians fail to identify significant neuropathic components in a number of people with LBP and that the true incidence of CLBP patients with a significant neuropathic component may be underdiagnosed (Freynhagen et al., 2006). In addition, evidence shows that neuropathic LBP is not restricted to patients that present with a typical radicular presentation (Attal et al., 2011; Forster et al., 2013). Patients with occult neuropathic symptoms may therefore be misclassified as nociceptive, in spite of a seemingly neuropathic symptom profile, or else idiopathic, which allows no indication of underlying pain mechanisms. Worst of all, an idiopathic classification may hint at a pejorative 'functional' label to a patient's symptoms (Cohen et al., 2011).

Importantly, failure to identify patients with occult neuropathic components may lead to sub-optimal treatment regimes. It is proposed that improved ability to identify these patients and target appropriate treatments will result in better outcomes.

The PainDETECT questionnaire (PDQ) was specifically developed to identify neuropathic components in patients with CLBP and to differentiate LBP patients with a significant neuropathic component from LBP patients with predominantly nociceptive, mechanical pain without the need for physical examination or confirmatory diagnostic markers. The PDQ has been shown to have a high sensitivity (85%), specificity, (80%) and positive predictive accuracy (83%) in LBP (Freynhagen et al., 2006). In addition, as clinical tests such as spinal palpation, slump testing and straight leg raising are largely qualitative in nature and therefore suffer from variability and limitations of sensitivity and specificity (Rubinstein and van Tulder, 2008; van der Windt et al., 2010), identification by PDQ was chosen to reduce possible inconsistencies in patient selection criteria and as a means to standardise the selection process.

We therefore chose to use the PDQ to identify two sub-groups within our CLBP population: LBP patients with predominantly nociceptive, mechanical pain (Group 1) and LBP patients with a significant neuropathic component (Group 2).

The primary objective of this study was to characterise these two groups. Our hypothesis stated that the psychophysical clinical profiles of our participants would reflect the clinical phenotypes and underlying pain mechanisms of Group 2 and Group 2 patients, identified using the PDQ. We also hypothesised that, in particular, Group 2 patients would display a more complex profile compared to Group 1 patients. If the profiles of each group were truly different, then diagnostic confidence that the PDQ is a valid tool, able to characterise pain phenotypes in a heterogeneous population, would be strengthened.

2. Methods

2.1. Recruitment

Fifty patients with CLBP were recruited from the same inner city London hospital, together with twenty age and sex-matched controls. All patients consented to clinical profiling by collection of behavioural questionnaire data, sensory examination and subsequent structural and functional neuroimaging (no neuroimaging data will be shown here but will form the basis of a subsequent paper).

In order to be eligible for inclusion, patients needed to report a history of LBP for at least 12 months and were required to score 3 or above on an 11 point numerical rating scale (NRS) on the day of screening. Subjects were excluded if they complained of chronic or current pain conditions other than LBP or if they were currently experiencing, or had any history of, clinically significant or unstable medical or psychological conditions that would compromise participation in the study. All control subjects, were required to be free of any painful conditions and other significant medical and psychological confounding factors. All subjects were screened for MRI safety. There were no exclusion criteria for pain medication and all subjects continued with their usual medication, which included paracetamol, non-steroidal anti inflammatory medication, neuropathic pain medication (anti-convulsants and anti-depressives) and opiates. Using chi-squared tests for independence (with Yate's continuity correction), no significantly different levels of medication usage across all categories were found for between groups. Further information on the recruitment process is given in Fig. 1. Formal ethical approval for the study was granted by XXXXX Research Ethics Committee (08/H0810/51).

Although all patients were initially selected at random, during the later stages of the recruitment process it was observed that more Group 1 than Group 2 patients (as determined by the PDQ) had been recruited at the first check point. This reflects the demographic incidence of neuropathic pain compared to non-neuropathic pain in clinical populations (Smith and Torrance, 2012; Torrance et al., 2006). It was therefore deemed necessary during the latter stages of recruitment to preferentially select Group 2 patients, as determined by PDQ, in order to balance patient numbers between the LBP groups.

2.2. Clinical and psychometric assessments

The following questionnaires were administered in order to assess pain, disability and psychological status: painDETECT Questionnaire (PDQ) (Freynhagen et al., 2006), numeric rating scale (NRS) for pain, Short Form McGill Pain Questionnaire (SFMPQ) (Melzack, 1987), RAND Medical Outcomes 36-Item Short Form Survey Instrument (SF-36) (Ware and Sherbourne, 1992), Centre for Epidemiologic Studies Depression Scale Questionnaire (CES-D) (Radloff, 1977), State Trait Anxiety Inventory (STAI) (Spielberger, 1983) and the Revised Symptom Checklist 90 Questionnaire (SCL-90-R) (Derogatis and Unger, 2010). Detailed information on each questionnaire is provided in Table 1.

2.3. Sensory testing

Sensory evaluation was carried out using two-point discrimination (2PD) and tactile threshold discrimination (TTD). Participants were positioned comfortably in prone lying with a pillow underneath the stomach to standardise lumbar position. The examiner identified and marked the spine in line with the spinous processes of L1, L3 and L5 bilaterally in line with the inferior angle of the scapula. The same assessor examined all patients in order to reduce the inter-rater variability inherent in these techniques (Catley et al., 2013). Testing was undertaken separately on left and right sides of the back and the order of testing was randomised, as was the order of levels tested.

2.3.1. TTD testing

Semmes-Weinstein monofilaments of varying thickness with corresponding target forces (1.65, {0.008g}; 2.83, {0.07g}; 3.61,