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Characterization of peripheral and central sensitization after dorsal root ganglion intervention in patients with unilateral lumbosacral radicular pain: a prospective pilot study

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Abstract

Background. Quantitative sensory testing (QST) has been used to predict the outcome of epidural steroid injections in lumbosacral radicular pain and has the potential to be an important tool in the selection of appropriate treatment (such as epidural steroid injections *vs* surgery) for patients with chronic radicular pain. In addition, QST assists in identification of the pain pathways of peripheral and central sensitization in selected groups of patients.
Methods. Twenty-three patients were given dorsal root ganglion (DRG) infiltration with local anaesthesia and steroid ('DRG block'), and those who demonstrated at least 50% pain relief were offered pulsed radiofrequency (PRF) to the DRG. Questionnaires and QST scores were measured before the DRG blocks and at 1 week and 3 months after their procedure. Those who received PRF also answered questionnaires and underwent QST measurements at 1 week and 3 months after their procedure.
Results. There was a significant increase in pressure pain threshold scores after DRG blocks. A reduced conditioned pain modulation response was seen before DRG, which increased after the procedure. Ten out of 23 patients underwent PRF to the DRG, and an increase in pressure pain threshold scores after PRF was observed. The conditioned pain modulation response was maintained in this group and increased after PRF.
Conclusions. The study demonstrates that patients with unilateral radicular low back pain who receive dorsal root ganglion interventions show changes in pressure pain thresholds and conditioned pain modulation that are consistent with a 'normalization' of peripheral and central sensitization.

Key words: conditioned pain modulation; dorsal root ganglion; quantitative sensory testing

Lumbar radicular pain is defined as pain perceived as arising in the lower limb. It is caused by ectopic activation of nociceptive afferent fibres in a spinal nerve or its roots, or other neuropathic mechanisms[1] resulting, for example, from disc protrusion, spinal stenosis, facet joint hypertrophy, or fibrosis after lumbar spine surgery. It is typically stabbing, shooting, and lancinating

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Editor's key points

- The authors conducted a pilot study (n=23) of the effect of dorsal root ganglion infiltration, followed, where suitable pain relief had been demonstrated, by pulsed radiofrequency treatment.
- They used quantitative sensory testing before and after dorsal root ganglion treatments, demonstrating observable effects on components of quantitative sensory testing, consistent with normalization of pain sensitization.

in quality, and may have a cutaneous element. The pathophysiology of chronic lumbar radicular pain involves mechanical, inflammatory, and immunological factors that affect the function of the dorsal root ganglion (DRG).[2]

Although both mechanical compression to the nerve root and associated inflammatory changes have been implicated in the pathogenesis of lumbar radicular pain, it is difficult to predict the dominant contributory factor in any particular individual. Animal studies have shown that injury can cause spontaneous and enhanced DRG activity.[3] In addition, inflammatory mediators released at the site of the herniated disc can alter sodium, potassium, and calcium ion channels on the DRG surface, causing ectopic and sustained firing.[4] Such sustained DRG discharges have been linked to sensitization of the spinal dorsal horn cells and the resulting state of hyperalgesia.[5] Based on these observations, the DRG is considered to be the most likely focus of ectopic impulse origin in patients with radicular pain and the prime target for neurodestructive and neuromodulator pain treatments.[6]

Injection of steroid into the epidural space for the treatment of radicular pain does not always relieve pain.[7] One alternative is the use of pulsed radiofrequency (PRF) to the DRG. Unlike conventional radiofrequency ablation, where a high-frequency alternating current is used to produce non-selective coagulative necrosis by heating target tissue, PRF uses short, high-voltage bursts of current followed by a silent phase, allowing for heat dissemination and a controlled target temperature of 42 °C. Although the exact mechanism of action of PRF in pain relief remains poorly understood, proposed mechanisms for pain relief after PRF to the DRG include the interruption of afferent nociceptor impulses from the alteration of gene expression within the dorsal horn,[8] neuromodulation of synaptic transmission,[9 10] and suggestions that there is further disturbance with the opioid system, noradrenaline and serotonin pathways, and microglia.[11] Despite its relatively widespread use in the treatment of a variety of pain symptoms, there is a lack of well-designed randomized controlled trials to assess its efficacy. However, case series and individual case reports have confirmed the success and excellent safety profile of PRF in managing radicular pain refractory to appropriate pharmacological and physical interventions.[12–15]

Quantitative sensory testing (QST) is used to describe different types of psychophysical testing of skin, mucosa, or muscle tissue that assess sensory and pain perception pathways. Various forms of QST have been described, which include methods of sensory and pain detection threshold determination under different testing paradigms.[16] Nociceptive inputs can trigger a prolonged but reversible increase in the excitability and synaptic efficacy of neurones in central nociceptive pathways, resulting in central sensitization; this may manifest as pain hypersensitivity, in particular dynamic tactile allodynia, secondary punctate or pressure hyperalgesia, and enhanced temporal summation. Central sensitization is a hyperexcitability state in nociceptive pathways and has been suggested to be the main cause of chronic pain conditions. The descending pain inhibitory system may be inhibited or facilitated by pain and conditioned pain modulation (CPM). Conditioned pain modulation refers to the phenomenon of one noxious stimulus inhibiting the sensation of a second stimulus administered remotely from the first or 'pain inhibits pain' phenomenon.[17]

Quantitative sensory testing has been used to measure thresholds for different sensations in neuropathic pain (NP), reflecting the possible nerve fibres that may be implicated in the pathogenesis. The degree of dysfunction of the individual fibre types measured by the QST may identify the dominant mechanism of injury (compression *vs* inflammation) in patients with chronic lower radicular (CLR) pain.[18] For example, compression from a herniated disc can affect Aβ-fibre function, which can be measured in experimental conditions using QST. It can therefore be proposed that QST has the potential to identify the dominant cause of CLR in patients with disc herniation. Quantitative sensory testing has been used to predict the outcome of epidural steroid injections in lumbosacral radicular pain and has the potential to be an important tool in the selection of the appropriate treatment (such as epidural steroid injections *vs* surgery) for patients with CLR, in addition to its role in identifying the mechanisms of pain generation in these patients.[19] A number of studies have demonstrated selective nerve fibre dysfunction in CLR using QST techniques.[20–23] One study describes a correlation between QST findings and clinical outcome after disc surgery in patients with CLR;[24] another study reports on the usefulness of current perception threshold testing in assessing lower extremity sensory functions before and after surgery for lumbar disc herniation. However, the characterization of peripheral and central sensitization after DRG interventions has not yet been studied, and the role of QST as a possible predictor of the outcome after PRF to the DRG remains to be identified.

This is a pilot study characterizing the response to DRG interventions using QST. The aim of the study was to investigate whether there were any changes in QST measurements, specifically peripheral and central sensitization, after DRG injections and the infiltration of the relevant dorsal root with local anaesthetic and steroid, and after PRF.

Methods

Study design

This was a single-centre, prospective study carried out at the Pain and Anaesthesia Research Centre at St Bartholomew's Hospital, Barts Health NHS Trust London, UK. The study was approved by the local ethics committee (approval 10/H070/62) and was conducted in accordance with the Declaration of Helsinki, with written informed consent obtained from the participants. There was no external funding or conflicts of interest within the team.

Participants

The study population was identified from the chronic pain clinic at St Bartholomew's Hospital, Barts Health NHS Trust in London, UK. All participants had a history of unilateral lumbar radicular pain of >6 months' duration and disc herniation confirmed on imaging studies, such as computed tomography or

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