Received: March 2, 2018 Revised: July 25, 2018 Accepted: August 15, 2018

(onlinelibrary.wiley.com) DOI: 10.1111/ner.12862

Characterizing the Somatosensory Profile of Patients With Failed Back Surgery Syndrome With Unilateral Lumbar Radiculopathy Undergoing Spinal Cord Stimulation: A Single Center Prospective Pilot Study

Shankar Ramaswamy, MD*; Theresa Wodehouse, PhD*; Richard Langford, MBBS*; Simon Thomson, MBBS†; Rod Taylor, PhD‡; Vivek Mehta, MD*

Objectives: Currently little objective evidence exists regarding the phenotype or somato-sensory profile of patients with Failed Back Surgery Syndrome (FBSS). The aim of this study is to characterize the somato-sensory profile of the patients with FBSS undergoing spinal cord stimulation (SCS).

Methods: A combined quantitative sensory test and questionnaire approach was used to characterize the somatosensory profiles of patients undergoing SCS.

Results: Baseline somatosensory profiles were obtained from 23 patients and full three-month data was obtained from 19 patients. At baseline, there was a high prevalence (>50% prevalence of moderate to severe sensation) of burning, tingling, electric shock, numbness, and pressure pain sensitivity. None of the sensory symptoms were present at significant levels at three months following SCS. At baseline, 65% of patients had an inefficient conditioned pain modulation (CPM). Three months post-SCS, 95% of patients had an efficient CPM. All the patients who had an inefficient CPM at baseline had a successful implant at three months and their CPM became efficient in all but one patient. Only 50% of the patients with an efficient CPM at baseline, had a successful implant at three months post-SCS.

Conclusion: Although very low numbers, we could demonstrate the somatosensory profiles of patients with FBSS undergoing SCS. Early indication may associate an efficient CPM profile having a higher chance of an unsuccessful implant at three months.

Keywords: Conditioned pain modulation, phenotyping, somatosensory profile

Conflict of Interest: Richard Langford reports personal fees from Grunenthal, grants and personal fees from Napp/Mundipharma, personal fees from Pfizer, personal fees from Astrazeneca, personal fees from BioQuiddity, and personal fees from The Medicines Co, all outside the submitted work. Simon Thomson has received consultancy from Boston Scientific, Mainstay Medical, and Axonics. His hospital has received research grants from National Institute of Health Research, Boston Scientific and Mainstay Medical. Rod Taylor is a paid consultant to Medtronic and Nevro. Vivek Mehta is the principal investigator for this investigator-initiated study. He is on Medical Advisory Board for Boston Scientific and received unrestricted educational grants and travel support for educational events. Shankar Ramaswamy and Theresa Wodehouse report no conflict of interest.

INTRODUCTION

Currently there is a growing interest in characterizing the somatosensory profile of patients with chronic pain using both validated questionnaires and quantitative sensory testing (QST) (1–6). This may not only allow us to subgroup patients based on underlying mechanisms but also helps us to identify suitable targets for treatment and perhaps might help us differentiate responders from non-responders (7–9). QST is a psychosensory measurement tool used to measure large and small afferent fiber function and to characterize the peripheral and central sensitization models in neuropathic pain (10–15). It includes static tests, which measures sensory and pain thresholds or pain magnitude rating to various stimuli and dynamic tests that either tests the central integration (Temporal summation TS) or descending

Address correspondence to: Dr. Shankar Ramaswamy, Consultant in Anaesthesia and Pain Management, Pain and Anaesthesia Research Centre, Barts Health NHS Trust, St Martin's Le Grand, West Smithfield, London, EC1A 7BE, Email: shankar.ramaswamy@bartshealth.nhs.uk

* Pain and Anaesthesia Research Centre, Barts Health NHS Trust, London, UK;
† Basildon and Thurrock University Hospitals, Basildon, UK; and
‡ South Cloisters, University of Exeter Medical School, University of Exeter, Exeter, UK

For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to www.wiley.com/WileyCDA/Section/id-301854.html

Source(s) of financial support: This study is part of an investigator-initiated study funded by the Boston Scientific.

modulation (conditioned pain modulation or CPM). The dynamic tests have the advantage of capturing the endogenous pain modulatory process and testing of central integration (16–21). Yarnitsky et al. have also characterized the patients as pro- and anti-nociceptive profiles based on dynamic QST measurements (22). They categorized patients with efficient CPM as having an anti-nociceptive profile and patients with inefficient CPM as having a pro-nociceptive profile.

Questionnaires such as painDetect grades different pain characteristics from none to severe, which gives us some understanding about the somatosensory profile of the patients (23,24). These tests have been validated in characterizing differential profiles including existence of "trans-etiological" clusters with distinct somatosensory characteristic profiles (2).

Lumbar spine surgeries are commonly performed in patients with chronic low back pain (25–27). The International Association for the Study of Pain (IASP) define Failed Back Surgery Syndrome (FBSS) as Lumbar spinal pain of unknown origin either persisting despite surgical intervention or appearing after surgical intervention for spinal pain originally in the same topographical location (28,29). The incidence of FBSS in various studies range between 4 and 50% (25,30–33).

Spinal cord stimulation (SCS) is an evidence-based treatment for patients with neuropathic pain associated with FBSS and is recommended in the UK as a treatment option by the National Institute for Health and Clinical Excellence (NICE) Technology Appraisal (TA) 159 (34–43). In the UK, currently the patients are screened subjectively by a multidisciplinary team as recommended by the NICE TA159 (34). However, little objective evidence exists regarding the phenotype or somato-sensory profile of FBSS patients, which we believe is a heterogenous condition.

Several theories have been proposed to explain the mechanism of action of SCS (44–47). Although several studies have looked into the effect of SCS on peripheral and central sensitization and the somatosensory sensory profile, it still remains to be established (16,17,48–53). Furthermore, there is a need to ascertain the somatosensory profile of these patients and the impact of SCS, thereby developing an objective tool or a phenotypic marker to evaluate the response of SCS. We hope that developing such profiles, before and after SCS, will inform us about the clinical decision-making as potentially certain pain sensitivity profiles may be better targeted by SCS. This we hope will allude toward mechanism based pain intervention treatment.

MATERIAL AND METHODS

This was a single center, prospective open label, pilot investigation to characterize the somatosensory profile of patients with FBSS, with unilateral lumbar radiculopathy with predominant leg pain undergoing SCS using a combined QST and questionnaire approach.

Following ethics committee approval (10/H070/62), 23 patients with FBSS and unilateral radicular pain, due to undergo percutaneous SCS as part of their standard treatment for lumbar neuropathic pain as per the national UK guidelines (NICE TA 159) at Barts Health NHS Trust, London, UK, were consented for this study. All patients were assessed by a multidisciplinary team and were confirmed to experience chronic pain (measuring at least 50 mm on a 0–100 mm visual analogue scale) for at least six months despite appropriate conventional medical management prior to consideration of SCS.

Somatosensory profiling using QST and questionnaire (painDetect) was collected before the first stage SCS trial (dual lead eight contact linear leads, Boston Scientific [BSCI]). The first stage was performed with the leads placed at T9–10 level with on-table mapping of the neuropathic pain as per the standard operating procedure using tonic stimulation parameter. All patients received one-week trial period. Patients reporting at least 50% pain relief during the trial stage were offered to have the permanent implant as per our standard policy. The permanent implant was done using the Precision Spectra™ implantable generator, BSCI. All implants (first and second stage) were jointly done by VM and SR. Paraesthesia mapping was performed to ensure adequate coverage as per our standard policy. Repeat somatosensory measurements including QST and painDetect were taken at 18 days and three months following the second stage implant.

The following measurements were recorded at baseline (pre-SCS), 18 days post-SCS and three months post-implant. To minimize operator related variability, same- trained operator (SR/ TW) performed all QST's on each patient using the standardized protocol.

1. **Mechanical detection threshold (MDT):** MDT is the weakest stimulus that a subject can detect. Seventeen, progressively rigid, monofilament, von Frey fibers (filaments represent stimuli from 0.039– 4386 mN) were used for this test. The painful leg area was tested with von Frey's filament, starting from the lowest/thinnest monofilament. Each filament was applied to the skin at a 90° angle with sufficient force to bend or bow the filament. The filament was held in place for 1.5 sec and then removed. The exact threshold was found by repetitive testing ascending fiber sizes. The patient was instructed to respond "Yes" when a stimulus was felt. Each filament was applied up to three times in increasing filament thickness and the patient should say "Yes" at least twice for the threshold filament.
2. **Pain perception threshold (PPrT) or punctate hyperalgesia:** PPrT is the lowest intensity of a painful stimulus at which the subject perceives pain. This test was performed similar to ST but the response is the monofilament producing discomfort/ pain.
3. **Measurement of pressure pain threshold (PPT):** A hand-held pressure algometer (Algometer type II, Somedic Production AB, Sosdala, Sweden, diameter contact tip 10 mm; cover 2 mm thick rubber; standardized and constant speed of pressure increase of 0.3 kg/s) was used to measure the PPT's in kPa (kilopascal). The probe was placed perpendicular to the skin and standard incremental pressure was applied until the subject perceived the pressure as pain when the procedure was immediately terminated. Measurements were taken at the most painful site in the leg as mentioned by the patient and also at corresponding non-painful site on the contralateral side and also in the back. At each site, three measurements were taken at four predefined points and an average PPT value was calculated from the 12 measurements.
4. **CPM paradigm:** CPM paradigm was measured using PPT as the test stimulus and ischaemic arm technique as the conditioning stimulus applied to the upper arm (54). To evoke the conditioning stimulus, the blood pressure cuff was inflated above systolic pressure (200 mmHg) for up to 10 min, or until a Numerical Rating Scale (NRS) of 6/10 was achieved. The point on the painful site with the lowest PPT value in the back as well as on the painful leg was chosen to measure the CPM response. Three PPT measurements were taken at these points using the parallel testing method (with cuff inflated) and then the cuff was deflated. The difference between the mean PPT measurements (pre-cuff inflation minus post-cuff inflation PPT) was taken as the absolute value of CPM response. A negative value suggests that CPM was efficient and the patient is likely

to have an anti-nociceptive profile. On the contrary, a positive value suggests that CPM was inefficient and the patient is likely to have a pro-nociceptive profile.

5. **Temperature thresholds:** Four different thresholds including Cold Detection Threshold (CDT), Warm Detection Threshold (WDT), Cold Pain threshold (CPT), and Heat Pain Threshold (HPT) were measured using a computer-controlled thermode with surface area of 9 cm^2 (TSA-II Quantitative NeuroSensory Analyzer; Medoc, Ramat Yishai, Israel). A pre-loaded software was used to set the baseline temperature at 32 °C degrees and changed the temperature at a constant rate of 1 °C /s until the subject pressed the patient-activated push-button. CDT and WDT measured the temperature, which was perceived as a "change" when the temperature was decreased or increased from 32 °C , respectively. Similarly, CPT and HPT measured the temperature, which was perceived as "painful" when the temperature was decreased or increased from 32 °C, respectively. Four consecutive measurements were taken with the thermode returning to baseline temperature each time. CDT and WDT were determined as the mean of the four measurements. Subsequently, CPT and HPT were determined in a similar manner, and in that order but by taking an average of three consecutive measurements.
6. The somatosensory profile of the patient was elicited using the individual questions from the painDetect. Seven different sensory profiles were evaluated including burning, tingling, touching, electric shock, heat or cold, numbness, and pressure pain sensation. Each of these characteristics was graded between 0 and 5 (0, no sensation, 1–2: mild sensation, 3: moderate sensation, 4–5: severe sensation).

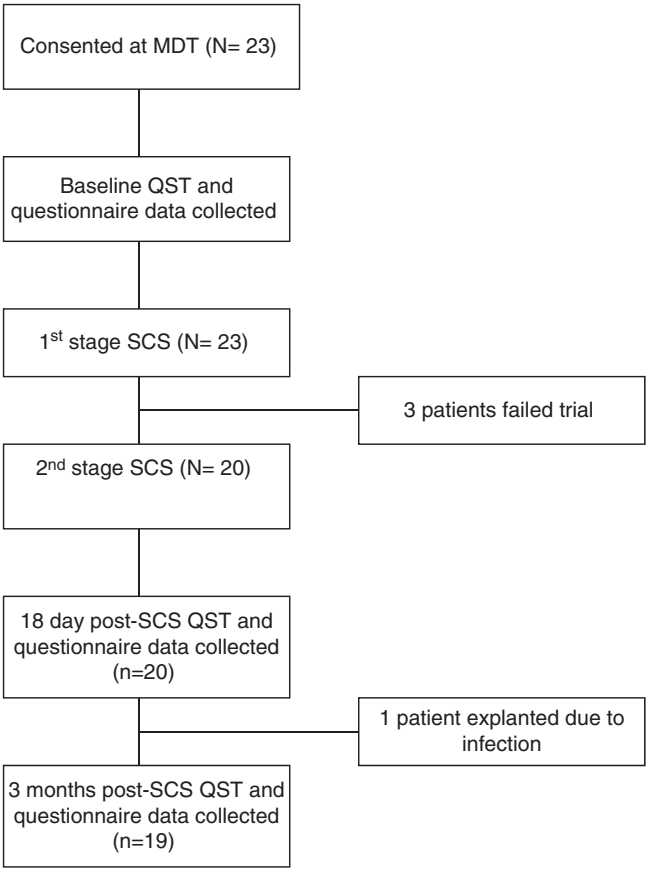

Figure 1. Consort diagram: Patient flow.

Statistical Analysis

Outcomes at baseline and follow up are presented as means and standard deviations (SD), medians and interquartile ranges (IQR). Normality and symmetry of the data was checked by visual inspection of the histogram and box plot prior to statistical analysis. None of the QST and sensory profile data was symmetric or normally distributed and hence we used sign test to calculate the *p* values. *p* values were calculated for baseline vs. 18 day/three months post-SCS. *p* values <0.05 were deemed statistically significant. STATA 14.2 software was used for the analysis of the data.

RESULTS

Demographic and Programming Data

A flow diagram shows the study scheme as summarized in Figure 1. The mean age was 60 ± 9.2 years and M:F ratio was 8:15. The Visual Analogue Scale (VAS) scores at baseline, 18 days post-SCS and three months post-SCS are summarized in Table 1. Eighty three percent of the patients had a neuropathic component to their pain.

Somatosensory Profile of the Patients With FBSS and the Effect of SCS on the Profile

The distribution of the somatosensory symptoms in the patient groups at baseline, 18 days, and three months post-SCS are shown in Figure 2. The change in the somatosensory profile following SCS is shown in Table 2.

Patients with unilateral radicular pain due to FBSS awaiting SCS reported a high prevalence (>50% prevalence of moderate to severe sensation) of baseline pain characteristics with burning, tingling, electric shock, numbness, and pressure pain sensitivity and a lower prevalence of touch and temperature sensitivity (<50% prevalence of moderate to severe sensation).

Following SCS, there was a definite shift in the somatosensory profile of these patients (Fig. 2). There were significant improvements in burning, tingling, electric shock, and pressure sensation both at 18 days and three months and significant improvement in numbness at three months. Patient reported that touch and temperature sensitivity were less of a problem at 18 days and improvement in temperature sensitivity reached statistical significance at three months following SCS ($p < 0.05$). None of the sensory symptoms were present to significant levels at three months following SCS. The patients moved from "likely" to "unlikely" neuropathic pain category following SCS. This demonstrates a significant shift in the various somatosensory characteristics of the patient following SCS.

CPM Profile of Patients With FBSS and the Effect of SCS on the CPM Profile

CPM paradigms of individual patients measured at back and painful leg are shown in Figures 3 and 4. Median (IQR) for CPM is summarized in Table 3. Of the 23 patients, 15 patients (65%) had an inefficient CPM at baseline, but all of them (15/15 or 100%) had a successful implant at three months. Of these, only one patient (1/15) continued to have an inefficient CPM at three months. Eight patients had an efficient CPM at baseline, of which only four patients (50%) had a successful implant at three months. CPM remained efficient in all the four patients.

Table 1. VAS Scores at Baseline, 18 Days Post-SCS, and Three Months Post-SCS.

VAS (N = 19)	Baseline	18 day post-SCS	Three months post-SCS
Median (IQR)	8.4 (7.5–9)	3 (2–7)	4.1 (1.3–5.6)
p value (comparison to baseline)		$p < 0.001$	$p < 0.001$

IQR: interquartile range.

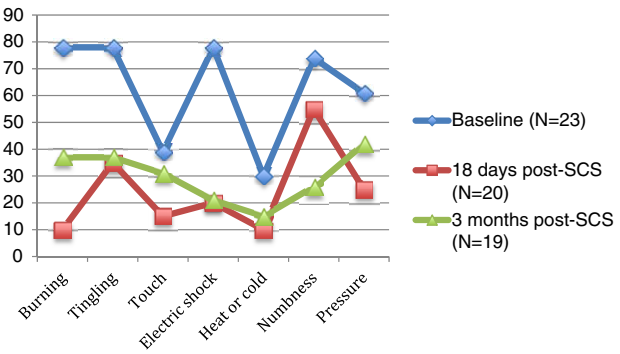

Figure 2. Sensory profile as measured using individual painDetect questions—Percentage of patients reporting moderate or severe scores (score 3–5). [Color figure can be viewed at wileyonlinelibrary.com]

Effect of SCS and Other QST Parameters

There was a statistically significant improvement in PPT's measured at the painful leg but not in the back and non-painful leg (Table 4). There was no significant difference in the temperature thresholds (CDT, WDT, CPT, and HPT), touch allodynia, and punctate hyperalgesia (Table 4). There was a greater difference in PPT between non-painful and painful side at baseline (p = 0.0558) compared to at 18 days (p = 0.18) or three months (p = 0.36). PPT in the painful leg was lower than the PPT in the non-painful leg (Δ mean 60.56 at baseline; vs. Δ mean 30.69 at three months). Following SCS, PPT improved significantly only in the painful leg.

DISCUSSION

Sensory characteristics using QST has been studied in patients undergoing SCS for chronic intractable neuropathic pain due to various etiologies. We have previously characterized CPM and PPT's in patients with unilateral lumbosacral pain undergoing dorsal root ganglion block. We have demonstrated that both CPM and PPT's (measured in the painful leg) improved significantly following the block (55). There have been limited studies, which looked to establish a phenotypic profile or a biomarker in predicting the response to SCS (16,17,49–53,56). The studies were focused on simple reporting of static measures but more recently, there has been a greater interest in using the dynamic measures such as CPM paradigms. A number of QST techniques have been used in these studies to evaluate the effect of SCS on the various somatosensory characteristics. Due to the varying methodologies used in these studies, it is difficult to come to any unifying conclusions. Eisenbergh et al. found a correlation between vibration threshold and tolerance to electrical stimulation with successful SCS trials (49). Van Eijs et al. found a negative correlation between brush evoked allodynia and response to SCS in patients with CRPS, that is, patients with significant allodynia had less chance of having a successful trial with SCS (52). To the best of our knowledge, this is the first study that has attempted to characterize the somatosensory profile of patients with FBSS undergoing SCS using the combined QST and questionnaire approach.

CPM seems to have an interesting relationship with chronic pain and as a predictive tool for response to intervention. Yarnitsky et al. categorized patients with efficient CPM as having an antinociceptive profile and patients with inefficient CPM as having a pro-nociceptive profile (22). Correa et al. reported an inefficient CPM in patients with CLBP compared to a normal healthy population (48). Yarnitsky et al showed that patients with less efficient CPM had a higher risk of development of chronic post-surgery pain and higher pain intensity (57). They in fact reported that CPM efficiency was the sole predictor of chronic postthoracotomy pain. In a study on patients with painful diabetic neuropathy, Yarnitsky et al. showed that inefficient CPM at baseline had a predictive value for response to duloxetine (r = 0.628, $p < 0.001$) (58). They also showed that in patients with less efficient CPM who demonstrated this improvement found a correlation between the efficacy of duloxetine and improvement in CPM (r = −0.411, p = 0.033). Campbell et al showed that patients with pro-nociceptive pain modulation profile with enhanced TS and reduced baseline CPM

Table 2. Patient Reported Sensory Phenotypes.

Sensory phenotype	Baseline	18 days post-SCS	Three months post-SCS
Burning	3 (3,4)	0 (0,2) ($p < 0.001$)	1.5 (0,3) ($p < 0.01$)
Tingling	4 (3,4)	2 (0,4) ($p < 0.01$)	1 (0,3) ($p < 0.001$)
Touch	2 (0,3)	1 (0,2) (p = 0.13)	0 (0,3) (p = 0.31)
Electric shock	4 (3,5)	0 (0,3) ($p < 0.01$)	0 (0,2.5) ($p < 0.001$)
Heat or cold	1 (0,3.25)	0.5 (0,1.25) (p = 0.15)	0 (0,0) ($p < 0.05$)
Numbness	4 (3,4)	2.5 (0,4) (p = 0.06)	1 (0,2.5) ($p < 0.01$)
Pressure pain	3 (2,4.25)	1 (0,3) ($p < 0.05$)	2 (0,3) ($p < 0.01$)
PainDetect	21 (16,26)	10 (4,15) ($p < 0.001$)	9.5 (5,15) ($p < 0.001$)

N = 19 (patients with full three months dataset). Median (IQR) and p values at baseline, 18 days, and three months post-SCS.

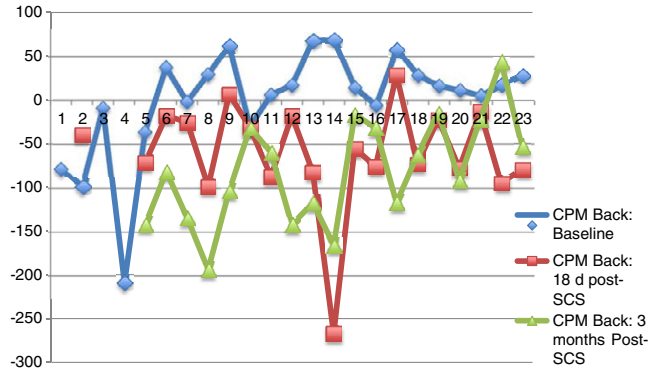

Figure 3. CPM Back—Baseline, 18 days, and three months post-SCS—individual patient values (absolute value of CPM in kPa). [Color figure can be viewed at wileyonlinelibrary.com]

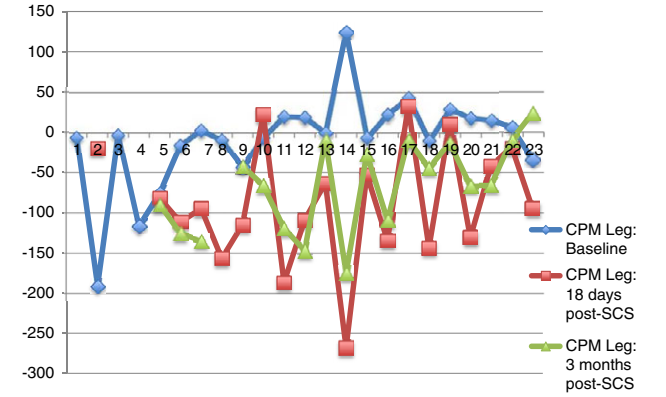

Figure 4. CPM Leg—Baseline, 18 days, and three months post-SCS—individual patient values (absolute value of CPM in kPa). [Color figure can be viewed at wileyonlinelibrary.com]

were associated with lower pain scores three months following SCS (17). Sixty five percent of the patients in our cohort had an inefficient CPM at baseline suggestive of a pro-nociceptive profile. Three months post-SCS, 95% of the patients had an efficient CPM, suggestive of an anti-nociceptive profile, which is similar to what we would expect in a normal population. All the patients in our cohort, who had a pro-nociceptive profile at baseline had a successful implant at three months and their profile became anti-nociceptive in all but one patient (14/15). This would suggest that SCS might normalize the pro-nociceptive profile to anti-nociceptive profile. Only 50% of the patients in our cohort with an efficient CPM at baseline had a successful implant at three months post-SCS. Although very low numbers, early indication may associate an anti-nociceptive profile having a higher chance of an unsuccessful implant at three months.

Our overall impression is that patients with chronic pain seems to have a pro-nociceptive profile with an inefficient CPM and patients with no chronic pain tend to have an anti-nociceptive profile with an efficient CPM. Furthermore, if a patient has an efficient CPM, perhaps they are less likely to develop chronic pain, however if efficient CPM profile is associated with chronic pain they are probably less likely to respond to an intervention. On the contrary, if a patient has an inefficient CPM, they are perhaps more likely to develop chronic pain and more likely to respond to an intervention.

Somatosensory Profiles Based on PPT

Patients with FBSS had lower PPT measured at back, painful and non-painful leg compared to healthy volunteers as reported previously in the literature (48,59,60). PPT in the painful leg was lower than the PPT in the non-painful leg but did not reach statistical significance. Following SCS, PPT improved significantly but only in the painful leg. Given that the current evidence for SCS is strongest for an improvement in leg pain in FBSS, a significant improvement in the PPT only in the painful leg is perhaps a reflection of the true local benefit of SCS on the peripheral sensitization.

Developing the Somatosensory Characteristics as a Phenotypic Biomarker for Patients With FBSS With Unilateral Radicular Pain and the Effect of SCS on the Profile

Freeman et al. defined three different pain types based on the somatosensory symptoms (pinpointed pain includes burning, electric shock, stabbing, pins and needles, and tingling; deep pain includes squeezing and pressure and provoked pain includes provoked brushing, pressure, and cold) and two different pain types based on QST measurements (evoked by touch pain and evoked by cold pain) (2). They performed a hierarchy cluster analysis to classify pain due to various etiologies into different clusters. It is beyond the scope of this study to perform such cluster analysis due to the small sample size. However, our data demonstrates that patients with FBSS have a high incidence (> 50%) of moderate to severe pinpointed and deep pain along with a high incidence (> 50%) of a pro-nociceptive profile. Following SCS, this profile changes to none to mild levels for all types of pain with an anti-nociceptive profile. This suggests how the patients with FBSS present and how we can expect their presentation to change following SCS, along with the suggested predictive value of a pro-nociceptive profile for a successful implant as mentioned above. This we hope makes a strong case for a future larger study to establish the phenotypic clusters of patients with FBSS and to study the effect of SCS on these clusters. This will enable us to successfully predict the phenotypes that may be associated with a successful implant.

One of the main limitations of this study is the small sample size. Despite the wide inter-patient variability of the CPM paradigms of individual patients measured at back and painful leg, the overall trend for the CPM measurements in the cohort of FBSS measured at two different sites, showed remarkable consistency. Our study demonstrates that CPM is reliable and a

Table 3. Effect of SCS on CPM (Median and IQR) (N = 19).

QST Sensation	Baseline	18 days post-SCS	Three months post-SCS
CPM back	17 (5, 37)	−71 (−82.63, −18) ($p < 0.001$)	−82 (−135, −31.67) ($p < 0.001$)
CPM painful leg	3 (−10, 20)	−95 (−134.7, −41.66) ($p < 0.001$)	−66.34 (−121, −12.4) ($p < 0.001$)
CPM (efficient: inefficient)	4 (21%):15 (78%)	17 (89%):2 (11%)	18 (95%):1 (5%)

Table 4. Effect of SCS on Other QST Parameters: PPT, Temperature Thresholds, Mechanical, and Punctate Hyperalgesia at Baseline, 18 Days, and Three Months Post-SCS (Median and IQR) ($N = 19$).

QST sensation	Baseline	18 days post-SCS	Three months post-SCS
PPT back	180.8 (154,289)	250.67 (213.75, 365) ($p = 0.076$)	259 (200.5, 392) ($p = 0.064$)
PPT painful leg	165 (99.49,272.56)	235 (189, 284) ($p = 0.0534$)	282.17 (223, 362.99) ($p < 0.001$)
PPT non-painful leg	225.98 (186,341)	283.92 (216.84, 330) ($p = 0.15$)	344.2 (222.6, 401.9) ($p = 0.06$)
CDT	28.7 (27.65,29.5)	28.14 (27, 29.34) ($p = 1$)	27.78 (26.65, 28.64) ($p = 0.42$)
WDT	35.8 (34.46,38.38)	36.46 (35, 38.7) ($p = 0.45$)	35.77 (34.9, 37.6) ($p = 0.42$)
CPT	23.58 (6.85,26.52)	22 (5.6, 25.8) ($p = 1$)	23.05 (15.27, 24.72) ($p = 0.18$)
HPT	44.88 (37.99,48.45)	44 (41.92, 48.28) ($p = 1$)	41.78 (38.87, 47.08) ($p = 0.58$)
MDT	3.84 (3.3,4.25)	4.08 (3.84, 4.56) ($p = 0.34$)	3.61 (3.22, 4.37) ($p = 0.09$)
Punctate hyperalgesia	5.18 (4.6,5.88)	5.46 (4.93, 5.88) ($p = 0.61$)	5.46 (5, 5.99) ($p = 1$)

consistent phenotype as has been previously reported in the literature (61–65). We feel that it may be possible to infer from this study that the trends in the relationship between CPM and FBSS, the effect of baseline CPM on a successful implant and the impact of SCS on CPM very much mirrors what has been reported in the literature in other chronic pain interventions. Given the small sample size, we feel it would be statistically incorrect to try to demonstrate a correlation between CPM and a successful implant in this study.

It will also be useful to collect long-term data (12 months) on somato-sensory profiling following SCS.

CONCLUSION

This pilot study shows that patients with FBSS have distinct somatosensory profiles and these profiles can be modified with SCS. However, the predicted value of the profile and opportunity for personalizing the delivery of SCS requires an adequately powered study specifically designed to address this issue.

Authorship Statement

Shankar Ramaswamy was involved in recruitment, implanting spinal cord stimulation, data collection including performing QST, analysis of data, writing the manuscript. This work is part of his PhD thesis. Theresa Wodehouse was involved in data collection and writing the manuscript. Richard Langford was involved in writing the manuscript. Simon Thomson was involved in designing the protocol and writing the manuscript. Rod Taylor provided the statistic support and writing the manuscript. Vivek Mehta was involved in writing the protocol, recruitment, implanting spinal cord stimulation, and writing the manuscript.

How to Cite this Article:

Ramaswamy S., Wodehouse T., Langford R., Thomson S., Taylor R., Mehta V. 2018. Characterizing the Somatosensory Profile of Patients With Failed Back Surgery Syndrome With Unilateral Lumbar Radiculopathy Undergoing Spinal Cord Stimulation: A Single Center Prospective Pilot Study.
Neuromodulation 2018; E-pub ahead of print. DOI:10.1111/ner.12862

REFERENCES

1. Cardoso JS, Riley JL 3rd, Glover T et al. Experimental pain phenotyping in community-dwelling individuals with knee osteoarthritis. *Pain* 2016;157:2104–2114.
2. Freeman R, Baron R, Bouhassira D, Cabrera J, Emir B. Sensory profiles of patients with neuropathic pain based on the neuropathic pain symptoms and signs. *Pain* 2014;155:367–376.
3. Frey-Law LA, Bohr NL, Sluka KA et al. Pain sensitivity profiles in patients with advanced knee osteoarthritis. *Pain* 2016;157:1988–1999.
4. Baron R, Maier C, Attal N et al. Peripheral neuropathic pain: a mechanism-related organizing principle based on sensory profiles. *Pain* 2017;158:261–272.
5. Vollert J, Kramer M, Barroso A et al. Symptom profiles in the painDETECT Questionnaire in patients with peripheral neuropathic pain stratified according to sensory loss in quantitative sensory testing. *Pain* 2016;157:1810–1818.
6. Vollert J, Maier C, Attal N et al. Stratifying patients with peripheral neuropathic pain based on sensory profiles: algorithm and sample size recommendations. *Pain* 2017;158:1446–1455.
7. Westermann A, Krumova EK, Pennekamp W, Horch C, Baron R, Maier C. Different underlying pain mechanisms despite identical pain characteristics: a case report of a patient with spinal cord injury. *Pain* 2012;153:1537–1540.
8. Baron R, Forster M, Binder A. Subgrouping of patients with neuropathic pain according to pain-related sensory abnormalities: a first step to a stratified treatment approach. *Lancet Neurol* 2012;11:999–1005.
9. Simpson DM, Schifitto G, Clifford DB et al. Pregabalin for painful HIV neuropathy: a randomized, double-blind, placebo-controlled trial. *Neurology* 2010;74:413–420.
10. Arendt-Nielsen L, Yarnitsky D. Experimental and clinical applications of quantitative sensory testing applied to skin, muscles and viscera. *J Pain* 2009;10:556–572.
11. Rolke R, Baron R, Maier C et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. *Pain* 2006;123:231–243.
12. Rolke R, Magerl W, Campbell KA et al. Quantitative sensory testing: a comprehensive protocol for clinical trials. *Eur J Pain* 2006;10:77–88.
13. Zaslansky R, Yarnitsky D. Clinical applications of quantitative sensory testing (QST). *J Neurol Sci* Jan 08 1998;153:215–238.
14. Cruccu G, Sommer C, Anand P et al. EFNS guidelines on neuropathic pain assessment: revised 2009. *Eur J Neurol* 2010;17:1010–1018.
15. Haanpaa M, Attal N, Backonja M et al. NeuPSIG guidelines on neuropathic pain assessment. *Pain* 2011;152:14–27.
16. Campbell CM, Jamison RN, Edwards RR. Psychological screening/phenotyping as predictors for spinal cord stimulation. *Curr Pain Headache Rep* 2013;17:307.
17. Campbell CM, Buenaver LF, Raja SN et al. Dynamic pain phenotypes are associated with spinal cord stimulation-induced reduction in pain: a repeated measures observational pilot study. *Pain Med* 2015;16:1349–1360.
18. Granot M. Can we predict persistent postoperative pain by testing preoperative experimental pain? *Curr Opin Anaesthesiol* 2009;22:425–430.
19. Granot M, Weissman-Fogel I, Crispel Y et al. Determinants of endogenous analgesia magnitude in a diffuse noxious inhibitory control (DNIC) paradigm: do conditioning stimulus painfulness, gender and personality variables matter? *Pain* 2008;136:142–149.
20. Graven-Nielsen T, Wodehouse T, Langford RM, Arendt-Nielsen L, Kidd BL. Normalization of widespread hyperesthesia and facilitated spatial summation of deep-tissue pain in knee osteoarthritis patients after knee replacement. *Arthritis Rheum* 2012;64:2907–2916.
21. Sprenger C, May A, Buchel C. Pain contra pain: the concept of DNIC. *Schmerz* 2010;24:569–574.
22. Yarnitsky D, Granot M, Granovsky Y. Pain modulation profile and pain therapy: between pro- and antinociception. *Pain* 2014;155:663–665.
23. Freynhagen R, Baron R, Gockel U, Tolle TR. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. *Curr Med Res Opin* 2006;22:1911–1920.
24. Freynhagen R, Tolle TR, Gockel U, Baron R. The painDETECT project—far more than a screening tool on neuropathic pain. *Curr Med Res Opin* 2016;32:1033–1057.

25. Taylor RS, Taylor RJ. The economic impact of failed back surgery syndrome. *Br J Pain* 2012;6:174–181.
26. Deyo RA, Mirza SK. Trends and variations in the use of spine surgery. *Clin Orthop Relat Res* 2006;443:139–146.
27. Weir S, Samnaliev M, Kuo TC et al. The incidence and healthcare costs of persistent postoperative pain following lumbar spine surgery in the UK: a cohort study using the Clinical Practice Research Datalink (CPRD) and Hospital Episode Statistics (HES). *BMJ Open* 2017;7:e017585.
28. Thomson S. Failed back surgery syndrome—definition, epidemiology and demographics. *Br J Pain* 2013;7:56–59.
29. North RB, Campbell JN, James CS et al. Failed back surgery syndrome: 5-year follow-up in 102 patients undergoing repeated operation. *Neurosurgery* 1991;28: 685–690. discussion 690–681.
30. Weber H. Lumbar disc herniation. A controlled, prospective study with ten years of observation. *Spine (Phila Pa 1976)* 1983;8:131–140.
31. Brox JI, Reikeras O, Nygaard O et al. Lumbar instrumented fusion compared with cognitive intervention and exercises in patients with chronic back pain after previous surgery for disc herniation: a prospective randomized controlled study. *Pain* May 2006;122:145–155.
32. Fritzell P, Hagg O, Nordwall A. Swedish Lumbar Spine Study G. Complications in lumbar fusion surgery for chronic low back pain: comparison of three surgical techniques used in a prospective randomized study. A report from the Swedish Lumbar Spine Study Group. *Eur Spine J* 2003;12:178–189.
33. Peul WC, van Houwelingen HC, van den Hout WB et al. Surgery versus prolonged conservative treatment for sciatica. *N Engl J Med* 2007;356:2245–2256.
34. NICE. *Technology Appraisal Guidelines 159: spinal cord stimulation for chronic pain of neuropathic or ischaemic origin*. Manchester, UK: National Institute for Health and Care Excellence, 2008.
35. Kumar K, Hunter G, Demeria D. Spinal cord stimulation in treatment of chronic benign pain: challenges in treatment planning and present status, a 22-year experience. *Neurosurgery* 2006;58:481–496. discussion 481–496.
36. North RB, Kidd DH, Farrokhi F, Piantadosi SA. Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial. *Neurosurgery* 2005;56:98–106. discussion 106–107.
37. North RB, Kidd DH, Lee MS, Piantodosi S. A prospective, randomized study of spinal cord stimulation versus reoperation for failed back surgery syndrome: initial results. *Stereotact Funct Neurosurg* 1994;62:267–272.
38. North RB, Kidd DH, Piantadosi S. Spinal cord stimulation versus reoperation for failed back surgery syndrome: a prospective, randomized study design. *Acta Neurochir Suppl* 1995;64:106–108.
39. Kumar K, Taylor RS, Jacques L et al. Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome. *Pain* 2007;132: 179–188.
40. Taylor RS, Desai MJ, Rigoard P, Taylor RJ. Predictors of pain relief following spinal cord stimulation in chronic back and leg pain and failed back surgery syndrome: a systematic review and meta-regression analysis. *Pain Pract* 2014;14:489–505.
41. Taylor RS, Van Buyten JP, Buchser E. Spinal cord stimulation for chronic back and leg pain and failed back surgery syndrome: a systematic review and analysis of prognostic factors. *Spine (Phila Pa 1976)* 2005;30:152–160.
42. Mailis-Gagnon A, Furlan AD, Sandoval JA, Taylor R. Spinal cord stimulation for chronic pain. *Cochrane Database Syst Rev* 2004;3:CD003783.
43. Turner JA, Loeser JD, Deyo RA, Sanders SB. Spinal cord stimulation for patients with failed back surgery syndrome or complex regional pain syndrome: a systematic review of effectiveness and complications. *Pain* 2004;108:137–147.
44. Meyerson BA, Linderoth B. Mechanisms of spinal cord stimulation in neuropathic pain. *Neurol Res* 2000;22:285–292.
45. Oakley JC, Prager JP. Spinal cord stimulation: mechanisms of action. *Spine (Phila Pa 1976)* 2002;27:2574–2583.
46. Raslan AM, McCartney S, Burchiel KJ. Management of chronic severe pain: spinal neuromodulatory and neuroablative approaches. *Acta Neurochir Suppl* 2007;97:33–41.
47. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science* 1965;150:971–979.
48. Correa JB, Costa LO, de Oliveira NT, Sluka KA, Liebano RE. Central sensitization and changes in conditioned pain modulation in people with chronic nonspecific low back pain: a case-control study. *Exp Brain Res* 2015;233:2391–2399.
49. Eisenberg E, Backonja MM, Fillingim RB et al. Quantitative sensory testing for spinal cord stimulation in patients with chronic neuropathic pain. *Pain Pract* 2006;6: 161–165.
50. Meier K, Nikolajsen L, Sorensen JC, Jensen TS. Effect of spinal cord stimulation on sensory characteristics: a randomized, blinded crossover study. *Clin J Pain* 2015;31:384–392.
51. Rasche D, Ruppolt MA, Kress B, Unterberg A, Tronnier VM. Quantitative sensory testing in patients with chronic unilateral radicular neuropathic pain and active spinal cord stimulation. *Neuromodulation* 2006;9:239–247.
52. van Eijs F, Smits H, Geurts JW et al. Brush-evoked allodynia predicts outcome of spinal cord stimulation in complex regional pain syndrome type 1. *Eur J Pain* 2010;14:164–169.
53. Ahmed SU, Zhang Y, Chen L et al. Effects of spinal cord stimulation on pain thresholds and sensory perceptions in chronic pain patients. *Neuromodulation* 2015;18:355–360.
54. Kosek E, Hansson P. Modulatory influence on somatosensory perception from vibration and heterotopic noxious conditioning stimulation (HNCS) in fibromyalgia patients and healthy subjects. *Pain* 1997;70:41–51.
55. Mehta V, Snidvongs S, Ghai B, Langford R, Wodehouse T. Characterization of peripheral and central sensitization after dorsal root ganglion intervention in patients with unilateral lumbosacral radicular pain: a prospective pilot study. *Br J Anaesth* 2017;118:924–931.
56. Pluijms WA, Slangen R, Bakkers M et al. Pain relief and quality-of-life improvement after spinal cord stimulation in painful diabetic polyneuropathy: a pilot study. *Br J Anaesth* 2012;109:623–629.
57. Yarnitsky D, Crispel Y, Eisenberg E et al. Prediction of chronic post-operative pain: pre-operative DNIC testing identifies patients at risk. *Pain* 2008;138:22–28.
58. Yarnitsky D, Granot M, Nahman-Averbuch H, Khamaisi M, Granovsky Y. Conditioned pain modulation predicts duloxetine efficacy in painful diabetic neuropathy. *Pain* 2012;153:1193–1198.
59. Binderup AT, Arendt-Nielsen L, Madeleine P. Pressure pain sensitivity maps of the neck-shoulder and the low back regions in men and women. *BMC Musculoskelet Disord* 2010;11:234.
60. Binderup AT, Arendt-Nielsen L, Madeleine P. Cluster analysis of pressure pain threshold maps from the trapezius muscle. *Comput Methods Biomech Biomed Eng* 2010;13:677–683.
61. Valencia C, Kindler LL, Fillingim RB, George SZ. Stability of conditioned pain modulation in two musculoskeletal pain models: investigating the influence of shoulder pain intensity and gender. *BMC Musculoskelet Disord* 2013;14:182.
62. Pud D, Granovsky Y, Yarnitsky D. The methodology of experimentally induced diffuse noxious inhibitory control (DNIC)-like effect in humans. *Pain* 2009;144:16–19.
63. Kennedy DL, Kemp HI, Ridout D, Yarnitsky D, Rice AS. Reliability of conditioned pain modulation: a systematic review. *Pain* 2016;157:2410–2419.
64. Biurrun Manresa JA, Fritsche R, Vuilleumier PH et al. Is the conditioned pain modulation paradigm reliable? A test-retest assessment using the nociceptive withdrawal reflex. *PLoS One* 2014;9:e100241.
65. Martel MO, Wasan AD, Edwards RR. Sex differences in the stability of conditioned pain modulation (CPM) among patients with chronic pain. *Pain Med* 2013;14: 1757–1768.

