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ORIGINAL ARTICLE

Changes in quantitative sensory testing and patient perspectives following spinal cord stimulation for persistent spinal pain syndrome: An observational study with long-term follow-up

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Abstract

Background: Spinal cord stimulation (SCS) can impact sensory, pain and tolerance thresholds in various ways, which can be accessed via quantitative sensory testing (QST). The objectives of this study were to (1) assess the subjective sensory responses using QST in patients following SCS therapy for PSPS and (2) to get a clinical impression of the results of SCS during an interview of these patients with PSPS and SCS during long term follow-up.

Methods: Forty patients with PSPS who received SCS treatment underwent QST via electrical and mechanical pressure stimuli. QST was performed at four different moments (1) pre-implantation SCS, (2) two weeks postoperatively, (3) three months after permanent SCS implantation and (4) six months after permanent SCS implantation. Patients' perspectives on pain, use of drugs and quality of life were assessed via semi-structured interviews during a follow-up between 5 and 11 years.

Results: We found statistical significant differences in the changes of sensory, pain and tolerance thresholds. A decrease in pain complaints and analgesics use were reported by the patients during follow-up. The quality of life in patients increased from three to eight (NRS 0 [worst QoL imaginable] -10 [best QoL imaginable]) after receiving SCS.

Conclusions: The increased thresholds on areas without pain or being covered by the SCS induced paresthesias may indicate that there are central changes contributing to these deviations in thresholds. The overall QoL in patients improved greatly after receiving SCS.

Significance: This study provides an overview of the effect of SCS on sensory, pain and tolerance thresholds in patients with PSPS throughout the SCS treatment process. In addition, this study presents data from 40 patients with PSPS treated with SCS, analysing several long-term patient-reported outcome measures. The results serve to give more insight into the mechanism of SCS and document SCS as a possible treatment for PSPS.

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1 | INTRODUCTION

Low back pain is a condition with an estimated global point prevalence of 9.4%, creating more disability than any other health condition in the world (Hoy et al., 2014) and increases with the global population ageing (Smith et al., 2013). As a consequence, more surgery for (chronic) low back pain is performed (Rajaei et al., 2012), which in some cases might fail to provide sufficient pain relief. It is estimated that approximately 20% of the patients will suffer from a so-called 'persistent spinal pain syndrome' (PSPS) (Petersen et al., 2021; Thomson, 2013). Painful sensations resulting from PSPS, previously called 'failed back surgery syndrome' (Chan & Peng, 2011), are either localized in the back where the surgery was performed or radiate down to one or both lower limbs.

After multiple treatments such as physical therapy, analgesic drugs, transcutaneous nerve stimulation and nerve blocks, spinal cord stimulation (SCS) can be a 'last step' to treat PSPS. SCS is based on the Gate Control Theory as described by Melzack and Wall, which states that stimulation of large afferent fibres in the dorsal column overrides the transmission of nociceptive signals propagated by the small fibres (Melzack & Wall, 1965). By placing an electrode epidurally at the dorsal side of the spinal cord via a minimally invasive surgical procedure, electrical stimulation with an implantable pulse generator can be accomplished. SCS appeared to be more (cost-)effective than the long-term use of opioids (Kumar et al., 2007; Kumar et al., 2008; Simpson et al., 2009) and is considered to be a safe therapy with strong evidence and low risk for complications (Eldabe et al., 2016; Sdrulla et al., 2018). Since it is difficult to predict which patient will respond adequately to SCS (Campbell et al., 2013), the associated high costs indicate that proper patient selection is important to maintain cost-effectiveness (Zucco et al., 2015).

One way to look at the changes that take place in the nervous system as a result of a successful treatment with SCS is assessing subjective sensory, pain and tolerance thresholds with quantitative sensory testing (QST). With this technique, using a standardized stimulation of different sensory and nociceptive modalities, it is possible to assess patients' pain thresholds and to study patients' pain modulation system before and after an intervention, for example SCS (Wilder-Smith, 2013).

Early observations showed a significant increase in the pain threshold (50% to 250%) during SCS (Shealy et al., 1970). However, no changes in touch, position and vibration sensations during the SCS were found (Shealy et al., 1970). In a systematic review by Sdrulla et al. (2018), the effect of conventional SCS on both sensory and pain thresholds was explored. The included studies were highly variable, which might be caused by heterogeneous

experimental paradigms. Nevertheless, it would clinically be relevant if a specific sensory profile or an early change in these QST measurements during trial stimulation or follow-up could predict the long-term effect of SCS. A series of patients with PSPS were treated with SCS while a standardized QST measurement was performed at various timepoints before the start of treatment and during follow-up. The objectives of this study were to (1) assess the subjective sensory responses using QST in patients following SCS therapy for PSPS and (2) to get a clinical impression of the results of SCS during an interview of these patients with PSPS and SCS during long-term follow-up. The primary outcome measures include changes in sensory, pain and tolerance thresholds, while quality of life, pain and use of pain-related medication were studied as secondary outcome measures.

2 | METHODS

In this observational study, all patients were treated with an implanted, definitive spinal cord stimulation device after a 2-week trial period. In the first part of the study, they underwent a standardized QST measurement protocol and were followed prospectively. A total of 44 patients with PSPS who were treated with SCS between 2009 and 2020 at the Radboudumc Expertise Center for Pain and Palliative Medicine (Radboud University Medical Center, Nijmegen, the Netherlands) were invited by letter to participate in the second part of this study. Data were retrieved from patient records, and QST measurements were performed within the care as usual during regular outpatient visits. When patients met the inclusion criteria and showed willingness to participate, they received an interview by telephone. Inclusion criteria for the patients consisted of (1) age at the day of SCS implantation between 18 and 75 years, (2) undergoing a treatment trajectory at the Radboudumc Expertise Centre for Pain and Palliative Medicine and (3) the patient has received spinal surgery before SCS implantation. The study design and patients at each stage of the study are shown in Figure 1.

2.1 | Patient data

Data from patients were collected in EPIC and included age, SCS implantation date and technique of SCS.

2.2 | Patient selection

All patients underwent back surgery previously and had no indication for repeat surgery as determined by a

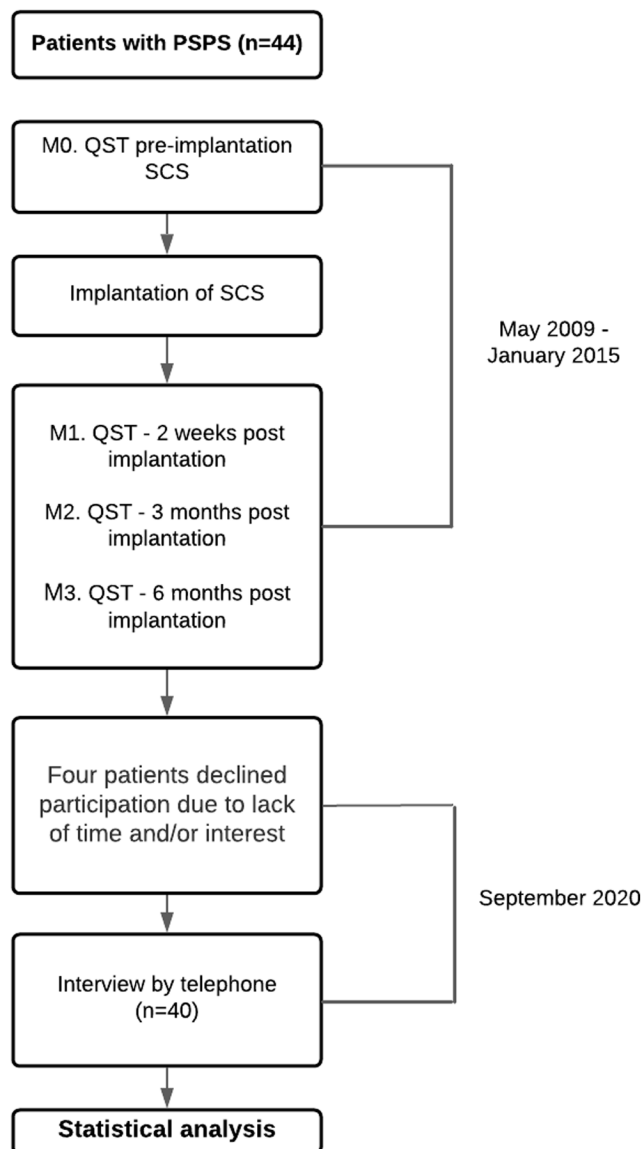


FIGURE 1 Flow-chart of study design. M0, Baseline QST measurement before implantation of the epidural lead of the SCS system; M1, The first QST post-operative measurement; M2, The second QST post-operative measurement; M3, The third QST post-operative measurement.

consultant neurosurgeon. Because of persistent neuropathic or nociceptive leg or back pain, they were seen by an anaesthesiologist-pain specialist, physical therapist and a clinical psychologist who, in consensus, decided that SCS would be an acceptable treatment modality after the failure of conservative treatment before. Patients received a permanent implant if a VAS decrease of at least 50% was seen after the 2-week trial phase. Thereafter follow-up of patients took place. The PSPS diagnosis was defined as lumbar spinal pain or radicular leg pain of unknown origin, either persisting following surgical intervention or beginning after surgical intervention for spinal pain that originated in the same anatomical location.

2.3 | SCS devices and implantation

Different SCS devices and stimulation strategies (conventional, burst, HF10) were used by the patients. The majority of the patients received conventional tonic treatment, which was the standard procedure available during the largest part of the study. The electrodes were all inserted under local anaesthesia and procedural sedation while using X-ray imaging. The electrode was positioned in the midline if one electrode was used, or parallel on both sides of the midline, when two electrodes were required. Most electrodes were positioned at the level of the T8-Th10. In those patients where back pain prevailed over leg pain, an HF-10 kHz or ‘burst’ SCS device was more frequently used after discussion in the treatment team. Usually, patients had a ‘dominant painful side’. During the operative procedure, it was possible in the majority of the patients to place the electrode in the midline or at the most painful side, measured by any occurring paraesthesias.

2.4 | QST

From May 2009 until January 2015, all QST measurements were performed at standardized timepoints during clinical admission by the same independent certified nurse specialist, who was not aware of the patient’s clinical response to SCS at the time of performing QST. The mechanical pressure and electrical stimulation were used in all QST sessions following the Nijmegen-Aalborg Screening QST (NASQ) protocol. The NASQ methodology as performed in this study has been extensively described by (Timmerman et al., 2014; Timmerman et al., 2018) and demonstrated in an instruction video by (van Helmond et al., 2018).

We retrieved the QST data before and after SCS implantation. Since we wanted to see whether QST changes had a clinical correlate, data were only used from the patients who participated in the neuromodulation interview.

The electrical sensory threshold (EST), pressure and electrical pain thresholds (PPT and EPT respectively) and electrical pain tolerance threshold (EPTT) were assessed. The fixed order in which QST was performed started with measuring the PPT followed by measuring the EST, EPT and EPTT.

A baseline QST measurement was executed before implantation of the epidural lead of the SCS system (M0). The first postoperative measurement (M1) was performed at the end of the 2-week SCS trial period, a few hours before the implantation of the battery for long-term treatment. Furthermore, the second postoperative measurement (M2) was performed at 3 months’ postimplantation of the permanent spinal cord stimulator. Finally, the

third postoperative measurement (M3) was performed at 6 month-follow-up. At least 1 h before the start of postoperative QST, the spinal cord stimulator was turned off to prevent a distracting effect of SCS.

2.5 | Sites of testing

QST was performed in six designated areas distributed over the body: bilateral clavicles (i.e., infra-midclavicular—C5 dermatome); bilateral iliac crests (middle part—L1 dermatome) and bilateral musculus rectus femoris (20 cm above the patella—L3 dermatome). The affected, most painful side of the body to be evaluated was noted as ipsilateral (ip.), while contralateral (co.) represents the less painful or unaffected side.

2.6 | PPT

During the study, two handheld electronic pressure algometers were used; initially a SenseLab AB Algometer (Somedic sales AB, Hörby, Sweden) and thereafter a Wagner pain test algometer FPX50 (Wagner, Greenwich, USA). The pressure algometer was placed on the skin of the designated areas with a 1.0 square centimetre probe under a 90° angle. Starting at zero Newton (N), the pressure was gradually increased by 5 N per second. For safety reasons, the maximum pressure was set at 200 N. Patients were instructed to say the word ‘now’ when they first perceived pain, indicating the PPT was reached.

2.7 | Electrical thresholds

Two self-adhesive ECG electrodes were placed adjacently at the marked spots on each testing site. The electrodes were placed at a distance of 4 cm from each other. The electrical QST apparatus (JNI Biomedical ApS, Klarup, Denmark) was used for delivering electrical stimulation to the electrodes. The tetanic stimulation was set on 100 Hz, 0.2 ms square waves with a ramping rate of 1 milliamperere per second (mA/s). The maximum current was set to 50 mA due to safety reasons. The electrical thresholds were derived three times and determined for each designated area by averaging the three threshold assessments per test site.

2.8 | EST

The patients were instructed to press and hold a button on the electrical QST apparatus and, release the button to

stop electrical stimulation as soon as they perceived any electrical sensation.

2.9 | EPT

The same methodology as during the EST measurement was adhered, but patients were instructed to release the button when they first perceived pain.

2.10 | EPTT

Again the same methodology as during the EST measurement was applied, but patients were instructed to release the button when the pain became unbearable. As such, the patient was able to withdraw from the stimulation at any moment. There were at least 15 s between the individual measurements to prevent possible wind-up.

2.11 | Neuromodulation interview

A semi-structured clinical interview was performed by telephone (September 2020) to evaluate pain scores, the use of analgesics, pain intervention history and quality of life. The interview protocol was judged by the Human Research Committee region Arnhem—Nijmegen, The Netherlands (WMO), as not burdensome for patients (CMO-number: 2020–6983). Due to COVID-19 restrictions, the decision was made to obtain verbal informed consent by telephone and the agreement was noted in the hospitals' medical records software system, Epic Systems Corporation (EPIC, Verona, Wisconsin, USA). The interview was recorded and stored on a secured database only accessible by the research team members. Data from the interviews were directly stored in a cloud-based Electronic Data Capture platform (CastorEDC, Amsterdam, the Netherlands) when performing the telephonic interview. A digital version of the interview was made in CastorEDC. Data from EPIC were imported into CastorEDC to complete the dataset. The complete interview can be found in Dutch as well as translated to English in [supplement A](#).

2.12 | Numeric pain rating scores

Patients were asked to rate their lowest, average and highest level of pain for the past month in a NRS (0 = no pain vs. 10 = worst pain imaginable). In addition, patients were asked if the pain they were experiencing in the past month was acceptable.

2.13 | Analgesics and other drugs

Patients were questioned to disclose their present use of analgesics, including paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids and other analgesics. Furthermore, the use of other drugs such as antidepressants, anti-epileptics and benzodiazepines to treat chronic pain was questioned. Dosages and frequency of use were recorded per drug. Additionally, patients were asked if the use of analgesics had changed after receiving SCS.

2.14 | Other pain treatments

Patients were requested to report further pain treatments (low back surgery, nerve blocks, rehabilitation, psychological treatment and physical therapy) other than SCS in the periods before and after receiving SCS.

2.15 | Quality of life

Questions were asked to indicate patients' QoL. These questions covered the topics: (voluntary) work, hobbies, domestic tasks, social activities, quality of sleep and personal care. Additionally, patients were asked to rate their QoL before SCS implantation and during the past month, both on a NRS (0 = worst QoL imaginable vs. 10 = best QoL imaginable). The questions regarding QoL were self-formulated based on the seven dimensions of the pain disability index (Tait et al., 1990). The dimension of sexual behaviour was left out to keep the interview load capacity low for patients.

2.16 | Effect of SCS treatment and satisfaction

Patients were given the following sentence and were asked to fill in the blank with one of the five multiple-choice options. '*Due to SCS therapy, my pain complaints: greatly deteriorated, slightly deteriorated, did not change, slightly improved and greatly improved*'. They also reported their satisfaction with the SCS treatment on a NRS of (0 = absolutely not satisfied vs. 10 = absolutely satisfied). In addition, patients were asked if they would recommend SCS to an acquaintance, loved one or family member with similar complaints.

2.17 | Statistical analysis

The normal distribution of data was assessed through normality plots and Shapiro–Wilk tests. Since the data were non-normally distributed, all analyses were performed in a

non-parametric way. We calculated and compared the medians with Inter Quartile Ranges [IQR] of PPT, EST, EPT and EPTT. A Friedman test was performed to compare the results on four different measurement moments (M0, M1, M2 and M3). A Dunn–Bonferroni post hoc test was performed to adjust for multiple testing. To analyse the interview data, descriptive statistics were used and calculated in n values and in percentages. As coefficient of concordance, the Kendall's W was used to calculate the results between subjects. Kendall's W ranges from 0 to 1, in which 1 means that for all subjects, the outcomes were ranked in the same way. Moreover, a Kendall's W of 0.1 means a small effect, 0.3 means a moderate effect and 0.5 or higher means a strong effect. All data were analysed using SPSS® Statistics for Windows, Version 28.0 (IBM Corp. Armonk, New York, United States of America). A p -value of ≤ 0.05 was considered to be statistically significant. Collected study data were stored in CastorEDC and is accessible by members of the research team.

3 | RESULTS

The four patients that declined participation mentioned lack of time or interest as reasons for declining participation. Forty patients, 23 males and 17 females, were included in this study. The median (IQR) age at implantation was 49.5 (40.5–59.0). All patient characteristics are shown in [Table 1](#).

3.1 | QST

[Table 2](#) shows the median pressure pain thresholds and the median of three different electrical thresholds at different QST measurement sites and at the different assessment moments. The data showed an overall increase in the medians of the pain and tolerance thresholds (PPT, EPT and EPTT) through time. However, there was, based on Kendall's W, only a small effect at maximum. Additionally, the median electrical and mechanical thresholds were compared at different assessment moments (M0 vs. M1/M2/M3) and shown in [Table 2](#).

3.2 | M0 versus M1

A statistically significant increase in the EPT was seen in the contralateral rectus femoral muscles ($p = 0.049$).

3.3 | M0 versus M2

Statistically significant increases in the QST parameters (EPT and EPTT) on the contralateral clavicle were

TABLE 1 Characteristics of included patients (interview data)

Characteristics	Total population (n = 40)	Male (n = 23)	Female (n = 17)
Age at day of implant median (IQR)	49.5 [40.5–59.0]	50.0 [42.0–59.0]	47.0 [37.0–60.0]
Technique of SCS—n (%) ^a			
Conventional	31 (77.5%)	18 (78.3%)	13 (76.5%)
Burst	1 (2.5%)	1 (4.3%)	0 (0.0%)
HF10	8 (20.0%)	4 (17.4%)	4 (23.5%)
NRS pain—median (IQR)			
Lowest	3 [2.0–5.0]	3 [2.0–5.0]	2 [1.5–4.5]
Average	5 [3.25–6.0]	5 [4.0–6.5]	5 [2.50–5.5]
Highest	7 [6.0–8.0]	7 [7.0–8.0]	7 [5.0–8.0]
Drugs—n (%)			
Analgesics	28 (70.0%)	15 (65.2%)	13 (76.5%)
Antidepressants	16 (40.0%)	6 (26.1%)	10 (58.8%)
Antiepileptics	9 (22.5%)	5 (21.7%)	4 (23.5%)
Benzodiazepines	7 (17.5%)	2 (8.7%)	5 (29.4%)
Analgesics—n (%)			
Paracetamol	19 (47.5%)	11 (47.8%)	8 (47.1%)
NSAIDs	14 (35.0%)	9 (39.1%)	5 (29.4%)
Tramadol	6 (15.0%)	3 (13.0%)	3 (17.6%)
Morphine / fentanyl / oxycodone	13 (32.5%)	6 (26.1%)	7 (41.2%)
Cannabinoids	2 (5.0%)	1 (4.3%)	1 (5.9%)
Frequency analgesics use—n (%)			
Daily use	25 (62.5%)	13 (56.5%)	12 (70.6%)
Incidental use	3 (7.5%)	2 (8.7%)	1 (5.9%)

Abbreviations: HF10, 10-kHz high frequency; IQR, interquartile range; n, number of patients; NRS, numeric rating scale; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs.

^aLast used technique of SCS.

discovered ($p = 0.012$, $p = 0.016$). Furthermore, the PPT statistically significantly increased on the contralateral iliac crest ($p = 0.003$).

3.4 | M0 versus M3

A statistically significant increase in the EPTT was seen on the contralateral clavicle ($p = 0.014$). Statistically significant increases in the QST parameters (PPT and EPT) on the ipsilateral iliac crest were discovered ($p = 0.031$, $p = 0.042$). Furthermore, the PPT and EPTT statistically significantly increased on the contralateral iliac crest ($p = 0.022$, $p = 0.010$).

3.4.1 | Neuromodulation interview

All patients completed the interview. The follow-up period was at median [IQR] 8 [6–9] years and ranged (min-max) from 5 to 11 years of postimplantation.

3.4.2 | Numeric pain rating scores

Patients reported the least, average and worst pain over the last month at a median [IQR] as 3 [2–5], 5.00 [3.25–6] and 7 [6–8] respectively. The reported pain concerning PSPS was acceptable for 70% (28/40 patients) and not acceptable in 30% (12/40 patients). The reported change in pain complaints after receiving SCS was reported as greatly improved (62.5%; 25/40 patients); slightly improved (27.5%; 11/40 patients) and as no change (10%; 4/40 patients).

3.5 | Analgesics and other drugs

Prior to SCS, all patients used analgesics for their pain concerning PSPS. During the interviews, 28 out of 40 patients (70%) disclosed that they still used some sort of analgesics for their pain concerning PSPS (daily use 89.3%; 25/28 and incidental use 10.7%; 3/28). Twenty-four out of these 28 patients reported a decrease in the use of analgesics after

TABLE 2 Results of the quantitative sensory testing (QST)

	Measurement										N	Pairwise comparison				Friedman's two-way analysis of variance by ranks	Kendall's W
	M0		M1		M2		M3		M0 vs. M1			M0 vs. M2		M0 vs. M3			
	N	Median [IQR]	N	Median [IQR]	N	Median [IQR]	N	Median [IQR]	Sig.	Adj. Sig.		Sig.	Adj. Sig.	Sig.	Adj. Sig.		
Clavicle ip	PPT	40	33.1 [21.5-59.2]	36	50.0 [25.5-62.1]	33	44.3 [26.8-70.6]	36	48.6 [27.7-69.2]	0.424	0.036	0.021	0.067	0.080			
	EST	40	2.2 [1.7-2.9]	37	2.2 [1.6-3.0]	34	2.0 [1.8-3.0]	35	2.2 [1.7-3.2]	1.000	0.214	0.129	0.816	0.010			
	EPT	40	5.6 [4.3-9.0]	37	7.0 [4.6-9.4]	34	7.1 [4.8-9.3]	35	7.0 [4.7-10.1]	0.882	1.000	0.481	0.315	0.039			
Clavicle co	EPTT	40	8.4 [6.4-13.4]	37	10.6 [8.3-14.0]	34	10.6 [8.2-13.6]	35	10.2 [7.9-14.0]	0.250	0.046	0.099	0.203	0.051			
	PPT	40	40.5 [25.6-51.6]	36	41.6 [26.8-62.7]	33	47.8 [31.4-69.5]	36	47.5 [33.2-68.4]	0.841	0.089	0.036	0.042	0.091			
	EST	40	1.9 [1.4-2.5]	37	1.9 [1.4-2.7]	34	1.9 [1.4-2.4]	35	2.1 [1.6-3.0]	0.881	0.582	0.424	0.740	0.014			
Iliac crest ip	EPT	40	5.4 [4.0-8.6]	37	5.6 [4.3-9.9]	34	6.8 [4.8-9.1]	35	7.0 [5.3-9.5]	0.064	0.002	0.024	0.015	0.116			
	EPTT	40	9.0 [7.0-11.5]	37	10.0 [7.2-13.1]	34	11.0 [8.5-13.3]	35	11.1 [9.0-13.1]	0.307	0.016	0.014	0.006	0.137			
	PPT	40	26.4 [15.9-43.6]	36	39.4 [28.4-47.6]	33	32.5 [26.8-57.2]	35	43.3 [24.6-63.9]	0.093	0.042	0.005	0.038	0.097			
Iliac crest co	EST	40	2.5 [1.9-3.5]	36	2.4 [1.6-3.4]	34	2.5 [1.6-3.0]	35	2.8 [2.1-3.5]	0.509	0.760	0.093	0.346	0.038			
	EPT	40	5.0 [4.1-8.2]	36	6.5 [4.0-9.3]	34	5.9 [5.0-8.1]	35	6.4 [5.2-11.0]	0.115	0.416	0.007	0.048	0.091			
	EPTT	40	7.5 [4.5-11.8]	36	9.3 [7.3-12.6]	34	8.6 [6.3-14.8]	35	9.1 [7.3-15.2]	0.075	0.127	0.075	0.219	0.051			
	PPT	40	31.5 [23.0-41.1]	36	35.9 [29.6-51.2]	33	37.7 [26.0-59.2]	36	40.2 [29.2-51.4]	0.016	<0.001	0.004	0.003	0.157			
	EST	40	2.4 [1.8-2.8]	36	2.5 [2.1-3.4]	34	2.3 [1.0-2.5]	35	2.6 [2.1-3.2]	0.098	0.003	0.022	0.087	0.075			
									0.22	0.053	0.060	0.359	0.087				

(Continues)

TABLE 2 (Continued)

	Measurement						N	Pairwise comparison						Friedman's two-way analysis of variance by ranks		Kendall's W
	M0		M1		M2			M3		M0 vs. M2		M0 vs. M3		Sig.	Adj. Sig.	
	Median [IQR]	N	Median [IQR]	N	Median [IQR]	N		Median [IQR]	N	Sig.	Adj. Sig.	Sig.	Adj. Sig.			
EPT	40	36	34	35	29	0.084	0.334	0.029	0.136	0.064	0.136	0.029	0.173	0.136	0.064	
	5.3 [3.8-8.5]	6.2 [4.4-9.4]	6.1 [4.4-9.1]	6.8 [5.4-8.9]		0.503	1.000	0.173								
EPTT	40	36	34	35	29	0.042	0.186	0.002	0.014	0.121	0.014	0.002	0.010	0.014	0.121	
	8.2 [5.7-12.6]	9.6 [6.6-13.4]	8.0 [6.0-12.6]	10.8 [7.6-13.7]		0.252	1.000	0.010								
m. rectus fem ip	38	35	33	35	27	0.833	0.292	0.527	0.726	0.016	0.726	0.292	1.000	0.527	0.726	
	47.2 [25.7-74.7]	53.7 [42.8-92.5]	64.0 [41.4-86.4]	58.5 [42.1-91.4]		1.000	1.000	1.000								
EST	40	36	34	34	28	0.836	0.301	0.408	0.319	0.042	0.319	0.301	1.000	0.408	0.319	
	6.6 [4.3-7.9]	6.2 [4.3-8.0]	7.1 [5.2-8.2]	5.7 4.6-7.9]		1.000	1.000	1.000								
EPT	40	36	34	35	29	0.684	0.360	0.127	0.453	0.030	0.453	0.360	0.763	0.127	0.453	
	9.6 [6.5-12.4]	10.4 [7.0-12.8]	10.3 [8.2-12.8]	11.5 [8.3-14.8]		1.000	1.000	0.763								
EPTT	40	36	34	35	29	0.576	0.104	0.022	0.085	0.076	0.085	0.104	0.622	0.022	0.076	
	11.5 [8.9-19.8]	13.1 [9.7-17.7]	13.1 [11.3-19.5]	15.0 [10.3-20.2]		1.000	0.622	0.133						0.133	0.076	
m. rectus fem co	40	36	32	36	30	0.147	0.211	0.271	0.468	0.028	0.468	0.211	1.000	0.271	0.468	
	54.1 [39.1-74.8]	53.6 [45.2-93.7]	63.9 [42.6-83.9]	63.3 [42.3-101.1]		0.882	1.000	1.000						1.000	0.028	
EST	40	36	33	35	29	0.222	0.799	0.959	0.450	0.030	0.450	0.799	1.000	0.959	0.450	
	6.2 [4.1-7.3]	6.1 [4.6-8.1]	5.6 [4.6-8.0]	6.3 [4.5-7.7]		1.000	1.000	1.000						1.000	0.030	
EPT	40	36	33	35	29	0.008	0.060	0.115	0.086	0.086	0.086	0.060	0.359	0.115	0.086	
	9.4 [7.0-12.1]	10.3 [6.4-13.2]	9.4 [7.1-13.3]	9.8 [7.9-13.0]		0.049	0.359	0.689						0.689	0.086	
EPTT	40	36	33	35	29	0.029	0.029	0.033	0.068	0.082	0.068	0.029	0.173	0.033	0.068	
	11.1 [9.3-16.5]	13.7 [8.9-16.9]	14.4 [10.4-16.9]	14.2 [9.4-17.0]		0.173	0.173	0.196						0.173	0.082	

Note: All p values showed in bold are statistically significant ($p \leq 0.05$).

Abbreviations: Adj, Sig, Adjusted Significance based on a Bonferroni-Dunn post hoc test to adjust for multiple testing; co, contralateral; EPT, Electrical pain threshold in milliamper (Median [IQR]); EPTT,

Electrical pain tolerance threshold in milliamper (Median [IQR]); EST, Electrical sensory threshold in milliamper (Median [IQR]); ip, ipsilateral; PPT, Pressure pain threshold in Newton (Median [IQR]); M0/1/2/3,

Measurement 0/1/2/3; m. rectus fem, musculus rectus femoris.

receiving SCS therapy (85.7%). Regarding the other four patients, two disclosed no change in analgesic drug intake (7.1%; 2/28), whereas the remaining two reported an increase (7.1%; 2/28). Postoperatively, 12 out of 40 patients did not use any analgesics for their pain-related to their PSPS (30%). Table 1 shows the medication use concerning PSPS.

Pain interventions other than SCS, both before and after implantation, are shown in Table 3.

3.6 | Quality of life

The reported QoL (NRS 0–10) before the start of SCS therapy was at a median of 3 [2–5] compared to 8 [7–8] after receiving SCS therapy. Enhanced quality of sleep was reported by 23 out of 40 patients (57.5%), compared to no change in 13 patients (32.5%; 13/40) and worse quality of sleep in three patients (7.5%; 3/40). In one patient (2.5%; 1/40), changes in the quality of sleep were not determined.

Furthermore, 31 out of 40 patients reported an increase in performing their daily activities with SCS (77.5%). Fifteen patients could still fully pursue their hobbies (37.5%; 15/40), another 19 patients partially (47.5%; 19/40), while six patients reported no improvement (15.0%; 6/40). Furthermore, 16 patients participated actively in social activities with family and friends (40.0%; 16/40), whereas in 19 this was partial (47.5%; 19/40) and in five no participation was possible (12.5%; 5/40).

In addition, 15 patients managed to do their household tasks independently (37.5%; 15/40) versus partially in 21 patients (52.5%; 21/40). Four patients failed to do so at all (10.0%; 4/10). Thirty-two patients reported that they could

still be active in the field of personal care (80.0%; 32/40) versus partially in six (15.0%; 6/40) and not being able in two patients (5.0%; 2/40). Data regarding the QoL are shown in Table 4.

3.7 | Effect of SCS treatment and satisfaction

Thirty-eight out of 40 patients (95.0%) said that they would undergo SCS implantation again if they had the option to do so. Common reasons included pain relief, decrease in opioid use, more social participation, increased physical activity, enhanced sleep and a better QoL. The two patients (5.0%) that would not undergo implantation again, mentioned insufficient pain relief of SCS as their main reason. One of these two patients also mentioned a history of postoperative complications as a secondary reason for not undergoing SCS implantation again. Moreover, 39 out of 40 patients reported that they would recommend the neurostimulator to an acquaintance, loved one or family member if they had similar complaints (97.5%). One patient would not have recommended SCS as it failed to sufficiently cover its painful area. Finally, 39 patients rated their overall satisfaction concerning SCS treatment at median with an 8 [7–10]

4 | DISCUSSION

The objectives of this study were to evaluate the changes in the subjective sensory responses using QST and to assess the long-term effect of SCS therapy on multiple outcomes

TABLE 3 Pain interventions

	Total population (n = 40)	Male (n = 23)	Female (n = 17)
Re-operation after SCS implantation—n (%)	3 (7.5%)	2 (8.7%)	1 (5.9%)
Nerve block after SCS implantation—n (%)	10 (25.0%)	5 (21.7%)	5 (29.4%)
Rehabilitation treatment—n (%)	21 (52.5%)	12 (52.2%)	9 (52.9%)
before SCS	6 (15.0%)	4 (17.4%)	2 (11.8%)
after SCS	7 (17.5%)	4 (17.4%)	3 (17.6%)
both	8 (20.0%)	4 (17.4%)	4 (23.5%)
Psychological treatment—n (%)	14 (35.0%)	9 (39.1%)	5 (29.4%)
before SCS	3 (7.5%)	1 (4.3%)	2 (11.8%)
after SCS	6 (15.0%)	4 (17.4%)	2 (11.8%)
both	5 (12.5%)	4 (17.4%)	1 (5.9%)
Physical therapy ^a —n (%)	14 (35.0%)	8 (34.8%)	6 (35.3%)

Abbreviation: n, number of patients.

^aReceived in the past year.

TABLE 4 Quality of life

Questions	Answers (%) (n = 40)		
	Yes	Partially	No
Can you still pursue your hobbies?—n (%)	15 (37.5%)	19 (47.5%)	6 (15.0%)
Can you still carry out your household tasks independently?—n (%)	15 (37.5%)	21 (52.5%)	4 (10.0%)
Can you actively participate in social activities with family and friends?—n (%)	16 (40.0%)	19 (47.5%)	5 (12.5%)
Can you be active in the field of personal care yourself?—n (%)	32 (80.0%)	6 (15.0%)	2 (5.0%)

Abbreviation: n, number of patients.

in patients receiving SCS therapy to treat PSPS. This study showed an increase in pain and tolerance thresholds (PPT, EPT, EPTT) after SCS implantation in patients with PSPS. Furthermore, the changes we found in quality of life long-term SCS follow-up are impressive. Additionally, we found an overall decrease in the use of analgesics and pain complaints after the start of SCS.

Also, enhanced quality of sleep and better performance of daily activities were seen in the majority of patients. All but one patient reported willingness to undergo SCS implantation again if they had the option to do so.

The QST data following the initiation of SCS illustrate a diverse pattern of changes in sensory, pain and tolerance thresholds. Since the changes occurred at different follow-up moments, it might be hypothesized that the nervous system of a particular patient requires a certain amount of time to adjust to this novel situation due to the influence by the implanted spinal cord stimulator (Ryan et al., 2019). Additionally, SCS programming was performed during outpatient visits as an iterative process, allowing ongoing fine-tuned adjustments of care (Sheldon et al., 2020).

Rarely, the optimum stimulation parameters are found in one session. These adjustments, therefore, can both affect SCS therapy and sensory, pain and tolerance thresholds over time. In our opinion, comparing our pre-implantation measurement versus the last QST measurement (M0 vs. M3) is most representative regarding the overall and long-term effect of SCS on sensory, pain and tolerance thresholds in these patients.

Interestingly, we also found an influence of SCS on the contralateral side (non-painful side). During SCS, there were statistically significant increases in pain and tolerance thresholds (PPT, EPT, EPTT) from the electrical and mechanical pressure stimuli on the less to non-painful, contralateral side suggesting that SCS has a generalized bilateral effect. In the clinical situation, this seems comparable with a medial placement of the electrode on the spinal cord, resulting in alleviating painful sensations bilaterally (Hunter & Ashby, 1994). Therefore, it is plausible

that there is an effect of both central, neuroplastic supraspinal as well as spinal changes, leading to an increased pain and tolerance threshold during electrical and mechanical pressure stimuli on the non-painful side of the body unrelated to the perceived paresthesias. These experienced paresthesias suggest that afferent pathways are tonically activated, and thereby changes in sensory thresholds could be anticipated.

A systematic review by (Sdrulla et al., 2018) highlights five studies that also found an increase in EST or EPT after receiving conventional SCS therapy. Additionally, EST and EPT were increased in patients implanted chronically compared with those receiving short-term stimulation (Doerr et al., 1978). Moreover, an increase in EPTT was seen in trial patients who ultimately went on to implantation but not in trial non-responders (Mironer & Somerville, 2000). Furthermore, this systematic review (Sdrulla et al., 2018) showed no changes in PPT after receiving conventional SCS therapy when looking at the studies published after 1990. In a study by (Youn et al., 2015), the PPT increased in patients after receiving high-frequency spinal cord stimulation. Nevertheless, It is difficult to draw clear conclusions from the studies analysed by (Sdrulla et al., 2018) due to diverse pain aetiologies, low subject numbers, acute versus chronic SCS state, differences in SCS lead locations (epidural vs. subdural), various stimulation frequencies and QST protocols.

The increase in quality of life, high treatment satisfaction and increase in function found in this study display the often cited beneficial effect of SCS in the patient's everyday life (Kapural et al., 2017). In line with this, a study performed by (Kumar et al., 2007) also showed enhanced health-related quality of life on seven of the eight dimensions of the SF-36 ($p \leq 0.02$) and superior function (ODI, $p < 0.001$) in patients with SCS compared to conservative medical management (CMM).

What also illustrates this high satisfaction with SCS therapy is the fact that almost all patients reported to undergo SCS implantation again if they had the option to do so. High treatment satisfaction and an overall decrease in

the use of analgesics and pain complaints are the major factors that determine the success of SCS therapy.

In our study, a decrease in the use of analgesics and pain complaints was seen. In a systematic review and meta-regression analysis (Taylor et al., 2014), the mean level of pain relief across the studies was 58% (95% confidence interval, 53%–64%) during an average follow-up of 24 months. A study by (North et al., 2005) reported an 87% decrease in analgesic use. Neither of them reported functional improvement as a result of SCS. Unfortunately, there were not enough patients with PSPS available to allow a perform adequate analyses exploring potential associations between QST responses and subjective clinical outcomes.

Changes in QST due to a pain-relieving intervention can be important for daily clinical practice as well as for research purposes during the follow-up of the patient. A recent qualitative study (Witkam et al., 2021) showed that pain reduction per se is not the only outcome patients are looking for; reductions in pain medication, improvement of sleep and QoL are also important domains that patients mention as possible positive effects of SCS therapy. Our study design gives us the opportunity to look at the value of SCS for each individual patient, even if the pain relief is not optimal. Our finding, that even the majority of the patients that reported their change in pain complaints following SCS as slightly improved or not changed at all, also had a high treatment satisfaction, underscores this phenomenon.

The strength of our study is that the QST sample concerned a large homogenous (PSPS) group of patients with a long-term follow-up period that enclosed the preoperative and longer term postoperative follow-up phase. Furthermore, one consistent QST protocol was performed at four different timepoints allowing a dynamic comparison through time by the same certified nurse specialist. Additionally, patients were interviewed by telephone by a researcher not being associated with the treatment team, which allowed patients to speak more freely. Finally, this live interview allowed a better picture of the patient's perspective in comparison with an online questionnaire because of the option to keep asking (in-depth) questions, which cannot be done in a standard, rigid format.

Although most patients received conventional SCS treatment, a limitation of this study was that burst stimulation, as well as 10-kHz High-Frequency (HF10), were also used, which might have led to other effects on the nociceptive system. Furthermore, recall bias was likely to occur due to the long interval between the moment of implant and the neuromodulation interview. Changes in the medication use during follow-up and other aspects of the pain treatment trajectory might have influenced the changes in the QST measurements. However, this could

not be discriminated from the possible neurophysiological changes in time, as is a result of a 'real-life' situation. We have not been able to correct for these factors.

Furthermore, five patients who got their SCS explanted were not invited in the study. This could have led to some form of selection bias. Finally, another limitation is the absence of a control group. This made it difficult to correct for non-specific, anti-nociceptive effects such as the placebo effect. However, using a PSPS control group means depriving chronic pain patients of a possibly effective pain treatment which we considered to be unethical.

We showed in these patients that not only pain relief but also many other changes (analgesic use, sleep quality, ADL) contribute to patient satisfaction and QoL. Therefore, ideally, a multidimensional scoring system (e.g. questionnaires, QST, physical testing and patient interviews) should be designed and validated instead of strictly adhering to a unidimensional pain intensity scale as a definition of a successful treatment outcome. For future studies, it would be desirable to be able to use the pre-operative QST outcomes as a predictor of a positive, longer lasting effect of SCS, thereby increasing the efficacy and cost-effectiveness of this treatment.

AUTHOR CONTRIBUTIONS

The study was designed by RvD, YP and HT. YP assisted in the data collection. YP and RvD reviewed the medical records and verified the PSPS diagnoses. Data analysis was performed by YP under the supervision of HT. YP, HT and RvD drafted the manuscript with substantive intellectual input from KV and JW. All authors discussed the results, critically reviewed the manuscript and approved the final version.

CONFLICT OF INTEREST

None of the authors have any conflicts of interest.

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SUPPORTING INFORMATION

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