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Neuropathic Pain Medication Use Does Not Alter Outcomes of Spinal Cord Stimulation for Lower Extremity Pain

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Abstract

Introduction—Spinal cord stimulation (SCS) for the treatment of lower extremity pain is believed to be the result of increased activity in the descending inhibitory and decreased activity in the ascending excitatory tracts. Evidence suggests that the analgesia afforded by SCS may be altered using certain neuropathic pain medications that also modulate neurotransmitters in these sensory tracts. We hypothesize that neuropathic pain medications may alter the response to SCS therapy.

Methods—One hundred and fifteen subjects undergoing SCS therapy for lower extremity pain were retrospectively examined. The pharmacologic profile, including stable use of neuropathic and opioid medications, were recorded. Three separate logistic regression models examined the odds ratio of primary outcomes; a successful SCS trial, a 50% decrease in pain or a 50% reduction in opioid use one year after implant.

Results—Neither the use of opioids or neuropathic pain medications were associated with changes in the odds of a successful SCS trial or a 50% pain reduction. A higher dose of chronic opioids use prior to a trial was associated with greater odds of having a 50% reduction in opioid use following implant. OR 1.02, 95% CI 1.01–1.02, p -value < 0.01).

Conclusions—The use of neuropathic pain medications did not change the odds of either a successful SCS trial, or of experiencing a 50% reduction in pain at one year. The association

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Authorship Statements

Dr. Maher conceived and designed the study. Drs. Maher, Bicket, Doshi, Hanna, Ahmed Chaves-Martins, and Zhang conducted the study, including review of medical information, data collection, and data analysis. Dr. Maher, Bicket, Doshi, Hanna, Ahmed Chaves-Martins, and Zhang prepared the manuscript draft. Drs. Bicket and Zhang were instrumental in statistical analysis. All authors approved the final manuscript. Drs. Maher, Bicket, Doshi, Hanna, Ahmed Chaves-Martins, and Zhang had complete access to the study data.

between higher opioid doses and greater odds of a 50% reduction in opioid use may be the reflective of SCS's ability to reduce opioid reliance in chronic pain patients.

Keywords

Chronic pain; epidural; failed back surgery syndrome; low back pain; neurostimulation

INTRODUCTION

Spinal cord stimulation (SCS) has been successfully utilized in the treatment of a diverse and increasing number of painful conditions including failed back surgery syndrome (FBSS), complex regional pain syndrome (CRPS), diabetic peripheral neuropathy (DPN), and radiculopathy without evidence of a disk herniation (1–3). As the technology is refined and the indications continue to expand, there is a need to better understand the mechanism of action and prognostication of SCS therapy outcomes.

The physiologic basis for SCS therapy has not been fully delineated but is believed to be, at least in part, due to electrically-induced modulation of spinal neurochemistry at the level of the integration and modulation neural circuitry, including the wide-dynamic range (WDR) neurons. SCS therapy increases release of gamma-aminobutyric acid (GABA), acetylcholine (ACh), serotonin (5-HT), and noradrenaline (NA) and decreases release of excitatory neurotransmitters, such as glutamate and aspartate (4–6). These findings suggests that SCS therapy augments inhibitory pathways in a feed-forward mechanism, and that pharmacological manipulation of these signaling pathways may present an opportunity to augment the clinical effects of SCS.

Previously published work suggests that SCS therapy may be amenable to pharmacologically modulated (5–9). In a rodent model of neuropathic pain, intrathecal administration of muscarinic antagonists, specifically inhibiting M_1 , M_2 , and M_4 receptors, decreased the observed efficacy of SCS-derived analgesia (5). Enhancement of SCS therapy in rodent models resulted from intrathecal administration of milnacipran, a selective serotonin/noradrenaline reuptake inhibitor (SNRI), and amitriptyline, a tricyclic antidepressants (TCA) that inhibits reuptake of 5-HT, NA, and ACh, but not fluoxetine, a selective serotonin reuptake inhibitor (SSRI) (9). The use of gabapentinoids, either pregabalin or gabapentin, decreased allodynia and potentiated the effects of SCS induced analgesia observed in a rodent model of neuropathy (10). A prospective randomized trial in subjects deriving unsatisfactory pain relief from implanted SCS devices successfully demonstrated that single injections of intrathecal baclofen, a $GABA_B$ receptor agonist, or intrathecal clonidine, an α_2 receptor agonist, increased analgesia (8). The role of opioids in modulation of SCS outcomes has not been firmly established. However, given the ongoing opioid crisis, reduction in opioid requirements is an increasingly prominent goal for SCS therapy.

Different degrees of analgesia derived from SCS therapy may be associated with the use of concomitant neuropathic pain medications that increase neurotransmission in the inhibitory pain pathways. In this retrospective analysis, we seek to characterize the effect of neuropathic pain medications use on SCS outcomes in subjects with lower extremity pain.

Outcomes that were examined included the odds of a successful SCS trial (greater than 50% pain relief), odds of 50% decrease in NRS-11 of baseline compared to one year following implant, and odds of a 50% reduction in opioid analgesic use of baseline compared to one year. This study will also provide insight into SCS's mechanism of action. The data may also allow for prognostication of SCS outcomes based on a subject's pharmacological profile. We hypothesize that the chronic use of a neuropathic pain medications, including SNRIs, anti-epileptics and TCA's, will augment SCS therapy and that the chronic use of SSRIs, opioids or benzodiazepines will not enhance SCS therapy.

METHODS

The Massachusetts General Hospital (MGH) Institutional Review Board approved the study protocol. Retrospective data was obtained from consecutive subjects who were treated at a single, urban, academic tertiary level pain management center between 2005 and 2015. Male and female subjects between the ages of 18 and 80 were included in analysis. All subjects who underwent a trial of SCS for treatment of a lower extremity pain syndrome were included in the analysis. Pain syndromes that met criteria for an SCS trial and inclusion in these analyses are CRPS, FBSS, DPN, and vascular claudication. Subjects with mixed axial and lower extremity pain or pure axial pain were excluded from analysis, as these pain conditions may have a different response rate to SCS when compared with pure lower extremity pain (1–3). All subjects were interviewed and examined by a board-certified pain physician in an outpatient clinic and confirmed to have a diagnosis responsive to treatment with SCS. All subjects underwent standardized medical, radiographic, and psychological evaluation to identify contraindications to implanted SCS hardware.

Subjects underwent a standardized SCS trial protocol. In an outpatient setting, subjects were placed in the prone position and had either one or two 8-contact dorsal column leads placed percutaneously in the dorsal epidural space under fluoroscopic guidance. The leads were then fixed to the skin with adhesive and attached to an external control unit as per the manufacturer's guidelines. No subject underwent a trial using an implanted lead technique. SCS systems were all tonic stimulation systems manufactured by Boston Scientific (Marlborough, MA, USA), St. Jude's Medical (St. Paul, MN, USA) or Medtronic (Dublin, Ireland). Typical tonic dorsal column stimulation settings included a pulse width between 100 and 400 msec and a rate usually between 20 and 120 Hz. The amplitude for tonic stimulation was individualized to subject perception of comfortable paresthesias. High frequency SCS (i.e. programmed rates - 1000 Hz) or burst SCS options were not clinically utilized during the study period and were not included in analysis. Following a trial period, percutaneous leads were removed. Subjects were evaluated for the degree of pain relief experienced. If subjects reported greater than 50% reduction in their pain, then implantation of a permanent SCS system by the same pain physician proceeded. All patients who underwent implantation of a SCS demonstrated at least a 50% reduction in pain with SCS trial. Subjects were then followed in the pain clinic for evaluation and reprogramming of the permanent SCS as necessary. Follow-up appointments were made at the following time points following permanent implantation: One week, four weeks, two months, three months, six months, and 12 months. This follow-up schedule is the standard practice at the clinic from which the data was collected.

Demographic information recorded in the chart for subjects included age, gender, and body mass index. Characteristics of pain that were recorded included laterality, pain diagnosis (if firmly established, e.g., the Budapest Criteria for CRPS), duration of pain, number of surgeries the subject had on the affected limb and pain severity as recorded on an 11-point numerical rating scale (NRS-11) on the day of placement of SCS trial leads. Pain descriptors were also recorded, including “sharp,” “burning,” “achy,” and “electric.” Subjects were allowed to define their pain with multiple descriptors. Complications arising from the device, such as hardware malfunction or infection, were also recorded.

The pharmacological profile recorded immediately prior to placement of SCS trial leads included medication name, classification, and total daily dose. All subjects remained on the same pain medication regimen during the interval between trial lead placement and implantation of a permanent SCS system. Following permanent implantation of the SCS system, medications were adjusted according to the evolving needs of the subject. Opioid medications were recorded and converted to the equivalent daily dose of oral morphine (MEQ) using previously published conversion ratios (11,12). Prior publications suggest that opioid utilization patterns in chronic pain populations are nonnormally distributed (13,14). To address nonnormality, the number and percent of patients using any opioids and the median and interquartile range of opioids use is reported. Some patients were allowed to start opioid therapy following implantation, which was continued long-term in some cases. Nonparametric tests were used to analyze opioid data. Subjects were not enrolled in an opioid reduction programs or formally encouraged to decrease opioid use following implantation as part of standard SCS therapy at the time of therapy. The types of neuropathic pain medications were recorded including tricyclic TCA’s, SSRI’s, SNRI’s, gabapentin or pregabalin, baclofen, and benzodiazepines. Tramadol, which is pharmacologically similar to both a TCA and an opioid, was counted as both an opioid and a TCA. For each medication, a binary variable was used to indicate whether a patient took it. Included subjects were on stable medication regimens for at least three months prior to an SCS trial. The subject’s medication regimen was then followed at the scheduled follow-up appointments.

Three separate multivariable regression analyses were used to compare subject pharmacologic profiles associated with SCS outcomes; 1) to odds of having 50% pain reduction with a trial, 2) the odds of having a 50% reduction in pain at one year and 3) the odds of having a 50% reduction in opioid use at one year. A 50% reduction in either pain or opioid use were chosen to reflect a clinically meaningful outcome in response to a relatively invasive therapy and to reflect a consistent degree of pain relief with a successful trial and a successful implant. Subjects that underwent a trial and subsequent implantation that required removal prior to one year were analyzed in the first analysis but not the latter two. Subjects were divided into “trial responders” that received 50% or greater analgesic benefit during an SCS trial and those that did not, “trial nonresponders.” Subjects who underwent a permanent stimulator placement were then divided into those “implant pain responders,” who experienced at least a 50% reduction in self-reported pain at one year after implant compared to baseline and “implant pain nonresponders” that did not. Finally, subjects were divided into “implant opioid responders,” those that could decrease the total equianalgesic dose of opioids by at least 50% at one year after implant, and “implant opioid nonresponders,” that were not.

All data were coded in an Excel file (Microsoft, Redmond, WA, USA) and imported into STATA/IC version 14.2 for Mac (StataCorp, College Station, TX, USA) for analysis. Continuous variables were reported as means $\pm$ standard deviations while categorical variables were presented as counts (proportions). A Shapiro-Wilk test was used to determine normalcy of data distribution. Nonnormally distributed data is indicated in the tables. Continuous variables were compared using *t*-tests for normally distributed data and a Mann-Whitney U test for nonnormally distributed data. Categorical variables were compared using a Chi-square test. Multivariable regression models incorporated pretrial NRS-11 pain score, pretrial opioid use as measured by converting the opioid regimen to equivalent mg of oral morphine, use of a SSRI, SNRI, TCA, gabapentin or pregabalin, baclofen, and benzodiazepines. A *p*-value of less than 0.05 and odds ratio with a generated 95% confidence interval that does not span 1.0 was deemed to be statistically significant. A Hosmer-Lemeshow goodness-of-fit test was performed to examine model calibration. Each of the three logistic regression models reported *p*-values greater than 0.05. To arrive at the presented models, consideration was given to alternative groups of variables by adding and subtracting them from each model in a forward selection stepwise fashion. Additionally, independence of factors included in the logistic regression models was confirmed using variance inflation factor tests (values less than 5).

RESULTS

A total of 201 subjects underwent an SCS trial for any reason at MGH between January 2005 and December 2015. One hundred and fifteen subjects underwent a trial of SCS for pain associated with a diagnosis of FBSS, CRPS, DPN or vascular claudication. The remaining SCS patients did not meet inclusion criteria due to the characteristics of their pain or indications for SCS therapy. For example, subjects who received SCS therapy for the treatment of cervical or thoracic pain were excluded. The subject demographics, pain descriptors, medication profiles, and trial characteristics are provided in Table 1. Subjects were most commonly males in the fifth decade of life. Their pain was most commonly described as unilateral (60.9%), burning (42.6%), sharp (23.5%), and shooting (22.6%). The average duration that subjects had experienced their pain was 7.7 ± 7.7 years with a pretrial intensity of 7.7 ± 1.9 . To treat their pain, subjects used the equivalent of 96.7 ± 189.7 mg of oral morphine. The most commonly used neuropathic pain medications were gabapentin or pregabalin (58.26%), followed by SNRIs (29.57%). The percent of trial responders and nonresponders using each type of pain medication is given in Figure 1a. Bivariable comparison of groups is provided in Table 2.

According to the first primary outcome of 50% pain relief with a trial, 97 subjects (79.13%) were trial responders and proceeded to have a permanent SCS system implanted which remained active for at least one year. The average duration of an SCS trial was 3.82 ± 1.57 days; with 89.57% of subjects having a two leads trial and the remainder trialing a single lead. Six subjects who were trial responders had their SCS system explanted prior to one year. Ninety-one subjects were evaluated at one year. Trial responders were older ($51.92, \pm 12.74$ vs. 43.00 ± 12.91 , *p*-value 0.01). Subjects using pregabalin or gabapentin prior to an SCS trial more frequently were trial nonresponders (52 [53.6%] vs. 15 [79.0%], *p* value 0.04).

With regards to the secondary primary outcome of 50% pain reduction at one year following implantation of an SCS, 34 (37%) were implant pain responders and 57 (63%) were not. With regards to a 50% reduction in opioid use at one year following SCS implantation, 26 (29%) were opioid responders and 65 (71%) were not responders. However, implant opioid responders were younger (48.82 ± 13.53 vs. 58.96 ± 10.46 , p -value 0.01). Implant opioid nonresponders reported higher NRS-11 pain scores prior to an SCS trial (8.40 ± 1.46 vs. 7.57 ± 1.86 , p -value 0.04). Implant opioid responders were also on higher doses of opioids prior to an SCS trial (131.4 ± 237.9 vs. 38.13 ± 53.2 , p -value 0.05) and more frequently were on stable opioid regimens prior to initiation of SCS therapy (100% vs. 55.38%, p -value < 0.01). The percent of implant pain responders and nonresponders or opioid responders and nonresponders using each type of neuropathic pain medication is given in Figure 1b,c, respectively.

A multivariable logistic regression model incorporating pretrial NRS-11 pain score, pretrial opioid use as measured by converting the opioid regimen to equivalent mg of oral morphine, use of a SSRI, SNRI, TCA, gabapentin or pregabalin, and benzodiazepines and is presented in Table 3. Only five subjects were using baclofen at the time of the trial and all went on to have a SCS system implanted. As a result, an odds ratio could not be calculated and this factor was excluded from this analysis.

Regression models incorporating the same variables were also used to analyze the outcomes with regard to pain and opioid use of the 91 subjects who had an SCS system implanted are also presented on Table 3. Subtracting the one-year pain score from the baseline pain score and dividing by the baseline pain score calculated a 50% reduction in NRS-11 pain. None of the incorporated variables were associated with increased odds of having at least 50% reduction in pain at one year. Subjects utilizing gabapentin or pregabalin again showed a nonsignificant trend towards decreased odds of 50% pain relief at one year. The preimplantation pain score was not associated with a change in the odds of achieving at least a 50% reduction in NRS-11 pain (OR 1.28, 95% CI 0.91–1.81, p -value 0.16). The final regression model examined the odds of a reduction in opioid use at one year. A 50% reduction in opioid use was calculated by first converting all opioids into equivalent milligrams of morphine and then subtracting the one year opioid dose from the baseline opioid dose and dividing by the baseline opioid dose. The five subjects who were using baclofen all had greater than 50% reduction in their opioid usage. As a result, an odds ratio could not be calculated and this factor was again excluded from this analysis. The analysis demonstrated a significant association between pretrial opioid dose and a subject's ability to achieve a 50% reduction in opioid dose at one year (OR 1.02, 95% CI 1.01–1.02, p -value < 0.01).

DISCUSSION

In subjects who underwent SCS trials, we found no difference in outcomes after the SCS trial or at one year follow-up regarding pain intensity or opioid use as a function of pain medications. However, the regression models indicate several important findings regarding medication management of subjects receiving SCS therapy. With regard to the SCS trial period, no medication was associated with statistically different odds of being a trial

responder or nonresponder, including opioid use. With regard to analgesia derived from SCS at one year, no medication was associated with a change in the odds of being an implant responder or not. Higher doses of opioids prior to implant were associated with statistically increased odds of achieving a 50% reduction in opioid use at one year. Other pain medications were not associated with changes in outcomes. This result is not surprising given subjects on higher doses of opioids may experience substantial decreases in use without increases in pain (15,16). Subjects were not actively encouraged to decrease opioid use following implantation.

Increased opioid use at the time of the SCS trial was associated with greater odds of experiencing a 50% reduction in opioid use at one year. This represents an important finding, especially given changing national attitudes regarding opioid prescribing. In the current climate, professional guidelines express reluctance to initiate and maintain long-term opioid therapy for patients with chronic noncancer pain, based on the unclear treatment efficacy and risk of critical events such as death and overdose (17). Recent recommendations from the CDC suggest that the preferred treatment of chronic noncancer pain occur with nonopioid medications and nonpharmacologic methods (18). It should be emphasized that interventional pain procedures such as SCS serve an important role as an opioid sparing treatment option for patients with chronic pain (18). However, a subject's ability to reduce opioid use may also be completely independent of SCS therapy as well.

SCS outcomes, such as a decrease in opioid use, have been inconsistently observed in prior research on patients with chronic pain. One RCT following 100 subjects receiving conventional SCS to treat FBSS demonstrated a nonsignificant trend towards a decreased percent of subjects using opioids in the SCS group (44%) at six months compared to conventional medical management (30%) (19). In the same study eight subjects in the SCS group ceased opioid use compared to one in the CMM group (19). A randomized controlled study following 90 subjects with 10 kHz SCS and 81 subjects with conventional SCS demonstrated a nonsignificant decrease in the number of subjects able to decrease opioid use at 12 months (35.5% vs. 24.6%) (20). Intragroup comparison of 10 kHz or traditional SCS indicates that neither therapy afforded a statistically significant decrease in opioid use (20). A retrospective study of 170 subjects, including 81 with FBSS and 46 with CRPS, were able to significantly decrease opioid use at one year (50.18 mg vs. 28.91 mg) (21). The same retrospective study also notes that other SCS indications, such as angina, neuropathy and chronic abdominal pain, did not have a decrease in opioid use associated with SCS therapy (21). A prospective cohort demonstrated nonsignificant difference in the percent of subjects that were able to cease opioid use; 14% of SCS subjects (51 total), 23% of pain clinic subjects, (39 total) and 23% of standard care subjects (68 total) (22).

The present study adds to the body of literature by demonstrating that SCS therapy can achieve a 50% reduction in pain that is not necessarily associated with either preimplantation pain intensity scores, preimplantation opioid use or neuropathic medication use. This observation further underscores the utility of SCS therapy in subjects on relatively high doses of opioids. One explanation for these results includes the tendency for subjects on very high doses of opioids being able to reduce their usage without a significant increase

in pain, whereas people on low doses may have experienced difficulty with opioid reduction below a certain level.

Evidence regarding the use of neuropathic pain medications for augmentation of SCS therapy in humans is also scarce. Medical indications for SCS therapy, such as CRPS and DPN, are commonly treated with neuropathic medications (23,24). This provides the foundational logic that medications used to treat a neuropathic pain condition may additively or synergistically augment the effects of SCS. The presented data does not provide evidence for this theory; use of neuropathic pain medications was not associated with a change in the odds of a successful SCS trial, 50% pain relief at one year or 50% reduction in opioid use at one year.

Findings from this retrospective cohort of SCS patients should be taken in the context of certain limitations. First, the present analysis lacks data as to why certain medications were or were not utilized in subjects. Potential reasons may have included medication availability, cost, undocumented side effects, ineffectiveness, or physician preference. An attempt was made to minimize a possible bias by only examining subjects who were on stable doses of opioids and neuropathic medications for at least three months prior to undergoing an SCS trial. Additionally, the use of multiple physicians in within the same institution may limit generalizability but may also decrease variance in prescription practices. Second, because baclofen was not commonly used in the studied population, this medication had to be excluded from two of the logistic regression models and comments regarding its effectiveness at SCS augmentation are limited. There was a nearly significant trend of gabapentin or pregabalin to be associated with decreased odds of pain relief and opioid reduction at one year. This may have represented a progression of pain with the need for additional analgesic treatment modalities. Finally, this study only examined subjects with lower extremity pain to create a homogenous pain cohort. The results may not be generalizable to pain in other regions of the body such as low back, thoracic or cervical pain.

In conclusion, the presented study provides several insights regarding the role of medication management in the setting of SCS therapy for chronic pain. In particular, patients on opioids prior to an SCS trial demonstrated increased odds of a 50% reduction in opioid use. The results suggest that SCS therapy could be a tool to help reduce opioid use. However, it is unclear if this is due subjects using relatively high doses of opioids being able to reduce usage without increased pain. The study also demonstrated that opioid use and increased pre-SCS trial pain are not associated with decreased odds of a successful trial or of pain relief at one year. The study did not demonstrate an association between neuropathic pain medications and augmentation of SCS. Controlled trials would be valuable in continued development of our understanding of SCS mechanisms and optimal medication management.

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Figure 1.

a–c. The percent of each analysis cohort was using a stable dose of each type of pain medication prior to the initiation of SCS therapy. Black bars represent responders and grey bars represent nonresponders for each outcome. Values are presented in Table 2. * indicates that a greater proportion of subjects who did not respond to a trial of SCS were using either gabapentin or pregabalin (53.61% vs. 78.95%, p -value 0.04) in Figure 1a and that a greater proportion of subjects who were able to reduce opioid usage by 50% at 1 year were

chronically using opioids at the start of SCS therapy (100% vs. 55.38%, p -value < 0.01). No other significant differences were noted.

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Table 1

Characteristics of Study Population.

	Average or count	Standard deviation or percentage
Age	50.52	13.12
Male	62	53.91%
Female	53	46.09%
BMI (kg/m ²)	29.37	6.37
Pain Descriptors		
Duration of Pain (years)	7.73	7.73
Bilateral Lower Extremity Pain	45	39.13%
Unilateral Lower Extremity Pain	70	60.86
Burning	49	42.61%
Sharp	27	23.48%
Shooting	26	22.61%
Electrical	9	7.83%
Achy	21	18.26%
NRS-11 Prior to SCS Trial	7.68	1.89
Number of Prior Surgeries At the Site of Pain	2.48	3.50
Pharmacologic Profile		
MEQ (mg)	96.65	189.70
SSRI	23	20.00%
SNRI	34	29.57%
TCA	27	23.48%
Gabapentin/Pregabalin	67	58.26%
Baclofen	5	4.35%
Benzodiazepine	30	26.09%
Trial Characteristics		
Trial Duration (days)	3.82	1.57
Single Lead Trials	11	9.57%
Dual Lead Trials	103.00	89.57%

BMI, Body Mass Index; NRS-11, 11 point numerical pain rating scale with 0 indicating no pain and 10 indicating the worst pain imaginable; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

Table 2

Bivariable Analysis of Patient Factors and Pain Medication Use on SCS Outcome.

	50% reduction in pain with trial Trial responders			50% reduction in pain at one year Implant pain responders			50% reduction in opioid use at one year [†] Implant opioid responders		
	Positive (n = 97)	Negative (n = 18)	p-value	Positive (n = 34)	Negative (n = 57)	p-value	Positive (n = 26)	Negative (n = 65)	p-value
Age	51.92 (12.74)	43.00 (12.91)	0.01	54.24 (13.50)	51.35 (13.24)	0.32	49.82 (13.53)	58.96 (10.46)	0.01
Male	53 (54.64%)	9 (47.37%)	0.56	17 (50.00%)	34 (59.65%)	0.98	34 (52.31%)	17 (65.38%)	0.26
Female	44 (44.36%)	9 (47.37%)	0.87	17 (50.00%)	23 (40.35%)	0.98	31 (47.69%)	9 (34.62%)	0.26
BMI (kg/m ²)	29.79 (6.15)	27.33 (7.20)	0.13	30.28 (5.23%)	28.96 (6.48%)	0.33	30.13 (6.42)	27.9 (4.80)	0.12
Pain Descriptors									
Duration of Pain (years)	7.41 (7.75)	9.53 (7.57)	0.30	5.98 (6.23)	9.34 (8.99)	0.06	8.62 (8.62)	6.94 (7.19)	0.38
Burning	42 (43.30%)	7 (36.84%)	0.60	13 (38.24%)	25 (43.85%)	0.60	26 (40.00%)	12 (46.15%)	0.59
Sharp	23 (23.71%)	4 (21.05%)	0.80	11 (32.35%)	13 (22.81%)	0.14	17 (26.15%)	7 (26.92%)	0.94
Shooting	22 (22.68%)	4 (21.05%)	0.88	11 (32.35%)	8 (14.04%)	0.31	17 (26.15%)	2 (7.69%)	0.05
Electrical	7 (7.22%)	2 (10.53%)	0.62	3 (8.82%)	4 (7.02%)	0.19	5 (7.69%)	2 (7.69%)	1.00
Achy	21 (21.65%)	0	0.25	9 (26.47%)	11 (19.30%)	0.42	15 (23.08%)	5 (19.23%)	0.69
NRS-11 Prior to SCS Trial	7.72 (1.86)	7.47 (2.06)	0.60	8.25 (1.59)	7.54 (1.85)	0.07	8.40 (1.46)	7.57 (1.86)	0.04
Number of Prior Surgeries At the Site of Pain	2.74 (3.74)	1.16 (1.26)	0.07*	3 (3.92)	2.51 (3.48)	0.54*	2.82 (4.02)	2.38 (2.48)	0.61*
Pharmacologic Profile									
MEQ (mg) mean	103.43 (203.38)	62.03 (88.29)	0.39*	115.06 (257.51)	98.59 (172.16)	0.64*	131.39 (237.88)	38.13 (53.19)	0.05*
MEQ (mg) median (IQR)	48 (8, 135)	7.5 (0, 90)		105 (56, 225)	60 (30, 180)		67.5 (20, 247.5)	60 (40, 154)	
Opioid Use %	75 (77.31%)	11 (61.11%)	0.15	22 (64.71%)	40 (70.17%)	0.52	26 (100%)	36 (55.38%)	0.01
SSRI	20 (20.62%)	3 (15.79%)	0.63	8 (23.53%)	10 (17.54%)	0.22	12 (18.46%)	6 (23.08%)	0.62
SNRI	27 (27.84%)	7 (36.84%)	0.43	8 (23.53%)	17 (29.82%)	0.26	19 (29.23%)	6 (23.08)	0.55
TCA	22 (22.68%)	5 (26.32%)	0.73	9 (26.47%)	10 (17.54%)	0.10	16 (24.62%)	3 (11.54%)	0.17
Gabapentin/Pregabalin	52 (53.61%)	15 (78.95%)	0.04	14 (41.18%)	33 (57.89%)	0.12	33 (50.77%)	14 (53.85%)	0.79
Baclofen	5 (5.15%)	0	0.31	2 (5.88%)	2 (3.51%)	0.59	3 (4.63%)	1 (3.85%)	0.87
Benzodiazepine	25 (25.77%)	5 (26.32%)	0.96	8 (23.53%)	14 (24.56%)	0.91	14 (23.08%)	7 (26.92%)	0.70
Trial Characteristics									
Trial Duration (days)	3.89 (1.47)	3.44 (2.01)	0.27						

Measured as the difference between baseline NRS-11 pain score and NRS-11 pain score at one year divided by baseline NRS-11 Pain score e.g. (baseline—one year)/baseline.

All patients on Baclofen had 50% pain reduction with a trial of SCS and were able to reduce opioid consumption by 50% preventing an Odds Ratio from being generated. This was omitted from these analyses.

* Indicates use of a nonparametric Mann-Whitey U test for comparison of groups.

[‡] Converted to equivalent mg of oral morphine. Measured as the difference between baseline opioid use and opioid use at 1 year divided by baseline opioid use e.g. (baseline—one year)/baseline.

CI, confidence interval; OR, odds ratio; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.

Table 3

Multivariable Regression Analyses of Pain Medication Use and SCS Outcomes.

	50% reduction in pain with trial Trial responders				50% reduction in pain at one year* Implant pain responders				50% reduction in opioid use at one year† Implant opioid responders			
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	OR	95% CI	p-value	p-value
Baseline NRS-11	1.09	0.83–1.44	0.52	1.28	0.91–1.81	0.16	0.82	0.49–1.39	0.82	0.49–1.39	0.46	0.46
Baseline Opioid Use	1.00	0.99–1.01	0.32	1.00	0.99–1.00	0.47	1.02	1.01–1.02	1.02	1.01–1.02	<0.01	<0.01
SSRI	1.26	0.29–5.53	0.76	1.74	0.43–6.93	0.44	2.21	0.27–18.07	2.21	0.27–18.07	0.46	0.46
SNRI	0.74	0.23–2.38	0.61	0.60	0.16–2.22	0.44	0.59	0.06–5.35	0.59	0.06–5.35	0.64	0.64
TCA	0.97	0.30–3.14	0.95	1.74	0.52–5.81	0.37	0.64	0.08–4.96	0.64	0.08–4.96	0.67	0.67
Gabapentin/pregabalin	0.30	0.9–1.02	0.05	0.37	0.12–1.13	0.08	1.18	0.19–7.21	1.18	0.19–7.21	0.85	0.85
Baclofen	Omitted			5.32	0.47–59.81	0.18	Omitted		Omitted			
Benzodiazepine	1.18	0.35–4.01	0.80	1.40	0.40–4.85	0.60	0.28	0.00–40.97	0.28	0.00–40.97	0.63	0.63

* Measured as the difference between baseline NRS-11 pain score and NRS-11 pain score at one year divided by baseline NRS-11 Pain score e.g. (baseline—one year)/baseline.

All patients on Baclofen had 50% pain reduction with a trial of SCS and were able to reduce opioid consumption by 50% preventing an Odds Ratio from being generated. This was omitted from these analyses.

† Converted to equivalent mg of oral morphine. Measured as the difference between baseline opioid use and opioid use at 1 year divided by baseline opioid use e.g. (baseline—one year)/baseline. CI, confidence interval; OR, odds ratio; SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressant.