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Burst Spinal Cord Stimulation Evaluated in Patients With Failed Back Surgery Syndrome and Painful Diabetic Neuropathy

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Objective: Spinal cord stimulation (SCS) is used for treating intractable neuropathic pain. Generally, it induces paresthesia in the area covered by SCS. Burst SCS was introduced as a new stimulation paradigm with good pain relief without causing paresthesia. Good results have been obtained in patients who were naive to SCS. In this study we assess the effectiveness of burst stimulation in three groups of chronic pain patients who are already familiar with SCS and the accompanying paresthesia.

Methods: Forty-eight patients with at least six months of conventional, tonic stimulation tested burst stimulation for a period of two weeks. They were classified in three different groups: a cross-section of our population with painful diabetic neuropathy (PDN), a cross-section of our population with failed back surgery syndrome (FBSS), and FBSS patients who over time had become poor responders (PR) to SCS. Visual analog scale scores for pain were assessed prior to implantation, with tonic stimulation, and after two weeks of burst stimulation.

Results: Burst stimulation reduced pain significantly for almost all patients. When compared with tonic stimulation, burst stimulation led to a significant additional pain reduction of on average 44% in patients with PDN ($p < 0.001$) and 28% in patients with FBSS ($p < 0.01$). Patients from the PR group benefitted less from burst stimulation on average. In addition, burst stimulation caused little or no paresthesia whereas tonic stimulation did induce paresthesia. Most patients preferred burst stimulation, but several preferred tonic stimulation because the paresthesia assured them that the SCS was working.

Conclusion: About 60% of the patients with tonic SCS experienced further pain reduction upon application of burst stimulation.

Keywords: Burst stimulation, diabetic neuropathic pain (DNP), failed back surgery syndrome (FBSS), paresthesia, spinal cord stimulation (SCS)

Conflict of Interest: Dirk De Ridder has submitted a patent application for burst stimulation. The other authors reported no conflicts of interest.

INTRODUCTION

Spinal cord stimulation (SCS) is an invasive technique that administers electrical stimulation to the dorsal columns of the spinal cord to reduce pain perception. SCS has shown to be an effective treatment for various neuropathic pain conditions (1–7).

To achieve the most beneficial pain relief for an individual patient, SCS parameters like the configuration of active electrodes, the stimulation frequency, pulse width, and pulse amplitude can be adjusted to the patient's needs. The electrical stimulation of the large-diameter fibers in the dorsal column elicits tingling sensations (paresthesia) in most patients (8,9). The perception and appreciation of this paresthesia varies to a great extent among patients and is heavily influenced by the stimulation parameters used.

The frequencies of SCS that are most often used in the clinic are around 50 Hz and generally vary between 30 and 120 Hz. New types of stimulation paradigms for SCS using high-frequency stimulation up to 10 kHz have been introduced (10,11). Recently, burst stimulation was introduced as a new stimulation paradigm (12,13) combining features of high-frequency stimulation with conventional, tonic stimulation. The burst stimulation used provided pulse trains of five high-frequency pulses at 500 Hz (= 500 Hz spike frequency) occurring 40 times a second (= 40 Hz burst frequency). The pulse width was fixed at 1 msec and the amplitude was optimized for each individual patient. Burst stimulation could be programmed in standard Eon implantable pulse generators (IPG) (St. Jude Medical, Plano, TX, USA). Burst stimulation was tested during a one-month trial stimu-

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lation period in 12 patients who were naive to SCS. The pain reduction obtained with burst stimulation was comparable or compared favorably with tonic stimulation and paresthesias were, in contrast to tonic stimulation, barely present (12). In a subsequent randomized placebo controlled trial in 15 patients, burst stimulation demonstrated to be significantly better than placebo stimulation and better for global pain than tonic stimulation (13).

The goal of this study is to assess the effectiveness of burst stimulation in chronic pain patients who are already receiving SCS treatment for at least six months. This is a challenging group, because these patients are used to feeling paresthesias when the SCS is active. It can be expected that these patients are conditioned to associate pain reduction with paresthesia, and will report lesser gains in pain reduction upon the introduction of paresthesia-free stimulation when compared with patients who never experienced SCS.

METHODS

Patients with an Eon IPG (St. Jude Medical) and using tonic SCS for at least six months tested burst stimulation for two weeks. Three groups of patients were included: two groups of patients who participated in previous studies—that is, patients with painful diabetic neuropathy (PDN) and patients with low back and leg pain (failed back surgery syndrome [FBSS] (14)), and one group of patients with low back and leg pain (FBSS) who over time had started to experience insufficient effect of tonic stimulation (poor responders: PR). The study conformed to the Declaration of Helsinki and was approved by the Institutional Review Board Twente. All patients gave written informed consent.

Prior to implantation of the SCS system, all patients underwent a psychological screening and filled out several questionnaires about their pain and quality of life, like Symptom Checklist 90, McGill pain questionnaire, EQ5D, and Rand SF-36. These data were used to define the baseline situation of the patients.

To acquire the data on tonic stimulation, patients visited the hospital and filled out questionnaires about their pain and experiences with tonic stimulation. Burst stimulation was programmed with settings similar to those used before (five spikes at 500 Hz spike mode, 40 Hz burst mode, 1 msec pulse width) (12) and amplitude was set at 90% of the paresthesia threshold. The patients evaluated the burst stimulation for two weeks, which was double the evaluation time used in previous studies in patients naive to SCS (12,13). During the evaluation period, patients were at home and kept a diary about their pain and its impact on daily life. After two weeks, patients visited the hospital again, filled out questionnaires about their pain and experiences with burst stimulation, and were asked whether they preferred to either return to tonic stimulation or keep burst stimulation.

Pain scores were acquired for feet, legs, and back separately for both tonic and burst stimulation conditions. Patients from the three groups had pain in various body parts. To be able to compare the different groups with each other, the highest pain score for any of their body parts was used for analyses. Within a group we assessed the effect of burst stimulation on feet, legs, and back separately.

To relate the electrical current output of tonic and burst stimulation in our patients to the electrical current in previous studies and modeling experiments (12,13,15), two quantities were determined by the charge per stimulation pulse, calculated as the product of the current amplitude (ampere) and pulse duration (sec), and the stimulation current, calculated as the product of the charge per pulse (coulomb) and the number of pulses per second. The data were normally distributed and paired samples *t*-tests were performed within each group of patients to detect statistically significant changes in current delivery.

A repeated measures analysis of variance was conducted with stimulation (baseline, tonic, and burst stimulation) as within-subjects variable and three different groups of patients (PDN, FBSS, and PR to conventional tonic stimulation) as a between-subjects variable. Within each group of patients, paired samples *t*-tests were performed to test whether there were statistically significant changes in pain perception due to burst stimulation as compared with tonic stimulation. In addition, paired samples *t*-tests were performed to compare the visual analog scale (VAS) scores between tonic and burst stimulation on, respectively, the pain patients perceived in their feet, legs, and back for three different groups of patients (PDN, FBSS, and PR) separately.

RESULTS

Study Population

Forty-eight patients from Medisch Spectrum Twente Hospital with an SCS system and tonic stimulation participated in the study. Their average age was 56 years (SD = 9; range: 29–80 years) and they had on average been experiencing pain for 10 years (SD = 6; range: 2–30 years). All patients had been using tonic stimulation for at least six months (mean = 2.5 years, SD = 2.6, range: 0.5–18 years) and evaluated burst stimulation for a two-week period.

Three different groups of patients were included: 12 patients with PDN, 24 patients with FBSS, and 12 patients belonged to the PR group (Table 1). Both the PDN group and the FBSS group represented a cross-section of the patient population who had an IPG implanted in Medisch Spectrum Twente Hospital. The PR group is a group of patients with low back and leg pain (FBSS) who had a successful trial stimulation period, but had reversion of their pain over time. This pain could not be ameliorated anymore by adjusting tonic stimulation. For this group, burst stimulation was the last option that could be offered.

Table 1. Overview of the Patients of the Three Groups, Including the Average Age, Average Duration of Pain, and Spinal Cord Stimulation and Average Pain Scores.

	Gender (M/F)	Age (years)	Duration of pain (years)	Duration of tonic SCS (years)	General pain scores VAS		
					Baseline	Tonic	Burst
PDN	6/6	57	9	1.8	70	28	16
FBSS	12/12	59	11	2.9	82	49	35
PR	4/8	50	9	2.4	82	74	64

SCS, spinal cord stimulation; PDN, painful diabetic neuropathy; FBSS, failed back surgery syndrome; PR, poor responders; VAS, visual analog scale.

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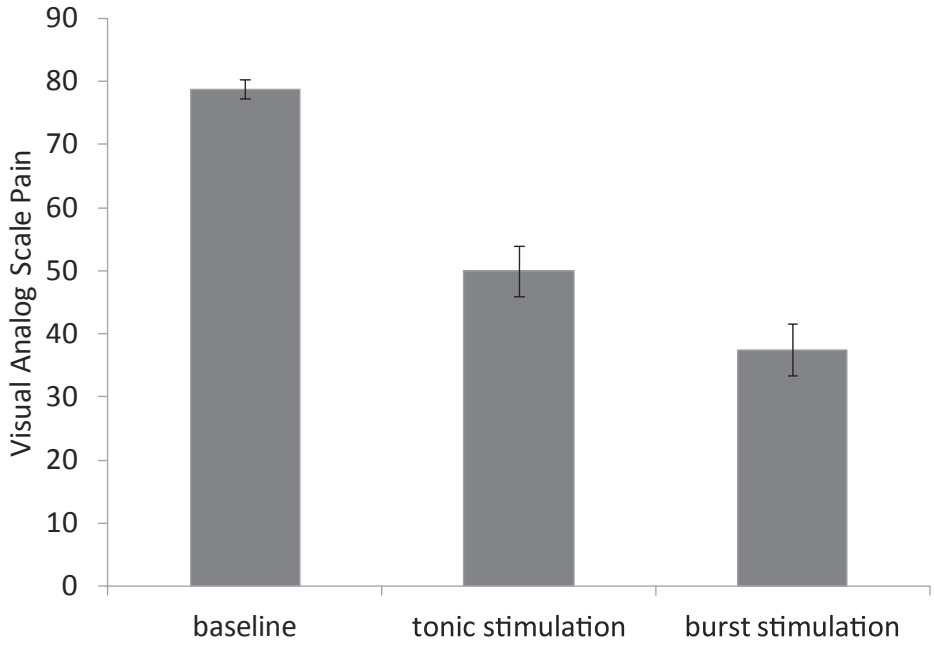

Figure 1. The average visual analog scale scores for pain for all 48 patients assessed preoperative, with tonic stimulation and with burst stimulation, respectively. Error bars represent standard errors.

Pain Reduction

Both tonic stimulation and burst stimulation led to pain reduction in almost all patients. Statistical analysis revealed that overall a significant effect was obtained for stimulation ($F = 66.3$; $p < 0.001$). Tonic stimulation caused an average reduction of 37% in VAS score in comparison with the baseline situation. Burst stimulation caused a 25% further pain reduction compared with tonic stimulation which resulted in an average reduction of 52% in VAS score in comparison with the baseline situation. Figure 1 shows the average pain patients perceived prior to stimulation, with tonic and with burst stimulation.

Pain reduction, however, was strongly dependent on etiology (i.e., PDN, FBSS, and PR). The effect for burst stimulation was strongest for PDN (decrease of 77%), followed by FBSS (decrease of 57%) and PR (decrease of 23%) in comparison with the baseline. A comparison between tonic stimulation and the baseline also revealed the strongest pain reduction for PDN (decrease of 58%), followed by FBSS (decrease of 41%) and PR (decrease of 10%). Figure 2 shows the average VAS scores for pain of the three groups of patients for the baseline, tonic, and burst stimulation, respectively.

PDN

The 12 patients with PDN had an average pain score of 70 prior to implantation. Tonic stimulation reduced their average pain score to 28 which was a significant reduction compared with baseline (see Table 2). After two weeks of burst stimulation, the average pain score was significantly further reduced to 16. There were 8 out of 12 patients (67%) who had extra pain reduction with burst stimulation as compared with tonic stimulation. One patient, however, experienced some pain increase comparing burst with tonic stimulation. Patients with PDN primarily had pain in their feet (see Fig. 3). Pain relief by burst stimulation is also predominantly in the feet, on average a further 50% ($p < 0.05$). No statistically significant effects were obtained for the legs or the back.

FBSS

The 24 patients with FBSS had an average pain score of 82 prior to implantation. With tonic stimulation a significant reduction in comparison with baseline was obtained, with an average pain score of 49. After two weeks of burst stimulation, the average pain score was further reduced to 35, with a significant effect in comparison with baseline and tonic stimulation. Fourteen patients (58%) experienced additional pain reduction with burst stimulation as compared with tonic stimulation; four patients experienced some pain increase.

Patients with FBSS primarily had pain in their legs and back. Forty-six percent of the patients also had pain in their feet. In this patient group, pain in the feet was generally not altered by burst stimulation in comparison with tonic stimulation, but average pain in the legs and back was reduced by burst stimulation from VAS score 35 to 20 and from 44 to 31, respectively (see Fig. 3).

PR

This group consisted of 12 patients with FBSS who experienced insufficient pain relief with tonic stimulation. They had an average pain score of 82 prior to implantation. After on average two and a half years of tonic stimulation, their average pain score was only reduced to 74. After two weeks of burst stimulation, the average pain score was further reduced to 64. Six patients (50%) experienced additional pain reduction with burst stimulation as compared with tonic stimulation, of which three patients experienced a pain reduction of more than 30%. However, one patient experienced a pain increase of 40%.

No significant effect was obtained for this group comparing pain in their feet, which was 46 with tonic stimulation and 38 with burst stimulation. A significant effect was obtained for the legs for burst stimulation (50) in comparison with tonic stimulation (65). A marginal significant difference was obtained for the back when comparing tonic stimulation (70) and burst stimulation (56).

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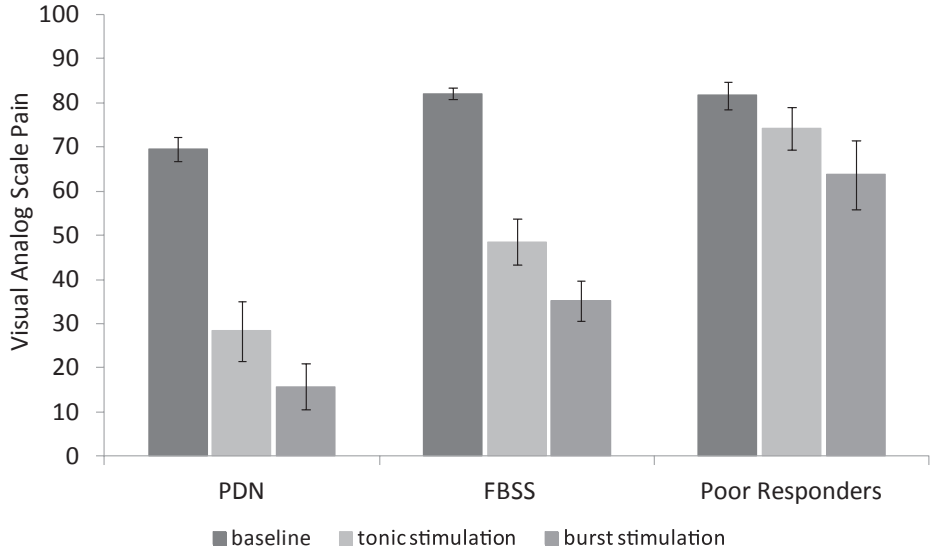

Figure 2. Visual analog scale scores for pain of the three groups of patients (painful diabetic neuropathy [PDN], failed back surgery syndrome [FBSS], and poor responders). Scores are assessed preoperative, with tonic stimulation and with burst stimulation. Bars represent the average pain score for all patients in a group; error bars represent standard errors.

Table 2. Average Pain Scores at Baseline, With Tonic and With Burst Stimulation for the Three Patient Groups.

	Baseline VAS (SD)	Tonic VAS (SD)	Burst VAS (SD)	*p*-Value base–tonic	*p*-Value base–burst	*p*-Value tonic–burst
PDN (*N* = 12)						
General pain	70 (9)	28 (23)	16 (18)	<0.001	<0.001	<0.05
Pain feet		28 (23)	14 (18)			<0.05
Pain legs		7 (12)	4 (8)			0.5
Pain back		3 (8)	0 (0)			0.2
FBSS (*N* = 24)						
General pain	82 (7)	49 (25)	35 (22)	<0.001	<0.001	<0.01
Pain feet		13 (16)	12 (18)			0.7
Pain legs		35 (25)	20 (22)			<0.01
Pain back		44 (28)	31 (24)			<0.05
PR (*N* = 12)						
General pain	82 (10)	74 (16)	64 (27)	<0.01	<0.05	0.1
Pain feet		47 (35)	38 (31)			0.1
Pain legs		65 (21)	50 (24)			<0.05
Pain back		70 (16)	56 (28)			0.09

SD, standard deviation; PDN, painful diabetic neuropathy; FBSS, failed back surgery syndrome; PR, poor responders; VAS, visual analog scale.

Patient Preference

Tonic stimulation is usually accompanied by paresthesia, while burst stimulation is aimed to be subthreshold for paresthesia and should therefore not be sensed by the patients. The perception and appreciation of paresthesias accompanying tonic stimulation varied to a great extent among the patients (see Table 3), which influenced the patients' preferences for either of the two types of stimulation. Phrases used by patients to describe their experience of the tonic paresthesias were, for example, annoying, irritating, neutral, part of me, comfortable, pleasant, and distraction from the pain.

In contrast to tonic stimulation, there is no possibility yet for patients to adjust the amplitude of burst stimulation themselves. Four patients of the PDN group and ten patients of the FBSS group saw that as a drawback of burst stimulation. These patients generally valued tonic paresthesia as comfortable or were used to increasing the stimulation amplitude during episodes of increased pain.

Eight patients with PDN and twelve patients with FBSS preferred burst stimulation over tonic stimulation. Six patients from the PR group preferred burst stimulation, even though pain relief obtained with burst stimulation was on average limited. For many patients the absence of paresthesia is an important advantage of burst stimulation.

Side Effects

Burst stimulation appeared to be accompanied by side effects, both positive and negative, in patients of all three groups. Negative

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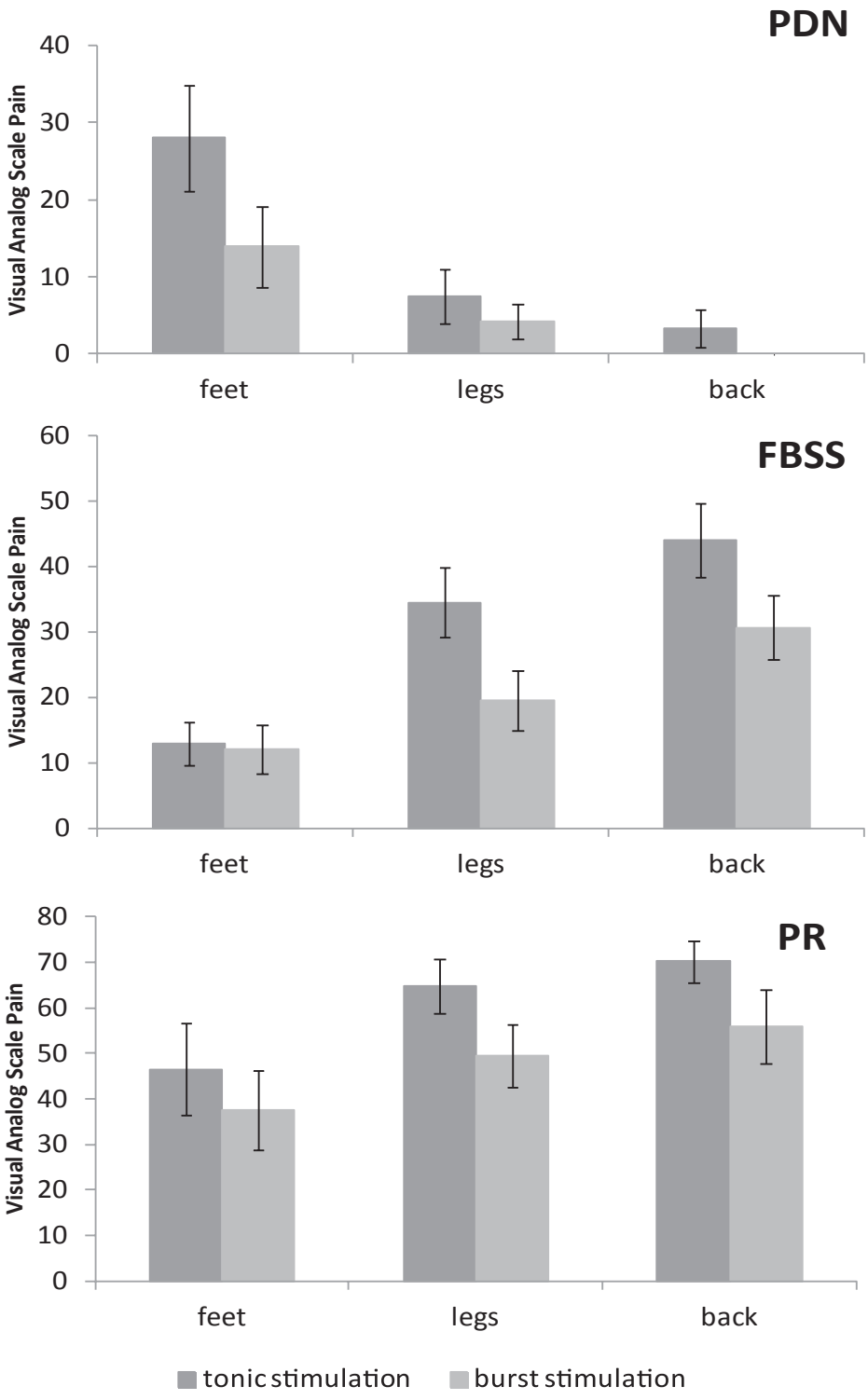

Figure 3. VAS scores for pain of the patients with painful diabetic neuropathy (PDN), failed back surgery syndrome (FBSS), and the poor responders (PR) perceived in their feet, legs, and back, with tonic and burst stimulation. Bars represent the average pain score in a body part; error bars represent standard errors.

side effects mentioned by patients were headaches, dizziness, and the sensation of "heavy legs." Three patients experienced headaches and dizziness; in two patients these side effects were sustained during the two-week evaluation period, while in the other patient these side effects diminished after a few days. The sensation of heavy legs appeared after half a day of burst stimulation in two patients and continued for the rest of the evaluation period. Positive side effects of burst stimulation mentioned by several patients were the sensation of warm feet and the sensation of peaceful rest in the legs. One patient reported having lower and more stable blood glucose levels during the evaluation period of burst stimulation.

Although burst stimulation should not elicit paresthesia, several patients did feel paresthesia when in supine position with burst stimulation at amplitudes that were used. Most of the time the

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Table 3. Overview of the Rating of the Perceived Tonic Paresthesia, the Desire to Adjust the Burst Stimulation Amplitude, and the Stimulation Preferences of the Number of Patients of Each Group.

	Tonic paresthesia			Adjust amplitude		Burst	Preference		Off
	Comfort	Neutral	Discomfort	Yes	No		Tonic	Either	
PDN	2	8	2	4	8	8	4	–	–
FBSS	8	9	7	10	14	12	11	–	1
PR	–	5	7	2	10	6	–	2	4

PDN, painful diabetic neuropathy; FBSS, failed back surgery syndrome; PR, poor responders.

sensation was not experienced as unpleasant, but in a few cases the sensations were perceived as very uncomfortable.

Electrical Charge Delivery

The electrical charge per stimulation pulse and the stimulation current were calculated for each patient. Pulse amplitudes used for burst stimulation were lower than for tonic stimulation. Therefore, converting patients from tonic to burst stimulation led to a reduction in the average charge per stimulation pulse from 1.1 μC to 0.85 μC ($p = 0.09$), from 2.8 μC to 1.6 μC ($p < 0.01$), and from 3.2 μC to 3.0 μC ($p = 0.81$) for the PDN, FBSS, and PR group, respectively. The average stimulation current, however, rose from 91 μA to 176 μA ($p = 0.09$), from 177 μA to 322 μA ($p < 0.001$), and from 218 μA to 669 μA ($p < 0.05$), respectively, for the same groups, as the number of pulses per second increased when burst stimulation was applied.

DISCUSSION

Burst stimulation caused pain reduction in almost all patients. On average, burst stimulation caused a significantly larger pain reduction in all three patient groups than tonic stimulation, and burst stimulation caused little or no paresthesia in most patients. About 60% of patients (67% for PDN, 58% for FBSS, and 50% for the PR group) experienced further pain reduction when applying burst stimulation in comparison with tonic stimulation. An increase in perceived pain as compared with tonic stimulation, starting after one to seven days of burst stimulation, was however mentioned by six patients.

Pain Reduction

In PDN patients, the neuropathic pain in their feet and sometimes lower legs already responded very well to tonic stimulation, but burst stimulation reduced the pain even further, in a statistically significant and clinically relevant way. With an average additional pain reduction of 44%, this patient group benefitted relatively most from switching to burst stimulation.

Eleven of the FBSS patients who participated in this study had pain in their feet as well, but burst stimulation was not able to reduce this pain in those patients. This could be due to the position of the electrode lead in the spinal cord, as it was placed to primarily target the lower back and legs. In FBSS patients the tip of the electrode was positioned T7-T10, while in PDN patients the electrode was positioned more caudal: T10-T12. When compared with tonic stimulation, the average pain-reducing effect of burst stimulation on leg pain (43%) is somewhat higher than on back pain (30%) in FBSS patients. These relative decreases in back and leg pain in this group are comparable with the results of burst stimulation in patients who were naive to SCS (13).

The PR group who had low back and leg pain and over time lost effect of tonic SCS was a more heterogenic group and consequently had more heterogenic responses as well. Two patients had no preference for either tonic or burst stimulation, four patients rather had their stimulator removed, and six patients preferred burst stimulation. Even though the average pain relief was limited in this group, three patients (25%) did benefit significantly from switching to burst stimulation.

Paresthesia

All patients in this study were familiar with tonic stimulation before they received burst stimulation. They were used to or at least familiar with the paresthesia. Several patients of both the PDN and the FBSS groups also indicated that they actually liked the paresthesia. The loss or change of the paresthesia and the inability to increase the stimulation amplitude and thereby the paresthesia intensity led some patients to prefer tonic stimulation over burst stimulation, in certain cases even despite of the larger pain reduction that was obtained by burst stimulation. In addition, some patients did not perceive the paresthesia as particularly comfortable, but were able to shift their attention from the pain to the paresthesia and therefore appreciated it as a distraction from the pain. These patients mentioned that they missed the paresthesia as a feedback signal that the SCS system is functioning.

In the studies performed by De Ridder et al. (12,13), patients were naive to any form of SCS. The test period of one week of tonic stimulation was probably too short to have patients get acquainted with the paresthesias accompanying pain reduction. Consequently, those patients did not associate pain reduction with paresthesia and were most likely able to focus primarily on the pain-reduction effects of the stimulation paradigms that were tested. As a result, all patients preferred burst stimulation.

The majority of the patients in this study, however, did associate paresthesia with pain reduction, which complicated the evaluation of the pain reduction effects of burst stimulation. This is possibly due to the fact that paresthesias reassure the patient that the stimulator is active, a prerequisite for conditioned pain relief. Twenty-six (54%) of all patients in this study preferred burst stimulation.

Stimulation Amplitude

In this study, only a two-week evaluation was performed, without the possibility to adjust the amplitude during or after the two weeks. This technical inadequacy is important as it can be expected that the efficacy of burst stimulation could be further improved if patients could control the intensity of the stimulation. This could give the patients a feeling of control over their pain, important features in subjective pain perception (16,17).

We have no neurological explanation for the side effects and sensations, both positive and negative, described by some of the

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patients. Except for the patient who had indeed lower and more stable blood glucose levels during the evaluation period, we were not able to objectify the side effects. However, the side effects must be induced by burst stimulation in general or by high amplitudes of burst stimulation, as they disappeared when the patients were converted to tonic stimulation again or when the amplitude was lowered during programming burst stimulation.

It is possible that many of the side effects and paresthesias could have been reduced or eliminated by lowering the amplitude, while further pain reduction might have been achieved by increasing the stimulation amplitude. A two-week evaluation period is, however, minimally necessary for patients who are already familiar with tonic stimulation. Patients need to get used to the change in sensation, considering the fact that they have been conditioned to associate pain reduction with the presence of paresthesias. An extended evaluation period that includes the option to adjust stimulation parameters after one or two weeks of stimulation might have been preferable to assess the full possibilities of burst stimulation.

It has been suggested by De Ridder et al. (12) that burst stimulation suppresses pain via the electrophysiologic gate-control mechanism before the clinical paresthesia threshold is reached, as the amplitude of effective burst stimulation pulses is lower than the amplitude of effective tonic stimulation pulses. In all three patient groups the charge per pulse in burst stimulation is lower than in conventional tonic stimulation. However, a larger pulse duration and higher pulse frequency in burst stimulation still lead to an increased average stimulation current, which in turn implies an increase in energy consumption and accelerated battery depletion. Future studies should look at intermittent burst stimulation in order to try and decrease energy delivery to the spinal cord. In view of the current calculations and the previously published calculations (12), a 1:2 or 1:3 ratio on : off would be theoretically ideal to exert an energy delivery that is equal to tonic stimulation.

CONCLUSION

Burst stimulation compares favorably with tonic stimulation for most patients, generally without eliciting paresthesia. On average, burst stimulation causes significantly more pain reduction in patients with PDN and in patients with FBSS. A trial period of at least two weeks of burst stimulation for every patient with a spinal cord stimulator would likely increase the efficacy of SCS therapy. Still, further research should elucidate optimal burst stimulation parameters for patients who are already familiar with SCS.

Authorship Statements

Ms. de Vos, Ms. Bom, and Drs. Vanneste, Lenders, and de Ridder designed the study. Ms. de Vos, Ms. Bom, and Dr. Lenders conducted the study, including patient recruitment and data collection. Ms. de Vos, Ms. Bom and, Dr. Vanneste performed data analysis. Ms. de Vos prepared the manuscript draft with important intellectual input from Ms. Bom, and Drs. Vanneste, Lenders, and de Ridder. All authors approved the final manuscript.

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REFERENCES

1. de Jongste MJL, Hautvast RWM, Hillege HL, Lie KI. Efficacy of spinal cord stimulation as adjuvant therapy for intractable angina pectoris: a prospective, randomized clinical study. *J Am Coll Cardiol* 1994;23:1592–1597.
2. Kemler MA, Barendse GAM, van Kleef M et al. Spinal cord stimulation in patients with chronic reflex sympathetic dystrophy. *N Engl J Med* 2000;343:618–624.
3. Kumar K, Toth C, Nath RK. Spinal cord stimulation for chronic pain in peripheral neuropathy. *Surg Neurol* 1996;46:363–369.
4. 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.
5. 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;56:98–107.
6. Pluijms WA, Slangen R, Joosten EA et al. Electrical spinal cord stimulation in painful diabetic polyneuropathy, a systematic review on treatment efficacy and safety. *Eur J Pain* 2011;15:783–788.
7. de Vos CC, Rajan V, Steenbergen W, van der Aa HE, Buschman HPJ. Effect and safety of spinal cord stimulation for treatment of chronic pain caused by diabetic neuropathy. *J Diabetes Complications* 2009;23:40–45.
8. Nordin M, Nystrom B, Wallin U, Hagbarth KE. Ectopic sensory discharges and paresthesiae in patients with disorders of peripheral nerves, dorsal roots and dorsal columns. *Pain* 1984;20:231–245.
9. Ochoa JL, Torebjork HE. Paraesthesiae from ectopic impulse generation in human sensory nerves. *Brain* 1980;103:835–853.
10. van Buyten JP, Al-Kaisy A, Smet I, Palmisani S, Smith T. High-frequency spinal cord stimulation for the treatment of chronic back pain patients: results of a prospective multicenter European clinical study. *Neuromodulation* 2012;16:59–66.
11. Tiede J, Brown L, Gekht G, Vallejo R, Yearwood T, Morgan D. Novel spinal cord stimulation parameters in patients with predominant back pain. *Neuromodulation* 2012; e-pub ahead of print. doi:10.1111/ner.12032.
12. de Ridder D, Vanneste S, Plazier M, van der Loo E, Menovsky T. Burst spinal cord stimulation: toward paresthesia-free pain suppression. *Neurosurgery* 2010;66:986–990.
13. de Ridder D, Plazier M, Kamerling N, Menovsky T, Vanneste S. Burst spinal cord stimulation for limb and back pain. *World Neurosurg* 2013; e-pub ahead of print. doi: 10.1016/j.wneu.2013.01.040.
14. de Vos CC, Dijkstra C, Lenders MWPM, Holsheimer J. Spinal cord stimulation with hybrid lead relieves pain in low back and legs. *Neuromodulation* 2012;15:118–123.
15. Wesselink WA, Holsheimer J, Boom HBK. Analysis of current density and related parameters in spinal cord stimulation. *IEEE Trans Rehabil Eng* 1998;6:200–207.
16. Grau JW, Huie JR, Garraway SM et al. Impact of behavioral control on the processing of nociceptive stimulation. *Front Physiol* 2012;3:262.
17. Muller MJ. Will it hurt less if I believe I can control it? Influence of actual and perceived control on perceived pain intensity in healthy male individuals: a randomized controlled study. *J Behav Med* 2012;35:529–537.

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COMMENTS

The test period for burst stimulation is too short compared to conventional SCS. There is no information about the positioning of the leads that were positioned for conventional SCS and therefore not ideally for burst stimulation. As the author said, there was no adjustment of the stimulation parameters in burst stimulation. How do they know the settings were optimal for pain relief as there are mostly no paresthesias?

The conclusions are poor. There is no explanation why the results are better in patients with PDN than in the other indications. It could be the amount of energy delivered to the spinal cord that has an effect on the fibers in the dorsal horn responsible for the sacral area and foot, which is difficult to reach with conventional SCS as demonstrated by both Barolat and Nakamura (1,2).

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REFERENCES

1. Holsheimer, J and Barolat, G. (1998). Spinal Geometry and Paresthesia Coverage in Spinal Cord Stimulation. *Neuromodulation: Technology at the Neural Interface*, Vol 1, 129–136.
2. Foerster, O. Motorische felder und bahnen, in Handbuch der Neurologie (ed. O. Bumke and O. Foerster). 1936, Springer-Verlag; Berlin, p. 1–357

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The purpose of this clinical research report was to determine how patients who had already experienced the effects of tonic SCS respond to burst SCS. The authors examined these comparisons in patients with painful diabetic neuropathy, failed back surgery syndrome and a poor responders group. The consistent and significant observation was that burst SCS provided a favorable comparison to tonic SCS but without generating paresthesia. It was also noted that burst SCS significantly reduced pain more than tonic SCS in patients with painful diabetic neuropathy and failed back surgery syndrome. Furthermore, numerous issues were presented in the results when comparing these two modes of stimulation in the different groups of patients. This study provides new and interesting information about the comparison of burst SCS and tonic SCS in patients who were previously implanted and treated with tonic SCS.

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The landmark demonstration by Bhadra and Kilgore of reliable and reversible peripheral nerve blockade in mammals using high frequency alternating current kindled an upsurge in higher frequency neurostimulation1. In peripheral nerves, the concept is easy to grasp: a cuff electrode is placed around the nerve and when high frequency stimulation (10 kHz–30 kHz) is applied, motor and sensory nerve blockade occurs. The concept is not as simply delineated with high frequency spinal cord stimulation (HFSCS). Standard (non-cuff like) leads are placed in the posterior epidural space similar to conventional non-high frequency SCS and no apparent disruption of nerve conduction is noted. Animal experimental data suggest potentially different peripheral and segmental spinal mechanisms for pain relief between conventional and HFSCS2; however, there appears to be no difference in effectiveness on mechanical hypersensitivity between low, mid and HFSCS in a rat model of painful diabetic polyneuropathy3.

Clinically, HFSCS has been used with frequencies as low as 500 Hz in a burst pattern4, 5 and as high as 10 kHz tonically6. Interestingly, and unlike conventional spinal cord stimulation, HFSCS does not result in perceptible paresthesias. Hence, HFSCS presents a golden opportunity to conduct double blind randomized trials on the efficacy of the therapy—an unfeasible feat with conventional SCS. To date, there has been one study that examined HFSCS compared to sham stimulation in a double blind format7. In this crossover study performed in 42 patients who have achieved stable relief with conventional SCS, HFSCS at 5 kHz was equivalent to sham as far as patient's global impression of change, pain scores (VAS) and functional outcomes (EQ-5D). However, a more recent smaller study examined burst stimulation vs. conventional tonic stimulation vs. placebo in 15 consecutive pain patients. Burst stimulation was found to be superior to conventional stimulation and to placebo5.

In the current paper by de Vos et al., in this issue of Neuromodulation, two weeks of burst stimulation resulted in significantly larger pain reduction in the majority of patients who were exposed to conventional SCS for at least six months. While adding to the literature on clinical use of HFSCS, this study fell short of its potential to test burst stimulation in a double blind fashion. According to the authors, the majority of patients were not willing to participate in the study if they were to be without stimulation for two weeks. However, this did not appear to be an issue for a similar group of patients in the two other studies that used a double blind paradigm of HFSCS5, 7. Hence, efficacy of HFSCS remains contested: open label studies of burst stimulation at 500 Hz4 or tonic HFSCS at 10 kHz6, as well as one small double blind study on burst stimulation5, suggest efficacy of HFSCS whereas a larger double blind randomized cross-over trial suggests the opposite: HFSCS at 5 kHz is equivalent to sham stimulation7. Clearly, larger well-controlled double blind randomized studies are needed to answer important questions of mechanisms, efficacy and parameters–especially in this day and age of evidence-based medicine.

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REFERENCES

1. Bhadra N, Kilgore KL. High-frequency electrical conduction block of mammalian peripheral motor nerve. *Muscle Nerve*. Dec 2005;32(6):782–790.
2. Shechter R, Yang F, Xu Q, et al. Conventional and Kilohertz-frequency Spinal Cord Stimulation Produces Intensity- and Frequency-dependent Inhibition of Mechanical Hypersensitivity in a Rat Model of Neuropathic Pain. *Anesthesiology*. Aug 2013;119(2):422–432.
3. Pluijms WA, van Kleef M, Honig WM, Janssen SP, Joosten EA. The effect of spinal cord stimulation frequency in experimental painful diabetic polyneuropathy. *Eur J Pain*. Oct 2013;17(9):1338–1346.
4. De Ridder D, Vanneste S, Plazier M, van der Loo E, Menovsky T. Burst spinal cord stimulation: toward paresthesia-free pain suppression. *Neurosurgery*. May 2010;66(5):986–990.
5. De Ridder D, Plazier M, Kamerling N, Menovsky T, Vanneste S. Burst Spinal Cord Stimulation for Limb and Back Pain. *World Neurosurg*. Jan 12 2013.
6. Van Buyten JP, Al-Kaisy A, Smet I, Palmisani S, Smith T. High-frequency spinal cord stimulation for the treatment of chronic back pain patients: results of a prospective multicenter European clinical study. *Neuromodulation*. Jan-Feb 2013;16(1):59–65; discussion 65–56.
7. Perruchoud C, Eldabe S, Batterham AM, et al. Analgesic efficacy of high-frequency spinal cord stimulation: a randomized double-blind placebo-controlled study. *Neuromodulation*. Jul 2013;16(4):363–369.

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