

C2 Subcutaneous Stimulation for Failed Back Surgery Syndrome: A Case Report

Dirk De Ridder, MD, PhD*[†], Mark Plazier, MD*, Tomas Menovsky, MD, PhD*, Niels Kamerling, MD*, Sven Vanneste, MSc, MA, PhD*[‡]

Objective: Failed back surgery syndrome (FBSS) is a term embracing a constellation of conditions that describes persistent or recurring low back pain, with or without sciatica following one or more spine surgeries. It has been shown in animals that electrical stimulation of the high cervical C2 area can suppress pain stimuli derived from the L5-S1 dermatome. It is unknown whether C2 electrical stimulation in humans can be used to treat pain derived from the L5-S1 area, and a case is reported in which subcutaneous C2 is applied to treat FBSS.

Case: A patient presents to the neuromodulation clinic because of FBSS (after three lumbar discectomies) and noninvasive neuromodulation is performed consisting of transcutaneous electrical nerve stimulation (TENS) at C2. The C2 TENS stimulation is successful in improving pain. It induces paresthesias in the C2 dermatome above a certain amplitude threshold, but does not generate paresthesias in the pain area. However, the patient becomes allergic to the skin-applied TENS electrodes and therefore a new treatment strategy is discussed with the patient. A subcutaneous C2 electrode is inserted under local anesthesia, and attached to an external pulse generator.

Methods: Three stimulation designs are tested: a classical tonic stimulation, consisting of 40 Hz stimulation, a placebo, and a burst stimulation, consisting of 40 Hz burst mode, with five spikes delivered at 500 Hz at 1000 μ sec pulse width and 1000 μ sec interspike interval.

Results: The patient's stimulation results demonstrate that burst mode is superior to placebo and tonic mode, and she receives a fully implanted C2 electrode connected to an internal pulse generator via an extension wire.

Conclusion: The burst design is capable of both suppressing the least and worst pain effectively, and she has remained almost pain-free for over three years.

Keywords: Burst, C2 stimulation, failed back surgery, pain, tonic

Conflict of Interest: The authors reported no conflict of interest.

INTRODUCTION

Failed back surgery syndrome (FBSS) is a term embracing a constellation of conditions that describes persistent or recurring low back pain, with or without sciatica following one or more spine surgeries (1).

The number of patients suffering from FBSS has increased with increasing rates of spine surgery (2). Despite advances in technology and surgical techniques, the proportion of FBSS is similar to what it was several decades ago (3) and varies with the type of surgical procedure: FBSS in lumbar discectomy is relatively low at approximately 10%, laminectomy at about 30–35%, and spinal fusion has the highest FBSS rates (2). The impact of FBSS on an individual's quality of life and functional status is considerable and more disabling when compared with other common chronic pain conditions (2). Treatment consists of conservative medical management, reoperation, or spinal cord stimulation (SCS). SCS has been shown to be superior to both conventional medical management and reoperation (4–11). Even though 60% of patients feel they are improved by SCS (12), its major disadvantages are the high rate of complications such as hardware failure (13) and the fact that the stimulation replaces pain by paresthesias, which can be disturbing as well (14).

The greater occipital nerve afferents enter the C2 segment of the spinal cord at the level of the nucleus caudalis of the trigeminal nerve forming the trigeminocervical complex. The nucleus caudalis projects to the thalamus, which relays sensory input to the cortex. Furthermore, animal studies have shown connections between neurons of the C2 spinal cord and the hypothalamus (15), the thalamus (16), the periaqueductal gray (16), the amygdala (15), anterior cingulate cortex (ACC) (17), and posterior insula (17). Thus, the C2 spinal cord is directly connected to most areas of the pain matrix. This was also demonstrated in a recent functional magnetic reso-

Address correspondence to: Dirk De Ridder, Brai²n, University Hospital Antwerp, Wilrijkstraat 10, 2650 Edegem, Belgium. Email: dirk.de.ridder@uza.be

* Brai²n, TRI & Department of Neurosurgery, University Hospital Antwerp, Edegem, Belgium; and

[†] Department of Surgical Sciences, Dunedin School of Medicine, University of Otago, New Zealand; and

[‡] Department of Translational Neuroscience, Faculty of Medicine, University of Antwerp, Edegem, Belgium

For more information on author guidelines, an explanation of our peer review process, and conflict of interest informed consent policies, please go to <http://www.wiley.com/bw/submit.asp?ref=1094-7159&site=1>

nance imaging study, showing that depending on the stimulation pattern (burst vs. tonic) and frequency, different brain areas are modulated (18). Positron emission tomography scans performed during C2 stimulation revealed significant changes in the regional cerebral blood flow in the dorsal rostral pons, ACC, and the cuneus, correlating to pain scores. Changes in the ACC and the left pulvinar correlated to paresthesia scores (19). As these structures are well known to be involved in the brain pain matrix, these data might suggest that stimulation of the greater occipital nerve results in a modulation of brain activity in pain-related cortical and subcortical structures.

This concept has been used to treat widespread bodily pain in fibromyalgia by subcutaneous C2 stimulation (20,21) and could potentially be extended to pain related to FBSS.

Case Report

A 37-year-old woman presents with FBSS after three lumbar spine operations. Three years prior to the consultation at the BRAI²N neuromodulation center she underwent a lumbar discectomy at L4-L5 twice followed by new discectomy at L4-L5 and L5-S1 one year later.

She develops typical neuropathic leg and back pain, and is treated by medication consisting of pregabalin, tramadol+paracetamol, venlafaxine, amitriptyline, vitamin B, and lormetazepam without much avail.

Due to FBSS, noninvasive neuromodulation is performed consisting of transcutaneous electrical nerve stimulation (TENS) at C2. The C2 nerve stimulation induces paresthesias in the C2 dermatome above a certain amplitude threshold, but does not generate paresthesias in the pain area. With TENS applied via skin electrodes at the C2 dermatome the pain in her leg improves to 3–4/10 without improvement of the back pain.

Once the patient becomes allergic to the electrodes a new treatment strategy is discussed with the patient. She gets the choice between a spinal cord stimulator and a subcutaneous C2 electrode. As both advantages and disadvantages of the SCS and C2 were explained she prefers a trial with a subcutaneous C2 electrode.

A subcutaneous C2 wire electrode (Octrode, SJMedical Neurodivision, Plano, TX, USA) is inserted under local anesthesia (Fig. 1). The single octrode is inserted 2.6 cm lateral to the midline, below the level of theinion. As the array length is 5.2 cm, four of the eight contacts are located on the left side, and four on the right side. A sharp turn and loop are used as means to prevent migration of the wire electrode (Fig. 1). The wire electrode is attached to an external pulse generator (EON, SJMedical Neurodivision, Plano, TX, USA) implanted in subcutaneous area at the buttock. The contact settings are +++++.

Three stimulation designs are tested, each during one week: a classical tonic stimulation, consisting of 40 Hz, a placebo, and a burst stimulation, consisting of 40 Hz burst mode, with five spikes delivered at 500 Hz at 1000 μ sec pulse width and 1000 μ sec interspike interval. All stimulations are performed subthreshold for paresthesias. The amplitude is increased progressively up to the moment paresthesias are perceived, and subsequently the stimulation amplitude is decreased so no paresthesias are felt in the C2 dermatome, even with manual compression on the area overlying the electrode. Placebo stimulation is performed by further decreasing the amplitude to 0 mA. Burst stimulation is performed with a custom-made programmer, commercially not yet available (18,22–24). The patient is asked to score her pain on a visual analog scale from 0 to 10 (0: no pain, 10 maximally imaginable pain). At each evaluation, after a week of tonic, placebo, or burst stimulation, pain

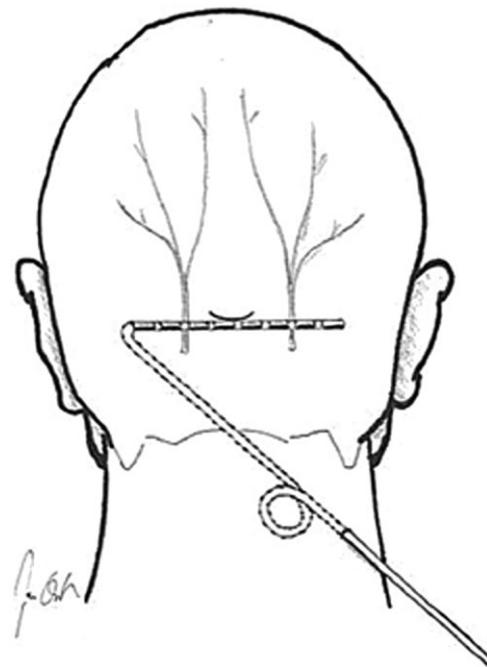


Figure 1. Graphical depiction of wire electrode (Octrode, SJMedical, Plano, TX, USA) inserted subcutaneously in the C2 dermatome. The single octrode is inserted 2.6 cm lateral to the midline, below the level of theinion. As the array length is 5.2 cm, four of the eight poles are located on the left side, and four on the right side. Note the sharp turn and loop to prevent migration of the wire electrode.

Table 1. Pain Scores Related to Stimulation Design.

	Baseline	Placebo	Tonic	Burst
Pain back	8.6	8.4	8	4.6
Pain limb	8.3	7.1	1.3	1.0
Pain general	8.5	6.1	5.4	2.5
PVAQ				
Attention to pain	11	13	18	10
Attention to changes in pain	16	15	15	14
VAS				
Pain now	8.3	8.2	1.1	1.4
Pain least	8.3	7.6	6.7	0.9
Pain worst	7.3	7.5	2.4	0.2
PVAQ, Pain Vigilance and Awareness Questionnaire; VAS, visual analog scale.				

scores are asked for back pain, leg pain, and pain in general during the stimulation period. Pain scores are also asked for the worst pain and least pain during the stimulation period as well as on the moment of the evaluation (pain now). Also changes in the Pain Vigilance and Awareness Questionnaire are used as a measurement of stimulation efficacy. The raw visual analog scale and Pain Vigilance and Awareness Questionnaire data are presented in Table 1 for the initial trial period, and the data after two years of stimulation are presented in Table 2.

Her stimulation results demonstrate that burst mode is superior to placebo and tonic mode (Table 1), and she receives a fully implanted C2 electrode connected to an internal pulse generator via an extension wire. The burst design is capable of both suppress-

Table 2. Follow-Up: A Comparison Between Baseline, Postoperative and Two Years Follow-Up on the Burst Results.

	Baseline	Postoperative burst	Follow-up burst
Pain back	8.6	4.6	3.1
Pain limb	8.3	1	2.9
Pain general	8.5	2.5	2.2
PVAQ			
Attention to pain	11	10	22
Attention to changes in pain	16	14	25
VAS			
Pain now	8.3	1.4	2.0
Pain least	8.3	0.9	2.9
Pain worst	7.3	0.2	.07
PVAQ, Pain Vigilance and Awareness Questionnaire; VAS, visual analog scale.			

ing the least and worst pain effectively, and she has remained almost pain-free for over three years.

DISCUSSION

Treatment options for FBSS consist of analgesic medication, functional rehabilitation, and in intractable cases SCS or reoperation. SCS in these intractable cases is superior to conventional medical management and reoperation (4–11), and because of this reason more than 50,000 spinal cord stimulators are implanted on a yearly basis (25). As C2 stimulation can be performed subthreshold for paresthesias and this results in similar activation patterns in the brain (26), it is possible to perform C2 stimulation in a placebo-controlled way to determine its efficacy for FBSS.

Initially noninvasive neuromodulation options were proposed to the patient, and TENS at C2 was successful, but because she became allergic to the electrodes applied to the skin, a subcutaneous C2 implant was offered, followed by a fully implantable device once this proved superior to placebo, as it did. Burst stimulation proved to be superior to tonic stimulation and placebo, and so the patient's internal pulse generator was programmed to burst mode.

Even though it might seem ludicrous at first sight to implant a subcutaneous electrode in the C2 dermatome for FBSS there is some literature to potentially explain the mechanism involved in this novel form of FBSS treatment.

C1-C3 cells represent 45% of all spinothalamic neurons and relay information from all levels of the cord to periaqueductal gray and/or thalamus (27) via a calbindin positive pathway (28). C1-C3 spinothalamic tract neurons process sensory information from widespread regions of the body (29). Upper SCS at C1-C3 modifies firing rate of >90% of lumbosacral spinothalamic cells (30), and may therefore modulate transmission of noxious stimuli from lumbosacral origin, analogous to what has been proposed for the modulation of widespread bodily pain in fibromyalgia (20,21).

The robustness of this novel treatment is demonstrated by the fact that the burst design is capable of both suppressing the least and worst pain effectively, and that she has remained almost pain-free for over three years.

The positive results of this case report warrant a prospective study of a larger sample of FBSS patients in order to verify whether this represents an exceptional case or whether this very safe and

relatively noninvasive procedure could be beneficial for a large group of FBSS patients. It should also be verified whether TENS applied to the C2 dermatome can reliably predict response to subcutaneous C2 stimulation via an implanted electrode, as this could be an easy prognostic test. However, group data are needed to confirm or disprove this possibility.

The exact mechanism of how this C2 stimulation can modulate FBSS still has to be elucidated. Performing functional magnetic resonance imaging (18), positron emission tomography, or source localized electroencephalogram studies before, during, and after the C2 stimulation and correlating the functional imaging data to clinical responses could help to elucidate the working mechanism.

CONCLUSION

This case report proposes a novel treatment for intractable FBSS, which is easily testable, is noninvasive, and carries less risk than SCS for the patient.

Acknowledgement

This work was supported by Research Foundation Flanders (FWO).

Authorship Statements

Professor Dr. Dirk De Ridder designed and conducted the study, including patient recruitment, data collection, and data analysis. Dr. Mark Plazier conducted the study, including patient recruitment. Dr. Tomas Menovsky conducted the study, including patient recruitment. Dr. Niels Kamerling conducted the study, including patient recruitment. Dr. Sven Vanneste designed and conducted the study, data collection, and data analysis.

How to Cite this Article:

De Ridder D., Plazier M., Menovsky T., Kamerling N., Vanneste S. 2013. C2 Subcutaneous Stimulation for Failed Back Surgery Syndrome: A Case Report. *Neuromodulation* 2013; 16: 610–613

REFERENCES

1. North RB, Campbell JN, James CS et al. Failed back surgery syndrome: 5-year follow-up in 102 patients undergoing repeated operation. *Neurosurgery* 1991;28:685–690; discussion 690–681.
2. Chan CW, Peng P. Failed back surgery syndrome. *Pain Med* 2011;12:577–606.
3. Burton CV. Failed back surgery patients: the alarm bells are ringing. *Surg Neurol* 2006;65:5–6.
4. Bala MM, Riemsma RP, Nixon J, Kleijnen J. Systematic review of the (cost-) effectiveness of spinal cord stimulation for people with failed back surgery syndrome. *Clin J Pain* 2008;24:741–756.
5. Bell GK, Kidd D, North RB. Cost-effectiveness analysis of spinal cord stimulation in treatment of failed back surgery syndrome. *J Pain Symptom Manage* 1997;13:286–295.
6. Kumar K, Malik S, Demeria D. Treatment of chronic pain with spinal cord stimulation versus alternative therapies: cost-effectiveness analysis. *Neurosurgery* 2002;51:106–115; discussion 115–106.
7. 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.

8. Mekhail N, Wentzel DL, Freeman R, Quadri H. Counting the costs: case management implications of spinal cord stimulation treatment for failed back surgery syndrome. *Prof Case Manag* 2011;16:27–36.
9. Simpson EL, Duenas A, Holmes MW, Papaioannou D, Chilcott J. Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin: systematic review and economic evaluation. *Health Technol Assess* 2009;13:iii; ix-x, 1–154.
10. Taylor RJ, Taylor RS. Spinal cord stimulation for failed back surgery syndrome: a decision-analytic model and cost-effectiveness analysis. *Int J Technol Assess Health Care* 2005;21:351–358.
11. Taylor RS, Taylor RJ, Van Buyten JP, Buchser E, North R, Bayliss S. The cost effectiveness of spinal cord stimulation in the treatment of pain: a systematic review of the literature. *J Pain Symptom Manage* 2004;27:370–378.
12. Kumar K, Wilson JR. Factors affecting spinal cord stimulation outcome in chronic benign pain with suggestions to improve success rate. *Acta Neurochir Suppl* 2007;97 (Pt 1):91–99.
13. Rainov NG, Heidecke V. Hardware failures in spinal cord stimulation (SCS) for chronic benign pain of spinal origin. *Acta Neurochir Suppl* 2007;97 (Pt 1):101–104.
14. Jang HD, Kim MS, Chang CH, Kim SW, Kim OL, Kim SH. Analysis of failed spinal cord stimulation trials in the treatment of intractable chronic pain. *J Korean Neurosurg Soc* 2008;43:85–89.
15. Newman HM, Stevens RT, Apkarian AV. Direct spinal projections to limbic and striatal areas: anterograde transport studies from the upper cervical spinal cord and the cervical enlargement in squirrel monkey and rat. *J Comp Neurol* 1996;365:640–658.
16. Edvinsson L. Tracing neural connections to pain pathways with relevance to primary headaches. *Cephalalgia* 2011;31:737–747.
17. Keizer K, Kuypers HG. Distribution of corticospinal neurons with collaterals to the lower brain stem reticular formation in monkey (*Macaca fascicularis*). *Exp Brain Res* 1989;74:311–318.
18. Kovacs S, Peeters R, De Ridder D, Plazier M, Menovsky T, Sunaert S. Central effects of occipital nerve electrical stimulation studied by functional magnetic resonance imaging. *Neuromodulation* 2011;14:46–55; discussion 56–47.
19. Matharu MS, Bartsch T, Ward N, Frackowiak RS, Weiner R, Goadsby PJ. Central neuromodulation in chronic migraine patients with suboccipital stimulators: a PET study. *Brain* 2004;127 (Pt 1):220–230.
20. Plazier M, Vanneste S, Dekelver I, Thimineur M, De Ridder D. Peripheral nerve stimulation for fibromyalgia. *Prog Neurol Surg* 2011;24:133–146.
21. Thimineur M, De Ridder D. C2 area neurostimulation: a surgical treatment for fibromyalgia. *Pain Med* 2007;8:639–646.
22. De Ridder D, Vanneste S, Kovacs S et al. Transcranial magnetic stimulation and extradural electrodes implanted on secondary auditory cortex for tinnitus suppression. *J Neurosurg* 2011;114:903–911.
23. 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.
24. De Ridder D, Vanneste S, van der Loo E, Plazier M, Menovsky T, van de Heyning P. Burst stimulation of the auditory cortex: a new form of neurostimulation for noise-like tinnitus suppression. *J Neurosurg* 2010;112:1289–1294.
25. Simpson BA. Preface. In: Simpson BA, ed. *Electrical stimulation and the relief of pain*, Vol. 15. Amsterdam: Elsevier, 2003: ix.
26. Kovacs S, Peeters R, De Ridder D, Plazier M, Menovsky T, Sunaert S. Central effects of occipital nerve electrical stimulation studied by functional magnetic resonance imaging. *Neuromodulation* 2011;14:46–57.
27. Mouton LJ, Klop EM, Holstege G. C1-C3 spinal cord projections to periaqueductal gray and thalamus: a quantitative retrograde tracing study in cat. *Brain Res* 2005;1043:87–94.
28. Craig AD, Zhang ET, Blomqvist A. Association of spinothalamic lamina I neurons and their ascending axons with calbindin-immunoreactivity in monkey and human. *Pain* 2002;97:105–115.
29. Chandler MJ, Zhang J, Foreman RD. Vagal, sympathetic and somatic sensory inputs to upper cervical (C1-C3) spinothalamic tract neurons in monkeys. *J Neurophysiol* 1996;76:2555–2567.
30. Djouhri L, Brown AG, Short AD. Effects of upper cervical spinal cord stimulation on neurons in the lumbosacral enlargement of the cat: spinothalamic tract neurons. *Neuroscience* 1995;68:1237–1246.