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'Pseudofailure' of spinal cord stimulation for neuropathic pain following a new severe noxious stimulus: learning points from a case series of failed spinal cord stimulation for complex regional pain syndrome and failed back surgery syndrome

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Abstract

Failure of spinal cord stimulation (SCS) may be due to hardware problems, migration of electrodes and, in the long-term, plasticity in the spinal cord with habituation to the stimulation current. We describe a series of seven patients who experienced acute therapeutic loss of SCS effects following an acute nociceptive event unrelated to primary pathology. There were no hardware problems. We called this 'Pseudofailure', as the effective stimulation returned in all patients following a period off stimulation or reprogramming. This phenomenon has not been reported previously in the literature. Over a 4-year period, we managed seven patients with this feature: four had received SCS for complex regional pain syndrome and three for failed back surgery syndrome. In all seven cases, there was cessation of the pain relief afforded by SCS following an acute painful event: four patients had trauma, two patients had domestic electric shock and one patient suffered shingles (varicella zoster infection). We excluded hardware-related problems in all cases. In two patients, SCS effects could be regained by an initial attempt at reprogramming. In the remaining five cases reprogramming was unsuccessful, and stimulation was switched off for several months before recommencing, when we discovered a return of good therapeutic effect. We conclude that SCS may seem to fail following a separate strong nociceptive stimulus. Stimulation may be regained with reprogramming or following a period with stimulation switched off. We would, therefore, advise against removal of SCS hardware in the first instance.

Keywords

Spinal cord stimulation, neuropathic pain, complex regional pain syndrome, failed back surgery syndrome, pseudofailure

Introduction

Following an initial period of successful spinal cord stimulation (SCS), subsequent failure of therapy may be due to hardware malfunction (e.g. resulting from physical damage to, or migration of leads) or habituation to stimulation. Replacement of components or reprogramming is, in these situations, able to restore therapeutic benefits.

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However, we identified that following an acute painful stimulus SCS therapy may temporarily cease, returning after a few months with stimulation switched off. This is not due to hardware or software malfunction but, we postulate, is due to reversible changes in the gating of sensory stimulus as a consequence of a new severe noxious stimulus.

Method

Over a 4-year (2009–2013) period, we encountered seven patients who had sudden temporary cessation of SCS following a new severe noxious stimulus. All patients had SCS implantation at our institution under the supervision of one consultant neurosurgeon, and all had successful SCS therapy initially. Implantable pulse generator (IPG) programming was performed at our institution exclusively, as were all patient follow-ups.

Following the loss of SCS therapy secondary to the experience of a severe nociceptive stimulus, all seven patients were investigated for hardware malfunction with radiographs of the implant to check for physical integrity, as well as IPG interrogation to check for function of the SCS implant.

In all cases, the stimulation was ultimately salvaged. This occurred either on initial reprogramming or after a period during which SCS therapy was switched off. We reviewed their medical notes and our management decisions and present them as a case series, to illustrate a phenomenon we term as ‘pseudofailure’ of SCS. Literature search using Medline showed no previously published documentation of such a phenomenon.

Results

All seven patients had *Medtronic Specify 2×8* electrodes: five patients had *Medtronic PrimeAdvanced Neurostimulators*, while the remaining two had *RestoreSensor* rechargeable IPG. The indication for SCS was complex regional pain syndrome (CRPS) in four patients and failed back surgery syndrome (FBSS) in three patients. None of these patients had SCS for phantom limb pain. Implantation site was cervical spine in two patients and thoracic spine in five patients. Post SCS radiographs were available for all seven patients; a practice we follow routinely after all SCS implantation procedures to document the exact location of electrodes.

All seven patients experienced a severe noxious stimulus, immediately followed by cessation of all paraesthesia sensation from the stimulator using previously active contacts, even at higher voltages. Radiographs were taken following these events and compared with those previously taken. In all cases, there had been no obvious lead migration, and the leads appeared to be physically intact.

IPG interrogation confirmed functional integrity of the systems. In all cases, the impedance remained normal, and the SCS was functioning, although the patients could not feel any stimulation. Hence, we were faced with intact systems but no perceptible or therapeutic stimulation.

In all seven patients, the effects of stimulation had stopped immediately following a new acute noxious stimulus, although the nature of this stimulus varied within the cohort. The loss of stimulation was abrupt and coincided with the noxious event. There had not been a gradual decline in therapeutic effect indicating a tolerance to stimulation prior to this in any of these patients.

In five of the patients, initial reprogramming was unsuccessful in achieving any paraesthesia. Therefore, a period with no stimulation was tried, following which a near complete return of stimulation was possible.

In the remaining two patients, SCS therapy was salvaged on initial reprogramming. Habituation following a period of SCS therapy is recognized and can also be managed with reprogramming. However, the abruptness of the loss of stimulation and its relationship to the noxious in these two patients suggests that habituation was not the mechanism. As such, we include these two patients in this series. The case summaries are as follows:

Patient 1

Patient 1 was a 53-year-old female patient with SCS implanted for CRPS of the right leg and foot. She initially had 100% coverage and more than 50% pain relief. Stimulation was lost following a road traffic accident (RTA), while she was a passenger in a car, during which she experienced pain from impact with the car interior. The SCS device was intact. Initial remapping attempts following RTA could only achieve stimulation in the upper thigh of the affected limb. No stimulation reached the target area with CRPS. The SCS device was switched off for 4 months following which 75% coverage was achieved. At 5 months, attempt at reprogramming achieved a larger area of coverage, but complete topographical coverage was never again achieved.

One year later, the patient had metatarsal fusion surgery of the CRPS affected limb, following which stimulation was lost completely again. Reprogramming achieved coverage between her thigh and knee but not further peripherally. Currently, the patient has had SCS stimulation switched off again and attempt at reprogramming will be made after another 3–4 months.

Patient 2

Patient 2 was a 56-year-old female patient with FBSS and left lower limb pain. Following SCS implantation

100% coverage and 70% pain relief had been achieved. A *PrimeAdvanced Neurostimulator* was initially implanted, but this became depleted within 23 months, and so, a rechargeable unit was subsequently implanted. There had been no change in the effect of stimulation following this procedure. This patient subsequently had a violent fall while standing on a moving bus, following which only stimulation in the leg was present (but not the foot). Initial reprogramming attempt was able to achieve 100% coverage again.

Patient 3

Patient 3 was a 34-year-old female patient with CRPS of the right arm. Initial coverage of 90% and more than 50% pain relief had been achieved with SCS therapy. She suffered recurrent episodes of shingles (varicella zoster infection) in the affected arm with loss of stimulation in the infected dermatomes. SCS therapy was switched off for 12 months due to recurrent reactivation of shingles. Following this, we were able to achieve the same coverage again.

Patient 4

Patient 4 was a 54-year-old female patient with FBSS and left leg pain. Initial coverage was 100% with more than 50% pain relief. Following an electric shock while on vacation abroad, she had a complete loss of stimulation. The IPG had been unaffected by the electrocution, as proven on interrogation of the device. We were unable to regain any stimulation in the target area on initial attempts at reprogramming. SCS was, therefore, switched off for 2 months, following which reprogramming was able to achieve 100% coverage, although the patient reported that pain relief was not as effective as previously (40%–50% pain relief).

Patient 5

Patient 5 was a 56-year-old man with CRPS affecting his left leg and foot. Initial coverage was 100% with 90% pain relief. Following a fall from standing height, he reported no coverage in his leg. Initial reprogramming was unable to restore stimulation in the leg. SCS was switched off for 2 months following which reprogramming was able to achieve full coverage again. Similar levels of pain relief were achieved but required a higher voltage.

Patient 6

Patient 6 was a 57-year-old woman with CRPS of the right hand. Initial coverage was 100% with more than 50% pain relief. Following a fall, she lost all stimulation

in the affected limb. Initial reprogramming allowed return of stimulation, however, a higher voltage was necessary as well as a change in the stimulation rate.

Patient 7

Patient 7 was a 44-year-old man with FBSS and right knee pain. Initial coverage was 100% with 80% reduction in pain. *RestoreSensor* IPG had been implanted. Following electrocution while carrying out electrical repairs at home, he had complete loss of stimulation, which could not be re-instituted on initial re-programming. The IPG was unaffected by the electric shock. After 2 months with the stimulation switched off, reprogramming was able to establish full coverage, although a higher voltage was necessary.

Table 1 summarizes the above data. Table 2 contains the programmes pre- and post-noxious stimulus. (These are 16 contact electrodes.)

Discussion

This series of cases shows that a cessation of beneficial SCS therapy following a severe nociceptive stimulus is likely to be temporary and can be restored after a period of time. Although the source of the stimuli varied within the cohort, what was common from patient reports is that they had experienced a severely painful event. The part of the body where the acute pain was felt was in all but one patient, different to the area already affected by neuropathic pain, but nonetheless, it altered the neuromodulation in the neuropathic region.

Our investigations showed no hardware malfunction in any of these patients. X-rays ruled out obvious lead fracture or migration. This cohort of patients had surgical paddle leads which makes micromigration (minute movements of the lead) unlikely due to the amount of fibrous scar tissue that tends to form within 6 months of implantation.

We considered the possibility of damage to the dorsal horns and neural substrate at the time of injury or a potentially reversible neurophysiological alteration leading to the cessation of SCS effect. Therefore, we elected to stop the external electrical field to allow time for repair or such that baseline can be re-achieved. The duration of SCS therapy 'off' time necessary to allow recovery of beneficial neuromodulatory effects varied between these patients, as did the degree of recovery experienced. In circumstances where we were unable to reprogramme the IPG to restore stimulation immediately, we elected to switch off the stimulator for a 2-month period in the first instance before reattempting SCS therapy. We postulated that this would be sufficient time to allow the acute pain to resolve. What is

Table 1. Case summary.

	Indication for SCS	Initial SCS efficacy	Incident	Findings after nociceptive event	SCS switch off interval	Return of stimulation
Patient 1	CRPS leg	100% coverage and >50% pain relief	High-speed RTA. Passenger in a car	Complete loss of stimulation	4 months	Near complete return of stimulation (75% coverage and >50% pain relief)
Patient 2	FBSS	100% coverage and 70% pain relief	Fall. Passenger in a bus	Complete loss of stimulation	0	Complete return of stimulation (100% coverage and 70% pain relief) on initial reprogramming
Patient 3	CRPS arm	90% coverage and >50% pain relief	Shingles – recurrent episodes	Stimulation lost in dermatomes affected by infection	12 months	Complete return of stimulation (90% coverage and >50% pain relief)
Patient 4	FBSS	100% coverage and >50% pain relief	Electrocution	Complete loss of stimulation	2 months	Return of stimulation in same region but less effective (100% coverage. 40–50% pain relief)
Patient 5	CRPS leg	100% coverage and 90% pain relief	Fall from standing height	Complete loss of stimulation	2 months	Complete return of stimulation (100% coverage and 90% pain relief)
Patient 6	CRPS hand	100% coverage and >50% pain relief	Fall from standing height	Complete loss of stimulation	0	Complete return of stimulation on initial reprogramming (100% coverage and >50% pain relief)
Patient 7	FBSS	100% coverage and 80% pain relief	Electrocution	Complete loss of stimulation	4 months	Near complete return of stimulation (100% coverage and 80% pain relief)

SCS: spinal cord stimulation; CRPS: complex regional pain syndrome; FBSS: failed back surgery syndrome.

uncertain is whether a longer duration of ‘off’ time following a noxious stimulus would allow a greater degree of therapeutic benefit to be salvaged.

As this interruption in SCS therapy was temporary and reversible to varying degrees, we coined the term ‘pseudofailure’ to describe it. The neurophysiological mechanism remains to be deciphered. Possible mechanisms for this phenomenon of ‘pseudofailure’ can be speculated from current theories on SCS mechanism of action.

Although Melzack and Wall’s theory of gate control from 1965 led to research which ultimately resulted in the development of SCS therapy, its explanation of the mechanism of action of SCS is now controversial, if not incomplete. According to the theory, stimulation of large fibres in the dorsal columns activates a gating mechanism in the dorsal horn.¹ However, one would be led to expect that nociceptive pain would be effectively blocked by SCS. In reality it is not, as demonstrated by our cohort of patients who suffered acute nociceptive pain despite the presence of SCS.

Another popular theory of the mechanism of neuropathic pain relates to hyperexcitability of multimodal wide dynamic range (WDR) cells in the dorsal horns^{2,3} and the release of glutamate and dysfunction of gamma-aminobutyric acid (GABA) systems.⁴

SCS therapy leads to a reduction of extracellular dorsal horn glutamate concentration,⁵ by way of activating GABA-B receptors.⁶ This is further supported by experiments showing potentiation of SCS efficacy when used in conjunction with intrathecal baclofen.⁷ Activation of the muscarinic M4 receptor has also been implicated in the mechanism of action of SCS.^{8,9} Descending serotonergic pathways additionally seem to have a role in the effect of SCS induced pain relief.¹⁰ Wallin et al.¹¹ showed that SCS inhibits long-term potentiation of WDR neurons.

The experience of nociceptive stimulus may alter the response of WDR cells to SCS, overcoming the beneficial effects, albeit temporarily. From our clinical experience of approximately 200 patients who have had surgically implanted SCSs, several have experienced

Table 2. Stimulator setting pre- and post-noxious stimulus.

	Pre-noxious stimulus settings				Post-noxious stimulus settings			
	Contacts	Voltage	Rate	Pulse width	Contacts	Voltage	Rate	Pulse width
Patient 1	4– 5+ 7–	2.8	70	300	Programme 1: 4– 5+ 7– Programme 2: 6+ 7–	3.4 3.4	60 60	470 450
Patient 1 (second stimulus)	Programme 1: 4– 5+ 7– Programme 2: 6+ 7–	3.4 3.4	60 60	470 450	Programme 1: 0– 1+ Programme 2: 6– 7+	3.5 3.5	60 60	270 270
Patient 2	9– 14+ 15–	3.3	70	210	Programme 1: 8+ 14+ 9– 15– 10+ Programme 2: 9+ 10– 14+ 15– Programme 3: 8+ 9– 14+ 15– 10+	6.8 7.2 7.2	70 70 70	450 450 450
Patient 3	Programme 1: 6– 7+ Programme 2: 10+ 11– 12+	6.4 2.4	60 60	200 90	Programme 1: 6– 7+ Programme 2: 10+ 11– 12+ Programme 3: 3– 4+	6.4 2.4 3.5	60 60 60	200 90 210
Patient 4	Programme 1: 6– 7+ Programme 2: 4+ 5– 6+ Programme 3: 14– 15+	2.6 2.1 4.6	80 80 240	240 240 240	Programme 1: 6– 7+ Programme 2: 5– 6+ Programme 3: 9– 10+	1.9 3.1 2.0	40 40 40	240 150 150
Patient 5	4+ 5– 6+	2.7	40	270	6+ 7–	10.2	70	450
Patient 6	13– 14+	0.8	60	190	Programme 1: 13– 14+ Programme 2: 12– 13+	1.0 0.9	60 60	190 200
Patient 7	10+ 11– 12+	5.5	60	210	Programme 1: 10+ 11– 12+ Programme 2: 10+ 11– 12+	8.8 9.2	80 190	510 520

noxious stimuli post-implantation (including surgical procedures and childbirth), but only 7 patients have experienced this complete loss of stimulation. Although it is a rare event, ‘pseudofailure’ should be kept in mind when managing patients with acute loss of stimulation following a noxious stimulus.

Conclusion

In patients who have experienced a loss of previously efficacious therapeutic effect of SCS following a new nociceptive stimulus, we suggest that in the first instance, all SCS hardware and software settings should be checked. If these appear unaltered, then an initial period (2–4 months) with SCS switched off is likely to allow subsequent return of beneficial SCS therapy. As such one should not be too hasty in removing SCS hardware due to such perceived failure of SCS therapy.

Declaration of Conflicting Interests

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References

1. Krames E. Implantable devices for pain control: spinal cord stimulation and intrathecal therapies. *Best Pract Res Clin Anaesthesiol* 2002; 16(4): 619–649.
2. Yakhnitsa V, Linderroth B and Meyerson BA. Spinal cord stimulation attenuates dorsal horn neuronal hyperexcitability in a rat model of mononeuropathy. *Pain* 1999; 79: 223–233.
3. Guan Y, Wacnik PW, Yang F, et al. Spinal cord stimulation-induced analgesia: electrical stimulation of dorsal column and dorsal roots attenuates dorsal horn neuronal excitability in neuropathic rats. *Anesthesiology* 2010; 113: 1392–1405.
4. Stiller CO, Cui JG, O'Connor WT, et al. Release of gamma-aminobutyric acid in the dorsal horn and suppression of tactile allodynia by spinal cord stimulation in mononeuropathic rats. *Neurosurgery* 1996; 39: 367–375.
5. Cui JG, O'Connor WT, Ungerstedt U, et al. Spinal cord stimulation attenuates augmented dorsal horn release of excitatory amino acids in mononeuropathy via a GABAergic mechanism. *Pain* 1997; 73: 87–95.

6. Cui JG, Linderorth B and Meyerson BA. Effects of spinal cord stimulation on touch-evoked allodynia involve GABAergic mechanisms. An experimental study in the mononeuropathic rat. *Pain* 1996; 66: 287–295.
7. Cui JG, Meyerson BA, Sollevi A, et al. Effect of spinal cord stimulation on tactile hypersensitivity in mononeuropathic rats is potentiated by simultaneous GABA(B) and adenosine receptor activation. *Neurosci Lett* 1998; 247: 183–186.
8. Song Z, Meyerson BA and Linderorth B. Muscarinic receptor activation potentiates the effect of spinal cord stimulation on pain-related behavior in rats with mononeuropathy. *Neurosci Lett* 2008; 436: 7–12.
9. Schechtmann G, Song Z, Ultenius C, et al. Cholinergic mechanisms in the pain relieving effect of spinal cord stimulation in a model of neuropathy. *Pain* 2008; 139: 136–145.
10. Song Z, Ultenius C, Meyerson BA, et al. Pain relief by spinal cord stimulation involves serotonergic mechanisms: an experimental study in a rat model of mononeuropathy. *Pain* 2009; 147: 241–248.
11. Wallin J, Fiska A, Tjølsenb A, et al. Spinal cord stimulation inhibits long-term potentiation of spinal wide dynamic range neurons. *Brain Res* 2003; 973(1): 39–43.