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Electroencephalographic evoked pain response is suppressed by spinal cord stimulation in complex regional pain syndrome: a case report

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Abstract

Purpose: Pain is a subjective response that limits assessment. The purpose of this case report was to explore how the objectivity of the electroencephalographic response to thermal stimuli would be affected by concurrent spinal cord stimulation.

Case report: A patient had been implanted with a spinal cord stimulator for the management of complex regional pain syndrome of both hands for eight years. Following ethical approval and written informed consent we induced thermal stimuli using the Medoc PATHWAY Pain & Sensory Evaluation System on the right hand of the patient with the spinal cord stimulator switched off and with the spinal cord stimulator switched on. The patient reported a clinically significant reduction in thermal induced pain using the numerical rating scale (71.4% reduction) with spinal cord stimulator switched on. Analysis of electroencephalogram recordings indicated the occurrence of contact heat evoked potentials (N2-P2) with spinal cord stimulator off, but not with spinal cord stimulator on.

Conclusion: This case report suggests that thermal pain can be reduced in complex regional pain syndrome patients with the use of spinal cord stimulation and offers objective validation of the reported outcomes with this treatment.

Keywords: complex regional pain syndrome; contact heat evoked potentials; electroencephalography (EEG); spinal cord stimulation

Introduction

Spinal cord stimulation (SCS) is considered as an option for the management of complex regional pain syndrome (CRPS); however, the clinical outcome data is limited to one randomised controlled trial of 24 patients [1]. Hyperalgesia, an increased pain response to a mechanical or thermal stimulus at normal or increased threshold is a common feature of CRPS. Animal studies have demonstrated that SCS significantly reduces mechanical hyperalgesia [2-4]. These studies suggest that SCS mechanisms may involve reduction of glial activation at spinal cord level and/or activation of μ-opioid and δ-opioid receptors. However, in humans it has been observed that SCS had no effect on experimental pain thresholds and did not produce decreased sensitivity for pressure, warmth, and cold induced pain in CRPS patients [5]. The majority of currently available studies on the effectiveness of SCS, including those using quantitative sensory testing (QST) rely on patient reported outcomes such as visual analogue or numerical rating scales. The current case report investigates the effectiveness of SCS based on electroencephalogram (EEG) analysis of contact heat evoked potentials following experimental induction of thermal stimuli.

Case History

The patient developed neuropathic pain in both hands in 1999, when she was 57 years of age. Investigations included magnetic resonance imaging (MRI) of the brain and cervical spinal cord which found only insignificant minor ischaemic areas of brain and spondylitic changes of cervical spine without nerve compression. Nerve conduction studies of upper limbs found minor carpal

tunnel compression on the right side. Several treatments were attempted to manage her neuropathic pain such as lidocaine, ketamine, phentolamine, carbamazepine, clonazepam, lamotrigine, valproate, levetiracetam, amitriptyline, venlafaxine, baclofen, tizanidine, fentanyl, and morphine. On review in 2004, her clinical features were considered to support a diagnosis of complex regional pain syndrome of upper and lower limbs including continuing pain, reported coldness, hyperalgesia (to pinprick), allodynia (to light touch), dystrophic features of the hands and weakness in upper and lower limbs, matching the now accepted diagnostic criteria for complex regional pain syndrome [6].

The patient was considered for SCS on 11/04/2005 and following a successful SCS trial period (≥ 50% pain relief during one week trial) had a permanent system (Advanced Bionics Precision SC-1110) with an octopolar lead placed at C4 and dual quadrupolar leads at T10 implanted on 06/11/2006. The patient's current SCS setting runs with co-stimulation with two programs: area one (upper limbs) ,3.5 mA threshold, 210 μs pulse width, 40 Hz rate, cathode at contact 0 (100%) and anode at contact 3 (100%) of octopolar lead; area two (lower limbs) 3.5 mA level, 390 μs pulse width, 40 Hz rate, cathodes at contacts 0 (55%) and 1 (45%) and anode at contact 3 (100%) of quadrupolar array.

In the month prior to participation in the current study, the patient used the SCS an average of 21.94 hours/day, the number of days in that month with stimulation was 29 days and without was only one day (we requested the patient to switch off the device the night prior to the test session). The patient reported a reduction in pain intensity from eight (with SCS off) to two (with SCS on) using a 0-10 numerical rating scale (NRS), which is equivalent to a 75% improvement.

Concomitant medication consisted of Duloxetine (60 mg/day) and Co-dydramol

(10/500 mg/day). Ethical approval was granted by NRES Committee West Midlands - South Birmingham (REC reference: 12/WM/0263) and written consent form obtained.

The patient switched off the implantable pulse generator (IPG) the night prior to the test session. This would ensure that the patient was free from the effects of the SCS, as it may take a few hours before the effects wear off. During the experiment, thermal stimuli were induced on the palm of the patient's right hand (predominant pain area) using the Medoc PATHWAY Pain & Sensory Evaluation System (Medoc Ltd, Ramat Yishai, Israel) with advanced thermal stimulator (ATS) and contact heat-evoked potential stimulator (CHEPS) (Figure 1). The test temperature was ascertained using the following method. The 30x30mm ATS thermode was used to evaluate pain tolerance from a baseline temperature of 32°C and programmed to increase the temperature at a rate of 1°C/sec. Three slowly ramping thermal stimuli were applied and the patient was instructed to press a button when the pain sensation reached their tolerance level. Using the 27mm diameter CHEPS probe programmed to increase the temperature at a rate of 70°C/sec followed by immediate cooling at a rate of 40°C/sec, five heat stimuli (pulses) were applied at the patient's tolerance level and the patient rated the pain intensity using a 0-10 NRS. The patient rated a stimulus temperature of 55°C as a seven out of ten. EEG recording during the no SCS condition now commenced with 25 stimuli (pulses) applied at 55°C with an interstimulus interval (randomised by software) ranging from 4-8 secs. The thermode was slightly moved to one of three adjacent but non-overlapping locations after each two stimuli to overcome habituation. Brain electrical activity recorded using EEG equipment consisting of a 10-channel system (BrainProducts, Munich,

Germany) consisting of nine Ag/AgCl scalp electrodes (AFz (ground), FCz (reference), Fz, Cz, Pz, C3, C4, T7, T8) and one electrode placed below the left eye to record eyeblinks. Impedance at all electrodes was <20 kΩ. The IPG was then switched on to being the SCS condition, and subsequent to a rest period (≈10 minutes), 25 additional stimuli were applied using the same programme. The patient reported the average pain intensity of the heat stimuli with SCS off as seven, and with the SCS on as two, using the NRS (71.4% reduction). Analysis of EEG recordings demonstrated the occurrence of contact heat evoked potentials (N2-P2 complex, average N2 latency = 500ms, average P2 latency = 552ms, average peak-to-peak amplitude = 4.54μV) at channel Pz during the SCS off condition, but these were not observed with SCS on (Figure 2).

Comment

A deflection in the waveform which resembles the N2-P2 complex that is characteristic of a contact heat evoked potential [7] was observed when the patient had the SCS switched off. There was no observable evoked potential when the patient had the SCS switched on. It should be noted that due to the small number of stimuli used, the EP is greatly affected by noise. In order to confirm and extend this limited observation, future work would benefit from an increase in the number of stimuli. Here, 25 stimuli were used in each condition, which were further reduced to 18/19 after removal of eyeblink artefacts. By increasing the number of stimuli to >40 the average waveform would benefit from an improved signal to noise ratio, making the presence or absence of an EP more obvious. It is possible that EPs were occurring during the SCS on condition, but were obscured by the presence of random noise, and an increase in the

number of stimuli would reveal any EP present in the data. We note that it is important to minimise participant discomfort, especially when the study involves inflicting pain on a person already suffering chronic pain. However, the present case study demonstrates the need for more stimuli, if we are to gather higher quality data in the future.

Earlier work by Kemler and colleagues reported that SCS had no effect on pain threshold [5]. We are unable to say if the pain threshold was affected by SCS in this case, as the maximum operating temperature of the Pathway system (55°C) was reached with SCS off, making any increase in threshold impossible to detect once the SCS was on. The patient did report a dramatic (71.4%) decrease in pain from the heat stimuli at the same temperature after the SCS was switched on. This implies that the SCS has a modulating effect on the perception of heat stimuli. How this modulation occurs is not clear.

The average waveform also shows a large artefact in all channels which begins around -100ms and ends around 300ms. This artefact is generated by the CHEPS machinery when the thermode is heating up, and is identical in all trials. Previous studies using CHEPS have reported such artefacts [8] and it has been possible to reduce or even completely eliminate this artefact by reducing the impedance at all electrodes to <5kΩ [9]. However it is not always possible to spend the extra time required to achieve minimal impedance, especially when the participant is experiencing discomfort.

In conclusion, this case report suggests that SCS for the management of CRPS may contribute to a decrease in both the subjective perception of thermal pain and the neuronal activity evoked by pain stimuli. EEG analysis of contact heat evoked potentials with SCS off and on allows for a more objective assessment of

response to SCS management. A case series in this patient population is warranted to corroborate these results.

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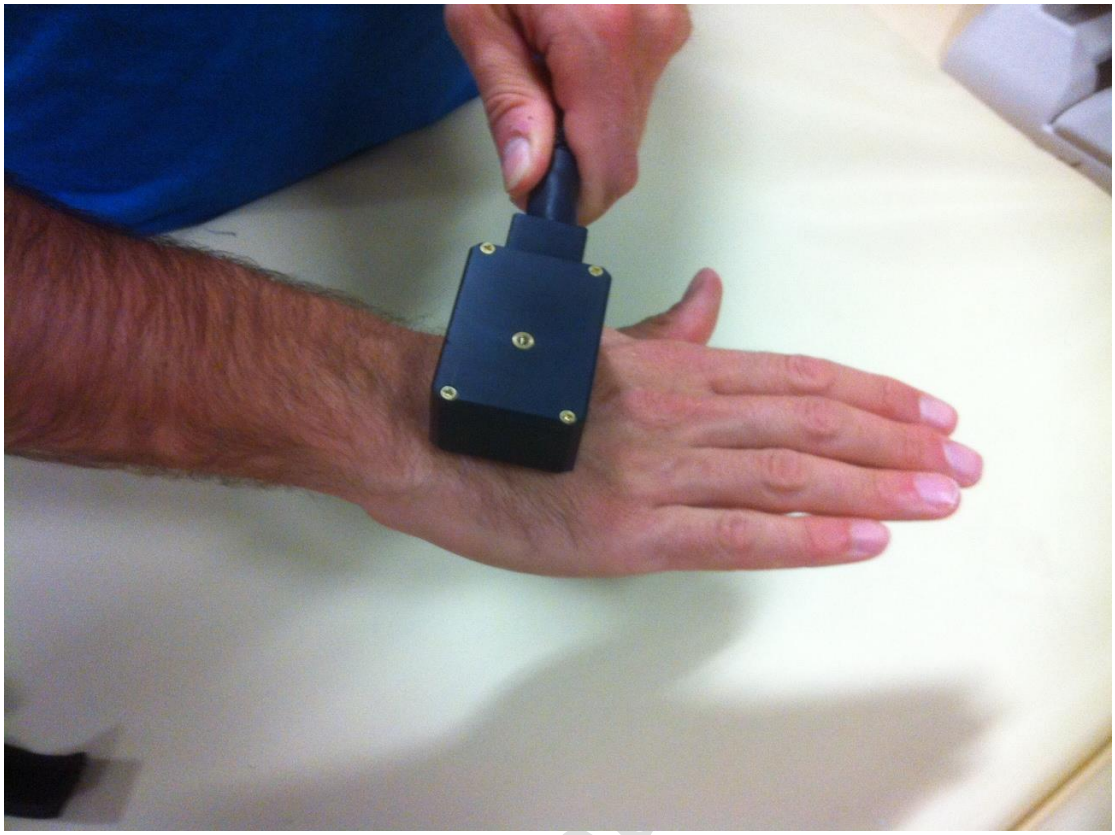

Figure 1. Demonstrative example of the thermode held onto the dorsum of right hand in a stimulation position.

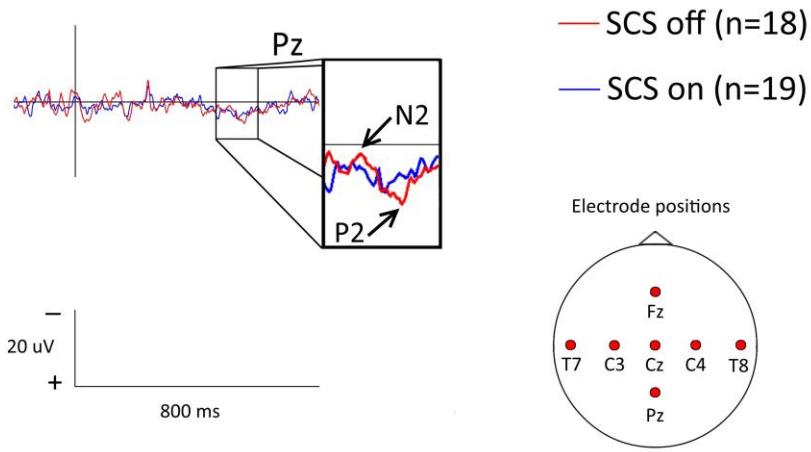

Figure 2. Scalp distribution of the effect of spinal cord stimulation on contact heat evoked potentials.