Efficacy of Spinal Cord Stimulation for Central Post-Stroke Pain

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1. Introduction

Central post-stroke pain (CPSP) is a neuropathic-type of pain that affects about 1-8\% of patients after stroke (Andersen et al., 1995; Bowsher 1993), and is characterized by pain and sensory dysfunction involving the area of the body that has been affected by the stroke (Leijon et al., 1998). Once present, CPSP rarely abates, causing a considerable long-term impact on patient’s quality of life (Wider & Ahlstrom, 2002). The first line of treatment for CPSP is usually tricyclic antidepressant amitriptyline or antiepileptic gabapentine. However, these drugs are often ineffective or cause intolerable side effects; including dry mouth, urinary retention, arrhythmias, and sedation; especially in elderly stroke patients (Finnerup et al., 2005).

Neuromodulatory techniques have been proposed for treatment of severe medically refractory CPSP (Kim, 2009). Deep brain stimulation (DBS) has yielded inconsistent results (Kumar et al., 1997). Motor cortex stimulation (MCS) has been the most popular technique to treat intractable CPSP. MCS involves implanting electrodes over the motor strip through a craniotomy. MCS has been reported to achieve pain relief in approximately half of patients (Katayama et al., 1998; Fontaine et al., 2009; Saitoh et al., 2007; Lazorthes et al., 2006). However, a large proportion of patients remain untreated due to either failure or decline of MCS (Aly et al., 2010). One group of patients declined MCS because of the need for a craniotomy (Aly et al., 2010). Another group of patients are considered poor candidates for MCS based on their poor response to repeated transcranial Magnetic Stimulation (r TMS) (Hosomi et al., 2008; Andre-Obadia et al., 2006). Moreover, MCS needs a special neurosurgical expertise and its use is correspondingly restricted to well-established functional neurosurgical centers (Kim, 2009). In these situations, there is practically no viable option to help these patients to relive their disabling medically refractory pain (Aly et al., 2010).

Spinal cord stimulation (SCS) is the most widely used neurostimulation technique for chronic pain because it is minimally invasive, has a low complication rate, and is generally effective (Kumar et al., 2006; Camerons, 2004). SCS has been proven effective for various
types of neuropathic pain of peripheral origin, in particular, failed back surgery syndrome (FBSS) and peripheral neuropathy (Kumar et al., 2006). In contrast, only a few reports to date have investigated the use of SCS for CPSP (Simpson, 1991; Katayama et al, 2001; Cruccu et al., 2007; Lopez et al., 2009; Aly et al., 2010). SCS is generally considered ineffective for central neuropathic pain, including CPSP in spite of the paucity of data in the literature to support this idea (Simpson, 1991; Katayama et al., 2001; Cruccu et al., 2007; Lopez et al., 2009; Aly et al., 2010). CPSP most often has a wide pain distribution and commonly occurs in a hemibody fashion (Kim, 2009). Because coverage of the entire painful area by stimulation paraesthesia is essential for success of SCS (Holsheimer, 1997), SCS was considered unsuitable for CPSP. From a pathophysiological point of view, it was argued how SCS which act on segmental spinal level would affect pain generators in CPSP which are located proximal to deafferentiation level i.e. supraspinal (Tsubokawa, et al., 1993).

In this chapter, we reviewed the literature about the use of SCS for CPSP with regard to patient selection, surgical technique, clinical outcome and, and mechanism of action.

2. Presurgical evaluation

The diagnosis of CPSP should be established based on the following criteria (Klit et al., 2009): 1) development of pain following stroke; 2) sensory disturbance correlated with the cerebrovascular lesion; 3) pain located within the territory of sensory disturbance. Other causes of nociceptive and peripheral neuropathic pain should be ruled out particularly those which are prevalent in this age group such as lumbar canal stenosis, peripheral neuropathy, and post-stroke shoulder pain (Kim, 2009; Aly et al., 2010).

Comprehensive neuropsychological assessment is essential in all patients to rule out serious psychiatric disorder or severe cognitive dysfunction (Kumar et al., 2006). To be eligible for SCS treatment, patients should have failed medical treatment for at least 6 months, including antidepressants and anticonvulsant drugs (Cruccu et al., 2007).

3. Patients selection for SCS

There is no doubt that MCS remains the primary option for treating intractable CPSP based upon the available literature (Fontaine et al., 2009; Saitoh et al., 2007; et al., 2008). The experience with MCS is larger and the outcome is more consistent. MCS has been implanted in more than 117 patients with CPSP with approximately 50 % success rate (Fontaine et al., 2009). However, a significant proportion of patients with intractable CPSP remain untreated either due to failure, poor prediction, or refusal of MCS by patients. In a recent study, out of 87 patients presented to neurosurgery department with intractable CPSP only 13 patients eventually had undergone MCS (Aly et al., 2010). Therefore, SCS may be an alternative option in the following situations:

3.1 Failure or poor predictors of MCS

Approximately 50 % of patients who undergo MCS fail to have satisfactory pain relief (Fontaine et al., 2009; Saitoh et al., 2007; Hosomi et al., 2008). Another group of patients may be considered poor candidates for MCS based on their poor response to TMS (Saitoh et al., 2007; Hosomi et al., 2008; Aly et al., 2010). For those groups of patients SCS may be one of the few viable options.
3.2 Patient preference

Some patients may prefer SCS over MCS because it does not need of craniotomy or general anesthesia as MCS does (Aly et al., 2010). Compared to MCS, percutaneous trial SCS is much better tolerated by patients can be done under local anesthesia, and the electrodes can be removed easily if a trial fails (Aly et al., 2010). In fact, the minimal invasiveness and simplicity of SCS is one of the most appealing aspects of SCS for clinicians and patients as well.

![Flowchart](image)

**Fig. 1.** Suggested algorithm for management of intractable CPSP.

3.3 Unavailability of MCS service

MCS service is generally less accessible than SCS. Because MCS needs a craniotomy and special neurosurgical expertise its use is limited to specialized neurosurgical centers (Aly et al., 2010). In contrast, the SCS technique is relatively simple, less invasive, and can be mastered not only by neurosurgeons but by many anesthesiologists and pain clinicians as well (Kim, 2009; Aly et al., 2010).
3.4 Pain distribution

3.4.1 Localized pain distribution

The distribution of CPSP throughout the body may be quite variable. CPSP most often occurs in a hemibody fashion, but may be restricted to distal parts of the body, such as the hand or foot (Kim, 2009). Because coverage of the entire targeted region of pain by stimulation-induced paraesthesia is essential for success of SCS (Holsheimer, 1997), it was thought that SCS may be unsuitable for CPSP. Obviously, patients who have localized pain may be the ideal candidate for SCS. Patients with putaminal hemorrhage that affects the posterior part of the internal capsule has the propensity to cause pain that is most severe in, or confined to, the leg (Kim, 2003). This explains why that group of patients represented (40%) of cases in Ali et al study (Aly et al., 2010). Some patients have a wide pain distribution but pain is more severe in distal parts such as foot or hand which cause substantial disability due to interfering with hand movement or walking respectively (Aly et al., 2010). It was reported that targeting these distal areas which are most painful may still improve the patient pain. In this context it is helpful to measure a separate VAS rating of different areas. Finally, some patients will benefit from insertion of 2 different electrodes in cervical and dorsal spine to target a wide area (Aly et al., 2010).

3.4.2 Lower extremity pain

Patients with leg-dominant CPSP were considered more suitable candidates for SCS than upper extremity pain because thoracic electrodes are technically less demanding and less susceptible to displacement than cervical electrodes. (Kumar & Wilson, 2007). In addition, lower-limb pain is not considered a good indication for MCS, given the technical difficulties associated with implanting electrodes on the medial surface of the brain (Fontaine et al., 2009; Aly et al., 2010).

4. Surgical procedure

4.1 Implantation of temporary electrodes

In the prone position, a percutaneous lead with quadripolar electrodes (Pisces Quad, Model 3487A; Medtronic, Inc., MN, USA) is inserted into the epidural space through a Touhy needle under local anesthesia. The tip was advanced to the required spinal level: C4 to C7 for upper limb pain or T9 to T12 for lower limb pain. The electrodes were manipulated with fluoroscopic guidance so that the stimulation-induced paraesthesia covered the entire region affected by pain (Aly et al., 2010; Stojanovic & Abdi, 2002; Kumar et al., 2006).

4.2 Trial stimulation

Using an externalized temporary lead connected to a test stimulator (model 3625, Medtronic), trial stimulation was performed to evaluate the efficacy of pain relief before permanent implantation. During the trial period (2 to 14 days), patients were allowed to test the pain-relieving effects of several stimulation parameters and combinations of active electrodes. Thereafter, the temporary electrodes are removed and patients were discharged. After counseling the patients in outpatient clinic, those who decided to proceed were
scheduled for implantation of a permanent SCS system (Aly et al., 2010; Stojanovic & Abdi, 2002; Kumar et al., 2006).

4.3 Implantation of permanent SCS system
A permanent lead was implanted in a similar manner as the trial lead and was anchored subcutaneously. Finally, an implantable pulse generator (IPG; Itrel III Model 7425 or Synergy Model 7427 V, Medtronic, Inc.) is implanted under general anesthesia in the left lower abdomen or anterior chest (Aly et al., 2010).

4.4 Evaluation of pain relief
Pain intensity was evaluated using a visual analogue scale (VAS) ranging from 0 (no pain) to 10 (worst possible pain) at baseline, during the trial, and at follow-up visits every 6 months. In patients with wide regions of pain, the VAS was assessed independently for each region and the target area for SCS was determined based on the area with greatest pain and disability (Aly MM, et al, 2010) (Fig. 2).

In addition, the patient global impression of change (PGIC) scale was assessed at the latest follow-up visit after the permanent implant. The PGIC scale indicates overall improvement according to a seven-point categorical scale: 1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; and 7, very much worse. The “rank 2” and “rank 1” were considered as clinically significant improvement (Aly MM, et al, 2010; Farrar, J., 2001).

During data analysis, the degree of pain relief was classified into three categories: good (≥50%), fair (30-49%), or poor (<30%) based on percent reduction of VAS (% reduction = [VAS pre-stimulation - VAS post-stimulation / VAS pre-stimulation] × 100%). Pain relief of “fair” or better was considered clinically significant based on a report documenting that pain reduction as low as 30% corresponds to clinically meaningful success (Aly et al., 2010; Farrar, 2001).

4.5 Stimulation parameters
The most common stimulation parameters were an amplitude of 1.5-3 V (range 1.5-6 V), a pulse width of 210 μsec (range 210-350 μsec), and a frequency of 31 Hz (range 10-50 Hz) with a bipolar configuration (Aly et al., 2010).

5. Clinical outcome
5.1 Previous studies design
To our knowledge, only 4 previous studies have investigated the use of SCS in CPSP (Table 1) (Simpson, 1991; Katayama, et al., 2001; Cruccu, et al., 2007; Lopez, 2009; Aly et al., 2010).

All previous studied were retrospective in nature and involved a small number of patients (6-45). Therefore, a prospective controlled study with a larger population of patients is needed to provide stronger evidence for the efficacy of SCS in CPSP. However performing such study poses certain challenges. Firstly, it is difficult to recruit a large number of CPSP patients in one center owing to the low prevalence and under-diagnosis of this condition.
It is also difficult to conduct placebo-controlled studies or blinded evaluations because SCS induces perceptible sensation (Camerons, 2004). Therefore, the role of placebo effect remains unresolved problem in SCS literature. Finally, it is difficult to conduct case-matched controls, as in surgical practice long-term follow-up care is available only for surgically treated patients (Aly et al., 2010).

Fig. 2. MRI reveals evidence of an old right putaminal hemorrhage (A). The distribution of pain in the left hemibody shows that pain was more severe in the left foot; the patient therefore underwent implantation of a lower thoracic electrode targeting the foot region (B).

5.2 Success rate

Simpson et al. first reported about long-term efficacy of SCS for CPSP in 10 patients (Simpson, 1991). Three out of the 10 patients (30 %) reported clinically significant improvement. The study done by Katayama was the main study reporting poor outcome from SCS (Katayama, et al., 2001). Katayama reported long-term pain reduction (≥60%) in

<table>
<thead>
<tr>
<th>Authors</th>
<th>No of cases</th>
<th>Outcome measure</th>
<th>Pain distribution</th>
<th>Success rate %</th>
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<td>Simpson, 1991</td>
<td>10</td>
<td>Subjective improvement</td>
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<td>30</td>
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<tr>
<td>Katayama, 2001</td>
<td>45</td>
<td>VAS &gt; 60 %</td>
<td>Not available</td>
<td>7</td>
</tr>
<tr>
<td>Ali, 2010</td>
<td>30</td>
<td>VAS &gt; 30 %, PGIC</td>
<td>Localized pain</td>
<td>25</td>
</tr>
<tr>
<td>Lopez, 2009</td>
<td>6</td>
<td>VAS &gt; 50 %</td>
<td>Localized pain</td>
<td>80</td>
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</tbody>
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Table 1. Summery of clinical outcomes of SCS studies for CPSP
only 3 of 45 patients (7%). Aly et al reported about 30 patients who underwent a trial of spinal cord stimulation, 10 underwent permanent placement, and 9 were available for follow-up (Aly, et al., 2010). Good or fair pain relief was seen in 7 of 9 patients (78%) with just over a mean 2-year follow-up. Lopez et al reported about 6 patients with SCS for CPSP. Good-to-excellent results were attained in 5 on long-term follow up (Lopez, et al., 2009).

5.3 Interpretation of outcome of previous studies

Three out of the 4 previous studies reported moderate to high success rate of SCS for CPSP (25-80 %). The fourth study reported a poor outcome from SCS with success rate of only 7 %. On interpreting the results of these studies it should be noted that these studies used different outcome measures and different inclusion criteria with regard to pain distribution (Table 1). Actually there is no consensus regarding what constitutes an optimum threshold for success in chronic pain studies. Most studies use the criterion of 50% pain relief as threshold of success. However, this criterion is increasingly challenged, because in clinical practice, patients will often be satisfied with 30% pain relief (Farrar et al., 2001; Cruccu et al., 2007). We therefore suspect that the use of > 60% VAS reduction by Katayama group might be unsuitably high threshold for success which may underestimated the clinical effect of SCS in this study (Aly et al, 2010).

5.4 Complications

Generally, the reported complication rate is low. Minor, clinically insignificant migrations were seen in 2 patients in one study (Aly et al., 2010). One electrode fractured and was replaced in another study (Lopez et al., 2009).

5.5 Predictors of success of SCS

Only one study analyzed the clinical factors predictive of success of SCS for CPSP (Aly et al., 2010). It was found that patients with hyperpathia tended to respond less well to trial stimulation than those without. This observation is consistent with a previous report in which SCS was less effective for control of evoked pain than spontaneous pain (Kim et al, 2001). It was also found that the effects of trial stimulation were sustained following permanent implantation in the majority of patients. SCS trial stimulation is thus advantageous for predicting efficacy in a minimally invasive manner before permanent implantation.

6. Mechanisms of action

The mechanism behind pain relieving effect of SCS is still not fully understood. Inhibition at spinal segmental level and activation of supraspinal mechanisms have been suggested as possible neurophysiologic mechanisms (Kishima et al., 2010). Positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies had detected brain activation during SCS (Stancák et al., 2008). Using H215O PET, we have recently observed activation not only in somatosensory areas but also in those areas concerned with emotional aspects of pain such as anterior cingulate cortex and prefrontal areas (Kishima et al., 2010). CPSP is thought to be due to abnormal processing of nociceptive information rostral to the level of deaffrentiation (Katayama et al., 2001).
Therefore, we speculate that the pain relieving effect of SCS in CPSP may be interpreted in light of its supraspinal mechanisms (Aly et al., 2010)

7. Conclusion

SCS may provide improved pain control in a group of patients with medically intractable CPSP. The efficacy of SCS in CPSP is generally modest; both in terms of success rate and degree of pain relief. However, this modest degree of efficacy is important considering the severity of pain in these patients, the refractory nature of their pain, and the paucity of alternative therapeutic options. A further prospective controlled study with larger population of patients is still needed to provide stronger evidence for the efficacy of SCS in CPSP and define patient population who are most likely to get benefit from SCS treatment. SCS should be one of the neurostimulation techniques available to treat the medically-refractory post-stroke pain patient.

8. References


Neuropathic pain is known to be pain with nerve involvement. The intensity of which depends on the severity, pain threshold and the ability of suffers to cope. Neuropathic pain may need mono-therapy or combination of therapies to be resolved. Neuropathic pain may not resolve completely, therefore patient's compliance and understanding is essential in its management. Awareness and patient's education on targets may be of help during therapies for neuropathic pain. All chapters treated introduction, characteristics, diagnosis and randomized interventions to certain management of neuropathic pain. We acknowledge all those involve in the making of this book.

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