Stereotact Funct Neurosurg 2013;91:288–289

DOI: [10.1159/000348272](https://doi.org/10.1159/000348272)

Spinal Cord Stimulation for Vegetative State: Is This Ready for Prime Time?

Michael G. Kaplitt

Weill Cornell Medical College, New York, N.Y., USA

One of the most attractive features of stereotactic and functional neurosurgery as a field is the opportunity to explore opportunities for novel neuromodulation or biological therapies for diseases not traditionally considered surgical diseases. Great strides are being made by functional neurosurgeons in both the laboratory and human studies in developing novel surgical therapies for a variety of such nontraditional disorders such as depression, drug addiction, obesity and many others [1, 2]. Among the most intriguing of these are disorders of consciousness. While patients can spontaneously recover from injuries such as trauma and stroke, those who continue to have altered consciousness over long periods of time have very limited treatment options and little hope for substantial recovery. Given our increased understanding of the functioning of the human brain, particularly with functional imaging, it is not surprising that efforts are being made to surgically intervene directly in the central nervous system to try to improve these devastating disorders. Deep brain stimulation (DBS), which is effective for movement disorders and epilepsy, has shown promise in those in minimally conscious states and has been tried in persistent vegetative state as well, based upon the belief that electrical modulation of specific targets may improve dysfunctional circuits governing arousal and consciousness [3, 4].

An alternative approach to neuromodulation for disorders of consciousness is spinal cord stimulation (SCS). This is a less invasive method of stimulating elements of the central nervous system, which is among the most attractive features of this approach. While SCS is mostly used for treating chronic pain, as with DBS, this is also being tested for a variety of new applications [5–8]. In the accompanying article by Della Pepa et al. [9], the literature describing the clinical experience to date with SCS for disorders of consciousness is reviewed. The rationale for performing SCS for this disorder is somewhat unclear, beyond simply the relatively low risk of the procedure. However, the authors provide a series of potential physiological mechanisms for functional improvement following stimulation. These include activation of the reticular formation and thalamic relay nuclei, as well as increasing cerebral blood flow. Whether these are simply nonspecific consequences of any type of neurostimulation or a specific response to SCS is unclear, but this provides some potential justification for studying this procedure. The authors also present a good summary of the

scope of the problem of disorders of consciousness, and in particular the potential cost to society that would justify SCS were it proven effective (although some of the data, particularly in the US, is fairly old).

The major problem with the entire field is a lack of rigorous, scientific testing to date. Ten publications were reviewed, and the authors should be credited for including a surgeon fluent in Japanese, since several of these articles are from Japanese-language journals. There have been no randomized, double-blind studies to date, which will be necessary if this were to be more seriously considered in the future. But even the open-label studies have utilized patients of variable presentation and vague indications. For example, most studies have used patients in a vegetative state for periods from one month to several years. While earlier patients have generally done better following surgery, they also are more likely to improve spontaneously. Furthermore, the outcome measures have been equally unclear. The largest and most recent study included in this review, by Kanno et al. [10], reported on an extremely large group of 201 patients, with a remarkable rate of 54.2% of patients with an ‘excellent’ or ‘positive’ response. An excellent response included a behavioral expression or swallowing food or water when placed in the mouth, while a positive response included eye movement in response to a visual stimulus or a pattern of opening and closing eyes when a specific stimulus is detected. Of 68 patients with traumatic etiology under 35, an astonishing 88.2% had an ‘excellent’ or ‘positive’ response. Greater detail is not provided and there is little further investigation other than exploration of cerebral blood flow, which did not correlate well with clinical outcome. The other studies cited are similarly vague in both patient selection criteria and outcome. Whether these types of unvalidated outcome measures have value is very unclear, and the functional significance of these outcomes is equally uncertain. SCS for disorders of consciousness may have value and functional neurosurgeons would welcome the opportunity to intervene in this devastating problem. This review highlights the need for more rigorous and careful clinical testing of this approach, with more careful pilot studies still needed even prior to considering more complex blinded studies.

References

- 1 Goodman WK, Alterman RL: Deep brain stimulation for intractable psychiatric disorders. *Annu Rev Med* 2011;63:511–524.
- 2 Tierney TS, Sankar T, Lozano AM: Deep brain stimulation emerging indications. *Prog Brain Res* 2011;194:83–95.
- 3 Schiff ND, Giacino JT, Fins JJ: Deep brain stimulation, neuroethics, and the minimally conscious state: moving beyond proof of principle. *Arch Neurol* 2009;66:697–702.
- 4 Sen AN, Campbell PG, Yadla S, Jallo J, Sharan AD: Deep brain stimulation in the management of disorders of consciousness: a review of physiology, previous reports, and ethical considerations. *Neurosurg Focus* 2010;29:E14.

- 5 Bernstein SA, Wong B, Vasquez C, Rosenberg SP, Rooke R, Kuznekoff LM, Lader JM, Mahoney VM, Budylin T, Alvstrand M, Rakowski-Anderson T, Bharmi R, Shah R, Fowler S, Holmes D, Farazi TG, Chinitz LA, Morley GE: Spinal cord stimulation protects against atrial fibrillation induced by tachypacing. *Heart Rhythm* 2012;9:1426–1433.e3.
- 6 Fuentes R, Petersson P, Nicolelis MA: Restoration of locomotive function in Parkinson's disease by spinal cord stimulation: mechanistic approach. *Eur J Neurosci* 2010;32:1100–1108.
- 7 Liu Y, Yue WS, Liao SY, Zhang Y, Au KW, Shuto C, Hata C, Park E, Chen P, Siu CW, Tse HF: Thoracic spinal cord stimulation improves cardiac contractile function and myocardial oxygen consumption in a porcine model of ischemic heart failure. *J Cardiovasc Electrophysiol* 2011;23:534–540.
- 8 Tator CH, Minassian K, Mushahwar VK: Spinal cord stimulation: therapeutic benefits and movement generation after spinal cord injury. *Handb Clin Neurol* 2012;109:283–296.
- 9 Della Pepa M, Fukaya C, La Rocca G, Zhong J, Visocchi M: Neuromodulation of vegetative state through spinal cord stimulation: where are we now and where are we going? *Stereotact Funct Neurosurg* 2013;91:275–287.
- 10 Kanno T, Morita I, Yamaguchi S, Yokoyama T, Kamei Y, Anil SM, Karagiozov KL: Dorsal column stimulation in persistent vegetative state. *Neuromodulation* 2009;12:33–38.