Neurol Med Chir (Tokyo) 52, 475～481, 2012

The 70th Annual Meeting Special Topics — Part I:
Validation and Prospects for Neuromodulation

Spinal Cord Stimulation for Treatment of Patients in the Minimally Conscious State

Takamitsu YAMAMOTO,[1] Yoichi KATAYAMA,[2] Toshiki OBUCHI,[2]
Kazutaka KOBAYASHI,[2] Hideki OSHIMA,[2] and Chikashi FUKAYA[1]

Divisions of [1]Applied System Neuroscience and [2]Neurosurgery,
Department of Neurological Surgery, Nihon University School of Medicine, Tokyo

Abstract

Minimally conscious state (MCS) is characterized by inconsistent but clearly discernible behavioral evidence of consciousness, and can be distinguished from coma and the vegetative state (VS). Ten MCS patients were evaluated neurologically and electrophysiologically over 3 months after the onset of brain injury, and were treated by spinal cord stimulation (SCS). A flexible four-contact, cylinder electrode was inserted into the epidural space of the cervical vertebrae, and placed at the C2–C4 levels. Stimulation was applied for 5 minutes every 30 minutes during the daytime at an intensity that produced motor twitches of the upper extremities. We used 5 Hz for SCS, considering that the induced muscle twitches can be a useful functional neurorehabilitation for MCS patients. Eight of the 10 MCS patients satisfied the electrophysiological inclusion criteria, which we proposed on the basis of the results of deep brain stimulation for the treatment of patients in the VS. Seven patients recovered from MCS following SCS therapy, and were able to carry out functional interactive communication and/or demonstrate the functional use of two different objects. Cervical SCS increased cerebral blood flow (CBF) diffusely in the brain, and CBF increased by 22.2% during the stimulation period compared with CBF before stimulation in MCS patients ($p < 0.0001$, paired t-test). Five-Hz cervical SCS could increase CBF and induce muscle twitches of the upper extremities. This SCS therapy method may be suitable for treating MCS.

Key words: minimally conscious state, spinal cord stimulation, vegetative state, prolonged coma, deep brain stimulation

Introduction

The concept of persistent vegetative state (PVS) was first proposed in 1972,[11] and The Multi-Society Task Force on PVS in 1994[19,20] defined PVS as a clinical condition of complete unawareness of the self and the environment, accompanied by sleep-wake cycles, with either complete or partial preservation of hypothalamic and brainstem autonomic function. We usually use the term of vegetative state (VS) instead of PVS, because some PVS patients may emerge from PVS. In 2002, the concept of minimally conscious state (MCS) was proposed,[7] which is characterized by inconsistent but clearly discernible behavioral evidence of consciousness, and can be distinguished from coma and VS by the presence of specific behavioral features not found in either of these conditions. Criteria were also proposed for determining emergence from MCS.

For the treatment of VS and MCS, chronic deep brain stimulation (DBS)[2,15,21,24,29] and chronic spinal cord stimulation (SCS)[5,6,12,17] have been reported, but the estimation of resting brain function in VS and MCS patients has been usually unclear. In addition, the definition of recovery from VS is different in various reports.[13,25,29] The definition of recovery and the estimation of resting brain function in VS and MCS patients are essential to evaluate the effects of these treatments. We previously investigated

Received February 27, 2012; Accepted March 29, 2012

electrophysiological evaluation to clarify the resting brain function of VS patients,[23,27,31] and found that DBS is useful for the treatment of VS patients if the candidates were selected on the basis of the electrophysiological evaluation.[26,28,29] We have mainly applied DBS to the treatment of VS patients and SCS to the treatment of MCS patients up to now.[26]

The present study describes the long-term follow-up results of chronic SCS for the treatment of MCS patients and compares the findings with the results of electrophysiological evaluation.

Methods

This study included 10 MCS patients aged from 16 to 67 years (mean 32 ± 15.9 years) treated by chronic SCS. The causes of the initial coma were head injury (6 patients), encephalomyelitis (1 patient), and cerebrovascular accident (3 patients). The clinical features of these 10 patients are summarized in Table 1. These patients underwent electrophysiological evaluations that included assessments of the auditory brainstem response (ABR), somatosensory evoked potential (SEP), pain-related P250, and continuous electroencephalography (EEG) frequency analysis expressed as a compressed spectral array (CSA) over 3 months after the onset of brain injury.

For ABR recording, needle electrodes were placed on the earlobes, vertex (Cz), and forehead (ground). The band pass was set from 10 Hz to 3 kHz. Binaural click stimuli were presented through earphones at 90 dB HL at a rate of 10/sec. In each trial, 2048 responses were recorded. For SEP recording, the recording electrode was placed over the primary cortical somatosensory regions on the head, with the reference electrode placed on the earlobe. The band pass was set from 0.5 Hz to 3 kHz. The pain-related P250[14] was recorded from the vertex in response to a train of electrical shocks to the finger pad at random intervals. The painful electrical skin stimuli consisted of constant current pulses of 0.5 msec duration applied at a repetition rate of 500 Hz for 50 msec. The stimulus was applied at an intensity that produced the withdrawal flexion reflex. Recording electrodes were placed on the vertex and hand region of the somatosensory cortex with reference to the electrode attached to the earlobe. The ground electrode was attached to the other earlobe or the wrist. Signals were amplified with the band pass in the range from 0.1 to 6000 Hz and were averaged over 16 sweeps with a signal processor (Fig. 1A). EEG recording was carried out using a monopolar

Table 1 Clinical features and long-term follow-up results of 10 minimally conscious state (MCS) patients treated by chronic cervical spinal cord stimulation (SCS)

Case No.	Age (yrs)/ Sex	Cause of brain injury	Start of SCS after initial injury (mos)	Positive electrophysiological items*	CBF (ml/100 g/min)		Long-term follow-up results after SCS
					Before SCS	During SCS	
1	26/M	head injury (cerebral contusion)	9	EEG, ABR, SEP, pain-related P250			recovered from MCS, use wheelchair alone
2	25/M	head injury (cerebral contusion, acute subdural hematoma)	9	EEG, ABR, SEP, pain-related P250			recovered from MCS, use wheelchair alone
3	16/M	head injury (diffuse brain injury)	3	EEG, ABR, SEP, pain-related P250	44.12	54.99	recovered from MCS, walk alone
4	22/M	head injury (diffuse brain injury)	3	EEG, ABR, SEP, pain-related P250	44.09	56.87	recovered from MCS, use wheelchair alone
5	28/M	head injury (diffuse brain injury)	3	EEG, ABR, SEP, pain-related P250	44.47	55.16	recovered from MCS, use wheelchair alone
6	52/M	head injury (cerebral contusion, acute subdural hematoma)	3	EEG, ABR, SEP, pain-related P250	35.1	40.69	recovered from MCS, difficult to use wheelchair alone
7	19/F	inflammatory (acute disseminated encephalomyelitis)	53	EEG, ABR, (SEP), pain-related P250	40.42	49.43	consciousness level: MCS, conscious but inconsistent
8	37/M	vascular (intracerebral hemorrhage)	8	EEG, ABR, SEP, pain-related P250	34.16	38.29	recovered from MCS, difficult to use wheelchair alone
9	67/F	vascular (subarachnoid hemorrhage)	12	EEG, ABR, SEP, pain-related P250	35.95	46.26	consciousness level: MCS, conscious but inconsistent
10	30/M	vascular (rupture of cerebral AVM)	11	EEG, ABR, SEP, (pain-related P250)	32.11	38.42	consciousness level: MCS, conscious but inconsistent

*( ) indicates absent in the electrophysiological evaluation. ABR: auditory brainstem response, AVM: arteriovenous malformation, CBF: cerebral blood flow, EEG: electroencephalography, SEP: somatosensory evoked potential.

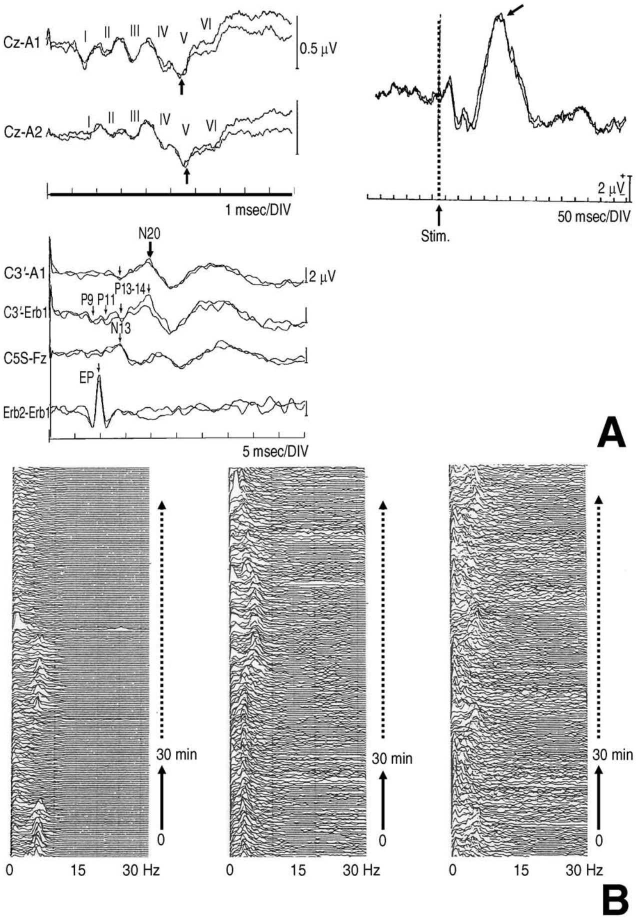

Fig. 1 A: Auditory brainstem response (*left upper panel*), somatosensory evoked potential (*left lower panel*), and pain-related P250 (*right panel*). DIV: division. B: Continuous electroencephalography frequency analysis: No desynchronization (*left*), slight desynchronization (*center*), and desynchronization (*right*).

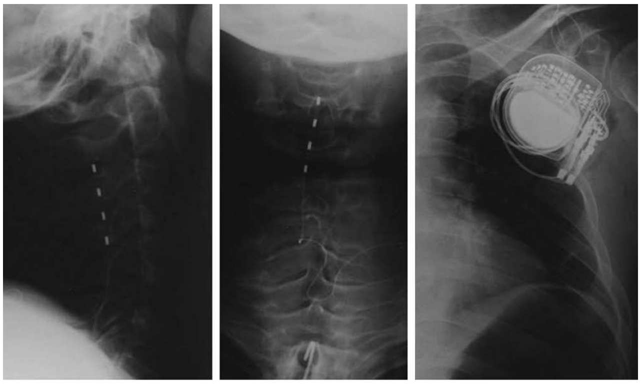

Fig. 2 Cervical spinal cord stimulation. Radiography images showing the location of the stimulation electrode and implantable pulse generator (IPG). *Left*: lateral view, *center*: anteroposterior view, *right*: IPG under the anterior chest wall.

lead, and electrodes were placed in the parietal area and earlobes on both sides. EEG recording was displayed as a CSA for EEG frequency analysis,[1,23] employing a fast Fourier transform. We classified the EEG frequencies into three patterns as follows: no desynchronization pattern in which changes in peak frequency were present only at alpha and low frequencies, but not at high frequencies; a slight desynchronization pattern in which desynchronization (a change to a low amplitude and a high frequency) was present but did not appear frequently, the duration was short (lower than 10% of the time course) and the high-frequency power was low; and a desynchronization pattern in which desynchronization appeared frequently and the increase in high-frequency power was clear at desynchronization (Fig. 1B).

On the basis of the results of DBS for VS patients, we established the electrophysiological inclusion criteria as follows: Vth wave of the ABR and N20 of SEP on at least one side were recorded even with prolonged latency; pain-related P250 was recorded with an amplitude of over 7 μV; and continuous EEG frequency analysis revealed the desynchronization or slight desynchronization pattern.

For SCS treatment, the patient was placed in the prone position, and an 18-gauge Touhy needle included in the electrode package was inserted into the midline epidural space at the cervical-thoracic junction under radiographic control. Through the Touhy needle, a flexible, four-contact, cylinder electrode (3487A PISCES-Quad; Medtronic, Inc., Minneapolis, Minnesota, USA) was inserted into the epidural space of the cervical vertebrae, and placed at the C2–C4 levels. The stimulation electrode was connected to the implantable pulse generator (7427 Synergy; Medtronic, Inc.), which was implanted under the anterior chest wall (Fig. 2). Stimulation was applied for 5 minutes every 30 minutes during the daytime, and at an intensity that produced motor twitches of the upper extremities. We used 5 Hz for SCS, considering that the induced muscle twitches can be a useful functional neurorehabilitation for MCS patients (Table 2).

All patients' families provided their written informed consent for this procedure. This study was approved by the Committee for Clinical Trials and Research on Humans of our university and conformed to the principles outlined in the Declaration of Helsinki.

Cerebral blood flow (CBF) was measured in 8 of the 10 MCS patients, excluding the first and second MCS patients treated by cervical SCS. Single photon emission computed tomography (SPECT) was per-

Table 2 Conditions and indications for spinal cord stimulation (SCS) in minimally conscious state patients

Subject	Minimally conscious state
Location of SCS electrode	C2–C4
Stimulation frequency	5 Hz
Stimulation intensity	Evoke muscle twitches on both sides of upper extremities (slightly higher than threshold)
Stimulation duration	210 μsec
Stimulation program	5 min ON, 25 min OFF alternately in the daytime
Start of SCS therapy	Over 3 mos after the onset of brain injury
Inclusion criteria	Electrophysiological evaluation

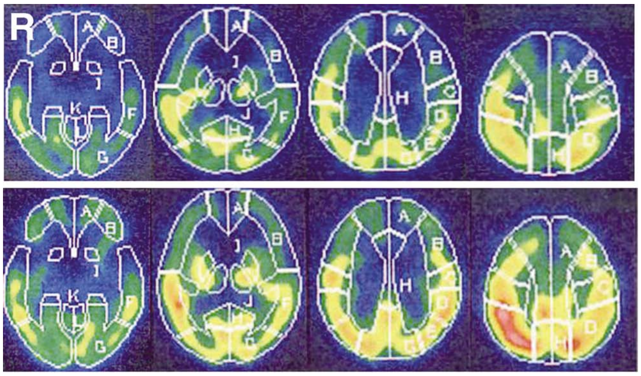

Fig. 3 Cerebral blood flow changes induced by cervical spinal cord stimulation (SCS) in Case 7. ***Upper row*****: before SCS,** ***lower row*****: during SCS.**

Fig. 4 Case 4. Twelve months after the start of cervical spinal cord stimulation therapy. The patient had recovered from minimally conscious state and was able to complete the 6 planes of Rubik's Cube.

Fig. 5 Case 8. Twelve months after the start of cervical spinal cord stimulation therapy. The patient had recovered from minimally conscious state and was able to play a rhythm on the guitar (*left*) and press a button to open the door of an elevator (*right*).

formed using the Prism 2000XP gamma camera system (Shimadzu Co., Kyoto). Using ethyl cysteinate dimmer, quantitative regional CBF (rCBF) images were converted from qualitative axial SPECT images by the application of Patlak plot graphical analysis with radionuclide angiography and Lassen's linearization. With this method, rCBF was estimated in the cerebral cortex and basal ganglia, and cerebellum as shown in Fig. 3. rCBF was estimated twice, without SCS and during SCS. CBF in the whole of these areas was compared for without SCS and during SCS (Table 1).

Changes in rCBF of the whole brain induced by SCS in MCS patients were compared using the paired t-test.

Results

Cervical SCS did not induce strong arousal responses similar to those induced by DBS, but induced muscle twitches of the upper extremities, which were not induced by DBS. Five-Hz SCS induced muscle twitches, whereas 25-Hz SCS induced muscle contraction of the upper extremities. Five-Hz cervical SCS increased CBF diffusely in the brain except at the lesion site (Fig. 3). In the eight patients, the mean CBF was 38.8 ± 5.1 ml/100 g/min before SCS and 47.51 ± 7.8 ml/100 g/min during SCS. CBF increased by 22.2% during the stimulation period compared with CBF before stimulation in MCS patients ($p < 0.0001$, paired t-test).

The criteria for determining emergence from MCS include the reliable and consistent demonstration of one or both of the following: functional interactive communication, and functional use of two different objects. On the basis of these proposed criteria, 7 of the 10 patients emerged from MCS following SCS therapy. Eight of the 10 MCS patients treated by SCS satisfied our electrophysiological inclusion criteria. All seven patients who recovered from MCS following SCS therapy satisfied our inclusion criteria. Among these seven patients, one had moderate disability and six had severe disability, as determined using the Glasgow Outcome Scale 1 year after the start of SCS therapy (Table 1). We present the cases of two patients who recovered from MCS following cervical SCS therapy.

Case 4 was a 22-year-old man who was involved in a traffic accident while riding a motorcycle. He suffered traumatic head injury leading to a comatose state, and the diagnosis was diffuse brain injury. He was diagnosed as MCS 3 months after the injury. He sometimes responded to our orders of grasping our hand and opening his hand, but not consistently. No other obvious form of communication was observed during this period. He satisfied the inclusion criteria for our electrophysiological evaluation. He underwent cervical SCS, and he was able to communicate consistently 7 months after the start of SCS. Twelve months after the start of MCS, he was able to rotate the six planes of a Rubik's Cube, and he was able to speak and communicate normally. He sufficiently recovered motor function of his upper extremities to be able to complete the Rubik's Cube, but recovery of motor function of his lower extremities was insufficient and he required the use of a wheelchair (Fig. 4).

Case 8 was a 37-year-old man who developed an intracerebral hematoma. The hematoma was removed to prevent impending herniation. He remained in MCS 8 months after the onset of intracerebral hematoma. He satisfied the inclusion criteria for our electrophysiological evaluation. He sometimes obeyed our orders such as to grasp our hand or to open and close his eyes. Six months after the start of SCS therapy, he was able to communicate consistently. He had left hemiparesis, but was able to play rhythms on his guitar as his hobby using his healthy right hand 12 months after the start of SCS. Compared with the recovery of the motor function of his right upper extremity, the recovery of lower extremities was insufficient and he required the use of a wheelchair (Fig. 5).

Discussion

Our method of electrophysiological evaluation to estimate the resting brain function of MCS patients is useful for evaluating VS patients who show individual differences in resting brain function.[23,29] We used ABR to evaluate brainstem function and SEP to evaluate thalamocortical function, and carried out continuous EEG frequency analysis to estimate the relationship between the brainstem and the cerebral cortex. We also performed pain-related P250 analysis to evaluate higher brain function.[26,29] We have also reported that only 16 (14.9%) of 107 VS patients satisfied the inclusion criteria for our electrophysiological evaluation, and the recovery rate from VS significantly differed between the DBS therapy group and the non-DBS therapy group, suggesting that DBS may be useful for the recovery of patients from VS if the candidates are selected on the basis of electrophysiological inclusion criteria.[29]

In this study, 8 of the 10 MCS patients satisfied our inclusion criteria. Seven of these 8 patients recovered from MCS, consistently showing functional interactive communication or functional use of two different objects. The remaining two patients who did not satisfy our inclusion criteria did not recover from MCS within 2 years after the start of SCS therapy. These findings indicate that electrophysiological evaluation is also useful for predicting the effectiveness of SCS for the treatment of MCS patients, and that MCS patients are good candidates for chronic SCS therapy. Although we previously observed minimal improvements following SCS for the treatment of VS, the present study confirmed that SCS therapy is effective for the treatment of MCS.

Cervical SCS was reported to induce a significant increase in CBF in the hemisphere ipsilateral to the induced paresthesia, whereas thoracic SCS showed no effect on CBF in 1985.[9] SCS therapy was administered to patients in VS and prolonged coma in 1989.[6,12,17] Subsequent studies also applied cervical SCS for the treatment of VS, and all of those studies used high-frequency SCS.[5,13,16] In contrast, we applied cervical SCS for the treatment of MCS patients, and selected 5 Hz for stimulation. Five-Hz stimulation induced clear and strong muscle twitches of the upper extremities compared with 3-Hz or 10-Hz stimulation. All patients who recovered from MCS showed good recovery of motor function of their upper extremities, compared with inadequate recovery of motor function of their lower extremities, and all required the use of a wheelchair. We selected stimulation for 5 minutes every 30 minutes to prevent muscle fatigue at the intensity for inducing muscle twitches. In addition, we speculate that intermittent SCS may be suitable for the recovery of motor function, because we previously found that excessive motor cortex stimulation worsens motor function owing to the increased rigidity and/or spasticity of the extremities.[32] We also speculate that dual-lead SCS, in which both cervical and lower thoracic levels are stimulated alternately, may be useful for recovery of motor function of the upper and lower extremities, since cervical SCS cannot induce muscle twitches of the lower extremities.

Bilateral DBS of the anterior intralaminar thalamic nuclei and adjacent paralaminar regions of thalamic association nuclei achieved good results in a

6-month double-blind alternating crossover study of the treatment of MCS patients.[21] Chronic DBS for the treatment of VS was first reported by Tsubokawa et al. (1990)[24] and Chohadon and Richer (1993).[2] Unilateral DBS of the intact side of the thalamic centromedian-parafascicular complex can induce a very strong arousal response in VS patients. We consider that increased arousal level in VS patients is important for recovery from VS.[3,4,8,10,18,22] In contrast to VS patients, MCS patients retain some consciousness. Considering the persistence of physical limitations after recovery from VS treated by DBS, as we have already reported,[29,32] we selected cervical SCS rather than DBS, because SCS can increase CBF in the entire brain, and can induce muscle twitches, which cannot be induced by DBS, for the recovery of motor function. Our comparison of the recovery of the motor function of the upper extremities in MCS patients found marked recovery of motor function following SCS compared with DBS. We speculate that cervical-level SCS at 5 Hz could induce muscle twitches of the upper extremities and these muscle twitches are useful for the functional recovery.[30] Further studies are necessary for the study of motor recovery induced by SCS.

Although the effect of cervical SCS is still difficult to distinguish from the spontaneous recovery of MCS patients, the recovery rate from MCS induced by cervical SCS was 70% in this study, which is relatively high. We consider that a comparison study between the SCS-treated group and non-SCS-treated group based on electrophysiological evaluation is necessary to obtain definite evidence of the effectiveness of cervical SCS for MCS. The cost of SCS therapy for MCS has been shouldered by the patients up until now, because SCS therapy for MCS patients is not covered by the health insurance in Japan. We intend to accumulate more scientific data that will support the effectiveness of this therapy to support coverage by the health insurance.

Acknowledgments

This work was supported by grants (Strategic Research Base Development Program for Private Universities and Strategic Research Program for Brain Sciences) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

References

1) Bricolo A, Turazzi S, Faccioli F, Odorizzi F, Sciaretta G, Erculiani P: Clinical application of compressed spectral array in long-term EEG monitoring of comatose patients. *Electroencephalogr Clin Neurophysiol* 45: 211–225, 1978
2) Cohadon F, Richer E: Stimulation cerebrale profonde chez des patients etat vegetatif post traumatique. *Neurochirurgie* 39: 281–292, 1993 (French)
3) Dempsey EWA, Morison RS: A study of thalamocortical relation. *Am J Physiol* 135: 291–292, 1942
4) Dieckmann G: Cortical synchronized and desynchronized responses evoked by stimulation of the putamen and pallidum in cats. *J Neurol Sci* 7: 385–391, 1968
5) Fujii M, Sadamitsu D, Maekawa T, Uesugi S, Ozaki S, Koizumi H, Uetsuka S, Sakamoto K, Yamashita T, Ito H: [Spinal cord stimulation therapy at an early stage for unresponsive patients with hypoxic encephalopathy]. *No Shinkei Geka* 26: 315–321, 1998 (Japanese)
6) Funahashi K, Komai N, Ogura M, Kuwata T, Nakai M, Tsuji N: [Effects and indications of spinal cord stimulation on the vegetative syndrome]. *No Shinkei Geka* 17: 917–923, 1989 (Japanese)
7) Giacino JT, Ashwal S, Childs N, Cranford R, Jennett B, Katz DI, Kelly JP, Rosenberg JH, Whyte J, Zafonte RD, Zasler DO, Zasler ND: The minimally conscious state: Definition and diagnostic criteria. *Neurology* 58: 349–353, 2002
8) Hassler R, Ore GD, Dieckmann G, Bricolo A, Dolce G: Behavioural and EEG arousal induced by stimulation of unspecific projection systems in a patient with post-traumatic apallic syndrome. *Electroencephalogr Clin Neurophysiol* 27: 306–310, 1969
9) Hosobuchi Y: Electrical stimulation of the cervical spinal cord increase cerebral blood flow in humans. *Appl Neurophysiol* 48: 372–376, 1985
10) Jasper HH, Naquet R, King LE: Thalamocortical recruiting responses in sensory receiving areas in the cat. *Electroencephalogr Clin Neurophysiol* 7: 99–114, 1995
11) Jennett B, Plum F: Persistent vegetative state after brain damage. *Lancet* 1: 734–737, 1972
12) Kanno T, Kamel Y, Yokoyama T, Shoda M, Tanji H, Nomura M: Effects of dorsal column spinal cord stimulation (DCS) on reversibility of neuronal function—experience of treatment for vegetative states. *Pacing Clin Electrophysiol* 12: 733–738, 1989
13) Kanno T, Morita I, Yamaguchi S, Yokoyama T, Kamei Y, Anil SM, Karagiozov KL: Dorsal column stimulation in persistent vegetative state. *Neuromodulation* 12: 33–38, 2009
14) Katayama Y, Tsubokawa T, Harano S, Tsukiyama T: Dissociation of subjective pain report and pain-related late positive component of cerebral evoked potentials in subjects with brain lesions. *Brain Res Bull* 14: 423–426, 1985
15) Katayama Y, Tsubokawa T, Yamamoto T, Hirayama T, Miyazaki S, Koyama S: Characterization and modification of brain activity with deep brain stimulation in a persistent vegetative state. *Pacing Clin Electrophysiol* 14: 116–121, 1991
16) Liu JT, Tan WC, Liao WJ: Effects of electrical cervical spinal cord stimulation on cerebral blood perfu-

sion, cerebrospinal fluid catecholamine levels, and oxidative stress in comatose patients. *Acta Neurochir Suppl* 101: 71–76, 2008

17) Matsui T, Asano T, Takakura K, Yamada R, Hosobuchi Y: Beneficial effects of cervical spinal cord stimulation (cSCS) on patients with impaired consciousness: a preliminary report. *Pacing Clin Electrophysiol* 12: 718–725, 1989

18) Moruzzi G, Magoun HW: Brain stem reticular formation and activation of the EEG. *Electroencephalogr Clin Neurophysiol* 1: 455–473, 1948

19) The Multi-Society Task Force on PVS: Medical aspects of the persistent vegetative state (1). *N Engl J Med* 330: 1499–1508, 1994

20) The Multi-Society Task Force on PVS: Medical aspects of the persistent vegetative state (2). *N Engl J Med* 330: 1572–1579, 1994

21) Schiff ND, Giacino JT, Kalmar K, Victor JD, Baker K, Gerber M, Fritz B, Eisenberger B, Connor JO, Kobylarz EJ, Farris S, Machado A, McCagg C, Plum F, Fins JJ, Rezai AR: Behavioural improvements with thalamic stimulation after severe traumatic brain injury. *Nature* 448: 600–603, 2007

22) Sturm V, Kuhner A, Schmitt HP, Assmus H, Stock G: Chronic electrical stimulation of the thalamic unspecific activating system in a patient with coma due to midbrain and upper brain stem infarction. *Acta Neurochir (Wien)* 47: 235–244, 1979

23) Tsubokawa T, Yamamoto Y, Katayama Y: Prediction of the outcome of prolonged coma caused by brain damage. *Brain Inj* 4: 329–337, 1990

24) Tsubokawa T, Yamamoto Y, Katayama Y, Hirayama T, Maejima S, Moriya T: Deep brain stimulation in a persistent vegetative state: Follow-up results and criteria for selection of candidates. *Brain Inj* 4: 315–327, 1990

25) Yamamoto T: Response to Kanno et al. ‘‘Dorsal column stimulation in persistent vegetative state’’. *Neuromodulation* 12: 315, 2009

26) Yamamoto T, Katayama Y: Deep brain stimulation therapy for the vegetative state. *Neuropsychol Rehabil* 15: 406–413, 2005

27) Yamamoto T, Katayama Y, Kobayashi K, Kasai M, Oshima H, Fukaya C: DBS therapy for a persistent vegetative state: Ten years follow-up results. *Acta Neurochir Suppl* 87: 15–18, 2003

28) Yamamoto T, Katayama Y, Kobayashi K, Oshima H, Fukaya C: DBS therapy for the vegetative state and minimally conscious state. *Acta Neurochir Suppl* 93: 101–104, 2005

29) Yamamoto T, Katayama Y, Kobayashi K, Oshima H, Fukaya C, Tsubokawa T: Deep brain stimulation for the treatment of vegetative state. *Eur J Neurosci* 32: 1145–1151, 2010

30) Yamamoto T, Katayama Y, Obuchi T, Kabayashi K, Oshima H, Fukaya C: DBS and SCS for vegetative state and minimally conscious state. *World Neurosurg* Epub 2012 Apr 24

31) Yamamoto T, Katayama Y, Oshima H, Fukaya C, Kawamata T, Tsubokawa T: Deep brain stimulation therapy for a persistent vegetative state. *Acta Neurochir Suppl* 79: 79–82, 2002

32) Yamamoto T, Katayama Y, Watanabe M, Sumi K, Obuchi T, Kabayashi K, Oshima H, Fukaya C: Changes in motor function induced by chronic motor cortex stimulation in post-stroke pain patients. *Stereotact Funct Neurosurg* 89: 381–389, 2011

Address reprint requests to: Takamitsu Yamamoto, MD, PhD, Division of Applied System Neuroscience, Department of Neurological Surgery, Nihon University School of Medicine, 30–1 Ohyaguchi Kamimachi, Itabashi–ku, Tokyo 173–8610, Japan.
e-mail: yamamoto.takamitsu@nihon-u.ac.jp