Deep Brain Stimulation and Spinal Cord Stimulation for Vegetative State and Minimally Conscious State

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Key words
- Deep brain stimulation
- Minimally conscious state
- Spinal cord stimulation
- Vegetative state

Abbreviations and Acronyms
CM-pf: Centromedian/parafascicularis
DBS: Deep brain stimulation
MCS: Minimally conscious state
PVS: Persistent vegetative state
r-CBF: Regional cerebral blood flow
SCS: Spinal cord stimulation
VS: Vegetative state


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OBJECTIVE: **On the basis of the findings of the electrophysiological evaluation of vegetative state (VS) and minimally conscious state (MCS), the effect of deep brain stimulation (DBS) was examined according to long-term follow-up results. The results of spinal cord stimulation (SCS) on MCS was also examined and compared with that of DBS.**

METHODS: **One hundred seven patients in VS and 21 patients in MCS were evaluated neurologically and electrophysiologically over 3 months after the onset of brain injury. Among the 107 VS patients, 21 were treated by DBS. Among the 21 MCS patients, 5 were treated by DBS and 10 by SCS.**

RESULTS: **Eight of the 21 patients recovered from VS and were able to follow verbal instructions. These eight patients showed desynchronization on continuous electroencephalographic frequency analysis. The Vth wave of the auditory brainstem response and N20 of somatosensory evoked potential were recorded even with a prolonged latency, and pain-related P250 was recorded with an amplitude of more than 7 μV. In addition, DBS and SCS induced a marked functional recovery in MCS patients who satisfied the electrophysiological inclusion criteria.**

CONCLUSION: **DBS for VS and MCS patients and SCS for MCS patients may be useful, when the candidates are selected on the basis of the electrophysiological inclusion criteria. Only 16 (14.9%) of the 107 VS patients and 15 (71.4%) of the 21 MCS patients satisfied the electrophysiological inclusion criteria.**

INTRODUCTION

In 1972, Jennett and Plum (11) first reported the concept of persistent vegetative state (PVS) and described it as wakefulness without awareness. In 1994, The Multi-Society Task Force on PVS summarized the medical aspects of PVS (25, 26) (**Table 1**). They reported that recovery of consciousness from a posttraumatic PVS is unlikely after 12 months, and recovery from a nontraumatic PVS after 3 months is exceedingly rare. In 2002, Giacino et al. (6) proposed the concept of minimally conscious state (MCS), which is characterized by inconsistent but clearly discernible behavioral evidence of consciousness and can be distinguished from coma and vegetative state (VS) by the presence of specific behavioral features not found in either of these conditions.

VS can be distinguished from MCS by neurologic evaluation. Although the clinical features of VS patients are similar, resting brain function differs from patient to patient (27, 31, 32). It is usually difficult to evaluate resting brain function correctly and to determine the prognosis of VS patients on the basis of only the findings of neurologic evaluation. Results of many medical and surgical interventions for the treatment of VS have been reported already, but the estimation of resting brain function in each reported VS patient has been usually unclear (26, 27). The estimation of resting brain function in VS patients is essential in the discussion about the effect of each treatment. We have carried out electrophysiological evaluation of VS patients to clarify their resting brain function (35, 36).

In 1969, Hassler et al. (7) transiently stimulated the basal part of the pallidum and basal portion of the lateropolar nucleus (VA) of the thalamus and observed a very strong arousal response in a comatose patient. The investigators were able to continue the stimulation for only 19 days, and no signs of awareness were observed in their patient. Recently, we have used the chronic DBS system for VS patients, and Tsubokawa et al. (1990) (28) and Cohadon and Richer (1993) (3) reported on chronic DBS in VS patients. In 2007, Schiff et al. (22) also applied chronic DBS to the treatment of MCS patients, and reported good results following a 6-month double-blind alternating crossover study. Together with DBS therapy, spinal cord stimulation (SCS) had also been tried for the treatment of VS (12, 16). We have applied SCS mainly to the treatment of MCS patients up to now, and obtained good results (34). On the basis of electrophysiological evaluation, we applied DBS to the treatment of VS and MCS patients, and examined long-term follow-up results. The long-term follow-up results of SCS were also examined in MCS patients, and compared them with the results of DBS.

Table 1. Criteria of Vegetative State (The Multi-Society Task Force on PVS)

1. No evidence of awareness of self or environment and inability to interact with others
2. No evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli
3. No evidence of language comprehension or expression
4. Intermittent wakefulness manifested by the presence of sleep–wake cycles
5. Sufficiently preserved hypothalamic and brainstem autonomic functions to permit survival with medical and nursing care
6. Bowel and bladder incontinence
7. Cranial-nerve reflexes (papillary, oculocephalic, corneal, vestibule-ocular, and gag) and spinal reflexes preserved at various extents

PVS, persistent vegetative state.

METHODS

Subjects for Electrophysiological Evaluation and Treatment by DBS or SCS

During 3 months after the onset of brain injury, electrophysiological evaluations that included assessments of the auditory brainstem response (ABR), somatosensory evoked potential (SEP), pain-related P250 (13), and continuous electroencephalographic (EEG) frequency analysis expressed as a compressed spectral array (CSA) were carried out in 107 VS patients and in 21 MCS patients. Among the 107 VS patients, 21 were treated by DBS. Among the 21 MCS patients, 5 were treated by DBS and 10 were treated by SCS (**Table 2**).

VS Patients Treated by DBS

All the 21 VS patients treated by chronic DBS were operated on from 4 to 8 months after the onset of comatose brain injury. These patients were followed up for a minimum of 10 years after DBS or until they died. Most of these patients were followed up in general hospitals in Japan, and we evaluated neurologic changes every month for 1 year, and twice a year in the following years. Their ages ranged from 19 to 75 (mean 43 ± 20.1) years, and the causes of the initial coma were head injury (nine patients), cerebrovascular accident (nine patients), and anoxia (three patients) (**Table 2**). On the basis of results of electrophysiological evaluation and DBS in the initial series of VS patients, we established the electrophysiological inclusion criteria for DBS therapy. Thereafter, we administered DBS in accordance with electrophysiological inclusion criteria (**Table 3**) as much as possible. Among the 21 VS patients, 10 satisfied the electrophysiological inclusion criteria, and the causes of their initial coma were head injury (four patients) and cerebrovascular accident (six patients). The remaining 11 VS patients who did not satisfy the electrophysiological inclusion criteria but received DBS therapy were included in our initial series of VS patients who received DBS.

Table 3. Electrophysiological Inclusion Criteria for Deep Brain Stimulation Therapy for Vegetative State

Patients

1. Vth wave of the auditory brainstem response (ABR) can be recorded even with a prolonged latency
2. N20 of somatosensory evoked potential (SEP) can be recorded even with a prolonged latency
3. Desynchronization pattern or slight-desynchronization pattern obtained by continuous EEG frequency analysis
4. Pain-related P250 is recorded with an amplitude of over 7 μV.

EEG, electroencephalography.

VS Patients without DBS

Eighty-six patients in VS did not receive chronic DBS therapy. All of these patients were treated similarly to the patients who received DBS therapy except for the DBS therapy. The ages ranged from 18 to 86 (mean 41 ± 18.3) years. The causes of their initial coma were head injury (18 patients), anoxia (28 patients), and cerebrovascular accident (40 patients). Among these patients, six satisfied our electrophysiological inclusion criteria for DBS. However, these six patients were not treated by DBS, because their families disagreed with our DBS protocol. The causes of the initial coma of these six patients were head injury (three patients) and cerebrovascular accident (three patients), and their ages ranged from 26 to 66 (mean 45 ± 17.4) years. We contacted the patients' families and the hospitals to which the patients were transferred 6, 12, 18, and 24 months after the electrophysiological evaluation.

Table 2. Summary of Data on Vegetative State and Minimally Conscious State Patients Treated by Deep Brain Stimulation or Spinal Cord Stimulation

	VS Patients	MCS Patients
Treated by DBS		
Age (years)	19–75 (43 ± 20.1)	18–47 (34 ± 14.3)
Cause of brain injury		
Traumatic brain injury	9 (2/4)*	3 (3/3)
Vascular brain injury	9 (6/6)	2 (2/2)
Anoxic injury	3	
Total	21 (8/10)	5 (5/5)
Treated by SCS		
Age (years)		16–67 (32 ± 15.9)
Cause of brain injury		
Traumatic brain injury		6 (6/6)
Vascular injury		3 (1/2)
Encephalomyelitis		1 (0/0)
Total		10 (7/8)

VS, vegetative state; MCS, minimally conscious state; DBS, deep brain stimulation; SCS, spinal cord stimulation.
*Values are expressed as *a* (*b*/*c*), where *a* = number of patients operated on; *b* = number of patients who recovered from VS or MCS; *c* = number of patients who satisfied electrophysiological inclusion criteria.