A case of persistent vegetative state treated with median nerve stimulation

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1. Introduction

Owing to rapid advancements in neurosurgery, the number of patients with severe brain injury due to cerebrovascular disorder, whose lives can be saved, has increased. Along with this phenomenon, however, the number of patients with persistent vegetative state has been increasing, and thus constitutes an important issue. No effective treatment method for persistent vegetative state has been established but some reports have recently shown that spinal epidural stimulation and median nerve stimulation are effective. However, the mechanisms of action of these methods, activation of nerve cells and increased cerebral blood flow, are unknown. We employed median nerve stimulation for a patient with persistent vegetative state due to an injury sustained in a traffic accident and obtained interesting results in terms of the patient's cerebrospinal fluid (CSF) findings.

2. Case reports and methods

The patient was an 18 year old woman who had sustained trauma in a traffic accident and had been transported to the Higher Life-Saving Emergency Center of our hospital. Computed tomography (CT) revealed findings of brain contusion and open head injury. On admission, her consciousness level was Glasgow Coma Scale (GCS) 4 and the extremities showed decerebrate rigidity. Anisocotia was absent, but the light reflex was slow bilaterally. Brain tissue leakage from the right eye was observed as a local finding. There was no serious trauma
in the thoracicoabdominal area. Immediately after admission, hypothermia was induced under monitoring of intracranial pressure. Since increased intracranial pressure was observed 3 days after the injury, wide-ranging decompression was performed. Cranioplasty was performed with a V.P shunt operation for hydrocephaly that developed 1.5 months after the injury, but the patient deteriorated to persistent vegetative state. Approximately 3 months after the injury, median nerve stimulation was started as a non-operative procedures.

The instrument was a Focus (Trade name: Empi Inc.) The right median nerve was percutaneously stimulated at an output of 20 mA and a frequency of 40 Hz for 300 ms (12 hours/day). Consciousness level was evaluated by single photon emission computed tomography (SPECT) using 123I-IMP as well as electroencephalography (EEG) and the determination of concentrations of neurotransmitters (GABA, dopamine, catecholamine and serotonin) in CSF before and one month after median nerve stimulation. Changes in these parameters were also investigated.

3. Results

The consciousness level was unchanged, GCS 7, after stimulation as compared to before stimulation. There were no marked changes in EEG findings after stimulation; there were almost no a waves but rather mainly low amplitude slow waves in the background. The evaluation by SPECT using 123I-IMP revealed decreased blood flow to the entire left cerebral hemisphere before stimulation. However cerebral blood flow to the entire left cerebral hemisphere before stimulation. There were essentially no changes in adrenalin, noradrenalin and serotonin, among the neurotransmitters measured in CSF, after stimulation. In contrast GABA increase from 289 pmol/ml to 455 pmol/ml and dopamine from 1.8ng/ml to 3.5 ng/ml after stimulation.
4. Discussion

Some reports have, in recent years, shown consciousness, EEG and cerebral blood flow to be improved by spinal epidural stimulation in patients with persistent vegetative State. However, the therapeutic procedure is operative, and difficult in patients whose general condition is poor and in those with injuries of the cervical vertebra(e) or the cervical cord. The median nerve stimulation employed for the present patient is, however, non-invasive and is thus anticipated to be useful. At the 5th meeting of this society, Jane et al. reported that a patient who had undergone median nerve stimulation immediately after injury had shown an improvement of 6.3 points in the GCS score after stimulation. Kanno et al. reported that one patient with hypoxia and another with a head injury had undergone median nerve stimulation 2 and 3 weeks after their injuries, respectively and shown improvements in cerebral blood flow and GCS scores. Our patient underwent median nerve stimulation 3 months after the injury, but consciousness showed no clinical improvement because the underlying damage to the brain was too severe. However, in considering the mechanisms of consciousness improvement with this procedure, it is very interesting that GABA and dopamine, among the neurotransmitters measured in CSF rose. These changes suggest that median nerve stimulation may directly activate the central nervous system itself. Some reports have shown that the CSF concentration of GABA is elevated by spinal epidural stimulation. It has also been demonstrated that consciousness can be improved by administering a dopamine agonist. These findings who that median nerve stimulation may become a non-operative procedure for persistent vegetative state if its indications are more strictly selected. The number of patients treated by this procedure will inevitably increase in the future and at the same time further study is needed on the mechanisms underlying the changes in various neurotransmitters induced by median nerve stimulation.

5. Conclusions

Median nerve stimulation was employed for a patient with persistent vegetative state, and CSF
concentrations of the neurotransmitters dopamine and GABA rose in response. These findings were considered to suggest one possible mechanism of the therapeutic effects of this procedure.

References


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Pilot study of electrical stimulation on median nerve in comatose severe brain injured patients: 3 month outcome.

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Primary objective: To determine if electrical stimulation (ES) benefits (waking time. 3-month outcomes) treated coma patients.

Research Design: Double blind randomized-controlled study.

Methods and procedures: Ten coma patients; six treatments and four controls. Using the ‘Respond Select’ by EMPI.

Experimental Interventions: Treatment group received radial nerve ES applied in 300 ms intermittent pulses at 40Hz. 15-20mA 8 hours a day up to 14 days of coma; control group received sham stimulation.

Main outcomes and results: ES group emerged from coma mean 2 days earlier than controls although this result was not statistically significant. At 3 month post-injury, there was no group difference in Glasgow Outcome Scale, although the ES group had improved function over controls as measured by the FIM/FAM (mean of 114 and 64.5 respectively, n.s.

Conclusions: These data show an interesting trend, although statistical power was limited in this small pilot study, suggesting the need for a larger trial.

Introduction

Electrical stimulation (ES) has been used as a therapeutic method in physical therapy and
rehabilitation for decades. The therapeutic potential of electrical currents being used for inverse applications was postulated more than a century ago. This includes treatment of lesions and diseases of the nervous system. ES has been used to treat patients with pain syndromes and Alzheimer's disease [1,2]. The interest in ES for severe traumatic brain injury (TBI) and its consequences is not new; it started more than a decade ago when electrical stimulation was noted to be beneficial in severely brain injured patients [3].

Significant research related to ES in vegetative states post-stroke, post-trauma and prolonged hypoxia has been performed in the last decade [3-7] using oral column stimulation (DCS) [3-5] and median nerve stimulation [6-8]. DCS consists of low electrical currents applied through an epidural or subdural electrode at the C2 level. DCS may hasten arousal increase cerebral blood flow, improve EEG increasing a-waves while decreasing 8-waves, raise dopamine and noradrenaline levels and lower serotonin in the cerebrospinal fluid (CSF).

In a report published in 1992, after a study of 42 cases of post-traumatic and post-stroke vegetative patients treated with DCS, Kanno et al, [4] reported that 42.9% of patients showed clinical improvement. The authors mentioned that the interval from the start of DCS therapy to the first sign of improvement is variable: from 6 months to 5 years [3-5].

The effect of ES via the median nerve was studied in acutely and severely brain injured patients [9]. A low intensity electrical current (20 mA) was used to stimulate the peripheral median nerve of subjects with a Glasgow coma Scale (GCS) who scored between 4-8.

The authors reported noticeable improvements of clinical status in stimulated patients in comparison with non-stimulated cases [9].

The median nerve has also been used for the treatment of post-stroke, post-trauma, hypoxic states and imaging, and laboratory measures (EEG, SPECT, catecholamine metabolism) have shown clinical improvement in ES patients versus non ES patients [6-8]

The concept of ES in severe TBI is based on the hypothesis that electrical currents applied through peripheral routes may reach central areas, activating the neuro-endoerine system to improve functioning after traumatic cerebral damage. It is proposed that the peripheral stimuli go to the ascending reticular activating system (ARAS), which further connects with intralaminar nuclei of the thalamus and then stimulates the cortical layer 1. The locus coeruleus (releasing norepinephrine), and the forebrain basal nucleus of Meynert (releasing acetycholine) are also involved and stimulate the cortical layer one enhancing arousal. However, some other mechanisms may also be possible [7, 10].
Thus, a pilot study was planned to specifically investigate whether patients will have a shorter time out of coma and better functional outcomes at 3 months following severe TBI.

**Methods**

**Subjects**

Patients were eligible for the study if they presented with a non-penetrating TBI with an admission Glasgow Coma Scale between 3-8, and enrolled within 72 hours of injury. Patients were required to be between the ages of 18-66. Patients were excluded if they were found clinically to be under alcohol and/or drug intoxication, unless their GCS remained 4-8 in the 24 hours post-admission. Patients with implanted pacemakers or defibrillators were excluded, as were patients with spinal cord injury or pregnancy, to preclude possible negative interactions with ES. Subjects were recruited from a daily survey of the General Surgery and Neurosurgery Intensive Care Units. Since these patients were in coma, written consent from the patient’s closest relative was obtained, with patient consent collected as soon as they were cognitively able. This study was conducted with full approval of the University of Virginia Investigational Review Board. Subjects were recruited from October 1998 to August 1999.

**Experimental design and random assignment to group**

This study is a double-blind, randomized, controlled pilot study of the effect of ES on severe TBI outcome. Patients were randomly assigned to either the treatment or the control groups. A list of random numbers was generated in Microsoft Excel 97 using RANDOM function, and subjects were assigned a number as they were enrolled in this study. All odd-numbered subjects were assigned to the treatment group and all even-numbered subjects were assigned to the control group. Control subjects were given ‘sham’ stimulation and, thus and they received no ES, in that they were hooked to a machine that did not have electrodes completing a circuit between the device and the patient. The ‘sham’ machine had no discernable difference from the functional machine. Patients and families were kept blind to treatment intervention.

**Electric stimulation treatment**

The device used to provide electrical impulses was the ‘Respond Select’ by EMPI. This device has multiple settings that allow various trains of electric pulses. It is connected to two electrodes attached to a cuff that is applied on the volar surface of the right forearm for patients who are right-handed, in order to stimulate the right median nerve (one subject was left handed
and therefore ES was applied on the subjects left median nerve. Stimulation was applied in 300 μs pulses at 40 Hz, and 15-20 mA given intermittently (20 seconds on, 40 seconds off) This regimen was found effective in previous studies [10]. The patients in the treatment group received ES 8 hours a day each day they remained in coma (GCS 48 hours in this study) will be difficult to collect, given that these patients are relatively rare. The prevalence of severe non-penetrating TBI is decreasing [14], probably as a result of improvements in safety, such as the use of air bags. Therefore, a multicentre-trial will be needed to collect data with sufficient subjects to determine if ES results in a truly significant improvement in this population. Until that point, TBI prevention remains the ‘treatment of choice’ for severe TBI.

References


Median Nerve Stimulation


Median Nerve Stimulation Method for Severe Brain Damage, with Its Clinical Improvement

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[Introduction]

We reported at the previous meeting that in cerebrospinal fluid the concentration of catecholamine, which is related to the expression of consciousness and motor control, increased as an influence of median nerve stimulation to the brain. The fact that the concentration of catecholamine, especially dopamine, a neurotransmitter in cerebrospinal fluid, was increased by stimulation of the peripheral nerve at the hand joint portion of the median nerve is clinically an interesting finding that indicates the possible influence of the stimulation reaching the central nervous system. Further study about its correlation with neurological symptoms should be carried out, but there has been no such report to this date.

In this study we continuously observed the change of clinical symptoms caused by median nerve stimulation and tried to find out which neurological symptoms would improve on which neurological change we could get the stimulation effectively. We discuss them hereby together with their relation to the action mechanism of this stimulation method and determination of its application.

[Subjects & Methods]

Subjects were 17 cases, from among 37 cases of severe brain damage, where clinical symptoms apparently improved after stimulation of the median nerve. The details of the damage were 9 cases of cerebral injuries (GCS

We scored the clinical change of consciousness disorders and neurological findings according to the State and Reaction scale (scoring of consciousness disorder in chronic stage) defined by the Society for Treatment of Coma (STC) and evaluated their clinical conditions before stimulation, 3 days after stimulation started, and one week after stimulation stared (Table 1, Table 2)
[Results]

Starting days of median nerve stimulation were 14-39 days after admission, 22.8 +/- 5.8 days on average. In the state scale, within the applicable 17 cases, the number of

Right median nerve electrical stimulation to hasten awakening from coma

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Electrical stimulation of the right median nerve may hasten the awakening of closed head injury, comatose patients. A series of 25 comatose patients have been treated. These patients made better recoveries than similar individuals reported in the literature. In a double-blind pilot project patients in the treated group scored better on interval Glasgow Coma Scale Scores, spent fewer days in the intensive care unit, and showed better Glasgow Outcome Scores at 1 month post-injury. Peripheral electrical stimulation of the right median nerve, through activation of the ascending reticular activating system, may be sufficient to arouse the moderate to severely comatose patient.

Introduction
Dorsal column electric stimulation of the cervical spinal cord has been successfully used in treating persistently vegetative individuals, those in coma for greater than 3 months. 43% of this severely compromised population have shown clinical improvement to the point of following simple commands and self-feeding. Dorsal column stimulation has been shown to increase norepinephrine and dopamine while reducing serotonin levels assayed in the cerebrospinal fluid. In Japan, right median nerve stimulation (RMNS) has been shown to cause significant increases in cerebral blood flow and improved electroencephalogram.

The median nerve serves as a peripheral gateway to the central nervous system. This is reflected in that the sensory distribution of the hand exhibits disproportionately large cortical representation. Within the brainstem, the ascending reticular activating system (ARAS) maintains wakefulness. The spinoreticular component of the median nerve synapses with neurons of the ARAS. The nearby locus coeruleus releases norepinephrine, using a monoaminergic arouse of the cortex directed to cortical layer 1. The intralaminar nuclei of the thalamus are activated by acetylcholinergic input from ARAS. These intralaminar thalamic nuclei provide non-specific 

encintory
input to the cortical layer 1, and are responsible, in part, for the initiation of awakening. The excited ARAS also stimulates the forebrain basal nucleus of Meynert which delivers diffusely spread acetylcholine to the cerebral cortex.

The right median nerve was chosen as a portal to stimulate the brainstem and cerebrum because increased alertness and better speech have been observed after RMNS (clinical observation). Broca’s motor speech planning area in the left front temporal region has been shown in position emission tomography (PET) to become more active when a subject moves, or even contemplates moving his hand, a process which is mimicked in RMNS.

Electrical stimulation has a variety of accepted clinical applications. Functional electrical stimulation (FES) is most commonly used in physical therapy for muscle strengthening. Individuals suffering from cerebrovascular accidents with hemispatial neglect may also benefit from FES. Transcutaneous electrical neuromuscular stimulation (TENS) has been well accepted in controlling pain. Peripheral electrical stimulation has been used to increase memory and verbal function of individuals with Alzheimer’s Disease. All of these peripheral applications of surface electrical stimulation cause changes in neuronal function and
The authors’ interest in stimulation began 26 years ago with a study involving a paraplegic individual at University of Virginia in Charlottesville, VA. Radio-linked, implanted electrodes strengthened muscles and allowed crude ambulation. From 1987 to 1989 individuals suffering from quadriplegia were helped to use their forearm muscles through voice-activated electrical stimulation to produce hand opening and closing at Duke University in Durham, NC. Significant improvement was observed in distal motor abilities. However, proximal and contralateral increases in performance were also noted during strength testing. Concurrently, stimulation was applied to individuals with severe mental/motor delays at Caswell Center in Kinston, NC, in hopes of improving function and awareness. While viewing serial videos of patients in the treated group, progressive augmentation of mental awareness was noted. The observed cross-over effect in the quadriplegic population, along with the central arousal of the retarded population, led to the postulation that stimulation of the median nerve causes significant central nervous system activation.

Methods

Comatose traumatic brain injury patients at University of Virginia and East Caroline University (ECU) in Greenville, NC, were screened for inclusion in the median nerve electrical stimulation trial. Those patients receiving a post-resuscitation Glasgow Coma Scale (GCS) score between 4 and 8 were enrolled in the study after consent of a legal representative. All patients received neurosurgical standard of care and were included with or without craniotomy. Patients under 6 years old, above 64 years old, with severe cardiac arrhythmias, implanted defibrillators, pacemakers, uncontrolled seizures, cerebral palsy, mental retardation, cervical spinal cord injury, brachial plexus injury, large intracranial hematomas, gunshot wound to the head, right median nerve injury or positive pregnancy test were excluded. In the pilot study at U of VA, patients were randomly assigned to a control or treated group. Sham stimulation was applied to control patients. GCS evaluators and families of patients were blinded to the experimental assignment. Stimulation was initiated when the patient’s medical condition stabilized and within 1 week of admission.

Empi Incorporated’s Respond Select (U of VA) and Respond II (ECU) battery powered, electrical neuromuscular stimulators supplied trains of asymmetric biphasic pulses at an
amplitude of 20 mA with pulse width of 300 at 40 Hz for 20 sec/min. Each day for 2 weeks, 12 hours of stimulation (ECU) or 8 hours of stimulation (U of VA) were delivered to the volar aspect of the right distal forearm over the median nerve via surface rubber electrodes measuring 2.5 cm². The electrodes, convex nerve via surface rubber electrodes, convex lubricated side applied to skin, were embedded 2 cm apart in the midline of plastic cuffs from Carolina Ortho Prosthetics, Greenville, NC. Peripheral electrical stimulation was cleared by the institutional review boards of U of VA and ECU for the coma projects.

Results

A group of six patients were enrolled in the pilot project at U of VA between 1994 and 1995. There were two males and four females ranging in age from 13 to 42 years. The average age of the treated group was 32 years and the average age of the control group was 24 years, with an average GCS of 7.3 and 7.0, respectively. Changes in GCS were scored at 7 and 14 days. Days spent in the intensive care unit (ICU) and Glasgow Outcome Scale (GOS) at 1 month post-injury were recorded for each patient.

In the U of VA study at 1 week, the treated group had improved by an average of 4.0 on the GCS and the control group had improved by an average of 0.7 on the GCS. By 2 weeks, the treated group had improved by an average of 6.4 on the GCS and the control group had improved by an average of 1.3 on the GCS.

The treated group stayed in the ICU for an average of 7.7 days and the control group stayed in the ICU for an average of 17.0 days. The GOS for the treated group averaged III and the GOS for the control group averaged II.

The following are three short case presentations of patients treated at ECU:

Table 1. Patient age, initial Glasgow Coma Scale (GCS), GCS at 7 days, GCS at 14 days, and the change in GCS over 14 days of the patients in the U of VA pilot project.
<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Age</th>
<th>Initial GCS</th>
<th>7 days</th>
<th>14 days</th>
<th>14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treated group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SI</td>
<td>16</td>
<td>7</td>
<td>10</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>DS</td>
<td>37</td>
<td>8</td>
<td>11</td>
<td>14</td>
<td>6</td>
</tr>
<tr>
<td>AC</td>
<td>42</td>
<td>7</td>
<td>13</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>32</td>
<td>7.3</td>
<td>11.3</td>
<td>13.7</td>
<td>6.4</td>
</tr>
<tr>
<td><strong>Control Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RB</td>
<td>13</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>WM</td>
<td>42</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>-2</td>
</tr>
</tbody>
</table>
Table 2. The number of day spent in the ICU and Glasgow Outcome Score at last assessment of the patients in the U of VA pilot project.

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Days spent in ICU</th>
<th>at 1 month</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treated group</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SI</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>DS</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>AC</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td><strong>Mean</strong></td>
<td>7.7</td>
<td>3</td>
</tr>
</tbody>
</table>

| **Control Group** | |
| 18 / 27           | |
Table 3. Patient age, initial Glasgow Coma Scale (GCS), GCS at 7 days, GCS at 14 days, and the change in GCS over 14 days of representative patients at ECU

<table>
<thead>
<tr>
<th>Patient Name</th>
<th>Age</th>
<th>Initial GCS</th>
<th>7 days</th>
<th>14 days</th>
<th>over 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI</td>
<td>16</td>
<td>4</td>
<td>7</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>CP</td>
<td>16</td>
<td>5</td>
<td>9</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>AT</td>
<td>14</td>
<td>4</td>
<td>6</td>
<td>8</td>
<td>4</td>
</tr>
</tbody>
</table>
Case 1

CP, a 16 year old female, was involved in a motor vehicle collision (MVC) and sustained a severe closed head injury. She had a mandibular fracture and an intracranial pressure of 18. Initial evaluation yielded a GCS of 5. Her initial head CT scan was normal, but she was dependent on a respirator and had a brief cardiac arrest. One week later she remained comatose and RMNS was commenced. After 1 week of stimulation her GCS had improved to 9. After a total of 2 weeks of stimulation she scored 14 on the GCS, an improvement of 9 and near the fully alert state. Within 1 month of her injury, CP could speak, eat and walk with assistance. CP was discharged to home within 2 months of her trauma. She made a full recovery and now holds a steady full-time job as a cashier.

Case 2

AT, a 14 year old female, was involved in a MVC and sustained a severe closed head injury. She had a haemothorax and pulmonary contusion. Her right mandibular condyle penetrated the base of her skull through the temporal bone in to the middle cranial fossa. CT scan showed haemorrhagic foci in the left cerebral hemisphere. She exhibited alternating decerebrate and decorticate posturing and received a GCS of 4. Within the first week of stimulation she began gripping spontaneously. After 1 week of stimulation her GCS was 6. After 2 weeks of stimulation she began to open her eyes spontaneously and received a GCS of 8. At 2 months post-injury she was eating well and speaking. Within 5 months she was playing volleyball and doing well in school.

Table 4. Glasgow Outcome Scores on hospital discharge of each of the 22 patients treated at ECU.
<table>
<thead>
<tr>
<th>Glasgow Outcome Score</th>
<th># of patients in category</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>27</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>23</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>100</td>
</tr>
</tbody>
</table>

**Case 3**

CI, a 16 year old female, was involved in a MVC and sustained severe closed head injury. She suffered a basilar skull fracture, cerebrospinal fluid otorrhea, left facial fracture, and left pelvic fracture. CT scan revealed left internal capsule contusion, right cerebellar subarachnoid haemorrhage, and blood in the fourth ventricle. Decerebrate posturing was observed and she received a GCS of 4. Within 1 week of stimulation, she exhibited semi-purposeful movement of her right arm and leg and scored 7 on the GCS. After a total of 2 weeks stimulation, she scored 10 on the GCS, and increase of 6, consistent with the U of VA pilot project. One month after the injury, CI followed simple commands. At 2 months post-injury CI could walk with assistance.
and read aloud. CI talks and walks well, has resumed dancing and diving, and now attends college.

All patients admitted into the study at ECU were treated with RMNS. No patients received a GOS of 2 which indicates persistently vegetative state. At hospital discharge, three patients died and received a GOS of 1. Eight patients received a GOS of 3 and were considered to be severely disabled. Five patients received a GOS of 4 with moderate disability. Six patients received a GOS of 5, having made good recoveries.

Discussion

Electrical Stimulation of the right median nerve may help acutely brain-injured people recover from coma more rapidly. This article presents the results of a pilot project at U of VA, the case histories of three comatose patients treated at ECU, and a summary of early outcome scores for 22 patients treated with RMNS at ECU. The patients whom were observed receiving RMNS have suffered no ill consequences. Many have recovered more quickly than was anticipated.

Through maintenance of existing neuronal circuitry, earlier awakening from coma may lead to higher final level of rehabilitation. Increased cerebral activity, as observed in RMNS, may also facilitate synaptogenesis in damaged cortex. The clinical observations indicate that RMNS has a beneficial effect on the resumption of language capabilities, possibly through stimulation of Broca’s motor speech area.

The pilot project at U of VA reflects the observations at ECU, in that treated patients’ GCS scores rose more quickly than those in the control group. Compared to the pre-treatment GCS score of U of VA patients, mean of 7.3, ECU patients had lower GCS scores, mean 4.7. The percentage of patients at ECU who made a satisfactory recovery at hospital discharge (good plus moderate disability groups) was 50%. In comparison to 746 patients who were included in a study of severe closed head injury conducted at U of VA, the University of Texas, Galveston, the Medical College of Virginia, Richmond, and the University of California, San Diego the patients at ECU showed a satisfactory recovery rate approximately twice that of the multi-center trial (50 versus 26%)[14].

In the double-blind pilot project at U of VA at 1 month post-injury, the treated group showed a
Median Nerve Stimulation

better GOS of III, indicated severe disability. The control group GOS was II, indicating persistent vegetative state. The treated patients spent an average of 9.3 days less in the ICU. It is believed that the days spent in ICU serves as an unbiased measure beyond the binding of the experiment, as the physicians ordering the step down to other units were not affiliated with the project. A shorter stay in the ICU reduces costs substantially for the patient and is attractive in today’s managed care environment. None of the patients in the treated series from ECU or U of VA remained in a persistent vegetative state at discharge from the hospital.

The burden of proof in establishing a cause and effect relationship in the comatose population is immense. However, both the treated group in the U of VA pilot project and the three cases presented from the ECU series showed a mean improvement of 6.4 on the GCS after 2 weeks of treatment. This suggests that the treatment may show dose-dependent efficacy in a larger trial. It is hoped that the ongoing clinical trial at U of VA will produce more substantial results. The observations gained from the series of patients at ECU and the pilot project at U of VA suggest that peripheral electrical stimulation may have a positive effect on brain-injured comatose individuals. It is promoted that non-invasive right median nerve electrical stimulation may improve outcomes, may be easily employed, carries little risk, and is cost effective.

References

Usefulness of Median Nerve Stimulation in Patients with Severe Traumatic Brain Injury Determined on the Basis of Changes in Cerebrospinal Fluid Dopamine

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[Introduction]

At the 1999 and 2000 annual meeting of our society, we reported on the usefulness of median nerve stimulation (MNS) in the treatment of consciousness disturbance in patients with severe brain damage. MNS produces noticeable changes, including vigilance, motor and emotional responses. MNS also elevates cerebrospinal fluid (CSF) catecholamine levels, especially dopamine levels. An interesting finding suggesting that dopamine is involved in the maintenance of consciousness and motor control. In the present study, we assessed the therapeutic effects of MNS on patients with severe traumatic injuries (TBIs), in relation to the mitigation of clinical symptoms, including a discussion of dopamine changes. This paper also reports on changes in CSF dopamine levels between before and after MNS, and discusses their significance.

[Subjects and Method]

The subjects of this study comprised 24 patients (10 males and 14 females) with TBIs rated as a Glasgow Coma Scale (GCS) of 3 through 8 on hospital arrival. Their ages ranged from 16 to 68 years, the mean GCS being 6.4 points on hospital arrival. The study population breakdown by disease was as follows: acute subdural hematoma in 11 patients, cerebral contusion in 7, and diffuse brain injury in 6. All patients, except 3 with diffuse brain injury, underwent brain hypothermic therapy, with craniectomy and intracranial pressure control performed in some patients. MNS was initiated at an average of 20.4 days after onset of injury, when management in the acute stage had nearly been completed. CSF was obtained from lumbar drainage after informed consent to patient’s family. At 2 weeks after initiation of MNS, CSF dopamine levels were compared between a group of 11 patients with clinical symptom changes achieved by MNS and a group of 13 patients with no changes. The method and conditions of stimulation were the same as those specified in the previous protocol.

[Results]
Each of the two groups, with or without clinical symptom, mitigation was roughly divided into three subgroups by pre-MNS CSF dopamine level: low-level group, normal-level group (8-16 pg/ml) and high level group. Of the 11 patients in the group with improvement of clinical symptom, 8 (73%) had lower dopamine levels, whereas 7 (54%) of the 13 patients in the group without had higher dopamine values. Furthermore, in all patients, except 1, in the group with improvement of clinical symptom, MNS more than doubled the CSF dopamine level. In contrast, in the group without improvement of clinical symptom, all patients except 2 were free from such elevations.

[Discussion]

The results of the present study show that peripheral nerve stimulation elevated spinal fluid dopamine concentration and that MNS was effective in improvement of clinical symptom in patients with low pre-MNS levels and ineffective in those with abnormally high levels. This finding suggests profound involvement of dopamine in the improvement of clinical symptoms. Although the mechanism of action of MNS on the brain remains to be not clarified, some researchers have reported improved EEG findings and increased cerebral blood flow. Dopamine is bilateral: it induces neurotoxicity by being released in large amounts into the extracellular cavity in the acute stage, and, it is also used as a therapeutic drug for the improvement of neurological symptoms, including consciousness disturbance, after the acute stage. Hayashi et al. Reported that dopamine is necessary in the treatment of severe TBIs in the acute and later stages. Since dopamine is involved in vigilance and motor control via the A-10 nervous system, which centers on the limbic system, consistency with the improvement of clinical symptoms after MNS is believed to be significant when associated with cerebral changes caused by dopamine.

Having been shown to alter cerebral catecholamine dynamics through continuous stimulation of the peripheral nerve, median nerve stimulation is expected to have potential as a new therapy for consciousness disturbance in the context of an interdisciplinary treatment of TBIs.

[Conclusion]

Better responders to MNS with low spinal fluid dopamine levels achieved improvement of clinical symptoms at a higher incidence. It is suggested that dopamine likely serves as an
important neurotransmitter in the course of recover from TBI's.

References


