

FO-1. Pisa Syndrome in Dystonia and Pallidal Deep Brain Stimulation: A Case Report

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Objective: Pisa syndrome (PS) refers to the forceful lateral flexion of the trunk. To our knowledge, only three reports of deep brain stimulation (DBS) at subthalamic nucleus or pedunculopontine nucleus have been made on PS associated with parkinson's disease. Pallidal DBS has been shown to be the effective for treatment of generalized and cervical dystonia. Thus far, however, there is no report with its use for PS associated with dystonia in the world. The authors report a case of PS associated with idiopathic dystonia in a 45-year-old man treated with pallidal DBS.

Methods: He had been suffering from lateral trunk flexion and cervical dystonia since 2 yr ago. His dystonic symptoms did progressive worse with various medications at other hospitals in Seoul. He had constant deviation of right lateral trunk flexion that interferes with sitting, standing, and walking. Brain MRI, DYT1 gene, and other laboratory findings were negative. Bilateral DBS electrodes were implanted to the internal globus pallidus under microrecording. After a day of a trial test at ward, the stimulation device was implanted.

Results: The post-op follow-up was 40 days. The last following parameters were used for bilateral stimulations: monopolar 0-case+: amplitude 3.0 V; pulse width, 60 milliseconds; frequency 60 Hz. He obtained over 90-percent improvement of the axial dystonia without side effects.

Conclusion: This case report demonstrates that the internal globus pallidus area is a valuable target for the control of PS in dystonia.

MEMO



FO-2. Dose-dependent Changes in Gait Pattern after Intrathecal Baclofen Bolus Injection in Adult Ambulatory Cerebral Palsy: A Case Report

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Intrathecal baclofen (ITB) therapy has been proven to reduce severe spasticity in cerebral palsy (CP). However, few results reported the objective gait pattern change after ITB bolus injection in adult ambulatory CP. We therefore evaluated observational and kinematic gait patterns at different ITB bolus injection doses. We performed a test trial of 3-day ITB bolus injections at doses of 12.5 µg, 25µg, and 50 µg in ambulatory CP. We evaluated modified Ashworth scale, visual analogue scale, observational gait scale, and kinematic gait analysis after ITB bolus injection. Intrathecal administration of low-dose baclofen 25 µg was successfully used not only for the treatment of spasticity but also for the treatment of gait disturbance, whereas the higher dose baclofen 50 µg induced foot drop and deteriorated gait pattern. We experienced dose-dependent changes in gait pattern confirmed by the observational and kinematic gait assessments after ITB bolus injection in adult ambulatory CP.

MEMO



FO-3. C-reactive Protein Levels Following Deep Brain Stimulation

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Objective: Acute cerebral infection following deep brain stimulation (DBS) is rare. But it has until recently been under-reported. Acute cerebritis manifests as vague prodromal symptoms and elevated C-reactive protein (CRP) level, and low density around the implanted electrode on computed tomography (CT). The aim of the present study was to establish the magnitude and time-course of CRP increases following routine DBS procedures in the absence of clinical and laboratory signs of infection.

Methods: A retrospective evaluation of serial changes of plasma CRP levels in 46 patients undergoing bilateral DBS was performed. Because most DBS was performed as a two-staged procedure involving; implantation of lead and internal pulse generator (IPG), CRP was measured preoperatively and post-operatively every 2 days until normalization of CRP (post-lead implantation day 2 and 4, post-IPG implantation day 2, 4, and 6).

Results: Compared with preoperative CRP levels (0.12 ± 0.17 mg/dL, n=51), mean CRP levels were significantly elevated after lead insertion and IPG implantation [1.68 ± 1.83 mg/dL (n=46) and 3.41 ± 2.56 mg/dL (n=46), respectively, $p < 0.001$]. The mean postoperative CRP levels were highest on post-IPG insertion day 2 ($p < 0.05$) and decreased rapidly, returning to the normal range on post-IPG implantation day 6.

Conclusion: Information about the normal response of CRP following DBS could help to avoid unnecessary diagnostic and therapeutic efforts. Imminent signs of infection are a secondary rise or a sustained elevation of CRP concentration.

MEMO



FO-4. Time-staged Gamma Knife Stereotactic Radiosurgery for Large Cerebral Arteriovenous Malformations: A Preliminary Report

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Objective: We retrospectively analyzed our experience with time-staged gamma knife stereotactic radiosurgery (GKS) in treating large AVMs ($\geq 10 \text{ cm}^3$).

Methods: Forty-five patients who underwent time-staged GKS between March 1998 and December 2011 were included in this study; 37 patients underwent 2-stage GKS and 8 patients underwent 3-stage GKS. The mean volume treated was $20.42 \pm 6.29 \text{ cm}^3$ (range, 10.20-38.50 cm^3). The obliteration rates of AVMs and the associated complications after GKS were evaluated.

Results: The mean AVM volume (and the median marginal dose) at each GKS session in 39 patients who underwent 2-stage GKS was as follows: 1st session, $19.67 \pm 6.08 \text{ cm}^3$ (13 Gy); 2nd session, $6.97 \pm 6.92 \text{ cm}^3$ (17 Gy). The median interval period was 39 months. After follow-up period of 37 months, the complete obliteration rate was 64.9%. The mean AVM volume (and the median marginal dose) at each GKS session in 5 patients who underwent 3-stage GKS was as follows: 1st session; $23.90 \pm 6.50 \text{ cm}^3$ (12.25 Gy); 2nd session, $19.43 \pm 7.46 \text{ cm}^3$ (13.5 Gy); 3rd session, $7.48 \pm 6.86 \text{ cm}^3$ (15.5 Gy). The median interval durations between the each GKS sessions were 37.5 months and 38 months, respectively. After a median follow-up period of 47.5 months, 5 patients (62.5%) achieved complete obliteration. Postradiosurgical hemorrhage developed in 5 patients (11.1%) including 1 case of major bleeding and 4 cases of minor bleeding.

Conclusion: The present study demonstrates that time-staged GKS could be an effective and safe treatment option in the management of large AVMs.

MEMO



FO-5. Cerebrospinal Fluid Egress from the Quadripolar Deep Brain Stimulation Electrode for Anterior Nucleus of the Thalamus for Refractory Epilepsy

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Objective: Deep brain stimulation (DBS) of the anterior nucleus of the thalamus (ANT) is an effective treatment for refractory epilepsy. Due to the unique location of ANT in the thalamus facing the lateral and third ventricles, transventricular DBS lead placement is an essential part of ANT DBS. However, there is no report regarding hardware problems including impedance variability in transventricular ANT DBS due to limited experience.

Methods: A 45-year-old male patient with previously effective, bilateral ANT DBS presented with increasing seizure frequency and a shortened battery longevity within two years. Magnetic resonance imaging showed that the left-sided DBS lead was in the third ventricle leaning on the medial wall of ANT. Electrode revision was performed.

Results: Upon disconnecting the proximal lead from the extension connection, cerebrospinal fluid egress through fine gaps between the metallic electrode contacts and electrode spacing was observed.

Conclusion: This case raises a concern about the transventricular approach for ANT lead placement because the currently available DBS electrode lead is not waterproofed. A careful, longitudinal follow-up of DBS impedance for ANT DBS is warranted.

MEMO



FO-6. Optimizing of Various Blood-brain Barrier Opening Factors Using Low Intensity Focused Ultrasound

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Objective: For the treatment of neurodegenerative disorders and neuro-oncological disorders, various drug and chemotherapy agents have been developed and tried in clinical field. However, these drugs or chemotherapeutic agents showed limited efficacy because of blocking by the blood brain barrier (BBB). Recently, a local and selective drug delivery method using focused ultrasound (FUS), which was traditionally used for tissue destruction, was introduced for localized and transient opening of BBB. In this study, we tried to evaluate various parameter factors for optimized BBB opening condition in small animals.

Methods: We have observed changes of BBB in motor and somatosensory cortex of SD-rat during transcranial sonication with microbubble (MB) using low-intensity focused ultrasound (N=20). Moreover, to find the optimal sonication parameters for BBB-disruption, we examined various sonication factors: MB injection type (bolus vs infusion pump), MB type (monolayer vs bilayer), pulse frequency (0.5 vs 1.1 MHz), acoustic pressure (0.1-2 MPa), pulse repeated frequency (1 Hz) and duty cycle (1%). The animals were sacrificed and perfused 4 h after FUS sonication. Brain tissues were obtained, sectioned and stained with hematoxylin and eosin (H&E) for histological examination.

Results: BBB opening at the sonication region was visualized using Evans blue (EB), which has a very large molecular weight of about 900 Da and normally does not pass through the BBB. When BBB was disrupted, however, EB diffused through the barrier. Moreover, we were able to detect various amounts and forms of EB extravasation depending on the various sonication factors. Based on these results, we also demonstrated the optimal BBB-disruption condition of the ultra-sonication for drug delivery.

Conclusion: In this pre-clinical study, we demonstrated that FUS can facilitate optimized opening of BBB at the focal area. It is expected that this technique can be applied to targeted drug delivery into a localized brain area. However, further investigation regarding the limitation of molecular weight for transposition across the BBB, controlling of focus size and location, and optimal parameters for drug delivery according to the molecular weight is necessary before application to the clinical field.



FO-7. Availability of Pediatric Gamma Knife Radiosurgery Under General Anesthesia

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Objective: Gamma knife radiosurgery (GKS) may have an important role for treating unresectable lesions in pediatric patients with brain tumors or vascular malformations. However, there are several factors to limit the application of GKS for children such as skull thickness, harmful radiation effects or psychiatric trauma. The purpose of this retrospective study was to evaluate the effectiveness of pediatric under general anesthesia particularly in pediatric patients.

Methods: The authors performed GKS for 20 pediatric patients. All participants were given general anesthesia from frame fixation to the end of irradiation. Among them, 4 patients had brain tumors and the others had arteriovenous malformation. The results were assessed by parents' satisfaction about the whole procedure, patient's fear as well as postoperative complications.

Results: A total of 18 patients were involved because 2 children were foreigners whom were difficult to contact. The mean score of parents' satisfaction got 9.6 points out of 10. Seventeen patients (94%) could not remember the GKS procedure, therefore, they were not repulsed by the procedure. Two patients demonstrated anxiety after the procedure, but relieved in several days. No severe complication was reported related to procedure itself or anesthesia.

Conclusion: The authors found that GKS under general anesthesia provided advantages in terms of safety and efficiency. GKS under general anesthesia can be an useful option to treat pediatric patients with intracranial lesions.

MEMO



FO-8. Twiddler's Syndrome, a Rare Hardware Complication in Spinal Cord Stimulation

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Objective: Twiddler's syndrome is an uncommon hardware complication involving the lead and pulse generators in cardiac pacemakers and defibrillators, deep brain stimulators, and vagal nerve stimulators. However, it has not been reported in spinal cord stimulators until early 2016. Considering the incidence of hardware complication of spinal cord stimulation, there may be an under-reporting of Twiddler's syndrome due to lack of awareness.

Methods: Two cases of Twiddler's syndrome as a hardware complication of SCS were identified between 2005 and 2015.

Results: One patient with hardware failure due to Twiddler's syndrome refused to have a revision surgery. The other patient who had a lead migration associated with coiling of the lead and twisting of pulse generator needed a revision surgery.

Conclusion: Twiddler's syndrome in patients treated with spinal cord stimulation is an uncommon but important adverse event. Awareness of characteristic presentation and radiologic finding is essential in identification of Twiddler's syndrome in spinal cord stimulation.

MEMO



FO-9. Experience of Burst Spinal Cord Stimulation

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Objective: Spinal cord stimulation (SCS) is a well-established treatment for medically intractable chronic neuropathic pain. However, conventional tonic stimulation evokes paresthesia which is not a pleasant sensation for SCS implanted patients. Recently, paresthesia-free burst stimulation has been developed and there have been a few publications discussing its efficacy and superiority over the tonic stimulation. However, physician's experience of burst stimulation is still limited and more clinical results are necessary to understand its mechanism and to establish more adequate indications for the treatment.

Methods: From July 2015 to March 2016, eleven consecutive patients, six men and five women, with total thirteen SCS leads were included in this study. During external trial stimulation, all patients received tonic and burst stimulation on alternative days. Pain intensities of preoperation, with tonic stimulation and with burst stimulation were assessed with 11-point numerical rating scale (NRS). Permanent stimulation type was chosen by patients' preference and degree of pain relief. Stimulation threshold for paresthesia and paresthesia awareness of permanent burst stimulation were also investigated.

Results: Average NRS reduced 38.4% from a mean of 7.8 (± 0.77) to 4.8 (± 1.41) with tonic stimulation and 56.4% to 3.4 (± 1.00) with burst stimulation. Burst stimulation was preferred by 9 patients (81.8%), tonic by 1 (9.1%), and 1 (9.1%) showed no preference. Patients without previous tonic experience showed 100% (6/6) preference for burst stimulation, while 60% (3/5) of patients who had tonic experience preferred burst stimulation. Threshold for paresthesia with tonic stimulation was 1.98 (± 1.45) mA and 1.30 (± 0.80) mA with burst stimulation. Among the patients who received permanent burst stimulation, 22.2% (2/9) presented paresthesia awareness.

Conclusion: Burst stimulation showed superior pain relief over the conventional tonic stimulation and patients' preference for burst stimulation was significantly higher than tonic stimulation. Patients with previous tonic stimulation experience showed lower preference for burst stimulation than patients without tonic experience. More well-controlled, randomized, long-term studies with large case series are necessary to improve treatment outcomes by investigating adequate indications of burst stimulation.



FO-10. Odor Discrimination Using Local Field Potentials in Rat Main Olfactory Bulb

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Objective: Rats have superior olfaction to protect themselves and thrive their species. Main olfactory bulb (MOB) is one of the key parts of the rat olfactory system, and various studies have tried to reveal its underlying mechanism in the last few decades. However, in spite of its outstanding abilities, most of these studies were focused on basic researches in perspective of physiology and/or molecular biology. Previously, we reported the possibility of odor discrimination using single unit activities (SUA) in rat MOB evoked by odorant presentation. SUA is a promising technique with high signal-to-noise ratio, but has limits in long-term signal acquisition due to micro movement of electrodes and immune reactions that ruin the recording pore. As an alternative, local field potential was introduced, which can provide long-term stable recording with good spatial and temporal resolution. We evaluated the possibility of odor discrimination using LFP which is a less invasive and safer method in long-term.

Methods: Five male adult Sprague-Dawley rats (350-400 g) were used in this experiment. Rats were mounted on the stereotaxic frame under full anesthesia (Urethane 1.5 g/kg, I.P.). Dorsal part of MOB was exposed and 5 electrodes were lowered to the glomerular layer using manipulators. We recorded the low signal (cut off frequency: 300 Hz) following odor presentation. Three odorants (350 ppm; isomylacetate (IAA), isopropylbenzene (IB), 2-heptanone (2-Hep)) were used as stimuli. Odor presentation was done by customized olfactometer based on Aduino.

Results: We observed that different odorants induced different responses in LFP frequency (theta, 2- 12 Hz; beta, 15-35 Hz; low Gamma, 36-55 Hz; high Gamma, 65-90 Hz). To determine the optimal number of features for SVM discrimination, accuracy variation following the changes of feature numbers were tested, and 7 features of each rat were used for odor discrimination. The overall accuracy of odor discrimination in 5 rats was 72% (The highest was 82.3% and the lowest was 66.7%), which is much higher than chance level (33.3%).

Conclusion: These findings suggest that odor discrimination using LFP signal is possible, which has advantage in terms of less invasiveness and long term stability.



FO-11. Clinical Outcome and Location of Active Contacts in the Centromedian Thalamic Nucleus Deep Brain Stimulation in Refractory Epilepsy

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Objective: To investigate the clinical outcome and location of active contacts in chronic centromedian nucleus (CM) deep brain stimulation (DBS) for refractory epilepsy.

Methods: The outcome of CM stimulation was evaluated with percent (%) seizure reduction compared to the baseline three months. To determine the location of active contacts, 27 leads in 14 patients with refractory epilepsy were studied. An analysis was conducted to determine whether any coordinates of the center of the active contacts predicted percent seizure reduction.

Results: With an average follow-up of 18.2 ± 5.6 months, the mean percent seizure reduction ($n=14$) was $68 \pm 22.4\%$ (25-100%). Eleven of 14 patients (78.6%) could achieve $>50\%$ improvement in the frequency of seizure. Specifically, all four patients (100%) with generalized epilepsy (Lennox-Gastaut syndrome) and seven out of 10 patients (70%) with multilobar epilepsy showed $>50\%$ reduction in seizure frequency. The mean coordinates of center of the active contact were located in the superior part of anterior ventrolateral CM. The calculated coordinates of laterality from midline (x), anterior-posterior (y) and height (z) from posterior commissure (PC) did not correlate with seizure outcome measured by percent seizure reduction. However, the locations of active contacts used during chronic CM stimulation in multilobar epilepsy were identified more dorsal to those used in generalized epilepsy.

Conclusion: Chronic CM stimulation is a safe and effective means in the treatment of refractory epilepsy.

MEMO



FO-12. Auditory Brainstem Implantation for Neurofibromatosis Type II via Trans-labyrinthine Approach: Early Experience for 5 Patients

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Objective: Neurofibromatosis type II (NFII) is genetically predisposed disease causing acquired hearing loss at mid-and late stage of life. The level of hearing loss in NF II patients is cochlear nerve, therefore, previous methods for hearing improvement such as hearing aid and cochlear implant had limited values for NF II patients. Auditory brainstem implantation (ABI) have been introduced for the patients with hearing loss, and according to previous reports, the clinical results seemed to be acceptable.

Methods: We performed ABI for 5 patients with NF II patients from Mar 2015 to Mar 2016. All patients were underwent ABI by translabyrinthine approach. During ABI electrode implantation, brainstem electrophysiological response to test stimulation was monitored, and final locations of electrode were decided according to the result of surgical findings and result from monitoring.

Results: 4 of 5 patients were showed reliable auditory response during procedures, and electrode location for 1 patient was decided by only surgical findings. ABI was switched on at 1 to 2 months after implantation, and patients expressed brainstem response including hearing sense. No serious complications related to SBI implantation were observed but 1 patients suffered from CSF collection at wound.

Conclusion: ABI is known to be acceptable methods for hearing loss. However, because the mechanism of hearing loss and anatomical changes of each underlying disease were quite different, the indication and surgical approach should be decided carefully. Early our experience ABI for NF II would be seemed acceptable, however, long term follow-up periods and careful analysis of surgical result should be needed.

MEMO

