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Microelectrode recording (MER) findings during sleep–awake anesthesia using dexmedetomidine in deep brain stimulation surgery for Parkinson's disease

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ABSTRACT

Objective: The preferred choice of anesthesia for deep brain stimulation (DBS) has been local anesthesia due to the need of patients' cooperation during the procedure, and concern on the interference of sedatives on microelectrode recording (MER) results. However, local anesthesia during the whole procedure may be impossible in some patients due to uncontrolled anxiety, fear, delirium or exhaustion. Therefore, sedative drugs have been used for DBS, but findings of MER during the procedures have not been reported in detail, especially in the globus pallidus internus (GPi). We introduce our experience using 'asleep–awake' technique by dexmedetomidine (DEX) anesthesia with MER findings during DBS in idiopathic Parkinson's disease (IPD) patients.

Patients and methods: Data from 14 different subcortical nuclei from 8 consecutive IPD patients whom had DBS at the GPi (6 patients) and subthalamic nucleus (STN) (2 patients) were retrospectively reviewed. We used continuous DEX and intermittent small boluses of propofol during the painful procedure ('asleep phase'), accompanied with continuous intraoperative monitorings of bispectral index (BIS) and modified observer's assessment of sedation (MOAA/S). Then sedatives were discontinued during MER recording ('awake phase'). Characteristic findings and firing rates of neurons were analyzed and compared to those from other 6 patients who underwent surgery under local anesthesia.

Results: All patients were satisfactorily sedated using this technique without any respiratory or hemodynamic complications. Characteristics of spike activities of each nucleus were inspected and analyzed quantitatively. We could inspect changes of spike activities according to level of patients' consciousness in some cases, but the localizing value was good to decide the target in all cases. Firing rates of group whom sedatives were given during asleep phase ('sedatives') were significantly lower than those of group under local anesthesia ('no sedative'). Intraoperative length of target nuclei, postoperative imaging and postoperative changes of UPDRS III score indicated satisfactory outcome.

Conclusion: We concluded that though MER findings may change during DEX-based monitored 'sleep–awake' anesthesia, it did not affect the results of target localization for the clinical purpose. However, it should be considered that use of sedatives before MER could result in changes of firing rate and pattern depending on the patient's state of consciousness.

1. Introduction

Deep brain stimulation (DBS) has been widely performed successfully for patients with various intractable movement disorders such as idiopathic Parkinson's disease (IPD), dystonias or tremors. Previously, DBS has been performed mostly under local anesthesia considering the quality of microelectrode recording (MER) results and the necessity of patient's cooperation during DBS. However,

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the duration of DBS intervention, especially in bilateral implantations at the same day, is sometimes too long and some patients suffer from intolerable exhaustion, anxiety or fear. Main concerns of using sedatives during DBS are its possible effect on the quality of MER and respiratory function. Gamma-aminobutyric acid-ergic (GABAergic) sedatives such as propofol have been used most commonly for DBS, but there are concerns on its interference on MER [1] or its fatal complications such as respiratory depression [2]. Dexmedetomidine (DEX) is a highly selective alpha-2-adrenergic receptor agonist which is a well known alternative sedative, which shows dose-dependent rapid action without respiratory depression [3–5]. However, undesirable effects such as changes of neuronal activities in the subthalamic nucleus (STN) during surgery [6], or prolonged impairment of consciousness [7], have also been reported. There has been a quantitative study of neuronal spikes during the STN DBS using DEX-based anesthesia [8]. In this study, the authors even recommended not to use high-dose DEX during the STN DBS [8] based on their results that spike patterns were changed.

In this paper we report our experience of MER during 'asleep–awake' anesthesia using DEX-based sedative technique in 8 consecutive IPD patients, mainly from GPi DBS. We stopped the infusion of DEX before the MER and observed the characteristics of neuronal spikes if they are acceptable for the clinical purpose to decide the optimal target. In addition, we analyzed the firing rate of each nucleus and tried to correlate them with the BIS of 'awake-phase'. To our knowledge, there has been no quantitative analysis using neuronal activities during GPi DBS of IPD patient using DEX-based anesthesia.

2. Methods

2.1. Patients

A total of eight consecutive patients whom underwent DBS for medically intractable IPD under DEX-based anesthesia between January 2013 and July 2015 in our institute were retrospectively studied. Neurologists and neurosurgeons specializing in movement disorders diagnosed all patients. A multi-department team including neurosurgeons, neurologists and psychiatrists made decision of surgical candidates and target nuclei for DBS, after considering the patients' main symptoms, unified Parkinson's disease rating scale (UPDRS) scores and the results of psychiatric evaluations. This study was approved by the Institutional Review Board.

2.2. Surgical procedure and anesthesia protocol

We followed the standard DBS surgical protocol as described in previously reported articles [9]. All operations were performed by a single experienced surgeon. IPD patients for STN DBS had been off all dopaminergic medications for at least 12 h before the surgery. For patients whom underwent globus pallidus internus (GPi) DBS for severe dyskinesia, their dopaminergic medications were administrated until the operation day as usual to verify the anti-dyskinetic effect of test stimulation during the surgery. Magnetic resonance images (MRI) were taken in the operation day morning after placement of the Leksell stereotactic head frame (Elekta Instrument, Stockholm, Sweden). The images were imported into the stereotactic planning software (Framelink^{TM}, Medtronic, US), and then coordinates of the initial target were decided by the neurosurgeon.

We used standard 'asleep–awake' anesthetic technique. Patients were sedated during the painful procedure ('asleep-phase') using loading and continuous infusion of DEX. Then sedatives were discontinued and patient was awakened for MER and test stimulation ('awake-phase'). The neuronal data from 'awake-phase' were used for analysis ('sedatives' group). For the quantitative analysis to compare firing rates and patterns, another group of patients (total 6: 2 GPi and 4 STN) whom underwent surgery under local anesthetics without any sedatives ('no sedative' group) were included. In addition, we used a data from two patients (patient 1 and 7) whom underwent surgery with one site with sedatives and the other site without, for within-patient analysis.

All patients were monitored by an experienced anesthesiologist during the whole procedures. Initially DEX was given by a loading dose of 0.5–1 μg/kg over 10 min, followed by a maintenance dose of 0.1–0.5 μg/kg/h infusion. If the patient was not sedated enough during the painful procedure, we increased the infusion rate of DEX or used small boluses of propofol (10–20 mg) for rapid effect. Low dose of remifentanil (REM) was also given (0.01–0.1 μg/kg/min) continuously with an adjustment as needed to control pain in 4 out of 8 cases. Continuous infusion of DEX and REM were stopped after the placement of burr holes. In case of bilateral implantation, DEX infusion was restarted before the intervention of the second side. Detailed control of the amount and doses of sedatives were done by the anesthesiologist, based on the patients' intraoperative conditions. Additionally, bispectral index (BIS) monitoring system (Aspect Medical System, US) was applied at the patient's forehead to monitor the depth of sedation. The maintenance dose of DEX was adjusted aiming the target BIS lower than 80. Modified observer's assessment of alertness/sedation (MOAA/S) scale was also checked by the anesthesiologist to evaluate the level of patients' consciousness.

2.3. Intraoperative microelectrode recordings procedure and postoperative evaluation

For the physiological mapping, MER was started from 15 mm above the estimated target. The tungsten/stainless steel microelectrode (model FC 1003, FHC Inc.) was advanced carefully, and stopped whenever good and consistent target neuronal activities appeared. Characteristic spike activities representing each target nuclei were displayed on the Leadpoint system (Medtronic). At the same time, the amplified signal was sent out to the Analog Output Board (Medtronic) installed on the system and separately digitized by an analogue-to-digital converter (ADC) (Micro1401, CED, UK). The sampling rate was 50,000 Hz for spike activities and digitized data was stored on a computer for the off-line analysis. After finishing of physiologic mapping according to intraoperative MER findings and evoked responses, testing macro-stimulation effect was performed at depths by more than two experienced movement disorders specialists. Once an agreement was made that the electrode was placed at the best effective target site, the therapeutic electrode (Model 3389 or 3387, Medtronic) was implanted. The final position of the electrode was verified postoperatively once again by co-registration of post-operative thin sliced computed tomography (CT) with preoperative MRI. Postoperative clinical effectiveness was evaluated by comparison of pre- and postoperative UPDRS III score, which represents the patients' clinical status related to motor function. We also compared preoperative OFF-medication state and postoperative OFF-medication/DBS-ON state at least 6 months after the surgery.

2.4. Spike sorting and analyses

Once the spontaneous neuronal activity was found during MER procedure, advancement of microelectrode was stopped and stayed at least 20 s to record stable spike activities, and then was stored for off-line analyses. Digitally recorded spike activities were sorted using Spike2 software (CED, Cambridge, UK) by template matching of action potential waveforms [9]. Spikes with high signal to noise ratio at least two times of background activities were chosen for