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Contribution of local field potential to subthalamic nucleus deep brain stimulation in Parkinson's disease

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INTRODUCTION

The subthalamic nucleus (STN) is the main target for deep brain stimulation (DBS) in Parkinson's disease. We analysed the relationships between magnetic resonance imaging (MRI) anatomy and electrophysiology done during surgery. In addition to extracellular recording of spontaneous neuronal activity (carried out conventionally in our Hospital), we performed simultaneous recordings of local field potential (LFP), i.e. deep EEG activity. We hypothesized that the contribution of LFP to neuronal firing rate with detailed MRI anatomy should allow to explore finely anatomo-electrophysiological relationships and also to determine precisely functional surgical targets.

PATIENTS, MATERIAL AND METHODS

Patients

10 patients with Parkinson's disease (5F – 5M; mean 62±4 years old; 11±3 years disease duration) underwent bilateral STN DBS surgical procedure.

Surgical technique

Stereotactic MRI: On the first day, the stereotactic Leksell G frame (Elekta, Sweden) was placed with its repositioning kit (Leksell repositioning kit, Elekta, Sweden) under local anesthesia. A stereotactic MRI was performed (1.5 Tesla, Siemens, Germany) with notably a White matter Attenuated Inversion Recovery (WAIR) sequence on the coronal plane: TR = 4500 msec; TE = 13 msec; TI = 160 msec; 2 × 15 images (two interleaved series). The frame was removed.

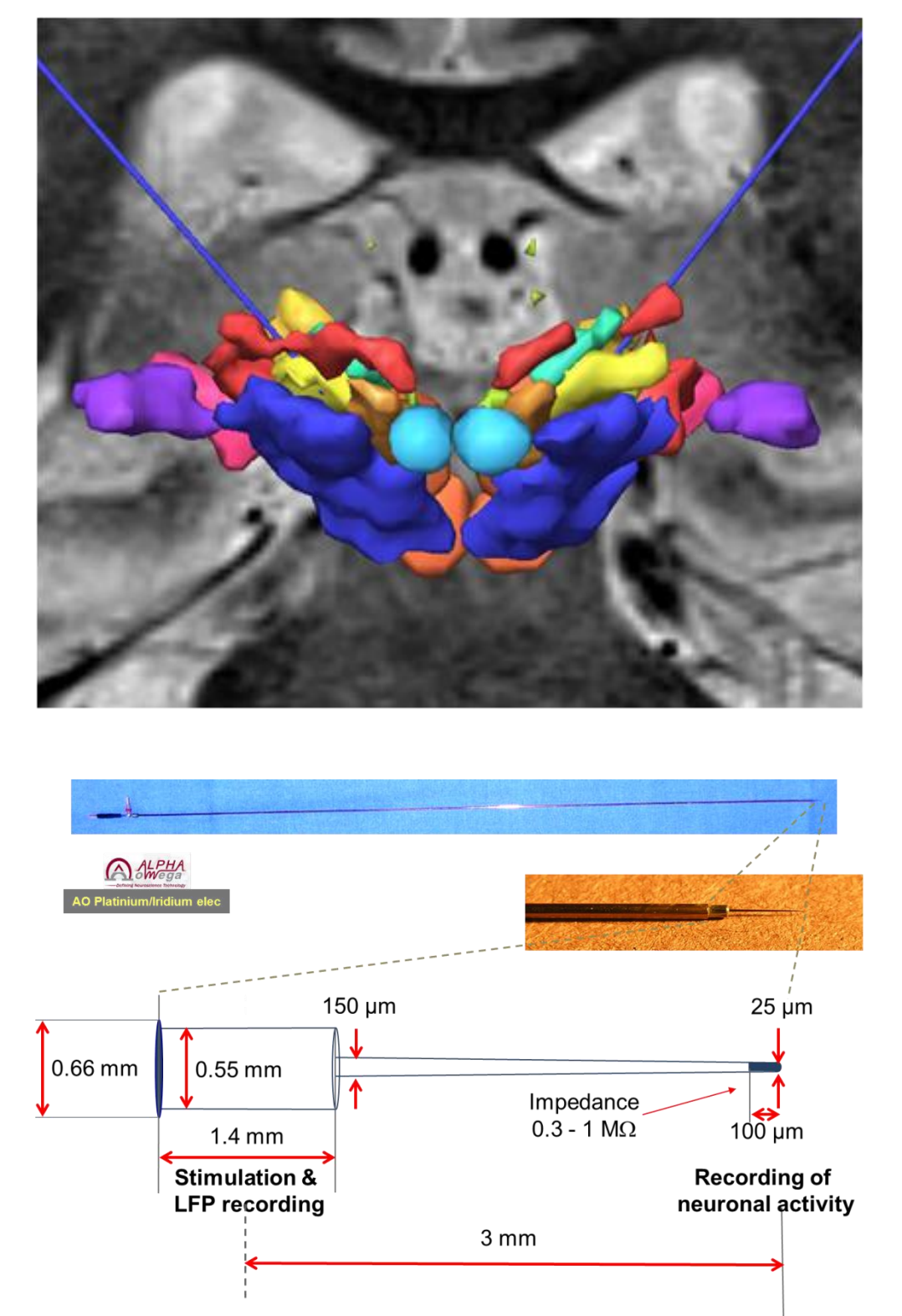
Planning: Direct targeting of STN region was performed using a stereotactic software (*Iplan, BrainLab, Germany*). We identified all the nuclei of the subthalamic region. With the help of probe view reconstructions, we determined a trajectory, with a double obliquity, avoiding the main vessels, going strictly through the parenchyma and with an endpoint located in the STN. We planned two parallel tracts, a central one centered on the best anatomical target, a 2mm-distant one.

Implantation surgery: The following day, the stereotactic frame was repositioned. Under local anesthesia, after recording of neuronal activity and LFP, an acute stimulation (monophasic, negative current, frequency: 130 Hz, pulse width: 0.06 msec) was performed using unshielded tungsten microelectrodes (stimulation tip: length 1.2 mm, diameter 550 µm) with a MicroGuide Pro system (*Alpha Omega, Israel*). We explored the clinical effects every 0.5 mm (current up to 3 mA) along the distal 10 mm on the 2 parallel tracts. Then a quadripolar electrode (*DBS 3387, Medtronic, USA*) was placed on the selected tract with one or two contacts in the clinically most efficient area. Peroperative tele radiographic X-rays controls and postoperative CT scanner acquisitions were performed to control the electrode positioning. Postoperative clinical assessments (6 months) showed a mean improvement of 63.6% (±14.9; ranging from 30.0 to 75.5) of motor control (part III of UPDRS).

Electrophysiology

> 715 unitary electrophysiological recordings of spontaneous extracellular neuronal activity (calculating the mean frequency of neuronal activity, and the occurrence of burst activity)

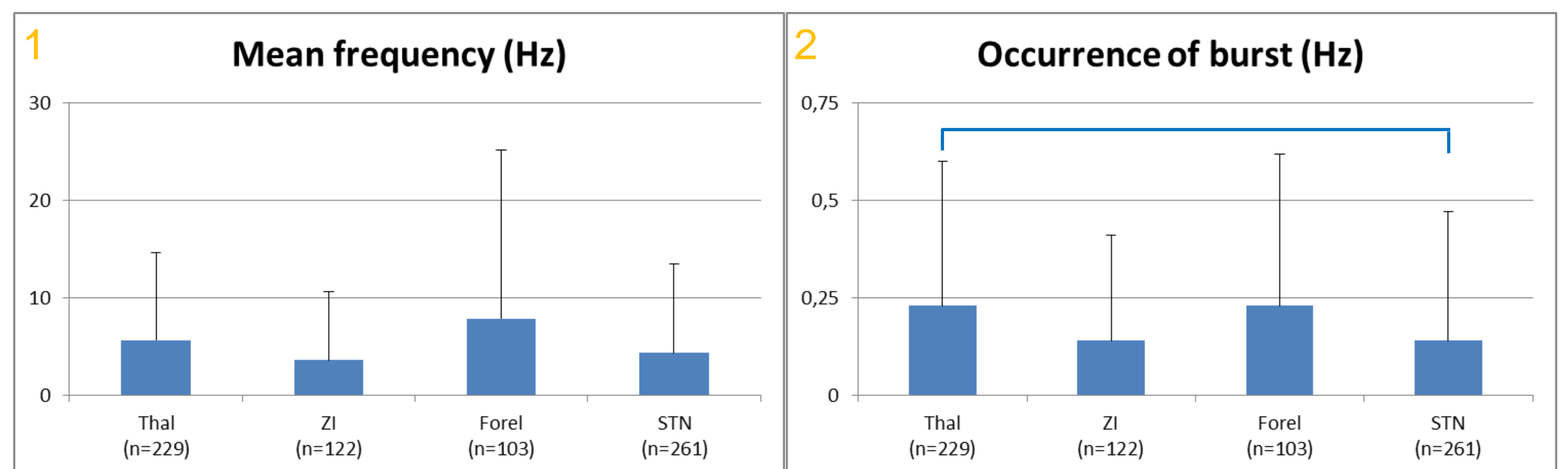
> 693 LFP recordings (Power spectral densities from 0 to 100Hz; 1024 frequency values; Normalization: percent of total PSD; Calculation for δ (0-4 Hz), θ (4-7 Hz), α (7-13 Hz), β (13-30 Hz), γ (30-50 Hz) and (50-100 Hz) frequency range) in MRI-outlined anatomical structures (Thalamus [Thal], Zona Incerta [ZI], Forel Field [Forel] and STN) were analyzed.



RESULTS

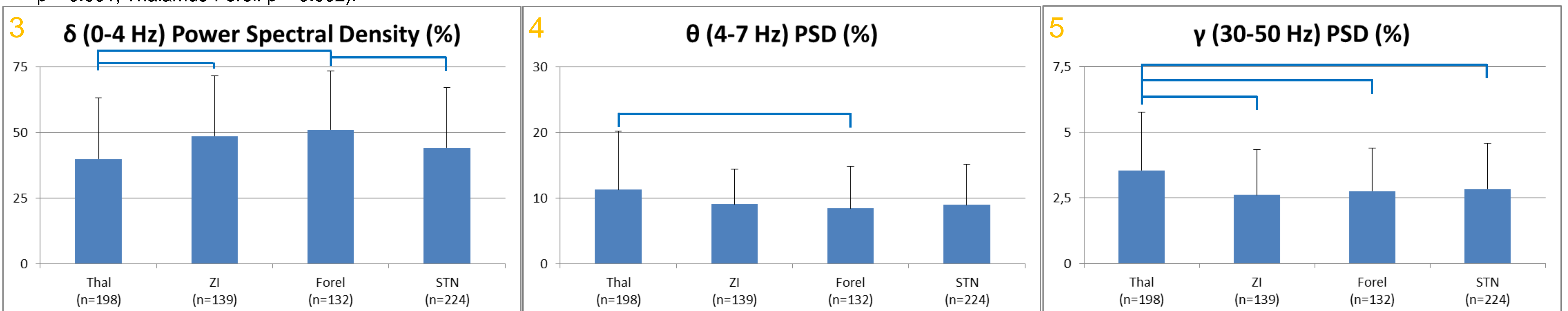
Electrophysiological recordings of spontaneous unitary extracellular neuronal activity

- In this study, the mean frequency failed to discriminate between the structures of the region of interest (non-parametric Kruskal-Wallis ANOVA; $p = 0.13$).
- The frequency of burst activity was significantly different between structures (K-W; $p = 0.01$). Burst activity in thalamus was statistically higher than in the STN (pairwise comparisons: $p = 0.002$).



Local field potential power spectral density analysis

- Delta band power spectral density (PSD) of LFP was significantly different between structures (K-W: $p = 0.0003$). Post hoc tests showed differences between Thalamus and Forel Field ($p = 0.0001$), between Forel Field and STN ($p = 0.003$) and between Thalamus and Zona Incerta ($p = 0.008$).
- Theta band PSD was significantly different between structures (K-W: $p = 0.02$). Thalamus had higher θ band activity than Forel Field ($p = 0.001$). Alpha and 50-100Hz bands showed the same statistically different pattern between Thalamus and Forel Field.
- Beta band PSD failed to discriminate between the structures of the subthalamic region (K-W: $p = 0.2$; data not shown).
- Gamma band activity was significantly different between structures (K-W: $p = 0.0003$). Thalamus γ activity differed from all other structures (Thalamus-ZI: $p = 0.00004$; Thalamus-STN: $p = 0.001$; Thalamus-Forel: $p = 0.002$).



CONCLUSION

- This study suggests the interest of LFP, which is at least as effective as extracellular neuronal activity (Coste et al., EJM, 2009), to discriminate between structures in the subthalamic region using exploration electrode with patient at rest during DBS surgery. Contrary to previous studies reporting an increase in β band when entering the STN (Chen et al., Exp Neurol, 2006), no significant difference was shown between structures concerning the β band.
- Another part of this study will consist in correlating extracellular neuronal activity and LFP, and analyzing modulations on LFP during voluntary movements of the patients.