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Local field potential oscillations of the globus pallidus in cervical and tardive dystonia

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ABSTRACT

Background: Reports about neural oscillatory activity in the globus pallidus internus (GPi) have targeted general (GD) and cervical dystonia (CD), however to our knowledge they are nonexistent for tardive dystonia (TD).
Methods: Local field potentials (LFPs) from seven CD and five TD patients were recorded intraoperatively. We compared LFP power in thetadelta, alpha and beta band during rest and sensory palmar stimulation (SPS) in patients with general anesthesia and local/analgo sedation.
Results: We found prominent LFP power activity in thetadelta for both CD and TD. Unlike TD, a significant difference between rest and SPS was revealed for CD.
Conclusions: Our data support the presence of LFP oscillatory activity in CD and TD. Thetadelta power modulation in the GPi is suggested as a signature for sensory processing in CD.

1. Introduction

Dystonia is a movement disorder characterized by persistent muscle contractions and abnormal postures that may be idiopathic as in the case of segmental or focal dystonia which includes cervical dystonia (CD) [1]. Tardive dystonia (TD) is a secondary dystonia, occurring as side effect of prescribed drugs. To date, the pathophysiology of CD and TD remain poorly understood [2]. Nevertheless, several studies point towards neural dysfunction of multiple brain regions [3] and particularly the basal ganglia which are targeted by deep brain stimulation (DBS). This therapy aims to modulate changes in oscillatory activity mostly in the globus pallidus internus (GPi) of dystonia and myoclonus dystonia patients [4,5,6,7,8,9,10]. In particular, some authors reported that neuronal synchronization indexed by LFP oscillations in the globus pallidus is correlated with movement parameters and signals such as dystonic muscle activity by focusing on theta, alpha, low beta and gamma bands [11,12,13]. It was also shown that such oscillations in the 8–12 Hz frequency range synchronize with local neuronal discharges (microelectrode activity) in the GPi and possess higher amplitude than in the globus pallidus externus [14]. LFP oscillatory activity in the GPi has also been reported from Huntington's [15] and Parkinson's disease [16], while the spatial pattern of spectral power corresponding to intraoperative trajectories has been studied by our group [15,17,18,19,20]. In this report, we address the spatial oscillatory pattern of intraoperative trajectories targeting GPi (frequency range up to 100 Hz) by focusing on the mentioned dystonic groups and also comparing LFP power between conditions: CD vs. TD, with vs. without general anesthesia, and rest vs. sensory palmar stimulation (SPS) at specified frequency bands. Based on our findings, we suggest thetadelta modulatory activity in the GPi as a correlate of sensory processing in CD rather than TD.

2. Materials and methods

2.1. Participants

A total of 18 GPis (eleven CD and seven TD) in seven CD and five TD patients who underwent deep brain stimulation (DBS) surgery of the GPi, were recorded (Table 1). The study was in compliance with the Helsinki Declaration and had been approved by the local Ethics Committee at the University Hospital Düsseldorf (Study Nr. 2459). Informed consent was obtained from each patient.

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Table 1
Patient's characteristics. (CD: cervical dystonia, TD: tardive dystonia).

Patient #	Gender	Disease	Years since disease onset	Age in years at surgery	Anesthesia during surgery
1	Male	CD	12	59	General
2	Male	CD	15	68	Local/analgo sedation
3	Female	CD	26	66	Local/analgo sedation
4	Male	CD	17	45	General
5	Female	CD	25	66	General
6	Female	CD	16	56	Local/analgo sedation
7	Female	CD	36	45	General
8	Female	TD	21	44	General
9	Male	TD	11	48	Local/analgo sedation
10	Female	TD	28	57	General
11	Female	TD	24	72	General
12	Female	TD	13	66	General

2.2. Micro- and LFP macrorecordings

DBS target was determined by fusion of stereotactic CT and preoperative 3 Tesla MRI. Intraoperative multiunit activity (MUA) and LFPs were recorded simultaneously with up to 5 combined micro-macroelectrodes (microelectrode and macroelectrode tip 1.5 mm apart) (M: medial, C: central, L: lateral, A: anterior and P: posterior or alternatively AM: anteriormedial, AL: anteriorlateral, PM, posteriormedial, PL: posteriorlateral) (Fig. 1A) in steps of 0.5 to 1 mm, starting 10 mm above the target point by using the INOMED ISIS microelectrode recording system (Inomed Medizintechnik GmbH, Emmendingen, Germany).

It was not possible to measure the impedance of the macroelectrodes, although the manufacturer of the INOMED system reports a generic value of 1 kΩ. LFP-signals were amplified by a factor of 2000 and sampled at 2.5 KHz. Patients were awake or sedated during surgery by taking into consideration their particular symptoms and physical condition. The protocol for patients in general anesthesia included propofol (mean dosage 6.088 ± 1.730 mg/min) and remifentanil (mean dosage 15.110 ± 5.984 μg/min). Patients without general anesthesia underwent analgosedation with the above mentioned drugs that were paused before recordings.

Determined by optimal microelectrode activity around the calculated target point (±1 mm) two conditions were recorded with LFP: 1) twice 1 min of rest before and after (to avoid order effects) 2) two minutes of SPS of the contralateral hand (palm) with cotton swabs. We applied the same stimulation protocol for all the patients (CD and TD).

2.3. Off-line analysis

Postoperative (offline) analysis of macroelectrode trajectories around the target point (±1 mm) was carried out by using BrainVision Analyzer software (version 2, Brain Products GmbH, Munich, Germany). Data were down-sampled to 512 Hz, band-passed between 0.5 and 160 Hz, and notch-filtered at 50 Hz. The fast Fourier transform (FFT) was applied over each recorded segment of 120 s, with a Hanning window of 0.5 s and 50% overlap, leading to a spectral resolution of 1.2 Hz. By using the FFT, power spectral density (PSD) was subsequently calculated as implemented in the mentioned software. PSD was used to study the strength of LFP's spectral power variation as a function of frequency. Throughout the text "PSD of LFP" is just referred to as PSD for brevity.

2.3.1. Peak analysis

For each GPi, the trajectory with the highest PSD peak amplitude in the frequency range 1–30 Hz during rest condition was selected for further statistical comparison. Analysis of LFP oscillatory activity was performed by comparing amplitude and frequency of selected PSD peaks between the considered conditions: CD vs. TD, rest vs. SPS and with vs. without general anesthesia. The analysis focused on the frequency bands (thetadelta (θ-δ): 1–7 Hz, alpha: 8–12 Hz, beta: 13–30 Hz).

For the comparison of PSD peaks between conditions, we took the peak with maximum amplitude (within a specified frequency band) in the rest condition and compared it with the one in the SPS condition by allowing a variance of ±1 Hz.

2.3.2. Grand average of PSD/mean PSD analysis

Grand average (GAV) of PSD was calculated for CD and TD across all trajectories regarding the condition rest vs. SPS. For each PSD spectra used in the calculation of these GAVs, mean PSD in the frequency ranges thetadelta (θ-δ) (1–7 Hz) and theta-alpha (θ-α) (5–12 Hz) were calculated.

In addition, GAV of PSD was calculated for each trajectory across all patients regarding the condition rest vs. SPS. For each PSD spectra used in the calculation of these GAVs, mean PSD in the frequency range thetadelta (θ-δ) (1–7 Hz) was calculated.

SEM bar graphs were calculated for mean PSD values (rest and SPS) in the case of CD for the frequency bands θ-δ and θ-α.

2.4. Statistical analysis

For selected trajectories in the peak analysis, we compared peak amplitudes and their corresponding frequencies for the considered conditions. Because the assumption of normality in the distribution of most variables was violated (Shapiro–Will test), we made use of the Mann–Whitney and the Kruskal–Wallis tests for comparisons between independent groups, and the Wilcoxon signed rank test (alternatively the sign test for non-symmetrical distributions) for intra-individual differences.

For variables meeting the assumption of equality of variations a mixed design ANOVA was additionally performed to study a possible effect of anesthesia between groups, although with caution considering the limitation of a small sample-size for both dystonic groups.

For the comparison of mean PSD values between rest and SPS for CD, TD and each trajectory, the Wilcoxon signed rank test (alternatively the sign test) was applied.

Statistical analysis was performed through SPSS software (IBM SPSS Statistics, IBM Corp). The level of significance for all statistical tests was fixed at $p < 0.05$.

3. Results

We obtained the oscillatory pattern of trajectories targeting the GPi in CD and TD by focusing on the selected frequency bands.

With regard to CD (rest), we found prominent LFP oscillatory activity in thetadelta (all GPis), alpha (5 GPis) and beta (4 GPis) as reflected by the presence of PSD peaks with maximum amplitude within each considered frequency band. With regard to TD (rest), oscillatory activity was found in thetadelta (all GPis), alpha (6 GPis) and beta (1 GPi).

Based on the number of recordings with a peak within a specified frequency band for each trajectory (Table 2(A, B)), we found that each considered frequency band was represented in each trajectory and that the highest number of recordings with PSD peak occurrences corresponded to the central trajectory. Note that Table 2 summarizes the number of recordings over the whole group of patients/recordings.

The comparison between recording conditions revealed the following details.

3.1. CD vs. TD

We found no significant difference between CD and TD by considering PSD peak frequency and PSD peak amplitude in the frequency bands thetadelta, alpha and beta, which suggests a similar oscillatory pattern for both dystonia groups.