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Research report

Subthalamic local field potential oscillations during ongoing deep brain stimulation in Parkinson's disease

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Abstract

How deep brain stimulation (DBS) acts and how the brain responds to it remains unclear. To investigate the mechanisms involved, we analyzed changes in local field potentials from the subthalamic area (STN-LFPs) recorded through the deep brain macroelectrode during monopolar DBS of the subthalamic nucleus area (STN-DBS) in a group of eight patients (16 nuclei) with idiopathic Parkinson's disease. Monopolar STN-DBS was delivered through contact 1 and differential LFP recordings were acquired between contacts 0 and 2. The stimulating contact was 0.5 mm away from each recording contact. The power spectral analysis of STN-LFPs showed that during ongoing STN-DBS whereas the power of beta oscillations (8–20 Hz) and high beta oscillations (21–40 Hz) remained unchanged, the power of low-frequency oscillations (1–7 Hz) significantly increased (baseline = 0.37 ± 0.22; during DBS = 7.07 ± 15.10, $p = 0.0003$). Despite comparable low-frequency baseline power with and without levodopa, the increase in low-frequency oscillations during STN-DBS was over boosted by pretreatment with levodopa. The low-frequency power increase in STN-LFPs during ongoing STN-DBS could reflect changes induced at basal ganglia network level similar to those elicited by levodopa. In addition, the correlation between the heart beat and the low-frequency oscillations suggests that part of the low-frequency power increase during STN-DBS arises from polarization phenomena around the stimulating electrode. Local polarization might in turn also help to normalize STN hyperactivity in Parkinson's disease.

Keywords: Local field potentials; Deep brain stimulation; Parkinson's disease; Subthalamic nucleus; Electrical polarization

1. Introduction

The mechanisms underlying the action of deep brain stimulation (DBS) are still debated [3,13,31,35,36,38,49]. The electrical field induced by neuronal activity around the electrodes implanted in the human basal ganglia for DBS produces recordable oscillations known as local field potentials (LFPs) [5]. These oscillations reflect the synchronized activity of large neuronal populations [14,24,28,50]. LFPs can be recorded after electrode implantation, when the electrodes are still available for recording before being connected to the subcutaneous neurostimulator. LFPs recorded from the human subthalamic nucleus area (STN) are characterized by multiple rhythms operating at various frequencies. LFPs are specifically responsive to drug administration [6,14,32,33,34,42], and movement execution [1,9,15,23,29,40], and correlate with various clinical features [2,16,26,50]. Analysing STN-LFPs recorded during ongoing STN-DBS could disclose oscillatory responses from the stimulated area thus increasing our understanding of the mechanisms underlying the action of DBS. LFP recordings during DBS

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Table 1
Clinical features of patients

Patient	Age (years)	Disease duration (years)	Levodopa equivalent (mg)	UPDRS III off therapy	UPDRS III on therapy
Fre	61	8	500	13.5	5.5
Sab	55	7	1500	17.5	0
Sta	55	10	1125	64	11
Fum	48	16	1000	32.5	7
Rab	59	7	450	24.5	5
Sol	61	18	750	41.5	5
Sal	61	11	500	19	6
Car	48	8	800	17	4

are also interesting because they can be used to develop adaptive DBS systems driven by changes in the oscillatory activity in the target structure. Even though understanding the relation between STN-DBS and STN-LFPs could clarify DBS action mechanisms, DBS-induced oscillations have so far been only indirectly – and controversially – inferred from LFPs recorded in the STN after turning DBS off [18,43,52] or recording LFPs from another structure (e.g. the globus pallidus internus, GPi) during STN-DBS [7]. Owing to the large STN-DBS-generated artefact in the recording system no published study has described STN-LFPs recorded from the stimulating electrode during STN-DBS.

In this study, to find out how the brain responds to STN-DBS we assessed the functional changes in the subthalamic neuronal population during ongoing stimulation. To do so, using a specifically developed novel methodology for artefact free recording [45] we analyzed the effect of ongoing monopolar STN-DBS on the power spectrum of STN-LFPs simultaneously recorded from the DBS macro-electrode in the stimulated STN in patients with idiopathic Parkinson's disease.

2. Materials and methods

2.1. Patients

The study was performed under a protocol approved by the Local Ethic Committee and all patients gave their written informed consent after study procedures and risks involved had been explained. Patients were undergoing in our department functional neurosurgery for bilateral implantation of DBS electrodes in the STN. The patients' average age was 56 years (range 48–61), disease history 10 years (7–16), levodopa equivalent therapy pre-surgery 830 mg/day (500–1500), and Unified Parkinson's Disease Rating Scale III (motor part, UPDRS) [21] pre-surgery off therapy 29 (13.5–64), on therapy 5 (0–12) (Table 1). Patients were predominantly rigid-akinetic. All patients fulfilled inclusion criteria for DBS [30]. STN-DBS procedures included pre-operative direct visualisation of the nucleus through computed tomography-magnetic resonance imaging (CT-MRI) based targeting [12,44], intra-operative neurophysiology with micro-recordings [37,41], intra-operative stimulation (i.e. through the exploratory electrode) and macrostimulation (i.e. through the implanted macroelectrode), and post-operative neuroimaging for final assessment of the electrode position [12,44]. The implanted electrode for DBS (Model 3389, Medtronic Inc., Minneapolis, USA) had four metal contacts, designated 0-1-2-3 in caudal-rostral direction. In all patients, the STN-DBS procedures collectively indicated that contact 1 was within or close to the STN [14].

2.2. Experimental protocol

Post-operative LFPs were recorded 2 days after DBS electrodes were implanted. Each post-operative experimental session lasted approximately 2 h during which the patient sat comfortably in an armchair. Four of the eight patients were studied after overnight withdrawal of antiparkinsonian medication (off levodopa), and four were studied after taking antiparkinsonian medication (on levodopa). The experimental recordings in patients on levodopa started about two-and-a-half hours after the morning dose of antiparkinsonian medication. The on levodopa condition in this study therefore differed from that of previous studies in which patients received levodopa during the experimental recordings after overnight withdrawal of antiparkinsonian medication [2,6,14,15,29,32,33,42,50]. None of the four patients studied on levodopa had dyskinesias during the recording sessions.

The FilterDBS system for artefact-free recording [45] was connected to contacts 0–2 on the 3389 Medtronic electrode leaving contact 1 (target STN contact) free for DBS delivery (Fig. 1). A skin Ag/AgCl electrode (RedDot, 3M, USA) was used as recording reference. The amplified signal was digitalised with the Micro1401 device (Cambridge Electronic Design Inc., Cambridge, UK) at 500 samples/s and 12 bit resolution with 10 V range.

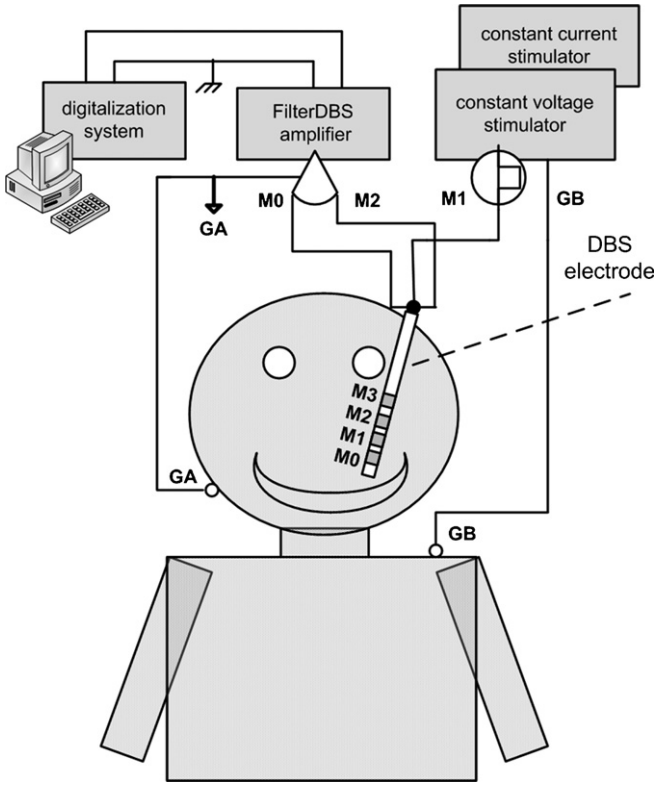

Fig. 1. Schematic diagram of the experimental set-up. The implanted 3389 electrode for deep brain stimulation (DBS) (contacts M0–M1–M2–M3) was connected to the FilterDBS (contacts M0–M2). The electrical stimulator delivering DBS was connected to the contact M1. GA is the reference for differential amplification and the GB is the anode for the stimulator.