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DOES INCREASED GAMMA ACTIVITY IN PATIENTS SUFFERING FROM PARKINSON'S DISEASE COUNTERACT THE MOVEMENT INHIBITING BETA ACTIVITY?

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Abstract—Akinesia and rigidity are cardinal symptoms of Parkinson's disease (PD). Previous studies analysing event-related desynchronization during movement onset associated both symptoms with pathologically increased oscillations in the beta frequency range. By focusing on the movement onset only, these studies cannot, however, shed light onto the question how oscillatory activity is changed during continuous movements. To investigate this issue, we compared the power of the local field potentials (LFP) within and above the subthalamic nucleus (STN) during rest, an isometric hold condition of the forearm, and a fist flexion and extension task in 13 patients with idiopathic PD during implantation of deep brain stimulation (DBS) electrodes. During fist flexion and extension (relative to rest), significantly increased activity in the low beta (12–18 Hz) and gamma (30–48 Hz) frequency ranges was observed within the STN, while during hold (compared to rest) no significant difference was found. For the regions above the STN the power during fist movements (compared to rest) was significantly higher, i.e. in the range of 18–30 Hz, with no significant changes in the gamma frequency range. Beta activity is claimed to inhibit movement and thereby could render fist movements more exhausting. Therefore, the observed increase in beta activity in the STN during fist movements might result in bradykinesia as experienced by many patients. We hypothesise that in order to enable repetitive fist movement despite increased beta activity, ''prokinetic'' gamma activity may be increased as a compensatory mechanism.

Key words: deep brain stimulation, power, nucleus subthalamicus, local field potentials.

INTRODUCTION

Neural oscillations have been described as one key mechanism for large-scale communication within the human brain (Singer, 1999; Schnitzler and Gross, 2005). Particularly in the motor system of the human brain, such oscillatory communication between different areas has been demonstrated. In the case of movement disorders several studies have shown that these oscillatory interactions are changed (Brown and Marsden, 1998; Timmermann et al., 2003). For example, in patients suffering from Parkinson's disease (PD) an increase of oscillatory activity in the beta frequency range (12–30 Hz) within the subthalamic nucleus (STN) has been associated with akinesia and rigidity (Wichmann et al., 1994; Marsden et al., 2001; Hutchison et al., 2004; Kuhn et al., 2004). Furthermore, for patients suffering from PD suppression in beta activity in the STN prior to and during movement onset has been observed as well as an ensuing increase of beta activity (Cassidy et al., 2002; Kuhn et al., 2004; Alegre et al., 2005).

The above mentioned studies have so far concentrated on the event-related development of the oscillatory activity before movement onset and shortly thereafter. Accordingly, the aim of this study was to analyse oscillatory activity during continuous movements. In healthy controls, a decrease of beta activity has been described during continuous movement (Gross et al., 2005), which suggests that beta activity might be related to movement inhibition. In contrast, gamma activity, i.e. in the range of 30–100 Hz, is supposed to promote movement (Brown et al., 2001; Brown, 2003; Hutchison et al., 2004). Furthermore gamma oscillations increased during movement in dystonic patients (Brucke et al., 2008; Liu et al., 2008).

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Abbreviations: DBS, deep brain stimulation; LFP, local field potentials; MCP, midcommissural point; MRI, magnetic resonance imaging; PD, Parkinson's disease; STN, subthalamic nucleus; UPDRS, Unified Parkinson's Disease Rating Scale; ZI, zona incerta.

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Based on these findings we here tested the following hypotheses: First, we expected a decrease in the beta frequency band within the STN for patients suffering from akinetic-rigid PD during continuous movement (compared to rest). This hypothesis is based on the fact that before movement onset a desynchronization in the beta band has been described (Cassidy et al., 2002; Kuhn et al., 2004; Foffani et al., 2005) and in healthy controls a decreased beta activity compared to rest was found (Gross et al., 2005). Second, based on the results in healthy subjects and dystonic patients we expected a change of the power in the gamma frequency range during movement (compared to rest). Furthermore gamma activity has been attributed particularly to the zona incerta (ZI) and the upper border of the STN (Trottenberg et al., 2006). Hence, we expected to find differences of oscillatory activity in regions above the STN compared to within the STN. In particular a difference in modulation in the gamma frequency range was expected (Trottenberg et al., 2006).

To test these hypotheses, we analysed local field potentials (LFP) within the STN of 13 patients suffering from akinetic-rigid PD. During recordings patients were asked to perform a resting condition, an isometric contraction task, and a continuous fist extension and flexion task. Furthermore, to confirm that these changes are specific for the STN we also recorded LFPs from regions above the STN.

EXPERIMENTAL PROCEDURES

Patients

In total, data obtained from 13 akinetic-rigid PD patients were analysed. The PD classification as akinetic-rigid was made according to the patients' preoperative Unified Parkinson's Disease Rating Scale (UPDRS) motor score (part III) (Fahn and Elton, 1987). If the average of the UPDRS items 22–26 was larger than the average of the UPDRS items 20 and 21, the patient was classified as akinetic-rigid. A summary of preoperative data is given in Table 1. The decision for STN-deep brain stimulation (DBS) was made in accordance with the preoperative selection criteria reviewed in Lang et al. (2006) and the German guidelines for DBS in PD (Hilker et al., 2009). All patients suffered from ON/OFF fluctuations due to long-term side effects of dopaminergic medication. In all patients, DBS electrodes were implanted bilaterally in the STN, the well-established target point (Deuschl et al., 2006).

All patients gave written informed consent to the implantation of electrodes and the micro- and macroelectrode recordings. The study was approved by the local ethics committee (Study No. 2459 (Düsseldorf-Cologne cooperation) and 08-158 (Cologne)) and conducted in accordance with the Declaration of Helsinki.

Implantation and intraoperative recordings

All patients were withdrawn from their anti-parkinsonian medication for at least 12 h in order to minimize influences due to medication during the operation and to perform intraoperative test-stimulation with an OFF state of the patient as "baseline". The DBS target points in the dorso-lateral STN were assessed by stereotactic coordinates, as well as fused stereotactic magnetic resonance imaging (MRI) and computed tomography (Voges et al., 2002). The standard coordinates to target the dorsolateral part of the STN used in our centre are 1.8 mm posterior to the mid AC (commissura anterior)–PC (commissura posterior) line (midcommissural point, MCP), 3.8 mm ventral to MCP and 12 mm laterally to midline.

During implantation of the stimulation electrode, LFPs were recorded with up to five combined micro- and macroelectrodes using the INOMED ISIS MER-system (INOMED Corp., Teningen, Germany). In 10 of the 13 patients LFP recordings were made only unilateral due to fatigue and anatomical constraints by, e.g., blood vessels. Furthermore due to the individual anatomy and blood vessels in some patients less than five micro-/macroelectrodes could be implanted. The number of recorded electrodes for each patient is given in Table 1. The combined micro-/macroelectrodes record single cell activity with a microtip 1 mm below the ring of the macroelectrode. LFPs were recorded with the macroelectrode ring. Simultaneously, surface EMGs were recorded of the M. extensor digitorum communis (EDC), M. flexor digitorum longus superficalis (FDL), and first dorsal interosseus (FDI). The EMGs were used to monitor that the patients performed the respective tasks correctly. Both EMG and LFP signals were sampled at 2500 Hz (Florin et al., 2010). The unit activity was sampled with 25,000 Hz. During recording a 1000 Hz low-pass filter was applied for the LFPs.

Table 1. Patient characteristics: A total of 13 PD patients aged between 39 years and 71 years at implantation and with disease durations between 4 years and 20 years were implanted bilaterally with electrodes in the STN. The number of trajectories indicates the number of recording electrodes for the respective implantation side

Patient No.	Gender	Age	Disease duration	UPDRS (ON/OFF)	Recording site	Number of trajectories
1	f	70	15	17/32	STN le	4
2	m	39	5	10/25	STN ri	5
3	m	58	9	43/54	STN le	5
4	m	61	10	21/61	STN le/STN ri	5/3
5	f	64	20	21/64	STN le/STN ri	5/4
6	f	58	14	14/41	STN le	5
7	m	63	9	25/62	STN le	5
8	f	44	6	9/31	STN le	3
9	m	71	10	27/56	STN le	4
10	m	62	12	24/60	STN le	5
11	f	66	18	29/58	STN le	4
12	m	71	16	14/21	STN le/STN ri	5/5
13	f	44	4	10/30	STN le	5

Abbreviations: m = male, f = female, le = left, ri = right; UPDRS – motor score of the Unified Parkinson's Disease Rating scale; ON – with medication; OFF – without medication.