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Research Paper

Subthalamic nucleus beta and gamma activity is modulated depending on the level of imagined grip force

Petra Fischer [a,b,*], Alek Pogosyan [a,b], Binith Cheeran [b], Alexander L. Green [b], Tipu Z. Aziz [b], Jonathan Hyam [c], Simon Little [c], Thomas Foltynie [c], Patricia Limousin [c], Ludvic Zrinzo [c], Marwan Hariz [c], Michael Samuel [d], Keyoumars Ashkan [d], Peter Brown [a,b], Huiling Tan [a,b]

[a] Medical Research Council Brain Network Dynamics Unit at the University of Oxford, OX1 3TH Oxford, United Kingdom
[b] Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, OX3 9DU Oxford, United Kingdom
[c] Unit of Functional Neurosurgery, Sobell Department of Motor Neuroscience and Movement Disorders, University College London Institute of Neurology, WC1N 3BG London, United Kingdom
[d] Departments of Neurology and Neurosurgery, King's College Hospital, King's College London, United Kingdom

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ABSTRACT

Motor imagery involves cortical networks similar to those activated by real movements, but the extent to which the basal ganglia are recruited is not yet clear. Gamma and beta oscillations in the subthalamic nucleus (STN) vary with the effort of sustained muscle activity. We recorded local field potentials in Parkinson's disease patients and investigated if similar changes can be observed during imagined gripping at three different 'forces'. We found that beta activity decreased significantly only for imagined grips at the two stronger force levels. Additionally, gamma power significantly scaled with increasing imagined force. Thus, in combination, these two spectral features can provide information about the intended force of an imaginary grip even in the absence of sensory feedback. Modulations in the two frequency bands during imaginary movement may explain the rehabilitating benefit of motor imagery to improve motor performance. The results also suggest that STN LFPs may provide useful information for brain-machine interfaces.

1. Introduction

Mental imagery, in addition to physical practice, is known to boost motor performance in comparison to physical practice alone (Avanzino et al., 2009). Two studies have indicated that physical training combined with mental imagery or autogenic training can improve motor performance more than physical exercises alone in patients with Parkinson's disease (Ajimsha et al., 2014; Tamir et al., 2007). Accordingly, it has been suggested that motor imagery exercises might be useful in improving motor control during physical rehabilitation in Parkinson's disease (Abbruzzese et al., 2015). This might be fruitful, as in Parkinson's disease not only motor execution, but also motor planning seems to be impaired (Avanzino et al., 2013; Conson et al., 2014). This idea is corroborated by imaging and transcranial magnetic stimulation studies that have demonstrated abnormal network activity during motor imagery in this patient group (Cunnington et al., 2001; Helmich et al., 2007; Maillet et al., 2015; Rienzo et al., 2014; Thobois et al., 2000; Tremblay et al., 2008). However, the neural basis of the rehabilitating effect of motor imagery in Parkinson's disease is still not known. Better understanding of the network activity underpinning motor imagery might help inform how best to leverage this potential therapeutic adjunct to physical rehabilitation in Parkinsonian patients.

Here we hypothesize that motor imagery involves the basal ganglia in humans in a similar fashion to real movements. We test this by investigating if activity recorded during motor imagery in the basal ganglia is modulated in a task-dependent manner similarly as during real movements. It has already been shown that beta activity decreases in the subthalamic nucleus (STN) local field potential (LFP) during mental imagery of brief wrist extension movements, and that this is not the case during non-motor visual imagery (Kühn et al., 2006). Similar decreases in beta activity have also been reported during passive action observation in the STN (Alegre et al., 2010; Marceglia et al., 2009). But it is still not established whether the extent of such beta changes depends on the intended effort or force of the movement that is imagined. In addition, in motor cortex, mu and beta activity are reduced during motor imagery whereas gamma activity tends to increase, with the

* Corresponding author at: Nuffield Department of Clinical Neurosciences, Level 6, West Wing, John Radcliffe Hospital, University of Oxford, OX3 9DU Oxford, United Kingdom.
E-mail address: petra.fischer@ndcn.ox.ac.uk (P. Fischer).

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latter outperforming changes in mu/beta for decoding of individual imagined finger movements (Liao et al., 2014). Whether gamma activity also increases in the STN during motor imagery is not known. However, there is some reason to suspect that reciprocal changes in beta and gamma activity in the STN might occur during motor imagery and scale with task demands. When patients with Parkinson's disease perform real manual grips at different force levels, beta and gamma activity in the STN are modulated such that the change in the gamma-band subtracted by the change in the beta-band linearly scales with the amount of force applied (Tan et al., 2013). If imagined gripping involves similar network dynamics as real gripping (Jeannerod, 2001), we would predict not only a beta decrease in the STN but also a gamma increase that is amplified with increasing force. Here we test this prediction by analysing local field potential recordings from the STN in Parkinson's disease patients who have undergone deep brain stimulation surgery.

2. Materials and methods

2.1. Participants

We recorded 11 Parkinson's disease patients who had undergone bilateral implantation of deep brain stimulation (DBS) leads in the STN 2–7 days prior to the recording. Patients underwent DBS surgery to receive chronic high-frequency stimulation of the STN to improve motor symptoms. In the first operation, electrode extension cables were externalized through the scalp to enable recordings. In a second operative procedure, up to 7 days later, a subcutaneous DBS pacemaker was implanted and connected to the electrodes used for chronic stimulation. In this relatively small cohort the number of post-operative days before recording had no obvious effect on the spectral reactivity patterns. The study was approved by the local ethics committee and patients were recorded after obtaining informed written consent. One patient had to be excluded because of excessive movement artefacts during real gripping. This patient had Boston Scientific DB-2201™ leads implanted. Clinical details of all patients included (mean age 61.3 ± 7 years, mean disease duration 9.6 ± 4 years, all right-handed, three female) are listed in Table 1. Recordings were performed in three surgical centres: King's College Hospital and University College Hospital in London and the John Radcliffe hospital in Oxford, UK. For each patient one of the following three macroelectrode models was used: Medtronic 3389 (quadripolar, n = 6), Boston Scientific DB-2201 Vercise (octopolar, n = 2) and Boston Scientific DB-2202 Vercise directional (octopolar, directional, n = 3).

2.2. Task

Patients were seated in a comfortable chair with their elbows flexed at about 90°. They held a dynamometer (G200; Biometrics Ltd., Cwmfelinfach, Gwent, UK) in each hand and were asked to grip it with maximal effort three times to obtain the maximum sustainable force before starting the main session. They had to hold the grip for as long as a white dot was presented on a computer screen (4.5 s), and performed this procedure separately for each hand. The time point of the most stable force production was selected manually in each trial and the maximum sustainable force was then computed as the maximum of the three trials.

In the first part of the main experiment, patients were presented with a red bar on the screen that instructed them to grip at 15, 50 or 85% of the maximum sustainable force (Fig. 1). The white dot and red bar both appeared either on the left or right field of the screen, which instructed them with which hand they should grip (left or right respectively). These were selected in a pseudo-random order. The red horizontal bars were presented at three different heights, corresponding to the different desired forces. The horizontal red bars were presented for 4.5 s in each trial. The exerted grip force was presented in real time as a vertical red column that increased in proportion to the force delivered. It replaced a vertical white column that corresponded to maximal sustainable force. The inter-trial interval was chosen randomly between 4 and 4.5 s. The time windows and force levels requested were set such that fatigue was kept to a minimum in the context of a time-limited post-operative study. Prior to the first recorded block, patients performed practice trials until they were comfortable with the task. We recorded three blocks in each condition. Each block contained 3–5 trials for each hand and force level (depending on the patient's fatigue, see Fig. 2). After completion of a block, patients were allowed to rest for as long as they wished. This resulted in an overall average number of 11 ± (SD) 2.8 trials per hand and force level.

In the second part of the main experiment, the dynamometers were put aside and patients were asked to rest their arms still on their lap for imagined gripping. Patients were instructed to imagine the gripping action they had just performed without activating any muscles. They were told to keep their arms fully relaxed, and it was pointed out that this would be assessed via recordings from the electromyographic (EMG) electrodes placed on their forearm (Fig. 3). However, they were not provided with real-time visual feedback of EMG or electrophysiological activity. The duration of the cue presentation was shortened to 2.5 s for the imagery condition to make it easier for patients to maintain imagery at the correct level for the whole trial duration and to avoid mind-wandering. Otherwise timings were kept the same as above. The imagery recordings were also split into three blocks allowing for breaks between blocks. Each block contained three trials per hand and force level resulting in an overall average number of 9 ± 1 trials for each hand and force level.

2.3. Recordings

Monopolar LFPs were recorded with a TMSi Porti amplifier (2048 Hz sampling rate, common average reference, TMS International, Netherlands) simultaneously with the force data from two dynamometers

Table 1
Clinical details. Age and disease duration are given in years. UPDRS-III: Unified Parkinson's disease rating scale part III. Levodopa equivalent dose was calculated according to Tomlinson et al. (2010). JR = John Radcliffe hospital, KC = King's College Hospital, UCL = University College London Hospital.

ID	Age/sex	UPDRS-III off/on levodopa	Disease duration	Main symptom	Medication (mg/day)	DBS lead	Surgical centre
1	71/m	22/8	12	Tremor	923 mg	Medtronic 3389™	KC, London
2	55/m	27/8	6	Rigidity, gait	1009 mg	Medtronic 3389™	JR, Oxford
3	56/m	17/9	3	Tremor	328 mg	Boston Scientific DB-2201™	KC, London
4	75/m	31/10	11	Gait, tremor	565 mg	Medtronic 3389™	KC, London
5	55/f	84/25	7	Gait, dystonia	1618 mg	Boston Scientific DB-2202™	JR, Oxford
6	62/m	27/4	12	Freezing of gait	955 mg	Medtronic 3389™	KC, London
7	60/m	52/30	8	Freezing of gait,	1282 mg	Medtronic 3389™	UCL, London
8	59/m	53/18	7	Tremor, bradykinesia, dyskinesia	1195 mg	Boston Scientific DB-2202™	JR, Oxford
9	60/f	56/31	14	Tremor, dyskinesia	1750 mg	Medtronic 3389™	KC, London
10	64/f	66/36	16	Rigidity, tremor	1628 mg	Boston Scientific DB-2202™	JR, Oxford