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Low-beta cortico-pallidal coherence decreases during movement and correlates with overall reaction time

Bernadette C.M. van Wijk [a,b,*], Wolf-Julian Neumann [a], Gerd-Helge Schneider [c], Tilmann H. Sander [d], Vladimir Litvak [b], Andrea A. Kühn [a,e,f]

[a] Department of Neurology, Charité - University Medicine Berlin, Germany
[b] Wellcome Trust Centre for Neuroimaging, University College London, UK
[c] Department of Neurosurgery, Charité - University Medicine Berlin, Germany
[d] Physikalisch-Technische Bundesanstalt, Institut Berlin, Germany
[e] Berlin School of Mind and Brain, Charité - University Medicine Berlin, Germany
[f] NeuroCure, Charité - University Medicine Berlin, Germany

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ABSTRACT

Beta band oscillations (13–30 Hz) are a hallmark of cortical and subcortical structures that are part of the motor system. In addition to local population activity, oscillations also provide a means for synchronization of activity between regions. Here we examined the role of beta band coherence between the internal globus pallidus (GPi) and (motor) cortex during a simple reaction time task performed by nine patients with idiopathic dystonia. We recorded local field potentials from deep brain stimulation (DBS) electrodes implanted in bilateral GPi in combination with simultaneous whole-head magneto-encephalography (MEG). Patients responded to visually presented go or stop-signal cues by pressing a button with left or right hand. Although coherence between signals from DBS electrodes and MEG sensors was observed throughout the entire beta band, a significant movement-related decrease prevailed in lower beta frequencies (~13–21 Hz). In addition, patients' absolute coherence values in this frequency range significantly correlated with their median reaction time during the task ($r = 0.89$, $p = 0.003$). These findings corroborate the recent idea of two functionally distinct frequency ranges within the beta band, as well as the anti-kinetic character of beta oscillations.

1. Introduction

The importance of basal ganglia structures in controlling movement has been demonstrated by the success of deep brain stimulation in the treatment of movement disorders (Kleiner-Fisman et al., 2006; Perlmutter and Mink, 2006). Local field potential recordings from these electrodes in target structures such as the subthalamic nucleus (STN) (Cassidy et al., 2002; Kühn et al., 2004; Alegre et al., 2005; Androulidakis et al., 2007b; Litvak et al., 2012), globus pallidus internus (GPi) (Brücke et al., 2008; Tsang et al., 2012; Talakoub et al., 2016), and ventral lateral thalamus (including Vim) (Paradiso et al., 2004; Klostermann et al., 2007; Brücke et al., 2013) have revealed movement-related modulations in the amplitude of beta (13–30 Hz) and gamma (~40–90 Hz) oscillations that are strikingly similar to those found in motor cortex. This suggests that neural activity throughout the cortical-basal ganglia-thalamus network is closely coordinated.

Beta band coherence in rest recordings has been reported between the STN and motor cortex (Hirschmann et al., 2011; Litvak et al., 2011a), and between STN and GPi (Brown et al., 2001) in Parkinson's disease patients, and between GPi and motor cortex in dystonia patients (Neumann et al., 2015). Although spectral beta power is clearly reduced during movement, it is less clear whether beta coherence follows the same pattern. Some studies report a decrease in STN-cortical coherence with movement (Kühn et al., 2006a; Lalo et al., 2008; Alegre et al., 2010) but others failed to observe a significant effect (Litvak et al., 2012; Hirschmann et al., 2013). This discrepancy might be related to the recent notion of a functional subdivision in the beta band into a low and high frequency range. Whereas Parkinsonian symptoms of bradykinesia and rigidity are

* Corresponding author. Department of Neurology, Movement Disorder and Neuromodulation Unit, Campus Mitte, Charité - University Medicine Berlin, Charitéplatz 1, 10117, Berlin, Germany.
E-mail address: vanwijk.bernadette@gmail.com (B.C.M. van Wijk).

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associated with low-beta power in the STN (Litvak et al., 2011a; Neumann et al., 2016; van Wijk et al., 2016), disease-unrelated coherence between STN and motor cortex was reported predominantly for high-beta frequencies in the same studies. When low-beta STN-cortex coherence is present, it is often of a slightly more lateral cortical location than the mesial high-beta coherence (Toledo et al., 2014; Oswal et al., 2016). It might therefore be relevant to look more closely at which beta frequencies experimental effects occur when interpreting results.

As the main output structure of the basal ganglia, the GPi is of special interest in studying the influence of basal ganglia on movement initiation. In our previous work involving dystonia patients (Neumann et al., 2015) we identified three sources of cortico-pallidal connectivity that were spatially distinct and frequency specific. In the theta range (4–8 Hz) pallidal activity was mainly coherent with temporal cortical regions; in the alpha range (7–13 Hz) with the cerebellum, and in the beta range (13–30 Hz) with sensorimotor regions. Only the pallido-cerebellar alpha coherence showed an inverse correlation with severity of dystonic symptoms. This leaves the possibility that the other networks are not disease-related but inherent to normal brain physiology. As these networks were found in rest recordings, it remains to be tested whether they have functional correlates, such as the control of movement.

The aim of this study was to investigate whether beta band cortico-pallidal coherence significantly reduces during movement, and whether it shows evidence of a subdivision into a low- and high-beta range. In addition, we correlated coherence values with measures of reaction time and clinical scores, in order to test for a link with behavior or disease severity. Results substantiate desynchronization in the low-beta band as a prerequisite for fast motor performance, and add to a more complete picture of cortical-basal ganglia oscillation patterns and the anti-kinetic role of beta band synchronization.

2. Methods

2.1. Patients and surgery

Nine patients (six female) with either segmental ($n = 2$), cervical ($n = 4$), Meige Syndrome ($n = 1$) or generalized dystonia ($n = 2$) took part in this study. 8 of them also participated in the rest recordings presented in Neumann et al. (2015); all except case 3. Patient characteristics are summarized in Table 1. Their mean age at time of recording was 51.4 (±12.1 SD) years, with an average disease duration of 14.0 (±6.7 SD) years. All patients were right-handed by self-report. Severity of clinical symptoms was assessed via the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) for patients with cervical or segmental dystonia and the Burke Fahn Marsden Dystonia Rating scale (BFMDRS) for patients with generalized dystonia. All patients were implanted with deep brain stimulation (DBS) macroelectrodes (model 3389, Medtronic, Minneapolis, MN, USA) in left and right globus pallidus internus. Each electrode lead had four contact points with a diameter of 1.27 mm, length of 1.5 mm and an inter-contact spacing of 2 mm centre-to-centre. Correct placement of the DBS electrodes was guided by intraoperative microelectrode recordings and confirmed by postoperative MRI (Neumann et al., 2015).

2.2. Recordings and experimental task

Recordings took place off medication and between 1 and 7 days after implantation while electrode leads were still externalized. Pallidal local field potential (LFP) recordings were obtained simultaneously with 125 channel magneto-encephalography (MEG, Yokogawa ET 160) at the Physikalisch Technische Bundesanstalt in Berlin. All patients were informed of the experimental procedures and gave written informed consent prior to the recordings. The study was approved by the local ethics committee of the Charité - University Medicine Berlin, Campus Virchow Klinikum, and was conducted in accordance with the declaration of Helsinki. Recordings for the stop-signal task included in this study took place after the 3–4 min rest recordings presented in Neumann et al. (2015) in the same session.

Stimuli were presented in black against a white background on a screen in front of the subjects. An experimental block comprised a mixture of left and right hand 'go' and 'stop' trials presented in a random order. Each trial started with a fixation cross displayed with a random duration between 4 and 6s. This was followed by presentation of a cue in the form of a '<' or '>'-sign indicating the response hand. Subjects were instructed to press a button with the corresponding left or right index finger as soon as the cue appeared. They were told to withhold their response when a red box appeared around the cue ('stop'). Each block contained 100 trials in total, of which 66% were 'go' and 33% 'stop' trials. Subjects completed at least one block and performed (part of) a second one depending on their level of fitness. Signals were low-pass filtered with 250 Hz and sampled at a rate of 2000 Hz. LFP signals were off-line converted to a bipolar montage between adjacent contact pairs.

2.3. Data analysis

We focused our analysis on the time window around the button press after the go-cues. Stop signal related changes were not analyzed due to limited number of trials and technical shortcomings for stop signal recording. Only go-trials in which subjects responded with the correct hand between 100 and 2000 ms after cue presentation were included. After applying notch filters at 50 Hz and higher-order harmonics (5th order bi-directional Butterworth filter with cut-off frequencies ±2 Hz), and downsampling to 1000 Hz, continuous time series were epoched from -3.5s until 3.5s around each button press (at 0s). Trials containing LFP amplitude values exceeding 7 standard deviations of the trial's time series were discarded. This resulted on average in 29 trials per left or right hand condition (range 18–44). For one patient (case 9) we were only able to record the right hand condition due to temporary technical failure of the left hand button. This patient was also the only subject not

Table 1
Patient characteristics. Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) was used for patients with cervical or segmental dystonia and the Burke Fahn Marsden Dystonia Rating scale (BFMDRS) in generalized dystonia (indicated with an *). Median reaction time was taken across the entire experiment, hence combining left and right hand trials. Likewise, average absolute coherence in the low-beta range (13–21 Hz) was averaged across left and right hemispheres.

Case	Age	Gender	Diagnosis	Preoperative TWSTRS/ BFMDRS*	Disease duration (years)	% Correct go-trials	Median reaction time (s)	Average absolute low-beta coherence
1	48	F	Generalized Dystonia	16*	20	98	0.98	0.010
2	55	M	Segmental Dystonia	20	12	68	1.20	0.016
3	52	F	Meige Syndrome	na	15	51	0.65	0.002
4	51	F	Cervical Dystonia	23	3	97	0.69	0.003
5	52	F	Cervical Dystonia	22	11	82	0.91	0.005
6	48	F	Segmental Dystonia	25	6	100	0.66	0.006
7	68	M	Cervical Dystonia	16	23	94	0.65	0.007
8	58	M	Cervical Dystonia	18	20	88	0.92	0.009
9	24	F	Generalized Dystonia (DYT1)	27*	16	74	0.48	0.002