Oscillatory activity in the subthalamic nucleus during arm reaching in Parkinson's disease

Raed A. Joundi a,b,⁎, John-Stuart Brittain a,c, Alex L. Green a,d, Tipu Z. Aziz a,d, Peter Brown a, Ned Jenkinson a

a Functional Neurosurgery and Experimental Neurology, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK
b Department of Physiology, Anatomy, and Genetics, University of Oxford, Oxford, UK
c Centre of Excellence in Personalised Healthcare, Institute of Biomedical Engineering, Department of Engineering Science, University of Oxford, Oxford, UK
d Nuffield Department of Surgical Sciences, John Radcliffe Hospital, University of Oxford, Oxford, UK

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A B S T R A C T
Oscillatory activities in the brain within the beta (15–30 Hz) and gamma (70–90 Hz) ranges have been implicated in the generation of voluntary movement. However, their roles remain unclear. Here, we record local field potential activity from the region of the subthalamic nucleus during movement of the contralateral limb in 11 patients with Parkinson’s disease. Patients were on their normal dopaminergic medication and were cued to perform arm-reaching movements after a delay period at three different speeds: ‘slow’, ‘normal’, and ‘fast’. Beta activity desynchronized earlier in response to the cue indicating an upcoming fast reach than to the cues for slow or normal speed movement. There was no difference in the degree of beta desynchronization between reaching speeds and beta desynchronization was established prior to movement onset in all cases. In contrast, synchronization in the gamma range developed during the reaching movement, and was especially pronounced during fast reaching. Thus the timing of suppression in the beta band depended on task demands, whereas the degree of increase in gamma oscillations depended on movement speed. These findings point to functionally segregated roles for different oscillatory frequencies in motor preparation and performance.

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Introduction

Changes in oscillatory brain activity are known to occur during the processing and execution of voluntary movement. Beta oscillatory activity (15–30 Hz) desynchronizes prior to and is sustained during movement in the cortex (Muthukumaraswamy, 2010; Zhang et al., 2008) and basal ganglia (Doyle et al., 2005; Kühn et al., 2004). Evidence suggests that beta oscillations facilitate maintenance of the current motor state while inhibiting the generation of new movements (Androulidakis et al., 2007a; Gilbertson et al., 2005; Joundi et al., 2012). Beta desynchronization is thought to play a ‘gating’ role to facilitate processing and initiation of movement, and accordingly is often observed up to 1 or 2 s prior to movement onset in self-paced movements (Klostermann et al., 2007; Kühn et al., 2004). In contrast, synchronization of neuronal activity at gamma band frequencies (70–90 Hz) has been observed during movement at cortical (Ball et al., 2008; Crone et al., 1998) and subcortical (Androulidakis et al., 2007b; Brücke et al., 2012; Kempf et al., 2009) sites. The prominence of movement-related increases in gamma activity in the contralateral cortex (Gonzalez Andino et al., 2005; Muthukumaraswamy, 2010) and the tight temporal relationship between gamma increase and movement advance the idea that it plays a ‘pro-kinetic’ role in the motor system (Brown, 2003; Lalo et al., 2008).

Nevertheless, data relating oscillatory activity in the basal ganglia to motor performance are sparse. One recent study has demonstrated a scaling of gamma synchronization with movement amplitude and velocity in the globus pallidus of dystonic patients, whereas beta desynchronization did not differ between movements (Brücke et al., 2012). However, responses to the cue and motor-related processing were not disambiguated. Here, we determine whether the same changes in oscillatory activity during movement are found in the region of the subthalamic nucleus (STN) in patients with Parkinson’s disease, using a paradigm that separates cue responses from movement. Recordings from the STN have previously revealed desynchronization in beta and synchronization in gamma activity concurrent with movement (Androulidakis et al., 2007b; Ray et al., 2012). Furthermore, dopamine replacement therapy reduces beta synchrony and increases 70 Hz oscillations (Brown et al., 2001; Lalo et al., 2008), furthering the possibility of gamma activity being physiologically, dopamine dependent, and ‘pro-kinetic’ (Brown, 2003).

Therefore, we tested people with Parkinson’s disease on their normal therapeutic dopaminergic medication to maximize the possibility of capturing spectral changes in their most normalized state. We recorded activity during a naturalistic reaching task where patients were asked to perform arm movements of the same distance but at
three different speeds. We sought to identify any differential modulation of beta and gamma activity in response to cues during motor preparation and subsequent movement.

Methods

Patients and surgery

Eleven patients with idiopathic PD (1 female, mean age 63.5±9.4 years (SD), disease duration 8.1±5.6 years) who had deep brain stimulation (DBS) electrodes implanted targeting the STN for the treatment of PD participated in the study. All patients gave their informed written consent to participate in the study, which was approved by an Oxford Research Ethics Committee according to the Declaration of Helsinki. Five patients were implanted unilaterally, and the remaining bilaterally. Clinical details are summarized in Table 1. The macroelectrodes used in all cases were Medtronic model 3389 (Medtronic Neurological Division, Minneapolis, USA) with four platinum–iridium cylindrical surfaces (1.27 mm diameter and 1.5 mm length) and a contact-to-contact separation of 0.5 mm. Intended coordinates for the STN were 12 mm lateral from and 1.5 mm length) and a contact-to-contact separation of 0.5 mm. Intended coordinates for the STN were 12 mm lateral from the midline, 3 mm behind the midcommissural point, and 4 mm below the AC–PC. Individual adjustments were made according to pre-operative stereotactic T2-weighted magnetic resonance imaging. During the surgical procedure intra-operative macroelectrode stimulation and clinical evaluation were carried out to identify the best placement for the electrode. Post-operative MRI were fused to pre-operative MRI to confirm accurate targeting.

Recordings

Recordings were obtained 4–6 days after surgery to implant the electrodes and prior to internalization of the DBS leads and pacemaker. Local field potentials (LFPs) were recorded from the DBS electrodes at 2.5 kHz and amplified (CED 1902 amplifiers, Cambridge Electronic Design, Cambridge, UK), digitized at a sampling rate of 1 kHz (CED 1401, CED Cambridge, UK), and recorded to disk (CED Spike2, CED, Cambridge, UK). Data were analyzed off-line using in-house scripts written in Matlab (Mathworks, Natick, MA, USA). STN LFPs were recorded as bipolar channels, in order to cancel out common signals due to volume conduction and ensure the LFPs recorded were as focal as possible to the electrode. Three bipolar channels in the STN contralateral to the task limb were acquired from each patient for analysis.

Task

The patients were seated on a comfortable chair in front of a keyboard and LCD monitor, positioned 50 cm apart. Stimuli were presented on the monitor using Presentation software (Neurobehavioral Systems Inc., CA, USA). The full paradigm is displayed in Fig. 1. The patients were first instructed to lightly depress the spacebar on a keyboard, to start the task. There followed a 1 s period in which the screen was blank, of which the latter 500 ms (or PRE-CUE period) was used as a baseline period for the LFP recordings for subsequent power changes. The PRE-CUE period was followed by a cue consisting of the speed instruction: the word “FAST”, “NORMAL”, or “SLOW” presented on the screen for 500 ms. The speed cue then disappeared, followed by a random delay between 500 and 1500 ms. The patients had to maintain their hold on the spacebar during this delay period, which will be referred to as DELAY. The gap was intended to identify activity that may be involved in the preparation of movement at different speeds. A randomized period was selected so that subjects would not anticipate the subsequent imperative cue. After the gap, a movement cue of a green square (5×5 cm) was presented at the middle of the monitor screen. On this cue the subject released the spacebar and reached towards the movement cue at the instructed speed. The brief period between presentation of the movement cue and release of the spacebar will be referred to as REACT. No explicit instruction was given regarding the reaction time itself, only to adjust speed of the subsequent reach. If “NORMAL” was presented, the subjects were to reach at a comfortable speed towards the cue. During

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Table 1

Clinical Details.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age, sex</th>
<th>Disease duration (years)</th>
<th>Predominant symptoms</th>
<th>Levodopa equivalent daily dose at surgery (mg)</th>
<th>Pre-op motor UPDRS off-meds</th>
<th>Pre-op motor UPDRS on-meds</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>58, M</td>
<td>2</td>
<td>Tremor</td>
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<td>19</td>
<td>6</td>
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<tr>
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<td>963</td>
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<tr>
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<td>63, M</td>
<td>10</td>
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<td>1610</td>
<td>40</td>
<td>22</td>
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<tr>
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<td>12</td>
<td>Gait, tremor</td>
<td>1000</td>
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</table>
“SLOW” trials the subjects were instructed to make a slower than normal (‘slow-motion’) movement towards the cue, while for “FAST” trials subjects were instructed to reach as quick as possible to the screen. Subjects were instructed to press the target on the screen with their index finger, whereupon they received an auditory beep, providing feedback. The period between spacebar release and touching the target will be referred to as REACH. Subjects then returned their finger to the spacebar to start the next trial. Each block consisted of 45 trials in total, with a pseudo-randomized distribution of 15 of each fast, normal, and slow trial. Between each block patients were reminded to keep their slow movements ‘slower than normal’ and their fast movements ‘as fast as possible’. The number of blocks varied from 2 to 4 for each patient, with the exception of 1 patient who completed a single block due to fatigue.

Analysis

Due to the relationship between contralateral gamma and movement we analyzed data only from the STNr contralateral to the movement. Data were imported into Matlab, band-pass filtered between 2 and 100 Hz, and notch filtered to remove main noise. Data were epoched to speed cue onset (−200 to 500 ms) and reach onset (−1000 to 2000 ms). Spectrograms were generated using a Hermite functions approach (Bayram and Baranuik, 2000). Hermite functions represent an extension of Thomson’s multitaper method (Thomson, 1982) to the time–frequency plane, providing improved bias and variance properties that are beneficial when examining non-stationary data. With an emphasis towards time-evolving spectra, spectrograms were generated using a time–frequency localization parameter A/2 = 5 (see Brittain et al., 2007) providing a full-width half-maximum resolution of 167 ms × 2.7 Hz. The electrode contact with the highest movement-related gamma synchronization was determined and chosen for subsequent analysis. Spectrograms were evaluated through point-wise paired t-tests over log-spectral values at p = 0.05. A baseline period for subsequent analysis. Spectrograms were evaluated through point-wise paired t-tests over log-spectral values at p = 0.05. A baseline period for subsequent analysis. Spectrograms were evaluated through point-wise paired t-tests over log-spectral values at p = 0.05. A baseline period for subsequent analysis. Spectrograms were evaluated through point-wise paired t-tests over log-spectral values at p = 0.05.

Finally, to quantify the relative changes in power within beta (15–30 Hz) and gamma (70–90 Hz) bands, percentage change differences were averaged for the three different task periods (DELAY, REACT, REACH) for each data set. In addition, each task period was normalized to the oscillatory power in the preceding period (REACT to DELAY, and REACH to REACT) to determine any sequential change in power for each time period.

All statistical analyses were conducted using SPSS v12 (SPSS Inc., Chicago, IL, USA), except significance spectrograms, which were generated using one-sample t-tests in MATLAB. Percentage change values of beta and gamma were normally distributed as confirmed by the one-sample Kolmogorov–Smirnov test. Mauchley’s test confirmed the sphericity of the data. One-way repeated measures analysis of variance (ANOVA) tests were conducted for movement time as well as power in both the beta and gamma bands in each task period (DELAY, REACT, REACH). Post-hoc paired t-tests, with Bonferroni correction, were used to compare between conditions (significant p value < 0.05). Significant differences from baseline for each condition were also calculated using one-sample t-tests (significant p < 0.05). Reach times were also correlated with increases in beta and gamma activity using Pearson’s product moment correlation.

Results

Selected contacts

The contact pairs demonstrating the highest movement-related gamma modulation were selected for analysis. All patients demonstrated a clear maximum in one of the 3 contact pairs on the side contralateral to movement. The largest increase in gamma power was 67.4 ± 17.6% (SEM) higher than the mean of the remaining contact pairs from the same electrode. We used the contact with the highest gamma activity to generate the spectrograms and band-limited measures of gamma change for all conditions. However, for band-limited changes in the beta range (15–30 Hz), we similarly selected the contact with the highest movement-related modulation in beta activity. There was 57.9 ± 6.7% more beta desynchronization in the selected contact than the mean of the remaining contact pairs. 8 out of 11 patients had the same contact selected for gamma and beta activity. Furthermore, recordings in 10 out of 11 patients exhibited polarity reversal across two of the contact pairs, suggesting local generation of potentials. In those patients, all contacts selected for analysis were among those with polarity reversal.

Movement time

Patients successfully varied the speed of their reaching movements according to the cued instructions, demonstrating significantly different movement times (F 2,20 = 51.3, p < 0.0001; Fig. 1B). ‘Slow’ movement (1612 ± 211 ms) had significantly longer movement times than ‘normal’ (1126 ± 109 ms; t10 = 4.27, p < 0.0001) and fast (647 ± 57 ms; t10 = 5.73, p < 0.0001) movements. Importantly, ‘fast’ movements were significantly shorter than ‘normal’ (t10 = 7.34, p < 0.0001).

General pattern of oscillatory activity during DELAY

Fig. 2A displays the spectrogram of selected channels aligned to speed cue onset for slow, normal and fast trials. Significance Fig. 2B shows areas of oscillatory change at p < 0.05 across patients. Apparently is a significant desynchronization in the lower beta range of around 13–20 Hz, beginning at cue onset only in the fast condition. In contrast, the slow and normal trials have no major oscillatory changes in response to the cue.

Band-limited activity for beta (15–30 Hz) and gamma (70–90 Hz) is plotted in Fig. 2C. Here again, a significant beta desynchronization occurs after the fast cue, with non-significant decreases in beta activity after normal and slow cues. Activity in the low (13–20 Hz) and high (21–30 Hz) beta ranges is plotted in Fig. 2D, showing a more dramatic decrease in low beta after fast cue onset. In contrast, there is no obvious change in band-limited gamma activity in response to the cue.

General pattern of oscillatory activity during REACH

Fig. 3 displays the spectrograms of the LFP activity during the reach period. Decreases in beta activity were evident before reach onset (especially for the fast condition), and beta activity was further suppressed after reaching began. This decrease was significant and continuous throughout the reach period for all three conditions.

Increases in gamma activity were observed around the time of reach onset in all three conditions; however, there was a substantially larger increase in gamma activity immediately after reach onset in the fast condition. Areas of significance for gamma activity were apparent only in the fast condition between approximately 70 and 90 Hz. There were also large increases in 40–60 Hz activity but this was not significant as power increases in this range occurred in only 2 patients (cases 8 and 9).

Beta activity averaged over 15–30 Hz demonstrated a significant decrease prior to and during reaching (Fig. 3C), resolving to non-significant levels approximately 500 ms after reach end. There were no differences in absolute power changes between speeds, apart from a quicker resynchronization in the fast condition due to the reduced movement time. There was an increase in band-limited gamma activity immediately prior to and during the reach. Slow and normal speeds had a modest increase in gamma activity, peaking
at about 25%, with very brief periods of significance from baseline. Fast reaching resulted in a substantially higher increase in gamma, achieving a peak increase of approximately 60%, and remaining significantly above baseline throughout the reach period.

Average beta power in the three task periods

To quantitatively assess changes in oscillatory activity, the average percentage change in beta band power was calculated for the three task periods, from a common baseline period of 500 ms preceding speed cue presentation (PRE-CUE). We additionally baselined REACT to DELAY, and REACH to REACT, in order to visualize the incremental change across task periods (Fig. 1A).

In DELAY (Fig. 4A), there was a significant decrease in beta activity for fast \((t_{10} = -2.9, p = 0.017)\), but not slow \((t_{10} = -2.0, p = 0.079)\) or normal speeds \((t_{10} = -1.7, p = 0.13)\). An ANOVA across the three speeds revealed a differential effect \((F_{2,20} = 15.1, p = 0.001)\), accounted for by significantly more suppressed beta activity in fast compared to slow \((t_{10} = -3.6, p = 0.016)\) and normal \((t_{10} = -6.8, p = 0.0001)\) trials.

In REACT as compared to DELAY (Fig. 4B), beta activity decreased significantly for slow \((t_{10} = -3.7, p = 0.0041)\), normal \((t_{10} = -4.3, p = 0.0016)\), but not fast \((t_{10} = -1.2, p = 0.26)\) trials. There was a significant difference across conditions \((F_{2,20} = 12.6, p = 0.0002)\), accounted for by a larger change in slow compared to fast trials \((t_{10} = -4.2, p = 0.005)\) and normal compared to fast \((t_{10} = -4.3, p = 0.005)\). When compared to the pre-cue period (Fig. 4D), REACT showed significant beta desynchronizations for slow \((t_{10} = -4.0, p = 0.0024)\), normal
(t10 = −3.5, p = 0.0061), and fast (t10 = −3.5, p = 0.0058) trials. However, there was no difference between conditions (F2,20 = 2.1, p = 0.066). Thus beta desynchronization in slow and normal speed trials caught up with the earlier desynchronization in the fast trials.

Beta activity did not change significantly between REACT and REACH (p > 0.05) and there was no difference between conditions (F2,20 = 0.18, p = 0.93, Fig. 4C). When comparing REACH to the PRE-CUE period (Fig. 4E), beta activity was significantly suppressed during slow (t10 = −5.9, p = 0.0001), normal (t10 = −4.4, p = 0.0013), and fast trials (t10 = −3.7, p = 0.0038). However, there was no differential effect between the three speeds (F2,20 = 0.29, p = 0.75).

In summary, the 'fast' cue elicited early beta desynchronization in DELAY and maintained this decrease throughout reach preparation and execution. In contrast, beta desynchronized later (during REACT) in the slow and normal conditions. In all conditions, there was no change between REACT and REACH, suggesting that most of the drop in beta occurred prior to movement.

Average gamma power in the three task periods

In DELAY (Fig. 4F), gamma activity showed no significant change in slow or normal trials (p > 0.05), but a significant increase for fast trials (t10 = 2.9, p = 0.016). However, there was no significant difference between conditions (F2,20 = 1.7, p = 0.211).

There were no significant changes from DELAY to REACT (p > 0.5, Fig. 4G), and no difference between conditions (F2,20 = 0.88, p = 0.43). Similarly, there were no significant increases as compared to the PRE-CUE period (Fig. 4I) across speeds (p > 0.05), and no significant difference between conditions (F2,20 = 2.3, p = 0.13).

Comparing REACT to REACH, a significant increase in gamma activity emerged (Fig. 4H; slow: t10 = 3.3, p = 0.0077, normal: t10 = 3.2, p = 0.0085, fast: t10 = 4.7, p = 0.0008). Furthermore, there was a significant difference between conditions (F2,20 = 8.56, p = 0.002). The difference was due to significantly higher gamma in the fast compared to slow (t10 = −3.1, p = 0.033) and normal
(t_{10} = -2.8, p = 0.033) trials, but not between slow and normal trials (t_{10} = -1.2, p = 0.76). Overall power compared to the PRE-CUE period (Fig. 4) showed significant gamma increases across all three conditions (slow: t_{10} = 2.9, p = 0.014, normal: t_{10} = 2.9, p = 0.015, fast: t_{10} = -3.3, p = 0.0075). Furthermore, there was a significant difference between conditions (F_{2,20} = 7.7, p = 0.015), due to significantly higher gamma in the fast reach (58.4 ± 0.15%) compared to slow (17.9 ± 0.06%, t_{10} = 2.8, p = 0.04) and normal (25.2 ± 0.09%, t_{10} = 3.1, p = 0.037) trials, but not between slow and normal speeds (t_{10} = -1.3, p = 0.42).

In summary, gamma power changed minimally during preparation but increased dramatically upon the onset of reaching. The increase in gamma power was most pronounced for the fast reach trials.

Correlations between speed of reach response and gamma activity

To determine if gamma activity was related to speed of movement on a trial-by-trial basis we correlated the mean gamma increase (as percentage change) from REACT to REACH with the mean speed of movement (taken as the log of the reach time) for each subject. The average of the R value in all patients was -0.29 ± 0.07, and this was significant when tested against zero (t_{10} = -4.0, p = 0.0027, Fig. 5A). Thus, shorter reaching times (higher speeds) were associated with larger gamma increases. For beta activity, the mean R value was 0.16 ± 0.39 which was not significantly different from zero (t_{10} = 1.4, p = 0.20, Fig. 5A). Gamma and beta R values were also significantly different from each other (t = 2.5, p = 0.03). Examples of two individual gamma correlations are shown in Fig. 5B. There was no significant correlation across subjects between reach time and the average gamma (R = -0.27, p = 0.13) or beta (R = 0.25, p = 0.47) band power change or between the ON-drug motor UPDRS score and the gamma (R = -0.02, p = 0.95) or beta (R = 0.25, p = 0.27) band power change.

Discussion

We sought to determine if beta and gamma activity in the region of the subthalamic nucleus was related to task demands during arm reaching. We found a dramatic increase in the amplitude of gamma oscillatory activity with fast reaching movements. In contrast, activity in the beta range desynchronized prior to and during movement. Although the eventual level of beta desynchronization did not differ between slow, normal and fast speed movements, the desynchronization in fast movements had an earlier onset. Thus, for a movement that can be programmed before execution—as in the task here—the depth of beta desynchronization is relatively fixed (see also Brücke et al., 2012), consistent with the hypothesis that...
beta activity serves to ‘gate’ motor output. This gate can be opened earlier if the anticipated task is demanding. The latter is in accord with the notion that beta suppression is important in securing resources for the planned action (Jenkinson and Brown, 2011).

The above may be an over-simplified account of the behavior of beta activity as it does not consider variation within the frequency band. Subdivision of the beta band revealed that the earlier onset of beta desynchronization in fast movements occurred in the lower beta frequencies (13–20 Hz). Kempf et al. (2007) likewise found that the earliest motor-related reactivity was seen over 6–18 Hz, although this study failed to distinguish alpha from lower frequency range beta activity. Still, the latter authors found that the early desynchronization occurred when more demanding movements had to be performed. That the timing of beta desynchronization has functional consequences is supported by the correlation between the onset of beta desynchronization and reaction time under conditions of time pressure (Doyle et al., 2005; Kühn et al., 2004). Thus beta suppression, particularly that in the lower range of the frequency band, may occur earlier when more demanding movements have to be executed or when cued movements are made under time pressure.

Gamma activity has been observed in a variety of neural systems and in different frequency bands depending on function and brain area. The most consistent gamma activity in our records was between 70 and 90 Hz. Such activity has been previously reported in the basal ganglia (Alegre et al., 2005; Androulakis et al., 2007b; Brücke et al., 2012; Kempf et al., 2009) and primary motor area of the cortex (Ball et al., 2008; Crone et al., 1998; Gonzalez Andino et al., 2005; Muthukumaraswamy, 2010). The increase in 70–90 Hz gamma with increased speed seen here compliments a recent study demonstrating a similar relationship between gamma and movement velocity seen in LFPs from the globus pallidus of dystonic patients (Brücke et al., 2012). In the latter study gamma activity scaled with both amplitude and velocity, but not direction, yet it was not fully possible to disentangle the former two. Here we kept amplitude constant and observed an increase in gamma with speed alone. Alternatively, the gamma modulation could be related to the presumed increase in force with higher speeds. There is prior evidence that cortical gamma activity may be important in the coding of force, as gamma increases in the cortex are more prominent with large rather than small force production (Muthukumaraswamy, 2010), and electrical stimulation of the motor cortex at 70 Hz can produce increases in force rate production in healthy humans (Joudi et al., 2012).

However, any relationship between gamma activity and force could also be secondary to the coding of motor effort by oscillatory activity in the 70–90 Hz band. Recent evidence implicates the basal ganglia in the scaling of effort in response to the energetic demands of a particular movement (Mazzoni et al., 2007). Gamma activity has also been considered to play a role in attention and arousal (Bauer et al., 2006) and it could be argued that the higher gamma activity with faster movements related to the higher degree of attention required. However, slow reaching trials also necessitated attention in order to inhibit oneself from moving at normal speeds. In addition, the major component of gamma synchronization occurred after movement onset, whereas attention might be expected to have been highest immediately following the imperative cue.

Recording from the STN of patients with Parkinson’s disease creates inherent challenges, as any attempts to study physiology are potentially affected by the known pathology in the basal ganglia. Additionally, bradykinesia will have prevented many patients from generating very fast speeds thereby limiting the range of velocities that could be studied. However, we opted to study patients on their normal dopaminergic medication so as to increase motor performance during the task, reduce fatigue, and, as far as possible, restore physiological functioning to the STN. Dopaminergic therapy is known to suppress the heightened pathological beta activity and increase gamma activity in PD (Brown, 2003), allowing us to more effectively study gamma oscillations compared to studies off medication.

Even so, our results may still have been influenced by the presence of motor dysfunction and pathological alteration in the basal ganglia. The usual approach to delineating the role of pathology in these circumstances is to contrast OFF and ON medication recordings. Several studies have taken this approach; however these have involved investigation of the resting state or extremely simple tasks (Androulakis et al., 2007a; Doyle et al., 2005; López-Azcárate et al., 2010; Moran et al., 2008; Trottengberg et al., 2006; Williams et al., 2002), conditions that can be adequately compared between off and on medication states as performance differences are less of an issue compared to our more demanding reaching task. Other on–off studies have focused on pre-movement activity (Kühn et al., 2004; Williams et al., 2003), again eliminating the confound of differences in future motor performance and have suggested that cue-related beta reactivity increases with dopamine (Doyle et al., 2005; Williams et al., 2005).

However, the primary goal of our study was to examine the role of oscillations in the subthalamic nucleus during a demanding and naturalistic motor task, in a state that was as close to normality as possible. Thus, we opted to study patients on medication for four main reasons: 1) the task would be rather taxing and fatiguing (repetitive ballistic movements with the whole arm) for patients off their anti-Parkinson medication, 2) large differences in performance would confound on–off comparisons, 3) dopaminergic treatment would facilitate a motor state as close to normal as possible, and 4) we wished to contrast beta and gamma band reactivities and movement-related gamma activity is minimal—and often not present—when off medication.

The similarity between our results and those of other non-invasive studies in healthy subjects (Alegre et al., 2003; Muthukumaraswamy, 2010) and those from recordings in the pallidum in patients with dystonia (Brücke et al., 2012) supports the suggestion of a physiological—rather than PD-related pathological—underpinning to the gamma activities observed in the present study.

In summary, we have shown that beta and gamma activity in the region of the subthalamic nucleus is modulated prior to and during naturalistic reaching movements. In line with previous reports, the direction and the timing of the changes differ between the frequency bands. The differences lead us to suggest that beta band desynchronization gates motor processing and thus necessarily develops before movement. In contrast, gamma band changes are only fully developed once movement has started. We suggest that gamma band increases are more closely related to motor processing, and in particular help scale movement through the coding of velocity, force or possible motor effort.

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