Persistent suppression of subthalamic beta-band activity during rhythmic finger tapping in Parkinson’s disease

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Objective: The function of synchronous oscillatory activity at beta band (15–30 Hz) frequencies within the basal ganglia is unclear. Here we sought support for the hypothesis that beta activity has a global function within the basal ganglia and is not directly involved in the coding of specific biomechanical parameters of movement.

Methods: We recorded local field potential activity from the subthalamic nuclei of 11 patients with Parkinson’s disease during a synchronized tapping task at three different externally cued rates.

Results: Beta activity was suppressed during tapping, reaching a minimum that differed little across the different tapping rates despite an increase in velocity of finger movements. Thus beta power suppression was independent of specific motor parameters. Moreover, although beta oscillations remained suppressed during all tapping rates, periods of resynchronization between taps were markedly attenuated during high rate tapping. As such, a beta rebound above baseline between taps at the lower rates was absent at the high rate.

Conclusion: Our results demonstrate that beta desynchronization in the region of the subthalamic nucleus is independent of motor parameters and that the beta resynchronization is differentially modulated by rate of finger tapping.

Significance: These findings implicate consistent beta suppression in the facilitation of continuous movement sequences.
suggested that beta levels may provide a measure of the likelihood that a new voluntary action will need to be actuated and hence facilitate the resourcing and preparation of potential actions (Jenkinson and Brown, 2011). In this theory salient external and internal cues serve to suppress beta activity and this helps determine motor readiness. All these theories consider beta suppression to subserve a global function within the motor system rather than the explicit coding of the biomechanical parameters of any given movement. Accordingly the level of task-related beta suppression should be unrelated to such parameters. However, reports differ in the extent to which activity in the beta frequency band behaves in the predicted way (Kempf et al., 2007; Brücke et al., 2012). The hypothesis that beta activity is suppressed according to the likelihood of new motor processing leads to a further specific prediction: that phasic suppression of beta activity prior to a voluntary action will be replaced by a persistent suppression during a sequence of related movements, such as in rhythmic tapping.

Hitherto, the above predictions have been supported by magnetoencephalographic and electroencephalographic studies showing that beta activity in the cerebral cortex of healthy humans during finger tapping maintains a constantly desynchronized state with faster finger movements (Toma et al., 2002; Erbil and Ungan, 2007; Muthukumaraswamy, 2010). Here, we test these predictions in the basal ganglia by recording local field potential (LFP) activity from the subthalamic nucleus region (STN) in patients with PD. In contrast to an earlier study (Androulidakis et al., 2008), we recorded from patients following treatment with the dopamine prodrug levodopa, so as to normalize as far as possible the function of the basal ganglia, and maximize possible inferences about physiological functioning. We studied patients while they made externally paced rhythmic tapping movements with their index finger as this provided a predictable sequence of movements. We asked subjects to perform finger tapping at different rates so that the dependence or otherwise of beta activity on sequential movement and velocity could be determined. Moreover, we could reasonably expect changes in beta activity in the subthalamic nucleus of treated patients in this task as the basal ganglia are implicated in the execution of movement sequences (Georgiou et al., 1993).

2. Methods

2.1. Patients and surgery

Eleven patients with idiopathic PD (one female, mean age 64 ± 2.9 (SD) years, mean disease duration 8.2 ± 1.6 years) who underwent implantation of deep-brain stimulation (DBS) electrodes in the STN participated in the study. All patients were on their normal medication, and dosages were deliberately unchanged in the peri-operative period, as the surgical team’s policy is to delay therapeutic stimulation to allow for the effect of post-operative stun to dissipate before titrating the stimulation parameters. All patients self-reported right-hand dominance in normal day-to-day-activities. All patients gave their informed written consent to participate in the study, which was approved by the Oxfordshire Research Ethics Committee A and carried out according to the Declaration of Helsinki. Three patients were implanted unilaterally, and the remaining bilaterally. Clinical details are summarized in Table 1. The macroelectrode used was model 3389 (Medtronic Neurological Division, Minneapolis, USA) with four platinum–iridium cylindrical contacts (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 the midline, 3 mm behind the midcommissural point, and 4 mm below the anterior commissure – posterior commissure line. Individual adjustments were made according to pre-operative stereotactic T2-weighted MRI. Intra-operative macrostimulation and clinical evaluation of the patient was also carried out to identify best placement of the electrode. Post-operative CT in conjunction with image fusion of pre-operative MRI confirmed targeting.

2.2. Recordings

Recordings were obtained 4–6 days after the initial implantation of the DBS electrodes, prior to internalization of the pacemaker. STN LFPs were recorded bipolarly from consecutive contacts of each DBS electrode (01, 12, 23) in order to provide common-mode rejection and ensure recorded activity was as focal as possible to the individual electrode contact. LFPs were recorded from the DBS electrodes through CED 1902 amplifiers, low-pass filtered at 1000 Hz and digitised at a sampling rate of 2.5 kHz with a CED 1401 (Cambridge Electronic Design, Cambridge, UK). Data were recorded onto hard-disk using CED Spike2 software, notch filtered to remove line noise, band-pass filtered between 2 and 100 Hz and down-sampled to 1000 Hz. Data were then analyzed using in-house scripts written in Matlab (Mathworks, Natick, MA, USA).

2.3. Task

All patients performed a synchronized tapping task. Patients were seated comfortably in a chair with their right arm supported by a cushion and their hand resting on a table. The left hand was used in one patient due to a right-sided unilateral electrode implantation. The tapping apparatus consisted of a 5 × 5 cm square force-sensitive resistor (FSR; Steadlands, Surrey, UK) and pre-amplifier (built in-house) connected to a data acquisition box (NIDAQ 6008, National Instruments), which relayed data to a laptop computer. Mattap toolbox (Elliott et al., 2009) was used to output repetitive sound pulses (700 Hz, 30 ms duration, approximately 80 decibels) from the speaker of the laptop. Although hearing loss was not objectively assessed, all patients had no difficulty in hearing and responding to the sounds. Sound pulses were output at three different rates: 0.5 Hz (once every 2 s), 1 Hz (once every 1 s), and 2 Hz (once every 0.5 s). These tapping rates will subsequently be referred to as low rate (0.5 Hz), medium rate (1 Hz), and high rate (2 Hz).

The FSR was centred under the participant’s index finger. The large size of the force plate ensured that individual taps occurred within the sensitive range of the pad. The patients were instructed to relax all of their fingers except their index finger, which they were to flex and extend at the metacarpophalangeal joint. A short plastic bar (3 cm) stood directly in front of the FSR and index finger to indicate the height to which the finger should be raised, so as to keep consistency in tap amplitude across conditions and patients. In nine out of 11 patients, we objectively quantified the tapping movements with a goniometer (Biometrics Ltd., Newport, United Kingdom) over the MCP joint on the index finger in order to relate the continuous movements to LFP activity.

One trial block consisted of 30 consecutive auditory beeps. During auditory cueing, patients were instructed to tap in time to the beat over the full 30 taps. Each run lasted either 1 min (low rate), 30 s (medium rate), or 15 s (high rate). Following each run the participant rested for at least 30 s before the start of the next run. Runs were randomized in order to avoid sequence effects such as fatigue, with a single block being defined as one run for each rate. The number of blocks differed from 2–4 depending on the patient’s level of fatigue. A control task was performed in eight of the 11 patients. In this, the sound cue only was played while the patient was instructed to be attentive to the cue but not respond; this was interleaved with the movement runs.
2.4. Analysis

Due to the fact that three patients had unilateral electrode implantation, we focused our analysis on the contralateral side to task performance. Data was also recorded from the ipsilateral STN region in the patients with bilateral implants, as addressed in the results section. Epochs were generated around each tap onset for a period of 2 s before until 2 s after. Spectrograms were generated from 5–35 Hz using a Hermite functions approach (Bayram and Baraniuk, 2000). 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 baseline period was taken as a 30 s period of rest before beginning the task for each patient. We determined the ratio of beta power (15–30 Hz) to overall power (2–100 Hz) in the baseline period for each contact in each patient. Previous studies have demonstrated that maximal beta power is a marker for accurate electrode position within the STN (Weinberger et al., 2006; Ray et al., 2008), and as such can be used during surgery to locate the STN (Chen et al., 2006). Therefore, the contact pair with the highest mean beta and as such can be used during surgery to locate the STN (Chen et al., 2006). Therefore normalization is required for adequate comparison across patients and methods such as these are commonly used to characterize local field activity in the STN during movement (Kühn et al., 2004; Andruleikaitis et al., 2007; López-Azcárate et al., 2010; Brücke et al., 2012). Even at rest, beta activity is known to have a relatively high variability (Little et al., 2012) and undergo periods of desynchronization (Park et al., 2010); however, the averaging of movement-related modulations across 60–120 epochs (depending on patient) would mitigate such random fluctuations and produce smooth time-locked traces. Once extracted, the traces were compared across the three movement frequencies. Analysis was first conducted over broadband beta activity (15–30 Hz). However, since we were also interested in relative rebound activity, we determined the frequency with the maximal rebound (FMR) within the 15–30 Hz range for each subject and condition. Similarly, we determined the frequency with the maximal suppression (FMS) for each subject and condition. For FMR and FMS, percentage change measures across the epoch were extracted for that particular frequency and averaged across subjects. We then quantified two different parameters from the broadband, FMR, and FMS beta traces for each patient: (i) maximal desynchronization, and (ii) maximal synchronization or rebound, representing the peak in beta power between movements. Goniometer traces were epoched around contact with the FSR as with LFPs. Maximum tap amplitude was taken for each patient at each movement rate. The goniometer position trace was then differentiated to obtain velocity. Goniometer values were sampled at a high rate (1000 Hz) and therefore differentiation produced smooth velocity profiles. Lastly, we calculated the relative stationary period when no movement occurred in between consecutive taps for all conditions. We accomplished this by first determining a threshold of the maximal point of the mean goniometer trace for each subject. We designated a threshold of 10% of the maximum deviation in that cycle and found the points that crossed this threshold in either direction from the maximum. This provided time points at which the finger rose over and fell under the 10% threshold, and the time difference between them served as our stationary period. This method was reliable in isolating the area in which relatively little movement occurred. All statistical analyses were conducted using SPSS v12 (SPSS Inc., Chicago, IL, USA), except significance levels for spectrograms, which were generated using one-sample t-tests in MATLAB. Percentage change values of beta were normally distributed as confirmed by the one-sample Kolmogorov–Smirnov test. One-way repeated measures analysis of variance (ANOVA) was conducted over the three movement rates to determine differences between the tapping rates. Mauchley’s test was used to assess sphericity of the data, and when significant deviations from sphericity

**Table 1**

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Disease duration (years)</th>
<th>Predominant symptoms</th>
<th>Levodopa equivalent daily dose at surgery (mg)$^a$</th>
<th>Pre-op UPDRS$^b$ off-meds</th>
<th>Pre-op UPDRS on-meds</th>
<th>Most affected side</th>
<th>Unilateral or bilateral electrode</th>
<th>Contra-lateral contact pair with highest beta</th>
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<td>17</td>
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<td>Right</td>
<td>Bilateral</td>
<td>12</td>
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<td>17</td>
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<td>17</td>
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$^a$ As per Tomlinson et al., 2010.

$^b$ Unified Parkinson’s Disease Rating Scale (Fahn and Elton, 1987).
occurred Greenhouse-Geisser correction was applied. Post hoc paired t-tests between conditions were Bonferroni corrected and thus we maintained our significant p threshold at 0.05. Furthermore, one-sample t-tests were used to assess changes in power from baseline for each tapping condition, with significant \( p < 0.05 \). Correlation between log of stationary period time and beta rebound was conducted using Pearson’s product moment correlation.

3. Results

3.1. Selected contacts

The contact pair demonstrating the highest beta power during the rest period was selected for analysis (see Table 1). In all patients there was a clear maximum at one of the three contact pairs on the side contralateral to movement. The mean reduction in beta power between this contact and the mean of the remaining two contacts was \(-51.5 \pm 15.3\%\) (standard error of the mean (SEM)). Furthermore, recordings in nine out of 11 patients exhibited polarity reversal across two of the bipolar contact pairs on each side, and all contacts selected for analysis were among those with polarity reversal. Polarity reversals suggest that the potential recorded is being generated local to the contacts (Kühn et al., 2004).

3.2. Behavioral data

Mean goniometer amplitude did not differ between conditions \((F_{2,20} = 0.36, p = 0.71)\). However, mean velocity was different across conditions \((F_{2,20} = 4.4, p = 0.03)\). Post hoc t-tests revealed no significant velocity difference between low and medium rate tapping \((t_{10} = -0.86, p = 0.41)\), or between medium and high \((t_{10} = -1.92, p = 0.091)\). However, the high rate condition had significantly higher velocity than low rate \((t_{10} = -2.6, p = 0.032)\). Therefore, patients maintained the same size of tap throughout the three movement rates, but had unexpectedly higher velocities during the high rate movement compared to the low rate.

We also calculated the timing of taps (impact with the force transducer) with respect to the onset of the auditory cue. An ANOVA showed that tap asynchrony differed according to tapping rate \((F_{2,20} = 15.47, p = 0.003)\), and this was due to the high rate condition having an earlier tap with respect to the cue (\(-24.8 \pm 17.2\) ms) as compared with low rate \((32.9 \pm 15.3\) ms, \(t_{10} = -3.1, p = 0.021)\), and medium rate \((29.9 \pm 14.6\) ms, \(t_{10} = -3.67, p = 0.005)\).

3.3. General pattern of tapping-related change in oscillatory activity

An example of recorded LFPs and concurrent goniometer movements is shown in Fig. 1. Fig. 2A demonstrates the normalized spectrograms constructed from the LFPs for frequencies from 5–35 Hz for all three rates of tapping, epoched from 2 s before to 2 s after the tap. Two features can be observed. Firstly, there was a suppression of beta power (desynchronization) before and after the onset of the tap for all conditions. Secondly at the low and, partially, at the medium tapping rate, periods between taps were punctuated with bursts of relative rebound activity (synchronization) in the beta band. However, the latter never become significantly different to baseline (Fig. 2B).

3.4. Time course of spectral changes in the beta range

Percentage change in power was averaged across the beta range (15–30 Hz) and is displayed in Fig. 3A for all three rates of tapping on the contralateral side. At all three rates, a similar maximal suppression of beta of about 35–40% occurred. However, whereas in the low and medium rates beta resynchronized to near baseline levels, beta in the high tapping rate remained suppressed throughout the task.

We explored the responses in the beta band still further by selecting, to the nearest Hz, the frequency of maximal rebound (FMR) power between taps, and the frequency with the maximal suppression (FMS) for each subject. The average FMR was 17.3 ± 1.4 Hz for low, 20.9 ± 1.6 Hz for medium, and 20.0 ± 1.3 Hz for high rate tapping. FMS was 24.5 ± 0.9 Hz for low, 25.9 ± 0.8 Hz for medium, and 23.7 ± 1.1 Hz for high rate tapping. Thus the frequency of maximal suppression was higher than that of maximal rebound in all three conditions \((p < 0.05)\). The average traces for these selected frequencies are plotted in Fig. 4 along with the simultaneously recorded mean goniometer trace. FMS showed a clear tap-related suppression of activity, with a resynchronization after the tap that remained below baseline for all conditions. This relative synchronization was diminished in the high rate condition. Overall, beta activity was continuously suppressed in the FMS, regardless of condition. In contrast, the FMR showed rebound activity with low and medium tapping rates, with increases in power above baseline. In low and medium-rate tapping, rebound above baseline coincided with periods of no or minimal movement, whereas rebound activity during high tapping was effectively absent.

3.5. Quantitative comparison of beta changes between tasks

Task related changes in beta power were quantitatively assessed (Fig. 5). Maximal desynchronization (Fig. 5A) was significantly different to baseline for all beta power measures and tapping rates \((p < 0.05)\). However, there were no differences in maximal desynchronization between tapping rates in either broadband beta \((F_{2,20} = 1.39, p = 0.27)\), FMR \((F_{2,20} = 0.036, p = 0.965)\) or FMS \((F_{2,20} = 2.96, p = 0.075)\).

For broadband beta power, maximal synchronization (Fig. 5B) was not significantly different from baseline during low and medium tapping, but was below baseline during tapping at the high rate \((t_{10} = -3.19, p = 0.01)\). There were also differences between tapping rates \((F_{2,20} = 8.05, p = 0.01)\). Post hoc tests revealed that maximal synchronization was less during high compared to both low \((t_{10} = 3.06, p = 0.036)\) and medium \((t_{10} = 3.15, p = 0.031)\) tapping rates.

Similarly, FMS only differed from, and was lower than, baseline at the high tapping rate \((t_{10} = -4.29, p = 0.002)\). There were also differences in FMS between tapping rates \((F_{2,20} = 15.75,
accounted for by a significantly reduced maximal synchronization during high compared to low ($t_{10} = 4.74, p = 0.002$) and a trend between high and medium ($t_{10} = 2.60, p = 0.08$) tapping rates. Maximal synchronization was also reduced during medium compared to low-rate tapping ($t_{10} = 3.49, p = 0.017$).

Lastly, FMR displayed maximal synchronization significantly above baseline for low and medium tapping rates (low: $t_{10} = 3.61, p = 0.005$, medium: $t_{10} = 4.02, p = 0.002$), but there was no difference from baseline in the high rate. There were also significant differences across conditions ($F_{2,20} = 4.90, p = 0.039$), between low and high ($t_{10} = 2.83, p = 0.049$), and medium and high ($t_{10} = 3.19, p = 0.024$) tapping rates.

In summary, the results showed similar maximal desynchronization during tapping rates, but a consistently reduced maximal synchronization during tapping at the high rate.
3.6. Relationship between stationary period and beta rebound

The timing of the strong FMR rebound in relation to the goniometer (Fig. 4) suggested that this effect may be related to the relatively stationary period between taps during which minimal movement occurred. To investigate this possibility we calculated the average stationary period for each tapping rate in each subject and plotted the log of these values against the maximal beta rebound (Fig. 6A). The analysis demonstrated that the lack of rebound during tapping at high rates was associated with a reduced stationary period. In contrast, tapping at medium and low rates had longer stationary periods and involved maximal synchronizations above baseline. Taking all conditions and subjects together (Fig. 6A), there was a significant correlation between log stationary period duration and rebound size ($R = 0.55, p = 0.029$).

Fig. 6B shows an example of a similar relationship within a condition (medium tapping rate) in a single patient.

3.7. Ipsilateral side

Although we had fewer recordings from the ipsilateral STN ($n = 8$), we observed a similar task-related beta modulation as the contralateral side (Fig. 3B). There was no difference in maximal desynchronization between tapping rates ($F_{2,14} = 3.3, p = 0.07$), however there was a significant difference for maximal synchronization ($F_{2,14} = 8.4, p = 0.004$). Post hoc tests revealed significant differences between low and high rate ($t_7 = 4.1, p = 0.014$), medium and high rate ($t_7, p = 3.7, p = 0.023$), but not low and medium rate ($t_7 = 0.3, p = 0.8$). Although among the eight patients with ipsilateral recordings there was overall less mean suppression of beta on the ipsilateral side ($47.5 ± 4.2\%$ ipsilateral versus $48.0 ± 4.4\%$ contralateral), there was no significant difference in the maximal desynchronization (side: $F_{1,7} = 1.8, p = 0.22$; rate: $F_{2,14} = 2.9, p = 0.089$; interaction: $F_{2,14} = 0.46, p = 0.64$) or maximal synchronization (side: $F_{1,7} = 0.46, p = 0.84$; rate: $F_{2,14} = 19.1, p < 0.0001$; interaction: $F_{2,14} = 0.20, p = 0.72$) between sides.

3.8. Auditory cues

To ensure that the auditory cues alone were not an important contributor to the changes in beta activity observed, we recorded activity in the STN in eight of the 11 patients during trains of auditory cues while participants were at rest, but attending to the cue. Runs of auditory cues were interleaved with tapping runs. Beta activity showed a similar pattern of modulation as in trials with tapping, but the amplitude of the modulation was greatly attenuated and did not differ between rates of auditory pacing. Thus there were no effects of sound rate in separate ANOVAs of maximal desynchronization ($F_{2,14} = 0.044, p = 0.96$) and maximal synchronization ($F_{2,14} = 2.48, p = 0.11$) during auditory pacing by itself. In

Fig. 4. Time-evolving profile of selected frequencies. Frequency of maximal suppression (FMS) is shown for low tapping rate (A, light green), medium tapping rate (B, light blue), and high tapping rate (C, light red), averaged across all patients on contralateral side. Power is always below baseline for FMS and shares a similar minimum of about $–50\%$ for all frequencies. Frequency of maximal rebound (FMR) is shown for low tapping rate (A, dark green), medium tapping rate (B, dark blue), and high tapping rate (C, dark red). Here, a prominent rebound between taps is observed in low and medium conditions, but is absent in the high rate condition. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 5. Quantitative analysis of power changes on contralateral side during tapping for low rate (L, green), medium rate (M, blue), and high rate (H, red). There is similar maximal desynchronization across tap rates (A), but diminished maximal synchronization (B) during tapping at the high rate. Significant differences from baseline taken as $p < 0.05$, and differences between conditions as $p < 0.05$, Bonferroni corrected. *$p = 0.08$. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)
addition, maximal desynchronization during auditory cues was $-20.3 \pm 3.8\%$ compared to $-48.1 \pm 5.7\%$ during paced tapping in the same subjects, averaged over all rates ($t_9 = 6.4, p < 0.0001$).

4. Discussion

We observed two main task-dependent patterns of modulation in the beta-frequency band. First is a desynchronization which was greatest at around 24 Hz, seen around the time of tapping, with an amplitude of desynchronization that was comparable across all tapping rates. Second is a relative rebound in synchronization which was greatest at around 20 Hz and which was only present for low and medium rates of tapping, coinciding with the time between taps when there was minimal movement of the finger. The defined separation between tapping rates captures major changes in beta activity but likely obscures a phenomenon that emerges gradually as movement rate increases. Nevertheless, the overall pattern of activity suggested a persistent beta desynchronization of similar depth across tapping rates, and superimposed on this, a beta rebound synchronization only when tapping rates were low enough to contain appreciable periods of minimal movement. Although we focused on activity contralateral to the tapping hand, ipsilateral activity also displayed the same modulation, which is in line with previous reports demonstrating comparable beta reactivity in both hemispheres (Doyle et al., 2005; Androulidakis et al., 2007; Hebb et al., 2012).

These two components of beta-band modulation may be related to the features of discrete phasic movements. Firstly, it would seem reasonable to relate the desynchronization, which reaches a maximal value at the time of tapping, with the desynchronization that precedes and occurs during phasic movements. An important finding of this study is that the absolute level of beta suppression was similar despite varying velocities between the tapping tasks, suggesting that it is not bound to any particular kinematic variable of the movement. The finding adds to the literature that movement related afferent feedback and sensorimotor recalibration processes of active immobilization after movement or the termination of a motor plan (Salmelin et al., 1995; Alegre et al., 2004; Erbil and Ungan, 2007), analogous to the increases in beta activity seen when a motor act must be stopped or inhibited (Zhang et al., 2008; Ray et al., 2012). Alternatively, it has been thought to reflect movement related afferent feed-back and sensorimotor recalibration following a period of change (Cassim et al., 2000). The dependence of the relative rebound upon the duration of the static period in our study would argue against a simple all-or-nothing termination signal, although we cannot rule out a possible contribution from sensory re-afference.

There are three potential, but not mutually exclusive, explanations for the persistently suppressed beta activity found in the high-rate tapping condition. Firstly, as has been argued elsewhere (Jenkinson and Brown, 2011), a drop in beta levels could enable the predictive resourcing of motor actions. A major prediction of this hypothesis is that suppression of beta activity will be sustained under conditions of sequential movement, as the likelihood of imminent movement after each successive component is high. Here, the persistence of beta suppression for the entire sequence of movements at the higher rate of tapping, as well as the anticipatory nature of tapping at the high rate whereby taps precede the auditory cues by about 25 ms, is consistent with the predictive and hence persistent suppression of beta activity. Secondly, the sustained suppression might represent a dynamic shift from discrete to continuous movement which is known to occur at around 2 Hz (Huys et al., 2008). The presence of a beta rebound with tapping at frequencies <2 Hz, and its absence during tapping at frequencies >2 Hz has been previously reported at the level of the cortex – the disappearance of the rebound at higher tapping rates also led to a sustained suppression of beta activity (Toma et al., 2002).
These and other authors have argued that finger taps performed at <2 Hz are programmed as independent movements timed to occur with the auditory cue, whereas tapping at >2 Hz becomes anticipatory or even syncopated, and is programmed as a continuous rhythmic movement (Mayville et al., 1999; Toma et al., 2002). Indeed, a distinction has been made between an ‘automatic’ timing system controlling sub-second movement intervals and a ‘cognitively controlled’ system involved in the production of supra-second intervals and discrete movements (Lewis and Miall, 2003). The continuous reduction of beta activity observed here during high-rate tapping may reduce the resourcing required for sequential movements and contribute to the perceived automaticity under such conditions. This thinking is in line with the possible role of the basal ganglia in controlling the automatic output of entire behavioral sequences or representations (Graybiel, 1998; Jin and Costa, 2010). Lastly, and perhaps the most parsimonious explanation, is that during high rate tapping the beta rebound is partly canceled out by the beta desynchronization of the next tap. Nevertheless, this simple effect could serve to maintain a consistent desynchronization and further promote continuous or sequential movement.

There are some limitations to the present study. Because our recordings were made in patients, any attempts to study normal physiology are necessarily confounded by the pathological state of PD. Dopaminergic therapy is known to suppress the heightened pathological beta activity in PD (Brown and Williams, 2005; Giannicola et al., 2010; Kühn et al., 2006a,b; Levy et al., 2002; Priori et al., 2004). Although DBS is also thought to suppress beta activity while improving symptoms (Eusebio et al., 2011; Rosa et al., 2011), this study was not designed to record activity during STN stimulation. Thus our results may still have been influenced by the presence of motor impairment and pathological changes in the basal ganglia. Although the usual approach to addressing the role of pathology is to contrast OFF and ON medication recordings, the primary goal of our study was to examine the role of oscillations in the subthalamic nucleus during a tapping task under near-physiological conditions. Thus, we opted to study patients on medication because: (1) the task would be fatiguing (at high tapping frequencies) for patients off their anti-Parkinson medication, (2) differences in performance would confound on–off comparisons, and (3) dopaminergic treatment would facilitate a motor state as close to normal as possible. In addition the changes shown here are in line with studies of cortical activity in normal subjects (Toma et al., 2002), supporting a physiological, rather than pathological, basis to the observed activity. It is also important to stress that the evidence suggested our LFP signals were locally generated and were very unlikely to have represented volume conduction from the cortex.

We should also acknowledge that auditory pacing alone resulted in some rhythmic modulation of beta activity in the STN, although this was less than half of that occurring during paced finger tapping. It is possible that the modulation related to imagined movements as auditory pacing was not specifically performed before tapping blocks, and motor imagery is known to induce substantial beta desynchronization in the STN (Kühn et al., 2006a,b). However, the basal ganglia have been implicated in timing and sequence learning (Lehéricy et al., 2005; Teki et al., 2011) and it is conceivable that the rhythmic modulation of beta activity with auditory pacing is physiological (Fujikawa et al., 2012). As such, it may even underlie some of the performance benefits of external rhythmic cuing (Thaut et al., 1996; Baker et al., 2008; Rochester et al., 2009) through the promotion of additional beta suppression at the time of taps.

In conclusion, the beta oscillations recorded in the region of the subthalamic nucleus in medicated PD patients are modulated by finger tapping. The effects can be considered as twofold. First, beta desynchronization becomes sustained for higher rates of tapping, in line with recent theories that suggest beta desynchronization relates to the prospective resourcing of action (Jenkinson and Brown, 2011). Thus beta desynchronization relates to the global sequence of movements rather than individual movement during high rate tapping. Second is a relative beta rebound the size of which depends in a graded fashion on the duration of static periods between taps. The latter would seem to exclude a function as an all-or-none termination signal at the end of movement, although a role in sensorimotor recalibration remains a possibility. Together these different forms of beta modulation may facilitate the motor performance of tapping, as suggested by the fact that finger tapping is characteristically compromised when PD patients are withdrawn from their anti-dopaminergic medication, with beta activity exaggerated and its reactivity diminished (Doyle et al., 2005).

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