The patient was a 54 year old woman with 14 year history of parkinsonian dyskinesias. We recorded local field potentials (LFPs) in a patient with Parkinson’s disease and left surgery induced dyskinesias with double, bilateral deep brain stimulation electrode implants in the subthalamic nucleus (STN) and the globus pallidus internus (GPI). Synchronisation was studied through coherence analysis. In the nuclei contralateral to the dystonic side of the body there was decreased STN-GPI coherence in the high beta range (20–30 Hz) and an enhanced coherence at low frequencies (<10 Hz). Despite the possible limitations arising from single-case observations, our findings suggest that parkinsonian dyskinesias are related to altered synchronisation between different structures of the basal ganglia. Firing abnormalities within individual basal ganglia nuclei are probably not enough to account for the complex balance between hypokinetic and hyperkinetic symptoms in human parkinsonian dyskinesias and altered interactions between nuclei should also be considered.

**METHODS**

**The patient**
The patient was a 54 year old woman with 14 year history of rigid-akinetiParkinson’s disease. The onset of the disease was on the left side of the body. She was on levodopa+dopamine agonists therapy for a daily dose of 1500 mg levodopa equivalents. She had a previous bilateral GPI DBS implant that was poorly effective and she therefore received a bilateral STN DBS implant after fulfilling specific inclusion criteria. Soon after implantation of the DBS electrodes in the STN she developed dyskinesias mainly at the left upper limb, which were worsened by levodopa. The phenomenology of dyskinesias resembled involuntary movements triggered by levodopa before surgery. On the right side there was no dyskinesia. Despite these transient dyskinesias, which lasted less than a week, the DBS had a good long term outcome. Before the STN surgery, the patient motor performance measured by Unified Parkinson’s Disease Rating Scale (UPDRS) part III was 62 “off” therapy and 23.5 “on” therapy. At 1 year after surgery the UPDRS III “off” medication “on” STN stimulation was 19. Dyskinesias and fluctuations (UPDRS IV part A and B, respectively) were reduced from 7 and 7 before the surgery to 1 and 2, respectively, at 1 year after surgery. The patient was studied after informed consent and local ethical committee approval.

**Electrode localisation**
The pre-operative CT-MRI targeting of the STN, intra-operative clinical and neurophysiological procedures, post-operative CT-MRI electrode confirmation, and clinical evaluation of efficacy are described in detail elsewhere. As in our previous work, the STN electrodes were verified to be within (or close to) the nuclei. Using the same imaging techniques, the distal contacts of the pallidal electrodes were confirmed to be within the GPI. Postoperative neuroimaging ruled out significant asymmetries of electrode positions and/or of lesion effect induced by the surgical procedures.

**Postoperative recordings**
The patient was comfortably seated in an armchair. LFPs were recorded from the STN and GPI ipsilateral electrodes (3389 Medtronic, contacts 0-1 and 0-2, respectively; Medtronic, Minneapolis, MN, USA) after overnight withdrawal of dopaminergic medication. The patient was asked to maintain a totally relaxed position, but she had spontaneous dyskinetic jerks on the left side of the body almost continuously during the recording session. As a control, LFPs were also recorded on the left side of the brain at rest and during voluntary contractions of right forearm muscles. Signals were preamplified, differentially amplified, and filtered (2–1000 Hz) through a CED 1902 amplifier (Cambridge Electronic Design, Cambridge, UK). A/D converted (sampling rate 2500 Hz) through a CED 1401 interface (Cambridge Electronic Design), on-line analysed on a personal computer, and stored using CED Signal software.

**Abbreviations:** DBS, deep brain stimulation; GPI, globus pallidus internus; LFPs, local field potentials; STN, subthalamic nucleus; UPDRS, Unified Parkinson’s Disease Rating Scale.
averaged to form the cross-spectrum (PSTN-GPi). The coher-
Fourier transforms of the sections of the two signals were

The coher-

The pattern of STN and GPI autospectra was dominated by
activity at frequencies <10 Hz (fig 1A and B). Ipsilaterally to
the dyskinetic side of the body at rest (fig 1C, continuous
line), the STN and GPI showed virtually no coherence at low
frequencies but were well synchronised at high-beta fre-

RESULTS

The synchronisation between the nuclei was analysed
through coherence analysis. The coherence, which is a
function of frequency with values between 0 and 1 that
indicate how well two signals match at each frequency, was
estimated from the LFPs of STN and GPI on ~160 s long data
segments at rest using Fourier analysis (Matlab routine
"cohere"). Signals were divided into 195 sections of 2048
samples, with no overlap; each section was detrended and
windowed by a Hanning window; the magnitude squared of
the discrete Fourier transforms of the sections of the two
signals was averaged to estimate the autospectra of the
two nuclei (PSTN and PGPi). The products of the discrete
Fourier transforms of the sections of the two signals were
averaged to form the cross-spectrum (PSTN-GPi). The coherence
C_{STN-GPi} was given by

\begin{equation}
C_{STN-GPi} = \frac{\text{abs}(P_{STN-GPi}) \cdot 2}{P_{STN}^2 + P_{GPI}^2}
\end{equation}

The recordings and the analyses were conducted separately on both sides of the brain.

DISCUSSION

In our patient a transient lesion effect due to electrode
introduction lowered the threshold for drug induced dys-
kinesias. In the nuclei contralateral to the dyskinetic side of
the body (in comparison with the nuclei contralateral to the
parkinsonian non-dyskinetic side of the body), there was a
reduced STN-GPi synchronisation of LFP oscillations at high-

...
was not anaesthetised and was drug free for several hours. Moreover, the pattern of STN-GPi synchronisation contralateral to the non-dyskinetic side was consistent with the STN-GPi synchronisation described in parkinsonian patients.11

Beta LFP oscillations are pathologically high in Parkinson’s disease both in the GPi12 14 15 and the STN.11 15 17 and the two nuclei are synchronised at these frequencies.13 Levodopa reduces beta oscillations within and between nuclei.11 13 14 15 In patients with dystonia, GPi beta oscillations are reduced even more than in parkinsonian patients after levodopa.10 Here we add a further piece to this picture, showing that even without levodopa administration STN-GPi high-beta synchronisation is lower—but apparently wider—in parkinsonian dyskinesias compared to non-dyskinetic Parkinson’s disease. This finding is in agreement with the antikineti

cron interpretation of beta oscillations.12 In addition, the different patterns of STN-GPi synchronisation we observed at high-beta and low-beta frequencies support the hypothesis that two different rhythms could operate in the beta band.12 14 15

Low-frequency LFP oscillations in Parkinson’s disease increase after dopaminergic medication both in the STN19 and the GPi.12 Dopaminergic medication does not induce low-frequency STN-GPi synchronisation.11 In patients with dystonia, GPi low-frequency oscillations are increased more than in parkinsonian patients after levodopa.15 Here we show that, differently from treated or untreated Parkinson’s disease, parkinsonian dyskinesias can be characterised by extremely strong STN-GPi low-frequency synchronisation. It should be noted that changes in coherence at frequencies <10 Hz might potentially include movement related artefacts,17 20 but the presence of synchronisation only in the dyskinetic nuclei makes this possibility unlikely. Hence, although several other possible factors might have contributed—at least partly—to coherence asymmetry, we believe that STN-GPi low-frequency synchronisation reflects a specific pathophysiological feature of parkinsonian dyskinesias.

According to the classical basal ganglia model,25 hyperkinetic symptoms arise from pathologically low firing rates in the STN and GPi, whereas hypokinetic symptoms arise from pathologically high firing rates in the STN and GPi. Thus, the coexistence of hypokinetic and hyperkinetic symptoms, as in our patient, leads the classical model to a paradox. Firing abnormalities within individual basal ganglia nuclei are not enough to account for the compound phenomenology of parkinsonian symptoms and more complex interactions between nuclei should be considered. As a possible solution of the paradox, our observations suggest that parkinsonian dyskinesias could arise not only from abnormal firing patterns within the GPi and the STN,11 but also from an altered synchronisation between these and, possibly, other basal ganglia nuclei.

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Altered subthalamo-pallidal synchronisation in parkinsonian dyskinesias

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