# First steps towards adaptive deep brain stimulation in Parkinson's disease

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*Introduction:* Deep brain stimulation (DBS) is used to treat Parkinson's disease (PD), when medical therapies are not efficient enough [1]. DBS requires the implantation of stimulation electrodes reaching into deep brain areas, commonly into the subthalamic nucleus (STN) that is one of the relay of the extrapyramidal circuit. Electrical pulses are sent on a fixed regular pace. Despite the proven efficacy of DBS on rigidity, bradykinesia and tremor, the principle clinical features of PD, its underlying principles and mechanisms are still not completely clear. Moreover, stimulation side effects such as speech problems, heat or numbness sensations, and dyskinesia can be caused by the stimulation. Current DBS systems are still in their early stages and can be compared to the early generation of heart pacemaker systems. Stimulation parameters (amplitude, frequencies or pulse-width) are typically fixed shortly after the implantation and remain unchanged. Altogether, the current practice –providing continuous stimulation with fixed parameters– may be suboptimal since it does not take into account any symptoms fluctuations. Adaptive DBS, where stimulation is triggered by certain neurophysiological markers, has emerged as an improvement over conventional systems. Such systems would reduce the amount of stimulation provided, thus extending battery life and potentially reducing side effects [2]. An adaptive DBS should be able to record the local field activity via the same electrodes as used for stimulation, recognize pathological brain activity, and finally drive the stimulation based on the specific needs of the patient [3]. Here we present our initial results on the development of a closed-loop adaptive DBS system.

*Methods and Results:* We recorded brain activity from the subthalamic nucleus via the deep electrodes while stimulating simultaneously. This was made possible because of the design of a custom-made system that allowed filtering out stimulation artifacts from the underlying brain signals. Tests of the closed-loop adaptive DBS have been performed in 3 PD patients. The protocol consisted of three stimulation conditions over 3 days: continuous (normal), adaptive, and no stimulation, whereby each condition was 20 min long. A neurologist evaluated the clinical assessments of the motor effect via the Unified Parkinson's disease rating scale (UPDRS) before, during, and after each condition. In the no-stimulation condition, we found a pathological synchronization of the beta band in both hemispheres and a strong coherence between both hemispheres in the high-beta and low-gamma band (Fig. 1a). Therefore, detection of increased (over the 50 percentile) beta band activity (22-28 Hz) was used to trigger the stimulation in the adaptive condition. During the adaptive condition, the stimulation time was reduced along the recording time (Fig. 1b), while the UPDRS improved over the recording days (Fig. 1c).
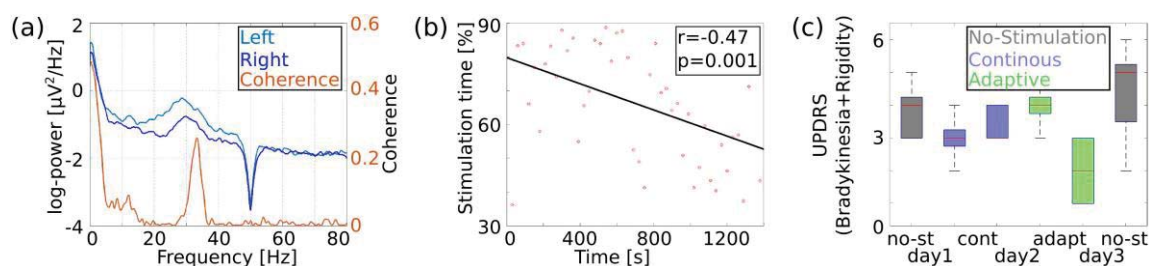


**Figure 1.**   *Exemplarily results of one subject: (a) Log power of left and right hemisphere during no-stimulation condition and their coherence. (b) Stimulation amount in % over the recording time. (c) UPDRS results for all conditions over the experiment.*

*Discussion:* Our initial results demonstrate that we can successfully record local field potentials, detect the physiological biomarkers of motor symptoms in PD patients and adaptively trigger the DBS. The subject-specific closed loop stimulation yielded similar efficiency to conventional continuous DBS. Nevertheless, more subjects and tests over longer periods of time are necessary to confirm these preliminary findings.

*Significance:* Closed-loop adaptive DBS is possible which opens up strategies to better tune the stimulation leading to increased battery life and better control over symptom variations.

*References:*
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