# Biomarkers for Deep Brain Stimulation

**Title of project or programme**

Title of PI Biomarkers for Deep Brain Stimulation

**Principal Investigators of project/programme grant**

| Title | Forname | Surname | Institution | Country |
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| Professor | Peter | Brown | University of Oxford | UK |

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|---|---|
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**Country**

- United Kingdom

**Source of funding information**
**Total sum awarded (Euro)**

1760962.23

**Start date of award**

01-01-2011

**Total duration of award in months**

48

**The project/programme is most relevant to**

- Parkinson's disease

**Keywords**
**Research abstract in English**

Parkinson's disease (PD) and dystonia are two of the most common movement disorders. Recently there has been immense interest in the neurosurgical treatment of these debilitating disorders through deep brain stimulation (DBS). However, the cost of DBS, its partial efficacy and side-effects mean that there is still a need to improve current therapy. One major problem is that present neurostimulators only provide continuous and fixed 'open-loop' stimulation which increases side effects and habituation, while reducing battery life. Our growing understanding of how different patterns of activity in the basal ganglia (BG) are associated with different symptoms raises the possibility of improving DBS through closed loop stimulation. In closed-loop mode, stimulation is titrated using a biomarker to determine when and how much stimulation is necessary. Here we will extend our studies of BG local field potential (LFP) activities in patients undergoing neurosurgery in

order to clarify the pathophysiology of PD and dystonia and thereby to identify local biomarkers suitable for closed loop stimulation regimes. To this end we will refine our 'noisy signal' model of BG disease, based on the hypothesis that it is the balance between synchronised activities indexed in the LFP, rather than one activity per se, which determines motor state. Our intention is to equate these diverse changes with psychophysical processes, and thereby formulate a model that links various levels of observation, has heuristic value and proffers more sophisticated biomarkers. The reliability and mechanistic importance of these biomarkers will then be assessed through a series of correlational and interventional experiments in patients. Establishing which biomarkers are causally linked to symptoms is critical in both understanding disease processes and in identifying legitimate targets for emerging smart stimulation approaches. In addition, we will define how current DBS works. Specifically we will test the hypothesis that DBS acts as a high frequency dither injection similar to that used to quench low frequency oscillations in nonlinear feedback control loops. Our intention is to model this process in the BG, which will in turn allow the identification of the most effective stimulation regime in individual patients. Finally, we will optimise algorithms for closed-loop stimulation based on LFP features, and prove closed loop stimulation can be effective in a double-blind cross-over trial of closed-loop versus current open-loop DBS in PD. Understanding gained in this research program will lay the foundation for improved DBS therapy for motor and other disorders.

**Lay Summary**
**In which category does this research fall?**

- Clinical research