Temporally patterned closed-loop stimulation for therapy of brain disorders

https://neurodegenerationresearch.eu/survey/temporally-patterned-closed-loop-stimulation-for-therapy-of-brain-disorders/

Principal Investigators

Professor P Brown

Institution

University of Oxford

Contact information of lead PI
Country

United Kingdom

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Temporally patterned closed-loop stimulation for therapy of brain disorders

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MRC

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The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords
Research Abstract
Parkinson’s disease (PD) and Tremor can be treated using continuous high-frequency deep brain stimulation (DBS) of basal ganglia or thalamus. Both diseases are characterised by neuronal synchrony in the cortex, basal ganglia and thalamus that occurs concurrently with symptoms. In tremor, this neuronal synchronisation occurs at the same frequency as the tremulous limb. In PD, there is mounting evidence for elevated neural synchrony in the beta

(~20 Hz) frequency band, and this correlates with severity of akinesia and rigidity. Our goal is to utilise this pathological activity to deliver a closed-loop brain stimulation framework that will significantly improve the treatment of these diseases. Although novel, these treatments will be tractable, based as they are on electrical stimulation that, even in its rawest forms, has already proven beneficial to tens of thousands of patients. To this end, we will develop three closed-loop strategies. Firstly, and most simply, we will limit stimulation to those periods during which pathological activity is elevated to give adaptive high frequency DBS (aHF DBS). We have shown that acute aHF DBS affords improved therapeutic benefit in PD patients as compared to continuous stimulation. We will continue to develop this strategy in both PD and tremor patients. Secondly, we will deliver stimulation locked to a particular point (phase) in the cycle of the underlying pathological activity to give adaptive phase locked DBS (aPL DBS). As oscillatory activity seems likely to be mechanistically important in driving symptomatology in PD and tremor, aPL DBS may be more specific and selective than conventional DBS by interacting directly with the pathological activity. We have demonstrated the potential efficacy of this strategy in tremor and will continue this work in patients. In PD, we will develop this methodology in the rat model and test the most successful protocols on patients. The pathological oscillatory activity in these conditions is likely an emergent property of altered functional connectivity, arising across specific circuit components as a consequence of chronic disturbances in neurotransmission. To this end, for our third strategy will use spike-triggered stimulation to progressively and selectively weaken or strengthen key connectivities over time to rebalance networks and ameliorate disease related impairment. These experiments will be carried out using animal models, to allow flexibility in stimulation protocols and the examination of structural changes in connectivity. Our approaches are intended to be generic and applicable to other brain targets and diseases, and eventually implementable by alternative, more selective forms of stimulation, when these become suitable for use in patients.

Lay Summary
Further information available at:

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Investments > €500k

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Parkinson's disease & PD-related disorders

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