Exploration of the Generation and Suppression of Pathological Oscillatory Neural Activity in a Model of Deep Brain Stimulation in Parkinson's disease (BINI 2015)

This study explores possible mechanisms for the generation of pathological neural oscillatory activity associated with Parkinson's disease in theoretical models. The suppression of the model oscillations with high frequency stimulation, analogous to the use of deep brain stimulation (DBS) in the treatment of Parkinson's disease, is also examined. The relationship between oscillation amplitude and the amplitude of the applied stimulation is explored theoretically and then compared with experimental data recorded in patients. The suppression of beta frequency (13-30Hz) local field potential oscillations with the application of DBS has been shown to occur in parallel with an improvement in motor symptoms of the disease, particularly bradykinesia and rigidity, although the exact mode of action through which this occurs is not clearly understood. The models, each comprised of two interconnected nuclei, are used to represent pathological synchronous oscillatory activity within the cortico-basal ganglia network in Parkinson's disease. Each nucleus is comprised of a nonlinear sigmoidal element in series with a second order transfer function. The high frequency stimulation was applied additively at the input to one nucleus. The relationship between stimulation amplitude and the amplitude of oscillatory activity in the models was explored theoretically and through simulation. The parameters of one of the models were optimized to fit the theoretical results to data recorded via implanted stimulation electrodes from the STN of four Parkinsonian patients at the University of Oxford and the University of London. The local field potential was recorded as the amplitude of applied stimulation was increased. The theoretical model of pathological beta band neural activity predicts a reduction in oscillation amplitude as the amplitude of the applied stimulation is increased. This result is in agreement with that observed in the recorded patient data. The models presented in this study examine some possible mechanisms through which oscillatory activity at frequencies associated with the pathology of Parkinson's disease may emerge. The simplified model used in this study to examine the relationship between oscillatory neural activity associated with Parkinson's disease and its suppression by DBS can be optimized to fit clinically recorded data on a patient by patient basis, conceivably representing the pathological state of an individual patient. The agreement observed between the predictions of the model and the local field potential data recorded from patients, suggests that the model captures key features of the cortico-basal ganglia system, and offers the possibility that the model could be translated to a clinical environment to aid in DBS parameter selection.