PARKINSONIAN PATTERN TRANSDUCTION BY GPI

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Abstract

It is hypothesised that Parkinson's disease is explained as a change in the pattern of synchronisation of discharges between neurons within the subthalamo-pallidal-thalamo-cortical circuit. By simulating a single GPi neuron receiving non-synchronous and oscillatory inputs the conditions required for the generation of normal and Parkinsonian patterns are determined.

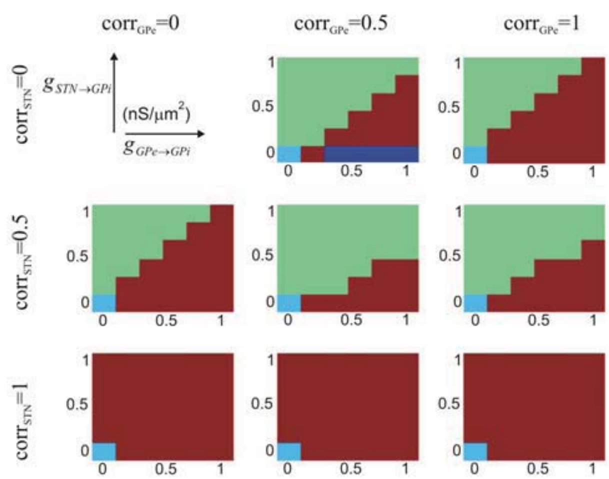
1 Introduction

Current hypotheses of basal ganglia (BG) action are based on the distinction of a direct and indirect pathway both projecting to the internal part of the globus pallidus (GPi), the output nucleus of the basal ganglia. The two pathways have reciprocal actions on movement and are inversely affected by dopaminergic denervation (i.e. Parkinson's disease (PD)) resulting in an imbalance between the two pathways and changes in neuronal firing patterns. From experimental data it was found that in PD (and MPTP treated primates) the neurons of the BG show a tendency toward bursting and abnormal synchronisation [1] with neurons collaborating in clusters [2,3]. Principal modes of synchronised activity can be distinguished: <10 Hz, 11-30 Hz, and >60 Hz, the first two are associated with anti-kinetic (Parkinsonian) symptoms; the third is expected to be pro-kinetic, ameliorating the effects of Parkinson's disease [1]. The GPe-STN loop is considered to be the central pacemaker of the oscillatory behaviour that via GPi causes rhythmic thalamic activity [4]. However, the number of neurons of either STN or GPe involved in each cluster, the connections within and between clusters and how they connect to GPi is not known. Therefore, irrespective of these connections, GPi activity is investigated for a range of inputs from GPe and STN.

2 Method

The activity patterns generated by a single GPi neuron are simulated using a conductance-based model [5]. Input from GPe and STN is modelled in both cases as a constant activity level on top of which a sinusoidal input may be present representing synchronisation within the respective nucleus with a certain correlation coefficient 'corr' (corr=0: uncorrelated input; corr=1: complete synchronisation). The classification of the GPi output pattern as 'normal' or 'Parkinsonian' is based on the occurrence of bursts.

3 Results



GPi behaviour for different levels of correlation (corr=0, 0.5, and 1) for both GPe and STN input with an oscillation frequency of 5 Hz, zero phase. Black: Parkinsonian; green: normal; dark blue: no spiking; light blue: zero input. $g_{STN\to GPi}$, $g_{GPe\to GPi}$ indicate the connection strength (conductivity) of the input from STN and GPe to GPi, respectively.

4 Discussion

It can be shown that with highly synchronous GPe and STN input patterns with frequencies up to 30 Hz Parkinsonian patterns are generated by GPi. For frequencies in the pro-kinetic area (>60 Hz), including those used for deep brain stimulation, normal patterns are again generated even for highly correlated inputs.

References

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