

THE PEDUNCULOPONTINE NUCLEUS AS ALTERNATIVE TARGET FOR DEEP BRAIN STIMULATION

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1 Introduction

Parkinson's disease (PD) is a neurodegenerative disease associated with motor and nonmotor symptoms. Deep brain stimulation (DBS) is a surgical treatment where an electrode is implanted in a certain area in the brain. In PD this is mostly done in the subthalamic nucleus (STN) or the globus pallidus interna (GPi). High frequency stimulation (~130 Hz) is often a successful treatment.

The pedunculopontine nucleus (PPN) has recently been suggested as a new therapeutic target for DBS, particularly for patients with severe gait and postural impairment [2]. Stimulation at this site is typically delivered at low frequencies in contrast to the high frequency stimulation required for therapeutic benefit in STN [2].

Despite real therapeutic successes, the fundamental physiological mechanisms underlying the effect of DBS are still not understood. To get a better understanding of PPN stimulation we constructed a computational conductance based model for PPN Type I neurons.

2 Method

The PPN model is based on neurophysiological data of the thalamocortical relay neuron and the pre-Böttinger neuron. Persistent sodium current is responsible for subthreshold membrane oscillations in PPN Type I neurons, which underlies spontaneous repetitive firing [3]. The low threshold spikes, which are responsible for bursts, are mediated by T-type calcium currents [3]. In addition the PPN model contains a leak, a sodium, a potassium and a hyperpolarization-activated current. The PPN Type I cell is modeled as a single compartment model using the Hodgkin-Huxley formalism, except for the calcium current, which is described by the Goldman-Hodgkin-Katz ion current equation. We have analyzed our model neuron within MATCONT, a bifurcation analysis tool [1].

3 Results

The PPN type I neuron model shows firing patterns as found in literature [3], i.e. a burst is generated after a period of hyperpolarization and spontaneous firing at 8 Hz. The model shows that switching

between low and high frequency spiking is possible. Bifurcation analysis confirms that there is bistability between high and low frequency tonic spiking. Both tonic spiking regimes have a Type II phase response curve, which means a perturbation of the limit cycle can produce a phase advance or phase delay depending upon the timing.

4 Discussion

PPN plays a role in the control of the muscle tone by means of its excitatory projections to the muscle tone inhibitory system in the brainstem. In PD the inhibitory basal ganglia output is overactive. An increase in basal ganglia inhibition, together with a decrease in cortical excitation of the PPN, may increase the muscle tone level, leading to rigidity [4]. Our next step will be to incorporate the PPN model in a basal ganglia network and to investigate the effects of DBS in STN and PPN on the behavior of the network. In particular: we shall analyze the output to the brainstem and describe the effects on the muscle tone.

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