MEASURING ACTIVITY OF THE SUBTHALAMIC NUCLEUS IN ACUTE SLICES USING MULTI ELECTRODE ARRAYS

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1 Introduction

The symptoms of Parkinson's disease (a.o.: tremor, rigidity) can be suppressed by electrical stimulation of the basal ganglia [1]. The most common target nucleus of this so called Deep Brain Stimulation (DBS) is the subthalamic nucleus (STN). Good clinical results are obtained by the application of pulses of 200 μs, 1-3 V amplitude at a constant rate of about 130 Hz. However, the mechanism(s) responsible for the clinical improvements are not yet elucidated.

The involvement of the basal ganglia in PD has been well established. The main hallmark is the loss of dopaminergic neurons in the substantia nigra. However, due to the vast interconnectivity, it is difficult to interpret exactly how this leads to PD symptoms and how high frequency stimulation modulates the associated neuronal activity patterns. The location of the basal ganglia, at the base of the forebrain, necessitates invasive methods in order to measure activity *in-vivo*. As such, activity is mostly measured at a single site and it is difficult to relate the activity in one nucleus to activity in another nucleus.

The use of acute brain slices as a model is therefore widely used, despite the inevitable loss of many connections [2]. Accurate (i.e. subthreshold) measurements of single neuron and multiple neuron (up to ~3, for practical reasons) membrane potentials are obtained by patch-clamp technique. Thus, acute slices of the basal ganglia have contributed vastly to our knowledge of the interrelationships between the various nuclei of the basal ganglia.

2 Methods

We propose to use multi electrode arrays (MEAs) for measuring the activity in brain slices at 60 different sites simultaneously. In our lab, MEAs consist of cone shaped electrodes protruding through a glass substrate in a square grid with a spacing of 200 μm. They allow observation through a microscope and the extracellular recording of action potentials. Figure 1 shows the recorded area, using a standard MEA.

3 Results

We will describe the first results using this new approach, focusing on the spontaneous activity patterns in STN and comparing these to results which have been obtained using other methods.

4 Discussion

The use of a multi electrode array enables the investigation of synaptic plasticity within the pallido-subthalamic circuit: Does synaptic plasticity in the STN/GPe network play a role in the generation of PD symptoms and does it play a role when high frequency stimulation is applied?

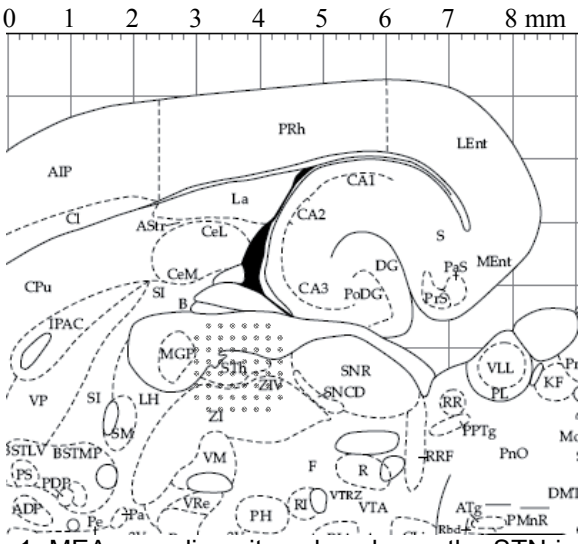

Fig 1. MEA recording sites placed over the STN in a horizontal slice (Rat Brain Atlas, Paxinos & Watson)

References

[1] Benabid AL et al. Deep brain stimulation of the subthalamic nucleus for Parkinson's disease: methodologic aspects and clinical criteria. *Neurology* 55, S40-S44, 2000.

[2] Plenz & Kital. A basal ganglia pacemaker formed by the subthalamic nucleus and external globus pallidus. *Nature* 400, 677-682, 1999.