

Impulse response analysis of neuromodulation for the treatment of motor symptoms in Parkinson's disease

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Popular science summary

In this thesis, a rat that have been made to display parkinsonian motor symptoms was used to investigate the brain responses to small electrical stimulation deep in the brain. The responses were recorded in the form of local field potentials (LFP), these measure the electrical potential inside the brain. The recording was done with a recording electrode with 128 channels. From the responses to three different stimulation protocols, models were created to simulate the recorded brain structures. Why? To answer that you will first be given some information about Parkinson's disease (PD) and its treatment options.

PD is a chronic neurodegenerative disease, this means that it causes nerve cells in the brain called neurons to die and the disease gets worse over time. In the case of PD particularly neurons in the brain structures that are related to movement are affected. That is what causes the so called motor symptoms of PD which can be tremors in the limb, face and jaw, slowness of movement, stiffness of limbs and postural instability. A treatment to the motor symptoms of PD is deep brain stimulation (DBS) where a small electrode is surgically implanted into the relevant brain structure. Then the electrode is configured to a stimulation protocol that suppresses the motor symptoms of PD. This configuration process can be quite complex and time consuming and require a specialist. Why DBS works is not exactly known but one hypothesis is that it cancels out disruptive signals sent by the damaged structures. The next step in the DBS development is adaptive deep brain stimulation (aDBS) in which the electrode stimulation would adapt itself to new circumstances on its own.

In this thesis, a new stimulation target called the reticular thalamus (RT) is investigated by looking at the responses to three stimulation protocols. The goal is to see how the stimulation affects the LFPs from relevant brain structures and if these responses can be modelled. If these responses could be modelled and predicted, this would be a small step forward in the development of aDBS.

The stimulation protocols were built up by the results from threshold testing. Threshold testing is a test where a rat was subjected to deep brain stimulation going from low charge amplitude and increasing the charge amplitude until a visual response could be seen. Next, these stimulation protocols were executed and the responses in the LFPs were recorded in two states, one parkinsonian, and one where the drug Levodopa, which supplies the brain with dopamine, were introduced to produce involuntary movements. This latter state is called dyskinesic and happens when a parkinsonian brain gets an overdose of dopamine. The way this rat model of PD worked is by leaving one half of the brain healthy and the other half parkinsonian, having the benefit of giving healthy and parkinsonian data to each state. The data were recorded with the 128 channel recording electrode, but some defects in the electrode caused many of the channels unusable.

The data were first inspected and normalised, any channels displaying saturation and noise were removed. The frequency component of the recordings revealed that the animal was a good example of the rat model of PD. The evoked potentials, or the average response to the stimulation, revealed that most of the recorded structures were sent into a 5-10 Hz oscillatory behaviour as a response to the stimulation. In the dyskinesic state these oscillations died out faster than in the parkinsonian state. The responses also revealed that the new stimulation target affected both hemispheres even though only one hemisphere was subject to the stimulation. The model created from the responses to one of the stimulation protocols could not predict the responses to the other two stimulation protocols tested here.

In this thesis it was seen that the RT is an interesting stimulation target that could use further study, especially since the RT seems to be connected to both hemispheres and the responses to stimulation were different in the parkinsonian, health and dyskinesic states. The modelled responses showed that the brain can not be completely modelled this way and that the brain is more complex than the author anticipated.

For further reading, please look at the master thesis [Hedström, 2016]. For general information about PD and deep brain stimulation try the web page of the Parkinson's Disease Foundation [PDF, 2016].

References

- S. Hedström. Impulse response analysis of neuromodulation for the treatment of motor symptoms in Parkinson's disease. Master's thesis, Faculty of Engineering (LTH), Lund University, Sweden, 2016. TFRT-5993.
- Parkinson's Disease Foundation (PDF). "What is Parkinson's Disease?", 2016. URL http://www.pdf.org/about_pd.