Personalised Parkinson's therapy using intelligent brain stimulation

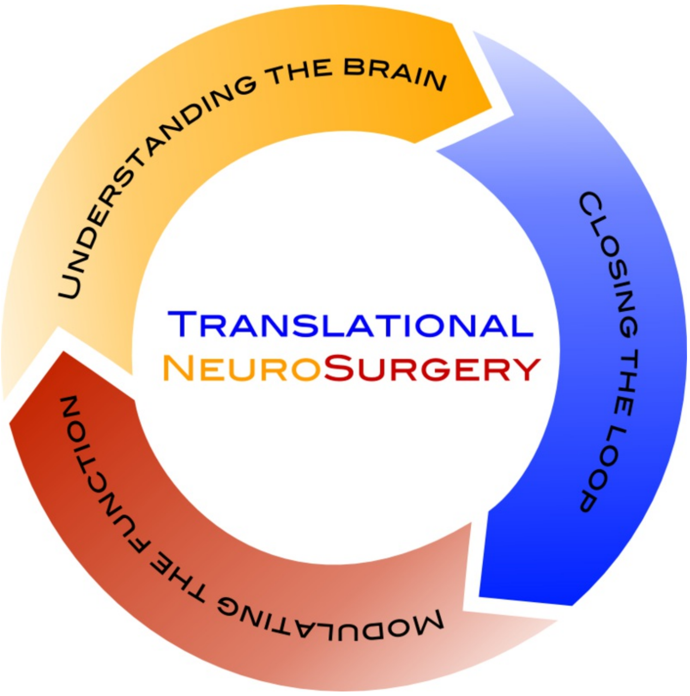
For many decades, deep brain stimulation has been used for treating neurodegenerative disorders such as Parkinson's disease. However, the mechanisms of the procedure, which involves implanting stimulation probes into low lying brain areas, are still not clear. Prof. Alireza Gharabaghi, Dr. Daniel Weiss and their teams of researchers at the University of Tübingen have now been able to demonstrate a direct relationship between deep brain stimulation and the neurophysiological basis of Parkinson's disease. The results could potentially contribute to the development of intelligent systems for the personalised treatment of Parkinson's patients based on specific requirements.

Deep brain stimulation (DBS) is a neurosurgical procedure that has been successfully used for treating patients with movement disorders since the 1990s. The procedure involves the implantation of electrodes (often referred to as "brain pacemakers") into deep brain areas. Therapy involves sending electrical pulses to the brain, which greatly improves symptoms such as tremor and rigor in most patients. Patients also regain autonomy and become more active than they were prior to surgery. More than 6000 patients in Germany have received such neuroimplants, and the University Hospital in Tübingen is one of the most active DBS centres in Germany. Although the efficacy of DBS for the treatment of neurodegenerative disorders such as Parkinson's has been demonstrated in clinical studies, further research is needed to clarify the principles and mechanisms of therapy on the neural level in greater detail.

Future Parkinson's disease therapy needs to be tailored to patient needs

Prof. Dr. Alireza Gharabaghi from the Werner Reichardt Centre for Integrative Neuroscience (CIN) at the University of Tübingen and Dr. Daniel Weiss from the Hertie Institute for Clinical Brain Research at the University Hospital of Tübingen and their teams have focused for quite some time on deep brain stimulation and its potential for treating Parkinson's disease. The two neuroscientists are specialists in both DBS research and clinical application. Gharabaghi carries out the implantation of the electrodes with an interdisciplinary team. It is a surgical intervention that he calls "highly standardised, yet sophisticated".

Gharabaghi and Weiss are both involved in research aimed at understanding the mechanisms of the procedure so that treatment can be further optimised. "We want to be able to treat each patient on an individual level as far as we can," says Gharabaghi. "We want to improve brain



Neuroscientists need to understand the neurophysiological basis of brain function before they can develop therapies tailored to the requirements of individual patients.
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stimulation to the extent that we can adapt treatment to the specific requirements of individual patients, and even adjust it to changing daily conditions." Weiss adds: "Our research focuses on therapies that target symptoms such as gait freezing. In order to develop therapies of this kind, we need detailed physiological insights into the neural basis of gait freezing and the mechanisms of deep brain stimulation."

Parkinson's disease is caused by a process known as neurodegeneration, which is the slow death of dopamine neurons in brain areas that are primarily responsible for controlling movement. In the early stages of the disease, only very specific brain areas are affected but functional disorders can nevertheless occur in widespread areas of the brain. "It's like a computer network where individual nodes are unable to communicate with each other when a particular part fails," says Gharabaghi. Weiss adds: "This is also true for Parkinson's disease: the death of neurons has a major negative affect on brain activity, leading to typical Parkinson's symptoms such as rigor and movement disorders. Brain stimulation has the potential to control some of the disease symptoms."

DBS stimulates extensive brain areas

In order to establish a relationship between the way DBS works and the physiological basis of Parkinson's disease, the neuroscientists from Tübingen have spent the past few months studying more than 20 patients and measuring their nerve activity at different points in time during and after implantation of electrodes. Surface EEGs on the scalp provided information on how stimulation of the subthalamic nucleus region affects the interconnection and communication of cerebral neuron groups. The electrophysiological measurements then provided the scientists with information on how nerve cells communicate with each other in the brain.

The researchers found that brain stimulation not only facilitated communication between the neurons; it also made it much more efficient. They also found that it was not just a relatively small brain region that was modulated as had previously been assumed. Gharabaghi comments: "Our findings suggest that stimulation affects extensive brain areas." The results could lead to a completely new way of treating Parkinson's disease symptoms. Gharabaghi says: "We are close to a paradigm shift. Whereas previously we used to try and detect certain areas by taking advantage of local characteristics, in future we will increasingly be looking for connection patterns between different brain areas and specifically stimulating these connections.

Development of new intelligent therapy systems

Neuroscientists refer to such measurements as electrophysiological biomarkers. The new biomarker provides valuable information that enables the researchers to better adapt deep brain stimulation to the requirements of individual patients. "Our idea is to make stimulators even smarter," says Weiss. While current devices need to be adjusted manually by physicians or patients, the researchers from Tübingen want to use their findings to produce new, intelligent stimulators, so-called closed-loop systems that can modulate stimulation parameters on the basis of physiological markers recorded online – even before the patient becomes aware that something is wrong. "A number of companies are already developing the required hardware," says Weiss. "We now need to develop algorithms for real-time calculations." In close cooperation with all partners, the neuroscientists from Tübingen hope to be able to offer personalised and customised treatment procedures for Parkinson's patients within the next few years. The intelligent stimulators will also take into account the possibility that the patient's condition may change from one day, or one hour, to the next. "We're aiming to develop a device that easily and instantaneously adapts to different situations, to prevent gait freezing, for example. We hope to achieve this within the next three to five years," says the neurologist.

Dr. Daniel Weiss is a neurology specialist with a particular interest in neurodegenerative diseases. He works at the Hertie Institute for Clinical Brain Research at the University of Tübingen.
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Article

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The article is part of the following dossiers

Neurodegenerative diseases

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