New ultrasound technique significantly improves brain performance

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In neurological diseases such as Alzheimer's disease, Parkinson's disease or Multiple Sclerosis, brain neurons are constantly being lost, resulting in memory lapses, speech disorders, mood swings and movement disorders,

for example, as well as muscle tremors in the case of Parkinson's. After six years of development, MedUni Vienna researchers from the Department of Neurology (Head: Thomas Berger), led by Roland Beisteiner, have developed a new method of treatment that represents a world first. Using a non-invasive ultrasound technique, it is now possible to reach all areas of the brain and activate neurons that can help to regenerate brain functions. The preliminary data, which have been prominently published on the international stage, show that this can improve brain performance. This has positioned Vienna as a world leader in an important sector of medicine.

The new method is called transcranial pulse stimulation with ultrasound (TPS) and was developed in collaboration with Swiss commercial partner Storz Medical and its project leader, Ernst Marlinghaus. "For the first time in the world, TPS enables us to penetrate into all areas of the brain by means of an ultrasound pulse delivered directly to the skull in a non-invasive, painless procedure, during which the patient is fully conscious, and to specifically target particular areas of the brain and stimulate them," explains Beisteiner. The study was part of the inter-university cluster led by Roland Beisteiner and Tecumseh Fitch, which is attempting to improve patients' brain functions by means of brain stimulation and is being jointly run by MedUni Vienna and the University of Vienna. Such clinical procedures must be carried out with great precision and must be tailored to the individual patient. However, the existing electromagnetic techniques such as e.g. Transcranial Magnetic Stimulation (TMS), in which magnetic fields act on the brain to stimulate or inhibit neurons, are currently incapable to provide the required clinical precision, or deep brain activation. An invasive method that is increasingly being used for serious illnesses involves placing stimulator electrodes in deep brain areas (deep brain stimulation [DBS]) – associated with a lengthy operation. It is hoped that TPS could also partially replace such invasive methods in the future.

TPS: Precision medicine in the brain

The stimulating pulse emitted by the ultrasound device is between 3 and 5 mm wide and approximately 3 cm long. An accurate "map" is first of all made of the patient's brain using magnetic resonance. "In the spirit of precision medicine, the area of the brain that is to be activated is very precisely targeted. These areas can be situated differently in each patient. Thanks to a navigation system, the treating neurologist can pinpoint on the screen where the pulse must be delivered and control everything very precisely," says Beisteiner.

The TPS pulse causes short-term membrane changes on the brain cells, bringing about local changes in the concentration of transmitters and other biochemical substances. This results in activation of neurons and the development of compensatory networks, which improve the affected brain function. This has been demonstrated in comprehensive laboratory studies. The result: the memory network is boosted and memory performance improves. Some patients also report a marked improvement in their mood, they find it easier to be physically active and to actively participate in conversations.

Says Beisteiner: "It is like starting up an old engine again. Those neurons that are still activatable show marked improvements after the procedure. The decline in performance is slowed down." Apart from Alzheimer's, Parkinson's or multiple sclerosis, any diseases that can be improved by activating viable neurons are potential applications for TPS. At the same time, TPS offers patients an "extra chance," says Beisteiner, since all ongoing treatments with drugs and physiotherapy or occupational therapy can be continued. However, the new technique is also significant for basic neuroscientific research.

In the clinical pilot study, which has now been published as cover-article in the prestigious journal *Advanced Science*, six one-hour sessions over

the course of two weeks were enough to bring about improvements in brain performance. If the results of the pilot study are confirmed, clinical neuroscientists expect a breakthrough in the treatment of brain diseases. However, before this method can be put into regular clinical use, further scientific studies are required to evaluate the results. "We are still looking for volunteers for these studies. They would be people who have a diagnosis of Alzheimer's or Parkinson's but no other brain disease," says Beisteiner.

More information: Roland Beisteiner et al. Transcranial Pulse Stimulation with Ultrasound in Alzheimer's Disease—A New Navigated Focal Brain Therapy, *Advanced Science* (2019). DOI: 10.1002/advs.201902583

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