

BRAIN STIMULATION VIA MRT-TRACKED TPS (TRANSCRANIAL PULSE STIMULATION) – A NEW METHOD FOR AMELIORATING DEFICITS IN PATIENTS WITH ALZHEIMER'S DISEASE

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INTRODUCTION

Alzheimer's disease (AD) is a very common cause of dementia in many countries all over the world and a common cause of death in elderly humans. No effective long-term treatment has been found yet.

TPS (Transcranial Pulse Stimulation), which can be individually tracked by MRT-scans, offers new perspectives to ameliorate deficits caused by AD. Pilot studies show beneficial effects on learning and memory of TPS. There are also reports of restorative structural changes in the thickness of the cerebral cortex due to the stimulation.

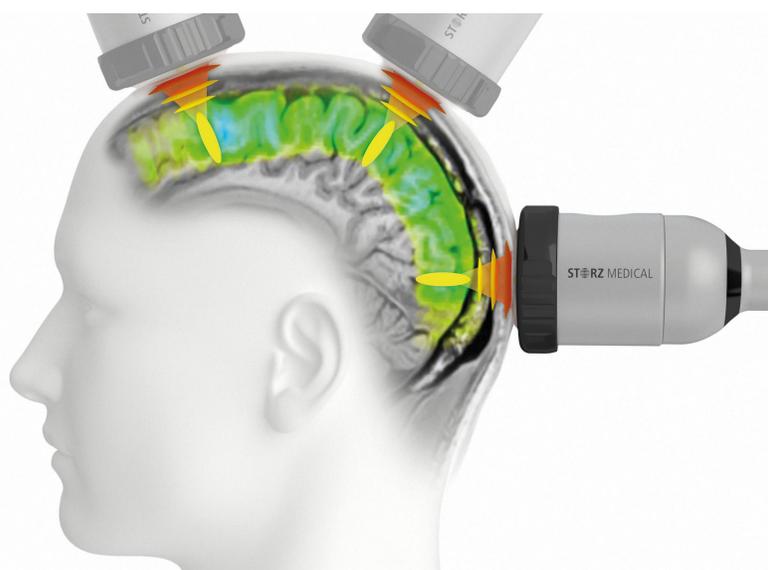


Fig.1 Stimulation-pulses are administered by MRT-tracking on the surface as well as in deeper structures of the brain.

METHODS

21 out-patients with Alzheimer's disease (with light to moderate symptoms) received 6.000 pulses of TPS (0.2 mJ/mm² per single pulse, with a frequency of 4 Hz) per session. The application of the pulses with Neurolith by Storz Medical was individually navigated by use of current MRT-images of the patients. TPS-pulses were administered bilaterally into the frontal, parietal and temporal cortex. Pulses were applied over a period of 2 weeks (3 sessions per week). Cognitive capabilities (especially executive functions) of the patients were tested using the Stroop-test (colour-word-interference-test) and CERAD. The Stroop-test is a standardized test for executive functions. Patients were tested using a pre – post design (t0 pre stimulation : t1 after 6 sessions, two weeks later).

LITERATURE

- (1) Tyler, S. et al., Ultrasonic modulation of neuronal circuit activity. Current opinion in neurobiology, 50, pp. 222-231, (2018).
- (2) Babakhanian, L. et al., Effects of low intensity focused ultrasound on liposomes containing channel proteins. Scientific Report, 8, 17250, (2018).
- (3) Min, P. et al., Focused ultrasound modulates the level of cortical neurotransmitters. Int. Journal of Imaging Systems and Technology, 21, pp.232-240, (2011).
- (4) Yang, P. et al., Transcranial focused ultrasound to the thalamus is associated with reduced extracellular GABA-levels in rats. Neuropsychobiology, 65, pp. 152-160, (2012).
- (5) Lin, W. et al., Protective effects of low-intensity pulsed ultrasound on aluminium-induced cerebral damage in Alzheimer's disease rat model. Scientific Reports, 5, 9671, (2015).

RESULTS

TPS-stimulation over a period of two weeks (6 sessions) showed ameliorating effects on performance in the Stroop-test. The mean-score was diminished significantly (pre vs. post ; $p < 0.05$ – paired T-test). Single patients showed extraordinary improvements by shortening completion times in the Stroop-test by half. No significant side-effects occurred during all the sessions in any of the patients.

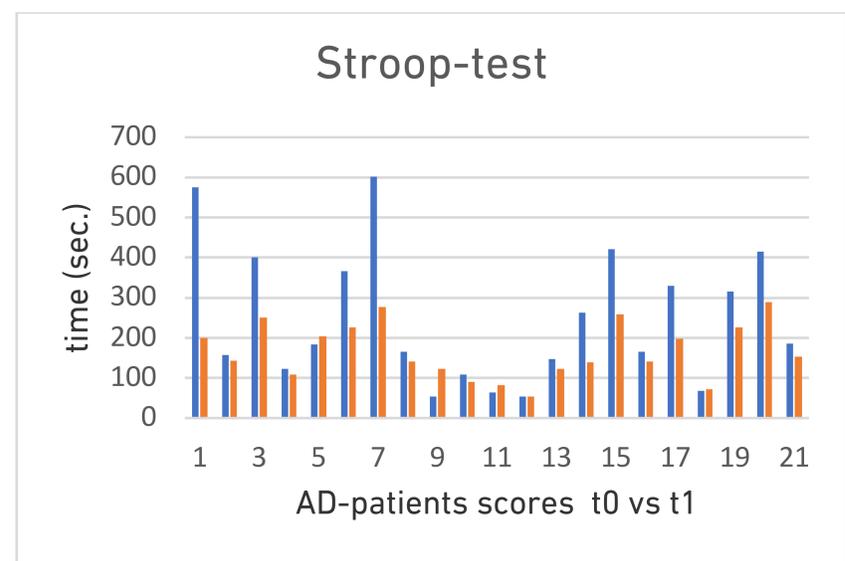


Fig. 2 Results of the Stroop-test. Executive functions improved from t0 vs t1.

DISCUSSION

The results of this pilot-trial show that cognitive impairments of executive functions in Alzheimer's disease may be ameliorated using TPS as a noninvasive brain stimulation method. No severe side-effects were observed.

Regarding the specific workingmechanism(s) of TPS various factors are to be discussed (1) Mechanical effects on the cell membranes influence ion channels and induce a membrane-poration in neurons and glia cells (2). Changes in various neurotransmitter levels have been observed after TPS (including an increase of dopamin and serotonin and a reduction of GABA (3,4). The blood-brain-barrier may be opened in stimulated areas of the brain. In addition, TPS may lead to an induction of trophic factors: BDNF (neurogenesis, proliferation of neurons) and VEGF (enriched vascularisation) (5).

In summary, the evaluation showed that TPS as an adjunctive therapy to a state-of-the-art treatment of AD could achieve an improvement of cognitive executive functions.