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POSTERS: A02.I. THERAPEUTIC TARGETS, MECHANISMS FOR TREATMENT: NEUROTROPHIC, SYNAPTIC PLASTICITY, REPAIR, REGENERATIVE MEDICINE

TRANSCRANEAL PULSE STIMULATION FOR THE TREATMENT OF MILD COGNITIVE IMPAIRMENT AND EARLY ALZHEIMER'S DISEASE

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Aims: Brain stimulation with transcranial pulse stimulation (TPS) is currently being studied for their increasing popularity as an approach to modulate and stimulate the human brain. Several publications have reported the benefits that TPS can deliver to the patients with a varied number of neurologic disorders, being specially so in patients with cognitive impairment due to Alzheimer's disease and other causes. Here we present the promising results from a short - medium follow-up of subjects with cognitive impairment treated with TPS.

Methods: The treatment protocol includes an initial evaluation with a neurologist and a neuropsychologist and an MRI scan. We perform an extensive cognitive battery, which includes MoCA test, clinical dementia rating (CDR), functional activities questionnaire (FAQ) and specific test to evaluate all cognitive domains. All patients received 6000 pulses/session. The session duration is 25 minutes. Subjects received 6 sessions delivered over 2 weeks, and a reinforcement session was administrated after 10 weeks. The protocol includes the evaluation of the patients after 3, 6 and 12 months post-treatment.

Results: Patients have experienced a sustained improvement in the following categories: orientation and attention. Improvement in fluency of language has also been documented. This study is yet to be concluded after collecting 12 month follow-up results.

Conclusions: Patients presented good tolerability and no side effects. This method shows promising results to slow down the progression of the disease and improve certain areas on the cognitive behavior. Shockwave stimulation is a non-invasive and well-tolerated technique that could support or enhance pharmacological treatment of patients with MCI and EAD.

P1166 / #298

POSTERS: K01.J. DEMENTIA AND COGNITIVE DYFUNCTION: OTHER

MRT-TRACKED TRANSCRANIAL PULSE STIMULATION – A NEW METHOD OF BRAIN STIMULATION TO AMELIORATE DEFICITS IN PATIENTS WITH ALZHEIMER'S DISEASE

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Aims: TPS (Transcranial Pulse Stimulation) which can be individually tracked by MRT-scans offers new perspectives to ameliorate deficits caused by Alzheimer's disease. 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. The aim of the application observation was to document behavioral benefits after treatment.

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).

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 none of the patients.

Conclusions: 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.

P0341 / #383

POSTERS: A03.Q. DRUG DEVELOPMENT, CLINICAL TRIALS: OTHER

TRANSCRANIAL PULSE STIMULATION IN ALZHEIMER'S PATIENTS: WHOM, HOW AND WHERE TO STIMULATE?

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Aims: Transcranial Pulse Stimulation (TPS) uses shockwaves for the treatment of Alzheimer's patients. Recently, our group published short-term clinical results after the first treatment cycle (Cont et al. 2022). However, many aspects remain unclear concerning patient selection and treatment protocols.

Methods: A consecutive series patients received TPS using the Neurolith System (Storz Medical). After the initial treatment cycle over 2 weeks patients were scheduled for monthly booster sessions. Safety data and different cognitive scores were assessed over 5-12 months. Individual symptomology, MRI- and CSF biomarker, disease stages, inclusion / exclusion criteria and treatment protocols where registered.

Results: The initial treatment was well tolerable with low number of only transient and not severe side effects even in selective patients with minor vascular lesions and platelet aggregation inhibitors. Cognitive and affective scores improved significantly after the first treatment cycle regardless of symptom severity at baseline and CSF biomarker. Standard protocol was 6000 pulses with 4 Hz stimulation of precuneus, bilateral frontal and parietal cortex but was extended to bitemporal cortex and / or motor areas such as SMA, M1, PMC to treat concomitant tremor or hypokinesia. Preliminary long-term data showed stable effects over months with the selected booster interval.

Conclusions: TPS might be an option for Alzheimer's not only in mild cases and regardless of the biomarker constellation und thus maybe for other dementia types. Minor vascular pathology and platelet aggregation inhibitors is generally acceptable. Treatment protocols can extend standard patterns and include e.g. motor areas to address concomitant hypokinesia or tremor. Imaging and electrophysiology biomarkers need to established. Systematic treatment protocols should be tested with a translational approach including basic neuroscience techniques and in comparison to other methods such as ultrasound and electric / magnetic stimulation.

P1084 / #434

POSTERS: J02. THERAPEUTIC TARGETS, MECHANISMS FOR TREATMENT

IMPLEMENTING TRANSCRANIAL PULSE STIMULATION AGAINST DEMENTIA AT PSYCHIATRIC DEPARTMENT SCHAFFHAUSEN

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Aims: Our very first patient treated with TPS (80y, mixed dementia) improved after the first block of 6 sessions in MMSE from 21 to 25 points (maximum 30). Even after pausing for 10 weeks, the result remained stable and after another block of 6 sessions TPS, the MMSE improved to 27 points, including improvement of short term memory. These results encouraged us to boost this therapy in our psychiatry clinic and the results are here demonstrated as well as tolerability and safety and maintenance aspects of TPS.

Methods: to be presented with poster

Results: to be presented with poster

Conclusions: to be presented with poster

P0304 / #1580

POSTERS: A02.R. THERAPEUTIC TARGETS, MECHANISMS FOR TREATMENT: OTHER

TPS (TRANSCRANIAL PULSE STIMULATION): SAFETY AND DOSES EVALUATION

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Aims: Low intensity shockwaves proved to be efficient for the treatment of non-unions, tendons and muscular pain, wound healing, heart insufficiency, erectile dysfunction and aesthetics since 1990. The working principle is the mechanical stimulation of biological processes called mechanotransduction. Transcranial Pulse Stimulation (TPS) uses shockwave pulses for mechanical stimulation of the brain tissue. In spite of the long term (since 1990) practical experience with shock wave application to the soft tissue, the application to the brain tissue required new safety evaluation, in order to exclude negative side effects. Bleeding is considered as the only significant risk factor.

Methods: Two animal trials were performed: 80 Sprague-Dawley rats were divided in 8 groups with 10 animals each and treated with:

0mJ/mm², the control group

0.1mJ/mm² with 100, 200 and 400 pulses

0.2mJ/mm² with 100, 200 and 400 pulses

0.3mJ/mm² with 100 pulses 5 Sprague-Dawley rats were treated with 0.2mJ/mm² with 400, 4000 and 8000 pulses.

Results: 80 Sprague-Dawley rats trial

The animals were euthanized and the brain histologically investigated with no bleeding found. 5 Sprague-Dawley rats trial The applied doses correspond to 15, 150 and 300fold human doses. MRI evaluation in-vivo showed minimal bleeding in only one animal treated with 300fold human doses.

Conclusions: This safety margin becomes even higher, when the stronger shockwave attenuation by the human skull compared to the rat skull is considered. Based on these investigations is the treatment with TPS safe.