Transcranial Pulse Stimulation (TPS) – New Perspectives in Treatment of Dementia in Alzheimer´s Disease?

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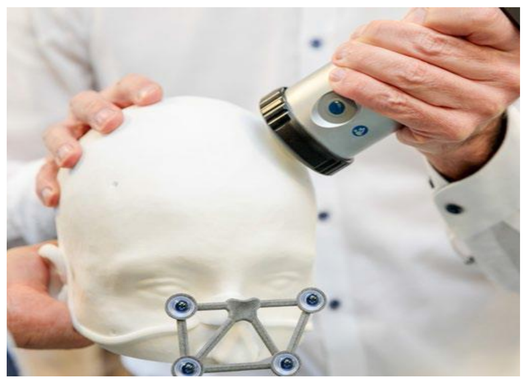
Introduction

Dementia is characterized by a decline or loss of cognitive functions, impairment of activities of daily living and often associated with psychiatric & behavioural symptoms [1, 2]. The course of this disease is progressive with an impairment of cognition, orientation, language, memory, autonomy, emotional control, motivation & social behavior [1, 2].
People with dementia are more likely to have comorbidities & shorter life expectancy [1, 2]. Dementia is associated with a high emotional burden & impairment of quality of life and can be seen as a severe illness [1, 2]. Most common cause of dementia syndrome is the Alzheimer's Disease (AD) [1, 2].
In last years TPS is used in the treatment of AD. TPS is a low-energy shock wave treatment, approved in mild to moderate AD. At TPS, sound pulses are introduced into certain brain areas to help improve blood flow & generation of new blood vessels in order to maintain or even increase cognitive performance for as long as possible.



Some studies indicate positive effects, which can be seen in significant improvement in neuropsychological test scores [3, 4, 5] and depressive symptom burden [5, 6]. But the effectiveness of this treatment is not conclusively confirmed. Therefore more studies are needed.
Our study examined the cognitive performance and depressive symptom burden of patients with an AD over the course of treatment with TPS.

Method & Selection

Measuring cognitive performance with Montreal Cognitive Assessment (**MoCA**) and depressive symptom burden with Geriatric Depression Scale (**GDS**) from patients with an AD who are treated with TPS in Wahrendorff Clinic in an outpatient setting.
Follow-up design of the study: Measuring MoCA and GDS at the beginning of the treatment and during the treatment, every three months over a time period of 12 months.

Table 1: **Sample Characteristic**

Feature	Women & Men n = 62 (100 %)	Women n = 35 (56 %)	Men n = 27 (44 %)	Sign.
Age *M (SD)*	71 (9.9) min = 48 max = 87	71 (10.7) min = 48 max = 83	71 (9.1) min = 53 max = 87	*n.s.*[a]
Diagnosis (AD, ICD-10) F00.0: Typ 2 (early onset)	16 (26 %)	9 (26 %)	7 (26 %)	*n.s.*[b]
Diagnosis (AD, ICD-10) F00.1: Typ 1 (late onset)	29 (47 %)	18 (51 %)	11 (41 %)	
Diagnosis (AD, ICD-10) F00.2: atypical / mixed	15 (24 %)	7 (20 %)	8 (30 %)	
Diagnosis (AD, ICD-10) F00.9: not specified	2 (3 %)	1 (3 %)	1 (3 %)	

Details: *M* = Mean Value; *SD* = Standard Deviation; [a] *t*-test; [b] χ^2-test; *n.s.* = not significant

Results

Comparison of the Mean Values of **MoCA** and the Mean Values of **GDS** at following time of measurement:
t1 (baseline)
t2 (1st interval, after 3 months of treatment)
t3 (2nd interval, after 6 months of treatment)

Selected statistical method: repeated measures ANOVA

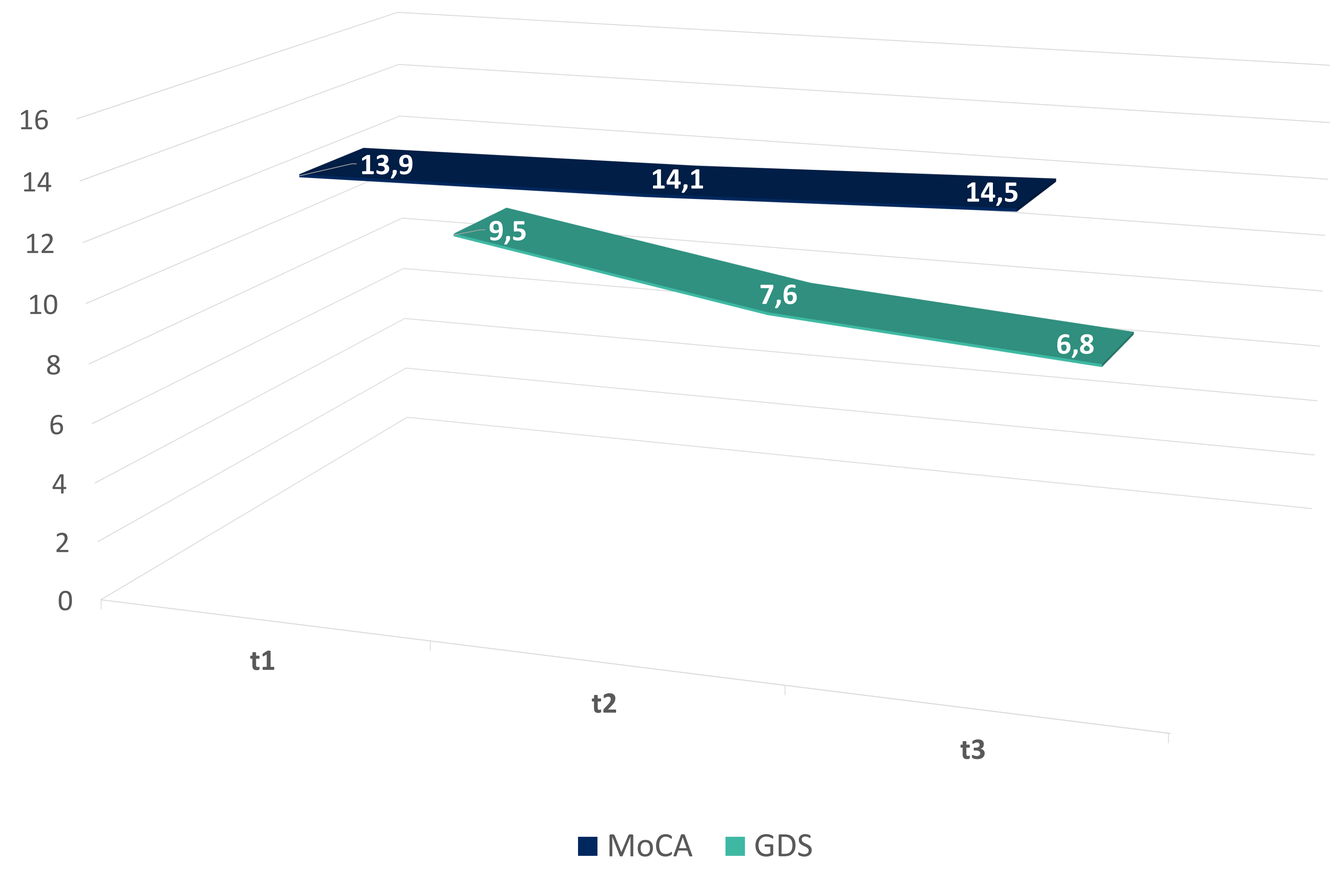
Degree of the Values of MoCA:
< 10 = severe cognitive disturbance
10 - 17 = moderate cognitive disturbance
18 - 25 = mild cognitive disturbance
≥ 26 = no or little cognitive disturbance

Degree of the Values of GDS:
< 10 = no or little depression
10 - 19 = mild depression
20 - 30 = severe depression

A repeated measures ANOVA with Mauchly-Test of Sphericity for **MoCA** revealed **no statistically significant difference of Mean Values for the different time of measurement**, $F(2, 66) = .749$, $p = .477$ (***Illustration 1***)

A repeated measures ANOVA with Mauchly-Test of Sphericity for **GDS** determined that Mean performance levels showed **a statistically significant difference between measurements**, $F(2, 32) = 4.410$, $p < .05$, partial $\eta^2 = .216$ (***Illustration 1***)

***Illustration 1*: Mean Values of MoCA & GDS over course of treatment with TPS (t1, t2, t3), n = 34**



Conclusion

The study examined the **cognitive performance** and **depressive symptom burden** of patients with an AD over the course of treatment with **TPS**. **Results indicate a minimal alteration of cognitive performance during the three time of measurement (*Illustration 1*)**. Therefore, treatment with TPS can contribute to maintain cognitive performance of patients with AD. **Furthermore the results indicate a reduction of depressive symptom burden in patients with AD over the course of treatment with TPS** (***Illustration 1***). Taking into account that patients rated their depressive symptom burden as rather low anyway. The results should be seen under consideration that cognitive performance and depressive symptoms can also be influenced by other factors. Furthermore, the study is being continued, so the results are preliminary data.
However, TPS therapy is not paid for by state or private health insurance companies and patients must therefore pay for the costs themselves. Furthermore, TPS therapy should only be carried out by qualified medical staff and contraindications should be taken into account. Like our study, some studies indicate positive effects, which can be seen in significant improvement in neuropsychological test scores [3, 4, 5] and depressive symptom burden [5, 6]. **But the effectiveness of TPS-treatment is not conclusively confirmed. Therefore more studies are needed.**
AD is a severe illness that is associated with considerable burden and impairments for those affected as well as their caregiving environment. It can be assumed that the number of cases will continue to increase and that this will result in further burden for healthcare systems. Dementia is still associated with challenges in diagnosis and treatment. For these reasons, special attention should be paid to AD. Maybe TPS can contribute to the maintenance of cognitive functions as well as to the improvement of psychiatric symptoms & behavioral symptoms in AD.
Possibly TPS appears to be a recommendable method for treatment of AD, naturally in addition to guideline-based therapies.

literatur:

[1] DGN eV, DGPPN eV (2023) S3-Leitlinie Demenzen Version XX 8.11.2023. Available at: https://register.awmf.org/de/leitlinien/detail/038-013, accessed on 20.02.2024.
[2] Jessen F, Frölich L, Hausner L (2016) Diagnostik und Therapie der Demenz (ICD-10 F0). Voderholzer U, Hohagen, F (Hrsg.) Therapie psychischer Erkrankungen – State of the Art. München Elsevier GmbH:1–22.
[3] Beisteiner R, Matt E, Fan C, Baldysiak H, Schönfeld M, Philippi Novak T, Amini A, Aslan T, Reinecke R, Lehrner J, Weber A, Reime U, Goldenstedt C, Marlinghaus E, Hallett M, Lohse-Busch H (2019) Transcranial Pulse Stimulation with Ultrasound in Alzheimer's Disease – A New Navigated Focal Brain Therapy. Adv Sci (Weinh) 7(3):1902583.
[4] Popescu T, Pernet C, Beisteiner R (2021) Transcranial ultrasound pulse stimulation reduces cortical atrophy in Alzheimer's patients: A follow-up study. Alzheimers Dement (NY) 7(1):e12121.
[5] Cont C, Stute N, Galli A, Schulte C, Logmin K, Trenado C, Wojtecki L (2022) Retrospective real-world pilot data on TPS in mild to severe Alzheimer's patients. Front Neurol 13:01–09.
[6] Matt E, Dörl G, Beisteiner R (2022) Transcranial pulse stimulation (TPS) improves depression in AD patients on state-of-the-art treatment. Alzheimers Dement (NY) 8(1):e12245.

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