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Assessment of Effectiveness and Safety of Transcranial Magnetic Stimulation (rTMS) combined with transcranial Direct Current Stimulation (tDCS) in Dementia Treatment in Alzheimer's disease

Lek. Emilia Frankowska
emilia.mielczarek1@stud.umed.lodz.pl
The Department of Old Age Psychiatry and Psychotic Disorders,
Faculty of Gerontology, Medical University of Lodz, Poland
Supervisor: Assoc. Prof. Jakub Kaźmierski, MD, PhD

Introduction

Alzheimer's disease is the most common disease responsible for dementia: it is responsible for 40-70% of all its cases. Alzheimer's disease is characterized by gradual and slow deterioration of memory and other cognitive functions and functioning.

Transcranial magnetic stimulation (TMS) is one of the youngest electrophysiological methods, enabling non-invasive and non-painful stimulation of the central and peripheral nervous system. Transcranial direct current stimulation (tDCS) is another non-invasive neurophysiological method used among patients with neurological dysfunctions and in selected psychiatric disorders.

The primary objective of the project is to assess whether the use of combined tDCS and rTMS therapies in patients diagnosed with mild to moderate Alzheimer's disease improves patients' cognitive function, including memory, attention, thinking, executive and language functions. Secondary objectives include assessing the impact of therapy on patients daily functioning, presence of neuropsychiatric symptoms/behavioral disorders, and the influence on the patients and their caregivers quality of life.

Methodology

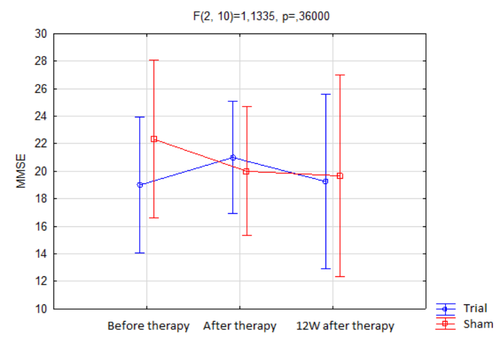
Patients are randomized to two parallel study groups – the active group receives rTMS and tDCS therapy with cognitive function exercise module and the placebo group with sham rTMS and tDCS with the cognitive function exercise module. The main part of the study consists of a clinical evaluation, conducting selected neuropsychological tests before the start of therapy, immediately after the end of therapy and 3 months after the end of therapy. Clinical evaluation is performed using MMSE, ADAS-Cog, NPI, ADCS, GDS, Zarit Burden Interviev, EQ-5D-3L, EQ-5D, clinical trials for evaluation of executive functions - Weigl-Colour Form Sorting Test, Memory Test Subtest from WAIS-R test, A-B Combination Test (TMT - Clinical Trial for Executive Function Testing). Safety is also evaluated and adverse events occurring at any time during the study are reported. The patient attends the clinic 5 times a week for 4 consecutive weeks, in total participates in 20 therapeutic sessions. Within one week of the end of therapy and 12 weeks after the end of therapy, patients and caregivers are re-evaluated using selected scales. Five randomly selected patients from active group and five of the control group will have a PET-CT scan of the brain before and after therapy to accurately determine the metabolic activity of different regions of the brain.

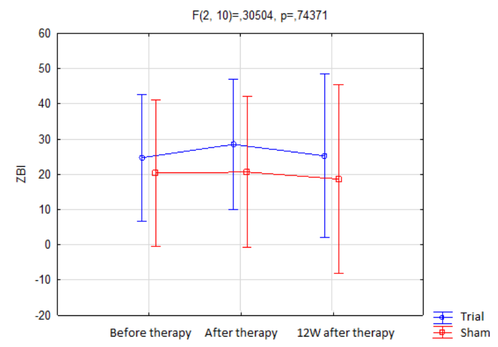
Results

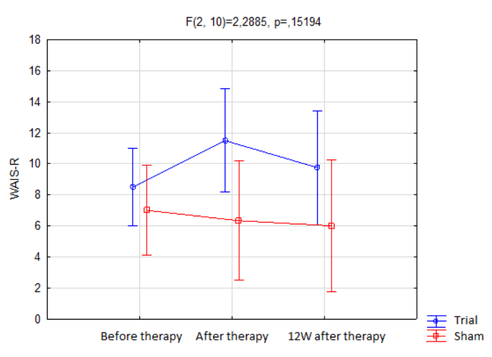
The study was completed by 10 patients. The analysis of the available data indicated tendencies to improve immediately after the therapy in the study group in tests that asses various aspects of cognitive functioning (ADAS-Cog, MMSE), the scope of immediate memory and the ability to concentrate (repetition of digits from the WAIS-R test), severity of depressive symptoms (GDS). There was no change in the test evaluating the ability to perceive and analyze forms and visual-motor coordination (Weigl-Colour Form Sorting Test), the patient efficiency and self-care (ADCS). There was a deterioration in the test that asses the caregiver burden (ZBI).

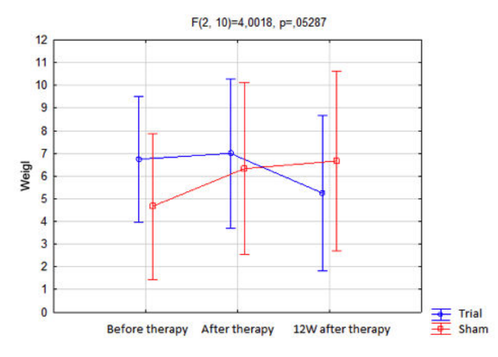
In the control group, a deterioration of the MMSE score was observed compared to the pre-treatment assessment. In the ADAS-Cog scale an improvement was observed compared to the result before the therapy, but lesser than for the study group. No difference was observed in the results of tests before and after therapy in the domains evaluating the scope of immediate memory and the ability to concentrate (repetition of digits from the WAIS-R test), the severity of depressive symptoms (GDS) or caregiver burden (ZBI).The improvement in the control group compared to the study group was observed only in the test evaluating the ability to perceive and analyze forms (Weigl-Colour Form Sorting Test).

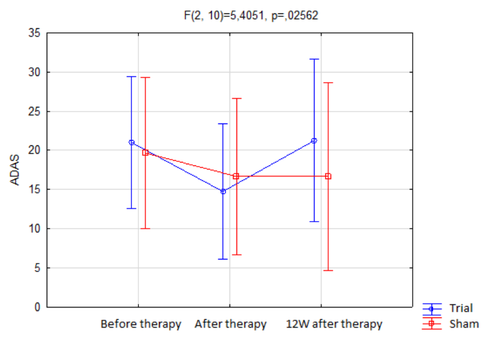
In the assessment performed 3 months after the therapy, the results were comparable to the results obtained before the therapy for the MMSE, ADAS-Cog and ZBI scales. The improvement was sustained in repetition of digits from the WAIS-R test and GDS scales. There deterioration was observed in the ADCS and Weigl-Colour Form Sorting Test scales. In the control group sustaining deterioration in domains evaluating cognitive functioning (MMSE, ADAS-Cog, repetition of digits from the WAIS-R test) was observed. There were no difference in the assessment of depressive symptoms (GDS) and caregiver burden (ZBI) compared to the results before the therapy. The improvement in the Weigl-Colour Form Sorting Test and ADCS tests was maintained.

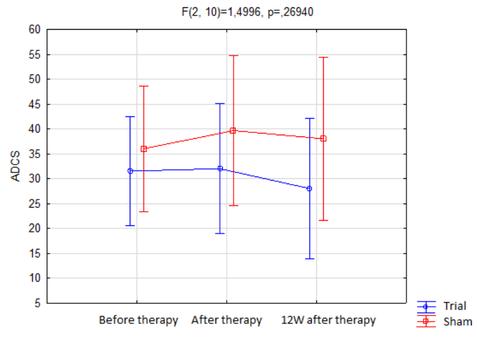


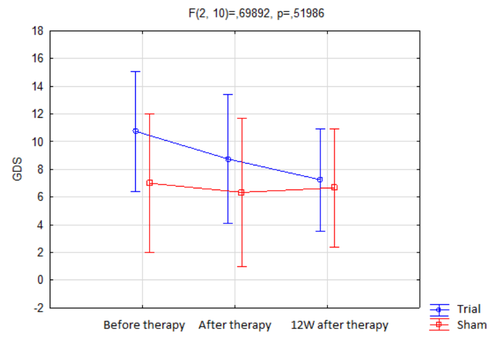












Group	Test	Before therapy	After therapy	12W after therapy
Trial	MMSE	19 (18-21)	23 (20-23)	20 (16-23)
	ADAS-cog	22 (15-24)	11 (11-14)	17 (16-27)
	ADCS	32 (21-32)	36 (33-37)	32 (19-38)
	GDS	8 (8-11)	7 (5-11)	7 (5-10)
	ZBI	20 (17-21)	23 (18-25)	16 (14-37)
	Weigl	7 (5-9)	7 (7-9)	5 (3-8)
	WAIS-R	10 (7-10)	12 (11-13)	11 (8-12)
Sham	MMSE	22 (22-24)	20 (20-21)	17 (16-26)
	ADAS-cog	19 (17-19)	15 (13-17)	16 (13-21)
	ADCS	36 (36-42)	37 (37-40)	39 (35-40)
	GDS	6 (5-7)	7 (4-8)	5 (5-10)
	ZBI	23 (11-28)	26 (18-27)	25 (5-26)
	Weigl	6 (4-6)	8 (7-8)	8 (4-8)
	WAIS-R	8 (7-9)	8 (7-9)	7 (4-7)

Conclusions

The described results may suggest a partial effectiveness of the therapy in terms of improving the cognitive functions and reduction od some neuropsychiatric symptoms e.g depression and apathy but probably in order to maintain the results the therapy should be repeated. The described analysis was based on a small number of patients, the results are not statistically significant. There were no adverse events reported yet in the study. The study need to be continued in order to fully assess the effectiveness and safety of the therapy.

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