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LETTER TO THE EDITOR

Transcranial direct current stimulation (tDCS) for treatment of phobic postural vertigo: an open label pilot study

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Some 30–50% of vertigo and dizziness symptoms cannot be explained by vestibular deficit or organic illness. They show co-morbidity with psychiatric disorders, i.e., anxiety and phobic disorders [1], illustrated in the concept of phobic postural vertigo (PPV) [2] describing patients with postural dizziness and subjective instability of stance and gait without pathological findings on otoneurological examination, vestibular, and balance tests. PPV exacerbates during perceptional stimuli and in social situations. The association between vertigo/dizziness and anxiety may be explained by neuroanatomical connections between the vestibular system and neuronal pathways modulated by monoaminergic influences [3].

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that modulates cortical neuroplasticity. Anodal stimulation of the left dorsolateral prefrontal cortex (DLPFC) improves cognitive control over negative stimuli such as anxiety and symptoms of psychiatric disorders, e.g., depression [4]. Currently, there is one case study reporting on tDCS in generalized anxiety disorder [5]. We hypothesized that tDCS can modulate PPV symptoms by strengthening cognitive control over fronto-limbic connections. Possible neurophysiological and neuroanatomical explanations of the effects might be (1) unspecific network changes in deeper frontal and subgenual regions [6, 7]; (2) shared neuroanatomical links of vestibular system and neural circuits of anxiety and depression [8, 9]; or (3) side and mode of stimulation, leading to differential effects in the laterality of the functional organization [10].

Eight outpatients (three female, five male) of the German Center for Vertigo and Balance Disorders IFB^{LMU} gave written informed consent for this open label pilot study as a precursor of a randomized placebo controlled clinical trial which has been acknowledged by the local ethics committee. Inclusion criteria were pertinent postitives in the medical history, supporting evidence from physical examinations and laboratory testing (normal findings on otoneurological examination and vestibular and balance tests), and symptom stability for at least 2 months. Five patients showed anxious control of posture. No one had a history of drug intake, brain injury, epilepsy, severe somatic disorders, or dermatologic disease. One patient was smoker, and two were suffering from migraine without aura (no long-term medication). One patient was treated with amitriptyline, two were undergoing psychotherapy, and all interventions were longer than 2 months. No patient received further medications. tDCS (anode: left DLPFC; cathode: right supraorbital; sponge size 35 cm^2; five stimulations in 5 days; 2 mA, 30 min, 15 s fade-in/fade-out) was performed with an Eldith DC stimulator (neuroConn GmbH, Ilmenau, Germany). All patients were informed to receive active stimulation; there was no sham condition.

For assessment, Edinburgh Handedness Test (EHT), Vertigo Symptom Scale (VSS), Dizziness Handicap Inventory

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(DHI), Beck Depression Inventory (BDI), and Hospital Anxiety and Depression Scale (HADS) were used. Measurements were performed at baseline before first stimulation (D1) (EHT, VSS, DHI, BDI, and HADS), before each stimulation on days D2–D4 (BDI, HADS) and after fifth stimulation (D5) (DHI, BDI, and HADS) and at follow-up examinations 1, 2, and 4 weeks after stimulation (FU1, FU2, and FU3) (DHI, BDI, and HADS).

Analysis of variance for repeated measures (rmANOVA; within-subject factor: time) was performed for DHI, BDI, and HADS sum scores. Greenhouse–Geisser correction and F value correction by a factor Epsilon (ε) were applied. Pearson's correlation coefficient was calculated for VSS and BDI at D1. DHI at D1, D5, and FU1–FU3 was correlated with mean age, HADS anxiety, and HADS depression at the five timepoints. Level of significance was Bonferroni-corrected to $p \leq 0.016$.

One left-handed and seven right-handed patients completed the study (mean age was 45.6 ± 12.3 years, range 24–59 years; demographic data: Table 1). Mean VSS score at baseline was 59.4 ± 26.5; VSS subscales "vertigo and related symptoms" were 32.5 ± 14.5 and and 26.8 ± 12.8, respectively, for "somatic anxiety and arousal". DHI score significantly decreased during tDCS treatment (D1: 48.8 ± 26.9; D65: 34.0 ± 22.7; $p = 0.03$), but showed no significant differences between D1 and FU1 ($p = 0.60$), FU2 ($p = 0.69$), and FU3 ($p = 0.31$) (Fig. 1a). Mean HADS score (Fig. 1b) decreased non-significantly (D1: 16.3 ± 9.0; D5: 12.6 ± 7.7; FU3: 10.6 ± 7.2; $p = 0.18$–1.00). An exploratory analysis of HADS anxiety subscale scores showed no significant changes over time ($p = 0.15$–1.00). BDI (D1: 15.3 ± 11.1; D5: 14.3 ± 10.1; FU3: 12.9 ± 8.4) did not show a significant change ($p = 1.00$) (Fig. 1b).

RmANOVA for level of dizziness (within-subject effect: DHI sum score D1–FU3) revealed no significant time effect ($F = 4.227$, $df = 1.369$, $\varepsilon = 0.342$, $p = 0.059$) and no significant effect in depressive symptoms (within-subject effect: BDI sum score D1–FU3; $F = 2.472$, $df = 1.947$, $\varepsilon = 0.353$, $p = 0.166$). A significant time effect was observed for HADS sum score (timepoints: D1–FU3; $F = 4.134$, $df = 7$, $p = 0.001$).

Severity of dizziness in the DHI scale (D1–FU3) was not correlated with mean age ($r = -0.390$–0.325; $p = 0.66$–0.93), to age > 50 years ($r = -0.461$–0.058; $p = 0.69$–0.96), or to age < 50 years ($r = -0.130$–0.526; $p = 0.36$–0.83). VSS, respectively, and its subscales "vertigo and related symptoms" and "somatic anxiety and arousal" showed a low correlation to BDI at baseline ($r = 0.284$–0.334; $p = 0.54$–0.70) and to HADS at baseline ($r = 0.030$–0.075; $p = 0.67$–0.92). Decrease of DHI (D1–FU3) showed mostly moderate-to-high correlation to the decrease in HADS anxiety (D1–FU3) ($r = 0.469$–0.858; $r = 0.006$–0.236) and in HADS depression over timepoints (D1–FU3) ($r = 0.455$–0.860; $p = 0.006$–0.142).

Side effects were mild, five patients reported itching sensation under the electrodes, each one patient reported perception of phosphenes, respectively, mild headache, and two patients reported transient increase of vertigo after stimulation and fading within 1 h.

In this first open label pilot study, eight PPV patients treated with left prefrontal anodal tDCS over 5 days showed a significant reduction in DHI sum scores. These effects were transient and significant results could only be achieved for DHI during treatment period. Anxiety or depression ratings also improved moderately, however, not significantly. Correlated changes in DHI and HADS subscales might indicate the potential relationship between enhancement of prefrontal cognitive control over anxiety and reduced vertigo symptoms. These results have to be interpreted cautiously due to the lacking significance, the lacking sham control, the small sample size, and a potential placebo effect. They should be seen as hypothesis driving for further controlled, randomized trials exploring the impact of tDCS in the treatment of PPV.

Table 1 Demographic data of patients ($n = 8$) and clinical data at baseline

Subject	Sex (M/F)	Age (years)	Handedness (%)	Education (years)	Tobacco abuse	Illicit drug abuse	VSS (total score)	DHI (total score)	BDI	HADS (total score)
1	F	29	100	10	No	No	65	84	20	16
2	M	49	100	10	No	No	46	66	20	24
3	M	53	100	12	No	No	6	18	3	9
4	F	24	90	12	Yes	No	57	46	21	22
5	M	49	100	8	No	No	76	72	32	28
6	M	49	100	8	No	No	2	12	5	10
7	M	59	100	8	No	No	92	28	3	1
8	F	53	−90	10	No	No	81	64	18	20

VSS Vertigo Symptom Scale, *DHI* Dizziness Handicap Inventory, *BDI* Beck Depression Inventory, *HADS* Hospital Anxiety and Depression Scale

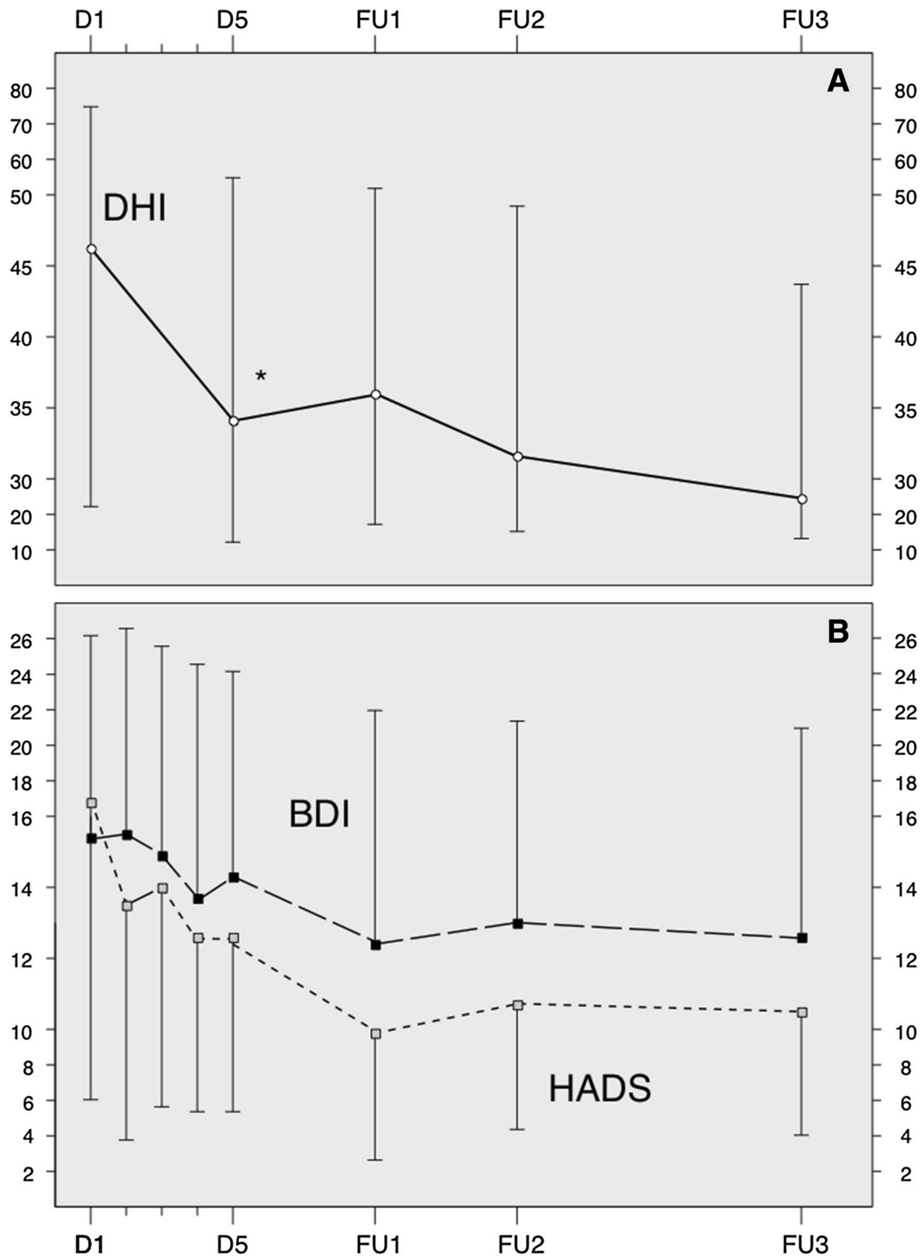

Fig. 1 Depiction of mean Dizziness Handicap Inventory (DHI; **a**), Hospital Anxiety and Depression Scale (HADS; **b**) and Becks Depression Inventory (BDI; **b**) sum scores and their standard deviation over the different timepoints. Measurements were performed at baseline before first stimulation (D1), before each stimulation on days 2–4 (D2–4), after fifth stimulation (D5) and at follow-up (FU) examinations 1, 2, and 4 weeks after end of stimulation (FU1, FU2, and FU3). Asterisk indicates significant results

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Compliance with ethical standards

Ethical standards This study was performed in accordance with the Declaration of Helsinki. All participants gave written informed consent prior to enrolment. This open label study is a precursor of a randomized double blind clinical trial, approved by the local ethics committee and registered at German Clinical Trials Register (DRKS00011844).

Conflict of interest U. P., D. K., and F. P. received paid speakership from neuroCare Group, Munich, Germany. U. P. has a private practice with neuroCare Group, Munich, Germany. The other authors declare that they have no competing financial interests regarding this study.

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