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LETTER TO THE EDITOR

Non-invasive electrical brain stimulation induces vision restoration in patients with visual pathway damage

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Dear Editor,

Non-invasive electrical stimulation may diminish functional deficits of visual perception. This concerns not only the application of transcorneal electrical stimulation (TES) in patients with retinal and optic nerve disease as reported by Gekeler and Bartz-Schmidt [1] but also non-invasive transorbital alternating current stimulation (ACS). Basic stimulation parameters of TES and transorbital ACS are similar since in both approaches current intensity is individually adjusted according to how well patients perceived phosphenes. TES evidence was obtained in a recent randomized study with patients suffering from retinitis pigmentosa [2].

Here, we wish to add further aspects that were not considered by Gekeler and Bartz-Schmidt. Firstly, non-invasive electrical stimulation has shown therapeutic efficacy in diminishing functional deficits of visual perception in patients with optic nerve disease when non-invasive transorbital ACS is applied [3–6]. Second, visual cortex excitability and related performance changes induced by transcranial direct current stimulation (tDCS) indicate that visual system functions can be altered by non-invasive currents [7].

Clinical findings of non-invasive transorbital alternating current stimulation In transorbital ACS weak current pulses well below 1.000 μA that elicit phosphene perception are delivered through electrodes that are placed at or near the right and left eye with eyes closed. In single case and clinical observations it was shown that transorbital ACS may reduce the defect depth and/or enlarge visual fields in patients with optic nerve damage well after the period of spontaneous recovery has been completed [3, 5]. We then carried out a prospective, double-blind, randomized, placebo-controlled clinical trial to assess the efficacy of transorbital ACS to improve visual functioning in patients with optic nerve damage [6]. In this trial, 22 patients with optic neuropathies were treated for 40 min daily (approx. 20 min per eye) for 10 days either with transorbital ACS or placebo-stimulation. In patients treated with transorbital ACS, the visual field detection deficit as well as visual processing speed significantly improved after the stimulation period and improvements in some perimetry parameters were maintained at a 2-month follow-up [6]. Patient-reported outcomes revealed that increases of detection ability in the scotoma were associated with improvement in the patients' vision-related quality of life as assessed by standard questionnaires (National Eye Institute – Visual Functioning Questionnaire) [4].

EEG-power-spectra analysis showed significantly increased alpha-activity, especially in occipital sites following ACS [6, 8]. It is assumed that electrical current stimulation at predetermined frequencies forces neuronal networks to propagate synchronous firing, which may induce a learned synchronization response in the brain, probably including residual areas surviving the injury. This idea of a "re-learned

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synchronization response" is compatible with the observation that synchronization can be entrained by external, transcranial-pulsed stimulations and such alpha entrainment has already been observed in normal subjects [9]. As a consequence of increased synchronization the injured visual system may react more sensitively to the reduced input and phosphene thresholds are lowered. A similar situation is probably present when spontaneous visual phosphenes occur during natural or training-induced recovery phases [10, 11].

Transcranial direct current stimulation in healthy subjects modulates visual cortex excitability tDCS is another stimulation technique that can alter cortical functions by modulation of spontaneous activity and excitability [12] leading to alterations in intracellular cAMP levels and calcium influxes [13, 14]. Generally, given a sufficiently long stimulation duration and adequate stimulation intensity, anodal stimulation increases neuronal excitability, while cathodal tDCS reduces it [15]. In healthy subjects, tDCS applied over visual areas induces changes in phosphene, contrast and motion perception thresholds and modifies the amplitude of visual evoked potentials. This suggests that anodal and cathodal stimulation can change the excitability of the visual cortex [16–19, for a recent review see 7]. tDCS-induced neuroplastic visual cortex changes in healthy subjects are in line with the observation of improved visual functions in patients after application of phosphene-generating current impulses. Recently, Olma et al. [20] provided additional evidence demonstrating the ability of anodal tDCS over the visual cortex in normal subjects to improve detection sensitivity for visual targets in a discrimination task. Whether tDCS has a positive impact on vision restoration in patients with damaged visual pathways is still an open question. Recent studies have shown that the combination of occipital anodal tDCS with visual field rehabilitation appears to enhance visual functional outcomes compared with visual rehabilitation alone [21, 22].

Finally, the more fundamental lesson to learn from these observations is that the damaged visual pathway has more potential for recovery and restoration then recently thought, even long after injury to the visual pathway has occurred. However, the extent of intra-individual change in vision parameters varies, which is common in neurorehabilitation. Thus, outcome may depend on the functional level that is available post lesion. The probability to achieve vision restoration seems to be a function of the residual visual capacities of the damaged system, which may predict functional outcome [23]. Future studies are required to optimize the stimulation parameters and explore the mechanisms of vision restoration as induced with methods such as TES and transorbital ACS to enhance recovery.

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Conflict of interest The authors declare that they have received financial support from EBS Technologies GmbH (Kleinmachnow, Germany) for performing studies in their university institution. B. A. Sabel is shareholder of EBS Technologies GmbH (Kleinmachnow, Germany), manufacturer of the alternating current stimulation device used in some cited studies [4, 6].

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