Title: Effects of the vestibular rehabilitation combined with transcranial cerebellar direct current stimulation in patients with chronic dizziness: An exploratory study

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Abstract:

Background: Vestibular rehabilitation is a useful approach for chronic dizziness in patients with intractable vestibular dysfunction. It can induce neuronal plasticity in the central nervous system, especially in cerebellum, to promote vestibular compensation. Recently, transcranial cerebellar direct current stimulation (tcDCS) has been reported to enhance cerebellar function.

Objective: We investigated whether the vestibular rehabilitation partially combined with tcDCS could more efficiently reduce dizziness than rehabilitation alone.

Methods: Patients with chronic dizziness by vestibular dysfunction received the rehabilitation concurrently with either 20-min tcDCS or sham stimulation for 5 days. Before and 1 month after the intervention, we evaluated Dizziness Handicap Inventory (DHI) scores, other psychometric and motor parameters.

Results: 16 patients completed the study. The DHI scores were significantly improved in the tcDCS group, than in the sham group (Mann-Whitney's U test, p=0.033).

Conclusion: The vestibular rehabilitation partially combined with tcDCS might be a promising approach.

Keywords: transcranial cerebellar direct current stimulation, vestibular rehabilitation, chronic dizziness, motor learning

Introduction:

Vestibular rehabilitation is used for management of chronic vestibular dysfunction [1, 2]. The mechanism is neuroplastic changes to compensate vestibular impairments in central nervous system, in which cerebellum readjusts the central processing of vestibular inputs [3]. Transcranial cerebellar direct current stimulation (tcDCS) can enhance cerebellar function and motor learning [4-6]. Here, we investigated whether the vestibular rehabilitation combined with tcDCS could be more effective than rehabilitation alone.

Methods:

An exploratory, single-blind, randomized controlled study was conducted. Thirty patients were recruited in the Departments of Ear Nose and Throat of the Tokyo National Medical Center and randomized into either of tcDCS group (n = 15) or sham group (n = 15). Six patients in the tcDCS group and 8 patients in sham group were lost to follow-up. The final sample on which data analyses were conducted included 16 patients (10 females), aged 41 to 73 years (mean±SD; 62.7 yrs ± 9.0). All the patients had chronic dizziness continued for at least 6 months (92.0 months ± 73.8) by unilateral vestibular dysfunction (5 vestibular neuritis, 8 sudden deafness, 1 endolymphatic hydrops, 1 Ramsay Hunt syndrome, 1 removal of acoustic neuroma). Exclusion criteria was orthopedic limitations, metallic implants, a history of head trauma or epilepsy. All patients stopped anti-dizziness medications before the study.

The study was approved by the ethical committee (R14-120), and written informed consent was obtained from all participants.

The patients in both groups underwent the Dizziness Handicap Inventory (DHI) grouped into three domains of functional, emotional and physical aspects to measure dizziness impact on daily-life [7, 8], the State-Trait Anxiety Inventory (STAI) [9], the Self-rating Depression Scale (SDS) [10], the timed up and go test (TUG) [11] and static posturography measuring total shift length (LNG) and enveloped area (EA) of the center of gravity with eye-opened conditions. They were evaluated before the intervention (pre) and 1 month after the intervention (post).

Interventions:

For 5 days, all patients received tridaily 25-min vestibular rehabilitation which was separated by 4 hours. TcDCS or sham stimulation was given concurrently with the 1st rehabilitation. For tcDCS, 2 mA of electrical constant direct current was delivered for 20 min through rectangular saline-soaked sponge electrodes: the anode was centered on the median line 2 cm below the inion with its lateral borders medial to the mastoid apophysis (over the cerebellum) (5×10 cm) and the reference (cathode) over the right arm (5×7 cm) since previous studies reported that 2mA could influence cerebellar activities [12, 13] and that the montages whose electrical intensity was maximum on the cerebellum [4-6]. For sham stimulation, electrodes

montage was the same as real stimulation, but the currents were given during the first 30 seconds. The rising and falling time was 10 seconds each. We used anodal tcDCS so that it enhanced motor functions [14-16] although the polarity effects were inconsistent [17-19].

Statistics:

All data were represented by mean ± SD values. A responder value was defined as at least a >1 point improvement on DHI scores. The improvements in both groups was compared using the Mann-Whitney *U* test. In addition, changes in psychometric parameters, TUG and posturopraphy in both groups were compared using the Mann-Whitney *U* test and Student's *t*-test, respectively. Normality of changes in TUG and posturopraphy was assessed by Shapiro–Wilk test. Differences were considered significant when the probability (*p*) of a type I error was .05 or less. The JMP statistical package (SAS Institute Inc., U.S.A) was used for all analyses.

Results:

No patients reported skin irritation and other adverse effect of the stimulation.

The baseline scores were following: DHI physical, 16.2 ± 5.7 and 14.6 ± 6.4, DHI emotional 19.6 ± 8.7 and 18.0 ± 6.1, DHI functional 19.1 ± 11.4 and 17.1 ± 7.4, DHI total 54.9 ± 22.3 and 49.7 ± 11.9, STAI state anxiety 52.7 ± 12.1 and 51.0 ± 11.0, STAI trait

anxiety 50.6 ± 12.6 and 45.3 ± 9.4, SDS 49.0 ± 10.5 and 43.9 ± 9.5, TUG 7.5 ± 1.2 and 9.8 ± 6.0 sec, LNG 110.3 ± 35.9 and 135.4 ± 56.1 cm, EA 4.5 ± 3.1 and 6.5 ± 3.5 cm^2 in the tcDCS and sham group, respectively.

Figure 1 represented the changes of physical, functional and total scores of DHI in both group. They were significantly improved in the tcDCS, compared with the sham group (physical, $p = 0.017$; functional, $p = 0.047$; total scores of DHI, $p = 0.033$). The other psychometric and motor parameters was not significantly different between the tcDCS and sham group ($p > 0.05$).

Discussion:

We found that the vestibular rehabilitation partially combined with tcDCS had a greater effect on reduction of dizziness in daily life of patients with chronic unilateral vestibular dysfunction than rehabilitation alone. To our knowledge, this is the first report about the vestibular rehabilitation using brain stimulation.

In the present study, the DHI physical and functional scores were significantly reduced in the tcDCS group. The handicaps are related to the both scores and less to emotional scores [20]. The tcDCS would be efficient to reduce dizziness and ADL handicaps in patients.

The cerebellum is important for sensory and error prediction and appropriate motor

outputs in motor learning [21]. Through enhanced cerebellar plasticity [4, 6], our rehabilitation might have promoted the curative processes such as habituation to reduce abnormal responses, adaptation for visual-vestibular interaction, substitution of sensory inputs for dysfunctional vestibular inputs and acquisition of reinforced postural controls [2]. The posturography data showed no difference between the tcDCS and sham groups. It suggested that body sways might not be changed but re-adaptation be reinforced so that they did not feel dizzy since anodal tcDCS enhanced adaptive motor learning to form a forward internal representation of movements [15, 19, 22-25]. More detailed investigations such as vestibulo-ocular reflex gain would be necessary.

The anodal electrode might not directly affect the brainstem because electrical field amplitude is sharply decreased in a deeper portion [26-28].

The limitation of this study is a small number of patients. A trial with more number of patients is warranted.

Acknowledgements:

This study was partly supported by a Grant-in-Aid for JSPS Fellows (16J40201), a Grant-in-Aid for Young Scientists (B) (26870321) from the Japan Society for the Promotion of Science, a the research grant (2015) from the Nakatomi Foundation (to S.K.), a Grant-in-Aid for Scientific Research (B) 15H03044, a Grant-in-Aid for Scientific Research on Innovative Areas

(15H05880, 15H05871) from the Japan Society for the Promotion of Science, STEP2 (27280201) and 2736040 from the Japan Agency for Medical research and Development, AMED (to T.M.).

The authors declare no competing financial interests.

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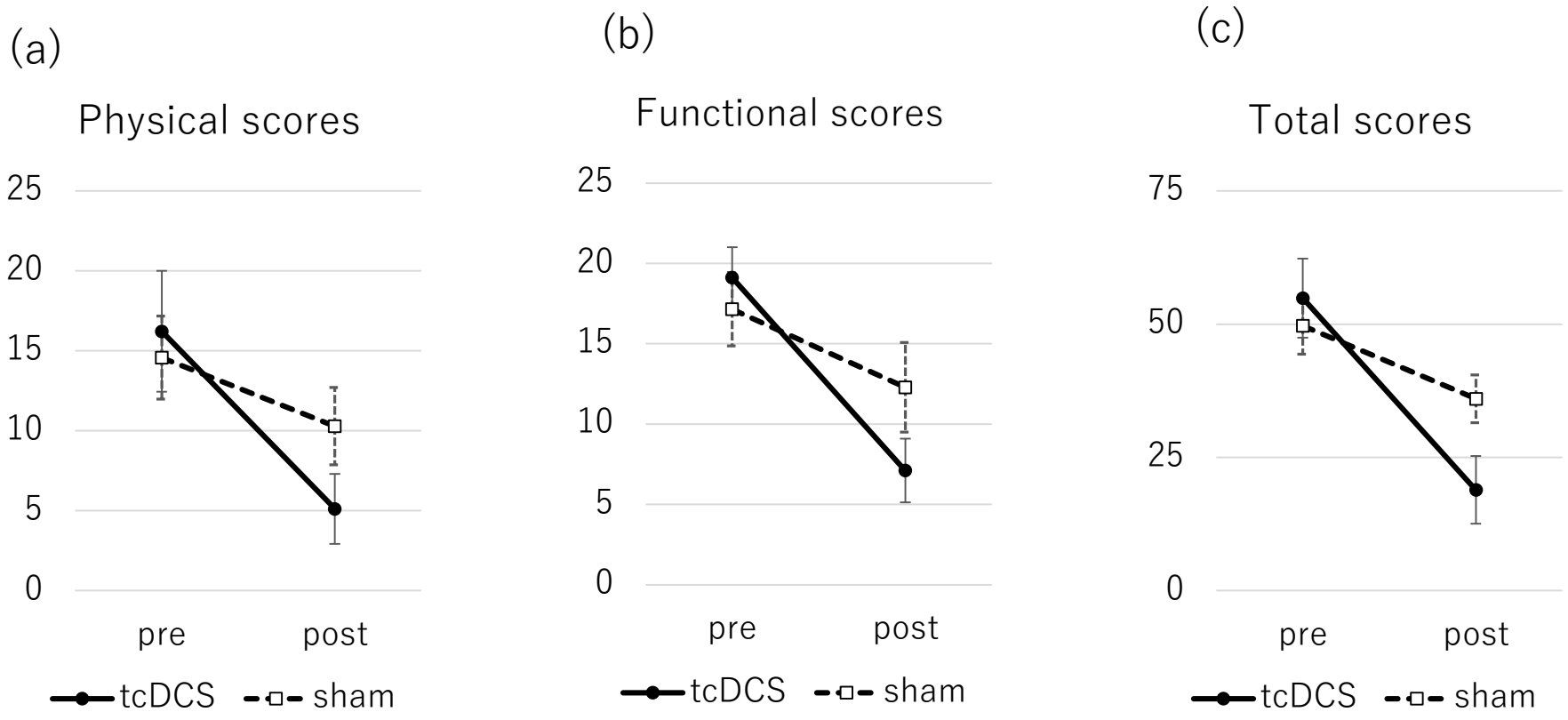
Figure legends:

Figure 1 *Changes of DHI scores in the tcDCS and sham groups*

The DHI physical (a), functional (b) and total scores (c) were chnaged after the intervention in the tcDCS group and sham group.

Figure 1: Changes of DHI scores in the tcDCS and sham groups



(error bars represent SEM)