Case Report
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A Functional Domain Based Approach in Neurocognitive Rehabilitation with Transcranial Direct Current Stimulation: A Case Report

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Transcranial direct current stimulation (tDCS) is a novel brain stimulation technique which has kindled hope in alleviating motor, language as well as cognitive deficits in neuronal injury. Current case report describes application of tDCS in two phases using two different protocols in a patient with hypoxic injury. In the first phase anodal stimulation of dorsolateral prefrontal cortex improved the language fluency. Subsequently, after 6 months second phase application of anodal stimulation over posterior parietal region targeted arithmetic and working memory deficits. Individualising the treatment protocols of brain stimulation, based on the lesion and the functional deficits, for neuro-rehabilitation is emphasised.

KEY WORDS: Transcranial direct current stimulation; Hypoxic ischemic encephalopathy; Acalculia; Language fluency; Dorsolateral prefrontal cortex; Posterior parietal cortex.

INTRODUCTION

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation method known to modulate neuroplasticity,[1] and is used in motor, cognitive and language rehabilitation in stroke.[2,3] Given the heterogeneity of deficits with neurovascular insult,[4] individualizing treatment protocols would be necessary. In this case report, we describe the first successful application of tDCS in a patient with cerebral hypoxic ischemia to treat significant language and cognitive deficits. The novelty of this report is that we implemented functional domain based tDCS, using two different tDCS treatment protocols (separated by a period of 6 months) to address the varying nature of the predominant cognitive deficit profiles over the course of one year.

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CASE

A 43 year old, right handed male, mechanical engineer, presented with a history of sudden cardiac arrest secondary to anterior wall myocardial infarction leading onto hypoxic ischemic encephalopathy. Magnetic resonance imaging during the episode showed restriction of diffusion involving the cortical ribbon in both parietal lobes and faint hyperintensities on fluid-attenuated inversion recovery (FLAIR) images. Behavioral and cognitive disturbances emerged following revival from acute state. Behavioral disturbances responded to psychotropic drugs (quetiapine 400 mg/day, valproate 1,000 mg/day, clonazepam 0.5 mg/day with ramipril 5 mg/day, metoprolol 25 mg/day, asprin 75 mg/day, and atorvastatin 10 mg/day) over the next few months. However, cognitive disturbances remained apparent thereafter, causing significant socio-occupational dysfunction in the absence of mood disturbances. The patient presented with predominant complaint of difficulty in engaging in a meaningful conversation.

A detailed clinical evaluation and neuropsychological assessment was conducted with category fluency test (CFT), trail making test (A and B), digit span, spatial span, letter number sequencing, controlled oral word association test (COWA), and mini-mental state examination (MMSE). Tests revealed a poor attention span, poor language comprehension and fluency with features suggestive of Gerstmann syndrome. An inability to perform in most of the assessments secondary to the above deficits was noted. As the medications and behavioral techniques failed in engaging the patient in cognitive retraining processes even after 6 months of the event, brain stimulation with tDCS was considered.

tDCS Phase-1

The first phase of tDCS was administered in June 2015. The patient and his primary caregiver were provided with adequate information regarding the tDCS procedure, and a video of the procedure was shown; following this, the patient agreed to participate in the tDCS sessions. We adhered to the ethical principles for medical research involving human subjects as per the World Medical Association Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/). A written informed consent was taken. The anode (35 cm^2 in size) was placed over the left dorsolateral prefrontal cortex (DLPFC; F3 of 10-20 system). A larger electrode (54 cm^2 in size) was used as the cathode and placed above the right eye-brow. Sessions were administered twice a day for 10 days using a standard equipment (TCT device model: M101-R-2012-V1.3; www.trans-cranial.com). The current intensity was set at 2 mA and each session was 20 minutes long. An improvement was noted in fluency in both categorical fluency test and controlled oral word association test after tDCS. However, the MMSE score remained at 16 with impaired working memory (Table 1).

COWA was applied for assessing phonemic fluency and CFT for semantic fluency. The normative score for the age, sex and education of the patient will be around 33.8±12.3 for COWA and 13.3±3.4 for CFT.[5] Thus implying larger deficits in phonemic fluency. Initial smaller improvement was noted in phonemic fluency with tDCS, which showed a significant leap in the six month (possibly with added vocabulary self-training adapted by the patient) (Table 1). The semantic fluency remained within normal limits after tDCS session, though the situation related performance fluctuations could be noted across the testing sessions. But overall clinical improvement in speech fluency and conversational skills with re-acquisition of language abilities, both subjective and objective were significant and incremental by 1st and 6th month follow-up. In the meantime, his motivation had improved significantly; he participated enthusiastically in the recovery process and persistently engaged in self-training by using dictionary to regain the vocabulary and lost language skills.

tDCS Phase-2

The second tDCS protocol was administered in January 2016. While the patient had shown significant improvement in language function, major deficits in arithmetic skills as well as working memory persisted with secondary functional impairment. Persisting deficits in gestalt ability, constructional apraxia and left-right disorientation were also noted on clinical evaluation. Targeting the predom-

Table 1. Neurocognitive scores across the two transcranial direct current stimulation (tDCS) treatment

Test	Pre 1st tDCS (16/6/2015)	Post 1st tDCS (26/6/2015)	FU 1st tDCS (13/7/2015)	Pre 2nd tDCS (7/1/2016)	Post 2nd tDCS (18/1/2016)
MMSE	16	17	16	21	23
DS	6	8	6	7	7
SS	10	11	13	13	12
COWA	9	11	8	24	24
CFT	7	13	11	9	9
LNS	4	3	3	2	2
TMT-A	4 min 55 sec	2 min 24 sec	3 min 11 sec	1 min 54 sec	1 min 32 sec
TMT-B	-	-	-	-	5 min 12 sec

Pre 1st tDCS, baseline; post 1st tDCS, after 1st tDCS phase; FU 1st tDCS, follow-up at 1 month of 1sttDCS phase; Pre 2nd tDCS, follow-up at 6 months of 1st tDCS protocol & before 2nd tDCS phase; Post 2nd tDCS, after 2nd tDCS phase.
MMSE, mini-mental state examination; DS, digit span; SS, spatial span; COWA, controlled oral word association test; CFT, category fluency test; LNS, letter number sequencing; TMT-A and TMT-B, trail making test part A and B.

Table 2. Neurocognitive scores in arithmetic, computerized DSST and mental rotation tests across the 2nd phase of tDCS treatment

SN.	Test	Pre 2nd tDCS (7/1/2016)	Post 2nd tDCS (18/1/2016)	FU 1 month (16/2/2016)	FU 3 months (11/4/2016)
1	Informal test (maximum score 6)	3	5	5	5
2	Digit forward	3 digits	4 digits	4 digits	4 digits
3	Digit backward	2 digits	2 digits	2 digits	3 digits
4.a	Forward digit (80-120) count: time taken	48 sec	40 sec	40 sec	30 sec
4.b	Forward digit (80-120) count: errors	2	0	0	0
5.a	Backward digit (120-80) count: time taken	187 sec	80 sec	70 sec	50 sec
5.b	Backward digit (120-80) count: errors	18	1	2	1
6.a	Numerosity sets-brief (each in 5 sec) numerosity estimate in 5 sets:approximate counting error	110	28	27	28
7.a	Numerosity sets-infinite time numerosity estimate in 5 sets: counting error	12	13	17	16
7.b	Numerosity sets-infinite time numerosity estimate in 5 sets: time taken	96	110	153	107
8	Digit-line comprehension: estimate number on a mark on the line (maximum score 5)	2	3	5	5
9	Digit-line comprehension: marking number on a line (maximum score 5)	2	2	4	5
10.a	Ordering the numbers (2 sets):total time taken	270 sec	452 sec	330 sec	312 sec
10.b	Ordering the numbers (2 sets): total errors	4	0	0	0
11	Transcode (written to reading) & (reading the written) (maximum score 4 each=8)	8	8	8	8
12	Mental arithmetic (addition and subtraction) (could not perform multiplication and division)	1 digit only	1 digit only	1 digit only	1 digit only
13	Verbal arithmetic puzzle	0	1 digit only	1 digit only	1 digit only
14	Written arithmetic	1 digit only (Addition and subtraction multiplication and division)	Maximum 3 digits - Addition and subtraction 1 digit only- multiplication and division	Maximum 3 digits- Addition and subtraction 1 digit only- multiplication and division	Maximum 3 digits- Addition and subtraction 1 digit only- multiplication and division
15	Arithmetic rule application (maximum score 4)	2	3	3	3
16.a	Computerized DSST: correct response	48	70	69	NA
16.b	Computerized DSST: average reaction time	10.65 sec	3.50 sec	3.81 sec	NA
17.a	Computerized mental rotation test-human percepts: correct response (maximum score 96)	37	44	43	NA
17.b	Computerized mental rotation test-human percepts: correct response (maximum score 96)	31	34	31	NA

DSST, digit symbol substitution test; tDCS, transcranial direct current stimulation; SN., serial number; Pre 2nd tDCS, before 2nd tDCS phase; Post 2nd tDCS, after 2nd tDCS phase; FU 1 month, follow-up after 1 month of 2nd tDCS phase; FU 3 months, follow-up after 3 months of 2nd tDCS phase; NA, not available.
See the Supplementary details (online) for this table.

inant arithmetic deficits, left posterior parietal (PP; P3 of 10-20 system) anodal stimulation was considered this time with cathode above left eye brow. Both the electrodes were 35 cm^2 in size.[6] This second tDCS protocol had other stimulation parameters similar to the first, and was again administered for 10 days with a different standard equipment (Neuroconn DC Stimulator Plus, http://www.neuroconn.de/dc-stimulatorplus/).

Neurocognitive assessments for arithmetic skills (Table 2) were undertaken using a special battery (consisting of 15 different tests adapted from numerical activities of daily living,[7] and proposed extension of EC301 battery by Ardila and Rosselli,[8] applied in a standard method on all the assessments) and spatial orientation by computerized mental rotation tasks[9] were tested before and after 10 days of tDCS and repeated during follow-up at 1st and 3rd month. Fluency for numbers (errors and time taken in digit forward and backward count) and numerosity (errors in estimation in a brief duration) showed significant improvement; there were concurrent improvement in constructional (clock and vase drawing) and gestalt perception (ordering and reading spaced words) abilities as well. These reflected in faster and more accurate verbal arithmetical operations and ability to gauge the rules. But time taken in tasks of evaluating numerosity for infinite duration and ordering numbers increased, possibly due to increased awareness of deficits and striving for perfection. Spatial orientation, tested by computerized mental rotation tasks showed good improvement in human percepts (correct response: pre-tDCS −77% to post-tDCS −92%) but not much for alphabetical letters and numbers (pre-tDCS −65% to post-tDCS −70%). He was able to perform the B part of trial making test for the first time, with minimal errors. Constructional ability improved with improvement in hand-writing. Upon first and third month follow up, the initial enhancements persisted with added enhancement in the ability in digit-line comprehension with near perfect scores. During the latest visit, working memory deficits as noted by digit span test (7) still persisted, impacting upon difficulties in mental arithmetic and hence the complex multiplication and division. The improvements reflected in enhancement of daily life activities in shopping, independent transportation and using electrical and technical devices. Motivation to retrain oneself for remediation of deficits emerged after first session of tDCS and currently being utilized for vocational rehabilitation.

DISCUSSION

Above case report describes the utility of tDCS in a patient with significant neurocognitive deficits secondary to hypoxic injury involving bilateral parietal cortex and its neuronal networks. Initial tDCS sessions targeting left DLPFC improved verbal fluency and attention. The second phase of tDCS targeting left PP brought changes in arithmetic abilities along with other complex cognitive abilities like construction ability, cognitive flexibility, and spatial orientation. This, to our knowledge is the first case reporting the successful use of anodal tDCS of posterior parietal region targeting acalculia.

In the first phase, anodal tDCS was applied to left DLPFC, as its activity is known to play a major role in post-stroke recovery, especially in non-fluent aphasia and cognitive deficits.[10] The left DLPFC acts as a compensatory and modulatory area for different regions involved in neurocognition including parietal lobe.[11] Enhancement of adaptive neuroplasticity by tDCS could be the mechanism underlying these changes. Neuroplastic processes sets in soon after acute cerebrovascular insult to continue till the achievement of recovery. Axonal regeneration and dendritic sprouting are known to occur at the initial part of spontaneous recovery.[12] Reorganization by remapping of the affected functional domain onto a non-lesional area would help in adaptive neuroplastic process after a brain insult in the later part.[12] tDCS sessions thus could have ignited the process of adaptive neuroplasticity as noted in progressive improvement till the end of 6 months.

The impact on deficits in behavioral inhibition, attentional system and general conversational abilities was noted with the first protocol. The core defects of parietal functions remained impaired, given the bilateral involvement of parietal cortices. In the view of prominent arithmetic deficits at the end of 6 months of first phase of tDCS, stimulation was considered over the peri-lesional area. Dominant hemisphere is known to mediate number processing and calculation abilities.[13] Left cathodal and right anodal oppositional tDCS of inferior parietal lobe/angular gyrus has been shown to impair numerical processing[13] as did inhibitory trans-cranial magnetic stimulation on number comparison performance.[14] Direct and oscillatory current stimulation studies on healthy controls demonstrated causal involvement of left posterior parietal cortex in arithmetic learning and arithmetic performance.[15,16] Though bilateral parietal damage was apparent in imaging and functioning, in view of above studies, anodal stimulation of left posterior parietal lobe was considered.

Attribution of improvement to tDCS could be challenged with the natural process of spontaneous recovery, but dysfunction prevalent for months before tDCS showed temporal correlation in its improvement with the tDCS. Also, the practice effect of the repeated assessments would have contributed to the change. An improvement in stagnant functional changes could definitively be attributable to 1st protocol and the differential montage specific improvements with the two protocols suggest the possible effect of tDCS. But, the lack of repeated structured neuropsychological assessments prior to tDCS remains a limitation of this report.

Communication skills, which forms a key focus in stroke rehabilitation,[12] improved after the first tDCS application. The second tDCS phase improved the basic arithmetic skills supporting the independence of living and initiation for vocational retraining. Modulating neuroplasticity by stimulation of two different brain regions resulted in improved neurocognitive and daily living functioning.[12] Personalizing tDCS with protocols specifically targeting the impairments could hold a significant neuro-rehabilitation potential.

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