Feasibility of Cerebellar Transcranial Direct Current Stimulation to Facilitate Goal-Directed Weight Shifting in Chronic Post-Stroke Hemiplegics

Shashi Ranjan, Zeynab Rezaee, Anirban Dutta, and Uttama Lahiri, *Member, IEEE*

***Abstract*— Neurological disorder such as stroke can adversely affect one's weight-bearing symmetry leading to dysfunctional postural control. Recovery after stroke is facilitated through functionally-relevant neuroplastic modulation. Functionally-relevant cerebellum coordinates voluntary movements. Specifically, the dentate nuclei and lower limb representations (lobules VII-IX) of the cerebellum are involved in error-correction, crucial for postural control. It is postulated that cerebellar transcranial direct current stimulation (ctDCS) of the dentate nuclei and lobules VII-IX can modulate postural control in chronic stroke survivors. The objectives of this work were to (1) present a refined Virtual Reality (VR)-based balance training platform (VBaT) that can measure Center of Pressure (CoP) and (2) carry out a study to understand the implication of ctDCS stimulating the dentate nuclei (Phase$_D$) and lobules VII-IX (Phase$_L$) on the postural control of chronic stroke patients when they interacted with VBaT. Also, we investigated whether hemiplegic patients (with intact cerebellum) having Basal Ganglia (BG) infarction had any differential abilities to correct postural sway from those with no BG infarction (while shifting weight to the Affected side). Results of a single-session single-blind crossover study on randomized Phase$_D$ and Phase$_L$ stimulation (with an intermediate resting state bipolar bilateral ctDCS) on 12 chronic hemiplegic patients on separate days indicated differentiated findings (post stimulation) on CoP-related indices. We observed an incremental effect on one's postural control during Phase$_D$ and inhibitory effect on the dentate nuclei during Phase$_L$. Clustering analysis showed that those with BG infarction demonstrated poor postural control and deficit in error correction ability irrespective of the ctDCS Phase.**

***Index Terms*— Cerebellar transcranial direct current stimulation, postural control, stroke, virtual reality.**

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Shashi Ranjan and Uttama Lahiri are with the Department of Electrical Engineering, Indian Institute of Technology Gandhinagar, Gujarat 382355, India (e-mail: shashi.r@iitgn.ac.in; uttamalahiri@iitgn.ac.in).

Zeynab Rezaee was with the Department of Biomedical Engineering, University at Buffalo SUNY, Buffalo, NY 14260 USA. She is now with the National Institute of Mental Health, Bethesda, MD 20892 USA (e-mail: zeynab.rezaee@nih.gov).

Anirban Dutta is with the Department of Biomedical Engineering, University at Buffalo SUNY, Buffalo, NY 14260 USA (e-mail: anirband@buffalo.edu).

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I. Introduction

One's ability to shift weight while standing and maintaining postural control during execution of activities of daily living are often adversely affected as a result of stroke [1]. In turn, this can lead to reduced autonomy and a high risk of fall [2] thereby affecting one's mobility, social presence and ability to earn livelihood. This can pose a socio-economic challenge given the global prevalence estimates of stroke as the third leading cause of disability [3]. About 85% of these patients experience hemiparesis immediately after stroke and ∼55% to 75% of them experience balance deficits [1] and exhibit weight bearing asymmetry, increased postural sway, etc. [4] while shifting weight during a standing balance task. Recovery after stroke is facilitated through functionally-relevant neuroplastic modulation [5] where the neuroplasticity refers to the ability of central nervous system to reorganize its structure, function and connections. Within the brain, the cerebellum is majorly involved via the cerebro-cerebellar network in making cortical adjustments as it modulates the command to motor neurons based on input received from vestibular receptors and proprioceptors. Also, the cerebellum plays a crucial role in planning and maintaining one's postural control [6] during a standing balance task. For this, the cerebellum has been postulated to use an error-driven algorithm leading to motor adaptation via Long-Term-Depression like plasticity of Purkinje cells [7]. In particular, this error-driven approach combines the feed-forward control by the cerebellum and feedback control by the cerebral motor cortex [6]. This in turn triggers the necessary output from the cerebellum [6], important for production of stable posture [8] and motor adaptation [9] that are adversely affected in post-stroke patients. Researchers have been investigating the contribution of cerebellar stimulation in post-stroke patients [10]–[12] towards motor adaptation and postural control.

One can electrically modulate the excitability of different regions within the cerebellum [13] by using Non-Invasive transcranial Direct Current Stimulation (tDCS *henceforth*). Previous research has shown the use of such technique for stroke patients (as therapeutic tool) to improve their motor ability [14] and to promote neuroplasticity [15]. The tDCS has emerged as an adjuvant therapeutic stimulant due to its low cost and ease of use [15]. Literature review indicates use of tDCS applied to different regions of the brain, such as Motor, Premotor and Supplementary Motor areas [16]–[18] in which researchers have shown that targeting the mid central region around the lower leg motor area can be beneficial for lower-limb motor functions. However, tDCS of the lower leg motor area can have bilateral effect on the lower limb muscles that is non-specific to single leg (e.g., in hemiplegia) and can result in their co-contraction [19]; thereby, facilitating maladaptive plasticity during post-stroke rehabilitation. Again, tDCS applied to the cerebellum (ctDCS *henceforth*) has been reported to facilitate cerebellar functions [20] by contributing to one's postural recovery [11]. This is possible since ctDCS can help modulate the cerebellar-M1 connections and has a facilitatory effect on M1 via disynaptic dentate-thalamo-cortical connection [21] with M1 being the lower limb representation in the motor cortex. A prior study [11] has looked to the contribution of ctDCS on motor adaptation and postural control of post-stroke patients. However, cerebellum has many functional sub-regions and lobule-specific ctDCS may be necessary. In principal accordance, we developed computational pipeline [22], neurophysiological testing, and portable neuroimaging approaches to evaluate the effects of lobule-specific ctDCS in line with [23], [24]. In this current study, we applied our computationally-derived ctDCS approach for stimulating specific functional regions of cerebellum to evaluate any differential effects on one's postural control.

In our present work, we have focused on investigating the implications of ctDCS applied to the dentate nuclei and the lower limb representations of the cerebellum (lobules VII-IX *henceforth*) on the postural control of post-stroke patients. We chose the dentate nuclei since it is the largest and most lateral of the four deep cerebellar nuclei (DCN *henceforth*) involved in planning and initiation of movements [25]. It receives the proprioceptive information from the spinocerebellar tract while premotor and supplementary motor cortices provide the planning and execution of movement-related information [25]. Also, it does error computation, necessary to maintain timing, balance and equilibrium [25]. Given the role of dentate nuclei in balance, researchers have been exploring the implication of ctDCS to the dentate nuclei on improving the standing balance of chronic stroke patients during visual tracking task [11]. Again, ctDCS of the dentate nuclei should have an excitatory effect on the disynaptic dentate-thalamo-cortical connection [23] with M1 and ctDCS of the Purkinje cells in the lobules VII–IX will have an inhibitory effect on the dentate nucleus [29]. This can cause differential implications on one's postural control – the goal of our present investigation. Also, since two of our participants (with intact cerebellum) had BG infarction, we wanted to see whether the patients can be clustered based on the implications of ctDCS on postural control ability. Rest of the paper is organized as follows: Section II describes the system design, Section III presents the experimental setup and procedure, Section IV discusses the results and Section V concludes our paper.

Given the importance of studying the differential effects of ctDCS to the dentate nuclei and the lobules VII-IX towards motor adaptation and postural control, in our study we have aimed to stimulate these two regions of the cerebellum in a crossover design. Our participants were chronic post-stroke patients (with intact cerebellum but with varying lesion areas, e.g., Lateral Cortex, Basal Ganglia, etc.) and they performed visuomotor goal-directed weight shifting task while standing on a balance board. The task was projected using Virtual Reality (VR *henceforth*) that was interfaced wirelessly with a portable Balance Board (BB *henceforth*) measuring one's Center of Pressure (CoP *henceforth*). Our VR-based Balance Training (VBaT *henceforth*) platform has been extensively studied in prior works for post-stroke rehabilitation [26]. In this study, we investigated the implications of ctDCS applied to the dentate nuclei and the lobules VII-IX of the cerebellum on one's postural control quantified in terms of displacement of CoP during weight shifting based on our VBaT platform. Here, although the cerebellum was free from lesions; however, Basal Ganglia infarction affected the ctDCS effects on the portable neuroimaging measures [23]. Therefore, in this study, we also investigated the implication of ctDCS on one's postural control when lesion is in specific regions of the brain involved in incorporating error correction during a weight shifting task, such as those with Basal Ganglia (BG *henceforth*) infarction [27]. The objectives of our research were to (1) refine BB-assisted VR-based Balance Training (VBaT) measures, and (2) conduct a study on the implication of ctDCS (targeting dentate nuclei and the lobules VII-IX) on the postural control of post-stroke subjects.

II. System Design

Our system consisted of two modules, namely (A) **V**irtual Reality-based **B**alance **T**raining platform and (B) Cerebellar Transcranial Direct Current Stimulator. The VR platform offered goal-directed weight shifting tasks to the user. The stimulator was used to deliver the ctDCS using two montages.

A. VR-Based Task Platform

The Fig. 1(a) presents an overview of the architecture of the platform. This platform consisted of (1) Graphical User Interface (GUI *henceforth*) projecting VR-based tasks, (2) Center of Pressure estimator, and (3) Performance evaluator.

1) Graphical User Interface Projecting VR-Based Tasks: A VR-based GUI was developed using Vizard software (from Worldviz Llc). The VR can offer flexibility in design of task environments along with options of delivering audio-visual feedback that can be motivating [2] for the user. The VR-based tasks, e.g., Figs. 1(b) and 1(c) (randomly chosen from a database of 30 templates) were projected for directional weight shifting towards East, North-East, North, North-West, and West. During each task, the GUI projected a VR

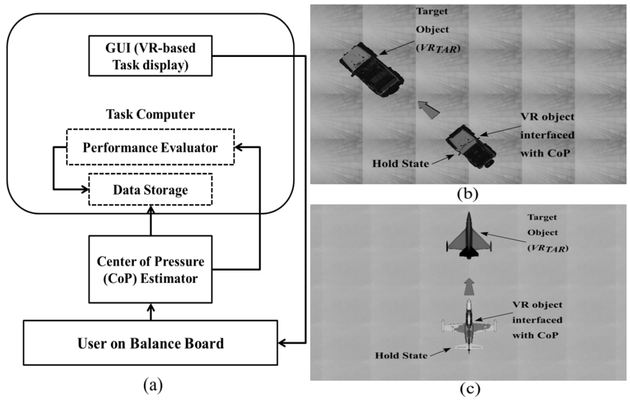

Fig. 1. (a) VR-based system architecture and typical GUI of task for (b) North-West and (c) North directions.

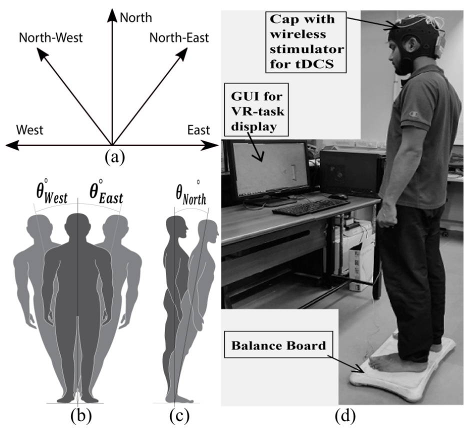

Fig. 2. (a) Directions for weight shifting (b) Weight shifting using ankle strategy towards East and West, (c) North and (d) Experimental setup.

environment that comprised of a static background along with a static target virtual object (VR_{TAR}) and a dynamic virtual object (VR_{DYN}) (Fig. 1(b) and 1(c)). Each pair of VR_{TAR} and VR_{DYN} was of different types, e.g., car, airplane, etc. The VR_{DYN} changed its position in the virtual environment based on one's Center of Pressure (CoP) estimated by the BB (Section II.A.2) in the physical environment. The task required one to shift weight through threshold angles ($\theta° = 3.38°$ for North, 5.11° for each of East and West, 4.25° for each of North-East and North-West; typical values based on a pilot study [2]) from central Hold State towards VR_{TAR} (Fig. 2(a)), thereby manoeuvring the VR_{DYN} (pose indicated in Figs. 2(b) and 2(c)) within maximum of 20 sec (for each direction). During each task, the VR_{TAR} appeared randomly in any of the five directions towards the end of the path away from the central Hold position where the VR_{DYN} initially appeared (Fig. 2(a)). To complete the task, one was expected to manoeuver his/her CoP (while standing on the BB (Fig. 2(d)) towards the VR_{TAR} thereby displacing the VR_{DYN}. The tasks were designed in a way that once the VR_{DYN} crossed the threshold (specific to each direction as indicated above) within the specified time duration and the individual (executing the weight shifting task) was able to hold the VR_{DYN} beyond the threshold point for 1 s, then the VR_{DYN} would shoot towards the VR_{TAR} thereby completing the task. Additionally, the GUI provided an audio feedback on task completion.

2) Center of Pressure Estimator: An in-house developed algorithm was used to acquire data from the BB at 30 Hz [28]. The BB (with pressure sensors e.g., F_1, F_2, F_3, and F_4 at the four corners) was used to compute the CoP coordinates (VR_{DYN_x}, VR_{DYN_y}) using Eqs. (1) and (2).

$$VR_{DYN_x} = 26.05 * \frac{(F_2 + F_4 - F_1 - F_3)}{(F_1 + F_2 + F_3 + F_4)} \tag{1}$$

$$VR_{DYN_y} = 16.75 * \frac{(F_1 - F_3 + F_2 - F_4)}{(F_1 + F_2 + F_3 + F_4)} \tag{2}$$

The coefficients represent the physical dimensions of the BB. The Wii-BB was used in our study to compute one's CoP and has demonstrated good test-retest reliability when compared to the laboratory-grade force platforms [29]. In turn, the CoP measured using the BB was further mapped to the dynamic virtual object (VR_{DYN}) in the VR-environment using coefficients based on the physical dimensions of the BB.

3) Performance Evaluator: For weight shifting task, we computed kinetic measures, since these measures can demonstrate the effects of tDCS on the quality of motor performance [30]. We computed different CoP based indices based on the CoP trajectory in the VR-environment during the goal-directed weight shifting task execution. The trajectory was obtained from the path followed by CoP (represented by the VR_{DYN} mapped using Eq.(1) and Eq. (2)). The CoP-based indices were (a) CoP path length (CoP_L *henceforth)*, (b) Normalized Effectiveness Index (NEI *henceforth*; 0-1 scale), and (c) Length Ratio (LR *henceforth*) for each direction. For our hemiplegic patients, we explored the deviation in the CoP trajectory towards the Affected side ($Sway_{AS}$ *henceforth*) and Unaffected side ($Sway_{UAS}$ *henceforth*). For example, for left hemiplegic patient, the $Sway_{AS}$ and $Sway_{UAS}$ were for West and East, respectively. We chose the CoP_L (length of CoP trajectory while shifting weight) to estimate one's balance [4]. In previous studies, the CoP_L was only used to measure one's limits of stability in BB-based task [4]. None have explored the CoP displacement capability-speed (of weight shifting) trade-off, crucial for daily living. Thus, we computed NEI (Eq. (3)) to account for this trade-off while computing one's performance.

$$NEI = \frac{1}{2}\left[\left\{1 - \left(\frac{D_M}{r_{th}}\right)\right\} + \left\{1 - \left(\frac{t}{t_{th}}\right)\right\}\right] \tag{3}$$

Here, D_M is the accuracy of task execution as mean error between one's actual CoP path and the shortest length path (L_{short}) between Hold State and VR_{TAR} (Figs. 2(b) and 2(c)). Again, t is the time taken to execute the VR-based task. The r_{th} (=1.8*L_{short}) and t_{th} (=20 s) are the distance and time thresholds (based on pilot study with age-matched healthy group).

We computed the LR in terms of the length of the CoP trajectory and the threshold length using Eq. (4).

$$LR = \frac{r_{th}}{CoP_L} \tag{4}$$

We computed Sway as deviation in CoP trajectory from the ideal straight path (Figs. 2(b) and 2(c)) for Affected

(AS *henceforth*) and Unaffected sides (UAS *henceforth*) (Eq. (5)).

$$Sway_{AS/UAS} = \frac{1}{N}\sum_{i=1}^{N}\sqrt{(VR_{DYN_x} - L_{short_x})^2 + (VR_{DYN_y} - L_{short_y})^2} \quad (5)$$

L_{short_x} and L_{short_y} represent the coordinates of the ideal straight path corresponding to instantaneous location of VR_{DYN} and 'N' is the total number of sample points.

B. Cerebellar Transcranial Direct Current Stimulation

The location of electrodes for cerebellar sub-region specific delivery of ctDCS was based on computational modelling from a prior work [22] that aimed to identify bipolar montage which target maximally (in terms of electric field strength) the dentate nuclei and uniformly target the lobules VII-IX during (i) Phase-dentate ($Phase_D$ *henceforth*) and (ii) Phase-leg ($Phase_L$ *henceforth*), respectively. However, the subject-specific magnetic resonance imaging (MRI) based head modelling [5] could be performed only in a subset of participants having MRI scans. Here, we applied age-specific (obtained from an online database [31]) and lobule-Specific dosage considerations for ctDCS [32]. The MRI data comprised of average T1-weighted MRI for the head and brain and segmenting priors for gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF). A Realistic volumetric Approach to Simulate Transcranial Electric Stimulation (ROAST) [33] was used to create a tetrahedral volume mesh of the head[5]. The ROAST used "Statistical Parametric Mapping" to segment the head and brain into Scalp, Skull, CSF, GM, and WM for the tetrahedral volume mesh. These brain tissues were modeled as different volume conductors for Finite Element Analysis in the ROAST. Here, isotropic conductivity used for the different brain tissues [34] were (in S/m): Scalp=0.465; Skull=0.01; CSF=1.654; GM=0.276; WM=0.126 [22]. We identified the best "one-size-fits-all" electrode montage for our post-stroke subject group [5].

In this study, we used two different montages during the two ctDCS Phases, namely (i) Phase-dentate ($Phase_D$) and (ii) Phase-leg ($Phase_L$). Specifically, 3.14cm^2disc anode and cathode were placed at PO10h and PO9h (10/5 EEG system), respectively for $Phase_D$. Then, for $Phase_L$, 3.14cm^2 disc anode and cathode were placed at xx8 [33] and Exx7, respectively. We used wireless STARSTIM 8 (from Neuroelectrics) for ctDCS according to the two montages from a prior work [23] for investigating their effects on postural control.

III. Experimental Setup And Procedure

A. Study Design and Ethical Approval

The study was designed as a single-session single-blind crossover study with randomized $Phase_D$ and $Phase_L$ stimulation (with an intermediate resting state bipolar bilateral ctDCS) in which the cerebellar stimulation was targeted to the dentate nuclei and the lobules VII-IX respectively. The ctDCS was delivered in a random order on two different days with a washout period of 2-3 days. During each ctDCS phase, the participant was expected to interact with the GUI offered by the VR-based task platform (Section II.A.1) while carrying out directional weight shifting that lasted for ~10 minutes prior to ctDCS (Pre-stage *henceforth*; study protocol shown in Fig. 3). Subsequently, 2mA bilateral ctDCS was administered for 15 minutes at rest in a repeated measure single-blind crossover design using two bipolar montages (Section II.B). The participants were blinded to the montage by keeping all the four stimulation electrodes (two anodes and two cathodes) always embedded in their cap. Post the cerebellar stimulation followed by a brief rest, the protocol required the participant to take part in the VR-based task that lasted for ~5 minutes (Post stage *henceforth*). Each phase required a commitment of ~1 hour from each participant. The study protocol was reviewed and approved by the institutional ethics committee with the approved proposal number as IEC/2019-20/4/UL/046.

Pre Stage (10 min)	Rest (2 min)	ctDCS (15 min)	Rest (2 min)	Post Stage (5 min)

Fig. 3. Study protocol.

TABLE I
PARTICIPANTS' CHARACTERISTICS (ALL MALE)

ID	Age (yrs)	AS	PSP (months)	BBS	Lesion Areas
S1	44	Right	23	52	Lateral cortex of MCA
S2	48	Left	8	47	NA
S3	53	Right	36	43	Anterior and Lateral cortex of MCA
S4	40	Left	15	41	Lateral cortex of MCA
S5	38	Right	9	52	Basal Ganglia, Lateral cortex of MCA
S6	32	Right	9	49	Basal Ganglia, Insula, Lateral cortex of MCA
S7	50	Left	18	50	Lateral cortex of MCA
S8	54	Left	7	55	NA
S9	45	Right	36	55	NA
S10	49	Left	24	55	NA
S11	61	Right	30	46	NA
S12	38	Right	27	55	NA

Note: PSP-Post-Stroke Period; BBS-Berg Balance Score; MCA-Middle Cerebral Artery; NA: Frontal Lobe affected with no detailed report; AS-Affected side
Note: Participant S1 and S3-S7 had MRI scans.

B. Participants

Post-stroke male patients (S1-S12; mean (SD)=46 (±8.16) years; Table I) were recruited from local civil hospital. The inclusion criteria were post-stroke period>6 months with intact cerebellum, ability to follow instructions, stand without any external support, Berg Balance Score (BBS) >40 (since this BBS threshold is related to the risk of fall [35], and no major surgery in the recent past. We had access to detailed MRI report only for S1 and S3-S7 with information on specific (brain) lesion location (Table I) and multi-slice segmentation masks from ROAST [33] (please see Supplementary Materials).

C. Procedure

After the participant arrived at the study room, he/she was asked to sit on a chair and relax for ~5 minutes.

The physiotherapist administered the Berg Balance Scoring (BBS) [35] and ensured that the inclusion criteria was satisfied (BBS>40). Then the experimenter described the experimental setup (comprising of a BB, stimulator, and a task computer (Fig 2(d)) and demonstrated the VR-based task. The participant was informed that he would be offered non-invasive brain stimulation. Also, the participant was told that he was free to discontinue from the study in case of any inconvenience. This was followed by administration of the signing of the consent form. Once the participant said that he has understood the task and was ready, the experimenter prepared him for ctDCS by placing the neoprene cap combined with wireless stimulator and the gel-based electrodes (Fig. 2(d)). While placing the cap on one's head, the scalp was prepared with gel for ctDCS. The experimenter ensured that the participant was comfortable with the cap (with the electrodes). Then the participant was asked to stand on the BB (placed in front of the Task Computer at a distance of ~150 cm) and execute the goal-directed weight shifting task using ankle strategy [2]. The tasks were offered using the VBaT platform followed by the ctDCS in the resting state. Again, post stimulation, the participant was asked to execute the goal-directed weight shifting task.

D. Clustering Analysis

Since our participants had varying lesion areas with two having BG infarction, we wanted to understand whether they can be clustered based on the implications of the ctDCS on their postural control ability. For this, we used k-means clustering approach [36], one of the most commonly used unsupervised algorithms that provides 'k' number of clusters for n-data points based on the mean of the data centroids. It tries to partition the data points into 'k' non-overlapping clusters in which each data point will have membership with only one cluster. The distinct clusters are formed in such a way that the sum of the Euclidean distance between each data point and the cluster's centroid would be least. In our work, we used k-means clustering approach to categorize a subgroup of the participants (S1 and S3-S7 (Table I)) having detailed MRI report into two different clusters based on the Sway (deviation in CoP trajectory). Specifically, we chose the sway while an individual shifted his weight towards his Affected side (Sway_{AS}) for the clustering analysis. Before clustering, we pre-processed the information on Sway_{AS} using the mean-normalization technique [37] as given by Eq. (6).

$$Norm.\ Sway_i = \frac{Sway_i - avg(Sway_{All})}{Range\left(Sway_{All}\right)} \tag{6}$$

$Sway_{All}$ indicates the feature vector formed from the estimated $Sway_{AS}$ of the participant pool and i indicates i^{th} individual.

E. Statistical Analysis

While our participants interacted with the VR-based tasks, we evaluated one's CoP-related indices during the Pre stage and Post stage in a time-synchronized manner. Given that the CoP-related indices were not normally distributed (using

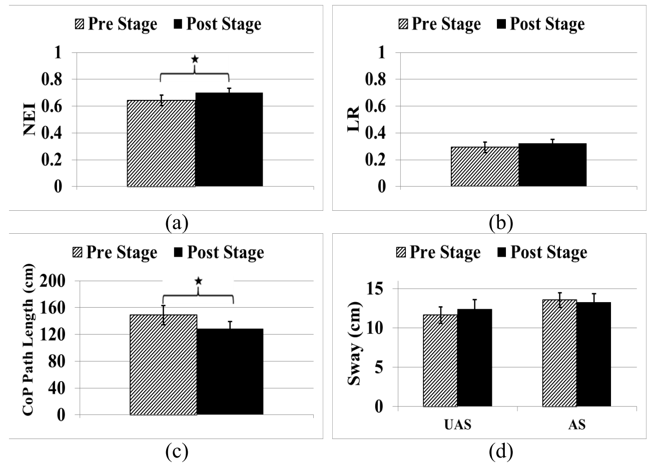

Fig. 4. Comparative analysis of (a) NEI, (b) LR, (c) CoP_{L} and (d) Sway on UAS and AS between pre and post stages of Phase_{D}. Note: * indicates p-value<0.05.

Shapiro-Wilk test [38]), we carried out non-parametric statistical test using Wilcoxon Signed-Rank test [38]. The null hypothesis for the dependent sample paired test was that there is effect of the ctDCS on one's Pre-to-Post stage postural ability. The statistical tests were carried out using the SPSS Statistics 20 software and effect size (r) was computed from the z value obtained using the statistical tests [39].

IV. Results and Discussion

While one interacted with the VR-based task platform in Phase_{D} and Phase_{L} with ctDCS being offered to the dentate nuclei and lobules VII-IX, respectively (during the intermediate rest state), we acquired one's CoP data in a time-synchronized manner. From this data, we extracted the CoP-related indices (Section II.A.2). The aim was to understand the implication of the stimulation during Phase_{D} and Phase_{L} on one's postural control in terms of comparative assessments between group average NEI, LR, CoP path length and sway. Also, having the detailed MRI report of S1 and S3-S7, we wanted to investigate whether the participants having BG infarction (namely S5 and S6) were different from the rest four in terms of ability to correct postural sway (while shifting weight to the Affected side) by k-means clustering (for $k = 2$).

A. Implication on CoP-Based Indices: Phase_{D}

In Phase_{D}, the participants were offered stimulation to the dentate nuclei. The idea was to understand the implications of this stimulation on the coordination ability of post-stroke patients while they executed goal-directed weight shifting tasks. Specifically, we wanted to understand the implication of ctDCS on the (i) accuracy of CoP displacement and speed of task execution, (ii) ability to reach the VR_{TAR} position and (iii) overall reduction in one's sway. Also, we wanted to understand the implications on the compensatory mechanism being employed by the patients during task execution.

Our data analysis showed that there was a group average Pre-to-Post increment ($\Delta\%$=~9%) in the overall NEI

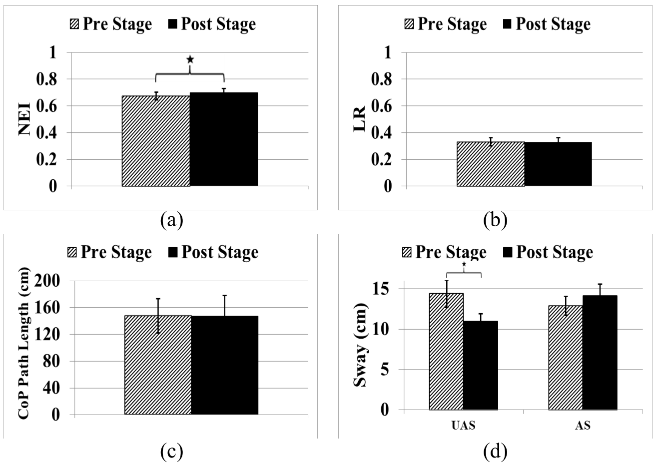

Fig. 5. Comparative analysis of (a) NEI, (b) LR, (c) CoP path length and (d) Sway on UAS and AS between pre and post stages of Phase_L. Note: * indicates p-value$<$0.05.

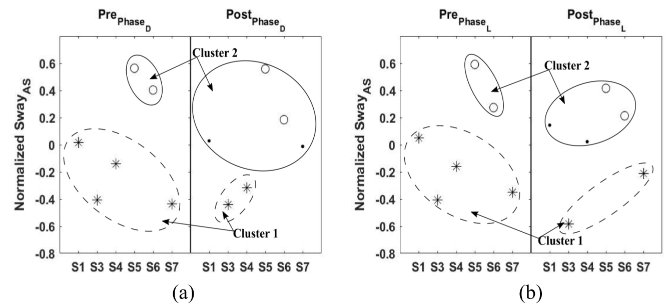

Fig. 6. Clustering analysis of six participants in pre and post stages of (a) Phase_D, and (b) Phase_L. Note: Subject S5 and S6 with BG infarction indicated with 'o' within the Cluster 2.

(Fig. 4(a)) that was statistically significant (p-value$<$0.05) with large effect size (r = 0.75). Such an improvement can be attributed to increased accuracy of CoP displacement ($\Delta\%=\sim 7\%$) and speed of task execution ($\Delta\%=\sim 9\%$). In short, there was improvement in the quality of performance in terms of both increased accuracy and speed. Also, we observed an increment ($\Delta\%=\sim 9\%$) in LR (not statistically significant) reflecting variation in one's ability while shifting CoP from Hold State to the VR_{TAR} position (Fig. 4(b)). Again, we observed altered weight shifting ability that was evident from the statistically significant Pre-to-Post reduction ($\Delta\%=\sim 14\%$) in the overall CoP_L (Fig. 4(c)) with large effect size (r = 0.63). Also, we wanted to ensure whether the participants employed any compensatory mechanism, commonly demonstrated by post-stroke patients to overcome the inabilities of AS [4]. For this, we computed the Sway_{AS} and Sway_{UAS} (Eq. 5) of the participants. The Figure 4(d) shows a decrease in the overall Pre-to-Post average sway on the AS ($\Delta\%=\sim 2\%$) coupled with a Pre-to-Post increase ($\Delta\%=\sim 6\%$) in the sway on the UAS. This infers that there was improvement in the coordination ability towards the AS. In addition, this improvement did not come at the expense of any compensatory move [40] initiated by the participant on the UAS. For both AS and UAS, the Pre-to-Post changes in the sway were not statistically significant. Given the limited sample size, our findings cannot be generalized.

B. Implication on CoP-Based Indices: Phase_L

In Phase_L, we wanted to understand the implication of stimulating the lobules VII-IX on one's postural control quantified in terms of CoP-based indices while an individual executed the goal-directed weight shifting tasks.

Our data analysis showed that there was a group average Pre-to-Post increase ($\Delta\%=\sim 4\%$) in the overall NEI (Fig. 5(a)) which was statistically significant (p-value$<$0.05) with large effect size (r = 0.63). However, this improvement in NEI had minimal contribution from improvement in accuracy of CoP displacement (with Pre-to-Post increment being $\sim 1\%$). In fact, the major contribution to the improvement in NEI came from reduction in VR-based task execution time (with Pre-to-Post reduction in time taken being $\sim 7\%$). In short, the improved NEI (indicating the quality of performance) was dominated by only speed of task execution (and not the accuracy of CoP displacement) unlike that we observed in Phase_D. In fact, in Phase_L, one's ability to perform coordinated movement reduced possibly inferring the inhibitory effect of ctDCS on the dentate nuclei. Again, in the case of LR (Fig. 5(b)), we observed a minimal Pre-to-Post reduction (not statistically significant) inferring almost unchanged ability of shifting CoP from the Hold State to the VR_{TAR} position. Similar was the finding for the overall CoP_L (Fig. 5(c)) with a negligible Pre-to-Post reduction. Further, we found an overall Pre-to-Post increase in the average sway on the AS ($\Delta\%=\sim 10\%$) along with a statistically significant (p-value$<$0.05) reduction ($\Delta\%=\sim 24\%$) on the UAS (Figure 5(d)) with large effect size (r = 0.77) unlike that in case of Phase_D. The increment in sway on the AS was possibly because of the inhibitory effect on the dentate nuclei mediated by the stimulation of lobules VII-IX. In fact, such inhibitory effect on the dentate nuclei mediated by the stimulation of lobules VII-IX has been reported to likely result in reduced co-contraction post-stroke [41]. This needs further investigation vis-à-vis reflex excitability with respect to postural sway [42] where a reduced ability to control the sway on the AS might be compensated by the participants by controlling the CoP sway (thereby reducing the sway) on the UAS unlike that in the case of Phase_D. Measures, such as overall postural sway and weight-bearing symmetry can each be an independently important measure of tDCS effects on post-stroke standing balance control [43] as discussed earlier [41]. Nevertheless, given the limited sample size, our findings cannot be generalized.

C. Clustering of Participants During Pre Stage and Post Stage of Phase_D and Phase_L

With the detailed MRI report of S1 and S3-S7, we investigated whether S5 and S6 with BG infarction can be distinguished from this subgroup of participants based on their postural sway (while shifting weight to the Affected side) which was motivated by portable neuroimaging evidence of BG infarction effects [23]. The BG motor circuit is known to be involved in fine tuning of one's coordinated voluntary movements and error correction during ongoing movements [27]. Here, we used normalized Sway_{AS} as a feature for the k-means clustering analysis. Our results for Phase_{D} and Phase_{L} (Figs. 6(a) and 6(b), respectively) show that S5 and S6 always grouped into a separate cluster (i.e., Cluster 2 with larger sway) irrespective of the stimulation both during Pre and Post stages inferring nearly unaltered deficit in their error correction ability during the directional weight shifting task offered by VBaT. Again, in the Post Stage of Phase_{D}, we observed that S1 and S7 teamed up with S5 and S6 (Fig. 6(a)). Also, in the Post stage of Phase_{L}, S1 and S4 teamed up with S5 and S6 (Fig. 6(b)). For S1, we observed minimal Pre-to-Post change that marginally shifted him to the other cluster (Cluster 2) in both the Phases. Again, S7 seemed to be more confident as his balance was good and his deteriorated performance during Post stage of Phase_{D} (that marginally shifted him to the other cluster) can be because of his not paying attention during the task (as reported by the experimenter). However, that was not the case with S7 during Phase_{L}, in which though his performance was deteriorated, it was not large enough to shift him to the Cluster 2. For S4, during Phase_{L}, we observed increase in sway post-stimulation (as expected) causing him to be shifted to the Cluster 2.

V. Conclusion

In this study, we have refined and utilized a BB-assisted VR-based Balance Training platform which offered different goal-directed weight shifting tasks to 12 post-stroke patients. Also, we have conducted a study to understand the implication of ctDCS on their postural control (quantified in terms of CoP-related indices). For ctDCS, we used two different montages, one stimulating the dentate nuclei (Phase_{D}) and the other stimulating the lobules VII-IX (Phase_{L}). Results indicated differentiated findings (post stimulation) with regard to kinetic measures in terms of CoP-related indices during Phase_{D} and Phase_{L}. Specifically, such observations were related to Phase_{D} having an incremental effect on one's postural control and Phase_{L} contributing to inhibitory effect on the dentate nuclei. Also, the clustering analysis over a subgroup of 6 post-stroke patients (for whom we had access to detailed MRI report) showed that the non-responders (namely S5 and S6) with BG infarction demonstrated poor postural control and deficit in error correction ability irrespective of the montage.

Though the results are interesting, yet our study had certain limitations. One of the limitations was the small sample size (n=6) for the clustering analysis based on MRI report although we had a total 12 subjects in this study. In future, we plan to extend the clustering analysis with larger participation pool stratified into post-stroke subjects with and without BG lesion. The other limitations were limited exposure (single exposure for each Phase) and participation from only male patients. In future, we plan to conduct longitudinal study with larger participant pool (both genders) and offer them multiple exposures. In addition, though we did not use the real sham configuration in our study due to the sham inconsistencies [44], yet we used alternate configurations as "active" sham with postulated differential behavioral effects based on prior neuroimaging evidence [23], e.g., dentate nuclei and lobules VII-IX with minimal spillover effects ($\sim$30% and $\sim$25% less compared to the target region, in terms of electric field strength for the dentate nuclei and lobules VII-IX stimulation, respectively [5]). However, in future, we plan to do extended study while considering the sham configuration under the sham inconsistencies [44]. However, this single-session preliminary study helped us to understand the effect of bilateral bipolar ctDCS targeting the dentate nuclei and lobules VII-IX on the postural control of post-stroke patients. In this study, we found heterogeneous deficits and improvements in the postural abilities of stroke survivors both within and outside the VBaT environment. However, questions on retention of such improvements during activities of daily living still remain and needs investigation in longitudinal study in the future.

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