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Original Research

Feasibility and Safety of Sequential Transcranial Direct Current Stimulation and Physical Therapy in Older Adults at Risk of Falling: A Randomized Pilot Study

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tDCS

Abstract *Objective:* To establish the feasibility and safety of administering transcranial direct current stimulation (tDCS) immediately prior to physical therapy (PT) sessions in older adults at risk of falls.
Design: A pilot randomized controlled study.
Setting: Outpatient geriatric physical therapy clinic.
Participants: Ten older adults living within supportive housing facilities (86.8±7.9 y/o, 8F) were enrolled in the study.
Interventions: Participants received tDCS or sham stimulation targeting the left dorsal lateral prefrontal cortex for 20 minutes, immediately prior to up to 10 of their PT visits.
Main Outcome Measures: Feasibility, safety, and functional outcomes were reported to inform the design of a larger and more definitive trial.
Results: Six fallers (88.8±5.0 y/o, 5F) completed the study and received 82.3% of the possible stimulation sessions, suggesting adding a 20-minute session of stimulation immediately prior to PT training sessions, along with pre- and post-assessments is feasible. The blinding strategy was successful and all reported side effects were expected and transient. While feasible and safe, the trial was met with numerous challenges, including selection bias, time and energy

List of abbreviations: dlPFC, dorsolateral prefrontal cortex; PT, physical therapy; tDCS, transcranial direct current stimulation

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commitment, and large variation in functional performance, that must be considered when designing and implementing larger more definitive trials.
Conclusion: This study provides preliminary evidence about the feasibility, safety, and challenges to combine PT and tDCS in very frail older adults.

Falls are common, costly, and correlated with both physical and cognitive declines in older adults.[1,2] Older adults at risk of falling are typically referred to physical therapy (PT). Traditional therapeutic strategies primarily target peripheral neuromuscular elements of motor control.[3-5] Such approaches often result in suboptimal improvements in gait and balance.[3-12] One likely reason is that traditional approaches do not sufficiently emphasize and train the higher-level "executive" control of movement.[13-15] Older adults require cognitive resources to plan and modify their movements, especially when walking in complex and ever-changing environments.[16,17] Recent evidence indicates that activity within the dorsolateral prefrontal cortices (dlPFC)[18,19] is closely linked with standing and walking performance, especially under challenging conditions.[20,21] Strategies that facilitate the activation of the dlPFC and its connected neural networks may be able to complement traditional PT interventions aimed at reducing falls and improving functional gait and balance in older adults.

Transcranial direct current stimulation (tDCS) is a noninvasive and safe means of modulating cortical excitability.[22,23] Although many previous studies have been deemed low-to-moderate quality,[24] mounting evidence suggests that tDCS interventions designed to facilitate the excitability of the left dlPFC improves numerous aspects of executive function related to mobility.[25-32] Recently, we demonstrated that a 2-week, 10-session intervention of this form of tDCS improved executive function and mobility in older adults with both slow gait and mild-to-moderate executive dysfunction for at least 2 weeks after the intervention.[33] Researchers have attempted to combine tDCS with PT to treat symptoms of Parkinson's disease[34,35] and stroke.[36,37] These studies suggest that this combination of therapies may lead to better outcomes as compared with either therapy.[34,35] However, as far as we know, limited studies have assessed tDCS as an adjunct to PT to improve gait and balance within outpatient geriatric rehabilitation focused on the mitigation of fall risk. Whether this combined approach can also be applied to an old and frail population within an outpatient clinical setting remains unclear.

This study aimed to establish the feasibility and safety of administering tDCS to facilitate prefrontal brain excitability *immediately prior to PT sessions* in older adults referred to PT due to high risks of falls. In particular, participants received stimulation in a private exam room within the PT clinic and then began their scheduled PT session with no additional activities in between. We aimed to identify factors that affected successful trial conduct including recruitment and evaluation of sample characteristics, intervention acceptability, safety, and participant response to intervention.

Methods

We conducted a pilot randomized controlled study in older adults at risk of falling who were referred to outpatient PT for gait and balance training. Participants were randomized into 1 of the 2 intervention arms: tDCS plus PT (ie, tDCS+PT) or sham stimulation plus PT (ie, Sham+PT). Each participant received a baseline assessment, tDCS or sham stimulation sessions prior to each of their scheduled PT sessions, and a final assessment, over approximately 2 months. The baseline assessment occurred on a separate day from the initial PT evaluation to minimize confounding due to fatigue. The final assessment occurred either after the 10 combined sessions or after the last scheduled PT session, whichever came first. All PT sessions were scheduled as usual and the research team scheduled all stimulation sessions accordingly. Participants and staff were blinded to intervention assignment. The study was approved and monitored by the Hebrew SeniorLife Institutional Review Board (IRB) and the National Clinical Trial (NCT) Number was NCT04181658.

Referral and recruitment process

Prior to implementation of the study, the research team met with the leadership team of the rehabilitation outpatient services to determine a strategy for recruiting participants. When an individual was referred to outpatient PT, the office administrator provided a study flyer to the patient, and at the same time, informed the research team about the new patient. The research team was authorized to review the patient's electronic medical record to identify the primary reason for PT referral. If the referral reason was related to falls or poor gait or balance, the research team would contact the patient, introduce the study, and determine their interest in study participation.

Interested patients completed a standardized screen process to determine study eligibility. Informed consent was obtained at the beginning of the in-person screening visit. Inclusion criteria were men and women aged 65 years and above who were referred to PT for gait and balance training due to recurrent falls or high risk of falling at the outpatient geriatric physical therapy clinic within the senior health care organization.

Exclusion criteria were designed to ensure safety and optimize compliance, while minimizing confounders due to overt disease or conditions that may significantly influence study outcomes. Specific criteria included inability to stand or walk unassisted for 60 seconds, Montreal Cognitive Assessment (MoCA) score <18, unstable medical condition, recent myocardial infarction, active cancer, psychiatric co-

morbidity, chronic use of any sedating medications, legal blindness, on vasodilators, or contraindications to tDCS.

Physical therapy sessions

Therapists provided standard care to each participant. At the first PT session, the therapist performed a comprehensive evaluation, determined short-term and long-term goals, and discussed their treatment plan with the patient. Therapists also completed selected objective measurements, which most frequently included the Berg Balance Scale (BBS). As nearly all participants in our cohort completed the BBS during their baseline and discharge evaluation, we extracted this information from the PT evaluation and included it in subsequent analyses.

After completing the initial evaluation, the therapist provided standard treatments and ongoing assessments based upon clinical judgment of individual need and progress. Each PT session took about 30-45 minutes and occurred twice per week. The total number of completed PT sessions and time to discharge were tracked for each participant.

Study-specific baseline and final assessments

Baseline and final assessments were conducted by the research team on separate dates before the first combined stimulation plus PT session and after the last combined session, respectively. These 2 visits included specific tests and questionnaires chosen based upon their widespread use within clinical and/or research settings and their sensitivity to future falls and/or tDCS designed to target the left dlPFC. ***Dual task walking*** was assessed by instrumenting participants with the portable wearable sensors[a] and having them complete 3, 60-second trials in each of 3 conditions: sitting while performing a verbalized serial subtraction task, walking quietly, and walking while completing the verbalized serial subtraction task (ie, dual-task walking).[33,38] The subtraction task entailed counting backward by 3's from a random 3-digit number ranging from 199 to 999, which was provided to participants just before the trial. ***Functional Mobility*** was assessed using the same equipment to time 2 trials of the timed Up and Go (TUG) test.[39,40] ***Fear of Falling*** was assessed by the Falls Efficacy Scale-International (FES-I) questionnaire.[41] ***Global cognitive function*** was assessed by MoCA,[42] and ***motor speed and aspects of executive function including visual search and task-switching*** was assessed by the Trail Making Test (TMT) A and B, respectively.[43,44] Alternant forms of the MoCA and TMT were used at each visit to minimize practice effects.

Participants were also asked to complete an exit interview after their final study assessment. The questions are provided in the Appendix (available online only at http://www.archives-pmr.org/).

Transcranial direct current stimulation

Participants received tDCS or sham stimulation targeting the left dlPFC for 20 minutes, immediately prior to each of their PT visits. tDCS was delivered using the device and software from the same company.[b] The tDCS system was connected to 6 electrodes positioned on the scalp and secured in place with a Neoprene cap. Conductive gel was applied below each electrode. This tDCS montage was designed to facilitate the excitability of the dlPFC, while optimally distributing the injected currents to minimize potential effects elsewhere in the brain. The amount of direct current delivered by any 1 electrode did not exceed 1.5 mA and the total amount of current injected by all electrodes was below 4 mA, to ensure safety and comfort.[21]

Sham stimulation was developed using the "acti-sham" approach.[45] The electrode placement was the same as the tDCS montage. However, the electrode current was extremely low and distributed primarily between electrodes in relatively close proximity to one another. This approach has been demonstrated to induce cutaneous sensations that are similar to those associated with tDCS, yet create only a minimal electric field at the level of the cortex.[45] tDCS side effects were recorded at each stimulation session and blinding efficacy was assessed at the end of the study. The details of the side effects questionnaire and the blinding efficacy are provided in the Appendix (available online only at http://www.archives-pmr.org/). Randomization was done by a computer-based program to ensure allocation concealment and by a personnel independent to this project. Participants were assigned in a 1:1 ratio to receive either tDCS or Sham stimulation.

Study outcomes and statistical analysis

Study outcomes were chosen primarily to inform the feasibility and design of a larger, more definitive trial and included (1) recruitment capacity, (2) acceptability and suitability of study procedures, (3) patient-reported outcomes, and (4) PT assessments and interventions within each PT session. We considered the study to be feasible while (1) the recruitment- and procedure-related achieved above 50%, (2) the prevalence of self-reported side effects was no more than the previous study, (3) the participants' guesses would be no significant difference between real and sham conditions, and (4) the satisfaction rate achieved above 70%.

Functional outcomes included the BBS score, gait speed during normal and dual task walking, stride time variability during normal walking, average TUG time, MoCA total score, and the adjusted TMT score (ie, B-A). We used the functional outcomes to estimate inter-subject variance over time, as a function of baseline status and intervention arm assignment.

Results

Recruitment, enrollment, and completion

Study recruitment was initiated on October 1st, 2019, and data collection was terminated on March 15th, 2020, due to the COVID-19 pandemic. Throughout this 5-month period, 34 potential participants were identified and contacted (fig 1). Thirteen (38.2%) were interested in participating in the study. Of these, 10 (76.9%) were eligible and successfully enrolled in the study. All 10 participants completed the baseline assessment, yet 4 (40%) then withdrew from the study *prior to intervention*. Of these 4, 1 withdrew because they stopped their prescribed PT course, 1 developed a schedule conflict, 1

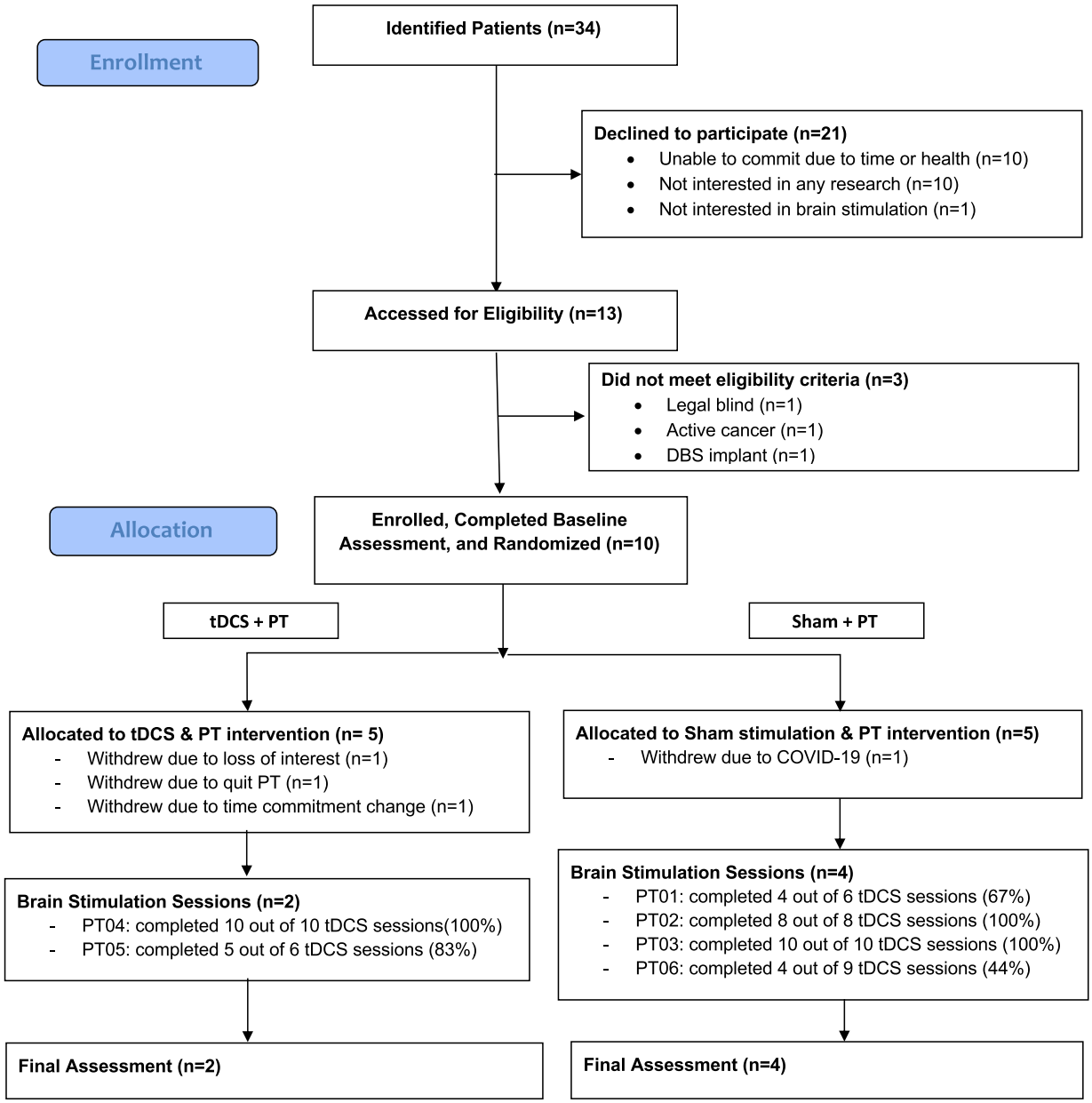

Fig 1 The CONSORT flow diagram of the progress throughout the phases of the study.

decided that they did not want to receive brain stimulation, and 1 tested positive for COVID-19.

The remaining 6 participants—of which 2 were allocated to the tDCS arm and 4 to the sham arm—completed between 6 and 10 PT sessions. The primary reason for completing fewer than 10 sessions were that the participants were discharged early. Participants completed, on average, 82% of the possible stimulation sessions (range: 44%-100%). This included 3 participants who were 100% compliant (details in fig 1). All 6 participants completed their final assessment.

Baseline characteristics of the 10 enrolled participants are provided in table 1. Participants were frail and at high risk of falls: 9 of 10 were >80 years old and all were at least moderately concerned about falling based upon the FES-I.

Effects of intervention on functional outcomes

Participants received 4-10 combined sessions (table 2). Across groups, all except 1 participant exhibited improved BBS performance, with changes from baseline ranging from 2 to 7 points.[46] Intriguingly, while participants in the sham +PT group exhibited either no change or an increase (worse) in gait stride time variability, each participant in the tDCS+PT group exhibited a pre-to-post reduction (improvement) in this gait metric. The effects on normal and dual task gait speed, TUG, FES-I, MoCA, and TMT adjusted were less consistent across individuals and no observable trends were present for potential between-group differences.

Table 1 Baseline characteristics of enrolled participants

ID	Age (y)	Sex	BMI (kg/m^2)	Reason for PT Referral	FES-I	Device	Gait Speed (m/s)	TUG (s)	MoCA	TMTadj (s)
Received intervention										
PT01	86	F	20.5	Evaluation and treatment of gait and balance impairments.	30 (high)	Cane	0.66	25.26	21	240.02
PT02	94	F	33.1	Evaluation and treatment of gait and balance impairments.	46 (high)	Walker	1.02	21.78	19	150
PT03	89	F	25.9	Unsteady gait.	33 (high)	None	1.10	12.54	26	29.29
PT04	81	M	30.4	Unsteady gait.	42 (high)	None	1.19	12.23	27	107.26
PT05	89	F	35.4	Unsteady gait and cervical immobility.	32 (high)	Walker	0.91	17.11	23	45.00
PT06	94	F	24.7	Evaluation and treatment of gait and balance impairments.	41 (high)	Cane	0.75	21.86	24	69.00
Withdrew BEFORE intervention										
PT07	92	F	22.6	Evaluation and treatment of gait and balance impairments.	22 (mod)	None	0.85	15.33	19	107.90
PT08	95	M	28.2	Evaluation and treatment of gait and balance impairments.	45 (high)	Walker	0.78	20.30	25	32.00
PT09	83	F	33.8	Low back pain and left hip pain limiting activity tolerance and mobility.	41 (high)	Cane	0.98	13.50	27	64.46
PT10	67	F	42.1	Total knee replacement	25 (mod)	Walker	0.74	22.44	30	78.35

Abbreviations: BMI, body mass index; FES-I, Falls Efficacy Scale-International (16-19: low concern of falls, 20-27: moderate concern of falls, 28-64: high concern of falls); TMTadj, the difference between the Trail Making Test (TMT) Part A and Part B.

Safety and efficacy response

There were no unanticipated side effects or adverse effects. Among the anticipated side effects, among the 2 participants who received tDCS, 1 reported no side effects and the other reported sensations under electrodes and skin redness. Among the 4 participants who received sham stimulation, 3 reported no side effects and 1 reported sensation under the electrode. Together, 2 out of 6 (33.3%) participants reported some type of side effects across their stimulation sessions. Sensations under electrodes were reported in 12.1% of the sessions, and skin redness was noticed in 2.4% of the sessions.

Participants appeared to be effectively blinded to the type of brain stimulation. No participants who received tDCS, and 2 out of 4 participants who received sham stimulation, correctly identified their intervention type.

Exit interview feedback

Average level of satisfaction was 7.8 on a scale of 1-10, suggesting the participants were relatively satisfied with their study experience. However, only 1 participant stated that they would be willing to participate in the study again or for a longer period. The answers to **"What do you like about the study?"** included *"I thought it was interesting to be part of research and I liked the research staff", "I enjoyed meeting with the research people" and "the research staff were wonderful"*. Four out of the 6 participants reported that the application of the gel was their main concern when they responded to the question "**What could the research team have improved on or done better?"**. The answers included *"the gel was terrible", "the gel was the main objection", and "If you continue using gel, you need to have a facility or hair salon to help people wash the gel out"*. Besides, the complexity of the cognitive tests and the commitment were mentioned as a barrier to the study.

Discussion

The primary purpose of this study was to assess the feasibility and safety of combining tDCS and PT focused on fall risk reduction in particularly vulnerable older adults with high risk of falling. Results indicated that it is feasible to add a 20-minute session of stimulation immediately prior to PT sessions, along with additional pre- and post-intervention assessments, in very old and frail adults. The approach using medical record reviews was successful and led to 1 enrolled participant for every 3 patients deemed potentially eligible. Among the identified patients who were interested and screened for eligibility, 76.9% were enrolled. 60% completed the study, and received 82.3% of the possible stimulation sessions. The blinding strategy was successful and all reported side effects were expected and transient. At the same time, the tested intervention was met with several challenges. Most importantly, receiving tDCS just prior to a demanding PT session created noticeable fatigue for some participants, and may have created significant burden for older adults, especially those who were frail and/or physically deconditioned. These challenges must be considered

Table 2 Functional outcomes before and after the combined intervention

	Intervention Sessions*			BBS (Score)		GS-NW (m/s)		GS-DT (m/s)		GV-NW (Unitless)		TUG (s)		FES-I (Score)		MoCA (Score)		TMTadj (s)	
	tDCS+PT, or Sham+PT	PT only	*Total Sessions*	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
tDCS+PT																			
PT04	10	0	*10*	45	50 (+5)	1.19	1.18 (-.01)	1.18	1.11 (-.07)	.043	.024 (-.019)	12.23	13.20 (+.97)	42	38 (-4)	27	25 (-2)	107.26	61.30 (-45.96)
PT05	5	1	*6*	43	48 (+5)	0.91	0.92 (+.01)	0.83	0.78 (-.05)	.050	.030 (-.020)	17.11	17.59 (+.48)	32	34 (+2)	23	27 (+4)	45.00	126.19 (+81.19)
Sham + PT																			
PT01	4	2	*6*	40	NA	0.66	0.56 (-.10)	0.70	0.55 (-.15)	.039	.042 (+.003)	25.26	21.15 (-4.11)	30	NA	21	17 (-4)	240.02	242.70 (+2.68)
PT02	8	0	*8*	37	39 (+2)	1.02	1.05 (-.03)	0.80	0.99 (+.19)	.035	.039 (+.004)	21.78	22.23 (+.45)	46	43 (-3)	19	23 (+4)	66.00	119.00 (+53.00)
PT03	10	0	*10*	50	53 (+3)	1.10	1.12 (+.02)	1.00	1.03 (+.03)	.023	.022 (-.001)	12.54	13.12 (+.58)	33	31 (-2)	26	26 (0)	29.29	36.77 (+7.48)
PT06	4	5	*9*	38	45 (+7)	0.75	0.73 (-.02)	0.60	0.61 (+.01)	.030	.050 (+.020)	21.86	21.70 (-.16)	41	54 (+13)	24	23 (-1)	69.0	158.40 (+89.40)

Abbreviations: DT, dual-task condition; GS, gait speed; GV, gait stride time variability; NW, normal walking condition; Post, the performance after the intervention; Pre, the performance before the intervention; Sham, sham stimulation; TMTadj, the difference between the Trail Making Test (TMT) Part A and Part B.

* The intervention sessions didn't include their first physical therapy session but counted from their second physical therapy session because the first physical therapy session was mainly evaluation, and no stimulation was provided.

when designing and implementing larger more definitive trials in the future.

While effective, recruitment via medical record review was somewhat difficult. One out of every 3 potential participants whom we identified via this approach agreed to learn more about the study. However, 2 out of every 3 of these individuals were not interested in participating after learning more about the study protocol. Stated reasons included concerns of receiving any type of brain stimulation, time commitment, their current health status, the potential for exposure to the COVID-19 virus, or not being interested in research participation in general. Future studies should work to implement strategies to maximize interest and reduce barriers to participation. For example, researchers may provide hands-on demonstrations of tDCS technology with physical therapists and potential participants to emphasize safety and ease common concerns about receiving this novel intervention.

For those participants who were enrolled and received the intervention, all participants completed the initial, final assessment, and 82.3% of possible stimulation sessions. Blinding to intervention assignment appeared successful and no unanticipated side effects or adverse events were reported. With respect to tDCS, approximately one-third of the participants reported some type of cutaneous sensation underneath the electrodes on just 12% of sessions, which is less than the ~36% reported by a review paper.[47] These results suggest that while recruitment may be difficult, tDCS can be comfortably delivered in the PT setting within a controlled trial, even in very old and frail cohorts.

The exit interview provided important patient-centered feedback that is expected to augment the design and implementation of related trials in the future. Although we provided participants with dry shampoo and a wet towel to clean the electrode gel off of their hair and scalp after each tDCS session, several participants reported dislike or mild discomfort associated with this procedure, especially since it occurred just prior to their PT session. Future studies may carefully consider the optimal approach to delivering tDCS relative to PT. Indeed, the timing of tDCS related to rehabilitation or other behavior interventions may affect its modulatory effects.[48-52] If the tDCS is to be applied *immediately* prior to (or during) a PT session, researchers may consider providing a hair salon voucher as an attractive incentive. Moreover, while important differences exist between gel- and (saline-soaked) sponge-based delivery of tDCS exist, the latter may be better tolerated by participants. The development of "dry" electrodes using novel materials such as the multilayer hydrogel composite appears to be a promising solution in the future.[53,54]

In addition to the dislike of gel electrodes, participants reported that it took considerable time, effort, and energy to undergo brain stimulation prior to each of their prescribed PT sessions. PT sessions alone are already time-consuming and often fatiguing for very old and deconditioned adults with elevated risk of falling. It was particularly difficult for participants to comply with the protocol when PT sessions were scheduled early in the morning. Moreover, several participants had conflicts arise from other appointments, or because they became the main caregiver for their spouse during the study. As such, research should explore the effect of the timing of tDCS administration relative to PT sessions. For example, while approaches that enable home-based, caregiver-led administration of tDCS[55] would not enable immediate transition to PT after stimulation, such an approach might facilitate compliance and minimize burden by adding flexibility to scheduling, providing adequate rest prior to PT, and enabling participants to wash their hair prior to interaction with the therapist.

Limitations

This study was conducted within a setting that benefits from close collaboration between research and clinical activities. Additional research is needed to fully assess feasibility and optimize recruitment and retention with larger samples recruited from multiple PT settings. Moreover, our sample was extremely small and heterogeneous with respect to baseline function, making it impossible to explore the effect size of tDCS+PT, as compared with Sham+PT, on functional outcomes. Still, our results provide initial estimates of within- and between-subject variance over time in functional outcome that can be used to determine sample sizes for future superiority trials.

Conclusions

Noninvasive brain stimulation including tDCS provides a promising neuromodulation tool that can be adjunct to standard rehabilitation services. This pilot work suggested it is feasible and safe to add a 20-min stimulation session prior to their PT sessions in very old fallers. This study also presented factors to be considered when designing and implementing larger more definitive trials in the future.

Suppliers

a. APDM Wearable Technologies Inc Mobility Lab.
b. Neuroelectrics Starstim 32.

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