MODULATING CORTICAL EXCITABILITY TO IMPROVE FUNCTIONAL MOVEMENTS IN INDIVIDUALS WITH PATELLOFEMORAL PAIN: A RANDOMIZED CONTROLLED TRIAL

By

Jeno Aquino

Bryce Broadwell

Connan Wallace

Makenzie Whimple

A doctoral project submitted in partial fulfillment of the requirements for the

Doctor of Physical Therapy

Department of Physical Therapy School of Integrated Health Science The Graduate College

University of Nevada, Las Vegas May 2024 Copyright by Jeno Aquino, Bryce Broadwell, Connan Wallace, and Makenzie Whimple, 2024 All Rights Reserved



Doctoral Project Approval

The Graduate College The University of Nevada, Las Vegas

May 9, 2024

This doctoral project prepared by

Jeno Aquino

Bryce Broadwell

Connan Wallace

Makenzie Whimple

entitled

Modulating Cortical Excitability to Improve Functional Movements in Individuals with Patellofemoral Pain: A Randomized Controlled Trial

is approved in partial fulfillment of the requirements for the degree of

Doctor of Physical Therapy Department of Physical Therapy

Daniel Young, Ph.D. Examination Committee Chair

Kai-Yu Ho, Ph.D. Research Project Advisor

Jing Nong Liang, Ph.D. Research Project Advisor

Merrill Landers, Ph.D. Chair, Department of Physical Therapy Alyssa Crittenden, Ph.D. Vice Provost for Graduate Education & Dean of the Graduate College

Abstract

Purpose/Hypothesis: Persons with patellofemoral pain (PFP) often exhibit increased knee valgus during functional tasks that is traditionally addressed by strengthening weak hip musculature. However, research related to this topic has revealed altered cortical reorganization in individuals with PFP contributes to dysfunctional movements and underscores the critical role of central neural control in this condition. Transcranial direct current stimulation (tDCS) is a neuromodulatory technique that alters cortical excitability to enhance neuroplasticity. Research using tDCS priming supports its feasibility as a possible treatment for other musculoskeletal conditions. However, its application specifically targeting the corticomotor function of the gluteal musculature in individuals with PFP has not been investigated. The purpose of this study was to investigate the acute effects of tDCS plus exercise to affect frontal plane kinematics during functional tasks in persons with PFP. We hypothesized that with tDCS priming, exercise would be more effective at improving frontal plane kinematics when compared to sham stimulation paired with exercise in persons with PFP.

Participants: Ten persons with unilateral or bilateral PFP. If bilateral PFP was the presentation, the involved limb was determined as being the more symptomatic side for a longer period of time. (6M/4F, age=28.2±6.88 yrs, BMI=26.83± 6.67).

Materials and Methods: Participants attended 2 sessions in which tDCS or sham stimulation was delivered using a bihemispheric montage with the anode over the primary motor cortex contralateral to the affected limb. During these conditions, participants performed four different hip strengthening exercises. Before and after each session, participants performed 5 functional tasks (single leg squat, single leg landing, single leg hop, forward step down, and lateral step down) on the symptomatic leg recorded in a frontal plane view. Pain on a visual analog scale (VAS) was also recorded. Kinematics were measured for each task, including trunk lean angle (TLA), hip and knee frontal plane projection angles (FPPA), and dynamic valgus index (DVI) at

iii

peak knee flexion. A one-way ANOVA with repeated measures and post-hoc pairwise comparisons was employed to compare the kinematics, while a Friedman test was used to compare VAS across the 3 conditions (pre-intervention, post-tDCS, and post-Sham). **Results:** No significant difference in TLA, hip FPPA, knee FPPA, or DVI was found among the 3 conditions during single leg squat, single leg hop, forward step down, and lateral step down (p>0.05). While knee FPPA was significantly lower post-Sham compared to pre-intervention during single leg landing (pre-intervention=7.73°±5.95°; post-Sham=3.70°±6.18°; p=.018), this change was less than calculated standard error of measurement. VAS scores were not different among the 3 conditions (p=.147).

Conclusions: A single session of tDCS with exercise was ineffective at improving frontal plane kinematics and reducing pain while performing functional tasks in persons with PFP when compared to exercise alone.

Clinical Relevance: Additional studies are needed to provide a more comprehensive understanding of the potential outcomes associated with tDCS in persons with PFP.

KEYWORDS: patellofemoral pain, transcranial direct current stimulation, dynamic valgus index

Acknowledgements

This research study was made possible by the University of Nevada, Las Vegas Physical Therapy Department Student Opportunity Research Grant (SORG) Program. The authors would like to thank Kai-Yu Ho, PT, MPT, PhD and Jing Nong Liang, PT, PhD for their excellent guidance as principal investigators of this study.

Table of Contents

Abstract	iii
Acknowledgements	v
Table of Contents	vi
1. Introduction	1
2. Methods	4
2.1 Recruitment & Participants	4
2.2 Procedure	4
2.2.1 Screening	4
2.2.2 tDCS/Sham Setup	
2.2.3 Functional Tasks	6
2.2.4 Data Analysis	7
2.2.5 Statistical Analysis	8
3. Results	10
3.1 Participant Demographics	10
3.2 Forward Step Down	10
3.3 Lateral Step Down	
3.4 Single Leg Squat	10
3.5 Single Leg Landing	
3.6 Single Leg Hopping	
3.7 Pain	
4. Discussion	12
5. Conclusion	15
Appendices	16
Appendix A	16
	10

Curriculum Vitae	27
References	. 20
Appendix D	. 19
Appendix C	. 18

1. Introduction

Patellofemoral Pain (PFP) is a common musculoskeletal condition that presents as chronic peri- and/or retro-patellar pain.¹ This condition becomes more aggravated by compression of the patellofemoral joint while in a flexed knee position, especially during daily activities such as walking, squatting, kneeling, jogging, or stair climbing.² PFP is reported to affect the general population annually at a rate of 22.7%.³ Most commonly affected groups are those with high activity levels such as adolescents, young active adults, elite athletes, and military personnel.⁴ PFP is differentially distributed across sexes, with reports of females being 2.23 times more likely than males to develop the condition.⁴

A common movement deficit correlated with PFP is knee valgus during weight-bearing activities due to a combination of excessive hip adduction, internal rotation, and knee abduction which results in lateral patellar translation. Increased ipsilateral trunk lean during functional tasks has also been found in this population, shifting the ground reaction force laterally and increasing the weight bearing load to the medial knee.^{5,6} Patellar maltracking is influenced by several factors including: thicker and tighter illoitbial bands, weakness of the quadriceps, and decreased strength in hip abductors, external rotators, and extensors. The traditional approach to addressing aberrant movements in persons with PFP is to strengthen targeted muscles that control those movements, most commonly weak hip musculature.⁷ This has been shown to reduce pain in the short term, but has been found ineffective in providing long-term relief. ⁷ However, recent systematic reviews suggest that hip weakness may be a result of PFP, and not a cause of it.⁸⁻¹⁰ Therefore, hip strengthening regimens may only be addressing a pain-induced strength deficit, and not the root of the problem.¹¹ As a result, it has been suggested that kinematic errors from altered excitability/function of the gluteal musculature can lead to prolonged joint overloading and pain in persons with PFP.^{12,13}

Recent literature highlights the significant role of descending central control in providing the body with efficient functionality, and shows how an altered motor cortical structure and

reduced excitability contribute to the dysfunctional movement patterns that are associated with PFP.¹⁴ Persistently affected PFP limbs have shown contralateral hemispheric changes in corticomotor organization of the quadriceps and gluteus maximus muscles when compared to asymptomatic controls when mapped using transcranial magnetic stimulation (TMS).¹⁵⁻¹⁷ Among the altered primary motor cortex organizational findings were increased overlap, reduced peak volume, and an anteriorly shifted motor representation.¹⁵ Furthermore, at the level of the spinal cord, reduced vastus medialis reflex excitability was observed in women with patellofemoral pain compared with asymptomatic individuals. This indicated impaired transmission efficacy between vastus medialis motor neurons and la afferent inputs. The reduced excitability was also associated with higher pain levels.¹⁸⁻²⁰ By that notion, increasing neuronal excitability may possibly be an avenue for pain reduction interventions.

Transcranial Direct Current Stimulation (tDCS) is a neuromodulatory technique that has been shown to alter cortical excitability. This is achieved by non-invasively delivering a weak direct current via electrodes placed over the scalp to modulate cortical excitability²¹ by altering neuronal firing rates.^{22,23} This modality has the capability to increase and/or decrease cortical excitability in a process known as neurological priming and can be paired with other interventions, such as exercise, in an effort to enhance neuroplasticity.^{21,24} Recent research using tDCS priming supports its feasibility as a possible treatment for chronic pain, deficits post-stroke, gait deviations, and other musculoskeletal conditions to address dysfunctional movement patterns, highlighting the importance of continued research in this area of rehabilitation.^{7,21-23,25,26} While tDCS has been previously utilized as an intervention to increase muscular strength and reduce pain in persons with PFP, ²⁶ targeting the corticomotor function of the gluteal musculature with tDCS has not been examined in persons with PFP to our knowledge.

When evoked by TMS, increased corticomotor potentials of quadriceps muscles in individuals with PFP have been found compared to asymptomatic individuals by using

electromyography.²⁷ Reorganization of cortical structures, along with diminished motor cortex excitability, has been suggested to contribute to dysfunctional movement patterns that are associated with PFP.^{14,15} The use of tDCS can be paired with traditional exercise to modulate these changes and increase neuroplasticity. However, there is a lack of understanding about corticomotor modulation to the contralateral hemisphere of the gluteal musculature as an intervention for PFP. Therefore, the purpose of this study was to investigate whether modulation of cortical excitability of the gluteal musculature via tDCS paired with exercise will improve frontal plane kinematics of the lower extremity and trunk during functional tasks in individuals with PFP. We hypothesized that tDCS targeting the corticomotor area of the gluteal musculature paired with exercise will be more effective at improving frontal plane kinematics of the lower extremity and trunk in individuals with PFP when compared to exercise alone via sham stimulation.

2. Methods

2.1 Recruitment & Participants

We recruited 10 individuals with PFP, defined as peri- and/or retro patellar pain of at least 3 months duration.^{15,28} With a Type I error of 0.05, power of 95%, and calculated effect size of 0.82,²⁹ this sample size was determined to be sufficient for detecting a reduction in knee valgus following an acute intervention protocol.

Participants were recruited by advertisement flyers and via email in the Las Vegas area between 2022 and 2023. Inclusion criteria consisted of knee valgus presentation (assessed using a forward step-down test),³⁰⁻³³ predominantly unilateral PFP for at least 3 months, and aged between 18-45 years old. Our study primarily targeted individuals with unilateral PFP. However, we also included participants who reported PFP on both limbs but consistently reported one limb that experienced greater chronicity and pain. This choice was driven by our tDCS protocol, which aimed to enhance the cortical representation of the gluteal muscles on the affected limb while simultaneously inhibiting the contralateral limb. Exclusion criteria were a history of any major musculoskeletal injury or knee surgery.³³ For safety concerning utilization of tDCS, additional exclusion criteria included: history of balance disorder, seizures, prescription of seizure medication, pregnancy, potential pregnancy, and/or metallic implants.³⁴

2.2 Procedure

2.2.1 Screening

This was a double-blinded, sham-control crossover study performed in the Rod Lee Bigelow Health Sciences building on the campus of the University of Nevada, Las Vegas (UNLV). Prior to initiating any screening protocol, an informed consent was gathered from each potential participant. All potential participants were then screened through physical examination to rule out concomitant sources of pain. This process included palpation of the soft tissues around the patellofemoral joint and a patellar compression test to identify the location of pain. The patellar

compression test involved applying pressure to the patella when the participant straightened their knee. Participants were excluded if the knee pain did not originate from their patellofemoral joint. Participants then performed the following tasks: single leg squat, single leg landing, single leg hop, forward step down, and lateral step down (Figure 3; Appendix C). Participants were excluded if knee valgus was not observed during the functional movement screen. If participants presented with pain from the patella and knee valgus during step down, they were given the opportunity to experience tDCS and decide if they would still like to participate. If they qualified and chose to move forward with enrollment into the study, they then filled out 4 paper forms that included information about their activity level (Global Physical Activity Questionnaire³⁵; GPAQ), pain level of the knee (Anterior Knee Pain Scale³⁶; AKP), medical history (Medical History Questionnaire; MHQ), and safety to receive tDCS (TMS / tDCS Screening Questionnaire). The MHQ and TMS / tDCS Screening Questionnaire are both standard forms created by the UNLV Department of Physical Therapy and were approved by the Institutional Review Board at UNLV, who also approved the study protocol outlined below. Each enrolled participant's mass and height was recorded.

2.2.2 tDCS/Sham Setup

Each participant attended two separate sessions of stimulation (tDCS and Sham) held two weeks apart in a randomized order. To pseudo-randomize conditions, a coin was flipped to determine the type of stimulation that the first participant received during their first session. From that point on, each participant received the opposite type of stimulation to that of the previous participant in their first session. Thus, five participants were initially assigned to receive tDCS as their first sessions, while the other five participants were initially assigned to receive the Sham intervention as their first sessions. During their second session, each participant was given the opposite stimulation of what they were given during their first session. The same researcher applied the stimulation for each session to all participants within the study. It was not

possible for this person to be blinded as application of each stimulation (tDCS or Sham) required entry of a code on the neuroConn DC-Stimulator (neuroCare, Germany) to the corresponding stimulation to be applied. All other researchers were blinded to the stimulation being received at each session. A bihemispheric montage was used in administering the stimulation, as it has been reported to prompt greater behavioral improvements than conventional unihemispheric montage.³⁷ tDCS was applied with the anode positioned over the primary motor cortex contralateral to the affected limb and the cathode was positioned above the ipsilateral cortex (Figure 1; Appendix A). Application started with a 30 second ramp up period using a 2-mA current, stimulation for 19 minutes, and ended with a 30 second ramp down. For the Sham stimulation, the current was ramped up for 30 seconds and then shut off for the remaining time.^{34,37} During the stimulation period, participants performed 3 sets and 12 repetitions of the following exercises: clamshells, quadruped hip abduction, standing 45° hip extension, and side-lying hip abduction (Figure 2; Appendix B). Exercise resistance was applied by using an ankle weight that was 30% of their one-repetition maximum (1RM), determined through the use of a handheld dynamometer. 1RM was determined in the first session and the same resistance was used in both conditions.³⁸ Rest periods between sets and exercises lasted 30 seconds and 1 minute, respectively.

2.2.3 Functional Tasks

Immediately after exercises, frontal plane videos were taken while participants performed multiple functional tests: single leg squat, single leg landing, single leg hop, forward step down, and lateral step down test (Figure 3; Appendix C).^{39,40} For the single leg squat test, participants stood on their symptomatic limb, squatted to 45° of knee flexion, and returned to the starting position over a 3-second period. For the single leg landing, participants stood on a 30 cm step with their symptomatic limb, hopped off and landed on their symptomatic limb onto a mark 30 cm forward from the step, and maintained balance for 3 seconds after landing. For the single leg hop task, participants hopped as far forward as possible on their symptomatic limb and

maintained balance for 3 seconds after landing. For the forward step down, participants stood on a 30 cm step with their symptomatic limb, lightly tapped the heel of the contralateral foot on the floor in an anterior direction while maintaining balance on the platform, and returned to the starting position over a 3-second period. For the lateral step down test, participants stood on a 30cm step with their symptomatic limb, lightly tapped the heel of the contralateral foot on the floor in a lateral direction while maintaining balance on the platform, and returned to the starting position over a 3-second period. The participants performed each task 3 times and a 1-minute break was provided between tasks. Additional breaks were allowed by participants' requests to avoid fatigue. A SonyCX405 Handycam® camera was placed 15 feet anteriorly to the participant to capture the knee valgus angle at peak knee flexion in a frontal plane view during functional tasks. 2D red dot stickers were placed as markers over the sternum, bilateral anterior superior iliac spine (ASIS) landmarks, ipsilateral patella, and bisection of ipsilateral malleoli to assist with measurement of joint angles across the various functional tasks.

2.2.4 Data Analysis

Frontal plane kinematics during video recorded functional tasks were assessed using a free online motion capture software (Kinovea; version 0.9.5) by an investigator blinded to the condition. The following measures were taken from video recordings: Trunk lean angle (TLA), knee frontal plane projection angle (FPPA), hip FPPA, and dynamic valgus index (DVI).²⁹ Measurement began by a vertical reference line drawn superiorly from the ipsilateral ASIS of the standing leg. The next line was drawn between markers on bilateral ASIS landmarks for the pelvic segment. Bisecting the thigh with a line drawn from the midpoint of the patella to the ipsilateral ASIS created a thigh segment. A line from the midpoint of the patella to the midpoint of the ankle created a shank segment. Angle measurements for the hip, knee, and trunk were taken at peak knee flexion as determined by the recording investigator through later analysis of the video recordings.²⁹ TLA was the angle between the vertical reference line created from the ipsilateral ASIS and the line from the ipsilateral ASIS to the sternal marker (Figure 3; Appendix

C). TLA has been found to have moderate agreement and reliability when compared to a 3D motion capture system for single leg movements.^{5,6}A lower TLA indicates greater ipsilateral trunk lean towards the symptomatic limb. Knee FPPA was calculated by the subtraction of the angle between the thigh and shank segments from 180° (Figure 3; Appendix C). A higher knee FPPA means greater knee valgus of the symptomatic limb. Hip FPPA was calculated by subtraction of the angle between the pelvic and thigh segments from 90° (Figure 3; Appendix C). A higher hip FPPA indicates greater hip adduction of the symptomatic limb. Dynamic valgus index (DVI)²⁹ was used to assess the degree of knee valgus, calculated by the summation of knee (FPPA) and hip FPPA (Figure 3; Appendix C). Two-dimensional DVI has been found to have a moderate intra-rater reliability with an ICC of 0.74.²⁹ It has also been found to be more highly correlated with kinematics measured by a 3D motion capture system than measured by knee (FPPA) alone.²⁹ A higher DVI angle would indicate a greater summation of knee valgus and/or hip adduction.

The researcher measured and averaged the angles of the performed 3 repetitions of each task, which was analyzed statistically. Participants' pain level before and after each session was recorded using the Visual Analog Scale (VAS), where zero represents no pain and 10 represents maximal pain.

2.2.5 Statistical Analysis

The outcome measures of this study included hip FPPA, knee FPPA, DVI, and TLA during 5 functional tasks, as well as pain on a VAS before and after tDCS or Sham intervention. To establish a baseline for the participants' pre-intervention data, we calculated the average of the data collected on two separate days. This approach was employed after confirming via paired t-tests that there was no statistically significant difference between the pre-intervention data from the two separate days.

We conducted a Shapiro-Wilk test to assess the distribution of the collected data. The

results indicated that the hip FPPA, knee FPPA, DVI, and TLA data followed a normal distribution. However, the VAS data exhibited a non-normal distribution. Therefore, one-way ANOVAs with repeated measures and post-hoc pairwise comparisons with Bonferroni corrections were used to compare the hip FPPA, knee FPPA, DVI, and TLA among the 3 conditions (pre-intervention, post-tDCS, and post-Sham). Friedman test was used to compare the VAS among pre-, post-tDCS, and post-sham conditions. All statistical analyses were performed using SPSS software (ver. 27, International Business Machines Corp. New York, USA). A significant difference was defined as p < 0.05.

3. Results

3.1 Participant Demographics

We included 6 males and 4 females with PFP whose age was 28.2 ± 6.88 . Their average AKP Scale score was 79.1 ± 7.29 . The average BMI among participants was 26.83 ± 6.67 kg/m². As measured by the GPAQ, the average activity level among participants was classified as being "moderate intensity" with an average measurement among all participants being 2017 metabolic equivalents (METs) per week. Among these participants, 8 had unilateral pain and 2 had bilateral pain. Both individuals with bilateral PFP reported a history of consistently more pain on one limb for the past 6 months.

3.2 Forward Step Down

The one-way ANOVA with repeated measures showed that there was not a significant difference in hip FPPA, knee FPPA, DVI, and TLA during forward step down among the pre-, post-tDCS, and post-Sham conditions (p>0.05) (Table 1; Appendix D).

3.3 Lateral Step Down

The one-way ANOVA with repeated measures showed that there was not a significant difference in hip FPPA, knee FPPA, DVI, and TLA during lateral step down among the pre-, post-tDCS, and post-Sham conditions (p>0.05) (Table 1; Appendix D).

3.4 Single Leg Squat

The one-way ANOVA with repeated measures showed that there was not a significant difference in hip FPPA, knee FPPA, DVI, and TLA during single leg squat among the pre-, post-tDCS, and post-Sham conditions (p>0.05) (Table 1; Appendix D).

3.5 Single Leg Landing

The one-way ANOVA with repeated measures showed that there was a significant difference in knee FPPA between 3 conditions (pre, post-tDCS, and post-Sham) (p = .011). The post-hoc pairwise comparisons showed that knee FPPA was significantly lower after Sham intervention compared to the pre-condition (p= 0.018). There was not a difference between pre-condition

and post-tDCS condition (p=0.394) or between post-tDCS and post-Sham conditions (p=0.365) in knee FPPA (Table 1; Appendix D).

The one-way ANOVA with repeated measures showed that there was not a significant difference in hip FPPA, DVI, and TLA during single leg landing among the pre- post-tDCS, and post-Sham conditions (p>0.05) (Table 1; Appendix D).

3.6 Single Leg Hopping

The one-way ANOVA with repeated measures showed that there was not a significant difference in hip FPPA, knee FPPA, DVI, and TLA during single leg hopping among the prepost-tDCS, and post-Sham conditions (p>0.05) (Table 1; Appendix D).

<u>3.7 Pain</u>

The Friedman test showed that there was not a significant difference in VAS among the pre-intervention, post-tDCS, and post-Sham conditions (pre-intervention = 1.78; post-tDCS = 2.44; post-Sham = 1.78; p = 0.147).

4. Discussion

The purpose of this study was to investigate whether modulation of cortical excitability of the gluteal musculature via tDCS paired with exercise would improve frontal plane kinematics of the lower extremity and trunk during functional tasks in individuals with PFP. It was hypothesized that tDCS targeting the corticomotor area of the gluteal musculature paired with exercise would be more effective at improving frontal plane kinematics of the lower extremity and trunk in individuals with PFP when compared to exercise alone. In contradiction with our hypothesis, our findings showed that a single 20-minute bout of tDCS paired with exercise did not improve frontal plane movements and pain in persons with PFP when compared to exercise alone via sham stimulation.

The literature is limited in regard to the use of tDCS as a potential treatment for PFP, but has been explored in a few recent studies outlined below. To our knowledge, there has not been any previous studies exploring the effect of tDCS on frontal plane kinematics during functional tasks in individuals with PFP. Lower extremity strength gains have been obtained in individuals with PFP through the use of tDCS with exercise,²⁶ whereas another study⁴¹ did not find such effects in healthy individuals. This may be that the neural modulatory capacity of tDCS was applied over an altered primary motor cortex organization, as has been found in PFP. In regard to pain perception, our findings contrast those of Rodrigues et al. (2022) who found a decrease in pain post-tDCS intervention when compared to baseline.²⁶ This contrast may be attributed to the lack of congruency in the tDCS protocols applied between the two studies. As with our study, there was considerable variability in the subjective reporting of pain by participants. Both studies utilized the patellar compression test and VAS. Although not in PFP, similar decreases in pain through the use of tDCS have been found in knee osteoarthritis, fibromyalgia, spinal cord injury, amputation, stroke, multiple sclerosis, and radiculopathy.⁴²⁻⁴⁴

Rodrigues et al. (2022) looked at the efficacy of a 20 minute tDCS stimulation at increasing lower extremity strength in both a treatment and control group undergoing the same

resistance training program over the course of 4 weeks (12 sessions), with 48-72 hours between sessions in persons with PFP.²⁶ They assessed baseline strength with a 10 RM test and reassessed participants at sessions 4, 8, and 12. While both groups demonstrated significant differences at sessions 0, 4, 8, and 12 weeks, a significant interaction was not found between the control and the tDCS group until session 8. This suggests that there may be a possible minimum intervention period for tDCS effectiveness and that participants may need to regularly attend exercise sessions in conjunction with tDCS in order to see greater improvements in strength over exercise alone. Future studies should also consider a greater tDCS intervention period to potentially affect biomechanical improvements in individuals.

Our findings demonstrated only significantly lower knee FPPA on the single leg landing task in post-Sham condition when compared with pre-intervention condition. While such an improvement may be due to an exercise effect, this result may not be clinically meaningful or translate to improvement of functional task performance. The statistically significant finding may also be affected by false positives arising from multiple comparisons.⁴⁵ Specifically, the 4° difference is less than the standard error of measurement (SEM) of 4.34° and minimum detectable change (MDC) of 12.03° calculated using the pre-intervention measurements from 2 sessions (pre-tDCS and pre-Sham).

Several limitations became apparent throughout conducting this study. Initially, only participants with unilateral knee pain were considered for participation, however this proved to severely limit the pool of potential participants as PFP tends to present bilaterally. Due to the use of bihemispheric montage in this tDCS protocol, the desired cortical modulation of contralateral excitation and ipsilateral inhibition may not apply to those 2 participants who presented bilaterally. Despite expanding our inclusion criteria, only 10 participants were eligible to participate, limiting the efficacy and generalizability of the results. Additionally, participants served as their own controls rather than being compared to healthy individuals. Again, the use of bihemispheric montage in this tDCS protocol for contralateral excitation and ipsilateral

inhibition would present a challenge for the inclusion of a control group of healthy individuals where cortical changes are not observed and they lack a PFP affected limb. The compensations each may have developed over time to cope with their knee pain may contribute to a varied baseline between them. In order to mitigate the potential for carryover effect between conditions, participants waited 2 weeks between sessions to fulfill a washout period for the effects of tDCS. Despite this, it is possible their performance during the second session was altered due to a training effect after their first session. Because of these potential effects, future studies should utilize a control group with healthy individuals. Finally, it should be noted that participants only received the active intervention of tDCS during one session for a period of 20 minutes, which was insufficient to affect change in kinematics.

5. Conclusion

This study examined how a tDCS protocol targeting the modulation of cortical excitability of the gluteal muscles paired with exercise affects frontal plane kinematics and pain in persons with PFP when compared to exercise alone. Our study found that a single session of tDCS paired with exercise was ineffective at improving frontal plane movements or reducing pain during functional tasks in individuals with PFP. While there was a reduction in knee FPPA after Sham intervention, the difference was likely not clinically meaningful.

Appendices

<u>Appendix A</u>



Figure 1: Bihemispheric tDCS montage. Anode (red) positioned over the primary motor cortex contralateral to the affected limb and cathode (blue) positioned above the ipsilateral cortex.

Appendix B



Figure 2: Hip strengthening exercises included in the tDCS protocol: (A) clamshells (B) quadruped hip abduction (C) standing 45° hip extension (D) side-lying hip abduction

Appendix C



Figure 3: Two-dimensional frontal plane kinematics measured during (A) SLS = single leg squat, (B) SLL = single leg landing, (C) SLH = single leg hop, (D) FSD = forward step down, and (E) LSD = lateral step down tasks; Trunk Lean Angle (TLA) = Y; hip Frontal Plane Projection Angle (FPPA) = 90 - α ; knee FPPA = 180 - β ; Dynamic Valgus Index (DVI) = knee FPPA + hip FPPA

Appendix D Table 1: Means, Standard Deviations, and Significance Values of Assessed Contrasts

	Pre (mean±SD)	Post-tDCS (mean±SD)	Post-Sham (mean±SD)	<i>p</i> value
Forward Step Down				
Hip FPPA	18.4° ± 5.0°	19.1° ± 5.2°	19.0° ± 6.9°	.898
Knee FPPA	0.9° ± 10.5°	-0.1° ± 11.8°	-0.5° ± 12.9°	.615
DVI	19.3° ± 13.1°	19.1° ± 15.4°	18.5° ± 18.6°	.953
TLA	11.4° ± 5.1°	11.7° ± 5.0°	12.9° ± 6.4°	.164
Lateral Step Down				
Hip FPPA	25.7° ± 4.7°	24.6° ± 6.4°	26.2° ± 6.6°	.403
Knee FPPA	17.1° ± 11.2°	14.8° ± 11.1°	16.4° ± 15.5°	.434
DVI	42.8° ± 14.3°	39.4° ± 15.4°	42.7° ± 20.6°	.357
TLA	15.4° ± 5.4°	13.0° ± 6.4°	14.8° ± 7.0°	.090
Single Leg Squat				
Hip FPPA	9.6° ± 3.2°	9.9° ± 3.1°	11.8° ± 4.4°	.383
Knee FPPA	1.9° ± 6.3°	1.1° ± 4.4°	2.1° ± 7.0°	.759
DVI	11.2° ± 8.8°	10.9° ± 6.8°	13.9° ± 12.4°	.442
TLA	12.2° ± 3.9°	12.7° ± 3.7°	13.5° ± 6.5°	.552
Single Leg Landing				
Hip FPPA	8.8° ± 6.8°	9.0° ± 7.9°	7.9° ± 8.9°	.739
Knee FPPA	7.7° ± 6.0°	5.7° ± 7.5°	3.7° ± 6.2°#	.011*
DVI	16.5° ± 12.1°	14.7° ± 14.8°	11.6° ± 14.1°	.151
TLA	12.1° ± 7.9°	11.4° ± 6.7°	10.5° ± 8.6°	.284
Single Leg Hopping				
Hip FPPA	7.8° ± 6.4°	7.5° ± 7.5°	9.1° ± 9.1°	.627
Knee FPPA	3.6° ± 4.7°	2.1° ± 6.8°	3.7° ± 7.6°	.655
DVI	11.4° ± 12.2°	9.6° ± 13.5°	12.8° ± 15.3°	.525
TLA	10.2° ± 6.5°	9.4° ± 7.4°	11.3° ± 10.9°	.698

*Highlights a significant difference using one-way ANOVA with repeated measures.

Highlights a significant difference using post-hoc pairwise comparisons from the pre-condition. Abbreviations: FPPA - frontal plane projection angle; DVI - dynamic valgus index; TLA - trunk lean angle

References

1. Te M, Baptista AF, Chipchase LS, Schabrun SM. Primary Motor Cortex Organization Is Altered in Persistent Patellofemoral Pain. *Pain Medicine*. 2017;18(11):2224-2234. doi:http://dx.doi.org/10.1093/pm/pnx036

2. Crossley KM, Stefanik JJ, Selfe J, et al. 2016 Patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester. Part 1: terminology, definitions, clinical examination, natural history, patellofemoral osteoarthritis and patient-reported outcome measures. *Br J Sports Med.* 2016;50(14):839-843. doi:10.1136/bjsports-2016-096384

3. Smith BE, Selfe J, Thacker D, et al. Incidence and prevalence of patellofemoral pain: a systematic review and meta-analysis. *PLoS One.* 2018;13(1):e0190892. doi:10.1371/journal.pone.0190892

4. Roush JR, Curtis Bay R. Prevalence of anterior knee pain in 18-35 year-old females. *Int J Sports Phys Ther.* 2012;7(4):396-401

5. Kingston B, Murray A, Norte GE, Glaviano NR. Validity and reliability of 2-dimensional trunk, hip, and knee frontal plane kinematics during single-leg squat, drop jump, and single-leg hop in females with patellofemoral pain. *Phys Ther Sport.* 2020;45:181-187.

doi:10.1016/j.ptsp.2020.07.006

6. Ulman S, Ulman S, Erdman A, et al. Concurrent validity of movement screening criteria designed to identify injury risk factors in adolescent female volleyball players. *Front Sports Act Living.* 2022;4. doi:10.3389/fspor.2022.915230

7. Willy RW, Hoglund LT, Barton CJ, et al. Patellofemoral pain: Clinical Practice Guidelines linked to the International Classification of Functioning, Disability and Health from the Academy of Orthopaedic Physical Therapy of the American Physical Therapy Association. *J Orthop Sports Phys Ther.* 2019;49(9):CPG1-CPG95. doi:10.2519/jospt.2019.0302

 Rathleff MS, Rathleff CR, Crossley KM, Barton CJ. Is hip strength a risk factor for patellofemoral pain? a systematic review and meta-analysis. *Br J Sports Med.* 2014;48(14):1088. doi:10.1136/bjsports-2013-093305

 Neal BS, Lack SD, Lankhorst NE, Raye A, Morrissey D, van Middelkoop M. Risk factors for patellofemoral pain: a systematic review and meta-analysis. *Br J Sports Med.* 2019;53(5):270-281. doi:10.1136/bjsports-2017-098890

10. Rabelo NDdA, Lucareli PRG. Do hip muscle weakness and dynamic knee valgus matter for the clinical evaluation and decision-making process in patients with patellofemoral pain? *Braz J Phys Ther.* 2018;22(2):105-109. doi:10.1016/j.bjpt.2017.10.002

11. Willy RW, Davis IS. The effect of a hip-strengthening program on mechanics during running and during a single-leg squat. *J Orthop Sports Phys Ther.* 2011;41(9):625-632. doi:10.2519/jospt.2011.3470

12. Glaviano NR, Bazett-Jones D, Norte G. Gluteal muscle inhibition: consequences of patellofemoral pain? *Med Hypotheses*. 2019;126:9-14. doi:10.1016/j.mehy.2019.02.046

13. Powers CM, Witvrouw E, Davis IS, Crossley KM. Evidence-based framework for a pathomechanical model of patellofemoral pain: 2017 patellofemoral pain consensus statement from the 4th International Patellofemoral Pain Research Retreat, Manchester, UK: part 3. *Br J Sports Med.* 2017;51(24):1713-1723. doi:10.1136/bjsports-2017-098717

14. Liang JN, Budge S, Madriaga A, Meske K, Nguyenton D, Ho K. Neurophysiological changes of brain and spinal cord in individuals with patellofemoral pain: a systematic review and meta-analysis protocol. *BMJ open.* 2021;11(7):e049882. doi:10.1136/bmjopen-2021-049882

15. Te M, Baptista AF, Chipchase LS, Schabrun SM. Primary motor cortex organization is altered in persistent patellofemoral pain. *Pain Med.* 2017;18(11):2224-2234. doi:10.1093/pm/pnx036

16. Ho K, Liang JN, Budge S, Madriaga A, Meske K, Nguyenton D. Brain and spinal cord adaptations associated with patellofemoral pain: a systematic review and meta-analysis. *Front Integr Neurosci.* 2022;16:791719. doi:10.3389/fnint.2022.791719

17. Shih Y, Fisher BE, Smith JA, Powers CM. Corticomotor excitability of gluteus maximus is associated with hip biomechanics during a single-leg drop-jump. *J Mot Behav.* 2021;53(1):40-46. doi:10.1080/00222895.2020.1723480

18. de Oliveira Silva D, Magalhães FH, Faria NC, et al. Lower amplitude of the Hoffmann Reflex in women with patellofemoral pain: thinking beyond proximal, local, and distal factors. *Arch Phys Med Rehabil.* 2016;97(7):1115-1120. doi:10.1016/j.apmr.2015.12.017

19. de Oliveira Silva D, Magalhães FH, Faria NC, et al. Vastus medialis Hoffmann Reflex excitability is associated with pain level, self-reported function, and chronicity in women with patellofemoral pain. *Arch Phys Med Rehabil.* 2017;98(1):114-119.

doi:10.1016/j.apmr.2016.06.011

20. Tsao H, Galea MP, Hodges PW. Reorganization of the motor cortex is associated with postural control deficits in recurrent low back pain. *Brain.* 2008;131(8):2161-2171. doi:10.1093/brain/awn154

21. Schabrun SM, Chipchase LS. Priming the brain to learn: The future of therapy? *Man Ther.* 2011;17(2):184-186. doi:10.1016/j.math.2011.12.001

22. Boggio PS, Amancio EJ, Correa CF, et al. Transcranial DC stimulation coupled with TENS for the treatment of chronic pain: a preliminary study. *Clin J Pain.* 2009;25(8):691-695. doi:10.1097/AJP.0b013e3181af1414

23. Celnik P, Paik N, Vandermeeren Y, Dimyan M, Cohen LG. Effects of combined peripheral nerve stimulation and brain polarization on performance of a motor sequence task after chronic stroke. *Stroke.* 2009;40(5):1764-1771. doi:10.1161/STROKEAHA.108.540500

24. Lefaucheur J, Antal A, Ayache SS, et al. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). *Clin Neurophysiol.* 2017;128(1):56-92. doi:10.1016/j.clinph.2016.10.087

25. Geroin C, Picelli A, Munari D, Waldner A, Tomelleri C, Smania N. Combined transcranial direct current stimulation and robot-assisted gait training in patients with chronic stroke: a preliminary comparison. *Clin Rehabil.* 2011;25(6):537-548. doi:10.1177/0269215510389497

26. Rodrigues GM, Paixão A, Arruda T, et al. Anodal transcranial direct current stimulation increases muscular strength and reduces pain perception in women with patellofemoral pain. *J Strength Cond Res.* 2022;36(2):371-378. doi:10.1519/JSC.00000000003473

27. On AY, Uludağ B, Taşkiran E, Ertekin C. Differential corticomotor control of a muscle adjacent to a painful joint. *Neurorehabil Neural Repair.* 2004;18(3):127-133. doi:10.1177/0888439004269030

28. Ho K, Keyak JH, Powers CM. Comparison of patella bone strain between females with and without patellofemoral pain: a finite element analysis study. *J Biomech.* 2013;47(1):230-236. doi:10.1016/j.jbiomech.2013.09.010

29. Scholtes SA, Salsich GB. A dynamic valgus index that combines hip and knee angles: assessment of utility in females with patellofemoral pain. *Int J Sports Phys Ther.* 2017;12(3):333-340

30. Earl JE, Monteiro SK, Snyder KR. Differences in lower extremity kinematics between a bilateral drop-vertical jump and a single-leg step-down. *J Orthop Sports Phys Ther.* 2007;37(5):245-252. doi:10.2519/jospt.2007.2202

31. Lopes Ferreira C, Barton G, Delgado Borges L, dos Anjos Rabelo ND, Politti F, Garcia Lucareli PR. Step down tests are the tasks that most differentiate the kinematics of women with patellofemoral pain compared to asymptomatic controls. *Gait Posture*. 2019;72:129-134. doi:10.1016/j.gaitpost.2019.05.023

32. Park K, Cynn H, Choung S. Musculoskeletal predictors of movement quality for the forward step-down test in asymptomatic women. *J Orthop Sports Phys Ther.* 2013;43(7):504-510. doi:10.2519/jospt.2013.4073

33. Ho K, Murata A. Asymmetries in dynamic valgus index after anterior cruciate ligament reconstruction: a proof-of-concept study. *Int J Environ Res Public Health.* 2021;18(13):7047. doi:10.3390/ijerph18137047

34. Liang JN, Ubalde L, Jacklin J, Hobson P, Wright-Avila S, Lee Y. Immediate effects of anodal transcranial direct current stimulation on postural stability using computerized dynamic

posturography in people with chronic post-stroke hemiparesis. *Front Hum Neurosci.* 2020;14:341. doi:10.3389/fnhum.2020.00341

35. Riley L, Guthold R, Cowan M, et al. The World Health Organization STEPwise approach to noncommunicable disease risk-factor surveillance: methods, challenges, and opportunities. *Am J Public Health.* 2016;106(1):74-78. doi:10.2105/AJPH.2015.302962

36. Kujala UM, Jaakkola LH, Koskinen SK, Taimela S, Hurme M, Nelimarkka O. Scoring of patellofemoral disorders. *Arthroscopy.* 1993;9(2):159-163. doi:10.1016/S0749-8063(05)80366-4

37. Waters-Metenier S, Husain M, Wiestler T, Diedrichsen Jö. Bihemispheric transcranial direct current stimulation enhances effector-independent representations of motor synergy and sequence learning. *J Neurosci.* 2014;34(3):1037-1050. doi:10.1523/JNEUROSCI.2282-13.2014

38. Kraemer WJ, Adams K, Cafarelli E, et al. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc.* 2002;34(2):364-380

39. Herrington L. Knee valgus angle during single leg squat and landing in patellofemoral pain patients and controls. *Knee*. 2013;21(2):514-517. doi:10.1016/j.knee.2013.11.011

40. Piva SR, Fitzgerald K, Irrgang JJ, et al. Reliability of measures of impairments associated with patellofemoral pain syndrome. *BMC Musculoskelet Disord.* 2006;7(1):33. doi:10.1186/1471-2474-7-33

41. Maeda K, Yamaguchi T, Tatemoto T, Kondo K, Otaka Y, Tanaka S. Transcranial direct current stimulation does not affect lower extremity muscle strength training in healthy individuals: a triple-blind, sham-controlled study. *Front Neurosci .* 2017;11:179. doi:10.3389/fnins.2017.00179

42. David MCMM, Moraes AAd, Costa MLd, Franco CIF. Transcranial direct current stimulation in the modulation of neuropathic pain: a systematic review. *Neurol Res.* 2018;40(7):557-565. doi:10.1080/01616412.2018.1453190

43. Antal A, PhD., Terney D, M.D., Kühnl S, Paulus W, M.D. Anodal transcranial direct current stimulation of the motor cortex ameliorates chronic pain and reduces short intracortical inhibition. *J Pain Symptom Manage.* 2010;39(5):890-903.

doi:10.1016/j.jpainsymman.2009.09.023

44. Ahn H, Woods AJ, Kunik ME, et al. Efficacy of transcranial direct current stimulation over primary motor cortex (anode) and contralateral supraorbital area (cathode) on clinical pain severity and mobility performance in persons with knee osteoarthritis: An experimenter- and participant-blinded, randomized, sham-controlled pilot clinical study. *Brain Stimul.* 2017;10(5):902-909. doi:10.1016/j.brs.2017.05.007

45. Ranganathan P, Pramesh C, Buyse M. Common pitfalls in statistical analysis: The perils of multiple testing. *Perspect Clin Res.* 2016;7(2):106-107. doi:10.4103/2229-3485.179436

Curriculum Vitae

Jeno Aquino

Department of Physical Therapy, University Of Nevada, Las Vegas 4505 Maryland Parkway, Las Vegas, Nevada 89154 jeno.d.aquino@gmail.com

Education

May 2024	Doctor of Physical Therapy (University of Nevada, Las Vegas)
May 2020	Bachelor of Science in Health Science (University of Guam)

Licensure

Apr 2024 Pending National Physical Therapy Examination

Certifications

Apr 2024 American Heart Association, BLS/CPR for Healthcare Providers

Clinical Affiliations

Jan - Mar 2024 | Encompass Health of Las Vegas (Inpatient Rehabilitation; Las Vegas, NV) Sep - Dec 2023 | Dignity Health Physical Therapy (Outpatient Ortho; Las Vegas NV) July - Sep 2023 | St. Rose Dominican - San Martin Campus (Acute Care; Las Vegas, NV June - July 2022 | Professional Physical Therapy and Sports Medicine (Outpatient Ortho; Orem, Utah)

Employment

Aug 2022 - Jun 2023 UNLVPT Graduate Teaching Assistant (Las Vegas, NV)

Research Activity

Sep 2021 - May 2024 Examining the Effects of Cortical Excitability Modulation on Functional Movements in Individuals with Patellofemoral Pain: A Randomized Controlled Trial

- Principal Investigators: Kai-Yu Ho, PT, MPT, PhD and Jing Nong Liang, PT, PhD
- Submitted for publication

Membership in Professional Organizations

Aug 2021 - Present American Physical Therapy Association (APTA) Member #: 961689

- Academy of Geriatric Physical Therapy
- Nevada Physical Therapy Association

Honors & Awards

UNLV Graduate Access Scholarship (2022, 2023)

Bryce Broadwell

Department of Physical Therapy, University Of Nevada, Las Vegas 4505 Maryland Parkway, Las Vegas, Nevada 89154 brycebroadwell@gmail.com

Education

May 2024 | Doctor of Physical Therapy (University of Nevada, Las Vegas) May 2020 | Bachelor of Arts in Biology, Minor in Chemistry (University of Redlands)

Licensure

Apr 2024 Pending National Physical Therapy Examination

Certifications

Apr 2024 American Heart Association, BLS/CPR for Healthcare Providers

Clinical Affiliations

Jan - Mar 2024 Optimal Physical Therapy (Underserved Outpatient Orthopedics; Henderson, NV)

Sep - Dec 2023 | St. Rose Dominican Hospital Siena Campus (Acute Care; Henderson, NV) July - Sep 2023 | Banner Baywood Medical Center (Acute Care; Mesa, AZ)

June - July 2022 PRN - Kelly Hawkins Physical Therapy (Outpatient Orthopedics; Henderson, NV)

Research Activity

Sep 2021 - May 2024 Examining the Effects of Cortical Excitability Modulation on Functional Movements in Individuals with Patellofemoral Pain: A Randomized Controlled Trial

- Principal Investigators: Kai-Yu Ho, PT, MPT, PhD and Jing Nong Liang, PT, PhD
- Submitted for publication

Membership in Professional Organizations

Aug 2021 - Present American Physical Therapy Association (APTA) Member #: 968442

- Academy of Orthopaedic Physical Therapy
- Academy of Geriatric Physical Therapy
- Nevada Physical Therapy Association

Honors & Awards

UNLV Graduate Access Scholarship (2022, 2023) University of Redlands Dean's List (2018)

Connan Wallace

Department of Physical Therapy, University Of Nevada, Las Vegas 4505 Maryland Parkway, Las Vegas, Nevada 89154 wallaceconnan@gmail.com

Education

May 2024 | Doctor of Physical Therapy (University of Nevada, Las Vegas) May 2020 | Bachelor of Science in Kinesiology (Utah State University)

Licensure

Apr 2024 Pending National Physical Therapy Examination

Certifications

Apr 2024 American Heart Association, BLS/CPR for Healthcare Providers

Clinical Affiliations

Jan - Mar 2024 | Neuroworx (Outpatient Neuro; Sandy, UT) Sep - Dec 2023 | Intermountain - Logan Regional Hospital (Acute Care; Logan, UT) July - Sep 2023 | Maple Springs of North Logan (Skilled Nursing Facility; Logan, UT) June - July 2022 | Family & Sports Physical Therapy (Outpatient Ortho; Las Vegas, NV)

Employment

Aug 2022 - Jun 2023 UNLVPT Graduate Teaching Assistant (Las Vegas, NV)

Research Activity

Sep 2021 - May 2024 | Examining the Effects of Cortical Excitability Modulation on Functional Movements in Individuals with Patellofemoral Pain: A Randomized Controlled Trial

- Principal Investigators: Kai-Yu Ho, PT, MPT, PhD and Jing Nong Liang, PT, PhD
- Submitted for publication

Membership in Professional Organizations

Aug 2021 - Present American Physical Therapy Association (APTA) Member #: 953880

- Academy of Orthopaedic Physical Therapy
- Academy of Neurologic Physical Therapy
- Nevada Physical Therapy Association

Honors & Awards

ACAPT National Student Honor Society Inductee (2024) UNLVPT Recognition of Achievement Award (2022, 2023, 2024) UNLVPT Kitty Rodman Award of Excellence (2023) UNLV Graduate Access Scholarship (2022, 2023) USU Dean's List (2017)

Makenzie Whimple

Department of Physical Therapy, University Of Nevada, Las Vegas 4505 Maryland Parkway, Las Vegas, Nevada 89154 makenziewhimple@gmail.com

Education

May 2024 Doctor of Physical Therapy (University of Nevada, Las Vegas) Apr 2019 Bachelor of Science in Exercise Science (Brigham Young University)

Licensure

July 2024 Pending National Physical Therapy Examination

Certifications

Apr 2022 American Heart Association, BLS/CPR for Healthcare Providers

Clinical Affiliations

Jan - Mar 2024 | Dignity Health Rehabilitation Hospital (Inpatient Rehab; Henderson, NV) Sep - Dec 2023 | Synergy Physical Therapy (Outpatient Ortho; Henderson, NV) July - Sep 2023 | Craig Neilson Rehabilitation Hospital (Inpatient Rehab; Salt Lake City, UT) June - July 2022 | Ruby Mountain Physical Therapy (Outpatient Ortho and Home Health; Elko, NV)

Research Activity

Sep 2021 - May 2024 | Examining the Effects of Cortical Excitability Modulation on Functional Movements in Individuals with Patellofemoral Pain: A Randomized Controlled Trial

- Principal Investigators: Kai-Yu Ho, PT, MPT, PhD and Jing Nong Liang, PT, PhD
- Submitted for publication

Membership in Professional Organizations

Aug 2021 - Aug 2023 American Physical Therapy Association (APTA) Member #: 959496

Honors & Awards

UNLV DPT Department Scholarship (2022) BYU College of Life Sciences Dean's List (2018)