Brain-Computer Interface Visualization Training to Optimize Muscle Activation Following Orthopaedic Surgery

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1. Abstract

Postoperative recovery following orthopedic surgeries often faces challenges due to Arthrogenic Muscle Inhibition (AMI), a neurological condition that impairs muscle activation and hinders rehabilitation. This study investigates the effectiveness of visualization training with neurofeedback as a supplementary method to standard physical therapy in reducing AMI and improving functional recovery. Neurofeedback, utilizing electroencephalography (EEG), provides real-time feedback on motor cortex activation during mental visualization of movements. The study focuses on patients recovering from four orthopedic procedures—anterior cruciate ligament reconstruction (ACLR), total knee arthroplasty (TKA), total hip arthroplasty (THA), and hip arthroscopy (HA) for femoroacetabular impingement syndrome (FAIS). Using iBrainTech™ technology, we aim to assess improvements in muscle activation, range of motion, strength, and patient-reported outcomes. Findings could enhance rehabilitation protocols, accelerate recovery, and deepen understanding of neuroplasticity in motor control.

2. Introduction

Background

Patients recovering from orthopedic surgical procedures require a comprehensive physical rehabilitation process to help recover pre-operative functional mobility and strength.

A limiting factor in physical rehabilitation is a patient's inability to activate the involved muscle groups postoperatively, a phenomenon termed Arthrogenic Muscle Inhibition (AMI) [1, 2]. AMI is a complex neurological process where the injury or surgery disrupts sensory and motor neurological pathways, resulting in decreased muscle activation and strength. AMI can be a major obstacle to a patient's return to normal mobility and muscular function [2]. For example, patients who have undergone anterior cruciate ligament reconstruction (ACLR), may experience ineffective quadriceps activation and persistent hamstring contracture, leading to loss of passive and active range of motion (ROM). Even with standard physical therapy rehabilitation, patients with AMI have ineffective recovery due to decreased muscular activation and movement dysfunction [3].

Visualization training with neurofeedback therapy is a non-invasive method that could be used with standard post-operative physical rehabilitation to decrease AMI and help patients recover pre-operative functional mobility and strength.

The motor regions of the brain (motor cortex) play a crucial role in planning, controlling, and executing voluntary movements. The motor cortex is not only active during actual movement; mentally rehearsing motor acts without physically moving also activates the motor cortex [4]. For example, one could imagine themselves performing squats without squatting (visualization), this process activates the brain regions related to squatting. Such visualization training can enhance the brain's ability to plan, control and execute movement without physical load on the body [5]. Theoretically, this training could help restore disrupted neurological pathways, leading to reduced AMI and improved patient recovery after surgery [6].

When a brain region has heightened activity, passive sensors on the scalp can detect the increased electrical activity, this technique is known as electroencephalography (EEG). A computer can process the EEG signal and provide users with real time feedback on their concentration level and whether they are activating their motor cortex through mental visualization of movements (neurofeedback). This feedback process enhances the visualization training [6].

This study aims to investigate the effect of visualization with neurofeedback on postoperative recovery in patients undergoing physical rehabilitation from 4 orthopedic surgical procedures: anterior cruciate ligament reconstruction (ACLR), total knee arthroplasty (TKA), total hip arthroplasty (THA), and hip arthroscopy (HA) for femoroacetabular impingement syndrome (FAIS). More specifically, neurofeedback training will be implemented using a novel technology developed by iBrainTech™ (**Figure 1**).

The findings of this study have the potential to revolutionize physical rehabilitation protocols for patients, offering a novel approach that integrates visualization therapy with neurofeedback to enhance standard physical rehabilitation. This could lead to faster, more complete recoveries, and potentially mitigate the long-term impacts of AMI. The successful application of this technology would also help deepen current understanding of neuroplasticity, specifically the malleability of the neuromuscular pathways and how this can improve motor control.

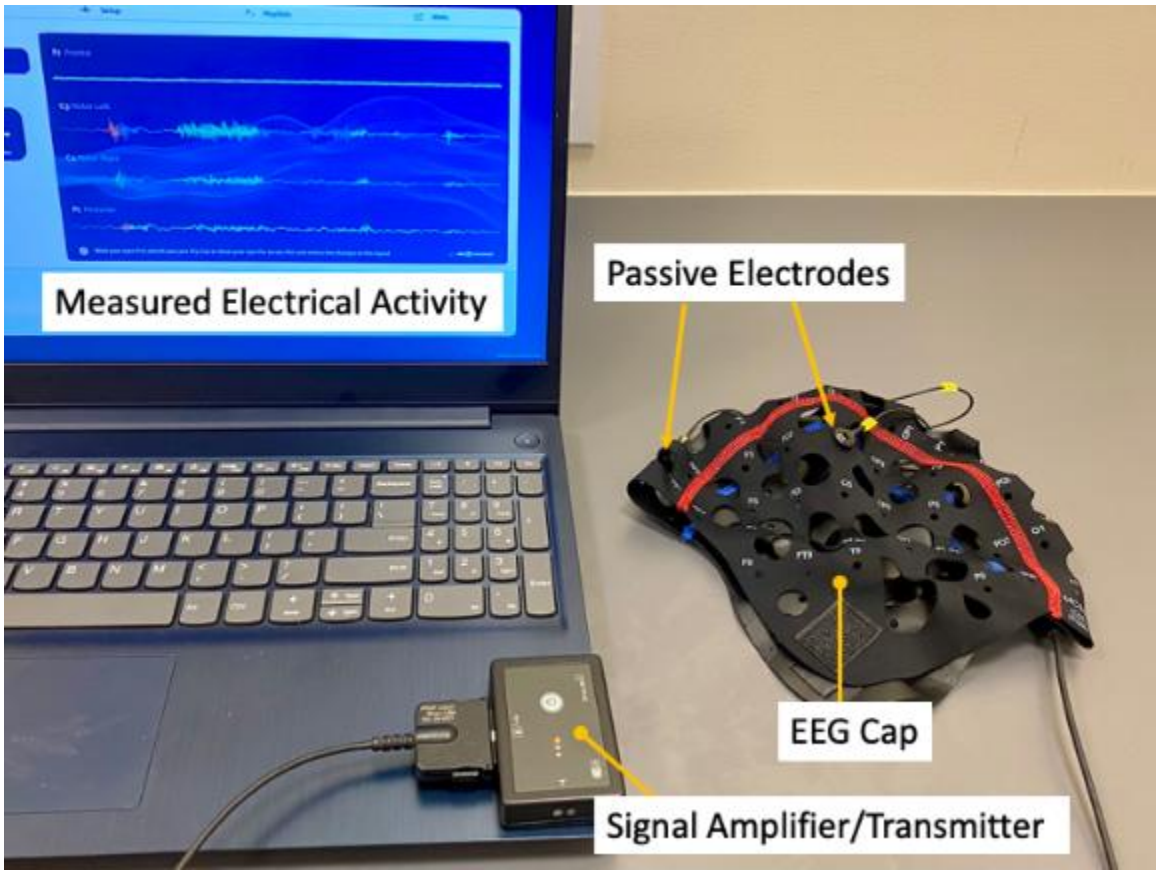

Figure 1 : The EEG device used in this study.

Purpose

The purpose of this study is to investigate the effect of visualization training with neurofeedback on postoperative recovery in patients rehabilitating from orthopedic surgeries.

Hypothesis

We hypothesize that through targeted visualization training with neurofeedback using iBrainTech™, post-surgical participants will experience improved muscle activation, which in turn will contribute to better rehabilitation outcomes, strength, such as range of motion, , and functional mobility. We also hypothesize that these improvements seen throughout the recovery period will have a positive impact on short-term patient-reported outcome surveys (PROs).

3. Methods

Trial Design

This study is a randomized, blinded (outcome assessors, physicians and statisticians) controlled trial investigating the effect of neurofeedback visualization training on AMI in patients following orthopedic procedures. The study will have two arms – a 1:1 allocation ratio for the control group and for the intervention cohort – stratified into four orthopedic surgeries:

- Anterior Cruciate Ligament Reconstruction (ACLR)
- Total Knee Arthroplasty (TKA)
- Total Hip Arthroplasty (THA)
- Hip Arthroscopy (HA) for Femoroacetabular Impingement Syndrome (FAIS)

There will be 30 participants per cohort arm for each procedure, totaling 240 participants for the project. In the event of any changes, modifications to eligibility criteria or study methods will be documented and justified in study amendments. In addition, any changes to data collection, analysis, or participant follow-up will be noted in trial records.

Participants

- Inclusion Criteria:
  - Patient age >18 years
  - Ability to complete neurofeedback training and follow study follow-ups
  - Indicated for one of the four investigated orthopedic procedures
- Exclusion Criteria:
  - Inability to participate in neurofeedback training
  - Lack of decisional capability
  - History of stroke, movement disorder (e.g. Parkinson's), peripheral neuropathy
  - Cardiac pacemaker or other internal electronic device
  - BMI >35

- Previous surgery or specific pathology on the affected joint (refer to procedure specific indications below)

Procedure Specifics:

Anterior cruciate ligament reconstruction (ACLR)

Procedure-specific Inclusion Criteria

- Patients undergoing primary ACLR with autograft or allograft tissue
- Adjunct lateral Extra-articular tenodesis will be included
- Additional meniscus debridement and repair will be included

Procedure-specific exclusion criteria

- Revision ACL surgery
- Moderate to Severe arthritis – Kellgren-Lawerence (KL) Grade > 3
- Patients with meniscus root repair
- Non-weight-bearing status exceeding 1 week postoperatively

Total knee arthroplasty (TKA)

Procedure specific inclusion criteria

- Patients undergoing primary TKA
- Preoperative total knee range of motion of at least 100 degrees (combined flexion and extension)
- Prior extensor mechanism tendon repair, quadriceps or patella tendon.

Procedure specific exclusion criteria

- Revision surgery
- Hinged implant
- Any open procedure involving the knee joint
- Symptomatic arthritis in the contralateral knee with planned or expected total knee arthroplasty within 6 months
- Inflammatory Arthritis

Total hip arthroplasty (THA)

Procedure Specific Inclusion Criteria

- Patients undergoing primary THA

Procedure Specific Exclusion Criteria

- Revision Surgery
- Any open procedure involving the hip joint
- Bilateral THA procedures
- Inflammatory Arthritis

Hip arthroscopy (HA) for femoroacetabular impingement syndrome (FAIS)

Procedure Specific Inclusion Criteria

- Patients undergoing HA for FAIS

Procedure Specific Exclusion Criteria

- Revision Surgery
- Diagnosis of hip dysplasia

Settings & Locations

Conducted at Rush University Medical Center, specifically within:

- The main campus of Midwest Orthopaedics at Rush (MOR) Sofija and Jorge O. Galante Orthopedic Building, 1611 W Harrison St, Chicago, IL 60612
- Motion Laboratory in the MOR Orthopedic Building
- Physical therapy facility (Chicago location)

4. Interventions

Control group: Standard post-surgical rehabilitation therapy
Intervention Group: Standard post-surgical rehabilitation therapy + iBrainTech neurofeedback training

- Procedure: Patients use EEG-based neurofeedback twice a week until 8 weeks post-operatively.
- Neurofeedback setup: EEG cap monitors motor cortex activation, guiding visualization exercises
- Training sessions: Patients visualize movements, and EEG feedback helps optimize motor activation
-

Physical Therapy

Patients will follow a standard physical therapy protocol. The protocol will be assigned by their respective surgeon who conducted the procedure and will be specific to the procedure that the patient underwent. The standardized physical therapy protocols will be attached in supplemental materials.

Treatment Group Intervention:

The main study intervention for the treatment group involves visualization training using the i-BrainTech™ Platform.

This is a technology that uses electroencephalography (EEG) to read the electrical activities in the brain [7]. Active neurons in the brain causes change in electrical activities on the scalp, detectable by electrodes placed on the scalp. The sensing electrodes are completely passive, incapable of sending electrical current to the wearer. An EEG cap will be used with sensing electrodes aligned to the frontal cortex and the motor cortex. The detected electrical activity from these locations of the scalp will transmitted to the computer, which allows for assessment of focus and motor cortex activity [8]. There are multiple cap sizes of the cap to ensure a comfortable fit.

By concentrating and imagining themselves performing the rehabilitation movements (visualization), patients activate their own motor and pre-frontal cortices. The EEG sensors detects the increased brain electrical activity, and the iBrainTech™ software translates the EEG

signal into a virtual avatar figure performing such movements on a computer monitor, providing feedback to the patients on their visualization efforts (neurofeedback)(**Figure 2**). Patients will effectively play a video game using their own brain signals. By turning this feedback process into a video game, the iBrainTech™ platform provides an incentive for the user to intensely focus and visualize the rehabilitation exercises, and in the process activate and strengthen the neural pathways responsible for these rehabilitation movements. The repeated activation of neural pathways theoretically improves their muscle control and reduces AMI [6].

Figure 2: Rendition of neurofeedback training process. Source: iBrainTech™

Instruction to Participants (how to play the "game")

The i-BrainTech™ training station has a laptop and EEG caps. Participants will be seated in front of the laptop and put on the appropriately sized EEG cap. A conductive gel is injected into 2 insertion points on the cap. The column of gel touches the participant's skin on one side and the sensor on the other. The gel is water-soluble and dries up in chunks and is not sticky. The conductive gel is routinely used in the clinic and pre-operative area for ultrasound. The wet gel can be wiped off with a paper towel and the dried gel can be pulled off the participant's scalp as it does not stick to hair. The remaining fragments will be washed away when the patient showers.

The session will be started and the i-BrainTech™ software will provide on screen prompts and feedback to the user.

First is a 2-minute calibration period. During this time, the user is prompted to relax their mind so baseline brain activity may be detected. The brain activity above the baseline is used to control the cartoon avatar performing rehabilitation exercises.

After calibration, a 20-minute visualization training with neurofeedback session begins. Participants are prompted to imagine themselves performing various rehabilitation exercises (visualization). The selections of exercises are the rehabilitation exercises they will eventually perform at a physical therapy session, specific to their surgical procedures (**Table 1**). The software provides real time feedback on how concentrated the user is with the task, and how well the user is at visualizing the specific therapy exercises. The video game incentivizes participants to concentrate on the visualization therapy to maximize their score.

When the participant finishes the i-BrainTech™ training session, they will remove the EEG cap and move on to their standard of care physical therapy session.

Table 1: Exercises performed during the sessions of visualization training with neurofeedback.

Day 1 to 3 weeks	3 weeks to 6 weeks	6 weeks to 8 weeks
Mini-Squats	Mini-Squats w/DB	Squats w/DB
Air Squats	Lateral lunge (involved)	Lunges/DB (uninvolved)
Lateral Lunge (involved)	Lunges w/DB (involved)	Reverse Lunge w/DB (involved)
Gastroc Stretch (uninvolved)	Reverse Lunges (involved)	Lunges/DB (involved)
Heel raises	Lunges w/DB (uninvolved)	Reverse Lunge w/DB (uninvolved)
Leg Raise (involved)	Heel Raises w/DB	SL Stance
Lunges (involved)	Air Squats	Heel Raises w/DB
Lunges (uninvolved)	Lateral lunge (uninvolved)	Lateral lunge (involved)

DB: Dumbbell. SL: Single leg

5. FDA Status of the Device

The i-BrainTech™ platform is approved by the Food and Drug Administration (FDA) as a Class II medical device.

Participant Flow

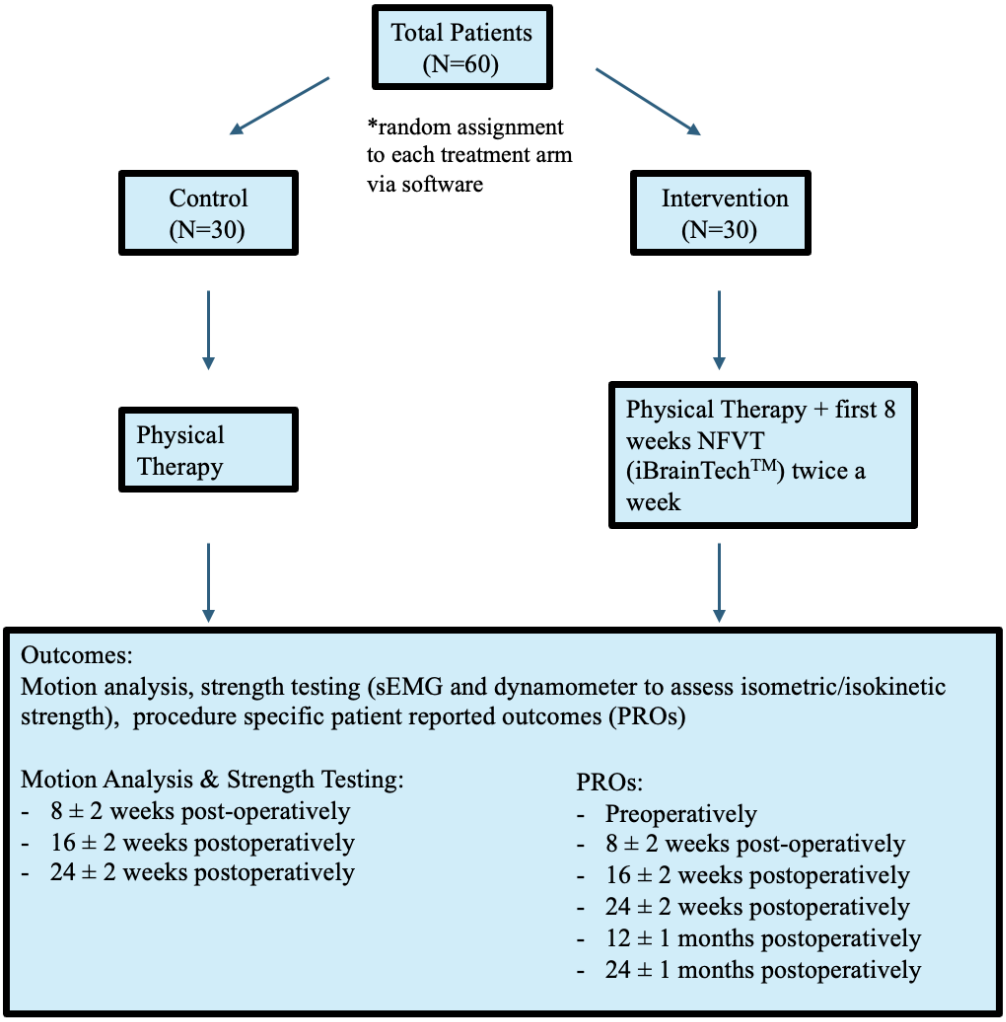

Figure 3: Participants Flow

6. Clinic Flow and Timing of Assessments

Participants in the intervention group will perform virtual rehabilitation exercises for 20 minutes 2 times per week for the first 8 weeks postoperatively.

Approximately 45 minutes total is required for setup, calibration, virtual rehabilitation, and clean up.

After the virtual rehab session, patients in the intervention group will move on to their standard-of-care PT session based on the surgeon's protocol specific to their operation. Patients in the control group go directly to their standard PT session.

The intervention group will spend an additional 45 minutes in clinic to perform the i-BrainTech™ training session for a total study visit time of no more than 1-1.5 hours.

The control group will spend 45 minutes to 1 hour of total study visit time.

Participants will continue receiving their standard clinical care with their attending healthcare team throughout the study. In addition, they will attend scheduled study visits at the Motion Laboratory in the Orthopedic Building at Rush University Medical Center for motion analysis and physical testing at 2 months, 4 months, and 6 months post-surgery.
At each visit, anthropometric data (age, height, weight, and BMI) will be collected first. Participants will then change into standardized clothing provided by the research team.

Surface Electromyography (sEMG)

sEMG data will be collected from five muscles: rectus femoris, vastus medialis oblique, vastus lateralis, semitendinosus, and biceps femoris, using a research-grade sEMG system. Electrode placement will follow the SENIAM (Surface EMG for a Non-Invasive Assessment of Muscles) protocol.

Per SENIAM guidelines, the skin will be shaved, lightly abraded with abrasion wipes, and cleaned with alcohol wipes before electrode application. Electrodes will be placed at least 2 cm apart to minimize crosstalk, and voluntary contractions will be performed to confirm correct placement.

Each muscle will be assessed individually before data collection. Once all sensors are verified, simultaneous sEMG and 3D kinematic data collection will be performed using Qualisys Track Manager software or similar.

Motion Capture

To evaluate patient-specific movement mechanics, a markerless multi-camera motion analysis system will be used to track kinematics, while instrumented force plates will measure ground reaction forces. The markerless system allows for accurate motion tracking while significantly reducing setup time—by up to 80% since no physical markers need to be placed on the skin

Participants will be evaluated while completing the following functional tasks (**Table *2***).

Table 2: Motion Capture and Strength Tests

Timeline	ACL	TKA	THA	Hip Arthroscopy

2 months	**Motion Analysis** Walk Bilateral Squats Forward Lunge **Strength** Knee Extension	**Motion Analysis** Walk Bilateral Squats Forward Lunge **Strength** Knee Extension	**Motion Analysis** Walk Bilateral Squats Forward and Lateral Lunge **Strength** Hip Extension Hip Abduction	**Motion Analysis** Walk Bilateral Squats Forward and Lateral Lunge **Strength** Hip Extension Hip Abduction
4 months	**Motion Analysis** Walk Bilateral Squats Forward Lunge Single Leg Vertical Jump **Strength** Knee Extension Knee Flexion	**Motion Analysis** Walk Bilateral Squats Forward Lunge Single Leg Vertical Jump **Strength** Knee Extension Knee Flexion	**Motion Analysis** Walk Bilateral Squats Forward and Lateral Lunge Single Leg Vertical Jump **Strength** Hip Extension Hip Abduction	**Motion Analysis** Walk Bilateral Squats Forward and Lateral Lunge Single Leg Vertical Jump **Strength** Hip Extension Hip Abduction
9 months	Similar to 4 months	Similar to 4 months	Similar to 4 months	Similar to 4 months

ACLR: Anterior Cruciate Ligament Reconstruction; TKA: Total Knee Arthroplasty; THA: Total Hip Arthroplasty.

At 2 months postoperatively, all patients—regardless of the surgical procedure—will undergo motion analysis and strength testing. The motion analysis will include walking, bilateral squats, and a procedure-specific lunge (forward lunge for ACLR and TKA; lateral lunge for THA and hip arthroscopy). Strength assessments will focus on knee extension for ACLR and TKA, and hip extension and abduction for THA and hip arthroscopy.

At 4 months postoperatively, all groups will repeat the same motion analysis tasks as at 2 months, with the addition of a single-leg vertical jump. Strength testing will now include two joint actions: knee extension and flexion for ACLR and TKA, and hip extension and abduction for THA and hip arthroscopy.

At 9 months postoperatively, assessments will mirror those conducted at the 4-month follow-up for all surgical groups, including the same motion tasks and strength tests.

This schedule allows for tracking recovery progression over time using both movement quality and strength performance.

Strength testing

Strength testing will be conducted after sEMG placement and motion analysis. Participants will keep the sEMG sensors on while performing maximum voluntary contractions (MVC) for knee flexion and extension.

Isometric and isokinetic strength will be assessed using either a Biodex dynamometer or a handheld dynamometer, depending on equipment availability and participant-specific considerations. Strength data will also be used to normalize sEMG signals, with mean amplitudes of each phase expressed as a percentage of MVC. A 30% MVC normalization will be applied to allow for valid comparisons across groups.

Total Testing Time

The full testing session—including subject setup, EMG placement, motion analysis, and strength testing—will take approximately 30 to 45 minutes. Participants will be offered opportunities for water and seated rest breaks as needed throughout the session to ensure comfort and minimize fatigue.

7. Outcomes

Primary outcomes

ACLR and TKA

- Outcome Measure Title
    - Knee extension strength
- Outcome Measure Description
- Maximal isokinetic knee extensor strength (Newtons/BMI). Maximal isokinetic knee extensor strength will be assessed using standardized dynamometry procedures with Biodex Isokinetic Dynamometer (Biodex System 3) at 2, 4 and 6 months after surgery. Each participant will perform three to five maximal voluntary isometric contractions of the knee extensors. The average of the peak torque values will be used for analysis. To account for individual differences in body size, values will be normalized to the participant's body mass index (Newtons/BMI). The first assessment will occur at 2 months to ensure patient safety and measurement consistency, as early postoperative conditions (e.g., pain, swelling) could compromise the reliability and validity of strength testing.
- Outcome Measure Time Frame
    - 2, 4 and 6 months
- Statistical Analysis
    - Linear mixed-effects models :
        - Linear mixed-effects models will be used to analyze changes in knee extensor strength between the intervention and control group across the 2-, 4-, and 6-month follow-up assessments. This approach accounts for repeated measures within participants and allows for the evaluation of group differences over time. Group (intervention vs. control), time (2, 4 and 6 months), and their interaction will be entered as fixed effects, with

subject-level random intercepts. Significant main effects or interactions will be further examined using pairwise comparisons of estimated marginal means, with Tukey's adjustment for multiple comparisons to determine pairwise differences. All results will be reported with estimated means, p-values, and 95% confidence intervals. .

Hip arthroscopy and THA

- Outcome Measure Title
    - Hip Abduction Strength
- Outcome Measure Description
    - Maximal isokinetic hip abductor strength (Newtons/BMI). Maximal isokinetic hip abductor strength will be assessed using standardized dynamometry procedures with Biodex Isokinetic Dynamometer (Biodex System 3) at 2, 4 and 6 months after surgery. Each participant will perform three to five maximal voluntary isometric contractions of the hip abductors. The average of the peak torque values will be used for analysis. To account for individual differences in body size, values will be normalized to the participant's body mass index (Newtons/BMI). The first assessment will occur at 2 months to ensure patient safety and measurement consistency, as early postoperative conditions (e.g., pain, swelling) could compromise the reliability and validity of strength testing..
- Outcome Measure Time Frame
    - 2, 4 and 6 months
- Statistical Analysis
    - Linear mixed-effects models :
        - Linear mixed-effects models will be used to analyze changes in hip abductor strength between the intervention and control group across the 2-, 4-, and 6-month follow-up assessments. This approach accounts for repeated measures within participants and allows for the evaluation of group differences over time. Group (intervention vs. control), time (2, 4 and 6 months), and their interaction will be entered as fixed effects, with subject-level random intercepts. Significant main effects or interactions will be further examined using pairwise comparisons of estimated marginal means, with Tukey's adjustment for multiple comparisons to determine pairwise differences. All results will be reported with estimated means, p-values, and 95% confidence intervals.

Table 3: Secondary outcomes

Assessment Type	Outcomes	Statistical Analysis	Timeframe

Motion Analysis Walk Bilateral Squats Lunge Single Leg Vertical Jump	**Kinematics:** Joint Angles: Hip, knee, ankle and trunk angles over the task cycle (waveforms: joint angle × % task cycle). **Segment Orientations:** Pelvis, thigh, shank, trunk and foot angles over the task cycle (waveforms: segment orientation × % task cycle). **Angular velocities/Accelerations**: Rate of change in joint angles during the task cycle. **Kinetics** **Joint Moments:** Hip, Knee and ankle external and internal moments in the three planes of motion (waveforms: joint moment × % task cycle). **Ground Reaction Forces (GRFs):** Vertical, medial-lateral, anterior-posterior components over the task cycle (GRF x % task cycle). **Spatiotemporal Parameters** Stride Length, Step Length Cadence (Steps/Minute) Gait Speed Stance Time, Swing Time Double Support Time **Muscle Activation (EMG)**	**Statistical Parametric Mapping (SPM):** **Kinematics and Kinetics** Differences between the intervention and control group across each task and at each timepoint. The outcome will be reported as statistically significant clusters (with associated p-values and confidence intervals - e.g. knee flexion angle at 75%–85% of the gait cycle), highlighting precise phases of gait where the intervention had effects. **Linear Mixed-effects models:** **Spatiotemporal parameters and EMG:** Differences between the intervention and control groups across each task and time point will be assessed using linear mixed-effects models. These models will include fixed effects for group (intervention vs. control), time (2, 4 and 6 months), and their interaction, with random intercepts for participants to account for repeated measures. This approach allows for the evaluation of both within-group changes over time and between-group differences across visits: Significant main effects or interactions will be further examined using pairwise comparisons of estimated marginal means, with Tukey's adjustment for multiple comparisons to determine pairwise differences. All results will be reported with	2, 4 and 6 months

	Key muscle groups (Vastus lateralis, rectus femoris, vastus medialis, semimembranosus, semitendinosus, gluteus maximus, and medius). Timing of Muscle Onset/Offset: Normalized mean and max amplitude EMG signals as a percentage of Maximum Voluntary Contraction (%MVC), averaged across trials. Co-contraction index to compare the quadriceps relative to the hamstrings Area under the curve (AUC) as a summary of the total activation during each task and its change over time	estimated means, p-values, and 95% confidence intervals.	
<u>Strength</u> Knee Extension Knee Flexion Hip Extension Hip Abduction	**<u>Kinematics</u>** Angular Velocity Maximal isokinetic and isometric strength (Newtons/BMI). **<u>Kinetics</u>** Peak Torque (raw and BMI normalized): Maximum hip and knee extension/flexion torque produced Torque Curve: The shape of the torque traces over the range of motion. Work and Power: Total work done and power generated during extension/flexion and abduction.	Differences between the intervention and control groups across each task and time point will be assessed using linear mixed-effects models. These models will include fixed effects for group (intervention vs. control), time (2, 4 and 6 months), and their interaction, with random intercepts for participants to account for repeated measures. This approach allows for the evaluation of both within-group changes over time and between-group differences across visits. Significant main effects or interactions will be further examined using pairwise comparisons of estimated marginal means,	2, 4 and 6 months

	<u>Muscle Activation (EMG)</u> Key muscle groups (Vastus lateralis, rectus femoris, vastus medialis, semimembranosus, semitendinosus, gluteus maximus, and medius). Timing of Muscle Onset/Offset: Normalized mean and max amplitude EMG signals as a percentage of Maximum Voluntary Contraction (%MVC), averaged across trials. Co-contraction index to compare the quadriceps relative to the hamstrings Area under the curve (AUC) as a summary of the total activation during each task and its change over each visit	with Tukey's adjustment for multiple comparisons to determine pairwise differences. All results will be reported with estimated means, p-values, and 95% confidence intervals.	
<u>Flexibility</u>	**<u>TKA and ACLR:</u>** Passive knee flexion ROM (^{o}) Passive knee extension ROM (^{o}) **THA and HA:** Thomas test (^{o}) Passive internal/external rotation (^{o})	Differences between the intervention and control groups across each task and time point will be assessed using linear mixed-effects models. These models will include fixed effects for group (intervention vs. control), time (2, 4 and 6 months), and their interaction, with random intercepts for participants to account for repeated measures. This approach allows for the evaluation of both within-group changes over time and between-group differences across visits. Significant main effects or interactions will be further analyzed using post	2, 4, and 6 months

		hoc comparisons and Tukey's adjustment to determine pairwise differences. Results will be reported with means, p-values, and 95% confidence intervals.	
Patient-reported outcome measures (PROs)	**ACLR:** International Knee Documentations Committee (IKDC) Questionnaire Knee Injury and Osteoarthritis Outcome Score for Joint Replacement (KOOS Jr) (Veterans RAND 12-Item Health Survey) VR12 Patient-Reported Outcome Measurement Information System-Pain Interference (PROMIS-PI) PROMIS Physical Function (PROMIS-PF) PROMIS depression short form Anterior Cruciate Ligament-Return to Sport after Injury (ACL-RSI) Tampa Scale of Kinesiophobia (TSK-11) **TKA:** VR12 KOOS Jr Knee Society Score Knee Single Assessment Numeric Evaluation (SANE)	Differences between the intervention and control groups across each task and time point will be assessed using linear mixed-effects models. These models will include fixed effects for group (intervention vs. control), time (pre-op, 2, 4 and 6 months), and their interaction, with random intercepts for participants to account for repeated measures. This approach allows for the evaluation of both within-group changes over time and between-group differences across visits. Significant main effects or interactions will be further analyzed using post hoc comparisons and Tukey's adjustment to determine pairwise differences. Results will be reported with means, p-values, and 95% confidence intervals..	Pre-op, 2, 4 and 6 months, 1 year, 2 years

	Joint Score EQ5D-3L Tampa Scale of Kinesiophobia (TSK-11) **<u>THA:</u>** VR12 Hip Dysfunction and Osteoarthritis Outcome Score for Joint Replacement (HOOS Jr) Harris Hip Score Joint Score EQ5D-3L Tampa Scale of Kinesiophobia (TSK-11) **<u>HA</u>** PROMIS-PF PROMIS-PI 12-item international Hip Outcome Tool (iHOT12) Hip Outcome Score-Activities of Daily Living (HOS-ADL) HOS-Sports Subscale (HOS-SS) Tampa Scale of Kinesiophobia (TSK-11)		
<u>Knee AMI Classification</u>	Sonnery-Cottet et al. knee AMI classification (Grade 0-3)	Differences in the distribution of knee AMI classification (grades 0–3, per Sonnery-Cottet et al.) between groups will be assessed using Fisher's exact test.	2, 4, and 6 months

Digital Avatar Performance Metrics	**Performance metrics generated during the neurofeedback training sessions will be collected directly from the iBrainTech software:** Attention, motor imagery, and session scores	Differences between the intervention and control groups across each task and time point will be assessed using linear mixed-effects models. These models will include fixed effects for group (intervention vs. control), time (pre-op, 2, 4 and 6 months), and their interaction, with random intercepts for participants to account for repeated measures. This approach allows for the evaluation of both within-group changes over time and between-group differences across visits.. Significant main effects or interactions will be further analyzed using post hoc comparisons and Tukey's adjustment to determine pairwise differences. Results will be reported with means, p-values, and 95% confidence intervals	2, 4, and 6 months

Notes: ACLR: Anterior Cruciate Ligament Reconstruction; ACL-RSI: Anterior Cruciate Ligament – Return to Sport after Injury; AMI: Arthrogenic Muscle Inhibition; ANOVA: Analysis of Variance; AUC: Area Under the Curve; BMI: Body Mass Index; CI: Confidence Interval; EMG: Electromyography; EQ5D-3L: EuroQol 5 Dimensions – 3 Level version; GRF: Ground Reaction Force; HA: Hip Arthroscopy; HKA: Hip-Knee-Ankle; HOOS Jr: Hip Disability and Osteoarthritis Outcome Score for Joint Replacement; HOS-ADL: Hip Outcome Score – Activities of Daily Living; HOS-SS: Hip Outcome Score – Sports Subscale; iHOT12: International Hip Outcome Tool – 12-item version; IKDC: International Knee Documentation Committee; KOOS Jr: Knee Injury and Osteoarthritis Outcome Score for Joint Replacement; MVC: Maximum Voluntary Contraction; N: Sample Size; PROMIS-PF: Patient-Reported Outcomes Measurement Information System – Physical Function; PROMIS-PI: Patient-Reported Outcomes Measurement Information System – Pain Interference; PROs: Patient-Reported Outcome Measures; ROM: Range of Motion; SANE: Single Assessment Numeric Evaluation; SD: Standard Deviation; SPM: Statistical Parametric Mapping; THA: Total Hip Arthroplasty; TKA: Total Knee Arthroplasty; TSK-11: Tampa Scale of Kinesiophobia – 11-item version; VR12: Veterans RAND 12-Item Health Survey; %MVC: Percentage of Maximum Voluntary Contraction.

8. Statistical Methods

Statistical methods are summarized in **Table 3**. For the primary outcome, linear mixed-effects models will be used to assess changes in knee and hip strength following ACLR, TKA, THA, and HA procedures. Strength outcomes will be compared between the intervention and control groups at 2, 4, and 6 months postoperatively. This modeling approach accounts for repeated measures within participants and allows for the evaluation of group differences over time. Group (intervention vs. control), time (2, 4 and 6 months), and their interaction will be entered as fixed effects, with subject-level random intercepts. Significant main effects or interactions will be further examined using pairwise comparisons of estimated marginal means, with Tukey's adjustment for multiple comparisons to determine pairwise differences. All results will be reported with estimated means, p-values, and 95% confidence intervals

Secondary outcomes will follow a similar analytic approach using linear mixed-effects models, accounting for repeated measures and assessing group-by-time interactions, with appropriate post hoc testing as needed.

To assess the time-series data of kinematics and kinetics across different conditions and time points, Statistical Parametric Mapping (SPM) will be utilized. SPM is a robust analytical approach that allows for the statistical evaluation of entire waveforms, reducing the limitations of discrete-point analysis in biomechanical research. SPM maintains the temporal structure of the data and enables the identification of significant differences across the entire movement cycle, offering a more comprehensive understanding of biomechanical adaptations post-surgery.

SPM will be applied to joint angle waveforms, ground reaction forces, and external moment profiles to compare surgical groups, timepoints, and control conditions. This approach will help detect subtle but functionally relevant alterations in movement patterns that may not be captured using traditional peak or mean value analyses.

Kinematic and kinetic data will be collected bilaterally to examine compensatory strategies in the contralateral limb. EMG and strength only in the affect side. The integration of markerless motion capture, inverse dynamics, and SPM analysis will provide a detailed and objective assessment of post-surgical movement patterns.

Differences in the distribution of knee AMI classification (grades 0–3, per Sonnery-Cottet et al.) between groups will be assessed using Fisher's exact test.

Statistical significance for all analyses will be set at an *a priori* α of 0.05. All data analyses will be completed using R version 4.2.3 (R Core Team).

Loss to Follow Up

Data analysis will be conducted according to the intention-to-treat (ITT) principle. Patients who are lost to follow-up for any reason will be included in the primary analysis using the last observation carried forward (LOCF) method.

9. Power Analysis

Strength

Separate power analyses were conducted for the knee surgery cohort (ACL and TKA) and the hip surgery cohort (HA and THA).

Knee Surgery (ACL and TKA)

The power analysis for the knee surgery group was based on data from a previous randomized controlled trial by Moukarzel et al. (Moukarzel et al., 2019), which evaluated the effects of motor imagery on quadriceps strength following total knee arthroplasty (TKA). The original study included 12 patients with unilateral TKA, assessed six months postoperatively (10 females, 2 males). The primary outcome was quadriceps maximum voluntary isometric contraction (MVIC), measured using a hand-held dynamometer. This method is highly correlated with the Biodex system currently used in the present trial ($R = 0.91$; Martin et al., 2006).

Statistical analysis was performed in R version 4.3.2 using the pwr package. The mean quadriceps MVIC reported was 20.58 N/BMI (SD = 1.85). Assuming a two-group parallel design (intervention vs. control) with 30 participants per group (total $n = 60$), the study is powered at 80% to detect a between-group difference of 1.31 N/BMI at a two-tailed $\alpha = 0.05$ (adjusted $\alpha = 0.025$ to account for multiple comparisons). This corresponds to a minimum detectable difference (MDD) of 6.31% between groups.

Hip Surgery (HA and THA)

The power analysis for the hip surgery group was based on data from a retrospective study by Servant et al. (Servant et al., 2022), which evaluated hip abductor strength before and three months after hip arthroscopy for femoroacetabular impingement (FAI). The study included 29 individuals (mean age 27.4 ± 7.5 years; 76% female). The primary outcome was hip abductor MVIC, also measured with a hand-held dynamometer.

The reported mean abductor MVIC was 1.97 N/kg (SD = 0.42). A two-group parallel design with 30 participants per group ($n = 60$ total) provides 80% power to detect a between-group difference of 0.31 N/kg at a two-tailed $\alpha = 0.05$ (adjusted $\alpha = 0.025$). This represents an MDD of 15.6%.

To contextualize the clinical relevance of the estimated minimal detectable differences (MDDs), previously published values for minimal clinically important differences (MCIDs) were reviewed. For quadriceps MVIC, Oliveira et al. (2021) (Oliveira et al., 2021) reported an MCID of 26.9% in older adults with COPD, with improvements associated with enhanced performance in the six-minute walk test. In patients undergoing ACL reconstruction, a limb strength asymmetry of 10% is considered a clinically relevant threshold and a predictor of reinjury. For hip abductor strength, although there is no universally accepted MCID after hip surgery, many studies consider a relative difference of 10–15% to be clinically meaningful. These values serve as important clinical benchmarks and support the interpretation that the proposed sample size ($n = 60$ per pathology group) is adequate to detect both statistically and clinically relevant between-group differences in strength outcomes.

Kinematics

A separate power analysis was conducted for the secondary kinematic outcomes to estimate the minimum detectable differences achievable with the current sample size and 80% statistical power. This analysis helps ensure that the study is adequately powered to detect changes that are not only statistically significant but also clinically meaningful.

The power analysis was based on data from a previous investigation (Antognini et al., 2024) conducted in the same laboratory where the current study will take place, using identical equipment, camera setup, and software configuration parameters. Individuals assessed in study were 5 healthy males (mean age 26) and 5 females (mean age 28) (n=10). The primary variables of interest for the power analysis were the knee peak flexion angle (for the ACL and TKA study arms) and the hip peak extension angle (for the hip arthroscopy and THA study arms) during the gait cycle, measured using a markerless motion capture system (Theia 3D, Theia Markerless Inc., Kingston, ON). The statistical analysis was conducted using R version 4.3.2 (R Core Team, 2023) and the pwr package (Champely, 2020).

For the knee flexion angle, Antognini et al. reported a mean of 19° with a standard deviation (SD) of 7.68° (Antognini et al., 2024). Using these values, a two-group parallel design with 30 participants per group (total n = 60) was powered at 80% to detect a between-group difference of at least 5.65° at a two-sided $\alpha = 0.05$ (adjusted $\alpha = 0.025$ for sidedness). Similarly, for hip extension angle (mean = 9.25°, SD = 5.11°), the same sample size and power would yield a minimum detectable difference of 3.76°.

To contextualize the clinical relevance of the estimated minimal detectable differences (MDDs), previously published values for minimal clinically important differences (MCIDs) were reviewed. For knee flexion angle, Guzik et al. (Guzik et al., 2020) reported an MCID of 6.81 degrees based on gait analysis of the unaffected limb in stroke patients. In a different clinical context, Kubo et al. (Kubo et al., 2021) identified an MCID of 5 degrees for passive range of motion following total knee arthroplasty, with improvements in flexion associated with better knee function and higher patient satisfaction. Regarding hip extension angle, Guzik et al. (Guzik et al., 2021) established an MCID of 2.86 degrees in stroke patients using motion analysis of the unaffected limb. These values serve as clinical benchmarks to interpret the statistical power and meaningfulness of the differences targeted in this study.

10. Randomization

Sequence Generation

Randomized list generation before trial commencement utilizing the National Institute of Health (NIH) Clinical Trial Randomization Tool. We will utilize a 1:1 allocation (intervention vs. Control) per procedure.

The randomization sequence will be generated before trial commencement by an independent data manager using the Clinical Trial Randomization Tool developed by the National Cancer Institute (NCI). The tool will use the Asymptotic Maximal procedure, a restricted randomization method that limits the imbalance between trial arms to a pre-specified Maximum Tolerated Imbalance (MTI) of 3. The randomization list will be created for a total of 70 participants, with no stratification applied.

Type of Randomization

A simple two-arm parallel group design will be used with a 1:1 allocation ratio for each procedure (ACLR, THA, TKA, and HA), with a separate randomization list of 35 participants per group (total n=70) generated independently for each procedure. Each procedure will be treated as a distinct trial with its own allocation sequence. The final participants will be randomly assigned in accordance with the MTI threshold, allowing minor tolerable imbalances between arms. No stratification or blocking will be implemented. The increased sample size per group (n=35 instead of n=30) accounts for potential losses or allocation issues during the study. Additional allocation slots beyond the target sample size will be generated to account for unexpected exclusions, dropouts before randomization, or technical errors during allocation.

Allocation Concealment Mechanism

Allocation concealment will be ensured using the REDCap (Research Electronic Data Capture) Randomization Module, which provides a secure, centralized, and automated platform for treatment allocation. The randomization sequence will be generated and implemented within REDCap by an independent data manager who will not be involved in participant enrollment, intervention, and outcome assessment. The system will be configured to assign participants in real time only after eligibility has been confirmed and baseline data have been entered, thereby preventing any foreknowledge of the upcoming assignment. Investigators, study staff, and participants will remain unaware of the allocation sequence prior to assignment (**Figure *4***). REDCap's access controls and audit logs will safeguard against manipulation and preserve allocation concealment throughout the trial.

Figure 4 Randomization and allocation concealment procedures

Implementation

All patients referred for ACLR, TKA, THA, or HA procedures in the physician's office will be referred to the research team to assess eligibility criteria and initiate the enrollment process, either in person or by phone. Eligible patients will be enrolled in the study during the pre-operative period and will complete baseline assessments. Following surgery, participants will be assigned to one of the intervention groups one day prior to the intervention date. Group allocation will be performed by an independent data manager using the REDCap Randomization Module and communicated only to the team responsible for delivering the NFVT. The individual

responsible for generating the allocation sequence will be distinct from those involved in enrolling participants and assigning interventions.

Blinding

Investigators and physicians will be blinded to group allocation to minimize bias in clinical decision-making and post-operative care. Patients will not be blinded due to the nature of the neurofeedback intervention, which cannot be masked. Both study groups will receive standard rehabilitation, with the only difference being the addition of NFVT in the intervention arm. The neurofeedback sessions will take place within the physical therapy clinic, immediately prior to scheduled physical therapy appointments.

The team delivering the neurofeedback intervention will be the only personnel aware of group allocation. Treating physicians, physical therapists, outcome assessors, and the statistical analysis team will remain blinded to participant allocation throughout the trial. Statistical analyses will be performed by the Rush Statistical Analysis team, an independent third-party ancillary resource, using a coded dataset to ensure blinding is maintained during data analysis.

Unblinding Procedures

Given the non-invasive nature of the EEG-based neurofeedback intervention, adverse effects are not expected. However, in rare cases where unblinding is required—such as equipment malfunction, unexpected clinical events, or participant withdrawal—a formal request must be submitted to the principal investigator (PI) or Data and Safety Monitoring Board (DSMB). All unblinding events will be logged with justification and date.

For emergencies, a dedicated study coordinator will have secure access to the REDCap randomization module and group allocation. This coordinator will be available to authorized clinical staff in urgent scenarios requiring immediate unblinding. Outcome assessors and data analysts will remain blinded throughout the study.

These procedures align with CONSORT guidelines and will be included in staff training to ensure adherence.

11. Recruitment

The investigators will identify eligible patients in the clinic, and the research study staff will discuss the study with eligible patients. The informed consent process may occur over a period of several discussions, culminating in the signing of a consent form in the office (iPad) or sent to their verified email address.

Informed consent will be obtained via the eConsent process through the secured platform Patient IQ. The patient will be prompted to reply with the appropriate passcode to access the consent form and then provide the passcode again with their signature (secured). A copy of the time stamped document will be sent to the study team through the electronic platform and a copy will

be sent to the participant. All participants will be consented prior to surgery and the performance of research related testing activities.

12. Risks

In any routine activities or exercise, there is an inherent risk of falling and musculoskeletal injuries. However, this risk will be minimized by using activities that are adequate for the training level of the subject. Subjects will only perform tasks that they are used to performing in their routines, and which they feel comfortable and confident to do. Furthermore, there will be staff supervision and close physical proximity to avoid falls and help in the execution of the task.

Reassurance of the possibility of study abandonment without compromise of current medical treatment will be provided during all study visits.

There are no alternative procedures, the only alternative to participation is not to participate. There are no additional risks for the participants than the ones that they are already exposed to during their normal training routines.

There is a risk of breach of confidentiality for participation in this study. Measures will be taken to protect patient privacy. To minimize this risk, data will be stored on a password-protected secure Rush server using Microsoft 365 OneDrive.

Side effects, risks, and/or discomforts from participation in this study may include fatigue during testing from the activities, minor skin irritation (i.e., reddening) from the adhesive used to place the sEMG sensors, discomfort in the limbs the following day due to the activities and potential minor muscle or joint soreness.

The risk for performing visualization exercises with neurofeedback training is minimal and does not exceed the risk of performing physical therapy.

13. Limitations

While there is a great effort to produce highly reliable and generalizable results, there are limitations to this study that must be addressed. One potential source of bias is patient adherence to neurofeedback therapy, which may vary and influence treatment outcomes. The sample size, limited to 240 participants with 30 interventions per procedure type, may constrain the statistical power and affect the broader applicability/generalization of results. Additionally, the novelty of using EEG neurofeedback in the postoperative setting presents challenges for comparative analysis, as there is a lack of precedent in the existing literature. The clinical treatment, including the surgical procedure and physical therapy, will follow a pragmatic approach, allowing for natural variations in clinical practice across patients and providers. While this enhances the external validity and real-world applicability of the findings, it may introduce variability that could influence outcomes.

Blinding poses another limitation; although physicians, researchers, and the data analysis team are masked to group allocation, participants are aware of their intervention, which could introduce potential expectation bias. Technological factors, such as EEG signal variability and the need for precise device calibration, may also affect the accuracy and consistency of data collection.

14. Generalizability

The generalizability of this study is inherently limited by its design. The population is restricted to orthopedic surgical patients, and the exclusion of individuals with a body mass index greater than 35, prior surgery on the affected joint, or underlying neurological disorders may further reduce external validity. As a single-center trial conducted at Rush University Medical Center, the findings may not be fully representative of broader or more diverse populations. Moreover, because the intervention relies heavily on patient engagement and adherence, its feasibility and effectiveness could differ across clinical settings. Differences in rehabilitation protocols across institutions may impact reproducibility and generalizability of the findings.

15. Interpretation

The results of this trial will be interpreted in the context of existing orthopedic rehabilitation literature, with a focus on balancing the potential benefits, such as enhanced neuroplasticity and AMI reduction, against risks related to adherence and technological constraints. If successful, this study may serve as a step toward integrating neurofeedback into postoperative rehabilitation protocols. Both patient-reported outcomes (e.g. PROMIS, KOOS Jr, IKDC) and objective measures (e.g. motion analysis, strength testing) will be used to evaluate the efficacy of the intervention.

16. Other Information

Funding

An internal department fund will be utilized for the majority of the study funding. The Walbert Sports Medicine Endowed Education Fund is dedicated to supporting high-quality research studies. The study utilizes the NFVT and EEG caps, provided by iBrainTech for research purposes. Participants in the study will receive compensation for their involvement, including parking, and a total of $150 for completing all three study visits. The compensation is progressive, with participants receiving a $25 Visa gift card after the first visit, a $40 Visa gift card after the second visit, and an $85 Visa gift card after the third (final) visit. There is no cost to participants, as all study-related expenses, including neurofeedback therapy and testing, are covered by the Walbert Sports Medicine Endowed Education Fund and the Midwest Orthopaedics at Rush Research team. Results will be shared with participants as soon as the study is peer-reviewed and published. Our team will be able to address via e-mail any questions or concerns.

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