**Title:** Use of an EMG-controlled computer game to improve muscle activation patterns in stroke survivors

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**PROTOCOL TITLE:** Use of an EMG-controlled computer game to improve muscle activation patterns in stroke survivors

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**VERSION NUMBER:**
*Version 2*

**VERSION DATE:**
08/08/2018

**STUDY SUMMARY:**

| | |
|---|---|
| Investigational Agent(s) (Drugs or Devices) | |
| IND / IDE / HDE # | |
| Indicate Special Population(s) | ☐ Children<br>☐ Children who are wards of the state<br>☐ Adults Unable to Consent<br>☐ Cognitively Impaired Adults<br>☐ Neonates of Uncertain Viability<br>☐ Pregnant Women<br>☐ Prisoners (or other detained/paroled individuals)<br>☐ Students/Employees |
| Sample Size | 20 |
| Funding Source | NIH R01-HD075813-03 |
| Indicate the type of consent to be obtained | ☒ Written<br>☐ Verbal/Waiver of Documentation of Informed Consent<br>☐ Waiver of HIPAA Authorization<br>☐ Waiver/Alteration of Consent Process |
| Site | ☐ Lead Site (For A Multiple Site Research Study)<br>☐ Data Coordinating Center (DCC) |
| Research Related Radiation Exposure | ☐ Yes<br>☒ No |
| DSMB / DMC / IDMC | ☒ Yes<br>☐ No |

**OBJECTIVES:**

Our immediate goal is to improve voluntary muscle activation patterns in stroke survivors with chronic hand impairment, with the ultimate goal of improving upper extremity function. We believe that training with visual feedback will help to increase the range and number of activation patterns which can be created.

We hypothesize that stroke survivors will experience a decrease in the time to complete a test of control with the EMG system after 9 training sessions. Furthermore, we believe this training will also lead to improvement in hand motor control, as measured with clinical measures and pinch strength. Furthermore, we hypothesize that a group using bilateral training will achieve better outcomes than a group training with only the impaired upper limb.

**BACKGROUND:**

Hand impairment is a common outcome following stroke. This impairment derives primarily from difficulty in creating appropriate muscle activation patterns. Specifically, stroke survivors typically exhibit problems in appropriately altering activation patterns, as well as in modifying the level of activation of different muscles, to accomplish the various tasks of daily living. Additionally, stroke survivors are limited by substantial hand weakness that arises from diminished capacity to fully activate muscles.

We have created novel software to focus hand therapy on retraining activation patterns. Electromyographic (EMG) signals drive a cursor on a computer screen; the cursor is used to play games such as moving through a maze, avoiding asteroids, or revealing a photograph. Vectors of EMG magnitudes across muscles are mapped to the axes of the screen. Thus, users have to create combinations of specified patterns in order to move the cursor to the desired location.

**STUDY ENDPOINTS:**

The endpoint for each participant is the completion of evaluation following the ninth training session. The endpoint for the study occurs when the 20$^{th}$ participant completes their post treatment evaluation.

**STUDY INTERVENTION**

The study involves only computer software and an FDA-approved EMG system, the Bagnoli 8-channel EMG system (Delsys, Inc., Natick, MA) with surface electrodes. The participant creates EMG signals to control a cursor on a computer screen to play different games, such as picture reveal, mazes, and a coin-collecting task. By controlling the mapping from EMG signal to cursor control, exploration of the activation workspace can be encouraged. The EMG signals are read into the computer and converted into the game controller through custom software written in Matlab (Natick, MA).

**PROCEDURES INVOLVED:**

Each participant will come to the laboratory to complete 9 one-hour training sessions with the EMG system, as well as two 1.5 hour sessions for clinical assessment during the 1$^{st}$ and 11$^{th}$ session.

Surface EMG electrodes (Delsys) will be placed over the following 4 muscles in each arm: flexor digitorum superficialis (FDS), extensor digitorum communis (EDC), first dorsal interosseous (FDI), and extensor carpi ulnaris (ECU). Then, participants will be asked to create maximum voluntary contractions (MVCs). EMG amplitudes will subsequently be normalized by these maximum values. A calibration phase will be performed next in which participants will be encouraged to fully explore their activation workspaces with each upper limb. Principal components (PCs) will be computed to describe each activation workspace. The PCs from the less impaired (ipsilesional) limb will serve as the target activation patterns assigned to the axes

of the screen. The calibration phase will be repeated at the end of each training session to monitor any changes in activation workspace volume or PCs.

During training, participants will attempt to create combinations of the target activation patterns to move the computer cursor to the desired location on the computer screen. To begin, the first two PCs (the two explaining the most variance in EMG patterns) from the less impaired side will serve as the target patterns. Study personnel will set appropriate ranges for the activation of each PC. As participant performance progresses, study personnel will increase the range for each PC, as well as alternate which PCs are mapped to the screen axes in order to challenge the participant to increase exploration of their activation workspace.

Half of the participants will control the cursor only with their impaired upper limb. The other half of the participants will use a combination of activation of the impaired and unimpaired limbs. Relative weighting of the activation patterns of the two limbs (totaling 100%) will be implemented to control the cursor. Thus, initially, only activation patterns from the less impaired limb will be used. The weighting of the more impaired (contralesional) limb will be linearly increased from 0% to 100% in steps of 12.5% each session (i.e.: 0%, 12.5%. 25%, 37.5%, 50%, 62.5%, 75%, 87.5%, 100%). Participants will be invited to take breaks as needed to mitigate soreness and fatigue.

Prior to the first and just after the ninth training sessions, participants will perform tests of control of the EMG game. Namely, they will be directed to move the cursor around a 5 x 5 set of tiles on the screen. The amount of time required to move the cursor into a total of 16 randomly presented, predetermined tiles at the outer limits of the workspace will be recorded. The same PC numbers (first and second) and ranges will be used during both of these testing sessions. Additionally, we will assess hand motor control. Participants will be asked to complete clinical measures such as: the Jebsen-Taylor hand function test, Wolf Motor Function Test, and the Action Research Arm Test (ARAT). They will also be asked to create maximal pinch and grip force, as well as a box and blocks assessment and 9-hole peg test. Maximum pinch force and EMG activity from FDS, EDC, FDI, and ECU will be recorded. At the end of each session, electrodes will be carefully removed and the contact area swabbed with alcohol to minimize irritation.

**DATA AND SPECIMEN BANKING: N/A**

**SHARING OF RESULTS WITH PARTICIPANTS:**

No genetic, imaging, or diagnostic tests will be performed.

**STUDY TIMELINES:**

Each participant will come to the laboratory 11 times over 3 weeks to complete the training and testing. Each training session will last one hour and each evaluation session (first and last) will last 1.5 hours.. We anticipate completing all activities with participants within 2 years.

**INCLUSION AND EXCLUSION CRITERIA:**

Adult stroke survivors (aged 18-80) who experienced a single, unilateral stroke at least 6 months prior to enrollment in the study will be recruited. Participants will have moderate hand impairment as defined by a rating of Stage 4-5 on the Stage of Hand of the Chedoke-McMaster Stroke Assessment. Individuals with visual neglect or visual deficits, upper extremity orthopedic conditions that interfere with movement, or cerebellar stroke will be excluded. We will not recruit children, prisoners, or adults unable to provide consent. As the procedures pose no increased risk for pregnant women, we will not specifically exclude them.

**VULNERABLE POPULATIONS**

Adult stroke survivors competent to provide informed consent will participate in this study. While we will not target pregnant women, we will not exclude them, as the proposed protocol does not entail any additional risk for pregnant women.

**PARTICIPANT POPULATIONS**

| Accrual Number: | Category/Group: (Adults/Children Special/Vulnerable Populations) | Consented: Maximum Number to be Consented or Reviewed/Collected/Screened | Enrolled: Number to Complete the Study or Needed to Address the Research Question |
|---|---|---|---|
| Local | Adults | 43 | 23 |
| | | | |
| Study-wide | | | |
| | | | |
| Total: | | 43 | 23 |

We expect to recruit 10 stroke survivors for each of the two groups, with a 15% drop out rate of 3 participants. We anticipate that 20 potential participants will fail the screening, totaling 43 potential participants.

**RECRUITMENT METHODS:**

Potential subjects will be recruited through IRB-approved flyers, the institutional website, and the IRB-approved stroke registry. A letter granting access to the registry is included in this submission.

**COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES**

Participants will be compensated $20 for each session for a possible total of $220. They will be paid at the end of each session. Payment will be prorated should the participant decide to end participation before completion of a session. Payment will be provided through a Shirley Ryan AbilityLab ClinCard assigned to each subject.

**WITHDRAWAL OF PARTICIPANTS:**

Participants could be withdrawn from the study under advice from their physicians or due to unanticipated health issues. Additionally, failure to appear for scheduled training sessions could result in withdrawal.

**RISKS TO PARTICIPANTS:**

Participation in the study entails minimal risk. The intensive training could result in temporary fatigue and muscle soreness. Placement and removal of EMG electrodes could result in temporary skin irritation.

**POTENTIAL BENEFITS TO PARTICIPANTS:**

Stroke survivors will participate in 9 sessions to train EMG patterns. Thus, participants may improve voluntary activation of muscles in the impaired arm and hand. This may result in improved motor control of the hand.

**DATA MANAGEMENT AND CONFIDENTIALITY**

The 4-dimensional volume encompassing the range of EMG values created during the calibration phase will be computed for pre-training and post-training for each of the 9 training sessions. The angle between the plane defined by the target PCs and the first two PCs of the more impaired limb will also be computed for each calibration session.

Repeated measures analysis of variance (rmANOVA) will be performed to examine the impact of the training with the EMG-controlled system. The between-subject factor will be participant Group (bilateral vs ipsilateral training). The within-subject factor will be Session. The primary outcome variable will be the time to complete the test. The variable Session will have two levels (data recorded during the testing for the first (pre) and after the ninth (post) sessions). We will be especially interested in any significant effects of Session or Group x Session. We will perform similar rmANOVA analyses for the secondary clinical measures and pinch strength.

Volume of the activation space and the planar angle between primary PCs for each limb will be examined across all 9 sessions. rmANOVAs will be run with the within-subject variables Session (9 levels) and Training (pre/post). The between-subject variable will again be Group.

The de-identified data will be stored on encrypted, password protected computers.

**PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS: N/A**

**PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS:**

As noted, subject identity will be encoded, with the key consisting only of a hard copy kept in a locked file cabinet. Sharing of personal subject information among study personnel will be limited to data necessary for performing the study.

Participants will be encouraged to address any questions about the study directly to study personnel, including the PI. Participants will be treated with the utmost respect.

The study doctor may access medical records or sensitive information for recruiting purposes.

**COMPENSATION FOR RESEARCH-RELATED INJURY:**

The hospital will not pay for medical care required due to an injury or illness as a result of subject participation in this research study. However, this does not keep them from seeking to be paid back for care required because of a bad outcome. Subjects are welcome to seek medical treatment through their doctor or treatment center of choice.

**COMMUNITY-BASED PARTICIPATORY RESEARCH:**

We have received considerable feedback from stroke survivors and lab personnel on use of the EMG-controlled game. A number of revisions have been made to improve system performance.

**ECONOMIC BURDEN TO PARTICIPANTS:**

There are no study costs for participants.

**CONSENT PROCESS:**

Authorized study personnel will obtain participant consent prior to enrollment in the study. We will obtain written consent to participate in the study. The consent document has been included with the application. The consenting process will occur at the Shirley Ryan AbilityLab. Study personnel will verbally explain the study and all potential risks and then the participant will read the consent form and sign if they wish to enroll in the study. If desired, a participant will be allowed to take the consent form home with them for further study before deciding whether to consent to continue.

**PROTECTED HEATH INFORMATION (PHI AND HIPAA)**

Research participants must be entered into the Shirley Ryan AbilityLab system to enter the building; however, no results from the study will be placed in a medical record.

**NON-ENGLISH SPEAKING PARTICIPANTS**

Interpreters will be found through the Shirley Ryan AbilityLab to translate for non-English speaking participants.

**QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE**

***RESOURCES AVAILABLE*:**

All equipment needed to conduct the study, such as EMG equipment, data acquisition boards, and the Action Research Arm Test kit, is already in place, as is the software.

Laboratory staff have considerable experience in conducting longitudinal interventions studies with stroke survivors. Two such studies, funded by federal grants, are ongoing. A total of 60 stroke survivors have been enrolled to date in one of these studies and a total of 20 stroke survivors in the other study. The targeted population for this study will have less hand impairment than the individuals participating in the first of the aforementioned ongoing studies. Thus, individuals recruited for that study who do not qualify may qualify for this study. The Shirley Ryan AbilityLab admits over 400 inpatients each year. Over 900 stroke survivors have agreed to be listed on an IRB-approved registry of individuals who wish to be contacted to participate in research studies. With these resources, we feel confident that we will be able to recruit the 20 individuals for this study.

Within the Shirley Ryan AbilityLab, a team of physicians is always available to respond to medical emergencies which may arise. They will arrive within minutes of receiving a call.

***SETTING:***

The study will be performed within the Shirley Ryan AbilityLab, where study personnel have laboratory and office space. Potential subjects will be recruited through IRB-approved flyers, the institutional website, and the IRB-approved stroke registry. A letter granting access to the registry is included in this submission.

The Shirley Ryan AbilityLab is highly supportive of research and is striving to further integrate research and clinical care. Therapists working in research typically split their time between research and the clinic. The Shirley Ryan AbilityLab currently hosts a number of federally funded centers, including the Rehabilitation Research and Training Center for Stroke, sponsored by the National Institute on Disability and Rehabilitation Research. Dr. Roth is the PI and Director for this Center. The Shirley Ryan AbilityLab is a new facility, opened March 2017, with a new floor concept to infuse biomedical science and research into the clinical environment. Thus, research laboratories will sit adjacent to clinical therapy space and a culture of interaction and cooperation will be fostered.