Study Title: Robotically Augmented Mental Practice for Neuromotor Facilitation

Document Title: Study Protocol and Statistical Analysis Plan

NCT: NCT04962698

Document Date: 08/25/2023

Protocol

This study consists of experiments on two non-consecutive days in the Human Neuromuscular Physiology Laboratory located in the Biological Sciences/Applied Physiology Building of Georgia Tech. If subjects qualify and agree to take part in this study, subjects will be asked to read and sign the consent form. The whole procedure will last about 3 hours per day, including preparation. Subjects will come to the lab on two separate days on the same tasks. The first day will serve as familiarization with the same tasks as the second day. Subjects will perform the following experiment.

Individuals will sit upright and relax their hands and shoulders. The right shoulder will be fixed with pads to the upper arm to prevent shoulder flexion/extension movement. The right hand and forearm will be rested on a plate hidden below a table. The robotic prosthesis will be placed on the table as one would normally place own arm on the table. There will be no physical connection between the hand and the robotic prosthesis.

Subjects will activate a pair of the front portion of the shoulder muscles and the upper part of the chest muscles for making a grasping movement of the robotic prosthesis. For making a releasing movement of the prosthesis, subjects will activate a pair of the back portion of the shoulder muscles and the back muscles. Muscle activity will be recorded with two small sensors on each muscle. Subjects will practice activation of each muscle pair while watching the signal on a monitor. In each pair, a clearer signal will be used for controlling the robotic digits.

Healthy subjects (N = 18):

Healthy subjects will perform the following tasks A-F. [A: Rest] Subjects will relax their muscles without physical or cognitive effort while gazing at the turned-off monitor. [B: Robotic action observation] Subjects will relax their muscles and focus on observing the computer-controlled grasp and release actions (2 s in each movement) of the robotic hand. [C: Visual MI] Subjects will relax their muscles and perform conventional visual mental imagery (MI). With the guidance of audio instruction, the subjects will imagine the grasp and release motions with the right arm for 2 s in each motion in their mind. There will be no proximal muscle contraction. [D: Kinesthetic MI] The same MI procedure as Task C will be performed, except that the subjects will focus on the kinesthetic sensation that they would feel with the imagined motions. [E: Robotic-Hand Interaction (see below detailed description)] Subjects will perform robotic-hand interaction for grasp and release motions with the activation control of the proximal muscles. During this task, subjects will also imagine the kinesthetic sensation that they would feel with the corresponding motions with the right arm. [F: Virtual-Hand Interaction] Subjects will perform Task E with visual feedback of virtual robot actions in 2D on a monitor. [G: Robotic-Hand Interaction without MI] Subjects will perform Task E without MI. As a reaction task, subjects will flex the index finger as soon as they hear an auditory cue.

Post-stroke subjects (N = 4):

Tasks C [Visual MI], E [Robotic-Hand Interaction], and A [Rest] above will be performed by post-stroke subjects with right-side hemiparesis who can volitionally activate fingers and proximal muscles. As a reaction task, subjects will flex the index finger as soon as they hear an auditory cue. The data on post-stroke subjects will be obtained to test the feasibility of the Robotic-Hand Interaction and observe potential trends. The data will not be used for statistical analysis.

Robot-Hand Interaction with and without MI (Task E and F above):

An individual will use proximal muscle contractions to flex and extend the robotic prosthesis digits for performing a grasp-release task. 1) Grasp. The individual will activate the proximal muscles as if for a retrieving motion (the back portion of the shoulder muscles and the back muscles) for 2 s. This muscle activation controls the prosthesis to flex the digits to grasp a cylinder-shaped object. 2) Release. The individual will relax the above-activated proximal muscles and activate the proximal muscles as if for a reaching motion (the front portion of the shoulder muscles and the top portion of the chest muscles) for 2 s. This muscle activation controls the prosthesis to extend the digits to release the object. After releasing the object, the individual will relax their proximal muscles. The individual will repeat this sequence while observing and hearing the actions of the prosthesis. The acceleration signal will be used to determine the slight displacement of the upper arm. EMG of the forearm and hand muscles will be monitored to ensure that those muscles are relaxed during proximal muscle activation.

TMS test

During the above-mentioned tasks, brain stimulation (called TMS) will be applied over the motor cortex in the left hemisphere. The TMS procedure will follow the one used in our previous studies. A TMS coil will be placed over a precise point on the scalp where we will stimulate the brain to make the muscle move. We will tell the subject when the stimulation portion of the procedure is about to begin. The first part of the procedure will be to find the area of the brain that controls muscles. We will position the TMS coil on the head and will give the subject a series of stimulations (called magnetic pulses). Once we find the spot that controls the muscles, we will find the least amount of stimulation needed to activate the resting muscles. The second part of the procedure will be to evoke muscle contraction with TMS at rest and during the tasks described above. We will apply single-pulse and paired-pulse TMS with 5-second intervals or more. Peak-to-peak amplitude of the motor evoked potential (MEP) will be determined.

Reaction time test

Subjects will be asked to exert finger flexion force with their index finger as soon as they hear an auditory cue for the reaction task. In this test, the focus was on immediacy, and there will be no instruction on the amount of force to produce. The audio cue timing will be randomly varied during the middle 60% during the flexion and extension phases of the artificial or imaginary finger. Reaction time, maximal rate of force development, peak EMG, and peak force will be determined.

Statistical Analysis

Statistical analysis will be peformed on data from 18 healthy subjects. The independent variable will be the task. The dependent variables will include MEP amplitude, reaction time, maximal rate for force development, peak EMG, and peak force. If the assumption of sphericity is not violated, the variable will be tested with one-way analysis of variance (ANOVA) with repeated measures on task, followed by a posthoc Bonferroni-corrected pair-wise comparison, when appropriate. If the assumption of sphericity is violated, the variables will be with the Friedman test, followed by the Wilcoxon signed-rank test when appropriate. The alpha value of 0.05 will be used to determine the significance. The alpha value will be corrected for repeated comparisons.