Neural adaptation after tendon transfer and training in tetraplegia.

ID number: N1772-P
NCT number: NCT02768103
IRB approval: March 31, 2019

Purpose
The purpose of the study is to improve upper limb function in people who have suffered injuries to their cervical spinal cord and have lost hand function. Many individuals with tetraplegia choose to undergo surgery, such as muscle-tendon transfers that restore function to their paralyzed upper limbs. In this study we will compare their ability to produce pinch force between the thumb and index finger before and after participating in a home exercise program. The exercises are designed to improve the strength and performance of the transferred muscle and also the muscles that are important to stabilize proximal joints.

The investigators anticipate the study will inform new postoperative treatment protocols designed to re-educate the transferred muscle in its new functional role. The objective is to determine if training to improve muscle strength and coordination will improve the ability to increase pinch strength after tendon transfer to restore pinch strength. Restoration of upper extremity function is rated among the highest priorities for individuals with tetraplegia. Use of the upper extremity is critical to functional independence, quality of life, ability to participate in society, and reduced burden of care.

Study Procedures
Recruitment and screening: We will invite individuals to participate if they have a SCI resulting in tetraplegia with a previous tendon transfer surgery to restore their ability to pinch and grasp. Individuals with tetraplegia will be recruited from the Upper Extremity Clinics for Spinal Cord Injury at the VA Palo Alto Health Care System, Stanford University Hospital Clinics, and Valley Medical Center in San Jose, CA. A hand surgeon and the PI will attend all of the clinics. A letter may be sent to individuals who have expressed interest in previous studies to be contacted for participation in any new studies.

Participants will be scheduled for 1 to 2 test sessions in the Laboratory for Upper Extremity Research in the SCI Center (UE Lab). In the first session a set of measurements will be taken for baseline data of strength, muscle activation, and ability to perform functional pinch tasks. An fMRI study will be included in the first session. Each participant with tendon transfer procedures will be given a set of exercise equipment to take home. The equipment will include a set of weights for resistance exercise (i.e. lifting weights), a digital pinch meter for biofeedback of the pinch force, a table-top device that is used to provide target locations the participants reach for and to practice pinch (using variable resistance pinch pins) in locations that simulate the actual functional pinch tasks, and a task board with tasks that require pinch strength (ex: key, atm card, zipper).

The participants will get verbal and written instructions about how to use the equipment and a log-book to record their practice sessions. They will be instructed to practice the exercises for 10 weeks. A second appointment in the UE Lab will be scheduled to measure any changes in pinch function after the exercise program. A set of measurements that are identical to the baseline data set will be obtained, including the fMRI study.

Home Exercise Training Program: Participants will be instructed to use resistance exercises to strengthen elbow flexor and extensor muscle groups. The exercises should be done 3 times per week and should take about 30 minutes to complete. They will be instructed to do the strengthening exercises and practice pinching using the table-top device and the task board to practice producing pinch force in specific locations that simulate the position of an ATM machine, horizontal and vertical zippers, using a fork, electric plug, remote control, and a key. All of the instructions for performing the exercises will be provided and each participant will practice the home exercises at the first test session. The participants will receive a log- book to document their participation in the exercise program. The participants will not be able to keep the exercise weights, brace, pinch meter, or table-top device. They will be used for other participants who are enrolled in the study over the next 2 years. The equipment in the exercise kit will be cleaned with anti-bacterial soap after use by individual participants.

Measurement of muscle structure and function: Quantitative measurements of UE impairment will be recorded in the UE Lab. These measures include: muscle activation patterns with surface and fine- wire electrodes; and muscle strength using commercially available force transducers. A standardized test (Canadian Occupational

Performance Measure) designed to detect self- perceived changes in performance over time will be administered by the examiner. In the test, participants will be asked to identify daily activities they want to be able to do and those which are difficult to complete to your satisfaction. The questions will relate to self-care, productivity, and leisure activities. This survey will be completed by the examiner before and after the training program.

The participants will have an fMRI study to determine if the training program or the tendon transfer procedure produced changes in the brain compared to the control participants (non-impaired and SCI without tendon transfer surgery). During fMRI, the participants will lie on an MR table within the magnet and will be asked to lie as motionless as possible while they perform the task. The participant may also be fitted with a bite bar (made of dental impression material) to keep the head immobile during the scans. fMRI will be obtained during an active motor task during which participants are asked to perform lateral pinch tasks, or attempt upper limb movements. These tasks will be done at a submaximal level and participants will have feedback for the level of effort from the examiner.

We will minimize risk by using research procedures that are routinely used in the clinical management of persons with tetraplegia. The testing procedures are minimal risk and the participants may improve their pinch strength after the home program.

We will use video recording to document upper extremity motor performance during our clinical evaluation. The primary purpose of this information will be to document the testing procedures. However, these videos may be shown at scientific meetings. Participants will provide informed consent for all video recordings. Videos will be digitally stored on a password-protected computer. No personal health information will be linked to the video as they will be labeled using a unique patient identification codes. Videos will only include the participants arm and hand.

There is no standard treatment that is being withheld. All of the participants will have completed conventional clinical rehabilitation following their tendon transfer procedure. There are currently no post-rehabilitation options for patients to participate in after discharge. The home exercise program will not be continued following the 10-week participation time and the equipment must be returned.

Study Endpoint: Individuals who participate in the study will be monitoring their pinch strength during the 10-week exercise phase of the study and will be aware of any negative effects of exercise, such as losing strength. It is unlikely there will be a loss of function during a 10-week exercise program. This study will end once all the participants are enrolled or the funded project period ends.

Statistical analyses

The main outcome measures for the fMRI data will be brain activation defined by intensity and cluster size in response to performing elbow flexion and pinch. Second level analyses will be mixed models effects derived using FSL FLAME for within participants (pre to post intervention) as well as cross-sectional (non impaired vs. SCI-ns; SCI-ns vs. SCI+TT) individual models (with outlier de-weighting and standard settings). Separately, T1 and T2 voxelwise models will regress EMG pinch amplitude for that time-point onto brain data to examine neural correlates of our standard EMG outcome metric. The difference between T1 and T2 will be tested similarly (fMRI con images and EMG calculated as [pre-post/pre+post]) before regressing EMG onto voxel-wise brain data.

Pinch and elbow extension strength. Pinch force is sampled simultaneously with the EMG data. A custom MATLAB program is used to locate the peak force that is maintained for at least 0.5 sec during the 10 sec trial. Mean pinch force is expressed in newtons (1 lb. = 4.454 N) before and after the training period.

EMG amplitude analysis. The EMG signals recorded during maximal pinch and maximal elbow flexion will be quantified by calculating a root-mean-square value over a 0.5 sec interval during peak force production. The ratio of the EMG amplitudes during maximal pinch to those during maximal elbow flexion will be calculated to normalize the EMG signals. During maximum pinch effort, the normalized EMG signals will be used to compare the amplitude of the transferred Br activation before and after the training program in each of the trials

and between participants. The normalized EMG activation will be expressed as a percent of the maximum voluntary contractions (MVC).