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Title of Study: Analysis of Tremor during Grasp Using Ultrasound Imaging
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Study Purpose

The purpose of the study is to use ultrasound imaging to characterize tremor in subjects as they perform grasping motion. In addition, functional electrical stimulation will be applied to study best pathways to suppress tremor.

Eligibility

- Participants without Tremors: be able bodied and between the ages of 18 and 90 years of age. Participants will fall under the able body category if they exhibit no movement disorders and can perform grasping motion with no inhibition. In addition, an ultrasound probe will be strapped to your hand/forearm
- Participants with Tremors: between the ages of 40 and 90 years old and who exhibit tremor in the forearm/hand during grasping motion, or whoexhibit tremor once the grasp is completed, and the object is being held for several seconds.
    - Participants will fall under the tremor subject category if they either:
        - Exhibit tremor with re-emergent properties during the grasping motion and exhibit no other health conditions other than their symptoms of Parkinson's disease that impact tremor severity and impairs motion
        - Exhibit tremor during grasping motion and exhibit no other health conditions other than their symptoms of Essential Tremor that impact tremor severity and impairs motion
    - Participants who have an implanted Deep Brain Stimulator (DBS) may be recruited. In this case, tremor data will be recorded both while the DBS is on their standard settings, as well as while it is turned off. This task will be performed with the assistance of Dr. Roque and will simply use your patient programmer to turn the device on and off under his supervision.
        - When turning off your DBS system, we will plan to perform this 1-2 minutes prior to the start of each grasping trial. Cumulatively, throughout the course of the experiment (all trials of grasping), you may be asked to keep DBS switched off for approximately 18-30 minutes.

Inclusion Criteria (Parkinson's **Tremor Group):**

1. At least 40 years of age, and no more than 90 years of age.

2. Meet UK Parkinson's disease brain bank diagnostic criteria

3. Have clinical evidence of tremor of one or both upper extremities defined as involuntary, rhythmic oscillations about any joint within the upper extremities.

4. Tremor amplitude must be at minimum 1 cm as determined by expert opinion by a movement disorders specialist. This will be determined by Dr. Daniel Roque.

5. People with an implanted deep brain stimulation (DBS) system may participate

6. Due to the nature of measurements occurring during a grasp maneuver, the tremor must be deemed to become re-emergent with a fixed posture. This shall be defined by development of postural tremor that does not begin immediately upon grasping the vertical object, but instead with a delay in development of oscillatory movement of at least half a second as timed by a stopwatch, and

that may grow in amplitude over seconds to maximum amplitude without changing the force of the grasp at first. Note that within-individual intermittency and variability of tremor can be influenced by anxiety, stress, cold temperature, and fatigue. In an effort to reduce this variability, we will have you perform tasks in a comfortable area, providing up to 20 minutes to allow you to relax in a temperature-neutral location, and reduce anxiety

Inclusion Criteria (Essential Tremor Group):

1. At least 40 years of age, and no more than 90 years of age.

2. Meet diagnostic criteria for essential tremor as defined by the 2018 consensus statement on the classification of tremors by the International Parkinson and Movement Disorders Society task force on tremor.

3. Have clinical evidence of tremor of both upper extremities defined as involuntary, rhythmic oscillations about any joint within the upper extremities.

4. Tremor amplitude must be at minimum 1 cm as determined by expert opinion by a movement disorders specialist. This will be determined by Dr. Daniel Roque.

5. People with an implanted deep brain stimulation (DBS) system may participate

6. Due to the nature of measurements occurring during a grasp maneuver, the tremor must be present during a fixed posture. This shall be defined by development of postural tremor beginning immediately upon grasping the vertical object. Note that within-individual intermittency and variability of tremor can be influenced by anxiety, stress, cold temperature, and fatigue. In an effort to reduce this variability, we will have you perform tasks in a comfortable area, providing up to 20 minutes to allow you to relax in a temperature-neutral location, and reduce anxiety

Exclusion Criteria (Tremor Group):

1. Muscle weakness as determined by Medical Research Council grade less than 5/5 on direct testing in the upper limb afflicted with tremor

2. Infection at the upper limb at time of assessment

3. Pre-existing, concomitant neuromuscular or cerebellar disorders

4. Use of medications that can alter the function of the neuromuscular junction.

5. Those with both essential tremor and Parkinson’s disease as determined by history or confirmed by movement disorders specialist prior to assessments. This will be determined by Dr. Daniel Roque.

6. You cannot participate in this study if you do not exhibit tremor during the grasping and holding motion.

In addition, an ultrasound probe will be strapped to your hand/forearm in order to measure the ultrasound activity as grasping is performed and if you have hair on your forearm you may be asked to shave before attaching the probe to your forearm. You cannot participate in the study if you are uncomfortable with this.

Protocol

Participants will be asked to perform different grasping motions with an ultrasound probe strapped to their forearm.

The initial number of visits to participate in the study will be 3, with each visit lasting an average of 1-2 hours, not exceeding 3 hours. These visits may be less or more depending on the quality of the collected data. If additional data is needed, participants may be invited to take part in up to 4 additional sessions. In total, you may take part in 3-7 visits.

The following procedures are experimental:

The experiment will start by securing up to two ultrasound probes, muscle signal recording sensor, and an inertial sensor to your hand/forearm. The probes will be strapped in such a way that the participants can still move their hand and forearm to perform grasping and pinching activities while their muscles are being imaged. In order to make sure the probes are securely strapped and captures the proper muscles, participants will be seated and then asked to grasp a object that is placed in a vertical upright position right in front of them.

To enhance the experimental setup, a wearable ultrasound transducer will be added to the existing sensors. This innovative device has been designed to conform to the shape of your limb, ensuring that it remains in place while you perform various activities. This allows continuous collection of forearm muscle ultrasound data and real-time analysis of muscle states, without restricting forearm movement. The device will be securely fastened to their forearm using medical tape, remaining non-invasive and comfortable to wear throughout the experiment.
Once it is certain that the correct muscles are being imaged through the duration of the grasping motion, data will be collected. The experiment involves grasping the object three different times, each time exerting a different force. The force will be measured through force sensors placed on the object and will be displayed along with the desired force. Before each trial you will be asked to attempt to grasp the object with the desired force in order to make sure it is achievable. This task will be repeated to image different muscles of the forearm that might cause tremor.

If a participant has an implanted deep brain stimulator (DBS), data will first be captured while their stimulation is turned off. They will then be asked to turn-off the DBS stimulation for a few trials, to collect tremor data in both settings. In total, they may be asked to keep the stimulator off for 18-30 minutes. All stimulation changes will be performed under the supervision of Dr. Daniel Roque and primarily utilizing your patient programmer. As needed, Dr. Roque's physician programmer will be used only if problems arise using your programmer.

FES (Functional electrical stimulation) will also be performed on you. FES is a low-level electrical current to the nerves that innervate the muscles to cause functional limb motion. It has the potential to suppress upper limb tremor since it aims to generate an opposing electrical pulse with respect to tremor movement, promote muscle contraction, and reduce tremor amplitude. During the experiment, you will be seated comfortably and attached with non-invasive electrodes securely applied on your forearm. The electrodes can be removed after the experiment.

The following two kinds of stimulation will be performed on you:

1. Electrical Stimulation Over the Motor Threshold: the pulse intensity of the electrical stimulation is high enough to activate muscle fibers and generate a muscle contraction.
2. Stimulation of Afferent Pathways/sensory activity for Tremor Management: low-level electrical stimulation applied at the wrist joint modulated the tremor frequency. In this way, sensory or afferent stimulation generates a response in the central nervous system that can modify tremor.

Each visit will take between 1-2 hours but no more than three (this includes time to setup and three trials of the grasping motion). You may be asked to return if data is not satisfactory.

Recording and images

During the grasping motion, video recordings will be taken of each trial. The video recordings will only be of the forearm/hand region and will not include any identifiable facial features. Video recording is optional and you can request to not have it done at any point during the study.

Risks and benefits

There are minimal risks associated with participation in this research. The risks because of this research include restricted forearm movement due to the ultrasound probe being strapped onto thehand, and possible skin irritation due to Velcro or ultrasound gel.

The risks/discomforts should be no different for participants with DBS. There would be a minor inconvenience when turning off your device, no different than if they did this voluntarily with the patient programmer at home, in that tremor would worsen while the stimulation is off. This instance would be similar if they chose to turn off their device to save battery life on their hardware.

The following are physical risks that may occur because of using FES in the study.

A). Skin irritation and redness due to the application of functional electrical stimulation. There could be a tingling sensation near the electrode site. These risks are mild and generally go away once the electrodes are removed.

B) Since it is an artificial means to produce muscle contractions, FES induces rapid muscle fatigue. The FES-induced muscle fatigue may cause pain. This risk can be avoided by reducing stimulation levels or stimulating within your comfort levels. To allow a person to recover from muscle fatigue, an appropriate amount of rest will be provided between successive experimental trials during a session.

C) Potential hyperextension during the experimental procedure. The FES stimulation program will have automatic mechanical safety stops to avoid this situation.

D) A rare risk of skin burn exist underneath the FES electrode. FES stimulators are FDA-approved and are designed to apply safe electrical current levels.

Additionally, here is a rare chance of skin reaction to ultrasound gel or adhesive tape.

Compensation

For your participation in this study, participants will receive $10/hour.