

Permission to Take Part in a Human Research Study

Do not sign this consent if today's date is later than the stated expiration date above.

Title of Research Study:

Effects of device-assisted practice of activities of daily living in a close-to-normal pattern on upper extremity motor recovery in individuals with moderate to severe stroke

Investigator: Jun Yao, PhD

Supported By: This research is supported by the National Institute of Health and the Northwestern University Department of Physical Therapy and Human Movement Sciences Departmental Fund.

Key Information:

The first few pages of this document include a summary of this study to help you decide whether or not to participate. Detailed information is provided after the summary.

Why am I being asked to take part in this research study?

We are asking you to take part in this research study because you previously experienced a stroke that resulted in insufficient control in one arm.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

The purpose of this study is to find out if using a device will help people who have had a stroke practice and improve the movements used in daily activities.

How long will the research last and what will I need to do?

The study includes: 1) 3 pre-intervention tests, ; 2) a 24-session intervention, each session lasting approximately 2.5 hours, 3) 3 post-intervention tests that are the same as the pre-intervention tests. We hope you can participate the whole study. However, you can withdraw from the study at any time. Your decision will not be held against you.

During the pre- and post-intervention clinical tests (~1.5 hours per session), you will be asked to perform a set of movements using your arm and hand, as well as answering some questions. The pre- and post-intervention tests also include a 1 hour MRI scan, and a 6-hour testing, during which you will be asked to repetitively open your hand with or without lifting up your arm while we measure your movements and your brain activity, all using non-invasive methods.

During the intervention, you will be asked to repetitively practice reaching, grasping, retrieving, and releasing (GR3) with progressively increased challenges, such as increased arm loading while lifting, and/or increased size of the object. Please note that there are 2 different groups, and you will be randomly assigned to one of the 2 groups. All the individuals in these 2 groups will

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participate the GR3 intervention. The only difference between these 2 groups is how we adjust the arm loadings while practicing.

More detailed information about the study procedures can be found under the section **What happens if I say “Yes, I want to be in this research”?**

Is there any way being in this study could be bad for me?

You may experience minor muscle soreness, fatigue, or muscle spasms, and minor irritation of the skin under the surface electrodes. Furthermore, the use of Electrical stimulator may cause high levels of soreness.

More detailed information about the risks of this study can be found under **“Is there any way being in this study could be bad for me? (Detailed Risks)”**

Will being in this study help me any way?

We cannot promise any benefits to you or others from your taking part in this research. However, the literature supports the use of an EMG-driven electrical stimulator device, which ReIn-hand is in this category, in the treatment of the hemiplegic wrist and forearm. Please note, such benefits are based on statistical data, may not apply to all the participants, and may not continue after the research has ended.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You decide whether or not to participate. If you choose to not participate, there will be no penalty to you or loss of benefit to which you are entitled.

Your alternative to participating in this research study is to not participate.

Detailed Information:

The rest of this document includes detailed information about this study (in addition to the information listed above).

Who can I talk to?

You can call us with your questions or concerns. If you have any illness or injury during your time on this study, you should call us promptly. Dr. Jun Yao is the person in charge of this research study. You may call her at telephone (312) 908-9060, Monday through Friday from 8am to 5pm. You may also call Dr. Sullivan at (312) 908-6789 or Dr. Carmona at (312) 503-4633, Monday through Friday from 8am to 4pm with questions about this research study. For problems arising evenings or weekends, you may call Dr. Yao at (773) 289-6920.

This research has been reviewed and approved by an Institutional Review Board (IRB). You may talk to them at (312) 503-9338 or irb@northwestern.edu if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

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How many people will be studied?

We expect about 60 people will be in this research study.

What happens if I say “Yes, I want to be in this research”?

If you say ‘yes’, you will participate in 2 baseline clinical assessment sessions, and 1 quantitative biomechanical measure session to evaluation your pre-intervention arm/hand ability. Then you will participate in a 24-session intervention. After the intervention, you will participate in another 1

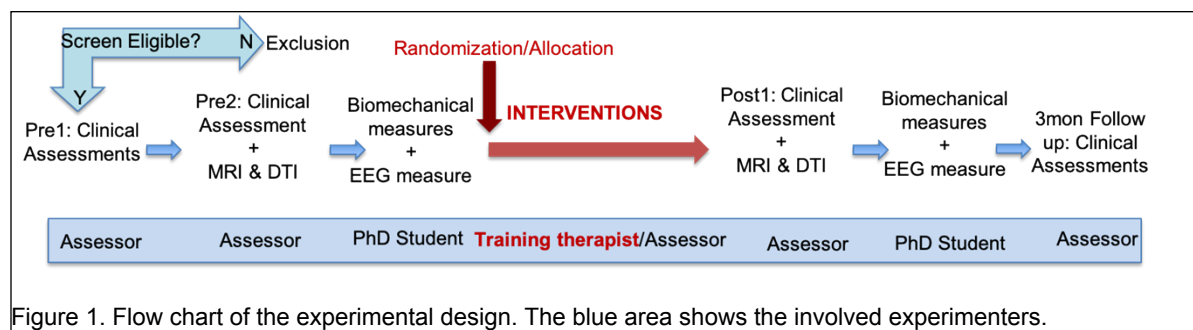


Figure 1. Flow chart of the experimental design. The blue area shows the involved experimenters.

quantitative biomechanical measure session, 1 MRI scan and a clinical assessment session, and a 3-month follow for clinical assessments again. A timeline description of the procedures is listed in figure 1. More details for each of the experimental sessions are listed below:

1. Clinical assessments

Clinical assessments will be performed at baseline (2 times before intervention), end of treatment, and 3 months after completion of treatment. During each of these sessions, a clinical researcher will ask you to perform a set of chosen clinical measures, including Box and Blocks Test (BBT), Quantitative Measure of Hand Opening Area and Closing Force (QMHOC), Cutaneous Sensory Touch Threshold (CSTT) Test using Semmes-Weinstein Monofilaments, the Action Research Arm Test (ARAT, Upper Extremity Fugl-Meyer Assessment (UE FMA), Chedoke-McMaster Stroke Assessment Hand portion, Sensory Assessment (Stereognosis) (SAS), Motor Activity Log, the Stroke Impact Scale (hand function domain), and Revised Nottingham Sensory Assessment: Kinaesthesia Subscale (NSA).

Each of the clinical assessment session will last about 1.5 hours. Furthermore, BBT (~5 mins), CSTT Test (~10 mins), and QMHOC (~10 mins) will be measured weekly.

2. MRI scanning

Within two weeks prior to and following the intervention, scans will be performed at Northwestern University's Center for Translation Imaging on a 3T Siemens Prisma scanner with a 64-channel head coil. Structural T1-weighted scans and Diffusion Tensor Images will be collected. This session will last about 1 hour. In order to reduce the number of your visits, we will schedule your MRI scanning session together with one of your clinical assessment session.

3. Analysis of arm/hand movement patterns and its related brain activity

Before and after one week of the intervention, we will collect data to analyze your arm/hand movement patterns, as well as your brain activity related to arm/hand movements. A stretchable fabric cap with 160 EEG surface electrodes will be put on your head. Skin under each of the electrodes will be prepared and the conductive gel will be used to fill the space between the scalp and electrodes. Subsequently, the positions of EEG electrodes will be recorded using a handheld scanner. This will allow for coregistration of EEG electrodes with your anatomical MRI data.

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Additionally, EMG signals from 3 arm/hand muscles will be recorded using surface electrodes. Furthermore, 5 markers will be placed on the tip of the thumb and the 4 fingers, with another marker on the back of the hand to record the movements of your fingers by 2 cameras (Metria Innovation, Inc., Wauwatosa, WI). Last, you will be seated in a Biodex seating system with straps across the chest and waist to prevent unwanted trunk movement. Your arm and hand will be positioned on a robot (Moog-FCR B.V., the Netherlands). The total setup time will be about 2 hours. A break (0.5-1 hour) may follow setup to avoid fatigue.

You will first be asked to maximally 1) lift up your arm, 2) grasp a cylinder, and 3) stretch your hand on a table top for normalization purposes. Then you will be instructed to move to a home position first, which will trigger the home position to change to a green ball. This sign will indicate the start of a trial. You will then be asked to relax in the home position for 5-7s and then to self-initiate a maximal hand opening for 2s, with the arm resting on the haptic table, or lifting up against 50% of your maximal lifting ability. You will be instructed to avoid blinking or moving your eyes. A set of 60-70 trials will be collected for each condition. These trials will be collected in blocks of 20-30 trials in a random order. Rest periods of at least 15 seconds between trials and ~10 min between blocks will be included to avoid fatigue. The total duration of data collection is about 3.5-4 hours.

4. Intervention

There are 2 different intervention groups. You will participate in one of the intervention groups. Your participation in which group will be chosen by chance, like flipping a coin. You will have a 50% chance of being given either treatment. Neither you nor the study assessor will choose or know what treatment you are getting. In both groups, the intervention will be ~2.5 hours per session, 3 sessions per week, for 8 weeks in total. The only difference between these 2 groups is how we adjust the arm loadings during the experiments.

All of the intervention sessions will be at one of the laboratories in the Department of Physical Therapy and Human Movement Sciences, Northwestern University. During each intervention session, the training therapist may stretch your paretic hand/arms as needed. Then the recording and stimulation electrodes will be placed, and the stimulation intensity will be adjusted to allow for a maximal hand opening without discomfort (ReIn-hand setup time will be approximately 30min).

You will be seated in a chair and then perform 40 trials of: 1) reaching towards a jar; 2) activating finger/wrist extensor muscles to trigger the ReIn-Hand device, which in turn assists the opening of the paretic hand while reaching; 3) grasping the jar; 4) retrieving the jar to the position closer to the chest and placing it on the table; and 5) releasing the jar. In order to avoid fatigue, a resting time of no less than 1 minute will be provided between each of the trials.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

1. Keep communication with our research team;
2. Try your best to keep your scheduled time;

What happens if I say "Yes", but I change my mind later?

You can leave the research at any time; it will not be held against you. If you decide to leave the research, contact the investigator so that the investigator can take you out of the contact list for future studies.

Choosing not to be in this study or to stop being in this study will not result in any penalty to you or loss of benefit to which you are entitled. Specifically, your choice not to be in this study will not negatively affect your right to any present or future medical treatment.

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If you stop being in the research, already collected data may not be removed from the study database. An investigator may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

Detailed Risks: Is there any way being in this study could be bad for me?

Performing different movements using your arm: The repeated movements may result in minor muscle soreness, fatigue, or muscle spasms. However, our protocols include many rest periods that should significantly reduce the risk of these adverse effects.

Surface electrodes for the purpose of recording the muscle activity and muscle-stimulating: The self-adhesive surface electrodes used to record muscle activity or stimulating muscles may produce minor irritation of the skin. The possibility of irritation will be minimized by cleaning the skin with alcohol before and after application of the electrodes.

Using Electrical stimulator: If the intensity progressively increases during the contraction period, then risk of muscle tear or injury is minimal. If a high intensity is applied, you will experience high levels of soreness. We will use 300 PV Complete Electrotherapy System, which is a FDA approved, clinically safe device. The stimulation configuration, including the stimulation intensity, will be set up by clinicians based on your feedback. There are many resting periods designed to avoid muscle fatigue.

MRI: This study uses structural and diffusion-weighted magnetic resonance imaging (MRI) to look at the brain. These structural and diffusion-weighted MRI are types of scans that use magnetic fields and radio waves to make a picture of the brain and will allow us to look at the anatomy and structure of the brain, including lesioned tissue and tracts. Some people cannot have an MRI because they have some type of metal in their body. For instance, if you have a heart pacemaker, artificial heart valves, metal implants such as metal ear implants, bullet pieces, chemotherapy or insulin pumps or any other metal such as metal clips or rings, they cannot have an MRI. During this test, you will lie in a small closed area inside a large magnetic tube. Some people are scared or anxious in small places (claustrophobic). The MRI scanner makes loud banging noises while taking a measurement, so either ear plugs or specially designed headphones will be used to reduce the noise.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

This study involves the use of your identifiable, personal information and there is a chance that a loss of confidentiality could occur. The researchers have procedures in place to lessen the possibility of this happening. See the section below titled: "What happens to the information collected for the research?".

What do I need to know about reproductive health and/or sexual activity if I am in this study?

You should not be or become pregnant while on this research study.

If you or your partner become pregnant while participating in this research study or immediately after you complete the study, it is important that you tell the study doctor or other research team member immediately. You may be required to stop participation in this study; however, other treatment options will be discussed with you at that time if necessary.

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Will it cost me anything to participate in this research study?

Taking part in this research study will not lead to any costs to you.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include: decreasing spasticity, improving muscle strength and range of motion.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution. Involvement in this research study may result in a loss of privacy, since persons other than the investigator and research team might view your study records. Unless required by law, only the following people can review your study records and they are required to keep your personal information confidential:

- Authorized members of the Northwestern University workforce, who may need to see your information, such as administrative staff members from the Office for Research, Office for Research Integrity and members of the Institutional Review Board (a committee which is responsible for the ethical oversight of the study),
- Representatives of the study sponsor, the National Institute of Health
- Representatives of Food and Drug Administration (FDA), and Office for Human Research Protections (OHRP)
- Registries or other research-related databases: the results of your examinations will be kept in a central computer or data registry at the NU Department of Physical Therapy and Human Movement Sciences. These results will be stored by research identifier code for privacy of records and your records will only be accessed by the investigators listed for this study.

The results of this study may also be used for local and regional scientific and healthcare conference presentations, as well as peer-reviewed scientific and medical journal papers. If your individual results are discussed, your identity will be protected by using a study code number rather than your name or other identifying information. We will not ask you about child [or elder] abuse, but if you tell us about child [or elder] abuse or neglect, we may be required or permitted by law or policy to report to authorities.

The sponsor, monitors, auditors, the IRB, the Northwestern University Office for Research Integrity, the US Office of Research Integrity (ORI), the US Office for the Protection of Human Research Protections (OHRP), the US Food and Drug Administration (FDA) may be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

A description of this clinical trial will be available at <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Your MRI data and questionnaire data will be uploaded using an encrypted connection to the Northwestern University Research Image Processing System (NURIPS), which is a secure

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storage and computing environment located behind the Northwestern firewall. Only study members will have access to this identifiable data.

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete secrecy. Organizations that may inspect and copy your information include the IRB and other representatives of this institution.

We will also contract to BuildClinical, LLC to enhance the participant's recruitment. Participants use BuildClinical service to join this study will need to agree BuildClinical to collect the participants' name, contact information, age and years-after stroke information. BuildClinical will pass it along to the team in a one-way transfer of data. The above-mentioned data will be stored in BuildClinical's participant management platform. After the study is over, Northwestern study team will maintain access to BuildClinical's platform for as long as this particular IRB is still active. Once this study's IRB is ended, BuildClinical will remove all the data relative to this study.

Data Sharing

De-identified data from this study may be shared with the research community at large to advance science and health. We will remove or code any personal information that could identify you before files are shared with other researchers to ensure that, by current scientific standards and known methods, no one will be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

How will the researcher protect my information?

MRI data and associated study data will be stored on our secured research computing environment, NURIPS. These data are protected and securely stored by following Northwestern's Information Technology (IT) policies and procedures. Only authorized users will have access, in order to minimize the risk of the data being disclosed to individuals outside of the study team.

How might the information collected in the study be shared in the future?

De-identified data from this study may be shared for future unspecified research studies with the Northwestern research community, with journals in which the study results are published, and our collaborators outside of Northwestern University. We will ensure that any personal information that could directly identify you will be removed. Despite these measures, we cannot guarantee anonymity of your personal data.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include changes in your health conditions, changes in experimental inclusion/exclusion criteria, inappropriate behavior (e.g., harassment, abusive/offensive, violence, etc), or other unpredictable conditions.

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We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

If you become ill or get injured as a result of this study (medications, devices or procedures), you should seek medical treatment through your doctor or treatment center of choice. You should promptly tell the study doctor about any illness or injury.

The researchers will not pay for medical care required because of a bad outcome resulting from your participation in this research study. This does not keep you from seeking to be paid back for care required because of a bad outcome.

If you agree to take part in this research study, we will pay you \$20 per hour for your participation of lab visits, with \$10 from NIH support and the other \$10 from Physical Therapy and Human Movement Sciences departmental funds. If your session lasts less than 1 hour, your participation time will be compensated as 1 full hour. If you are here for more than one hour, your participation time will be compensated as the nearest half or full hour, whichever is closer.

You will be given reimbursement for public transportation expenses or parking fee in Northwestern Medical School parking lots (located at 321 E. Erie St. or 222 E. Huron St.) where a parking voucher will be provided for your free parking when you drive here. If a cab or rideshare car (Uber or Lyft) is needed, we request that you contact lab staff to confirm that the fare can be covered before scheduling pickup. If using the rideshare program Lyft, the Lyft trip will be booked by a research team member through the Lyft application on your behalf. Since it will be booked through a Lyft Concierge account that has been set up by the Department of Physical Therapy and Human Movement Sciences, there is no cost to you. If using a cab or Uber, reimbursement will be paid by check and a receipt is required.

Reimbursement and payment will be submitted to the accounting department on a weekly basis. Typically, the accounting department will mail you a check 4 weeks after receiving the payment request.

The Accounting Services at Northwestern University will be given your name, address, and Social Security Number in order to issue a check for your study participation. Study payments are considered taxable income and reportable to the IRS. A Form 1099 will be sent to you if your total payments are \$600 or more in a calendar year.

HIPAA Authorization

We are committed to respect your privacy and to keep your personal information confidential. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, phone number or social security number. Your health information we may collect and use for this research includes:

- Name
- Street Address
- Telephone number
- Date of Birth
- Information from a physical examination including only: blood pressure reading, upper extremity range of motion, strength, and functional movement assessment.

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- Medical record related to your stroke, and any potential conditions that may impact your eligibility for MRI scan
- Social Security Number - needed for the Accounts Payable Department at Northwestern University in order to issue the study stipend to you and for the medical records department of most hospitals to identify your medical record file
- 3D movement analysis of your arm during reaching/grasping tasks

Involvement in this research study may result in a loss of privacy, since persons other than the investigator and research team might view your study records.

- Clinical affiliates, including but not limited to Northwestern Medical Group (NMG), Northwestern Memorial Hospital (NMH), and Northwestern Lake Forest Hospital (NLFH), for purposes including, but not limited to, the affiliate's provision of care to you and/or the affiliate's scheduling of appointments and/or billing activities.
- Other University research centers and University contractors who are also working on the study,
- Study monitors and auditors who make sure that the study is being done properly,
- National Institute of Health, who is sponsoring the study, and that company's contractors and partners.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).
- Registries or other research-related databases: the results of your examinations will be kept in a central computer or data registry at the NU Department of Physical Therapy and Human Movement Sciences. These results will be stored by research identifier code for privacy of records and your records will only be accessed by the investigators listed for this study.

Those persons who get your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it. Some of those persons may be able to share your information with others without your separate permission.

However, Illinois law does not allow the re-release of HIV/AIDS, genetic testing, mental health and developmental disabilities information by the recipients of the information except in precise situations allowed by law.

Also, Federal Confidentiality Rules, 42 CFR Part 2, prohibit making any further disclosure of substance use disorder information unless further disclosure of this information is expressly permitted by written consent of the person to whom it pertains or as otherwise permitted by 42 CFR Part 2.

The results of this study may also be used for teaching, publications, or for presentation at scientific meetings.

Unless you revoke your consent, it will expire by the "end of the research study".

Although you may revoke consent to participation in this research at any time and in any format, you must revoke authorization for use or disclosure of your health information in writing. To revoke your authorization, write to:

Dr. Jun Yao
Northwestern University
Department of Physical Therapy and Human Movement Sciences

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645 N Michigan Ave, Chicago, IL, 60611

You do not have to authorize the use or disclosure of your health information; however, you will not be allowed to take part in this research study. If you do not authorize the use or disclosure of your health information, it will not affect your treatment by health care providers, or the payment or enrollment in any health plans, or affect your eligibility for benefits.

Optional Elements:

The following research activities are optional, meaning that you do not have to agree to them in order to participate in the research study. Please indicate your willingness to participate in these optional activities by placing your initials next to each activity.

I agree

I disagree

The researcher may audio or video record me to aid with data analysis. The researcher will not share these recordings with anyone outside of the immediate study team.

The researcher may audio or video record me for use in scholarly presentations or publications. My identity may be shared as part of this activity, although the researcher will attempt to limit such identification. I understand the risks associated with such identification.

The researcher may contact me in the future to see whether I am interested in participating in other research studies by the Principal Investigator of this study.

Your signature documents your permission to take part in this research. You will be provided a copy of this signed document.

Signature of Participant

Date

Printed Name of Participant

Signature of Person Obtaining Consent

Date

Printed Name of Person Obtaining Consent