Clinical Studies for PPA

Eddie Europa, PhD, CCC-SLP
Assistant Professor, CSU Chico
Speech-Language Pathologist, CSU Chico
What is a clinical study?

Conducted by a research team
Requires specific plans to be followed
May include one visit, or multiple visits
Reasons for conducting a clinical study

- Learn about prevention
- Improve diagnosis
- Develop effective treatments
- Contribute to medical science
Two main types of clinical studies:

1. Observational Studies
2. Interventional Studies / Clinical Trials
Observational studies

Volunteers receive routine medical care

With permission, researchers use the volunteer’s health information for the study

Volunteers are not assigned to specific study conditions

Example:
Does diet affect brain health?
Interventional Studies / Clinical Trials

Volunteers are assigned to specific conditions

Experimental Condition: Teletherapy

Condition A: In-Person Therapy

Condition B: No Therapy

- Is this helpful?
- Is this harmful?
- Is it no different from the other conditions?

PURPOSE: Determine the safety and efficacy of the experimental treatment
How do I find opportunities to participate in clinical studies?

https://clinicaltrials.gov/
Step 1. Go to clinicaltrials.gov

IMPORTANT: Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

Before participating in a study, talk to your health care provider.
Step 2. Enter “Primary Progressive Aphasia” under Condition or disease. Then hit ”Search”.

You could also try different variants or terms that are related to your specific condition. Here are some suggestions:

• Progressive Nonfluent Aphasia
• Semantic Dementia
• Logopenic Progressive Aphasia
• Alzheimer’s disease
• Frontotemporal Dementia
• Pick’s disease
Step 3. Select “Recruiting”, then scroll down…

…and go to “Study Type” and make your selection. Most people are interested in “interventional studies,” or “observational studies.” Then select “Apply”
In-Person vs. Virtual Participation

- Some studies require in-person visits
  - If you are interested in these studies, you can narrow down your search by location (see next few slides)
How to filter by location

Select your country or continent.
For example, my country is the USA.

Select “On Map”

If you selected the US, select your state.
For example, my state is California.
In-Person vs. Virtual Participation

• Some studies require in-person visits
  • If you are interested in these studies, you can narrow down your search by location

• Other studies can be completed online
  • If you are interested in these studies, you should check the study information
  • If it’s a lot to read through, contact someone from the study (see the next few slides)
Sometimes, the title of the study shows that it can be done online.
Sometimes, if you read more about a study, it shows that it can be done online. If the study doesn’t say it can be done online, or if you have questions, you should contact the people listed on the study.
### Observational Studies for PPA in the USA
(as of July 14, 2021, there were about 17)

<table>
<thead>
<tr>
<th>Title</th>
<th>Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language in Primary Progressive Aphasia</td>
<td>Northwestern University, Chicago, IL</td>
</tr>
<tr>
<td>Florbetaben PET Imaging in PPA</td>
<td>Northwestern University, Chicago, IL</td>
</tr>
<tr>
<td>Investigating Complex Neurodegenerative Disorders Related to ALS and FTD</td>
<td>National Institutes of Health Clinical Center, Bethesda, MD</td>
</tr>
<tr>
<td>The Neurobiology of Two Distinct Types of Progressive Apraxia of Speech</td>
<td>Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td>Human CNS Tau Kinetics in Tauopathies</td>
<td>Washington University in St. Louis School of Medicine, MO</td>
</tr>
<tr>
<td>ARTFL LEFFTDS Longitudinal Frontotemporal Lobar Degeneration (ALLFTD)</td>
<td>Multiple Locations</td>
</tr>
<tr>
<td>4-Repeat Tauopathy Neuroimaging Initiative - Cycle 2</td>
<td>Multiple Locations</td>
</tr>
<tr>
<td>Phenotype, Genotype and Biomarkers 2</td>
<td>Multiple Locations</td>
</tr>
<tr>
<td>Clinico-Pathologic-Genetic-Imaging Study of Neurodegenerative and Related Disorders</td>
<td>Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td>Early-onset Alzheimer's Disease Phenotypes: Neuropsychology and Neural Networks</td>
<td>UCLA</td>
</tr>
<tr>
<td>UPenn Observational Research Repository on Neurodegenerative Disease</td>
<td>University of Pennsylvania</td>
</tr>
<tr>
<td>Longitudinal Study of Neurodegenerative Disorders</td>
<td>The Program for the Study of Neurodevelopment in Rare Disorders, Children’s Hospital of Pittsburgh of UPMC</td>
</tr>
<tr>
<td>Feasibility of Passive Data Collection in Dementia Subjects With Agitation</td>
<td>Tucson Neuroscience Research, LLC, AZ</td>
</tr>
<tr>
<td>Rare Disease Patient Registry &amp; Natural History Study - Coordination of Rare Diseases at Sanford</td>
<td>Sanford Health, Sioux Falls, SD</td>
</tr>
<tr>
<td>Longitudinal Cognitive Assessment by BoCA</td>
<td>Andrey Vyshedskiy, Miami, FL</td>
</tr>
<tr>
<td>Genetic Study of Familial and Sporadic ALS/Motor Neuron Disease, Miyoshi Myopathy and Other Neuromuscular Disorders</td>
<td>University of Massachusetts Medical School, Worcester, MA</td>
</tr>
<tr>
<td>DC Longitudinal Study on Aging and Specimen Bank</td>
<td>Georgetown University, Washington, DC</td>
</tr>
</tbody>
</table>
## Clinical Trials for PPA in the USA
(as of July 14, 2021, there were about 27)

<table>
<thead>
<tr>
<th>Title</th>
<th>Locations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effects of tDCS on Apraxia of Speech in Non-Fluent Primary Progressive Aphasia</td>
<td>Johns Hopkins Hospital, Baltimore, MD</td>
</tr>
<tr>
<td>Enhancing Language Function in Primary Progressive Aphasia</td>
<td>University of Arizona, Tucson, AZ</td>
</tr>
<tr>
<td>Treating Primary Progressive Aphasia (PPA) Using High-definition tDCS</td>
<td>University of Pennsylvania</td>
</tr>
<tr>
<td>Communication Bridge: A Person-centered Internet-based Intervention for Individuals With Primary Progressive Aphasia</td>
<td>Northwestern University, Chicago, IL</td>
</tr>
<tr>
<td>Rehabilitating and Decelerating Language Loss in Primary Progressive Aphasia With tDCS Plus Language Therapy</td>
<td>Johns Hopkins School of Medicine, Baltimore, MD</td>
</tr>
<tr>
<td>TMS for the Treatment of Primary Progressive Aphasia</td>
<td>Massachusetts General Hospital, Boston, MA</td>
</tr>
<tr>
<td>Treating Primary Progressive Aphasia (PPA) Using tDCS</td>
<td>University of Pennsylvania</td>
</tr>
<tr>
<td>Determining the Influence of Atrophy on Efficacy of tDCS in Treating Primary Progressive Aphasia</td>
<td>Johns Hopkins Hospital, Baltimore, MD</td>
</tr>
<tr>
<td>tDCS Intervention in Primary Progressive Aphasia</td>
<td>Johns Hopkins Hospital, Baltimore, MD</td>
</tr>
<tr>
<td>rTMS as a Treatment for PPA</td>
<td>Massachusetts General Hospital, Boston, MA</td>
</tr>
<tr>
<td>Phase 1/2 Clinical Trial of PR006 in Patients With Frontotemporal Dementia With Progranulin Mutations (FTD-GRN)</td>
<td>Bioclinica Orlando, FL</td>
</tr>
<tr>
<td>Gamma-Induction in FrontoTemporal Dementia Trial</td>
<td>Beth Israel Deaconess Medical Center, Boston, MA</td>
</tr>
<tr>
<td>PPA Tele-Savvy: A Pilot Study of an Online Intervention for Caregivers of Persons Living With PPA</td>
<td>Northwestern University, Chicago, IL</td>
</tr>
<tr>
<td>A Phase 3 Study to Evaluate Efficacy and Safety of AL001 in Frontotemporal Dementia (INFRONT-3)</td>
<td>Multiple Locations</td>
</tr>
<tr>
<td>A Phase 2 Study to Evaluate Safety of Long-term AL001 Dosing in Frontotemporal Dementia (FTD) Patients (INFRONT-2)</td>
<td>Multiple Locations</td>
</tr>
<tr>
<td>Intranasal Insulin in Frontotemporal Dementia (FTD)</td>
<td>HealthPartners Neuroscience Center, Saint Paul, MN</td>
</tr>
<tr>
<td>Low-Dose Lithium for the Treatment of Behavioral Symptoms in Frontotemporal Dementia</td>
<td>Columbia University Medical Center, NY</td>
</tr>
<tr>
<td>Treatment for Speech and Language in Primary Progressive Aphasia</td>
<td>UCSF, UT Austin</td>
</tr>
<tr>
<td>Tau PET Imaging in Atypical Dementias</td>
<td>Northwestern University, Chicago, IL</td>
</tr>
<tr>
<td>Rehabilitation and Prophylaxis of Anomia in Primary Progressive Aphasia</td>
<td>Georgetown University Medical Center, DC; Johns Hopkins University, Baltimore, MD</td>
</tr>
<tr>
<td>Circuitry Assessment and Reinforcement Training Effects on Recovery</td>
<td>Johns Hopkins Hospital, Baltimore, MD</td>
</tr>
<tr>
<td>Network Modulation in Alzheimer’s Disease</td>
<td>Massachusetts General Hospital, Charlestown, MA</td>
</tr>
<tr>
<td>Safety and Therapeutic Potential of the FDA-approved Drug Metformin for C9orf72 ALS/FTD</td>
<td>UF Health at the University of Florida, Gainesville, FL</td>
</tr>
<tr>
<td>Longitudinal Multi-Modality Imaging in Progressive Apraxia of Speech</td>
<td>Mayo Clinic, Rochester, MN</td>
</tr>
<tr>
<td>Rural Dementia Caregiver Project</td>
<td>UCSF</td>
</tr>
<tr>
<td>PET Imaging of Neuroinflammation in Neurodegenerative Diseases Via a Novel TSPO Radioligand</td>
<td>National Institutes of Health Clinical Center, Bethesda, MD</td>
</tr>
<tr>
<td>Longitudinal Imaging of Microglial Activation in Different Clinical Variants of Alzheimer’s Disease</td>
<td>Columbia University Irving Medical Center, NY</td>
</tr>
</tbody>
</table>
Example questions to ask

- What is being studied?
- What will I have to do?
- What tests and procedures are involved?
- How often will I have to visit the hospital or clinic?
- Will hospitalization be required?
- How long will the study last?
- Who will pay for my participation?
- Will I be reimbursed for other expenses?
- What type of long-term follow-up care is part of this trial?
- Will results of the study be provided to me?
- Who will oversee my medical care while I am participating in the trial?
- What are my options if I am injured during the study?
Example questions to ask for clinical trials

• Why do researchers believe the intervention being tested might be effective? Why might it not be effective? Has it been tested before?

• What are the possible interventions that I might receive during the trial?

• How will it be determined which interventions I receive (for example, by chance)?

• Who will know which intervention I receive during the trial? Will I know? Will members of the research team know?

• How do the possible risks, side effects, and benefits of this trial compare with those of my current treatment?

• If I benefit from the intervention, will I be allowed to continue receiving it after the trial ends?
Any questions?

ereuropa@csuchico.edu
How experimental drugs are approved

Clinical Trials

Preclinical: Drug Approved for Testing in Humans
Phase 1: 20-100 Participants
Phase 2: 100-1,000 Participants
Phase 3: 1,000-3,000 Participants
FDA Review: To Confirm Safety and Effectiveness
Phase 4: 1,000+ Participants
Drug Submitted for FDA Approval
Drug Approved
Aducanumab
(trade name Aduhelm)

- On June 7, 2021, the FDA approved aducanumab for use in Alzheimer’s disease
- This drug was developed to remove amyloid from the brain
- However, the evidence that ADUHELM offers clinical improvement or that it slows clinical worsening is not totally convincing
- ADUHELM is not a cure for Alzheimer’s disease
- There is no claim that it reverses existing disease or that it stops progression.
- ADUHELM requires monthly intravenous infusions, can have side effects that require monitoring by periodic brain scans, and it is likely to be very expensive.

Excerpts from statement by Dr. M. Marsel Mesulam, Director of the Mesulam Center for Cognitive Neurology and Alzheimer’s Disease
Weblinks about Aducanumab

- FDA News Release: FDA Grants Accelerated Approval for Alzheimer’s Drug
- FDA Label for Aduhelm
- FDA’s Decision to Approve New Treatment for Alzheimer’s Disease
- Northwestern University Feinberg School of Medicine: FDA Approval of Aducanumab
- UCSF Memory and Aging Center: Aducanumab
- New York Times: F.D.A. Approves Alzheimer’s Drug Despite Fierce Debate Over Whether It Works
- Alzforum: Aducanumab Approval Sparks Backlash
NON-INVASIVE BRAIN STIMULATION

- Electrical current to excite activity in targeted brain regions
  - Transcranial Magnetic Stimulation (TMS)
  - Transcranial Direct Current Stimulation (tDCS)
- Has primarily been used in conjunction with word-finding and spelling treatments (e.g., Kyrana Tsapkini and colleagues at Johns Hopkins University)
- May augment gains made in therapy
- Not widely available for clinical use

(Picture of TMS device from Johns Hopkins Medicine)

(Ekhtiari et al., 2019, Neuroscience & Biobehavioral Reviews)