Together, we can explore options that may help improve Long COVID symptoms
About This Study                      page 1
Why Your Participation Matters        page 1
What to Expect During the Study       page 2
About the Study Interventions         page 4
Setting Yourself Up for Success        page 5
About the RECOVER Research Biorepository  page 6
Welcome to RECOVER-NEURO

About This Study

RECOVER-NEURO is looking at how different interventions can help people who have cognitive dysfunction symptoms related to Long COVID. Symptoms can include brain fog, trouble thinking clearly, memory changes, fatigue, headache, slowed attention, anxiety, depression, and difficulty with problem-solving.

In this study, researchers are comparing 3 interventions to learn if they may help improve cognitive dysfunction symptoms. These include:

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BrainHQ</td>
<td>An online brain training program</td>
</tr>
<tr>
<td>PASC-CoRE</td>
<td>(Post-Acute Sequalae of SARS-CoV-2 Infection - Cognitive Recovery)</td>
</tr>
<tr>
<td>Transcranial Direct Current Stimulation (tDCS)</td>
<td>A safe, well-tolerated and noninvasive form of brain stimulation</td>
</tr>
</tbody>
</table>

These interventions have been used before to improve brain function in people with brain injuries and other conditions that cause cognitive dysfunction.

Why Your Participation Matters

More than 500 million people around the world have had COVID, and it's possible that millions of them could have long-term symptoms. We need more information to support the safe use of potential treatments for people with Long COVID. With your help, we can better understand why and how Long COVID affects people in different ways and explore possible treatments. This research may help you, your loved ones, and other people with Long COVID.
What to Expect During the Study

<table>
<thead>
<tr>
<th>Length of Study Intervention</th>
<th>Total Length of Study</th>
<th>Number of Study Visits</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 weeks</td>
<td>About 6 months, including a follow-up visit</td>
<td>3 clinic visits and 1 virtual visit</td>
<td>Answer follow-up questions about your health and well-being</td>
</tr>
</tbody>
</table>

What will I do at each visit?

- **Baseline (Week 1):** Enroll in the study and complete surveys, lab tests, and brain function tests at the clinic. Your study equipment will be mailed to you.
- **Middle of Intervention (Between Weeks 5 and 6):** Complete surveys and brain function tests at home.
- **End of Intervention (Week 10):** Complete surveys, lab tests, and brain function tests at the clinic. Mail back the study equipment.
- **End of Study (3 months after End of Intervention):** Complete surveys, lab tests, and brain function tests at the clinic.

When will I receive my study equipment?

You will be mailed a study kit box with all of the equipment you’ll need for this study. The study team will loan you the equipment and train you on how to use it during your study intervention period.

Before starting your study intervention, a study team member will review your study equipment with you in a video call. You will need to mail back the study equipment at the end of the 10-week period using a pre-paid shipping label and box that will be provided to you.

Please do not open the study kit box or use the study equipment until your first call with a study team member.

When will the study team contact me?

The study team will contact you each week during the 10-week study intervention period. You can expect:
- a brief check-in call each week to see how you are feeling
- a call about a day after the baseline, end of intervention, and end of study visits to ask you to complete follow-up surveys about your health and well-being
About the Study Interventions

BrainHQ or Active Comparator

BrainHQ is an online brain training program that targets memory, attention, and the time it takes to understand and respond to information. It works by continuously adapting activities to each participant's brain function and learning rate. The goal of BrainHQ is to engage the brain's ability to change at any age, and to restore brain function.

The Active Comparator is a set of cognitive activities that actively engage participants but do not continuously adapt to their brain function. These activities are accessed through the same BrainHQ platform. These activities are not the same as usual care.

BrainHQ and PASC-CoRE

In addition to completing BrainHQ sessions, some participants will also complete PASC-CoRe (PASC-Cognitive Recovery). This is an online goal management training program for people with Post-Acute Sequelae of SARS-CoV-2 infection (PASC), including Long COVID. Participants will work with trained study staff to:

• Plan and manage personal goals
• Learn mindfulness-based ways to work through distractions
• Learn skills to focus on goal-oriented tasks
• Develop strategies to manage mental tiredness.

BrainHQ and transcranial Direct Current Stimulation tDCS (active or comparator)

While completing BrainHQ sessions, some participants will also use tDCS (active or comparator). tDCS is a type of noninvasive brain stimulation currently under investigation for use in managing a variety of symptoms or as part of a rehabilitation program. Participants will wear a headset that directs a mild electrical current to specific parts of the brain. A single tDCS treatment lasts approximately 30 minutes. tDCS is thought to have the most benefit when repeated daily or nearly daily over a period of time.

tDCS (comparator) looks the same as the tDCS (active), but it will not deliver the same electrical current. tDCS is authorized by the FDA for investigational use since it is classified as non-significant risk by an ethics board.
About Your Study Intervention Assignment

You will have an equal chance of being assigned to any of the study intervention groups:

<table>
<thead>
<tr>
<th>Brain HQ</th>
<th>Active Comparator</th>
<th>BrainHQ and PASC-CoRE</th>
<th>BrainHQ and tDCS-active</th>
<th>BrainHQ and tDCS-comparator</th>
</tr>
</thead>
</table>

You, your study doctor, and the study staff will not know whether you are assigned to the active comparator group or the active intervention group receiving BrainHQ sessions. Similarly, you, your study doctor, and the study staff will not know if you are receiving tDCS-active or tDCS-comparator electrical current with the BrainHQ sessions, but they can quickly find out if there is ever a need to know for your safety or well-being.

Checking in with the Study Team During Virtual Sessions

At the beginning of each session, we will connect with you through a live video call using the provided iPad and Zoom.
- For your first 3 sessions, a study team member will attend each 30-minute session with you and help make sure you are able to access the BrainHQ training site. They will provide instructions and be available to answer any questions.
- For the rest of your BrainHQ sessions, a study team member will check in with you at the beginning of the session to answer any questions. You can then complete your session on your own for that day.

Potential Risks
Researchers believe these study interventions may help improve cognitive dysfunction symptoms. These study interventions may also worsen cognitive symptoms and post-exertional malaise (PEM). Please contact your study team if you experience any new or worsening symptoms, including PEM.

Setting Yourself Up for Success

- **Think about timing.** When can you consistently complete the activities? When would you feel most engaged?

- **Think about location.** Choose somewhere quiet and comfortable to complete your study activities.

- **Be consistent.** Try to complete the activities at the same time each day.

- **Plan ahead.** During the 10-week study intervention period, please work the study activities into your schedule so that you can complete them on time.

- **Allow for flexibility.** Consider scheduling the sessions early in the day, in case you need to reschedule for later in the day.
About the RECOVER Research Biorepository

The RECOVER Research Biorepository is designed to collect and store biospecimens for future research related to the RECOVER Initiative. Biospecimens may include samples of blood and stool (poop). These samples will be stored securely until they are used up. The samples may also be shared with other researchers for future research, such as developing new tests and treatments for Long COVID or other health problems.

Participating in this study means you agree to share your data and biospecimens with the RECOVER Research Biorepository. You can change your mind later, but researchers might still use your data and biospecimens if they have already been shared. If you choose to participate in this study, your data and biospecimens are subject to be shared for other research.

Why is a biorepository needed?
Biospecimens from a blood sample can provide valuable information to researchers. This information is called "biomarkers." For example, a person's blood sugar level is one of the biomarkers for diabetes. Biomarkers can be measured and may provide important information about Long COVID. They may also predict how a patient will respond to a treatment.

How could a biorepository help with Long COVID research?
Sharing your data and biospecimens with the RECOVER Research Biorepository may:
• Contribute to research that could help your family and others in the future and improve healthcare and public health
• Help researchers make important discoveries about health conditions and possible therapies
• Improve our understanding of how antiviral drugs and other interventions may work to reduce Long COVID symptoms
• Increase the possibility of developing new interventions and possible treatments related to Long COVID
• Enhance our understanding of how and why Long COVID affects people differently

What will the samples be used for?

RECOVER research
The samples will be used for research on COVID and the long-term effects of the virus that causes COVID-19. They may also be used for research on other health problems. Your data and samples will not include any information that can personally identify you, and researchers cannot easily link your identifying information to the data and biospecimens.

Genetic testing (optional)
The use of your samples for genetic testing is optional, and you can let the study team know your decision in the Informed Consent Form. If you give your permission, researchers may study your genes to look for links to Long COVID. Genetic tests can determine if a person or groups of people are more likely to have certain genetic diseases or conditions.
Blood Samples

When will I have blood drawn for the biorepository?
The study team will take about 5 tablespoons (80 ml) of blood from your arm during specified study visits.

Stool Samples

How will I provide stool samples?
After the baseline and End of Intervention, you will be asked to provide a stool (poop) sample using an at-home kit. The at-home kit will include a confidential pre-paid box for you to mail your sample directly to the RECOVER Research Biorepository where it will be stored securely.

Why are stool samples important to this research?
People who have had COVID can have changes in their microbiome (microorganisms like fungi, bacteria, and viruses that live in the intestines) in their stool after their infection. Collecting stool samples helps researchers understand changes in the microbiome caused by the COVID-19 infection.
If you must miss a session
• Contact the study team at (929) 455-5319.
• You may pause study activities 1 time for up to 3 days during the 10-week intervention period.

If you have questions about your equipment
• Contact the study team at (929) 455-5319.

If You Become Ill or Injured
Get the medical care that you need right away. Visit your doctor, go to urgent care, or go to the emergency room if needed.

Contact Your Study Team if You:
• Receive urgent or emergency medical care
• Experience new or worsening symptoms, including post-exertional malaise
• Start taking any new medicines
• Change your phone number, email, or home address
• Have questions about the study

For more information and study updates, visit trials.recovercovid.org/neuro

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