Title of research study:

Safety and feasibility of using low frequency deep brain stimulation of the subthalamic nucleus to improve cognitive performance in patients with Parkinson's disease

Investigator: Kiarash Shahlaie, MD, PhD (PI); Katherine Scangos MD, PhD

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you are an adult, diagnosed with Parkinson's disease, and are a candidate for bilateral subthalamic nucleus deep brain stimulation.

What should I know about a research study?

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document**.**
- If you agree to take part, you will be given a copy of this document.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at the UC Davis Department of Neurological Surgery and UC Davis Department of Psychiatry. The contact information is provided below:

Kiarash Shahlaie, MD, PhD
Department of Neurological Surgery
University of California, Davis School of Medicine
(916) 734-6511

Katherine Scangos, MD, PhD
Department of Psychiatry

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University of California, Davis School of Medicine
For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the Neurosurgery Resident on-call. In the case of an emergency, dial 911 from any phone.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). Information to help you understand research is on-line at http://www.research.ucdavis.edu/IRBAdmin. You may talk to an IRB staff member at (916) 703-9151, IRBAdmin@ucdmc.ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- 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 subject.
- You want to get information or provide input about this research.

Why is this research being done?

The purpose of this research is to determine whether deep brain stimulation can improve memory and thinking ability in people with Parkinson's disease. People with Parkinson's disease have difficulties with movements, tremor, and balance. However, people also have difficulty with thinking, planning, and remembering. Eventually many people with Parkinson's disease develop dementia. Currently there are few treatments available for difficulties with thinking. We believe that low frequency deep brain stimulation may improve thinking in people with Parkinson's disease. We hope that this research will help us develop new treatments for people with cognitive difficulties in Parkinson's disease, and slow the progression to dementia.

How long will the research last?

We expect that you will be in this research study for approximately 2 months.

How many people will be studied?

We expect about 20 people here will be in this research study.

What happens if I say yes, I want to be in this research?

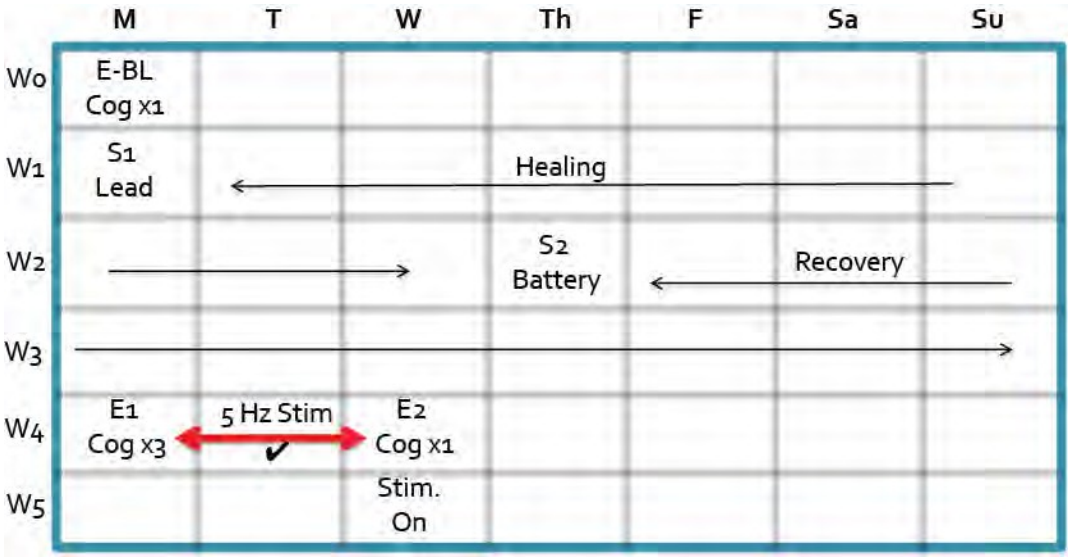
There will be three on-site research visits involved in this study and one telephone call. The first on-site visit will occur before the surgery scheduled by your doctor. In this first visit, you will sit at a computer and play a computer game that tests your thinking, planning, and memory. You will also be asked questions about your mood, emotional wellbeing, and your ability to come up with words. The session will take approximately 50 minutes.

The second two on-site research visits will occur after the surgeries scheduled by your doctor have been completed. These research visits will occur in the 4th week after your first surgery, and the week prior to the time when your doctor would normally turn your deep brain stimulator on. Participating in this study will therefore not delay your treatment in any way.

In the second research visit we will examine the effects of low frequency deep brain stimulation and standard frequency deep brain stimulation on your ability to think, plan, and remember. We will ask you to first complete the cognitive tests that you performed in the first research visit. We will then turn your deep brain stimulator on and ask you to repeat the cognitive tests two times, once when the stimulator is turned to low frequency, and again when the stimulator is turned to the standard frequency. The order of the frequency will be randomized. This second visit will last approximately 2 hours.

We will then examine whether sustained low frequency stimulation leads to improvements in your ability to think, plan, and remember. At the end of the second research visit, we will turn your stimulator on to low frequency stimulation. You will then return home. The next day we will call you at home to check on how you are feeling. During this telephone call, you will be asked questions about your mood and emotional wellbeing and will have the opportunity to describe any changes in your ability to move or think. A caregiver or relative will also be asked questions about your mood, behavior, and wellbeing. After 48 hours, you will return to the clinic for the third research visit.

At the third research visit the low frequency stimulation will be left on and you will again perform the cognitive tests on the computer. You will also be asked questions about your mood, emotional wellbeing, and ability to come up with words. This third visit will last about 50 minutes. At the end of the visit, your deep brain stimulator will be turned off. The following week, you will go to your regularly scheduled doctors appointment for the start of your deep brain stimulator treatment.



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E-BL Cog (baseline experimental cognitive testing, may occur 1-2 wks. prior to lead placement surgery), S1 Lead (DBS lead placement surgery), S2 Battery (DBS battery placement surgery), E1 Cog (experimental testing session 1), E2 Cog (experimental testing session 2). Checkmark indicates timing of telephone check-in.

All onsite research visits will occur at UC Davis in the ACC clinic exam rooms in the same building as your normally scheduled neurosurgery and neurology doctors visits. One research visit will occur by telephone as described above. Research will be conducted by members of the Department of Neurological Surgery and Department of Psychiatry as well as research assistants affiliated with the UC Davis School of Medicine.

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

If you take part in this research, you will have no responsibilities other than coming to the research visits.

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

You may decide not to take part in the research and it will not be held against you.

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

You can leave the research at any time and it will not be held against you.

Data that his been collected already will be used in the study if you agree. If you prefer that your data not be used, all information will be deleted. You will not be asked to explain why you are withdrawing from the study.

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

There are minimal risks to this study. The following risks may result:

1) Physical Risk: Physical risks to the study include minor, temporary, motor symptoms that may result from standard deep brain stimulation. If such side effects occur, the stimulation parameters will be adjusted so that you do not experience any motor side effects or discomfort.
2) Psychological Risks: Deep brain stimulation in the specific area of the basal ganglia known as the ventral subthalamic nucleus could lead to changes in your mood including feeling depressed, impulsive, manic, or psychotic. We expect such symptoms to be very rare, since the stimulation in the study is brief and at low frequency. Risks for these symptoms are not expected to be greater than the standard treatment for your Parkinson's disease. However, we will assess your mood and emotional wellbeing at the first research visit before the surgery, over the telephone, and at each on-site visit. Other psychological risks include boredom or uncertainty during the cognitive testing.

3) Although we expect low-frequency stimulation to improve cognition, we cannot rule out the possibility that some patients may experience temporary worsening of cognitive function.
4) Privacy Risks: Each subject will be assigned a unique identification number and there will be no reference to your name or any other personal identifier in any subsequent publication. All personal identifiers will be destroyed upon completion of the research and the required storage period. Data files will be stored on a secured server, which will be password-protected and access to data files will be given only to IRB approved research personnel.
5) Legal Risks: There are no legal risks.
6) Social Risks: There are no social risks.
7) Economic Risks: There are no economic risks.

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 temporary benefits in your ability to think, plan, and remember. We hope that your participation in this research will help us develop new treatments for cognitive difficulties in Parkinson's disease that may ultimately slow the progression of dementia.

What happens to the information collected for the research?

Efforts will be made to limit use or 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 confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study.

Cognitive performance data collected during this study will be kept for a maximum of 5 years. At the end of this period, all data will be destroyed.

This research is funded in part by a donation from the Chevo Foundation. The Chevo Foundation will not have access to any of the study documents including the data.
The sponsor, monitors, Auditors, the IRB, and the Food and Drug Administration will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your research records may be looked at by the sponsor of this study and government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/compliance/pdf/notice.pdf) and in an attached document.

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Can I be removed from the research without my OK?

You will not be removed from the research study without your approval.

What else do I need to know?

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury.

If you agree to take part in this research study, we will compensate you $10 per research visit for your time and effort. You will also be compensated up to $30 for travel expenses if needed. Compensation will be in the form of a gift card and will be given at the time of the visit. You may be asked for your social security number for payment purposes. It will not be used for any other purpose without your permission.

You will be given access to the results of the study at the closure of the study. If you desire, the results will be shared verbally with your treatment team at the Parkinson's clinic. The information will not be shared with any other health care providers.

Are there other research opportunities?

If you are interested in being contacted for future research, please provide your phone number and/or email. <u>This is completely optional.</u>

_____(initials) Yes, I am willing to be contacted for future research opportunities. My phone number and/or email is: _____.

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Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	Date
Printed name of person witnessing consent process	

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