RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Study Title: Role of GABA in motor symptoms and neurophysiological abnormalities in dystonia

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Sponsor: VCU Health

ABOUT THIS CONSENT FORM

You are being invited to participate in a research study. It is important that you carefully think about whether being in this study is right for you and your situation. This consent form is meant to assist you in thinking about whether or not you want to be in this study. Please ask the study doctor or the study staff to explain any information in this consent document that is not clear to you. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision. Your participation is voluntary. You may decide not to participate in this study. If you do participate, you may withdraw from the study at any time. Your decision not to take part or to withdraw will involve no penalty or loss of benefits to which you are otherwise entitled.

OVERVIEW OF STUDY AND KEY INFORMATION

Why is this study being done?

This study plans to assess the levels of a brain chemical known as GABA in individuals with dystonia and compare them to others without dystonia. Dystonia is a neurological disorder characterized by abnormal muscle spasms and posturing of body parts. This study also assesses the blink reflex response and ability to sense electrical stimulations in your hand in individuals with dystonia compared to others without dystonia. You have been asked to participate in this research study because you have been diagnosed with dystonia or you are volunteering as a healthy community control.

What happens if I participate?

In this study you will be asked to do the following:

1. Visit VCU/VCU Health on 3 different days for study visits
2. If you are currently taking medications that impact your GABA levels, you will be weaned off of the medication prior to your first study visit
3. Have a neurological exam
4. If you have dystonia, you will have your dystonia symptoms assessed
5. Have an MRI scan

6. Have non-harmful electrical stimulation studies of nerves above the eyebrow and on the hand
7. Give permission for researchers to collect information from your medical records about your medical history, diagnosis, and treatment during your participation in the study.

Your participation in this study will last up to 2 weeks. Approximately 60 individuals will participate in and complete this study.

What are the risks and benefits of participating?

There are both risks and benefits of participating in research studies. We want you to know about a few key risks right now. We will give you more information in the "WHAT RISKS AND DISCOMFORTS CAN I EXPECT FROM BEING IN THE STUDY?" section.

Risks and Discomforts	Benefits to you and others
1. The study questionnaires ask questions that are sensitive in nature and may make you feel uncomfortable. 2. The MRI scan may be uncomfortable if you do not like tight spaces. 3. There is a possibility that electrical stimulation studies may be uncomfortable. 4. Tapering off of any medications that impact your GABA levels may worsen dystonia and pain, anxiety, agitation, insomnia, and seizures.	This study may help the study doctors learn things that may help other people with dystonia in the future.

Now that you have a general overview of the study, we want to provide the details about what your participation involves. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask the study staff.

WHY IS THIS STUDY BEING DONE?

This study plans to assess the levels of a brain chemical known as GABA in individuals with dystonia and compare them to others without dystonia. This study also assesses the blink reflex response and ability to sense electrical stimulations in your hand in individuals with dystonia compared to others without dystonia.

The cause of dystonia is poorly understood, but research suggests that there is a loss of the brain's normal inhibition function. GABA is the primary brain chemical in the brains inhibitory system and is predicted to be involved in this loss of inhibitory function. An imaging tool called Magnetic Resonance Spectroscopy (MRS), which is obtained using a standard MRI scanner, will

measure GABA levels in your brain. The investigators hope to see if there is a difference in GABA levels between those with dystonia and those without dystonia.

Researchers also hope to see if differences in GABA levels are associated with differences is response to electrical stimulation, primarily the blink reflex and response to stimuli, between those with dystonia and those without dystonia. This will be studied through recording participant blink reflex recovery cycle (BRRC) and Temporal Discrimination Thresholds (TDT). These measure your blink reflex and your ability to detect two stimuli one after another, respectively.

WHAT WILL HAPPEN IF I PARTICIPATE IN THE STUDY?

Visit 1: Screening visit located at VCU Health Neuroscience, Orthopedics, and Wellness (NOW) building

- At your first study visit (Screening visit), we will review information about the study with you and give you the opportunity to read this consent form and to ask questions before agreeing to participate and signing this form. We will review the study in more detail and go over your health history to make sure you are eligible and safe to continue in this study.
- You will have a neurological exam. This includes assessment of your sensory and motor function, reflexes, coordination, and gait. You will be told and referred for appropriate care if the neurologist has any concerns based on your exam.
- If you have dystonia, you will have an assessment of your symptoms.
- We will also measure if you have any depression, anxiety, or thoughts about suicide. If you are found to have severe depression or anxiety, you will be referred to appropriate health care providers.

Visit 2 (~1-2 weeks later): MRI visit located at the Collaborative Advanced Research Imaging (CARI) Center

- You will have GABA MRS scanning in a Magnetic Resonance Image (MRI) scanner. An MRI involves lying down inside a large, tube-like scanner. Using magnet and radio waves, thousands of images are taken of your brain and skull.
    - You will be asked to rest quietly and not think about anything in particular during the MRI scan
    - You will be positioned and supported using belts and pillows to maximize comfort and prevent movement during your scan. These restraints can be removed at any time If you are uncomfortable.
    - If you can have children, you will be given a urine pregnancy test prior to the MRI. A positive pregnancy test means you cannot have an MRI. This study will not use your urine sample to sequence all or part of your DNA.

- The MRI used in the study is for research purposes only and is not of good enough quality for clinical use. Still, if we find abnormal results on the MRI you may be excluded from the study and will be referred for appropriate

Visit 3 (within 2 weeks of MRI visit): Electrophysiology visit located at the VCU Health Neuroscience, Orthopedics, and Wellness (NOW) building

- The last study visit is for electrophysiology testing. Your Blink Reflex Recovery Cycle (BRRC) and Temporal Discrimination Thresholds (TDT) will be recorded.
  - BRRC Recoding will involve a non-harmful electrical stimulation to a nerve above the eyebrow.
  - TDT recording will involve a surface skin electrode on the right index finger and a non-harmful electrical stimulus.

WHAT ARE THE BENEFITS OF BEING IN THIS STUDY?

This study may help the study doctors learn things that may help other people with dystonia in the future."

WHAT RISKS AND DISCOMFORTS COULD I EXPERIENCE FROM BEING IN THIS STUDY?

Risks of discontinuing GABAergic medications

Because certain medications may change your natural GABA levels, we will ask you to taper off the medication prior to participating in the research procedures of this study. There are some potential risks associated with discontinuing these medications including worsening of dystonia and pain, anxiety, agitation, insomnia, and seizures.

To ensure this process is safe, the medication tapering process will not begin until you have provided informed consent to participate in this study AND we have discussed the tapering with the doctor who prescribed this medication for you. We will work with you and the prescribing doctor to ensure we can safely taper you off the medication, and if it is felt that this cannot safely be done over a 30-day time period you will be withdrawn from the study. If you are not comfortable with the tapering plan or at any time during the tapering of your medication wish to no longer taper off your medication for any reason you may return to your usual dose of medication in a manner recommended by the principal investigator in consultation with the prescribing doctor and withdraw from this study.

Risks of MRI scan

In this study we will take a Magnetic Resonance Imaging (MRI) scan of your head. The MRI machine uses powerful magnetic waves to take pictures inside the body. The waves themselves are not harmful, but they can cause metal to heat up and electronics to stop working.

You should NOT have an MRI if you have metal or electronic devices inside your body. Heart pacemakers and insulin pumps are examples of electronic devices.

The MRI machine is a small round tube. It might make you uncomfortable if you do not like tight spaces.

If you are pregnant, be sure to tell the person giving you the MRI. We do not know if the MRI scan affects pregnancy or fetal development. Therefore, women who are able to become pregnant will have a pregnancy test done before the MRI. You will not be able to participate if the pregnancy test is positive.

Risk of answering Study Questionnaires

Some questionnaires will assess your memory and thinking. You may become fatigued, frustrated, or sad. You may take breaks. If you are found to have more trouble with these questions than expected, we will work with you to contact your personal physician and may provide you with referrals for further evaluation.

Questionnaires may contain questions that are sensitive or upsetting in nature. You may refuse to answer any question that makes you feel uncomfortable. This study will ask you questions about personal topics that might be embarrassing to talk about and that could affect your family relationships if this information were to become known outside of the study.

There is a risk that we may discover you have severe depression and or thoughts of suicide.

Risk of electrophysiology testing

You may experience discomfort from the non-harmful electrical stimulations that are used during electrophysiology testing. The stimulations are delivered for very brief amounts of time (less than a second) and are generally not bothersome to participants. If you feel the stimulation is too uncomfortable the testing will be stopped. The response to the electrical stimulation is measured with electrodes that applied to the skin. The adhesives from the electrodes may cause skin irritation, itching or discomfort.

Privacy risks

Participation in research might involve some loss of privacy. There is a small risk that someone outside the research study could see and misuse information about you.

Unknown/unforeseeable risks

The researchers will let you know about any significant new findings (such as additional risks or discomforts) that might make you change your mind about participating in the study.

WHAT ARE THE COSTS OF THIS STUDY?

Study exams, and any tests will be provided by VCU at no cost to you. You will not be charged for any study visits, tests, or procedures.

You will be paid via a mailed check $75 after you complete all the visits. If you leave the study early, or if we must take you out of the study, you will be paid $25 for each of the visits you have completed.

Total payments within one calendar year that exceed $600 will require the University to annually report these payments to the IRS and you. This may require you to claim the compensation you receive for participation in this study as taxable income. VCU is required by federal law to collect your social security number. Your social security number will be kept confidential and will only be used to process payment.

There are no plans to share any money or profits with you if the use of your sample(s) results in inventions or discoveries that have commercial value.

CAN I STOP BEING IN THIS STUDY?

You can stop being in this research study at any time. Leaving the study will not affect your medical care, employment status, or academic standing at VCU or VCU Health. Tell the study staff if you are thinking about stopping or decide to stop. Your participation in this study may be stopped at any time by the study doctor without your consent. The reasons might include:

- the study doctor thinks it necessary for your health or safety
- you are found to not be eligible for the study
- you have not followed study instructions
- administrative reasons require your withdrawal
- the sponsor stops the study

HOW WILL INFORMATION ABOUT ME BE PROTECTED?

VCU and the VCU Health System have established secure research databases and computer systems to store information and to help with monitoring and oversight of research. Your information may be kept in these databases but are only accessible to individuals working on this study or authorized individuals who have access for specific research related tasks.

Identifiable information in these databases are not released outside VCU unless stated in this consent or required by law. Although results of this research may be presented at meetings or in publications, identifiable personal information about participants will not be disclosed.

Personal information about you might be shared with or copied by authorized representatives from the following organizations for the purposes of managing, monitoring, and overseeing this study:

- Representatives of VCU and the VCU Health System
- Officials of the Department of Health and Human Services

In general, we will not give you any individual results from the study. If we find something of medical importance to you, we will inform you, although we expect that this will be a very rare occurrence.

If you tell us that you may hurt yourself or someone else, the law says that we must let people in authority know. The researchers may share information about you or your participation in the research project without your consent if you disclose to us your intent to hurt yourself or others.

In the future, identifiers might be removed from the information you provide in this study, and after that removal, the information could be used for other research studies by this study team or another researcher without asking you for additional consent.

The researchers cannot prevent you or others, for example a member of your family, from sharing information about you or your involvement in this research.

HOW WILL MY HEALTH INFORMATION BE USED AND SHARED DURING THIS STUDY?

As part of this research study, we will ask you to share identifiable health information with us and/or permit us to access existing information from your healthcare records. New health information may also be created from study-related tests, procedures, visits, and/or questionnaires. This type of information is considered "Protected Health Information" that is protected by federal law.

What type of health information will be used or shared with others during this research?

The following types of information may be used for the conduct of this research:

- Complete health record
- History and physical exam
- Information about mental health

Who will use or share protected health information about me?

VCU and VCU Health are required by law to protect your identifiable health information. By consenting to this study, you authorize VCU/VCU Health to use and/or share your health information for this research. The health information listed above may be used by and/or shared with the following people and groups to conduct, monitor, and oversee the research:

- Principal Investigator and Research Staff
- Data Coordinators
- Health Care Providers at VCU Health
- Institutional Review Boards
- Government/Health Agencies
- Others as Required by Law

Once your health information has been disclosed to anyone outside of this study, the information may no longer be protected under this authorization.

When will this authorization (permission) to use my protected health information expire?

This authorization will expire when the research study is closed, or there is no need to review, analyze and consider the data generated by the research project, whichever is later.

Statement of Privacy Rights

You may change your mind and revoke (take back) the right to use your protected health information at any time. However, even if you revoke this authorization, the researchers may still use or disclose health information they have already collected about you for this study. If you revoke this Authorization, you may no longer be allowed to participate in the research study. You may revoke this authorization at any time. To revoke this Authorization, you must write to the Principal Investigator at:

Dr. Brian Berman, VCU Neurology
1101 E. Marshall Street, Richmond VA 23298.

WHOM SHOULD I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY?

The investigator and study staff named below are the best person(s) to contact if you have any questions, complaints, or concerns about your participation in this research:

Dr. Brian Berman, (804) 628-5276, Brian.Berman@vcuhealth.org

Elizabeth Crump, (804) 446-0668, Elizabeth.Crump@vcuhealth.org

If you have general questions about your rights as a participant in this or any other research, or if you wish to discuss problems, concerns or questions, to obtain information, or to offer input about research, you may contact:

Virginia Commonwealth University Office of Research
800 East Leigh Street, Suite 3000, Box 980568,
Richmond, VA 23298
(804) 827-2157
https://research.vcu.edu/human_research/volunteers.htm

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all your questions

STATEMENT OF CONSENT

I have been provided with an opportunity to read this consent form carefully. All the questions that I wish to raise concerning this study have been answered. By signing this consent form, I have not waived any of the legal rights or benefits to which I otherwise would be entitled. My signature indicates that I freely consent to participate in this research study. I will receive a copy of the consent form for my records.

Adult Participants	
_____ Adult Participant Name (Printed)	
_____ Adult Participant's Signature	_____ Date
_____ Name of Person Conducting Consent Discussion (Printed)	
_____ Signature of Person Conducting Consent Discussion	_____ Date
_____ Principal Investigator Signature (if different from above)	_____ Date