UPMC | University of Pittsburgh Medical Center

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: Targeting the Auditory Control Network with Auditory Control Enhancement (ACE) in Schizophrenia

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Key Points:

- The purpose of this study is to learn about the relationship between perception and attention problems associated with auditory hallucinations in schizophrenia, schizoaffective disorder, schizophreniform disorder, psychosis NOS, and affective psychosis with mood incongruent hallucinations.
- If you agree to participate, we will ask you to do some tests to be sure you are eligible.
- If you qualify to participate, you will be one of 20 participants included in this study
- You will have three sessions of Auditory Control Enhancement (ACE) training, which is about 45 minutes of computer-based response time games with transcranial direct current stimulation (tDCS), a method of non-invasive stimulation of the brain for a short period of time.
    - For tDCS, one or two thin wet sponges will be placed on your head and/or upper arm. The sponges will be connected to electrodes which will deliver a very weak electrical current.
    - You may feel a slight tingling in the beginning of tDCS that goes away after a short time.
- You will have clinical interviews and cognitive testing before and after ACE sessions are completed to assess changes in symptoms.
- You will have an MRI session before and after ACE sessions are completed to assess changes in brain function:
    - MRI is an imaging technique used to collect information about energy use in the brain. MRI is obtained in a hospital setting at the MR Research Center at Presbyterian Hospital.
- You will have an EEG session before and after ACE sessions are completed to assess changes in brain function:
    - EEG is a technique used to collect the natural electric activity produced by the brain. EEG sensors are contained in a cap placed on the scalp.

- It is possible that participation in this study might alleviate some problems associated with psychotic disorders, leading to reduced symptoms, although that cannot be guaranteed.
- Neither you nor your insurance will be billed for you participation in this study.
- You will be paid $25 for completion of initial screening, $25 for initial cognitive tests, and $25 for initial clinical interviews, and $45 for each completed session thereafter (2 EEG sessions, 2 MRI sessions, 3 ACE sessions, and 1 post clinical session), plus a $45 bonus for completing all sessions (up to $480 total). If you are ineligible or unable to complete a session after arrival to the facility, you will be paid $25. Please note if you are a part of another study that collects the same data, that data may be shared so you do not have to repeat procedures. You will not be compensated for assessments that you have already completed.

What is the purpose of this research study?

This study is being done to learn more about people who suffer from psychotic symptoms such as hearing voices, having beliefs which other people do not share, and having difficulties concentrating and thinking. We are trying to learn about perception and attention problems associated with these symptoms. To do this, Dr. Coffman and colleagues are conducting a research study using computer-based training, transcranial direct current stimulation (tDCS), electroencephalography (EEG), and magnetic resonance imaging (MRI). The EEG measures the natural activity of the brain. We will collect EEG while you listen to sounds and/or see letters, numbers, or symbols. We will also ask you to respond to some of these sounds or pictures. The MRI uses a large magnetic field to capture a series of images of the brain which can later be reconstructed into a 3D image. Along with imaging, you will also perform interviews and tests that assess intellectual function, social function, and ratings of psychotic symptoms if applicable. You may also receive tDCS, which is used to non-invasively stimulate the way the brain works for a short period of time. For tDCS, one or two wet, thin sponges will be placed on your head. The sponges will be connected to electrodes which will deliver a very weak electrical current. You may feel a slight tingling as the current begins, but the tingling should go away after a short time. tDCS is non-invasive, meaning that it does not require piercing the skin or putting anything inside the body.

What procedures will be performed for research purposes?

If you decide to take part in this research study, you will undergo the following procedures:

Screening Procedures:

Procedures to determine if you are eligible to take part in a research study are called “screening procedures.” For this research study, the following screening procedures will take place during your initial visit:

- A 15 to 30 minute hearing test will be performed to determine if you have any hearing loss.
- Height, weight and head measurements to ensure the ability to fit into the scanning equipment. No participant exceeding 6’4” in height, 300 lbs. in weight,

or with a head circumference greater than 62 cm can be put in the scanning equipment.

- An interview about your feelings and experiences and family history of psychiatric illness. We may also obtain information from your medical records and, if applicable, treatment team.
- A vocabulary and problem-solving test.

If you are a suitable candidate after performing the screening procedures, you will be asked to enter the study. Subjects who don't pass the screen will be reimbursed $25. Participants will not be reimbursed for assessments they do not complete.

Experimental Procedures:

If you qualify to take part in this research study, you will undergo the experimental procedures listed below. Please note if you are a part of another study that collects the same data, that data may be shared so you may not have to repeat procedures.

- ***Auditory Control Enhancement (ACE)****:* You will be assigned by chance (such as a coin flip) into one of two groups to receive a different dosage or level of transcranial direct current stimulation (tDCS) during three sessions of cognitive training. tDCS is used to stimulate the brain for a short period of time. This is a single blind study. This means the person administering will know what group you are assigned to, but you will not be told. For tDCS one or two thin wet sponges will be placed on your head and/or upper arm. The sponges will be connected to electrodes which will deliver a very weak electrical current. You may feel a slight tingling as the current begins, but the tingling should go away after a short time. You may feel an itching or tingling feeling for a short time; if such a feeling occurs, we ask you to please announce it to the research team. You may or may not feel any sensation during tDCS. The Neuroelectrics Starstim 32 will be used to deliver tDCS. This specific device is not approved by the FDA, but it has been used in research studies for nearly ten years and the FDA has determined that the use of this device in this study does not pose significant risk.
- ***Interviews:*** Before and after ACE, in two separate sessions, you will be asked questions about a) your background; b) functioning in daily life and across different phases of your life. If you have experienced psychosis, we may obtain information (for example, psychiatric symptoms) from you and may obtain information from your treatment team and past, present and future medical records. These interviews will take approximately 1 hour.
- ***Cognitive Tests:*** During the interview sessions, you will also perform cognitive tests. You will be asked to complete computerized and pen-and-paper tests of your attention, concentration, reading, and problem-solving ability, which will take approximately 1.5 hours.
- ***EEG scan****:* You will be asked to complete EEG (electroencephalography) studies before and after ACE training. EEG will be measured using the same Neuroelectrics Starstim 32 system used for tDCS. EEG measures the natural activity of the brain using small sensors placed on the scalp. These sensors use

conductive gel to provide a connection suitable for recording brain activity. During EEG, you will watch a silent video while sounds are played over headphones, or sometimes count the sounds. In addition to these auditory tasks, you will also be asked to perform visual attention tasks, such pressing a button when you see a letter or image. You may be asked to complete a motor task. This motor task will require you to press a button at a specified rate and will take no longer than five minutes to complete. Following these tasks, we may record EEG when you are not engaged in any task. After the experiment, we will clean the gel from your scalp. When you get home, we recommend that you wash your hair to remove any remaining gel. The total time for EEG testing will be between 2 to 2.5 hours (including setup and clean up times). The actual testing will be about 1 to 1.5 hours.

- ***Magnetic Resonance Imaging (MRI) Scan:*** You will also be asked to complete MRI studies before and after ACE training. An MRI is a type of brain scan that takes pictures of the brain that will later be used to create a 3D model of your brain. The MRI does not use radiation, but rather radio waves, a large magnet and a computer to create the images. The actual MRI examination requires up to a half hour for transportation/preparation/debriefing and approximately 1 hour in the scanner.

  Prior to the scan, you will be asked questions to make sure you are eligible to participate in the scan. This includes whether you have certain types of metal in your body (if there is any question, you may be required to have an x-ray at UPMC to determine if you can safely enter the magnet). Females will also be asked to self-report any pregnancy. If you are pregnant AND have certain types of metal in your body, you cannot participate in the MRI part of this study and will be excluded from the study.

  If you like, you may first lie in a “practice scanner” which looks and feels like the real scanner. This will allow you to see what it is like before the actual scan.

  During the MRI, you will lie on your back on a table that moves into a hollow, cylindrical machine (the scanner). While you are lying in the MRI machine, you will hear a knocking noise the MRI machine makes when taking pictures of your brain. It is important to remain still while in the scanner, as moving your head, arms and legs can make the brain pictures blurry. You will always be able to talk with the technologist during the study.

The brain imaging studies are not tailored for clinical assessment and are designed solely for research purposes. If at the time of the scan, the MRI technologist detects a potential incidental finding, a neuroradiologist will assess its clinical significance. If the finding is judged by the radiologist to warrant clinical investigation, we will tell you and offer an appropriate referral for follow-up.

You will be asked to complete clinical and cognitive assessments, EEG, and MRI before and after three sessions of ACE. All together, these evaluations and tests (including the screening) will take about 20-30 hours.

What are the possible risks, side effects, and discomforts of this research study?

There are minimal potential risks associated with this research study. You may

experience uneasiness or anxiety during testing. If you feel uncomfortable or distressed at any point in testing, please let the researcher know immediately. You will be given a break and reassurance if you remain uncomfortable. Remember, you are not required to complete any procedures.

- MRI: The MRI scanner is a large magnet which can attract metal objects toward it. Although there are no known effects of the magnetism, radio frequencies or head coil used in MRI technology, there could be unknown risk. If you have certain types of metal in your body you cannot participate in the MRI scan. If you think you may be pregnant AND you have certain types of metal in your body, you will be excluded from this study. If there is any question of metal in your body, you may be required to have an x-ray before you complete the MRI scan. You will be asked to place all metal and magnetic objects in your possession (e.g., jewelry, keys, credit cards) in a locker outside the magnetic room. You will use ear plugs during the MRI to reduce the loud knocking noise made by the scanner. People commonly feel uncomfortable in the small space of the magnet, but rarely feel claustrophobic. Experience in the "practice scanner" helps to lessen the discomfort. The study will be stopped immediately if this is a problem for you. There is no radiation exposure associated with the MRI exam.
- tDCS: In a few cases subjects have reported mild skin damage or irritation. For example, a few subjects who had recently shaved their heads have described temporary redness and irritation at the electrode site. Before stimulation, your head will be checked for any redness, irritation, or recent shaving of the head. If any of these are seen, we will exclude you from the study. At the start of tDCS there may be a brief tingling, warming, or itching sensation on the head. If the warm feeling becomes a hotter, burning feeling, please tell us right away and the stimulation will be stopped. You will be asked at the beginning of and throughout the stimulation to report any pain or discomfort that you feel during the procedure on scale from 1 to 10, with 1 being "not at all" and 10 being the most severe imaginable. If you report an 8 or more, we will end stimulation right away. There is the chance of a small shock and/or a sensation of a short light flash during tDCS. The most common reason this can happen is that the tDCS electrodes are removed suddenly during stimulation. Please do not touch the electrodes or move them away from your skin during testing. There is a very small chance of a burn at the electrode site, much like sunburn, that may cause in a scab. This risk is minimized by removing any makeup prior to tDCS. Although these are the only known risks of tDCS as used here, there may be other unknown effects of tDCS in people with auditory hallucinations. More specifically, we do not currently know how participants with schizophrenia might perceive the effects and safety of an electric current passed into their brain. It is possible that procedures associated with tDCS will lead to the worsening symptoms. Also, the long-term effect(s) of tDCS are currently unknown.
- EEG: Risks associated with the EEG are slight skin irritation caused by the placement of the electrodes on the skin (rate–occurs in less than 1% of people, less than 1 out of 100 people). The EEG system we use is designed to avoid skin irritation.
- Interviews and cognitive tests: Some may find the interviews and tests stressful,

uncomfortable, or embarrassing. Our staff is highly trained in the administration of these measures; you are not obligated to answer any questions or perform any task you don't want to. You will be given breaks as needed.

- Breach of Confidentiality: There is a rare possibility of a breach of confidentiality, but we have safeguards in place to minimize that. All records related to your involvement in this research study will be stored in a locked file cabinet and in firewall- and password-protected electronic files. You will also be assigned a case number and it is this number, along with your initials (for proper identification by the research team), that is used on research assessments. Although every reasonable effort has been taken, confidentiality during Internet communication activities cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study.

What are possible benefits from taking part in this study?

Psychiatric illnesses are likely related to problems in certain brain areas. It is possible that participation in this study might alleviate some of these problems, leading to reduced symptoms and enhanced cognition, although that cannot be guaranteed.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?

Any new information that comes to the attention of the investigators during the course of the research and that may relate to your willingness to continue to participate will be provided to you.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?

Neither you nor your insurance provider will be charged for the costs of any of the procedures performed for the purpose of this research study. Research funds will pay for all costs related to your participation.

Will I be paid if I take part in this research study?

If you agree to participate in this study, in addition to travel reimbursement and meals, you will receive monetary compensation for your participation in these research procedures. Please note if you are a part of another study that collects the same data, that data may be shared so you do not have to repeat procedures. You will not be compensated for assessments that you have already completed.

You will be paid $25 for completing initial screening, $25 for initial clinical interviews, $25 for initial cognitive testing, and $45 for each completed session thereafter (2 EEG sessions, 2 MRI sessions, 3 ACE sessions, and 1 post clinical session), plus a $45 bonus for completing all sessions. In total, you can be paid up to $480 for completing all sessions of this study. If you are ineligible or unable to complete a session after arrival to the facility, you will be paid $25.

If you are currently enrolled in or recently completed the PRAC Screening Protocol (IRB#STUDY23070107), you may not be asked to complete the initial screening assessment, in which case the total compensation would be $455.

If all clinical measures and assessments are unable to be completed in one session, you will be paid $25 for each of two clinical assessment and interview appointments.

Also note that to receive payment through the Vincent Payment system you are asked to provide your social security number. If you do not wish to provide this information, taxes will be taken out of your payment and you will not receive full compensation.

Payment to participants is considered taxable income regardless of the amount. If a participant receives $600 or more in a calendar year from one organization, that organization is required by law to file a "Form 1099 – Miscellaneous" with the IRS and provide a copy to the taxpayer. We are required to give your name and social security number to the Accounting Office. Participants who do not provide a social security number may still participate in the research, but the IRS requires that 24% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 76% of the expected payment.

How will the privacy of my research information be protected?

Several procedures have been put into place to protect the privacy of your medical record information (see "Breach of Confidentiality" above). All records related to your involvement in this research study will be stored in a locked file cabinet and in firewall- and password-protected electronic files. Your identity on these records will be indicated by a case number, along with your initials (for proper identification by the research team), rather than by your name.

Who will know about my participation in this study?

Members of the research team and staff in the University of Pittsburgh Office of Research Protections, U.S. Food and Drug Administration (FDA) and this study's sponsor, the National Institute of Mental Health (NIMH) will have access to your research information. Additionally, authorized representatives of UPMC hospitals or other affiliated health care providers may have access to identifiable information related to your participation in this research study for the purpose of: (1) fulfilling orders, made by the investigators, for hospital and health care services associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance). However, just as with the use of your medical information for health care purposes, we cannot absolutely guarantee its privacy. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

It is possible that we may use the information obtained from this study in other research studies. This information may be shared with other researchers here and at other research centers, but those researchers will never be provided with any personal identifiers that would allow them to learn your identity. If you have consented or do consent to participate in a research study where an investigator is the same as an

investigator listed on this protocol or is another UPMC study, the data from the studies may be joined. Each study would have already collected identifying information from you. Sharing information provides new knowledge and avoids duplication of certain interviews and tests; it also allows us to answer new research questions.

In the event that any unusual or unexpected findings appear in the data collected from your MRI scan, a follow up review of the data will be performed by a trained Magnetic Resonance Research Center (MRRC) neuroradiologist. A member of the research staff will inform you if any abnormalities are found and will refer you to your PCP or provide you with a referral for a follow up. Release of this information can be requested by a signed form.

There is the possibility that you may be eligible for other research studies being conducted independently of this one. You may be contacted in person, by phone and possibly by mail/email by members of our research team to determine your interest in those other studies, but you are never under any obligation to participate in those. We will also give reminder calls/emails for follow-up appointments. Declining to participate in such research will not have any bearing on your clinical care or future relationship with the University of Pittsburgh or UPMC.

According to University of Pittsburgh policy all research records must be maintained for at least 7 years following final reporting or publication of a project, and records may be kept indefinitely.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings; if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

Your data used in this research study may contribute to a new discovery or treatment. In some instances, these discoveries or treatments may be of commercial value and may be sold, patented, or licensed by the investigators and the University of Pittsburgh for use in other research or the development of new products. You will not retain any property rights nor will you share in any money that the investigators, the University of Pittsburgh, or their agents may receive.

Will this research study use or disclose my identifiable medical record information?

For UPMC patients, we will review and record all past, present, and future medical record information related to their psychiatric care.

If you have experienced psychosis, we are requesting your authorization or permission to review your medical records to determine whether you meet the conditions for participating in this study as well as to aid in the identification of your psychiatric symptoms. We may obtain information (for example, about symptoms, birth history, family history) from you and may obtain information from your treatment team and past, present, and future medical records.

This research study may result in identifiable information that will be placed in your medical records held at UPMC WPH. This includes a copy of this signed consent form, progress notes and possibly other information collected as part of this research study. We may share the results of this research study with your treatment team and obtain information about your past, current and future treatment. In accordance with UPMC Notices of Privacy Practices document that you have been provided, you are permitted access to information (including information resulting from your medical records filed with your health care provider).

May I withdraw, at a future date, my permission for participation in this research study?

Yes. To do so, you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form. **Your participation is completely voluntary and your decision whether or not to participate in all or part of this study, or to later withdraw from all or part of it, will not affect your current or future medical care at UPMC, nor will it affect your relationship with the University of Pittsburgh. Additionally, you can always withdraw your authorization to allow the research team to review your medical records by contacting the investigator listed on the first page and making the request in writing.** Any information obtained from you up to that point will continue to be used by the research team**.** Your research information collected before you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

Can I be withdrawn from the study without my consent?

It is possible that you may be removed from the research study by the researchers, for example, if you have hearing loss or if you are unable to perform the tasks, or if at any point during the study you no longer meet study eligibility.

Who will pay if I am injured as a result of taking part in this study?

If you believe that the research procedures have resulted in an injury to you, immediately contact the Principal Investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. Currently, there is no plan for any additional financial compensation.

VOLUNTARY CONSENT: All of the above has been explained to me and all of my current questions have been answered. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

Any questions I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing below, I agree to continue my participation in this research study and provide my authorization to share my medical records with the research team. A blank copy of this consent form will be given to me.

_____
Printed Name of Participant

_____ _____
Participant's Signature Date

CERTIFICATION OF INFORMED CONSENT:

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study that I may always request that my questions, concerns and complaints be addressed by a listed investigator. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____
Printed Name of Person Obtaining Consent Role in Research Study

_____ _____
Signature of Person Obtaining Consent Date

FOR REMOTE CONSENT ONLY:

VOLUNTARY CONSENT: All the above has been explained to me and all of my current questions have been answered. I understand that I may always request that my questions, concerns or complaints be addressed by a listed investigator.

Any questions I have about my rights as a research participant will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

To indicate my agreement to participate in this research study, and to allow the use and disclosure of my medical record information for the purposes described above, I consent to participate in the study by clicking the 'I agree' box and by completing the fields below.

Click here to print a copy of the consent form to keep for your records.

I agree

Full Name: _____ ___ _____(first, middle initial, last name)

Birthdate: ____ / _____ / _____ (mm/dd/year)

Answer to ONE of 3 questions from drop-down box:

What is your mother's maiden name?

In what city were you born?

What high school did you attend?