UPMC | University of Pittsburgh Medical Center

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Testing the Causal Role of the OFC in Compulsive Behavior

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

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SUMMARY OF KEY POINTS

- Complete a one-time visit involving Transcranial Magnetic Stimulation (TMS) procedures. TMS is FDA-approved as a treatment for psychological conditions including depression and has been used safely in research and clinical care for 30 years.

- The most common risk of TMS is discomfort (e.g., pain, muscle contractions, itching) during administration of TMS, in the vicinity of the coil (forehead area).

- The TMS procedures are given in conjunction with a behavioral "shock avoidance task" involving unpleasant (but not painful or dangerous) shocks, which can be avoided by pressing the correct keys.

- Both the TMS procedures and the "shock avoidance task" may be given in either an "active" version or in a "sham" (or neutral/placebo) version. Which set of procedures you receive will be determined at random (similar to a coin flip).

- In addition to today's screening visit, complete an additional assessment visit, followed by the TMS day/visit, followed by one final 1-week follow-up visit.

- The second, third and fourth visits include a functional Magnetic Resonance Imaging (fMRI) scan.

- All procedures completed, compensation=$300

PURPOSE AND DESCRIPTION:
Compulsive behaviors (CBs), or unwanted, repetitive behaviors aimed at reducing distress, are a core feature of obsessive-compulsive (OC) spectrum disorders but appear across a very broad spectrum of psychological conditions from general anxiety (checking, perfectionism), to eating pathology, to substance dependence (seeking substances to avoid withdrawal-related symptoms). The purpose of this research study is to find brain patterns causing unwanted, repetitive behaviors (complusions). This work could ultimately lead to the ability to treat compulsions more effectively by targeting the right regions of the brain to overcome compulsions.

You have been asked to participate in this study because you have reported problems with compulsive behaviors.

PROCEDURES: Individuals who are currently experiencing clinically significant compulsive behaviors will be recruited for this study. If you agree to participate, you will undergo the following procedure(s) that are not part of your routine medical care. The experiment consists of up to four study visits which will span approximately 3-5 weeks.

It is very important for the purposes of the study to complete all study procedures on time. Failure to complete study procedures on time will result in being withdrawn from the study and referred for care outside the study. The following summarizes the conditions of participation, or what is expected of you during the study.

1. Study questionnaires must be completed on time throughout the duration of the study. These questionnaires ask how you are currently feeling both mentally and physically and about your past medical and psychiatric history. Some questionnaires are self-reports and others are administered by trained research staff.

2. To the best of your knowledge, you will be living in the Pittsburgh area for at least 3 weeks so that you can continue to attend study visits.

3. You agree to avoid using mood-altering drugs such as cocaine, cannabis or marijuana, opiates, amphetamines, and barbiturates. In addition, you agree to avoid using alcohol prior to any assessment or intervention visit.

4. Please notify the study coordinator or other personnel if you receive any additional treatment for psychiatric difficulties or start any new medications for anxiety or other psychological symptoms during the duration of the study.

5. You agree to have evaluations videotaped, which will include facial images. All videotapes will be labeled with subject study number, session number, and date. These audiotapes and videotapes will be used for research purposes only. These tapes will be viewed by research study staff to ensure that interviewers are adhering to protocol standards and to quantify compulsive behaviors in the laboratory.

Visit 1 (Eligibility/Screening) Procedures:
On the first visit, the study will be explained to you and you will review the entire study and sign the consent form before any study procedures begin. Then you will go through assessments about the symptoms you are experiencing to see if you are eligible to participate. You will be asked questions about your psychiatric and medical history and your basic demographics. You will then complete computer-based tests of cognitive abilities, a laboratory assessment of your compulsive behaviors, and a few questionnaires.

There will not be a change in your medication nor will you be subjected to any medical procedure as a result of participation in this study. All administered tests are for research purposes only. We will analyze the data collected from the study to better understand what brain regions are important in overcoming compulsive behaviors. You will receive payment for the first testing session whether or not you return for the other testing session(s).

Visit 2 Procedures:
If after the screening procedures you continue to be eligible for study participation and agree, on your second visit you will complete an assessment using Functional Magnetic Resonance Imaging (fMRI), and will undergo the following procedures: 1) entering a room in which a large magnet is located, 2) lying on a narrow bed and being slid into a small tunnel approximately 6 feet long and 25 inches wide; a mirror will be placed above your head to measure the diameter of your pupil, 3) completing computer-based tasks. On days when an fMRI assessment is also completed, the affective go/no-go task may be completed in the fMRI scanner (time permitting). All participants will be asked a series of screening questions before entering the scanner room to ensure the safety of the participant. In addition, you may be asked to complete a urine pregnancy or urine drug test. If either the pregnancy test or the drug test is positive, you will not be able to participate further in the study.

The fMRI tasks take up to 60 minutes total. These tasks will be completed while lying inside the scanner. The scanner tube will be noisy. A staff member will be with you throughout the procedure. The instrument used for MRI is a large machine employing a strong magnet, radio waves, and a coil to obtain pictures of brain activity. The instrument is FDA approved.

You will then be asked to complete computer-based tests of cognitive abilities, a laboratory assessment of your compulsive behaviors, and a few questionnaires.

This visit will take up to 2 hours.

Visit 3 Procedures:
Your third visit will take place about 1 week after Visit 2. You will complete a computer task, the "shock avoidance task," designed to train you to respond to different stimuli (e.g., letters and shapes) by pressing a button in order to avoid receiving a mild electrical shock to each foot, which may be unpleasant but not painful or dangerous. These shocks are very brief (1

millisecond, or one one-thousandth of a second) and their intensity will be individually tailored to you (within a safe range used often in research) so that they are not painful. At the very most, you could receive one of these brief shocks about once every 18 seconds during a 24min task. However, the shocks can be avoided entirely through a simple process of pressing the correct buttons, and you will be fully pre-trained in the task before the possibility of receiving a shock is introduced.

You will then undergo Transcranial Magnetic Stimulation (TMS) procedures. TMS involves very brief, noninvasive stimulation of a brain area beneath the left side of your forehead. It is FDA-approved as a treatment for psychological conditions including depression and has been used safely in research and clinical care for 30 years. Some of the TMS placements used in this study will involve no stimulation, and you will not be informed of whether you have received active stimulation or no (sham) stimulation. Following the TMS procedures, you will then immediately complete a new variation of the "shock avoidance task." This time, one of the electrodes may be disconnected from one of your two feet so that shocks can no longer be received on that side, and you may receive either an "active" version of the task or a "sham" (neutral/placebo) version, depending on the experimental condition you've been randomly assigned to. You will not be informed of whether you have received the active or the sham version.
After a short break, you will then repeat a second block of identical procedures—including both the TMS procedures and the "shock avoidance task" procedures.
Next, you will complete fMRI and other assessment procedures identical to the second visit, including computer-based tests of cognitive abilities, a laboratory assessment of your compulsive behaviors, and a few questionnaires.

This visit will take up to 3 hours.

Visit 4 Procedures:
Your fourth visit will take place about 1 week after your third visit, and will be similar to your other visits, but will NOT involve any Transcranial Magnetic Stimulation (TMS) procedures. At this visit, you will complete a final fMRI scan, complete computer-based tests of cognitive abilities, a laboratory assessment of your compulsive behaviors, a few questionnaires, and a portion of the clinical interviews you completed during the screening process. This visit will take up to 2.5 hours.

Communication after testing
The principal investigator of this study will be available to answer any questions you may have regarding this research or this form. If you have any questions, comments, or concerns about the study or the informed consent process, you may also contact the principal investigator at the number provided to you at the testing session (also located on the front page of this consent form).

New Information**:** You understand that if new information, either good or bad, about the study intervention or other aspects of this study is learned during the course of this study, you will be informed.

Clinicaltrials.gov
A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

Your research information may be shared with investigators conducting other research. This information may be identifiable.

Your information (even if identifiers are removed) may be used for commercial profit; however, you will not retain any property rights, nor will you share in any money that the that the investigators, the University of Pittsburgh, or outside agencies may receive.

You will not be notified of any individual research results.

ALTERNATIVES TO PARTICIPATION
There are many alternatives that effectively reduce compulsive behavior symptoms. These include psychotherapy, medication, and the combination of medications plus psychotherapy. If you agree to participate in the study, then you will be agreeing to postpone beginning any new treatments for the approximately 3 week period of your intervention visits. If you decide at any point during the study that you prefer to make changes to your treatments or newly pursue any of these alternatives, you should request a referral and not participate in this study.

PROCEDURES THAT MAY RESULT IN DISCOMFORT OR INCONVENIENCE/EXPECTED RISKS AND BENEFITS:

Risks of clinical, self-report, behavioral, and cognitive assessment tasks
You may become upset, anxious, bored, tired, and/or frustrated during this study. The interviews, questionnaires, cognitive assessments, and the compulsive behavior assessments, which involve brief exposure to a feared object/situation, may potentially cause you to feel upset. During the experiment, you will be asked a number of questions regarding how you "feel". You may become aware of feelings of happiness, sadness, anxiety, or other mood states that you had not considered before. You may also be asked to think about times in your life that were either very anxious or very sad. This could result in a transient anxious or depressed mood state. States such as these normally last 10-15 minutes and then disappear quickly and completely. If the experiment makes you uncomfortable in any way, you may discontinue your participation in the experiment, either temporarily or permanently. In the event of a serious emotional reaction, a recommendation for independent professional counseling will be provided.

Breach of confidentiality
Although extensive measures will be taken to keep all research records confidential, breach of subject confidentiality is a possible risk of this study. If during the course of clinical assessments you provide information that raises significant concerns about your safety or the safety of others, it may be necessary to breach confidentiality in order to ensure safety. In such an event, crisis intervention services available through WPIC may be notified of any information you shared that is directly pertinent to your safety and/or the safety of others.

Risks of shock avoidance task (computer-based habit override assessment and practice)

Some aspects of the "shock avoidance task" may be disturbing to you, including the possibility that you may receive a mild electrical shock. You may experience distress, boredom, fatigue, and/or frustration during the tasks. Although mild electrical shocks have been used safely in thousands of participants, there is a risk of serious injury if the device's electrodes were to be attached in a way that crossed the heart. For this protocol, electrodes will be attached and taped to the feet to fully prevent such an occurrence.

Risks of MRI

The risks associated with having an MRI are small. The MRI machine may attract or move metal objects. Thus, people who have metal in their body, such as aneurysm clips or pacemakers will be excluded from this study unless the device can be proven to be safe for MRI by the MR Research Center's trained staff. Before participating, you will also be asked whether you are wearing metal or have metal in your pockets and will be asked to remove such metal objects before entering the room with the scanner. There are no known risks of exposure to the magnetic fields used for these tests. The machine is loud when turned on and may cause some discomfort. Therefore, all participants will be given and must wear ear plugs. A staff member will be talking with you multiple times throughout the scan and an emergency squeeze ball will be provided so that you may stop the testing if you become uncomfortable or anxious at any time.

The space inside the MRI machine is fairly limited. Some people feel claustrophobic in the magnet. There is a chance you may be uncomfortable in a space this small. Some individuals panic in enclosed spaces, and thus may experience a panic attack in the scanner. You will have the opportunity to examine this space before the test starts. The study will be ended early if this is a problem for you; you may elect to discontinue the study at any time if you become anxious in the scanner. In the event that you do experience a panic attack, clinically trained personnel will be available to help you to relax; however, no medications will be provided**.**

After lying in the MRI machine, some people feel lightheaded upon sitting up. This feeling will go away within a few minutes. You will be assisted to make sure that you do not fall.

Conclusive tests to determine the risks of an MRI to a fetus (unborn child) have not been done. To avoid risk to a fetus, it is important that you not be pregnant during the MRI scan. If you are a woman of child-bearing potential, you will undergo a pregnancy test prior to the MRI.

There is also a risk of learning new health information that you were not expecting. The MRIs performed during the course of the experiment are not clinical measures. They will not be read by a radiologist. They are not guaranteed to reveal tumors or brain abnormalities. However, if the staff at the MRI center notices any abnormalities, we will communicate to you about these incidental findings and help you to seek appropriate follow-up care.

Risks of the Transcranial Magnetic Stimulation (TMS) procedures

The risks of the TMS procedures in this study involve almost exclusively minimal-mild adverse events. TMS is currently under investigation as a potential treatment for various neurological and psychiatric disorders and has been approved for the treatment of depression by the FDA in 2008. Repetitive TMS has also been used to probe various aspects of brain function, via noninvasive stimulation of specific brain regions, in the context of research studies. In this study, TMS will be delivered in compliance with the safety guidelines recommended by the International Workshop on the safety of repetitive Transcranial Magnetic Stimulation, which were reviewed

and updated in 2008.

There is a risk of discomfort (pain, muscle contractions) during administration of TMS. However, subjective pain reports in a prior study using nearly identical procedures dissipated within the first 15-30sec and no participant requested to discontinue the experiment. The total time that stimulation will be given at each visit is about 10min. You may choose to discontinue the stimulation at any time without penalty.

There is a risk of temporary effects on certain aspects of cognition. These effects are expected to mild and transient, lasting approximately 60min maximum, and fully resolving prior to the completion of any study visit.

Minimal-mild post-TBS discomfort (e.g., headache, nausea) has been reported in a small minority of participants (e.g., 5%). There is a very small risk of seizure (less than one-tenth of one percent), with only one such instance observed in over 1000 participants completing the current form of TMS in research settings.

Risks of videotaping:
Risks associated with videotaping include the potential for a breach in confidentiality if the recordings were misplaced or became available to non-study personnel. To protect against this risk, we will not record your name or identifying information anywhere on the recording, and will store recordings on a secure server to which only the research study staff have access.

As with any experimental procedure, there may be adverse events or side effects that are currently unknown and certain of these unknown risks could be permanent, severe or life-threatening.

Benefits of participation:
You may learn information about your symptoms through psychoeducational debriefings following clinical assessments. Additionally, you may derive benefits from the psychiatric evaluations by having the opportunity to talk about personal issues and concerns with a sympathetic listener and by having access to treatment referral services. Clinical monitoring throughout the course of treatment will be provided, which may provide faster access to a higher level of care if needed.

Although the benefits of the procedures have not been proven, you could experience beneficial effects from the study intervention in that your compulsive behavior symptoms could temporarily decrease. Referrals to appropriate alternative care will be made available to you at any time throughout the study. Finally, participation in the proposed research may help inform and improve the development of novel treatment strategies that could ultimately benefit patients, including you.

SPECIAL CIRCUMSTANCES: COSTS AND PAYMENTS: There will be no costs to you for your participation in this study. There will be no fees or charges for any of the psychiatric evaluations required for the study. There also will be no fees for the TMS procedures or any other research-only services including the MRI and associated pregnancy test (if one is required). You understand that you will be responsible for the costs of any other types of medical care that

you might need during the course of the study including all standard care costs not directly associated with this research study.
You will receive $30 for completing Visit 1, $70 for Visit 2, and $100 for each of Visits 3 and 4. Participants who complete all visits will thus receive a total of $300. You may refuse to participate or may withdraw from this study at any time, and you have the right to refuse to answer any question(s) without any negative consequences. The investigator may also stop the study at any time.

COMPENSATION FOR INJURY: 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. At this time, there is no plan for any additional financial compensation. You do not waive any rights by signing this form.

CONFIDENTIALITY:
Who will know about my participation in this research study?
Any information about you obtained from this research will be kept as confidential (private) as possible. All records related to your involvement in this research study will be stored in a locked file cabinet and/or in password-protected electronic files stored in locked offices or on university servers protected by a powerful security firewall. Your identity on these records will be indicated by a case number rather than by your name, and the information linking these case numbers with your identity will be kept separate from the research records. You will not be identified by name in any publication of the research results unless you sign a separate consent form giving your permission (release).

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.

Although every reasonable effort has been taken to de-identify your research information, confidentiality cannot be guaranteed, and it is possible that re-identification of research data/samples may occur. All research records will be maintained for a period of at least 7 years following final reporting or publication of the study.

Your physician is involved as an investigator in this research study. Before agreeing to participate, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

Will this research study involve the use or disclosure of my identifiable medical record information?
This research study will NOT involve the recording of current and/or future identifiable medical information from your hospital and/or other health care provider (e.g., physician office) records,

nor will any identifiable information obtained through this research study be placed in your medical records.

Who will have access to my identifiable information related to my participation in this research study?

In addition to the investigators listed on the first page of this consent form and their research staff, the following individuals will or may have access to identifiable information related to your participation in this research study:

- Authorized representatives of the University of Pittsburgh Office of Research Protections may review your identifiable research information for the purpose of monitoring the appropriate conduct of this research study.
- In unusual cases, the investigators may be required to release identifiable information related to your participation in this research study in response to an order from a court of law. 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.
- Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical 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 (e.g., laboratory tests, diagnostic procedures) 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).

Is my participation in this research study voluntary?

Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary.

Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

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

You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above. In other words, if you withdraw from the study, or if investigators remove you prior to completing the study, your research data will continue to be stored and protected in the same manner as if you had not withdrawn.

To formally withdraw your consent for participation in this research study 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 decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

If I agree to take part in this research study, can I be removed from the study without my consent?

It is possible that you may be removed from the research study by the researchers, for example, for serious noncompliance with the study protocol or failing to continue to meet eligibility criteria (for example, continued substance use). You may be removed from the proposed study if you cannot attend regularly scheduled sessions. You will be removed from the study if you miss a scheduled session and cannot reschedule sessions in accordance with the study protocols. However, every accommodation will be made for you to flexibly reschedule missed sessions. In addition, you may be withdrawn if it is determined that the information provided was incorrect and affected eligibility, e.g., if it is determined that reported medications, medical history, or substance use are inaccurate.

You may also be removed from the study if the research team determines that a different type of care is warranted in order to protect your safety, for instance, if you require treatment outside of study protocols (e.g., medications for compulsions, anxiety or depression) or if the procedures provided in the study are contraindicated.

For how long will the investigators be permitted to use my identifiable information?

The investigators may continue to use and disclose your identifiable information for the purposes described above for an indefinite period of time.

Certificate of Confidentiality

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, see below); 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.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law of abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

USE OF RESEARCH RESULTS:
Results of this study may be presented at scientific conferences and published in the medical or scientific literature. Data from this study, stripped of all identifying information, may be made available to other researchers.

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VOLUNTARY CONSENT:
The above information has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions, voice concerns or complaints about any aspect of this research study during the course of this study, and that such future questions, concerns or complaints will be answered by a qualified individual or by the investigator listed on the first page of this consent document at the telephone number given.

I understand that I may always request that my questions, concerns or complaints be addressed by the listed investigator. I understand that I may contact the Human Subjects Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668) to discuss problems, concerns and questions; obtain information; offer input; or discuss situations that occurred during my participating.

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

_____ _____
Printed Name of Participant Date

_____
Participant's Signature

Optional consent for sharing of contact information with other studies: If you answer affirmative to the question below, your identity may be shared with other researchers at the University of Pittsburgh seeking participants for similar studies focused on compulsive behaviors or related conditions. Your decision to agree to share your identity with other researchers, for research purposes only, will in no way affect your eligibility for the current study, and is completely voluntary. If you consent and are contacted by other research studies in the future, you will be told at that time about the details of the other research and will be able to freely decide at that time whether to participate or not.

Do you consent to have your contact information shared with researchers seeking participants like you for future studies?

___ Yes ___ No
_____initial here

CERTIFICATION OF INFORMED CONSENT:
I certify that I have explained the nature and purpose of this research study to the above-named individual(s), and I have discussed the potential benefits and possible risks of study participation. Any questions the individual(s) have about his 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