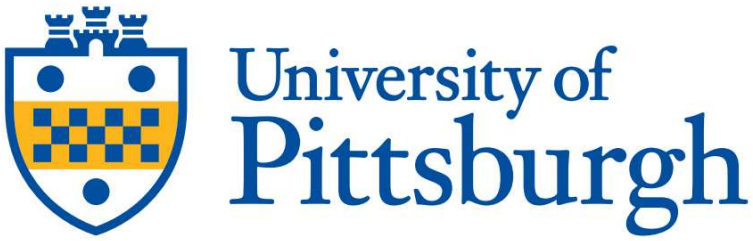

CONSENT TO ACT AS A SUBJECT IN A CLINICAL STUDY

TITLE: AAT + tDCS to reduce cue-induced craving and smoking behavior

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SOURCE OF SUPPORT: National Institute on Drug Abuse

Key Information

- You are being asked to take part in a research study. Research Studies include only people who choose to take part. The study team members will explain the study to you and will answer any questions you might have. You should take your time to make your decision.
- This is a 10-visit study to test interventions to reduce your urge to smoke. The intervention is not a drug. Each session will last between 1-3 hours.
- You will complete questionnaires about your smoking history, identify situations in which you experience an increased urge to smoke, and will take photos of the places where this occurs. You will either:
    - Learn an “Approach/Avoidance Task” or “AAT” which is using different images to help guide you to not smoking and avoid ones that trigger smoking.

      OR

    - Have transcranial direct current stimulation (tDCS). This involves placing two monitor pads on you, one on your head and one on your arm to deliver a low current to your brain.

      OR

    - undergo both of these techniques, while you look at pictures of your smoking situations.

Although tDCS is being studied for several conditions such as depression, anxiety, pain relief, it is not currently approved by the United States Food and Drug Administration (FDA) for this specific purpose, which is why we are testing it. You will also have an electroencephalogram (EEG) which is a test that detects electrical activity in your brain using small, metal monitors (electrodes) attached to your scalp while you are performing a word task on a computer. You will not feel anything from the electrodes during the EEG.

- Risks include feeling uncomfortable answering questionnaires, increased urge to smoke during exposure to photos, and mild skin irritations, brief tingling, warming, or itching during tDCS.
- Aside from being paid for participation, there is no direct benefit to you for participating in this research study; however, you may experience reduction in your urge to smoke in the short or long term, but this is not guaranteed. You may also benefit from gaining coping strategies to deal with situations that trigger your urges to smoke and/or potentially gain cognitive (thoughtful) control over the urge to smoke.

What is the purpose of this research study?

This study is being done to assess whether an Approach/Avoidance task (AAT) and transcranial direct current stimulation (tDCS) can:

- help intervention-seeking smokers with their urges to smoke
- reduce both their response when something triggers them to want to smoke and daily smoking
- increase their intent and confidence to quit.

We will enroll 160 subjects for this study.

What procedures will be performed for research purposes?

If you agree to participate and are eligible, you will be asked to come to our research clinic for ten visits including this visit.

Visit 1	Approx. 2 hours	Consent and initial study form completion	$20
Visit 2	Approx 2 hours	EEG	$50
Visit 3	Approx 1 hour	Picture viewing	$20
Visits 4-8	Approx 45 mins	Training sessions with tDCS device	$20 each visit plus $50 bonus session 4 only
Visit 9	Approx 2 hours	EEG	$50
Visit 10	Approx 1 hour	Picture viewing	$20 + $50 bonus
Follow up call (2)	Approx 5 min	Questionnaires over the phone at 1 week and 1 month	$25

Visit 1 – Screening/Enrollment:

This is today's visit during which we will explain the study and what is expected of you if you decide to participate. Your carbon monoxide (CO) level will be measured by giving a breath sample using our breath CO monitor. If your CO level is below 8 ppm you will not be able to continue with the study and we will pay you for today's visit.

You will then complete the following forms:

- Smoking History: This form will ask questions about you and your smoking history and

will also assess your level of nicotine dependence.

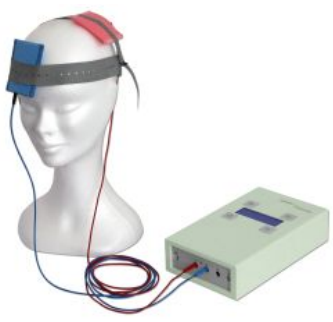
- Quit Interest: This is a questionnaire for evaluating your interest in quitting smoking.
- Intent to Quit: This measures your degree of intention to quit smoking.
- Confidence in Quitting: This questionnaire assesses your confidence in quitting smoking.
- BIDR-IM: This questionnaire lists different statements about you. You'll answer each statement based on how true or not true each statement is about you.

Next, we will identify your personal smoking and non-smoking cues of places. You will go through a brief interview during which we will identify places in which you regularly smoke or do not smoke. We will lend you a camera and teach you how to take pictures before the next visit. You will take pictures of your top 4 places that are 'smoking cues' and 4 places that are 'non-smoking cues' from various angles. **We ask that your pictures don't include people (passers-by or any other friends/family) or personal identifiers (license plates, street names, etc.) to protect privacy.** You will be given specific instructions on the collection of photos and guidelines in a separate document. You will bring the camera containing your pictures back with you to your second session. We will review the pictures at this time to be sure they will work for the study. If there are some pictures that need to be retaken, you will take the camera with you to retake these pictures and return them at the next scheduled session. You will be given specific instructions on the collection of photos and guidelines in a separate document. This allows us to ensure usable pictures and process them before your next visit. You will also complete a brief vision test during this visit. You will stand 10 feet from an eye chart, identify and read out loud the line you can see most comfortably.

- Randomization: You will be randomly assigned to one of four groups, meaning you will be assigned by chance, like the flip of a coin, to one of 4 groups.
    - AAT + tDCS
    - AAT + sham tDCS
    - AC + tDCS
    - AC + sham tDCS

  The components of these groups are defined as:

    - Approach/Avoidance Task (AAT): Pictures will appear on the screen and you will use a joystick to push pictures away from you or pull them in closer to you on the computer screen.
    - Transcranial Direct Current Stimulation (tDCS): is used to slightly change the way the brain works for a short time. One wet, thin sponge is placed on your head and another wet thin sponge is placed on your arm and connected to electrodes which will deliver a very weak electrical



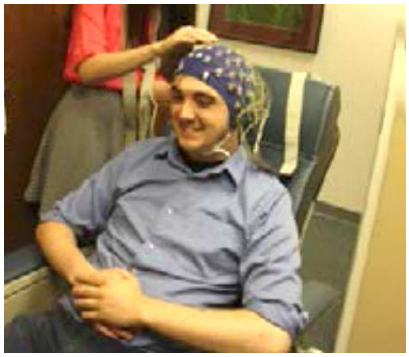
current. Before stimulation, your head and arm will be checked for any redness, irritation, or recent shaving of the head. If any of these are seen, we will exclude you from the study. Some individuals may feel a slight painless tingling as the current begins, but the tingling should go away after a short time. You will be asked at the beginning of and throughout the stimulation to report how much tingling you are feeling on a scale of 1 being "not at all" and 10 being "extreme". If at any point you are experiencing extreme discomfort, we will end the stimulation.

- Active Control (AC): You will determine if a picture presented on the computer screen is portrait (vertical) or landscape (horizontal) and make your selection with a key press on the keyboard.
- Sham tDCS: Two wet, thin sponges are placed one on your head and one on your arm. The sponges will be connected to electrodes which will not deliver any electrical current.

Thus, one group gets both active intervention methods (AAT + tDCS) two groups get either active tDCS or AAT, and one group gets no active intervention (AC + sham tDCS)

Visits 2 and 9: During this visit you will have an attentional bias assessment while undergoing an electroencephalography (EEG).

- Attentional-Bias: You will be seated in front of a computer with a four-button color response box. Four different word lists of 15 words each will be presented in a random order with no repeats. For each trial, a cross appears in the center of the screen followed by one word from the list in one of four colors. You will press the button that matches the color in which the word appears. This test is trying to determine how much you pay attention to certain signals.
- EEG: The EEG allows us to measure electrical activity in your brain. A cap containing sensors will be placed on your head. In addition, sensors will be placed behind your ears, and on the tip of your nose. Gel will be inserted into the cap (approximately 30-40 ml) to connect the sensors to the scalp. There is a slight possibility of a mild skin irritation from the gel. This would be expected to resolve once the gel has been washed completely off. You will not feel any sensations from these electrodes. While wearing the cap, you will complete the attentional bias training. Afterwards, we will clean as much of the gel from your scalp as possible.



- Cue-reactivity: Cue reactivity involves viewing pictures of your personal smoking-related and non-smoking-related pictures and rating how you felt while viewing those pictures.

The pictures and the ratings are presented on a computer and some pictures will be projected on the wall.

Visits 3 and 10: During these visits you will complete cue-reactivity to your personal smoking and non-smoking cues and smoke cigarettes using a special cigarette holder that will measure how you smoke your cigarette. You will be given special instructions on how to light the cigarette and place it into the holder before you smoke. You will be seated comfortably in front of a large computer monitor and view 12 picture trials. Each picture trial will be followed by post-trial ratings. After all the picture trials, a screen will appear informing you that when pictures begin to appear again you may smoke (using the cigarette holder) as much or little as you like, or not smoke at all, it is up to you and watch the pictures. At any point while viewing these pictures you may start or stop smoking.

Visits 4-8: During these visits you will go through cue-reactivity while either doing AAT while receiving tDCS (Group 1), doing AAT while receiving sham tDCS (Group 2), doing AC while receiving tDCS (Group 3), or doing AC while receiving sham tDCS (Group 4). You will not specifically know which group you are in.

Follow-Up: We will call you 1- week after your last visit and then also at 1-month after and ask you how many cigarettes per day you're smoking. We will also ask you the intent and confidence to quit assessments. Those who do not complete the study will not receive follow-up calls and will not be paid for those visits.

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

- Cue Reactivity: No negative effects of cue-reactivity are anticipated. Viewing pictures may increase your craving to smoke, like those cravings you feel when you are unable to smoke in real life. The discomfort of craving is anticipated to dissipate fairly quickly, and over the course of the training may lead to less robust craving.

- tDCS: The risk associated with transcranial electrical stimulation is minimal. There is a small risk of skin irritation which is minimized by using saline water as the conductive medium, and through the monitoring of participant discomfort throughout the procedure. There is a risk that you may have an allergic reaction to latex contained in the electrodes. You will be screened for latex allergy, and individuals with latex allergy will be excluded from the study. Participants with pacemakers or metallic implants in their head should not receive tDCS due to potential heating of the metallic components. You will be screened for metallic implants, and individuals with metallic implants will be excluded from the study. The risks associated with transcranial direct current stimulation (tDCS) are considered minimal or no significant risk. tDCS is seen as a non-invasive medical procedure, and the commonly reported side effects in active vs. sham interventions are itching (39.3% vs 32.9%), tingling (22.2% vs 18.3%), headache (14.8% vs 16.2%), burning sensation (8.7% vs 10%), and discomfort (10.4% vs 13.4%). Redness at the electrode site has also been reported.

- Questionnaires: Some people may find the interview and questionnaires uncomfortable. All interviews and questionnaires will be completed by trained personnel. You will be given breaks as needed and will be reminded that you do not have to answer questions you choose not to and may stop at any time.

- Collection and storage of private information: 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 all electronic records are password and firewall protected. Your identity on these records will be indicated by a case number rather than by your name, although we may use your initials on certain forms. The photo instruction sheet you will be given will explain to you the protections and disposition of the photos you will be taking.

As with any investigational study, there may be adverse events or side effects that are currently unknown, and it is possible that certain of these unknown risks could be permanent, serious or life-threatening.

What are possible benefits from taking part in this study?

There are no direct benefits to you from taking part in the study. You may reduce your cue reactivity to the smoking stimuli you encounter in your daily life and may reduce your daily smoking from the techniques being tested in this study. This would have health benefits in the short and long term, but this cannot be guaranteed. Even if you do not alter your smoking behavior you may benefit from gaining coping strategies to deal with stimuli that trigger smoking and potentially gain cognitive control over stimuli and manage cravings. Likewise, you may increase your intention and confidence to quit following participation in this study.

Will I be told of clinically relevant findings?

The EEG the study team will do is not being done for to diagnose any conditions. However, if the study team notices something of concern on your EEG, Dr. Conklin will discuss with you and refer you to a physician if needed.

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 over the course of the study 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 take part in this study, you will be paid. All participants will be paid up to $410. For each session you will be paid $20.00; however, you will be paid $50 for each of the two EEG visits. At session 4, you will a $50 bonus for taking your pictures and continuing on in the study, in addition to the $20 visit payment. If you attend all 10 study sessions as scheduled, you will receive a completion bonus of $50. If you attend a session as scheduled but are determined to be ineligible at any point, you will still be paid $20.00 for that session, but will be excused from the study and will not be eligible for the study completion bonus. In addition, you will be paid $25 for completing each remote follow-up visit where we will call and ask you questions about your smoking after the study, such as how much you're smoking and your intention to quit and your confidence in quitting. Your payment for these follow-up visits is not dependent upon your answers to our questions. We will add the payment to a UPMC/Pitt reloadable debit called a "Vincent" payment card. You will also be reimbursed for bus fare, if necessary, for your study visits. You will only receive and be paid for follow-up calls if you have completed the study.

Since you are being compensated for your participation in this study, your name, address, and social security number will be released to the Accounting Office. If the total reimbursement for your participation in research is greater than $600 in a year, this will be reported to the Internal Revenue Service (IRS) as income. Individuals who do not provide a social security number may still participate in the research, but the IRS requires that 26% of the payment be sent by the institution to the IRS for 'backup withholding;' thus you would only receive 74% of the expected payment.

Who will know about my participation?

In addition to the Principal Investigator listed on the first page of this consent form and the other investigators involved in this study and the study team, 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 for the purpose of monitoring the appropriate conduct of this research study.

• Authorized representative of the U.S. Food and Drug Administration (FDA), the National Institutes of Health and other regulatory agencies may review and/or obtain your identifiable information related to your participation in this research study for the purpose of monitoring the accuracy of the research data.

Several procedures have been put into place to protect the privacy of your information (see

above). Only members of the research team, staff in the Office of Research Protections will have access to your identifiable information. 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. Further, individuals from the funding agency, NIH, will have access to the study record.

We may share information that does not identify you in any way to other investigators or with research repositories in order to answer new research questions.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally-funded projects or for information that must be disclosed to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities if you or someone with whom you are involved, or a child, is in serious danger or facing potential harm.

Per University of Pittsburgh policy all research records must be maintained for at least 7 years following final reporting or publication of a project.

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.

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

Your participation is completely voluntary and your decision on whether 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. You may withdraw from this research study at

any time. 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 are unable to perform any of the required tasks. You will always be paid for a session you attended prior to being formally withdrawn from the study.

What if I believe I have been injured by participation 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 intervention 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 intervention, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency intervention, 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 give up any of your legal rights by signing this form.

VOLUNTARY CONSENT: All of the above has been explained to me and all of my current questions have been answered. I understand that I am encouraged to ask questions about any aspect of this research study during the course of this study, and that such future questions will be answered by the researchers listed on the first page of this form.

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 this form, I agree to participate in this research study. A blank copy of this consent form will be given to me.

Participant's Signature | Date

Printed Name of Participant

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. 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