Study Protocol

Official Title: tDCS and cognitive training intervention for chronic smokers with schizophrenia (TACTICSS)

ClinicalTrials.gov ID (NCT number): NCT03588728

Protocol Date: 12/12/2018

Scientific Background

Individuals with severe mental illnesses consume 35-44% of all cigarettes in the U.S., well above their representation in the population.[1] This disproportionate level of smoking and limited access to cessation treatment has led to exceptionally high tobacco-related mortality and morbidity rates among smokers with schizophrenia.[2] Of those who attempt cessation, relapse rates are much higher than found in the general population of smokers.[3] Recent literature suggests that this discrepancy may be related to deficits in cognitive processes mediated by the prefrontal cortex (PFC). Specifically, impaired executive function and working memory have been directly linked to cessation failure among smokers with schizophrenia[4,5], and low cognitive control of impulsivity is strongly correlated with time to relapse in the general population.[6,7] Moreover, schizophrenia is associated with persistent cognitive deficits, often linked to abnormal interaction among various brain regions, particularly right inferior frontal gyrus (IFG) and ventral striatum, making it difficult to cope with prepotent stimuli (e.g., smoking-related cues).[4,5] Unfortunately, pharmacologic cessation treatments (e.g., Chantix, Wellbutrin) are only modestly effective in helping smokers with schizophrenia quit.[8–11] To better assist this subset of highly vulnerable smokers achieve abstinence, development of new cessation adjuncts are needed. One promising route is the development of techniques that not only target underlying mechanisms that maintain smoking, but also specifically improve cognitive control.

Cognitive enhancement therapy increases cognitive performance in schizophrenia patients, particularly when working memory, processing speed, executive function, and social cognition are targeted.[12] Standard protocols are intensive, taking 18 months to complete, making standard therapy a sub-optimal candidate for smoking cessation. However, the Cognitive Remediation (CR) component of cognitive enhancement therapy focuses specifically on cognitive training and is less intensive and lengthy. When combined with another cognition enhancement method, namely Transcranial Direct Current Stimulation (tDCS), CR may provide a robust and time efficient method of improving cognitive control among patients with schizophrenia. tDCS studies in our lab and others have demonstrated clear enhancement of attention, working memory, and risk aversion using this technique[13–17]; as well as reductions in craving and amount of smoking. These findings, combined with knowledge of identified cognitive deficits in schizophrenia and the relationship between cognitive function and smoking cessation failure, suggest the potential of CR + tDCS to target cognitive deficits and smoking-related reactivity among smokers with schizophrenia. Specifically, we hypothesize that CR + tDCS will enhance cognitive control, reduce cue-induced craving and attenuate attentional bias (reaction time and ERPs) to smoking stimuli. Further, we will examine if these changes are associated with reductions in actual smoking behavior; and, we will explore the potential of CR + tDCS to increase quit intention and confidence in quitting among smokers with schizophrenia. Our specific aims are as follows:

Study Objectives

Aim 1: Examine the effectiveness of CR + tDCS to improve behavioral and neurophysiological measures of **cognitive control** among smokers with schizophrenia. Using a 2 X 2 factorial design (n=20 per group) we will examine main and interactive effects of CR and tDCS on multiple measures of cognitive control. Hypothesis: Combined CR + tDCS will result in greater improvement in MATRICS measures of cognitive control, as well as continuous performance task (CPT) relative to the other groups (CR + sham tDCS, AC + tDCS, AC + sham tDCS).

Aim 2: Determine the effectiveness of CR + tDCS to attenuate **reactivity to smoking stimuli** among smokers with schizophrenia. Hypothesis: CR + tDCS will lead to greater reductions in cue-induced craving, and improved reaction time and ERP measures of attentional bias relative to the other groups (CR + sham tDCS, AC + tDCS, AC + sham tDCS).

Aim 3: Examine if cognitive control enhancement (Aim 1) and/or changes in reactivity to smoking-related stimuli (Aim 2) predict reductions in measures of **actual smoking behavior**. Hypothesis: Enhanced cognitive control and attenuation of reactivity to smoking stimuli will be directly

related to reductions in smoking topography (i.e., Latency to light, puff volume, and number of puffs) within the CR + tDCS group.

Secondary Aim: To inform future clinical research, we will also explore whether changes in cognitive control and smoking reactivity measures are associated with changes in **quit intention** and **confidence in quitting** from baseline assessment to end of study by training condition.

Study design and methods

Using a 2 x 2 design we examined CR (CR, active control [AC]) X tDCS (active, sham) to enhance cognitive control, reduce cue-induced craving, and attenuate attentional bias measures of reaction time and ERPs to smoking stimuli; and, we determined the impact of these changes on smoking behavior and intent to quit and confidence in quitting among daily smokers with schizophrenia. Participants were assigned to active (2.0 mA) CR + tDCS, CR + sham (0.1 mA) tDCS, active control (AC) + active tDCS, or AC + sham tDCS, each with anode electrode placement over the right inferior frontal gyrus (IFG) and cathode electrode placement over the left bicep. Similar to our previous studies participants received 30 minutes of either active or sham tDCS during each visit, starting at the beginning of the CR training. AC consisted of a self-paced knowledge- and vocabulary-based task in which participants were given sequential multiple-choice questions about factual information at a 6th-grade level. Participants underwent consecutive CR + tDCS sessions, 5 days a week, for 2 weeks. Cognitive control, cue-induced craving and attentional bias (reaction time & ERPs), as well as smoking topography were assessed during Week1 baseline testing and Assessment Week 4.

Procedures and protocol

Eligible participants will be invited to the Clinical Neurophysiology Research Lab for informed consent and further screening, including CO, Smoking and Medical history, PANSS[18], Intention to quit[19], Confidence in quitting,[20] and hearing/vision testing to screen for sensory problems that may affect cognitive and/or EEG testing. After initial screening on Day 1, participants will be randomized. Randomization for the 4 groups will be stratified by current typical or atypical antipsychotic medication to control for the potential interaction of tDCS with medication class. A randomization assignment list will be generated for each category using a permuted 4 block design. Dropouts will be replaced. Participants will then be scheduled for two baseline testing sessions, completed the same week as initial screening. The first will utilize the MATRICS Clinical Consensus Battery (MCCB) for baseline testing of cognitive measures. Participants will perform form A of the MCCB at baseline, which includes composite scores for attention, processing speed, working memory, and reasoning/problem solving. Participants will also complete behavioral tests of cognitive control, cue reactivity and attentional bias during this visit. Participants will then complete a baseline EEG testing session on a separate visit in the same week. Electrophysiological measures of cognitive control will be examined using the 'AX'-type Continuous Performance Task (AX-CPT)[21,22]. Cue-induced craving and smoking topography will be assessed with a pictorial cue reactivity paradigm,[23] and attentional bias will be measured using a modified stroop task.[24] Following baseline testing (Week1), participants will return 5 days (M-F) for the next 2 weeks for cognitive training with CR / tDCS and will receive the same tDCS condition in each visit. In week 4, participants will perform follow-up testing using form B of the MCCB, behavioral tests of cognitive control, cue-reactivity, and attentional bias on the first day, and EEG testing on the second.

Interventions.

Cognitive Remediation (CR). CR incorporates a subset of components from Cognitive Enhancement Therapy found to have early benefits on the cognitive deficits of particular interest to the proposed studies and can be conducted more time-efficiently to achieve our specific goals. This abbreviated CR involves 20 hours of neurocognitive training using attention and processing speed training software developed by Ben-Yishay and colleagues.[25] Deficits in Attention are addressed with exercises used to enhance vigilance and rapid decision making, inhibit irrelevant stimuli, and shift attention between auditory and visual modalities. These exercises facilitate reaction time in a temporal mode using auditory cues (The Attention Reaction Conditioner), spatial focusing with visual cues (the

Zero Accuracy Conditioner), and temporal vigilance with auditory and visual cues (Time Estimates). Our experience with over 200 patients with schizophrenia reveals that they successfully progress through these training exercises over the 20 hours of training. For the active control (AC) condition, participants will complete a self-paced knowledge- and vocabulary-based task of the same duration as CR to equate time spent on task, while omitting the cognitive control training aspect that is central to CR.

Transcranial Direct Current Stimulation (tDCS). tDCS is a low-cost, portable method that is well-tolerated by participants. The polarity of the current and the location of stimulating electrodes is an important factor that influences its effects on neural activity, with positive polarization (anodal) at the scalp inducing excitation of the underlying cortex, and negative polarization (cathodal) at the scalp resulting in the opposite effect.[26–28] Functionally, cathodal tDCS suppresses while anodal stimulation facilitates cortical excitability.[29] Modeling studies suggest that layer IV and V pyramidal cells are most affected by tDCS.[30] In PFC, these cells receive direct and indirect regulatory signals from the striatal dopaminergic system, and striatal modulation of prefrontal pyramidal cells has been linked to cognitive control.[31] We believe right inferior frontal gyrus to be the prime candidate for cognitive control enhancement with tDCS, given recent published results showing that greater activation in the right IFG during a standard Stroop task, but not striatum, was associated with greater reduction in cotinine levels.[32,33] Participants across the 4 conditions will be assigned to a group involving either active (2.0 mA) or sham (0.1 mA) tDCS, with anode electrode placement over the right IFG and cathode electrode placement over the left bicep. tDCS will be administered the first thirty minutes of each of the 10 2-hour CR sessions. During tDCS, patients will be monitored for possible negative side effects.

Measures.

Cognitive Control:

MATRICS Clinical Consensus Battery (MCCB). An abbreviated MCCB will be completed before and after CR + tDCS. Subscales include: *Attention:* The Continuous Performance Test (CPT), the Continuous Performance Test—Identical Pairs (CPT-IP), and the A-X Continuous Performance Test (AX-CPT). *Working memory:* N-Back digit sequencing from the BACS, Spatial span from the Wechsler Memory Scale, 3rd ed. (WMS-III), Letter-number sequencing from the WAIS-III, Spatial delayed response task. *Reasoning/problem solving*: Block design from the WAIS-III, Tower of London from the BACS, Mazes and Categories from the Neuropsychological Assessment Battery, Penn Conditional Exclusion Test, Sorting test from the Delis-Kaplan Executive Functioning Scale. To reduce practice effects, two forms are available for most measures.

The Continuous Performance Test (CPT) is a go/no-go task requiring continuously responding to frequent stimuli, and witholding response to a rare target stimulus. EEG will be recorded this task. The AX-CPT also requires maintaining stimulus items in temporary memory store (respond to the letter 'X' only when it follows the letter 'A'). The AX-CPT can measure *proactive cognitive control* of response inhibition. Additionally, a negative ERP, a contingent negative variation (CNV), and a reduction in beta-band oscilations compared to baseline (event-related desynchronization (ERD)), occur between the alerting stimulus ("A") and target stimulus ("X"). Both are blunted in schizophrenia patients[34] and this proactive control deficit may be part of problematic cognitive coordination in schizophrenia[35].

Smoking-related reactivity.

Attentional Bias (Reaction time and ERPs) Participants will be seated in front of a computer with a four-button color response box. Four-word lists (two neutral and two smoking-related) of 15 words each, will be presented in a random order with no repeat. For each trial, a cross appears in the center of the screen for 500ms followed by one word from the list in one of the four colors. Participants respond by pressing the color button that matches the color in which the word appears. Reaction time to respond to each word is recorded within the nearest ms. These procedures are similar to those used

in a past modified-stroop test with smokers.[24] We will also examine EEG correlates of smoking reactivity. In past studies, smokers have increased electrophysiological responses to smoking compared to neutral images, such that their N200 and P300 ERPs are larger in response to smoking stimuli. We will assess this response before and after CR + tDCS to examine neural correlates of attentional bias related to increased N200 and P300 in smokers.

Cue-Induced craving and smoking topography. Participants' reactivity to smoking-related cues will also be assessed at Baseline and Week 4 Assessments. To equate time to last cigarette, participants will light a cigarette and smoke as much or as little as they like prior to each the testing session. Cue reactivity testing is computer automated. Following a practice trial, the participant will be viewed by the experimenter on a monitor outside of the subject room to verify compliance with instructions (sit back, focus on pictures, and fill out ratings), which appear on the screen. Four angles of each pictorial cue will be presented for 4 smoking and 4 nonsmoking picture trials with self-report ratings in between. Each cue trial will end with a computer prompt for subjects to complete post-trial craving ratings on a 0-100 scale (4-item Questionnaire on Smoking Urges)[36] After the ratings are filled out for the last cue-reactivity trial, a screen will appear informing subjects that when the pictures return they may smoke as much or as little as they like. They will then complete a 10-minute ad lib smoking / cue-viewing period during which all smoking will occur through a CReSS cigarette holder, allowing for topographical assessment of latency to light, puff volume, and number of puffs.

Eligibility Criteria

Inclusion Criteria:

1. Between the ages of 18 & 65.
2. Currently meets DSM-5 criteria for Schizophrenia, Schizoaffective Disorder, Schizophreniform Disorder, or Delusional Disorder.
3. Ability to provide written informed consent
4. Smoke ≥ 7 cigarettes per day
5. Expired breath CO ≥ 10 ppm at screening
6. Stable medication regimen for ≥ 4 weeks (If on more than one psychotropic medication, main antipsychotic will be considered for stability)

Exclusion Criteria:

1. Epilepsy or Current Seizure Disorder
2. Alcohol or Substance Dependence past 3 months (caffeine allowed, nicotine is part of inclusion criteria).
3. Pregnant or lactating
4. Psychiatric hospitalization in past 3 months
5. Suicidal and/or aggressive behavior past 3 months
6. Implanted cardiac or brain medical devices

Data Analysis

Prior to hypothesis testing, descriptive statistics and graphic displays will identify outliers and missing data and guide the use of transformations and appropriate tests. Correlation and principal component analysis will identify any outcomes reflecting the same underlying construct, and representative measures will be selected if necessary. We will use 2x2 ANOVA to assess the effects of tDCS (vs sham) and CR (vs AC) on pre-post change scores for all dependent variables. Should baseline differences be identified, post-training scores will be used as dependent variables, and baseline (pre-training) scores will be included as covariates in the analysis.

References

1. Lasser K, Boyd J, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *JAMA*. 2000;284(20):2606-2610. doi:10.1001/jama.284.20.2606

2. Williams JM, Steinberg ML, Griffiths KG, Cooperman N. Smokers With Behavioral Health Comorbidity Should Be Designated a Tobacco Use Disparity Group. *Am J Public Health*. 2013;103(9):1549-1555. doi:10.2105/AJPH.2013.301232

3. Evins AE. Nicotine dependence in schizophrenia: prevalence, mechanisms, and implications for treatment. *Psychiatr Times*. 2008;25(3):55-55.

4. Tidey JW, Rohsenow DJ, Kaplan GB, Swift RM. Subjective and Physiological Responses to Smoking Cues in Smokers with Schizophrenia. *Nicotine Tob Res*. 2005;7(3):421-429. doi:10.1080/14622200500125724

5. AhnAllen CG, Tidey JW. Personalized smoking environment cue reactivity in smokers with schizophrenia and controls: A pilot study. *Psychiatry Res*. 2011;188(2):286–288.

6. Mitchell SH. Measures of impulsivity in cigarette smokers and non-smokers. *Psychopharmacology (Berl)*. 1999;146(4):455-464. doi:10.1007/PL00005491

7. Sheffer C, MacKillop J, McGeary J, et al. Delay Discounting, Locus of Control, and Cognitive Impulsiveness Independently Predict Tobacco Dependence Treatment Outcomes in a Highly Dependent, Lower Socioeconomic Group of Smokers. *Am J Addict*. 2012;21(3):221-232. doi:10.1111/j.1521-0391.2012.00224.x

8. Evins AE, Cather C, Deckersbach T, et al. A double-blind placebo-controlled trial of bupropion sustained-release for smoking cessation in schizophrenia. *J Clin Psychopharmacol*. 2005;25(3):218-225.

9. Ziedonis D, Hitsman B, Beckham JC, et al. Tobacco use and cessation in psychiatric disorders: National Institute of Mental Health report. *Nicotine Tob Res*. 2008;10(12):1691–1715.

10. George TP, Ziedonis DM, Feingold A, et al. Nicotine Transdermal Patch and Atypical Antipsychotic Medications for Smoking Cessation in Schizophrenia. *Am J Psychiatry*. 2000;157(11):1835-1842. doi:10.1176/appi.ajp.157.11.1835

11. George TP, Vessicchio JC, Termine A, et al. A placebo controlled trial of bupropion for smoking cessation in schizophrenia. *Biol Psychiatry*. 2002;52(1):53–61.

12. Hogarty GE, Flesher S, Ulrich R, et al. Cognitive enhancement therapy for schizophrenia: Effects of a 2-year randomized trial on cognition and behavior. *Arch Gen Psychiatry*. 2004;61(9):866-876. doi:10.1001/archpsyc.61.9.866

13. Coffman BA, Trumbo MC, Clark VP. Enhancement of object detection with transcranial direct current stimulation is associated with increased attention. *BMC Neurosci*. 2012;13:108. doi:10.1186/1471-2202-13-108

14. Clark VP, Coffman BA, Mayer AR, et al. TDCS guided using fMRI significantly accelerates learning to identify concealed objects. *NeuroImage*. 2012;59(1):117-128. doi:10.1016/j.neuroimage.2010.11.036

15. Marshall L, Mölle M, Hallschmid M, Born J. Transcranial Direct Current Stimulation during Sleep Improves Declarative Memory. *J Neurosci*. 2004;24(44):9985-9992. doi:10.1523/JNEUROSCI.2725-04.2004

16. Fecteau S, Knoch D, Fregni F, Sultani N, Boggio P, Pascual-Leone A. Diminishing Risk-Taking Behavior by Modulating Activity in the Prefrontal Cortex: A Direct Current Stimulation Study. *J Neurosci*. 2007;27(46):12500-12505. doi:10.1523/JNEUROSCI.3283-07.2007

17. Fecteau S, Pascual-Leone A, Zald DH, et al. Activation of Prefrontal Cortex by Transcranial Direct Current Stimulation Reduces Appetite for Risk during Ambiguous Decision Making. *J Neurosci*. 2007;27(23):6212-6218. doi:10.1523/JNEUROSCI.0314-07.2007

18. Kay SR, Flszbein A, Opfer LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13(2):261.

19. DiClemente CC, Prochaska JO, Fairhurst SK, Velicer WF, Velasquez MM, Rossi JS. The process of smoking cessation: an analysis of precontemplation, contemplation, and preparation stages of change. *J Consult Clin Psychol*. 1991;59(2):295.

20. Gwaltney CJ, Metrik J, Kahler CW, Shiffman S. Self-efficacy and smoking cessation: a meta-analysis. *Psychol Addict Behav J Soc Psychol Addict Behav*. 2009;23(1):56-66. doi:10.1037/a0013529

21. Barch DM, Braver TS, Nystrom L, Noll DC, Cohen JD. Activation of prefronal cortex by the representation and maintainance of context information. *Schizophr Res*. 1997;24(1):163–163.

22. Carter CS, Braver TS, Barch DM, Botvinick MM, Noll D, Cohen JD. Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science*. 1998;280(5364):747–749.

23. Conklin CA, Vella EJ, Joyce CJ, Salkeld RP, Perkins KA, Parzynski CS. Examining the relationship between cue-induced craving and actual smoking. *Exp Clin Psychopharmacol*. 2015;23(2):90.

24. Drobes DJ, Elibero A, Evans DE. Attentional bias for smoking and affective stimuli: a Stroop task study. *Psychol Addict Behav*. 2006;20(4):490.

25. Ben-Yishay Y, Piasetsky EB, Rattok J. A systematic method for ameliorating disorders in basic attention. Published online 1987. Accessed July 11, 2016. http://psycnet.apa.org/psycinfo/1987-97860-008

26. Bindman LJ, Lippold OCJ, Redfearn JWT. The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. *J Physiol*. 1964;172(3):369.

27. Landau WM, Bishop GH, Clare MH. Analysis of the form and distribution of evoked cortical potentials under the influence of polarizing currents. *J Neurophysiol*. 1964;27(5):788–813.

28. Purpura DP, McMurtry JG. Intracellular activities and evoked potential changes during polarization of motor cortex. *J Neurophysiol*. 1965;28(1):166–185.

29. Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol*. 2000;527(3):633–639.

30. Radman T, Ramos RL, Brumberg JC, Bikson M. Role of cortical cell type and morphology in subthreshold and suprathreshold uniform electric field stimulation in vitro. *Brain Stimulat*. 2009;2(4):215–228.

31. Goldman-Rakic PS. Regional and cellular fractionation of working memory. *Proc Natl Acad Sci*. 1996;93(24):13473–13480.

32. Brewer JA, Worhunsky PD, Carroll KM, Rounsaville BJ, Potenza MN. Pretreatment brain activation during stroop task is associated with outcomes in cocaine-dependent patients. *Biol Psychiatry*. 2008;64(11):998–1004.

33. Krishnan-Sarin S, Balodis IM, Kober H, et al. An exploratory pilot study of the relationship between neural correlates of cognitive control and reduction in cigarette use among treatment-seeking adolescent smokers. *Psychol Addict Behav*. 2013;27(2):526.

34. Dias EC, Bickel S, Epstein ML, Sehatpour P, Javitt DC. Abnormal task modulation of oscillatory neural activity in schizophrenia. Published online 2013. Accessed January 6, 2017. https://books.google.com/books?hl=en&lr=&id=7QB7CgAAQBAJ&oi=fnd&pg=PA209&dq=Dias,+E.+C.,+Bickel,+S.,+Epstein,+M.+L.,+Sehatpour,+P.,+%26+Javitt,+D.+C.+&ots=21GJdfR-j8&sig=C0lJ95oZ2mCoe-gQfcdgCmJLot8

35. Phillips W, Silverstein S. Convergence of biological and psychological perspectives on cognitive coordination in schizophrenia. *Behav Brain Sci*. 2002;26(1). Accessed January 6, 2017. http://clin-eeglab.narod.ru/mmn/BBSCommentary.pdf

36. Carter BL, Tiffany ST. The cue-availability paradigm: the effects of cigarette availability on cue reactivity in smokers. *Exp Clin Psychopharmacol*. 2001;9(2):183-190.

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Cynthia Conklin,

From: Jamie Zelazny, PhD, Vice Chair

Date: 12/13/2018

IRB#: REN18110090 / PRO17080543

Subject: tDCS and cognitive training intervention for chronic smokers with schizophrenia (TACTICSS)

The Renewal for the above referenced research study was reviewed and approved by the Institutional Review Board, Committee G , which met on 12/12/2018.

Please note the following information:

The risk level designation is Greater Than Minimal.

Approval Date: 12/12/2018
Expiration Date: 12/11/2019

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least **one month** prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center),

FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

3500 Fifth Avenue
Ground Level
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

University of Pittsburgh
Institutional Review Board

Memorandum

To: Cynthia Conklin

From: IRB Office

Date: 6/14/2018

IRB#: MOD17080543-02 / PRO17080543

Subject: tDCS and cognitive training intervention for chronic smokers with schizophrenia (TACTICSS)

The University of Pittsburgh Institutional Review Board reviewed and approved the requested modifications by expedited review procedure authorized under 45 CFR 46.110 and 21 CFR 56.110.

Modification Approval Date: 6/14/2018
Expiration Date: 1/30/2019

The following documents were approved by the IRB:
TACTICSS

For studies being conducted in UPMC facilities, no clinical activities that are impacted by the modifications can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.

University of Pittsburgh
Institutional Review Board

3500 Fifth Avenue
Pittsburgh, PA 15213
(412) 383-1480
(412) 383-1508 (fax)
http://www.irb.pitt.edu

Memorandum

To: Cynthia Conklin, PhD

From: Margaret Hsieh, MD, Vice Chair

Date: 2/20/2018

IRB#: PRO17080543

Subject: tDCS and cognitive training intervention for chronic smokers with schizophrenia (TACTICSS)

At its full board meeting on 1/31/2018, the University of Pittsburgh Institutional Review Board, Committee H, reviewed the above referenced research study and approved it pending minor modifications. Your responses to these comments have been reviewed and the research submission, in its currently modified form, adequately addresses the concerns of the IRB and is therefore approved.

Please note the following information:

The risk level designation is Greater Than Minimal Risk.

This study is supported by the following federal grant application:
R21DA045137 Cognitive remediation and transcranial direct current stimulation to aid smokers with schizophrenia

The IRB has approved the waiver for the requirement to obtain a written informed consent for a screening interview.

The IRB has approved the waiver for the requirement to obtain informed consent to use protected health information to identify potential research subjects.

The IRB has approved the advertisement that was submitted for review as written. As a reminder, any changes to the advertisement other than to edit contact information requires IRB approval prior to distribution.

Approval Date: 2/16/2018
Expiration Date: 1/30/2019

For studies being conducted in UPMC facilities, no clinical activities can be undertaken by investigators until they have received approval from the UPMC Fiscal Review Office.

Please note that it is the investigator's responsibility to report to the IRB any unanticipated problems involving risks to subjects or others [see 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)]. Refer to the IRB Policy and Procedure Manual regarding the reporting requirements for unanticipated problems which include, but are not limited to, adverse events. If you have any questions about this process, please contact the Adverse Events Coordinator at 412-383-1480.

The protocol and consent forms, along with a brief progress report must be resubmitted at least one month prior to the renewal date noted above as required by FWA00006790 (University of Pittsburgh), FWA00006735 (University of Pittsburgh Medical Center), FWA00000600 (Children's Hospital of Pittsburgh), FWA00003567 (Magee-Womens Health Corporation), FWA00003338 (University of Pittsburgh Medical Center Cancer Institute).

Please be advised that your research study may be audited periodically by the University of Pittsburgh Research Conduct and Compliance Office.