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Transcranial Direct Current Stimulation Therapy for Central Hypersomnia Without Cataplexy

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Title: Transcranial Direct Current Stimulation Therapy for Central Hypersomnia Without Cataplexy

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Not applicable

IDE: non-significant risk (NSR) investigational device that meets the abbreviated Investigational Device Exemptions (IDE) requirements at 21 CFR 812.2(b)

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I. Objectives

1) To determine the effects of transcranial direct current stimulation (tDCS) on vigilance in subjects with central hypersomnia without cataplexy.
2) To determine the effects of tDCS on subjective measures of sleepiness and alertness in subjects with central hypersomnia without cataplexy.

The objectives of this study are to determine if active tDCS treatment in patients with central disorders of hypersomnolence will improve vigilance and subjective measures of sleepiness and alertness as compared to sham tDCS stimulation.

The risks associated with this study are minimal compared to the potential benefits. Knowledge about the effects of tDCS on vigilance and subjective sleepiness would be an important advance in the care of these patients.

II. Background and Rationale

Central disorders of hypersomnolence are conditions that are characterized by excessive daytime sleepiness as well as deficits in daytime attention despite adequate quantity of nocturnal sleep. It includes patients with narcolepsy type 1(with cataplexy), narcolepsy type 2 (without cataplexy), idiopathic hypersomnia, Kleine-Levin syndrome, and hypersomnia due to medication, medical or psychiatric disorders.[2]

While there are medications approved by the Food and Drug Administration (FDA) for patients with narcolepsy and in adequately treated obstructive sleep apnea (OSA) with residual hypersomnia, there is no FDA-approved therapy for the other central disorders of hypersomnolence. Current treatments being utilized include the off-label use of stimulant medications that promote wakefulness.[3] However, these medications are limited by side effects. Therefore, there is a need to develop non-pharmacologic treatment strategies for central disorders of hypersomnolence.

Multiple recent studies have used transcranial direct current stimulation (tDCS) as a novel therapy for central nervous system disorders including depression, anxiety, Parkinson's disease, and chronic pain.[4-7] tDCS is a form of noninvasive, painless, brain stimulation that uses a mild direct electrical current passed between electrodes on the scalp to modify neuronal membrane resting potential in a polarity dependent manner, elevating or lowering neuron excitability in a region.[1] It has several advantages over other brain stimulation techniques because it is noninvasive, painless and safe. It is also easy to administer and the equipment is easily portable. The most common side effect of tDCS is a slight itching or tingling on the scalp.[8] Importantly, no studies thus far have provided evidence that tDCS produces more than a minimal risk.[9] **An updated review that consolidated evidence on the safety of tDCS found that to date, the use of conventional tDCS protocols in human trials (≤40 min, ≤4 milliamperes, ≤7.2 Coulombs) has not produced any reports of a Serious Adverse Effect or irreversible injury across over 33,200 sessions and 1000 subjects with repeated sessions. This review included a wide variety of subjects, including persons from potentially vulnerable populations.[9]** In addition, several studies have shown that tDCS can be used safely in the home environment.[10-14]

Thus, tDCS is a non-significant risk (NSR) investigational device that meets the abbreviated Investigational Device Exemptions (IDE) requirements at 21 CFR 812.2(b) addressing labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion for an NSR device study.

Studies using tDCS have demonstrated improvements in vigilance and cognitive function under conditions of sleep deprivation and in a case of a patient with organic hypersomnia.[1,8,15] These studies, suggest potential benefit in central disorders of hypersomnolence. Our hypothesis is that patients with central disorders of hypersomnolence will demonstrate improvements in vigilance as a primary outcome after receiving active stimulation as compared to control (sham) stimulation.

III. Procedures

A. Research Design

This is a randomized, sham-controlled, parallel group study.

Subjects: Adult subjects aged 18-70 years with a clinical diagnosis of any of the following:

- Idiopathic Hypersomnia or Narcolepsy without Cataplexy (Narcolepsy Type 2). Idiopathic hypersomnia and narcolepsy without cataplexy are usually objectively differentiated based on the number of sleep onset rapid eye movement periods (SOREMP) during a multiple sleep latency test (MSLT). However, this diagnostic feature has been shown to be not stable over time making it difficult for clinicians to distinguish these two conditions.[16,17]
- Hypersomnia in OSA patients adequately treated with positive airway pressure (PAP) therapy or dental device
- Posttraumatic hypersomnia
- Unspecified hypersomnia

Patients with Narcolepsy with Cataplexy will be excluded from this study in view of the specific known loss of hypocretin in these patients.

Informed consent will be obtained from all participants. If the subject is agreeable, the consent form will be sent to them via mail or electronically so that they will have the opportunity to read the document ahead of time.

B. Subject Selection:

1. Inclusion/Exclusion Criteria

A. Key Inclusion Criteria

- Age 18 - 70 years
- Epworth Sleepiness scale score >10
- Stable medication dosage over previous 4 weeks
- Able to understand English and read and write at the 8th grade level and give a written informed consent document.
- Stable sleep/wake schedule (that is, no rotating shift work)
- Clinical diagnosis of any of the following:
    a. Idiopathic Hypersomnia
    b. Narcolepsy without Cataplexy
    c. Hypersomnia in OSA patients adequately treated with PAP therapy or dental device

d. Posttraumatic hypersomnia
e. Hypersomnia, unspecified

- Multiple sleep latency test (MSLT) shows fewer than two sleep onset REM periods (except for patients with Narcolepsy without cataplexy, a diagnosis that requires at least two sleep onset REM periods) and a mean sleep latency of ≤ 8 minutes. An MSLT is not required for inclusion of OSA patients provided their Epworth Sleepiness Scale (ESS) score is >10. Adequately treated OSA patients will be defined as: i) an average PAP usage of ≥ 4 hours per night and a residual apnea-hypopnea index (AHI) of <10/hour based on PAP machine download during at least a 30-day period, or ii) regular use of dental device during sleep based on self-report and a prior sleep study showing an AHI <10/hour while using the dental device.

- Subjects with idiopathic hypersomnia with an MSLT mean sleep latency of > 8 minutes will be included provided they have hypersomnia symptoms and habitually long sleep times (average of ≥10 hours per day) documented by actigraphy for at least 7 days.[18]

- Subjects currently on stimulant medications who upon discussion with their sleep medicine provider, are either scheduled to be on a medication holiday or are willing to discontinue their stimulants for at least one week before study enrolment, will be eligible for the study. Eligibility will be determined via a clinician note in the medical record stating the above plan.

B. Key Exclusion Criteria

- Self-reported habitual sleep period of < 7 hours/night
- History of automobile accident due to falling asleep while driving within the past 2 years
- Currently taking stimulant medications such as Modafinil, Armodafinil, Methylphenidate, or Dextroamphetamine.
- Inability to understand or read English
- Clear history of cataplexy
- Moderate or severe sleep apnea defined as an apnea-hypopnea index (AHI) of ≥ 15/hour based on a previous sleep study and non-compliant with treatment.
- Self-reported Substance abuse (current)
- Excessive alcohol consumption defined as:
    - More than 3 glasses of wine a day
    - More than 3 beers a day
    - More than 60 mL of hard liquor a day
- Presence of cardiac pacemaker or automatic implantable cardioverter-defibrillator (AICD).
- Pregnancy, lactation (will be screened with urine pregnancy test)
- Recent hospitalization for major surgery/major illness (within past 1 month)
- Non-removable metal or tattoos around head
- Use of implantable birth control device such as Implanon
- History of severe and frequent headaches
- Unstable coronary artery disease
- Uncontrolled Seizure disorder

- Uncontrolled hypertension
- Uncontrolled Congestive heart failure
- Anything that, in the opinion of the investigators, would place the subject at increased risk or preclude a participant's full compliance in completing the study

2. Vulnerable Populations

- Children, fetuses, neonates, or prisoners are not included in this research study.

3. Populations vulnerable to undue influence or coercion

Should an OSU employee or student (or their surrogate) be approached for enrollment, they will be given the opportunity and time to consider participation and will be reassured that declining to participate will not jeopardize or hinder their standard of care at the OSU Wexner Medical Center, nor will it have any bearing on either their student status or employment.

4. Inclusion of Women and Minorities

Both men and women of all races and ethnic groups are eligible for this study.

C. Study Plan

This is a randomized, sham-controlled, parallel group study. The study will last up to 5 weeks. After informed consent, subjects with idiopathic hypersomnia with an MSLT mean sleep latency of >8 minutes will undergo actigraphy and those with an average sleep time of ≥10 hours per day will continue with the study while those with <10 hours sleep time will be excluded. In addition, OSA subjects with complaints of hypersomnia with an ESS score <10 will also be excluded. Female subjects of child bearing age and not menopausal will have a pregnancy test performed as pregnancy is an exclusionary criteria.

Subjects will be randomized to receive either active tDCS or sham stimulation for 30 minutes daily for 4 sessions. The randomization scheme will be generated in permuted blocks of varying size. The randomization scheme will be prepared, uploaded, and overseen by the study's biostatistician. Investigators and research staff, other than the biostatistician, will not have access to the full randomization scheme. Randomization assignments will be delivered via RedCap.

Subjects will be blinded as to whether they are receiving sham or active tDCS treatments. The investigator who will conduct the analysis of all outcomes will be blinded as to subject treatment assignment.

All stimulation visits will be completed within a five-consecutive day period; that is one stimulation visit may be missed provided a total of four stimulation visits are completed within a five-day period. Outcome measures will include: psychomotor vigilance test (PVT), subjective measures of sleepiness, and the Center for Epidemiologic Studies Depression (CES-D) scale. PVT will be performed pre- and post- stimulation during the first and last stimulation sessions. Subjective measures of sleepiness include the following: Epworth Sleepiness Scale (ESS), Stanford Sleepiness Scale (SSS), Functional Outcomes of Sleep Questionnaire-10 (FOSQ-10), and Visual Analogue Scale (VAS).

Subjects who qualify for the study will receive up to $300 compensation for participating in the study. They will receive $75 for each study visit which will be provided in the form of a check at

the end of Visit 2 and Visit 4. The 4 study visits must be completed within the five-consecutive day period.

Visit Schedule

1) **Visit 1**

During this visit, the following will be obtained for all subjects **prior** to sham or active tDCS:

a. Informed consent (if not obtained on a prior separate visit)
b. Medical History
c. Pregnancy test, if applicable
d. Medication list
e. Height and weight
f. Resting blood pressure and pulse rate
g. Sleep study report
h. Psychomotor Vigilance Test (PVT)
i. Cognitive Tasks results
j. Responses to questionnaires (ESS, SSS, FOSQ-10, VAS, CES-D, side effects)

They will then receive either sham or active tDCS for 30 mins after randomization. PVT and side effects questionnaire will be repeated **during** the sham or active tDCS

k. VAS/Side effects Questionnaire **after** the sham or stimulation.
l. Actigraphy. Subjects will be provided instructions on how to wear an actigraph device around their wrist that measures both the rest-activity cycle. A sleep diary will also be provided.
m. Expected visit length: 90 minutes

2) **Visit 2**

During this visit, the following will be obtained for all subjects:

a. Resting blood pressure and pulse rate
b. Changes to Medication
c. Side effects questionnaire

They will then receive either sham or active tDCS for 30 mins after randomization. PVT/side effects questionnaire **during** the sham or active tDCS

d. Side effects questionnaire **after** the sham or active tDCS
e. Expected visit length: 60 minutes

3) **Visit 3**

During this visit, the following will be obtained for all subjects:

a. Resting blood pressure and pulse rate
b. Changes to Medication
c. Side effects questionnaire

They will then receive either sham or active tDCS for 30 mins after randomization. PVT/side effects questionnaire **during** the sham or active tDCS

d. Side effects questionnaire **after** the sham or active tDCS
e. Expected visit length: 60 minutes

4) Visit 4

During this visit, the following will be obtained for all subjects **prior** to sham or active tDCS:

a. Return actigraph device
b. Resting blood pressure and pulse rate
c. Changes to Medication
d. Psychomotor Vigilance Test (PVT)/VAS results/side effects questionnaire

They will then receive either sham or active tDCS for 30 mins after randomization. PVT/side effects questionnaire will be repeated **during** the sham or active tDCS

e. The following will be obtained **after** the sham or active tDCS
   i. PVT
   ii. Cognitive Tasks results
   iii. Responses to questionnaires (ESS, SSS, VAS, FOSQ-10, CES-D)
   iv. Side effects Questionnaire

f. Expected visit length: 90 minutes

Visit Schedule

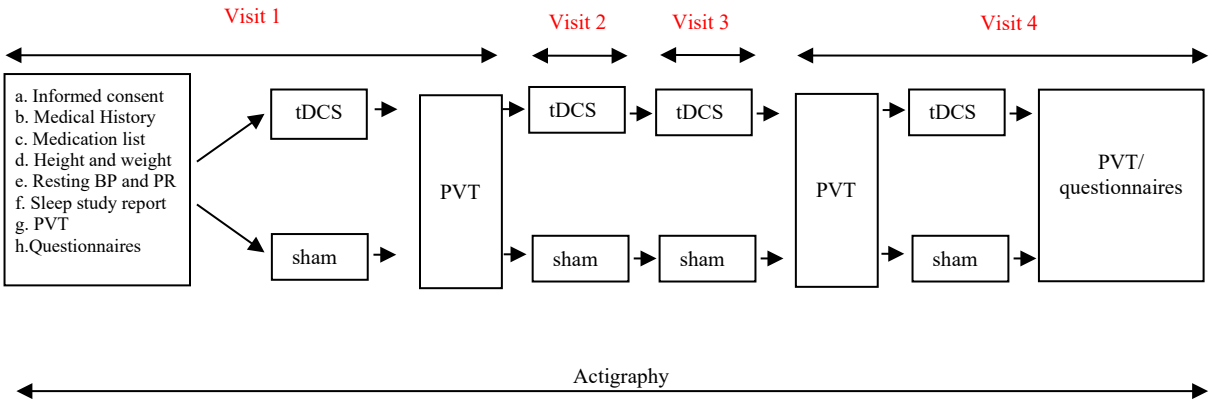
PROCEDURES	Clinical Care	Visit 1	Visit 2	Visit 3	Visit 4
Consent		•			
Sleep study*	•				
Medical History		•			
Pregnancy test, if applicable		•			
Medication List		•	•	•	•
BP and Pulse rate		•	•	•	•
Height and weight		•			
Questionnaires**		•			•
PVT/Cognitive Tasks***		•	•	•	•
tDCS (sham or active)		•	•	•	•
Actigraphy		•	•	•	•

* Sleep study is completed per standard clinical care.

** Done prior to stimulation during visit 1 and after stimulation during visit 4

*** Done prior to and after stimulation during visits 1 and 4

Study Schema



D. Detailed Procedures

1. Sleep study (is part of clinical care):

Subjects will undergo standard polysomnography and MSLT according to the evaluation of their physician. Each 30-second epoch will be analyzed for the number of apneas, hypopneas, arousals, and oxyhemoglobin desaturation.[19] Apnea will be defined as the absence of airflow for at least 10 seconds. Hypopnea will be defined as at least a 30% reduction in airflow lasting at least 10 seconds associated with at least a 4% decrease in arterial oxyhemoglobin saturation. Apneas and hypopneas will be classified as obstructive if respiratory effort was present, and central if respiratory effort was absent during the event. Sleep staging of the PSG and MSLT will follow standard scoring procedures.

2. Medication List

For all subjects we will obtain information about their medications or any changes to their medications.

3. Height and Weight

Weight and height measurements (to calculate BMI) will be done without shoes.

4. Blood Pressure

The standard operating procedure for obtaining sitting blood pressure will be followed.[20]

Medical Alert Procedure. Subjects in these protocols may be identified to have clinical abnormalities that require medical attention. Research staff would notify Dr. Magalang or a physician co-investigator immediately for Systolic BP >200 mmHg or diastolic BP >120 mmHg.

5. Questionnaires

The following questionnaires will be completed by the subjects:

1) Epworth Sleepiness Scale (ESS)

2) Stanford Sleepiness Scale (SSS)
3) Functional Outcomes of Sleep Questionnaire (FOSQ-10)
4) Visual Analogue Scale (VAS)
5) Center for Epidemiologic Studies Depression Scale (CES-D)
6) Side Effects

6. Actigraphy

This device is the size of a small wristwatch that measures activity and is a non-invasive method of monitoring human rest/activity cycle. The instructions for the device use as well as a sleep diary will be provided. The data is then downloaded into a computer.

7. Psychomotor Vigilance Test (PVT)/Cognitive Tasks

The PVT is a sustained-attention, reaction-timed task that measures the speed with which subjects respond to a visual stimulus. The PVT is a simple task where the subject presses a button as soon as the light appears. The light will turn on randomly every few seconds for 10 minutes. The purpose of the PVT is to measure sustained attention and give a numerical measure of sleepiness.[21] In addition, subjects will also be asked to make judgements or decisions on stimuli such as words or images presented on a computer screen to track memory and thought process (cognitive performance).

8. Transcranial Direct Current Stimulation (tDCS)- active and sham stimulation

The neuroConn DC stimulator (neuroCare Group, Munchen, Germany) will be used to provide the tDCS stimulation. This battery-powered device will be controlled with a microprocessor to ensure constant current at up to 2000 μA. For safety, multistage monitoring of the output current and electrode/tissue impedance will be included. The device automatically shuts off if the impedance becomes greater than 50 kΩ to prevent electric shocks or burns. This device will be investigational only (not FDA approved). As above, tDCS is a non-significant risk (NSR) investigational device that meets the abbreviated Investigational Device Exemptions (IDE) requirements at 21 CFR 812.2(b) addressing labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion for an NSR device study.

We will use a custom set of silver/silver chloride electroencephalographic (EEG) electrodes as described in McKinley et al.[21] These new electrodes were shown to be more stable over time, produce lower sensation levels, and produce fewer skin reactions when compared to standard sponge electrodes. Both the anode and cathode consist of a separate array of 5 EEG electrodes as pictured in Fig. 1. Each electrode has an inner diameter of 1.6 cm yielding a contact area of 2.01 cm^2 for each electrode. At 2 mA of supplied current, the average current density will be 0.199 mA/cm^2 as calculated by current (2 mA) divided by area (10.05 cm^2).

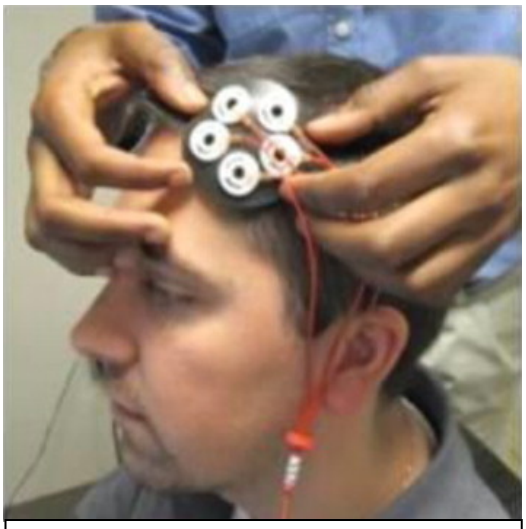


Figure 1. tDCS electrode array (anode only pictured). All five elements are standard silver-silver chloride EEG electrodes placed in a plastic cup which is then filled with a conductive gel.[1]

For the active anodal stimulation condition, tDCS will be applied at 2mA for 30 min. Sham tDCS will be applied at the same intensity but for only 30 seconds.[1] The anode will be applied to scalp location F3 according to the 10-20 EEG electrode placement system while the cathode will be placed over the contralateral (i.e. right) bicep. Electrodes will be secured using medical bandages, and connectivity will be ensured using highly conductive gel.[1]

IV. Data Analysis

Sample size:

The sample size is selected such that we have power to detect differences in the mean reciprocal reaction time (mean 1/RT) and ESS, which are our co-primary endpoints. Differences in co-primary endpoints will be assessed at Visit 4. We assume a loss to follow up rate of 15%.

We will enroll a total of 60 patients with 30 randomized to each group. Thus we anticipate at least 50 evaluable patients. We will control the type I error rate at 0.05 for assessing the primary endpoints conservatively using a Bonferroni correction. With this sample size, we have 80% power to detect a change of 0.90 standard deviations in mean 1/RT with an alpha level of 0.025 using a two-sided t-test. For the ESS, we assume a standard deviation of 3.2 [22]and have 80% power with this sample size to detect a change in ESS of 2.87 with an alpha level of 0.025 using a two sided t-test.

Statistical Methods:

The primary analysis will examine the co-primary endpoints. To analyze differences in mean 1/RT at Visit 4, we will use a linear regression model that is adjusted for baseline average inverse response time. To analyze differences in ESS at Visit 4, we will use a linear regression model that is adjusted for baseline ESS. We will employ a sequential testing procedure to control familywise type I error at 0.05 where we first test differences mean 1/RT and then test ESS.[23] If an endpoint is not stopped for early efficacy, it will be tested at the remaining alpha level, 0.023. If there is a significant difference in mean 1/RT, then ESS will instead be tested at the total remaining alpha level, 0.046.

Secondary analyses will include additional outcomes from the PVT and subjective questionnaires. To analyze differences in the number of lapses at Visit 4, we will use a Poisson regression model to compare the lapse rate of the treatment group to that of the control group that adjusts for the baseline lapse rate. Additional subjective sleep scores and questionnaires will be assessed using linear regression that adjusts for baseline sleep and questionnaire scores respectively. We will also explore differences in the magnitude of the change pre and post treatment at Visit 1 and pre and post treatment at Visit 4. Characteristics of participants will be summarized by randomized treatment group using appropriate descriptive statistics. We will also summarize any reported side effects of treatment. Additional exploratory analyses may be conducted at the discretion of the study team.

Interim Analysis

An interim analysis will be conducted after 34 patients have completed the study. The study will be stopped early for efficacy if both endpoints achieve the stopping boundaries. The analysis will assess both co-primary endpoints using the error spending approach described by Lan and Demets with the O'Brien-Fleming boundary.[24,25] For reaction time, the stopping boundary will be achieved if the two-sided p-value is less than 0.005 ($|Z|>2.813$). If early efficacy is achieved for reaction time, early efficacy for ESS will be evaluated and calculated using the total available type I error rate of 0.05. In that case, the stopping boundary will be achieved if the one-sided p-value is less than 0.013 ($|Z|>2.48$). If early efficacy is not achieved for reaction time, then the stopping boundary for ESS will be achieved if the two-sided p-value is less than 0.005 ($|Z|>2.813$).

V. Event Reporting

(a) Adverse Events

The ICH Guideline for Good Clinical Practice E6(R1) defines an adverse event (AE) as:

> Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

As this is a study that does not include a pharmaceutical product intervention, this definition would include AEs that occur as a result of protocol procedures and protocol treatment.

A serious adverse event (SAE) is any AE that:

- Results in death
- Is immediately life-threatening
  This term refers to an event in which the subject was at risk of death at the time of the event; it does not refer to an event that may have led to death.
- Requires inpatient hospitalization or prolongation of existing hospitalization

In general, hospitalization signifies that the subject has been detained (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in an outpatient setting.

- Results in persistent or significant disability/incapacity
  The term disability means a substantial disruption of a person's ability to conduct normal life functions.
- Is an important medical event that may jeopardize the subject or may require medical intervention to prevent one of the outcomes listed above.

  Medical or scientific judgment should be exercised in deciding whether expedited reporting is appropriate in this situation. Examples of medically important events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalizations; or development of drug dependency or drug abuse.

1. Collecting and reporting adverse events:
All AEs occurring after subject has signed consent and up to the study completion visit must be recorded on specific data collection forms.

2. Collecting and reporting Serious Adverse Events:
The OSU Event Reporting Form should be used to report untoward events that may affect participants in research approved by an OSU IRB. Events requiring prompt reporting include adverse events, protocol deviations, and other unforeseen problems or findings that suggest participants, research staff, or others are placed at greater risk by the research than previously expected. These events, classified broadly as **unanticipated problems involving risks to participants or others**, must be reported promptly to the IRB. Unanticipated problems can occur in any type of research and may involve physical, psychological, social, legal, or economic harms.

Events Requiring Prompt Reporting
Events that may represent unanticipated problems involving risks to participants or others and therefore require prompt reporting include the following:

- Adverse events or injuries that are serious, unexpected, and related;
- Events requiring prompt reporting according to the protocol or sponsor;
- Reports, interim analyses, or other oversight committee/monitoring reports altering the risk/benefit profile;

These events should be promptly reported (see below), regardless of whether they occur during the study, after study completion, or to a participant who has withdrawn from or completed study participation.

Timeframe for Reporting
All **internal events** (those occurring in research at OSU or at a site under an OSU IRB's jurisdiction) as described above should be reported **within 10 days** of the Investigator's or research staff member's learning of the event. Events resulting in temporary or permanent interruption of study activities by the Investigator or sponsor to avoid potential harm to participants should be reported **immediately (within 48 hours)** whenever possible.

Additional Information
Related adverse events and other problems involving risk that do not meet the reporting requirements and do not represent potential unanticipated problems involving risks to participants or others should be reported in summary form at the time of continuing IRB review. However, any problem or adverse event that an investigator believes could influence the safe conduct of the research should be reported promptly.

(b) Protocol Deviations
Protocol deviations are accidental or unintentional changes to the protocol or procedures. In the event that the protocol deviation involves risk to the subject or potential risk to future participants, or with the potential to recur or significantly impacts the integrity of the research data, the event should be reported to the IRB in a timely manner, in accordance with their reporting guidelines.

VI. Ethical Considerations

The study will be conducted in accordance with the ICH guidelines on GCP, the GCPs applicable to any region where the study is conducted, and the ethical principles set forth in the Declaration of Helsinki. Good clinical practice is defined as a standard for the design, conduct, performance, recording, analysis, and reporting of clinical studies in a way that provides assurance that the data and reported results are credible and accurate, and that the rights, safety, and well-being of study participants are protected.

Per GCP, the protocol will be reviewed and approved by the IRB or IEC of each participating center prior to study initiation. The investigator will keep the IRB/IEC informed as to the progress of the study.

(a) Consent procedures
The investigator/study personnel will explain the nature of the study, and will be available to answer questions regarding procedures, risks and alternatives to participation. The consenter will inform the subject that participation is voluntary and that the subject can withdraw or be withdrawn from the study at any time. The principal investigator or his/her entitled designee will obtain written informed consent from each subject. Documentation of the informed consent process along with the original consent form will be maintained in the subject's research folder. A copy of the signed informed consent will be provided to the subject for their records.

VII. Data Handling and Record Keeping

The investigator shall maintain the records of the study e.g.: subject research charts, regulatory documents and all other study specific documentation for a minimum of 15 years or in accordance with currently OSU-IRB regulations.

1. Confidentiality

- Confidentiality of all records will be maintained and data will be kept in a locked filing cabinet and only research staff and authorized members of the IRB will have access.
- Electronic data is protected by codes to which only research staff and authorized members of the IRB and OHR will have access
- The PHI to be collected; who will use the information within the institution and why; who may disclose the information and to whom; the subjects rights to access research information and their right to withdraw authorization (approval) for any future use of personal health information are all listed in the HIPAA form specific to the research
- The names of subjects and any other identifying information will be kept in a different secure location.
- Should publications result from this study all PHI will be removed.

VIII. Data Safety Monitoring Plan

The risks involved with tDCS, completion of questionnaires, PVT, and actigraphy are minimal.

This study will be monitored to ensure participant safety and data integrity. The monitoring for this study will be conducted by the Principal Investigator and the study team. The information that will be evaluated will be the incidence and severity of adverse reactions related to the study procedures, enrollment and efficiency of data capturing. The adverse events will be assessed on a case by case basis at the time the study team is aware of the event.

Overall study monitoring will take place on an ongoing basis with study review meetings taking place at least every 6 months. In the event the side effects suggest the risk outweighs the benefit, the study will be stopped and the IRB notified in order to evaluate possible solutions to the risk problem.

IX. References

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