Guidance on Research involving Transcranial Direct Current Stimulation

Introduction

Transcranial direct current stimulation (tDCS), is a non-invasive, painless brain stimulation treatment that uses direct electrical currents to stimulate specific parts of the brain. A constant, low intensity current is passed through two electrodes placed over the head which modulates neuronal activity. There are two types of stimulation with tDCS: anodal and cathodal stimulation. Anodal stimulation acts to excite neuronal activity while cathodal stimulation inhibits or reduces neuronal activity.

Although tDCS is still an experimental form of brain stimulation, it potentially has several advantages over other brain stimulation techniques. It is cheap, non-invasive, 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.

Several studies suggest it may be a valuable tool for the treatment of neuropsychiatric conditions such as depression, anxiety, Parkinson's disease, and chronic pain. Research has also demonstrated cognitive improvement in some patients undergoing tDCS.

tDCS Devices

There are tDCS administration devices that are FDA cleared for cortical stimulation (e.g. http://www.fisherwallace.com/) and many non-FDA cleared versions. All appear to use a maximum of 9 volts, but vary in waveform, frequency, constant current vs. constant voltage, as well as other parameters. It is important to know that the devices are different and safety information on one device may not apply to another. A well-studied device commonly used in research is the Magstim device (http://www.magstim.com/). On an acute basis, the devices appear to be benign. There is controversy about long term effects, both positive and negative.

tDCS and the FDA

The FDA defines a device as: *"An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is: (1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them, (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."*

In most cases, tDCS is being used as a "device" because it is affecting the function of the body. Namely, the device is being used to affect neuronal activity and to affect memory, cognition, etc.

FDA regulations define "clinical investigation" to include *"any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the Food and Drug Administration under section … 520(g) of the act."* This is the case regardless of whether data is being submitted to FDA or intended for marketing. Although it is often stated that the purpose of the research is NOT to study the device itself or to gather safety or effectiveness data, but this is seldom true. For example, FDA might consider the protocol to evaluate whether and how tDCS affects memory or whether and how tDCS affects neuronal activity, in which case FDA will consider this a clinical investigation. Therefore, in most cases, administration of tDCS involves an FDA-regulated clinical investigation of a device.

Researcher Responsibilities

If the study is an FDA-regulated clinical investigation, the researcher does **not** need to apply to FDA for an investigational device exemption (IDE). Instead, the following must occur:

- FDA requirements for informed consent must be followed:
  - Disclose in the informed consent that FDA may inspect the records
  - Participant must date his/her signature
  - No waiver of informed consent or documentation of informed consent
- Abbreviated IDE requirements
  - Researcher must submit a justification to the IRB as to why the device is non-significant risk (NSR; see Device Form).
  - A *significant risk* (SR) device is:
    - Intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
    - Purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
    - For a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
    - Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
  - Researcher must follow a subset of the IDE regulations:
    - Submit justification to IRB why the device is NSR using the Device Form;
    - Label the device as investigational (the name and place of business of the manufacturer, packer, or distributor, the quantity of contents, if appropriate, and the following statement: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use."
    - Do not market/promote the device;
    - Report unanticipated adverse device effects to the IRB, sponsor, etc.
  - Fully convened IRB must make a non-significant risk device (NSR) determination.

Study Participants

- tDCS should not be administered to individuals who are pregnant or may be pregnant. Urine pregnancy testing should be performed on any fertile female participants prior to administration of tDCS.
- Special consideration should be given to inclusion of vulnerable populations including children and the elderly, subjects with mood disorders, epilepsy, stroke, and implants.

Can tDCS studies be reviewed by the expedited procedure?

If the study is FDA-regulated and using a non-FDA cleared device, FDA guidance states: "IRBs should make the SR or NSR determination about a study by reviewing relevant information at a convened meeting." Therefore all initial reviews of abbreviated IDE studies will be done at convened meetings. If the committee makes an NSR determination and determines that the study is minimal risk and meets expedited review criteria, it can subsequently be reviewed via expedited procedures.

If the researcher uses an FDA-approved device, expedited review procedures may be used for initial review, at the discretion of the IRB.