**Project 1: Attention Project, Buxbaum**

The goal of the project is to examine whether the effects of TDCS and prism treatment in neglect are synergistic. Proposed subjects included patients with right hemisphere stroke, chronic (6 months out), without cerebellar lesions. Occipital lesions, presence of field cuts and severity will be used as covariates in the study. It is within subjects design with three cells (combo treatment, TDCS alone, and prism with sham). Anodal applied to lesioned right hemisphere and cathodal to unimpaired left hemisphere. Three separate baselines at three separate time points corresponding to treatment. Outcome measures include proprioceptive measures of shift, traditional neuropsychological measures and virtual reality task of navigation.

**Discussion:**

Whyte queries whether there was any intention to investigate differences in responses as a function of individual difference (e.g., neglect severity, extent of visual involvement). Buxbaum noted that examining these differences not realistic given expectations of patient recruitment. Examinations of lesion load and severity, as well as most other contrasts, would be post-hoc in nature.

Fregni raises concern about shunting from multiple electrodes and power issue with design. Walsh raised a possibility of requiring more control experiments, but agrees that one would first need to elicit an effect and then worry about follow-up studies. Clark notes that they have stimulated homotopic areas with some success, but that you need to do extra controls to determine mechanisms if you get positive effects. Schlaug noted that in dual versus unilateral stimulation approach, hair may be an issue for shunting. He also raised a question about power and noted opposite effects sometime seen in motor cortex with dual stimulation.

Buxbaum responded that the power issue mitigated by within subjects design. However, notes that might not be able to see synergistic effects of dual treatment if present due to lack of power. Barrett added that you can obtain power estimates from other within subject designs in stroke.

Celnik voiced a concern about intensity and location of stimulation and Buxbaum suggested that their putative location will be IPL, 1 milliamp for 10-12 minutes.

Buxbaum also queried as to whether it was better to stimulate first and then administer prism treatment or to do prism treatment during stimulation? Clark furthers this query by inquiring about stimulating after to improve consolidation. Cohen notes that caution has to be used when stimulating after treatment as in their experiments stimulation after did not produce an effect. Nitsche suggested concurrent task and stimulation for best efficacy.

**Project 2: Motor group, Celnik**
Group proposes phase 1 TDCS study in 100 sub-acute (within 7 days of injury) stroke patients. The patients will be recruited while in-patient, and treated for 10 days with both anodal stimulation ipsi-lesion motor cortex and cathodal in contra-lesional motor cortex. Subjects also sent home with unit so that TDCS can be done in conjunction with OT. Subject inclusion was not specific for cortical versus sub-cortical, or hemisphere of lesion. Main outcome goal is for safety. Major concerns were seizure activity, motor behavior functions (ie getting worse with intervention), and potential tissue damage. They also proposed the conjunctive use of imaging studies in smaller cohort. Outcome measures included standard clinical measures for stroke.

Whyte asked for clarification if they were interested in testing both detrimental and positive effects in both contra and ipsi-lesional motor functioning. Both Celnik and Fregni reported that there are no reports of detrimental functioning following TDCS in ipsi-lesional side for motor functioning. Schlaug notes that his IRB questioned him about proving a null effect. Clark added that their IRB questioned when it is safe to send someone home. Clark notes that they have not seen any changes in baseline measures for non-experimental manipulations an hour after TDCS administration.

Clark asked why bilateral stimulation on homotopic regions was proposed yet the studies that the group had presented were mostly on unilateral stimulation. Celnik responded that these early studies were proof of principle, while in the proposed study they will be trying to maximize the effect with dual anodal/cathodal stimulation.

Whyte questioned whether sample was going to be stratified or straight randomization. Schlaug responded that they would be stratified on the clinical measures. Again reiterated that this would be the first real-world study in the sub-acute phase so first we need to generate safety measures but also want to collect enough data for a larger study.

Hicks questioned whether there have been any animal studies in sub-acute stroke. Nitsche responded that he was not aware of animal studies, noted that some early work was done on spreading depression.

Fregni asked about shunting and whether modeling studies are needed at the individual level.

Project 3: Executive functions, Pascual-Leone

Proposed study is on prospective memory function in healthy group of normal aging subjects (65 plus year old) in parallel groups, as they were worried about carry-over effects. Goal is to determine if prospective memory can be improved to level of younger controls following stimulation (TDCS). Notes that currently there are limited applications for improving real-world behaviors (e.g., people forget to take lists with them when shopping). Stimulation applied to BA 10 and DLPFC with anodal and cathodal stimulation for a total of 6 active cells. At home, subjects will be asked to take a pill each day at a certain time. Information is uploaded to the computer based on when pill box is accessed. Other outcome measures include standard prospective memory tasks and
cafeteria task (to be developed). They also propose to test effects in FMRI with and without TDCS in a smaller cohort. Stimulation is 1.5 milliamps for a 15 minute period.

Fregni responded that he was in favor of the at-home clinical outcome measure but worried that negative effect will be present. Pascual-Leone responded that acute effects of TDCS should be present, and that he was hoping to translate these into long term effects that are observable in pill box test (i.e., TDCS and task will hopefully reinforce prospective memory).

Whyte raised a concern about regarding the pill measure, since some of the patients might not be used to taking regular medications. Furthermore, there is some concern as to whether the cafeteria task is (i) sensitive enough to yield results, (ii) whether results from this task can be validated, and (iii) whether the pill box manipulation is cost effective. Whyte conclude by suggesting that it was better to go with a validated measure. Pascual-Leone suggested that real-world ecologically valid measures such as pill taking were superior to laboratory measures and reiterated that the primary aim of the current study was to assess whether positive effects will go beyond initial period.

Fregni questioned how subjects would remain blind to the sham condition provided the stronger stimulation. Nitsche proposes to use local anesthesia cream to deaden senses to increase likelihood that subject would be blinded. Pascual-Leone also noted that efficacy of blinding depends on task order for motor studies.

Cohen suggests the need for active stimulation controls (eg TDCS over task-unrelated cortical regions). Pascual-Leone noted that the number of active controls is difficult to translate to a grant application because everyone wants to see a sham control. Clark notes that an active control is raising the empirical bar (i.e., better control than sham) but that it introduces a problem with experimental control (i.e., stimulation of the activity network as a secondary effect). Cohen agrees in that active control reduces explanatory power but provides the best control.

**Project 4: Language, Schwartz**

Propose a TDCS study in aphasic patients with the main outcome variable being picture naming. Test materials are eight separate matched confrontation word naming lists that are planned to evoke error rates of 30-70%. Outcome measures are types of errors, latency and reaction time. Exploratory study based on previous phase 1 study with TMS. Main question is where does TDCS promote the best effect? Within-subjects stimulation design under 8 different conditions (2x2x2 where factors correspond to right left hemisphere, anodal and cathodal (with reference on shoulder), anterior and posterior stimulation sites (anterior = BA 44, 45; pos = TPJ 37, 39 40)). 8 subjects per cell, 20 minute treatment at 1.5 milliamps, begin word naming test four minutes into treatment regimen. Group also proposes follow-up testing to assess replication.
Schlaug questions evidence of behavioral effect for naming and about timing of stimulation and testing (e.g., is four minutes too fast?) and suggests simplifying the study to look at anterior vs posterior placement.

Pascual-Leone raises an issue about cephalic versus non-cephalic reference. Fregni notes that with non-cephalic you have significant amount of current going to the cortex but it is not clear about the direction of the current. Nitsche cites two published studies that reported shoulder references to be less effective during a motor study. Cohen suggests that New York group performed modeling study for a cephalic and non-cephalic reference but indicates that replicable effects are more important than modeling. He also indicated that effects occur very early on in the time course so that 4 minutes should be adequate for seeing the effects in proposed task.

Schwartz questions how much has been done in terms of safety work for reference location. Schlaug notes case study on himself where the left shoulder reference seemed to affect his heart. Also notes Wassermann study reporting an effect with 2 but not 1 milliamp in FAS task. Fregni and Cohen both state that the current should be distributed and not go preferentially to the heart. Schlaug suggests using the mastoid and neck for the reference control.

Coslett again raises question about timing of stimulation and task. Schlaug suggests waiting for a longer duration as he thought that accuracy might not show that effect so soon whereas reaction time might be sensitive at four minutes.