

## Session VI: Motor Function Breakout

Recorder: Dawson

After determining that the majority of the group was interested in motor learning and plasticity, Cohen initiated a discussion of the effects of context on learning, a phenomenon sometimes known as **meta-plasticity**. A discussion of the roles of pre-existing regulation for LTD and LTP ensued. This concept was contrasted with **homeostatic plasticity** in which down regulation produces better or faster learning, but increased regulation worsens motor control learning.

Ziemann further went on to explain that conflicting results regarding the capacity for plasticity based on motor learning may occur because most studies simply increase activity. For example, in a Journal of Neuroscience article, there was a study using a paired associate stimulus followed by a motor learning paradigm in which the interval between the stimulus and the motor learning event was varied from immediately afterwards to a 90 minute delay. They found evidence of homeostatic regulation where the LTD protocol enhanced motor learning afterwards, and the LTP protocol reduced it. There was a non-homeostatic interaction because the timing of the two interventions mattered a lot. There is no direct connection between excitability, context and learning.

Further discussion ensued about whether homeostatic plasticity could be used as a diagnostic or therapeutic tool. Schlaug stated that we needed to agree on good outcome parameters which could be related to a particular outcome or intervention paradigm, or standardized to improve comparability to other studies, such as Excite or Northstar. The question was posed whether there are other physical measures that would help differentiate or predict recovery. A few possibilities were mentioned, such as the ability to get a corticospinal response; one difficulty with this measure is that one doesn't always find a corticospinal response in acute cases even though subjects demonstrate a high Fugl-Meyer score. Ziemann stated that motor evoked potentials are not adequate as an exclusive measure, but it is still better to have them than not in order to make outcome predictions. He also thought that a DTI or FA ratio on the spinal tract can improve outcome prediction.

After determining that there has not been a tDCS treatment study in acute stroke patients, it was decided that this topic was novel enough to warrant building a study around it. Further, the consensus was that tDCS was inexpensive, safe, could be used on in- or outpatients, and had the capacity to change motor learning and performance. Further, tDCS was thought to be preferable to TMS because it has the capacity to manipulate recovery.

No one had any idea how TDCS would work in acute patients when the brain is swollen and many metabolic processes are active. Schlaug proposed the idea to study sub-acute patients in order to reduce the likelihood that the data would be overwhelmed with noise. Patients could be started in the hospital and treatment could continue after they transitioned to outpatient care.

Cohen further defined the patient population as ischemic stroke with any size of lesion and that the treatment would only apply to the motor domain. He posed the question as to whether this study would be a proof-of-principle or a clinical trial. This initiated a long discussion. A clinical trial was considered to be preferable in terms of funding possibilities.

Schlaug advocated for a Phase 1 clinical trial because it would be necessary to show that tDCS is safe in acute stroke populations. A number of measures that would reflect safety were discussed. The rest of the time was spent discussing safety concerns and measures, and how these measures, while ostensibly focused on safety, could also be used to measure tDCS efficacy to assist in planning the next study. The discussion about the type and location of stimulation was very brief. Schlaug mentioned a study by Gottfried where chronic stroke patients were stimulated on both sides, and this methodology was quickly appropriated, as was the consensus to stimulate motor cortex. The following represents the outlines of the planned protocol:

Project: tDCS IN SUBACUTE STROKE

Project type: Phase 1 or 2 safety study

Hypothesis: tDCS will enhance motor recovery relative to sham.

Subjects: 1 week out from ischemic stroke, lesion size irrelevant

Protocol: Either stimulation or sham would be administered during OT or sensory stimulation sessions -- cathodal stimulation to the contralesional motor cortex and anodal stimulation to the ipsilesional motor cortex. Start treatment in the hospital and continue on outpatient basis for a total of 10 sessions, with a 3-month follow-up.

Safety outcome measures: seizure evaluation, EEG activity, getting worse or better on measures of motor performance (see below), tissue damage as evidenced by S100B and NSE (before stimulation and 1 hr. after), and imaging to look for hemorrhaging and mismatches between diffusion and perfusion

Efficacy outcome measures: motor evoked potentials, Fugl-Meyer or NIH Stroke Scale (impairment score), Wolf Motor (activity score), Stroke Impact Scale (subjective score), and Jebsen-Taylor hand function test or 9-hole pegboard (fast exam).

Objective: use data from this study to generate a power analysis and plan Phase 3 study