

## Session II Discussion

Discussant: Cohen

Recorders: Fecteau/Oberman

The first talk of the session was given by Dr. Celnik, who had three main points. The first was that TMS may be useful in studying mechanisms of motor recovery after stroke (specifically via such indices as motor thresholds, recruitment curves, and intracortical inhibition). For example, he reviewed several studies on the changing nature of interhemispheric interactions during recovery. Thus, TMS may be useful as a predictor of motor recovery. Dr. Celnik argued that the indices discussed were more reliably correlated with motor recovery in the acute as compared to chronic phase of recovery. To date, however, most studies have been conducted with chronic patients. The final segment of Dr. Celnik's lecture included the suggestion that combined stimulation and behavioral intervention techniques may lead to improved outcomes.

Following Dr. Celnik's talk, the discussion focused on two main points. First, several participants discussed the need for clinical trials that go beyond the proof-of-principle stage of research. Second, a concern was raised that all of the interventions explored to date have appeared to hit a "ceiling" of 10-20% improvement on the measure of interest.

The second talk of the session, given by Dr. Nitsche, focused on tDCS, and, in particular, specific methodological options for increasing contralesional and/or decreasing perilesional cortical plasticity, with the goal of maximizing rehabilitation of motor function. Dr. Nitsche focused largely on Constraint Induced Movement Therapy. He suggested that tDCS seems most effective when applied during task performance (not prior). Additionally, he outlined options for bilateral vs. unilateral stimulation, and discussed optimal intervals between stimulation sessions. Dr. Nitsche concluded by stating that the beneficial effects of tDCS were not likely restricted to motor function, but may also be effective in visual rehabilitation.

Following Dr. Nitsche's talk there was a question about how the frequently-observed 10-20% improvement on outcome measures translated to the subjective experience of patients. It was suggested that there are mixed results in this regard; one recent study reported that when patients recover 10-20% they feel that tDCS has been helpful.

The final talk of this session was given by Dr. Cohen, who discussed the benefits of somatosensory (i.e., peripheral) stimulation in motor recovery. He emphasized that the effects were comparable to the level of improvement shown by noninvasive brain stimulation. Dr. Cohen's major point was that combining somatosensory stimulation with brain stimulation may lead to lasting beneficial effects greater than either of the techniques alone. He highlighted several areas of research requiring additional investigation, including outcome measures (e.g., measures of adaptation, acquisition, compensation, speed/accuracy trade off, etc.), the form of learning (explicit, implicit, declarative and procedural), the stages of learning (online, offline, consolidation, and long-term retention), and task dependency. He concluded by showing a diagram of the "translational research pipeline" and suggesting that researchers are stuck at the stage of small proof-of-principle studies without clear transition to large-scale clinical trials. This inspired an animated discussion from the group.

During the discussion, Dr. Seltzer suggested that there are stages missing from the diagram – namely optimization between basic science and proof-of-principal and between proof-of-principal and clinical trial stages. Dr. Pascual-Leone commented that the positive results from small proof-of-principle studies often do not translate to larger clinical trials, but it is unclear why. Following this, a number of participants engaged in a discussion regarding whether it would be most effective to run smaller clinical trials with specific patient subgroups and a more homogeneous sample, or larger clinical trials with more heterogeneity. There were differing opinions on this matter. One suggestion for overcoming the roadblocks discussed was development of a data repository containing relevant (both positive and negative) findings that researchers could access across multiple institutions.