General Dicussion
Facilitators: Nick Ward and Myrna Schwartz
Summarizer: Steven Jax and Sarah Shomstein

The main framework of the closing discussion section was to consider the rationale and methods for conducting neuroimaging studies in the service of understanding mechanisms of recovery and of therapeutic interventions.

Rationale for rehab-inspired neuroimaging research
The consensus appeared to be that most early studies using functional imaging techniques were primarily observational. However, we are now entering the new and exciting phase of neuro-rehabilitative research in which is hypothesis driven.

The discussion progressed to ask whether hypothesis driven research is beneficial to the rehabilitative field. The point was made that a pragmatic approach to treatment will always be required. However, a distinction needs to be made between treatments which aim to help adaptation to impairment and those which aim to minimize the impairment itself. The former are well established and form the cornerstone of neurorehabilitation. The latter are less well developed, but it is in this field that neuroscience can help further understanding. In this framework, basic research is imperative for understanding the mechanisms of cognitive control and can later be used to develop rehabilitative techniques designed to minimize impairment. However, the current practice of neurorehabilitation will continue to be pragmatic until evidence suggests that changes in practice should be made.

The consensus appeared to be that both approaches are worthwhile. There is great value in both – having a clear theoretical notion of your treatment as well as having a treatment that works and adding a neuroimaging component to identify possible changes at the neural level. Whichever approach is taken, it is critical to have a research question that matches both the hypothesis and the method used to investigate that question.

Understanding the mechanisms
An important issue for future work will be to better understand the similarities or differences in neural changes following spontaneous recovery and following rehabilitation. Thus far, it is unclear whether rehabilitation techniques affect the brain in the same way as spontaneous recovery or if it is possible for rehabilitation to change the way recovery progresses. Future work should consider this issue.

Prediction (e.g., to predict the best way to deliver treatment)
One of the key themes has been that patients with brain injury have as many differences as similarities from one another. It is unlikely that a particular treatment will be equally effective in all patients as a result of differences in anatomical damage, time since damage, biological age, concurrent medication, genotype etc. Thus different patients might show different patterns of neural reorganization, either spontaneously or in response to treatments. If the goal of a treatment is to promote cerebral reorganization then structural and functional imaging might be able to predict whether an individual will respond to that particular treatment, thus allowing stratification of patients based on their likelihood of responding. However, at present the field is not yet mature enough to provide treatment prescriptions, but this is clearly a goal for future work.

Reliability of the tools and methods of analysis
The quality of the data acquired is critically important. Much care should be devoted to ensuring that the data is of the best quality possible. FMRI data sets are complex and it is worth remembering that they be analyzed in a number of ways. The following points were felt worthy of consideration.

- First, and foremost, experimental design should be given the most important consideration when designing any kind of a neuroimaging study. The suggestion is to attempt to focus on simple paradigms in which most of the experimental factors can be rather well controlled. This will reduce the noise and increase explanatory power for observed effects.
- Data may be contaminated by motion artifacts. It is suggested that most of the motion algorithms can filter out motion rather well. As long as movement is not task correlated (i.e., patient moves with every presentation of the stimulus) this motion can be filtered out effectively. However, there are methods (e.g. *uwarp* in SPM5) that are designed to deal with task correlated head movement. It was stressed that time spent making the subject comfortable in the scanning environment with adequate time to practice the task often helps reduce motion artifacts.

- More sophisticated statistical analyses may be employed. We mostly use mass univariate statistical techniques to provide information about relative increases or decreases in activation in brain regions. This kind of analysis is certainly valuable, but may not pick up other kinds of changes such as those designed to make inferences about changes in connection strength between regions
- Some considered that thresholding of data seems arbitrary. It was pointed out that the first level 'contrast images' from a single subjects that are used in a true mixed effects analyses (at group level) are not thresholded. When thresholding is used, it was pointed out that widely accepted methods and levels of thresholding are in use. This includes the use of correction for multiple comparisons and the option of restricting a search volume based on *a priori* anatomical hypotheses. It was suggested that an informative statistical measure is performing *power* analysis. This measure would be extremely useful in interpreting the results at any given threshold (i.e., power to threshold relationship).

Generalizability of the principles

It was agreed that different areas of neuro-rehabilitation seem to be at different stages of development, therefore the level of analysis that seems to be appropriate for one area might not be appropriate (or even feasible) for another. For example, research inspired by psycholinguistic theory has been very useful for understanding language related impairments after stroke, but a good understanding of TBI has been lacking. Also, stroke studies can go beyond descriptive methods because the physiological markers of stroke are better understood. In terms of the overall general method of approaching any single study, it was noted that the same standards cannot be applied to say stroke studies as to studies of TBI.

Barriers to collaboration

Several barriers to collaboration were identified:

- Differences in equipment (i.e., different MR machines) and analysis software need to be considered. Whether data from different scanners can be combined is unclear, but studies assessing this possibility are underway. Thus this question needs to be positively addressed empirically.
- Although most of the participants agreed that larger sample studies were needed, differences in research interest (e.g. language vs. motor abilities) and population of interest (stroke vs. TBI) make consensus about even the research question for multisite collaborations difficult. Collaborations therefore should be based on agreement about a particular research question and hypothesis to be tested.
- In order to convince a large organization to fund a significant multicentre study, it would be very useful to have some pilot data to demonstrate that such a project is at least feasible.
- Finally, it was again reiterated that some pilot funds for junior faculty are available from the NCRRN, and that proposals will be due in the few months following the conference.