Brainsynch-Hit: The influence of directional interactions in brain networks in predicting cognitive deficits post-stroke

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Abstract

The human brain is a complex dynamic non-linear system where hundreds of billions of neurons and astrocytes organized in columns, cells assemblies, and large scale networks communicate through fluctuating neurochemical signals that vary in frequencies from 0.05 Hz (or lower) and 500 Hz (or higher). Cognitive functions arise out of multiple neuronal interactions in space and time. One of the most successful approaches in understanding human cognition has been the study of cognitive deficits following focal lesions. More recently neuropsychology has been integrated with advance brain imaging methods. The PI (Dr Corbetta) has pioneered methods for measuring changes of functional connectivity (FC) with functional magnetic resonance imaging (fMRI) in stroke to predict cognitive deficits and recovery. Recently he showed that a few clusters of correlated, hierarchically organized, deficits explain ~70% of behavioral variability post-stroke in a large population2. Correspondingly, these behavioral clusters are predicted by low dimensional alterations of fMRI connectivity measured at rest. The two most common abnormalities are a disruption of inter-hemispheric integration and intra-hemispheric segregation, which correspond jointly to a global loss of modularity. Interestingly, different deficits are predicted by the topography, not the type, of altered connectivity3. This project funded by the National Institute of Neurological Disorders (NINDS) for five years has been renewed and will run for an additional five years to arrive to a target enrollment of n=400 subject.We propose to link this unique project to the Human Brain Project (HBP) to study fundamental issues about neural communication and behavior.The low dimensional alterations of FC in stroke represent potential biomarkers for prediction at the level of single subjects, one of the goals of the medical informatics core (SP8) (theme 11). Theoretically, these alterations can be modeled at the level of whole brain (SP4) or process oriented computational models of brain function (CDP4) to understand neuronal interactions and relationship to behavior. Finally, computational models can be used to scout novel treatment given the impossibility of trying different strategies on real patients (theme 13).A major limitation toward these goals is a deeper understanding of directional interactions in the brain since FC is a non-directional measure of interaction. Directional influences are difficult to study with slow methods like fMRI. However, Dr Andrea Brovelli has been a leader in the development of new methods to study directional interactions from neural signals. His approach is based on non-linear decomposition methods that hierarchically use mutual information, clustering, and Grangier causality. Here we plan to ask very straighforward questions related to the directionality of our low dimensional connectivity patterns in stroke. For instance, we plan to examine if disruption of inter-hemispheric interaction is the cause or the effect of intra-hemispheric connectivity changes.A second goal is to use computational tools being developed as part of CDP4 (Dr Rainer Goebel) and SP4 (Dr Gustavo Deco) to model the effects of lesions on neural activity and behavior. We have the rare opportunity of an iterative approach in which computer models of network dysfunction can be validated on real data and behavior.

Consortium

Maurizio Corbetta – University of Padua – Italy – Funded by: MIUR (Coordinator)
Andrea Brovelli – Centre National de la Recherche Scientifique Délégation Provence et Corse _Institut de Neurosciences de la Timone – France – Funded by: ANR
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