ATTENTION DYNAMICS CONSORTIUM
IN TRAUMATIC BRAIN INJURY (ADC-TBI)

I. EXECUTIVE SUMMARY

Traumatic Brain Injury (TBI) is a global health problem in terms of incidence, cost and impact on daily living.[1] Worldwide, an estimated 57 million individuals have been hospitalized with TBI.[2] More than 90% of individuals with TBI are classified as having mild TBI (mTBI) or concussion. In the United States, medical center emergency rooms report approximately 1.74 million cases of mTBI.[3] These estimates fail to include unrecognized or unreported mTBI cases that may number up to 3 million[2, 4] for sports-related injuries and up to 40% for personnel participating in current military engagements.[5, 6]

Currently, there is no causative explanation for the attention deficits and persistence of symptoms in TBI patients.[7, 8] An extensive review of TBI[9] finds no single psychological, physiologic, somatic, or demographic fact that can account for persistent post-concussive symptoms (PCS). Many PCS symptoms are equally compatible with diagnoses of depression, anxiety, and chronic pain as they are with disorders of cognition. The lack of a clear understanding of the mechanisms underlying concussive symptoms has important consequences for the diagnosis and treatment of these individuals.

We propose that cognitive deficits from mild Traumatic Brain Injury (mTBI) arise from traumatic disruption of white matter connectivity in a neural network that sub-serves attention and working memory. Furthermore we posit that one crucial and vulnerable function of this neural network is to produce predictive timing in order to reduce temporal variability in performance. This is consistent with the prevalent finding in mTBI patients, and other pathologies of attention, of an increase in reaction time variability. We hypothesize that impairments in this anticipatory process likely contribute to the fact that approximately 20% of individuals with mTBI end up being classified as chronically disabled.[10] Accordingly, we plan to characterize the chronic behavioral sequelae of mTBI in adults by quantifying and correlating these deficits along with structural and physiological abnormalities in cortico-cortical and cortico-subcortical network connectivity.

Structural imaging will assess the integrity of brain regions, and their *anatomical* connectivity most susceptible to mechanical stress, such as, anterior and lateral prefrontal white matter tracts, and long white matter tracts. These white matter pathways bi-directionally connect anterior to posterior regions of the brain, and cortical to sub-cortical regions. fMRI and MEG/EEG measures will assess the strength of *functional* connectivity by quantifying the degree of coherence in the attention network involving prefrontal and posterior parietal cortex, as well as other networks involved in adaptive compensation and error monitoring. *Behavioral* performance will be monitored using smooth pursuit eye movement tracking to assess predictive timing and performance variability in a continuous task that will enable on-line linkage of eye-tracking variability with network coherence measures.

The novel aspects of this investigation are the quantification and specificity of damage to white matter tracts using new imaging techniques and analyses, relating focal structural connectivity disruption to functional changes in neurophysiology and behavior using MEG/EEG and fMRI, and in correlating neural network coherence with behavioral performance using eye-tracking variability as a metric of attention.

The program will be divided into two phases over five years, with the first phase, over three years, testing coherence in neural networks with behavioral synchronization in relation to focal network connectivity lesions. The second phase, over two years, will test TBI rehabilitation interventions based on network connectivity disruption. The synergy of the consortium will be the commonality of experimental tasks, sharing of research fellows and the intense interest in bridging neurophysiology, anatomy and behavior through the analyses of coherence, connectivity and behavioral synchronization. The Brain Trauma Foundation will foster the collaboration and disseminate findings through interaction with other TBI organizations. This collaborative program will elucidate the neural and cognitive sequelae of TBI and increase our understanding of the mechanisms underlying attention. Importantly, the research will provide guidance in the development of new methods to recognize, treat and potentially prevent acute and chronic TBI symptoms.

II. ORGANIZATION

We formalized a collaborative network with a range of expertise including: clinical management of TBI, innovations in white-matter tract tracing techniques, assessment of network coherence using fMRI, MEG/EEG, motor synchronization tasks and coherence analyses. There are four groups in the consortium, based on expertise: fMRI-DTI, MEG/EEG, MRI-DTI and Synchronization analysis. The scientists are from renown clinical and research institutions: Washington University (fMRI-DTI), UC San Diego (MEG/EEG), UC San Francisco (MRI-DTI), Salk Institute (Synchronization), UC Berkeley (Synchronization), and Weill Cornell (Synchronization). This group of scientists and institutions represent a unique ensemble of human and scientific talents, as well as methodological and computational strengths, which is well positioned to significantly advance our understanding of mTBI.

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