

CONSORTIUM/CONTRACTUAL ARRANGEMENTS – INFORMATICS AND ANALYTICS CORE (IAC)

A project of this scale requires leadership with a demonstrable track-record of program administration and scientific excellence. The USC group has demonstrated leadership in large scientific efforts. Collectively the IAC team has experience in neuroscience imaging, epilepsy, data integration, scalable cloud technologies, electrophysiology, genetics, imaging, and multifactorial data analysis. We have an unmatched resource of knowledge to integrate and analyze multi-modal data towards the discovery of biomarkers of epilepsy. We have either led or participated in several national and international big data related initiatives, various NIH P- and U-class projects, NSF projects related to big data computing, as well as:

PPMI (<http://www.ppmi-info.org/>) is an international study to identify biomarkers of Parkinson's disease progression. Sites in the U.S., Europe and Australia collect imaging, biologic sampling and clinical and behavioral assessments. We developed and manage the informatics systems for this project. Since 2005, the longitudinal Alzheimer's Disease Neuroimaging Initiative (**ADNI**; <http://adni.loni.usc.edu/>) has been validating the use of biomarkers including blood tests, tests of cerebrospinal fluid, and MRI/ PET imaging for Alzheimer's disease (AD) clinical trials and diagnosis. It is one of the largest and most successful big data exchanges (now that it contains whole genome sequencing of the subjects), with heterogeneous data collected from almost 60 sites and distributed to thousands. We are responsible for the informatics of ADNI. The **ENIGMA** project (<http://enigma.loni.usc.edu>) is a network of imaging, genetics and informatics researchers studying brain structure and function, based on MRI, DTI, fMRI and genome-wide association scan (GWAS) data.

In short, ours represents a group of leading investigators particularly well suited to address the aforementioned issues and to provide novel solutions for meeting the challenges presented by big clinical data sets. Our team members have direct and immediate experience in managing large, multi-site investigations for brain research, are well known for our leading work in computer science, engineering, workflow development technologies, and informatics, as well as our world-leading efforts to develop systems-level computational approaches toward modeling biological processes. We have established noted approaches for large-scale data analysis as well as for operationalizing scientific workflow design and execution. Involving leading neuroscience, biology, and computer science research centers, ours is a collection of thought-leaders on the topic of big data, its present and promise, with a history of delivering unique outcomes of immediate relevance toward data science, thereby providing big data solutions to promote discovery brain science.

With our team of expert neuroimaging researchers and informaticists, we will hold monthly project phone calls to discuss project direction, identify challenges, and note progress. Annual all-hands meetings will be held at rotating locations to discuss plans, showcase results, confront challenges, etc. The project leader will work closely with the overall project PI, the overall project advisory board, as well as with NIH U54 program officials to ensure that project milestones are met as well as the timely release of informatics deliverables.

David McArthur, Ph.D., M.P.H., brings to this effort a broad range of expertise in biobehavioral research. For decades he has been involved in complex clinical studies in both laboratory and intensive care settings with particular focus on measurement and assessment (including EEG and other physiologic signals as well as behavioral and educational assessments), on data acquisition and computerization with special reference to massive datasets, and on cutting edge statistical analyses and research design. For the last 15 years he has served as the full-time principal statistician at UCLA's Department of Neurosurgery, a unique position that has demanded staying abreast of burgeoning developments in statistical theory and applications. He has developed a deep understanding of R, the preeminent software for cutting-edge data analytics with now over 8000 available specialized packages, and was elected chair of the premiere international meeting for R when it was held at UCLA in 2014. In addition to longstanding attention to traumatic injury, he has also been a key liaison regarding IRB issues involving patient rights and responsibilities of researchers working with comatose individuals, helping to develop the legislation that facilitates surrogate consent in California. His roles in the present study will include advice and analysis across multiple topics, from executing algorithms for robust statistical analytics to resolving data problems and IRB concerns and constraints.

Denes Agoston, M.D., Ph.D. brings expertise in TBI biomarkers, proteomics, and the understanding of the pathobiology of TBI. Dr. Agoston is a translational neuroscientist working for the last ~15 years on

experimental and clinical aspects of TBI, especially on the identification and validation of serum and CSF based protein biomarkers. Dr. Agoston has adopted and refined the high throughput, antibody based proteomics platform (reverse phase protein microarray, RPPM) for TBI research. He has been particularly successful in identifying biomarker changes in relation to neurobehavioral, histopathological, and MRI abnormalities. Using the RPPM platform, he has completed multiple projects and has identified the molecular pathologies in penetrating, diffuse, and blast-induced TBI. Furthermore, he has demonstrated that anti-inflammatory treatment and environmental enrichment can mitigate the molecular pathology and can prevent the long-term neurobehavioral and molecular abnormalities after blast-induced TBI (bTBI). He is leading a multinational clinical project aimed to determine TBI-induced changes in protein biomarkers in brain interstitial fluid (cerebral microdialysates), CSF, and blood using mass spectrometry and antibody-based proteomics. His role in the proposed research will also include interpreting protein biomarker data in the context of the other outcome measures.