

Title of Project: Multilevel Multimodal Biomarkers of Early Alzheimer’s Disease (MEMORIES)

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Brief Description:

A major rise in prevalence and impact of neurodegenerative diseases, such as Alzheimer’s disease (AD), is projected in the coming decades, resulting from increasing life expectancy, thus leading to substantially increased healthcare costs. Currently, there is no noninvasive biomarker available to detect and monitor early stages of disease progression in AD. The research to be done for this project aims to identify such biomarkers and is rooted in network medicine, an emerging field of study which seeks to explore systematically the complex functional interdependencies between various biological components, with the overarching goal of modeling the emergence of disease phenotypes.

Specifically, the proposed project aims at identifying multilevel (genotype - phenotype) and multimodal markers in early AD based on approaches inspired from complex networks analysis.

- i) At genotype (-omics) level, novel network-based approaches will be developed, to integrate various -omics data from patients’ blood: gene expression, epigenetic and SNP mutations. The approach extends our recent work in biological networks analysis and aims to identify network modules which have biomarker value.
- ii) At phenotype (brain connectomics) level, structural and functional connectivity (from MRI neuroimaging experiments) will be explored using brain connectivity methods, to reveal complex disruptions caused by AD in aging brain. Here, complex network analysis will be used to identify discriminative modular substructures, which may serve as biomarkers.

Results of this research will enable noninvasive diagnosis, provide support for monitoring therapies, and help understand heretofore unexamined relations between genetic and neuroimaging phenotype. In doing so, *MEMORIES* addresses critical questions with high implications and major societal and scientific impact.

