Abstract

Functional MR imaging and direct intracranial recordings are two of the most popular and effective methods for understanding how the human brain encodes and retrieves memories. However, to our knowledge, no one has attempted to understand how the patterns observed using these techniques are related to underlying differences in gene expression between brain regions or between individuals. Further, there is considerable heterogeneity among individuals for fMRI and intracranial EEG responses during the encoding and retrieval of memories; a direct comparison of fMRI and iEEG and employing gene expression profiles may provide an explanation for some of this variance. This proposal brings together expertise from across three disciplines (fMRI, direct human electrophysiology, and gene expression quantification) and across institutions in an effort to obtain pilot data to develop a comprehensive understanding of human brain processes during the encoding of episodic memories. We propose to test patients who will undergo stereo electroencephalography (SEEG) electrode implantation as part of an attempt to localize an epileptic focus; these patients will be drawn from the epilepsy surgery program at UT Southwestern. Patients will undergo a pre—operative fMRI as they perform the free recall task, a standard test of episodic memory. This will be performed at the Center for Advanced Imaging Research under the direction of Dr. Rugg, who possesses extensive experience in performing fMRI for episodic memory. After stereo EEG electrode implantation, the patients will perform the same episodic memory task as direct brain recordings are made using the clinical electrode array. Dr. Lega is a neurosurgeon with extensive experience in both performing the stereo EEG surgery and analyzing intracranial brain oscillations looking for patterns unique to successful item encoding. The most robust of these patterns is the gamma band subsequent memory effect. We will compare activity within locations and connectivity among brain locations (especially hippocampal connectivity) between fMRI and iEEG. For this we will use the psychophysical interaction analysis method for fMRI data. For electrophysiological analyses, we will use signal processing metrics such as synchrony, coherence, and phase—amplitude coupling. While activity *within* brain areas shows disparity between fMRI and iEEG, We hypothesize that hippocampal connectivity metrics (changes in connectivity during memory encoding) will be consistent between these modalities. When these patients go on to a resection of brain tissue, we will collect a specimen immediately at the time of surgery for the analysis of whole genome expression profiles. This will be led by Dr. Konopka, who has extensive experience in performing the requisite RNA assays and in correlating these data with behavioral activity. Based on preliminary data, we hypothesize that genes related to ion channel regulation will be most highly correlated with electrophysiolgical and fMRI signal during episodic memory encoding.

Significance

The data we hope to obtain in this pilot proposal will be useful to better understand how fMRI BOLD metrics of memory encoding are related to underlying physiology. This is important for developing non—invasive methods for accurately predicting the magnitude of functional memory deficits after seizure surgery. Further, improving our understanding of network—level interactions during the encoding and retrieval of memories will help develop new strategies for neuromodulation which may provide new therapeutic options for patients suffering memory loss due to epilepsy, brain injury, and degenerative processes. Finally, this proposal will generate “first of its kind” data examining how BOLD and iEEG signals during memory encoding are related to underlying gene expression profiles. This may identify targets for further investigation as well as genes of interest for the development of therapeutic interventions targeting the involved proteins. We believe the novelty of our proposal and the potential impact of the data, along with the complex cross—institutional collaboration required to execute it, make it an excellent candidate for UT BRAIN funding.