Title: Memory, epilepsy, and brain stimulation: oscillatory correlates of episodic and spatial encoding and retrieval in chronically implanted human epilepsy patients

Project summary:

Brain stimulation therapy in epilepsy patients is known to reduce seizures, but little is known about how such treatments might affect cognitive impairments associated with epilepsy. For example, epileptics often have substantial impairments in memory performance, which can in some cases be even more devastating for patients than the seizures themselves. This project is aimed at elucidating the oscillatory correlates of episodic and spatial encoding and retrieval in epilepsy patients with and without memory dysfunction. We will focus our study on patients with temporal lobe epilepsy who have been surgically implanted with a self-contained ambulatory electrocorticographic recording device (RNS®, Neuropace Inc.). Our central hypothesis is that brain stimulation therapies, which have been previously designed and calibrated with the sole goal of reducing the number of seizures, may also recalibrate to also correct memory dysfunction by restoring healthy oscillations. We will test this hypothesis and develop appropriate stimulation therapies through four specific aims: 1. Determine the oscillatory markers of short and long term free recall including the oscillations of especially disabling long-term accelerated forgetting. 2. Determine oscillatory markers of real world spatial navigation and memory as compared with virtual navigation. 3. Determine the influence of abnormal interictal epileptiform discharges on spatial memory and free recall. 4. Study whether scheduled hippocampal stimulation or responsive stimulation has an effect on memory acutely and long term. We will develop a series of experimental paradigms to test and examine patients’ episodic and spatial memory function. The patients’ memories will be tested at a variety of intervals, ranging from a few seconds up to 30 days, in order to estimate the effective viability of encoded memories. A critical component of each of these aims is to develop a clear understanding of how epileptiform discharges specifically disrupt memory encoding and retrieval, and how stimulation might be used to correct such disruptions. Our approach is innovative in that the Neuropace device will enable us to record and stimulate using implanted electrodes in chronically implanted, freely moving, humans. Further, it provides a clinically feasible means of using brain stimulation to enhance patients’ memory function in the long term (e.g. once the patients leave the hospital). Our proposed research is significant because the results of our study will inform the future design of brain stimulation devices used to treat epilepsy (and possibly for other disease states). The opportunity to study the detailed electrophysiological correlates of memory encoding and recall using implanted electrodes in “freely ranging humans” will provide unprecedented real-world, longitudinal data to facilitate our understanding of human memory.

Project narrative:

The memory impairments associated with epilepsy are often more debilitating than the seizures themselves. Brain stimulation therapies have been shown to reduce seizures, but more research is needed to understand whether and/or how brain stimulation might be used to restore full cognitive function to epilepsy patients. Our proposed research is aimed at elucidating our basic understanding of how epileptic activity disrupts memory function, and how stimulation therapies may be used to restore memory function in epilepsy patients. Our proposed research is critical to public health and the NIH's mission, because in addition to contributing substantially to the field’s understanding of memory encoding and retrieval, our research is likely to have direct applications to helping to correct memory impairments in epilepsy patients. The work will usher in a new line of “electrotherapeutic” devices intended to not only reduce seizures, but also to restore cognitive function.