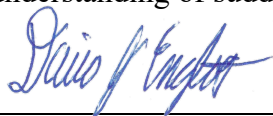Analysis of Subcortical Arousal System Connectivity in Temporal Lobe Epilepsy

Hernán F. J. González

Dissertation under the direction of Dr. Dario J. Englot

Temporal lobe epilepsy (TLE) is the most common form of epilepsy, a debilitating disease that affects 50 million people globally. In TLE, seizure onset is typically localized to an epileptogenic zone (EZ) in the mesial temporal lobe. Unfortunately, the negative effects of TLE are not limited to the EZ. Previous studies have shown widespread neocortical decreases in resting state functional connectivity (RSFC) in patients with TLE versus healthy controls and have related these RSFC decreases to neuropsychological impairments. Prior works have resulted in the "network inhibition hypothesis," that proposes that focal seizures may influence widespread neocortex by affecting deep arousal structures that are important for cortical activation. This research hypothesized that recurrent seizures in TLE result in altered connectivity between arousal structures and the neocortex, leading to decreased neocortical connectivity and impaired neurocognition. To test this, connectivity networks of subcortical arousal structures were examined using functional magnetic resonance imaging RSFC in TLE. Specifically, RSFC of brainstem arousal nuclei was examined before and after surgery in patients with TLE. Then, the effects of epilepsy surgery on RSFC of thalamic arousal nuclei were studied using a novel participant-specific thalamic nuclei atlas. Subsequently, in patients with TLE, using advanced network analyses, the role of the nucleus basalis of Meynert as a key node in abnormal connectivity networks was defined. Tying these studies together, the relationship of the abnormal connectivity between these arousal structures and intrinsic connectivity networks was related to impaired neurocognition. In summation, studying arousal network dysfunction in TLE may lead to improved neurosurgical treatment or behavioral therapies for this disorder, novel neuromodulation targets, and may improve the mechanistic understanding of sudden unexpected death in epilepsy.

Approved _____ Date March 1, 2021

Dario J. Englot, M.D., Ph.D.