Benjamin F. Gruenbaum, MD
Yale University School of Medicine, New Haven, CT
Neuronal Mechanisms of Unconsciousness in an Absence Seizure Model

Abstract

Each year, millions of people undergo general anesthesia. The fundamental mechanisms by which anesthetics induce unconsciousness, however, remain largely unknown. Several animal models of unconsciousness have been used to study these mechanisms, but are greatly limited by unwanted effects on cerebral blood flow and metabolism. In our laboratory, we use an absence seizure model to elucidate the neuronal mechanisms of unconsciousness, which is advantageous in that unconsciousness is achieved spontaneously with minimal systemic effects. Like other conditions associated with unconsciousness, the unconscious state induced by absence seizures is known to arise in the thalamocortical network, regulated by unknown neuronal mechanisms. Previous absence seizure animal models explored these mechanisms under general anesthesia, resulting in fMRI patterns that differed from unanesthetized human absence seizures. We recently habituated genetic absence epilepsy rats from Strasbourg (GAERS) to electrophysiologic, hemodynamic and behavioral testing while awake. Our strong preliminary data demonstrate that, without anesthetics, the absence seizures now closely resemble absence seizures observed in humans. Here, we propose to use our awake rodent model to define how auditory inputs are processed in the cortex during absence seizures by recording single cortical neurons during an auditory tone detection task in awake GAERS. The results will reveal the neuronal changes in sensory input processing that underlie alterations in consciousness during absence seizures. We expect that our findings will have broad applications to other conditions of unconsciousness and facilitate the development of novel, targeted therapeutic and anesthetic agents.