Astrocytic Involvement with Glutamatergic Excitotoxicity following Cortical Spreading Depolarization

Misha Lockamy and C. William Shuttleworth

Department of Neurosciences, University of New Mexico School of Medicine, Albuquerque, NM

Spreading depolarization (SD) is a neurological anomaly, involving near-complete failure of neuronal and glial ion-homeostasis, that propagates in waves across the cortical surface of the brain. It has thus far been detected primarily in collaboration with such events as migraine, subarachnoid hemorrhage, stroke and traumatic brain injury (TBI). The recovery outcomes of TBI are strongly correlated with the prevalence of SD, yet there is still no definitive medical intervention in place. As a result, there is currently a great deal of interest in discovering the mechanisms responsible for the deleterious effects of SD and determining the existence of potentially beneficial ones. My project seeks to investigate the astrocytic contribution to SD and to the recovery from the changes associated with it. Following a summer of rigorous analysis of the available literature on astrocytic activity accompanying SD, we have determined the role of astrocytes to be a substantial target for potential medical response. The pathophysiology of SD may be homologous to the surge of excitotoxic glutamate, and to astrocyte swelling. In a normally functioning central nervous system (CNS), astrocytes are the glial cells primarily responsible for monitoring many of the processes that malfunction during SD and may play a sizable role in the rehabilitation from these events. My initial immunohistochemistry research will include fluorescence confocal microscopy images of GFAP labeled mouse model brain slices to examine the morphology of control astrocytes in comparison with those following the experience of chemically induced SD. GFAP will serve as an astrocyte activation marker to evaluate the relationship between SD recovery and its potential benefits. In conjunction, the effects of astrocytic metabolic compromise on glutamate efflux following SD will be examined by pharmacologically inhibiting mitochondrial function using fluoroacetate (FA), while measuring extracellular glutamate with a fluorescent sensor (iGluSnFr). This research will test my hypothesis that astrocytic functioning is intensely intertwined with the progressive stages of SD and may support future research efforts involving improved outcomes for a variety of neurological damage, diseases and disorders.

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