2019 State NMJAS Research Paper Competition Winner
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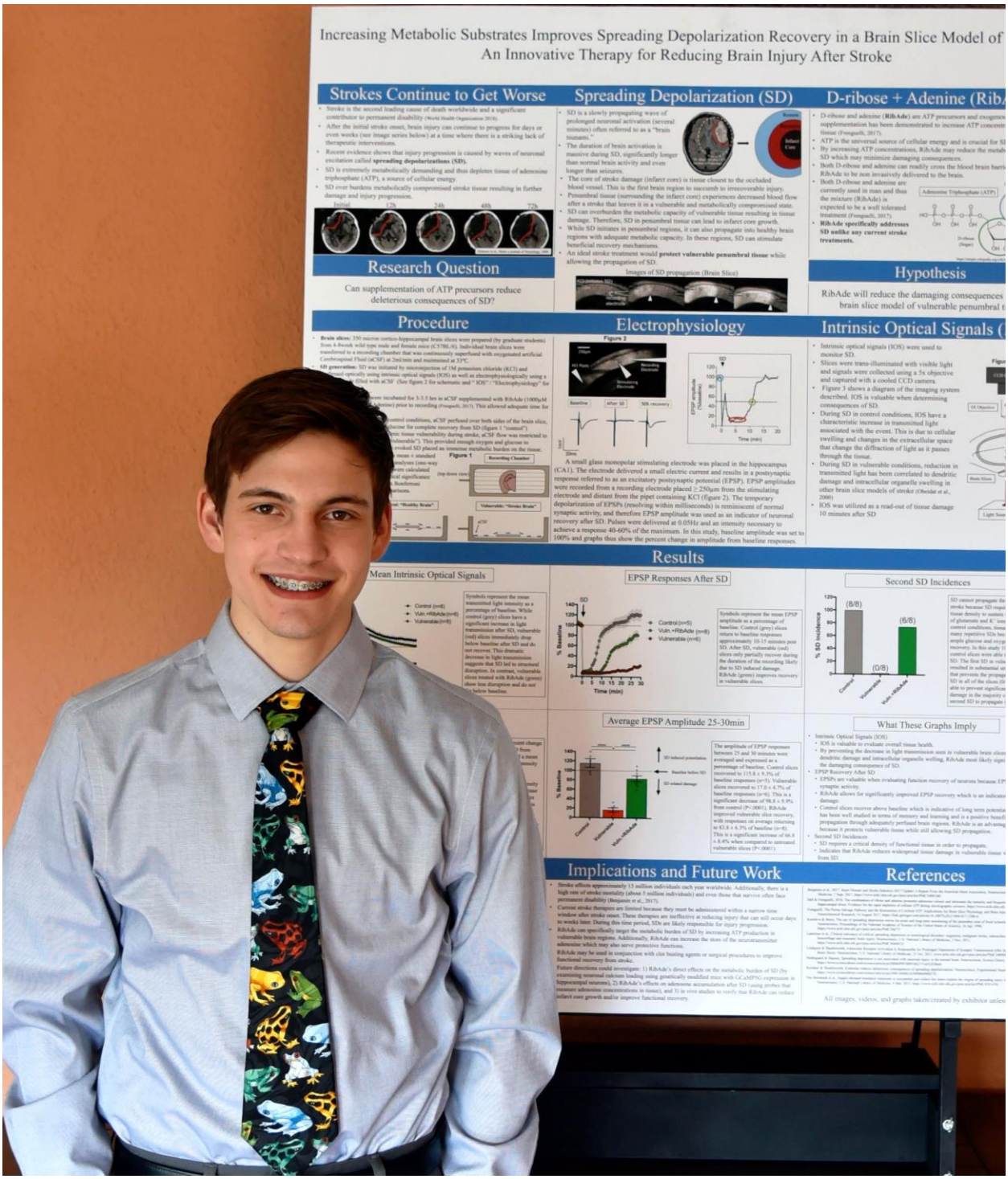

Increasing Metabolic Substrates Improves Spreading Depolarization Recovery in a Brain Slice Model of Stroke: An Innovative Therapy for Reducing Brain Injury After Stroke

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Worldwide, stroke is the second leading cause of death and the third leading cause of disability with approximately 15 million strokes reported each year. Recent work has demonstrated that an event in the brain referred to as a spreading depolarization (SD) is a significant contributor to injury progression in the days to weeks after stroke onset. SD, often referred to as a brain tsunami, is a slowly progressing wave of coordinated neuronal and glial depolarization. Even in the healthy brain, SD is extremely metabolically demanding and can deplete the building blocks of adenosine triphosphate (ATP), a source of cellular energy. In tissue compromised by a stroke or other acute brain injury, SD overburdens the metabolic capacity of tissue and results in irrecoverable injury. Clinically, there are no treatments available that target SD specifically. In this work, the exogenous supplementation of the mixture of the ATP precursors, D-Ribose and Adenine (RibAde), prior to SD was examined. RibAde supplementation has been shown to increase ATP production in brain tissue, and thus may reduce damaging consequences of SD in stroke conditions. Electrophysiology and transmitted light imaging were used to evaluate SD initiated by potassium chloride microinjection in metabolically compromised mouse brain slices. Exposure to RibAde improved recovery of brain slices likely by increasing ATP availability. These findings suggest that Adenine and D-ribose supplementation reduce the damaging consequences of SD in vulnerable tissue and may pose as an innovative approach in the treatment of ischemic stroke and brain injury worldwide.