

# An Investigation into the Current Use of Caffeine as a Migraine Treatment and Its Effects on Spreading Depolarizations: A Second Year Study and the Introduction of a Novel Therapy

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Migraines are the third most prevalent illness in the world, and migraine symptoms (e.g. severe pain, visual disturbances, nausea, and cognitive impairments) all impede daily life. At the neurological level, migraines are caused by a slowly progressing, wave of coordinated depolarization of neurons, referred to as a spreading depolarization (SD). SD places enormous metabolic demands on the brain, requiring blood vessels to dilate in order to provide oxygen and energy (i.e. adenosine triphosphate, ATP) necessary for repolarization. Blood vessels dilation produces migraine pain while depolarization causes the mental effects. SD is caused by overstimulation of neurons and imbalances of highly regulated neurotransmitters. A byproduct of cellular respiration is adenosine which activates adenosine 1 (A1) receptors and slow neuronal activity. This reduction may be an important protective mechanism to promote recovery. Caffeine, an A1 receptor antagonist and current migraine therapy, may disrupt protective cellular mechanisms necessary for recovery. In this work, the effects of caffeine were compared to Dipropylcyclopentylxanthine, a specific A1 receptor antagonist. SD characteristics were studied using transmitted light imaging, and electrical monitoring of brain tissue. Results suggest caffeine may be an undesirable treatment for migraines by negatively impacting recovery following SD. SD places such high metabolic demand on tissue, it is thought that ATP and ATP precursors are depleted which delays recovery. In this work the supplementation of the ATP precursors adenine and D-ribose was also studied. Results suggest that supplementation of ATP precursors positively impacts recovery and may pose a more beneficial therapy for recovery following SD. ,

## Awards Won:

Third Award of \$1,000

American Physiological Society: APS Exceptional Science Award for \$500