University of Rochester
Department of Biomedical Engineering

M.S. Defense Seminar

"Systemic Pituitary Adenylate-Cyclase-Activating Polypeptide (PACAP) and Calcitonin Gene-Related Peptide (CGRP) effects on balance and auditory sensitivities in preclinical migraine models"

by

Abigail Dweh

Supervised by: Dr. Anne Luebke

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2-6424 Medical Center

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Abstract:

Migraine is a prevalent neurological disorder, affecting 18% of females and 6% of males. Vestibular migraine (VM), characterized by episodic vertigo and balance impairments, affects ~3-4% of the population. Moreover, migraine and VM are disorders associated with increased motion sensitivity leading to symptoms of imbalance. Neuropeptides such as calcitonin gene-related peptide (CGRP) and pituitary adenylate cyclase-activating polypeptide (PACAP) are implicated in sensory hypersensitivity associated with migraines. While CGRP has been extensively studied in migraine pathophysiology, the role of CGRP and PACAP in balance and auditory sensitivities remain underexplored. Antagonism of CGRP signaling is an established therapy, but not all patients respond. In this study, we compared systemic PACAP and a blocker of PAC1 receptor with systemic CGRP and blocker of CGRP receptor to investigate imbalance and auditory sensitivities in mice. As behavioral surrogates, we performed center of pressure (CoP) postural sway and balance beam walking and auditory brainstem response (ABR) experiments in male and female C57B/6 mice. Mice were evaluated in these assays following intraperitoneal (IP) injections of i) vehicle control, ii) CGRP (0.1 mg/kg) (Sigma-Aldrich), or iii) 0.3 mg/kg PACAP-38 (Bachem) and corresponding blockers.

Our findings indicate that IP PACAP-38 significantly increased postural sway and caused balance beam imbalances. Our findings provide preclinical evidence supporting a potential role of PACAP-38 in vestibular migraine pathophysiology.