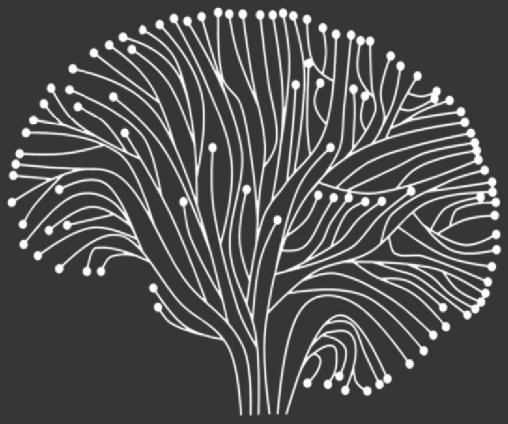

SAN2024

XXXIX Annual Meeting
Ebook

October 25th – 27th IFIBYNE Auditorium

Ciudad Universitaria, Universidad de Buenos Aires

D-020 | IMPAIRMENT OF THE MEDIAL OLIVOCOCHLEAR SYSTEM MATURATION DUE TO KCNQ4 DEFICIENCY

Cellular and Molecular Neurobiology

Author: Ezequiel Ignacio Rías | Email: e.rias@hotmail.com

Ezequiel Rías1°2°, Ingrid Ouwerkerk2°, Guillermo Spitzmaul1°2°, Leonardo Dionisio1°2°

1° Instituto de Investigaciones Bioquímicas de Bahía Blanca (INIBIBB), CONICET-UNS

2° Departamento de Biología, Bioquímica y Farmacia (BByF), Universidad Nacional del Sur

The medial olivocochlear (MOC) system regulates outer hair cell (OHC) excitability. In response to sound overstimulation, MOC activates Ca2+ influx through nicotinic acetylcholine receptors, which stimulates BK and SK2 channels, helping KCNQ4 to remove K+ and restoring membrane potential. KCNQ4 absence results in chronic depolarization, OHC damage, and hearing loss. We evaluated how the absence of KCNQ4 affects the organization and function of the MOC system. Confocal imaging was used to analyze MOC terminal locations on OHC in Kcnq4+/+ (WT) and Kcnq4-/- (KO) mice at 2, 3, 4, and 10 postnatal weeks (W). At 2W, both genotypes have 49% of synaptic contacts in the basal domain and 51% in the lateral domain. In mature animals (≥3W), WT show all terminals in the basal domain, whereas KO kept 8.7%, 16.5%, and 2.9% in the lateral domain at 3, 4, and 10W, respectively. KO mice also had fewer and smaller synaptic contacts per OHC at 4 and 10W compared to WT. Similar results were found in inner hair cells. Using qPCR we demonstrated that, KO mice had a 6-fold decrease in α10 subunit mRNA, with α9 unchanged, and a 3-fold decrease in BK and SK2 at 4W. By 10W, all tested genes returned to WT levels. Additionally, BK protein was also mislocalized, and some Ca2+-associated proteins showed altered expression at 4W in KO mice. These findings indicate that chronic depolarization alters MOC system development and efferent components expression, leading to functional impairment and hearing loss.