manitoba neuroscience network

Regulation of neuronal oxytocin receptor and novel lipid organizers of synaptic transmission

SEMINAR & VISITING SPEAKER SERIES

DATE Monday, May 6th, 2024

TIME 11:00 AM to 12:00 PM

LOCATION CHOWN A207 A&B

SPEAKER

Mohiuddin Ahmad, MBBS, PhD

Assistant Professor, Department of Cell Biology, University of Oklahoma Health Science Center

BIO

I obtained my medical degree from Jawaharlal Nehru Medical College at Aligarh Muslim University in India. I received my PhD in Neuroscience from Georg-August University, Goettingen, Germany with my thesis work on the role of neurexin family of proteins in synaptic transmission. For my postdoctoral training, I joined the laboratory of Robert C Malenka at Stanford University where I worked on the mechanisms underlying long-term synaptic plasticity. I made key discoveries regarding the trafficking of AMPA receptors during synaptic plasticity, including the role of complexin in mediating AMPA receptor exocytosis during long-term potentiation (Ahmad et al., 2012), and the role of Rab11Fip5 during long-term depression (Bacaj et al., 2015). I then joined the University of Oklahoma Health Sciences Center as an Assistant Professor. In my laboratory, I run a cutting-edge program in synaptic physiology. My laboratory has identified the role of neuroligin-2 in controlling the excitatory-inhibitory balance in the lateral septum (Troyano-Rodriguez et al., 2019a), the role of membrane protein PRRT1 as a critical regulator of AMPA receptor trafficking during long-term depression (Troyano-Rodriguez et al., 2019b; Martin et al., 2021), and the function of very long chain fatty acids in regulating synaptic transmission and plasticity (Nagaraja et al., 2021; Nagaraja et al., 2023). My laboratory also has a major focus on the neuromodulation mediated by oxytocin acting on the oxytocin receptor in the brain. In projects funded by the NIH and the Whitehall Foundation, we are working to elucidate the intracellular mechanisms that regulate the trafficking and activity of oxytocin receptors in neurons (George et al., accepted, Hoang et al., under review). My work utilizes multidisciplinary approaches including brain slice patch-clamp electrophysiology, in vivo molecular manipulations, microscopic imaging, receptor trafficking assays, and biochemical methods.

ABSTRACT

I will present the current work in my laboratory focused on two major themes. First, I will describe our latest findings on the intracellular mechanisms that regulate oxytocin receptor (OXTR) in neurons. We have identified robust and rapid-onset desensitization of OXTR response in multiple regions of the mouse brain. Both cell autonomous spiking response and presynaptic activation undergo similar agonist-induced desensitization. We identified that G protein-coupled receptor kinases (GRK) GRK2, GRK3, and GRK6 are recruited to neuronal OXTR following agonist binding, and their catalytic activity is required for agonist-induced desensitization and internalization in neurons. In contrast, beta-arrestin-1 and -2 are redundant for these processes, even though they are recruited readily to neuronal OXTR. I will present data on identifying a parallel pathway that may explain redundancy of beta-arrestins. This work defines unique aspects of the mechanisms governing OXTR regulation in neurons and has implications for advancing treatment strategies for autism spectrum disorder. In the second half of the talk, I will present the results of our efforts in determining the function of an understudied class of lipids called very long chain fatty acids in synaptic transmission and plasticity. The importance of these fatty acids is underscored by the fact that mutations of the enzyme ELOVL4 that mediates their biosynthesis results in neurological disorders, spinocerebellar ataxia (SCA34) and neuroichthyosis. Using animal models engineered to carry disease-associated mutations in Elovl4 gene that recapitulate these disorders, we have identified synaptic defects in the cerebellum and hippocampus. These defects include synapse-specific alterations in release probability, changes in vesicle pool size and reduction in dendritic spine density. These findings advance our understanding of the synaptic mechanisms regulated by very long chain fatty acids and describe the synaptic dysfunction that leads to ataxia in SCA34 and seizures in neuroichthyosis.

OBJECTIVES

1. Determine the intracellular mechanisms that regulate oxytocin receptor signaling and trafficking in neurons and the brain.

2. Determine the role of very long chain fatty acid-containing lipids in synaptic transmission and plasticity.

3. Decipher the mechanisms mediating AMPA receptor trafficking during synaptic plasticity

For more information:

T: 204-235-3939
E: info@manitobaneuroscience.ca

https://www.linkedin.com/in/mohiuddin-ahmad-67055920/
Website: https://basicsciences.ouhsc.edu/cb/People/category/primary-faculty/mohiuddin-ahma

Hôpital St-Boniface Hospital
RECHERCHE • RESEARCH
Division of Neurodegenerative Disorders

Health Sciences Centre Winnipeg

University of Manitoba