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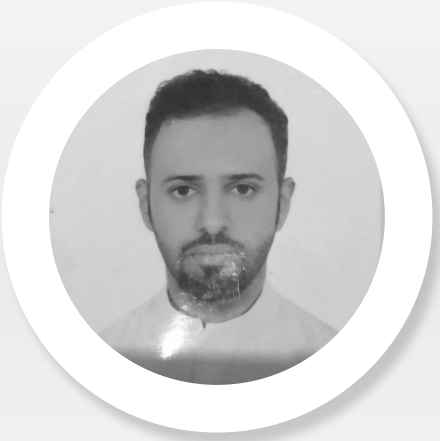

Fahad Somaa
King Abdulaziz University, KSA

Primary cilia-related genes and neonatal anesthesia neurotoxicity in congenital heart disease

A recent study found that protein-damaging de novo gene mutations are strong predictors of neurodevelopmental anomalies in CHD. At least 15% of these genes found to be associated with primary cilia structure and/or function. Interestingly, primary cilia play a key role in protecting neurons exposed to alcohol. Hence studying the combined effect of anesthesia and primary cilia gene mutation will determine the way by which CHD genetic alterations identified in CHD patients with neurodevelopmental abnormalities affect the molecular and cellular programs underlying brain development. Using conditional knockout mice; in which primary cilia are lost specifically in cortical excitatory neuron or gender matched heterozygous, we injected either saline or ketamine intraperitoneally at postnatal day 7 (P7). We examined caspase-3, fractin and cleaved tubulin, at P8 in the medial prefrontal cortex. At P30, mice were behaviorally tested using water T-maze. To assess the impact of primary cilia mutation and anesthesia on pyramidal neurons and their dendritic morphology, we used two other inducible cre-lox mice to specifically label layer II and layer V and cross it with flox mice. We found significant enhancement of caspase-3, fractin and cleaved-tubulin immunoreactivity in the knockout mice that are exposed to ketamine (cKO+Ket) compared to the other three groups (HT+PBS, HT+ket, and Cko+PBS). All groups displayed similar spatial memory performance during the acquisition stage, while in the reversal learning stage Cko+Ket mice failed to learn the task compared to other groups indicating a cognitive deficit in this treatment group. Our preliminary data showed that the primary cilia play a key role to protect cortical neurons from anesthesia-inducible neurodegeneration in the developing brain in layer II & V. We also found that dendrites morphology was only affected in ketamine injected primary cilia mutated mouse.

Biography

Fahad Somaa has completed his PhD from University of Melbourne and Post-doctoral studies from Children's National Medical Center affiliated with George Washington University. He is currently working as an Assistant Professor at King Abdulaziz University in Saudi Arabia. He has published 4 papers in reputed journals.

fsomaa6549@gmail.com

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