The Effect of NMDA Receptor Blockade on Neurogenesis and Neural Crest Development

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The NMDA receptor (NMDAR) plays an integral role in neuronal communication and neurodevelopment, and its malfunction has been linked to multiple neurodevelopmental diseases (NDDs) including autism spectrum disorder (ASD). Each receptor possesses a calcium ion channel, and an intracellular Carboxyl-terminus domain (CTD) that interacts with intracellular scaffolding and signaling proteins. Despite being a nearly ubiquitous receptor, little is known about the NMDAR's role in neurogenesis and neural crest development. Using the NMDAR antagonist MK-801 on the model organism zebrafish, the function of NMDAR as a Ca2+ channel was blocked, thus limiting the function of NMDAR to solely interactions with interior scaffolding proteins. Following NMDAR blockade, statistically significant increases in neuron quantity, pigmentation, cartilage formation and activity were observed. Additionally, zebrafish swimming patterns were classified and recorded using a novel ordinal scale, and analysis yielded distinct swimming patterns in treated zebrafish. These results suggest that the Ca2+ channel plays a critical role in regulating both neurogenesis and neural crest development, as pigmentation and cartilage are both neural crest derived cell types. The traits generated as a result of the Ca2+ channel blockade phenotypically resemble traits displayed by individuals with NDDs including increased neuronal densities, craniofacial abnormalities, and a hyperexcitable nervous system, suggesting that the Ca2+ channel malfunction is at the root of these diseases. Understanding the exact mechanisms by which the NMDAR dysfunction contributes to disease pathogenesis is crucial to the development of effective preventative and therapeutic treatments for patients with NMDAR mutations and NDDs.

Awards Won:
Third Award of $1,000