Loss of NMDA Receptor Signaling Results in Excess Proliferation of CNS and Neural Crest-Derived Cells

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In this study the N-Methyl D-aspartate (NMDA) receptor was perturbed, and the resulting phenotypic effects were studied. It was hypothesized that the role of the NMDAR in neurodevelopmental cell proliferation is to regulate the process by slowing down cell cycle progression. Embryonic zebrafish were used as the model organism for analysis due to their lifelong neurogenesis, external, rapid, and transparent development, and their pliancy to genetic manipulation. To quantify these various effects caused by the mutation of NMDARs a further inquiry into the loss of regulation in the CNS, the effects on an anatomical level, and the function and progeny of neural crest cells was completed through the analysis of confocal images. These images revealed a statistically significant increase in neuronal cell density in the forebrain and the hindbrain of the mutants, with one p-value less than 0.01, and the others less than 0.0001. Confirming receptor perturbation led to uncontrolled neuronal cell proliferation. There was no statistical difference in external brain proxy measurements, confirming that increased cell density resulted from uncontrolled cell proliferation. Furthermore, the discovery of increased pigmentation and craniofacial cartilage suggests the mutation resulted in dysregulated neural crest development. While numerous NMDAR mutations are already associated with neurodevelopmental disorders, the full disease etiology is not yet fully understood. Many symptoms of neurodevelopmental disorders are related to sensory processing, and numerous birth defects arise from malformations of the craniofacial cartilage. This novel data associates NMDAR disruption with sensory dysregulation in neurodevelopmental diseases and craniofacial defects.

Awards Won:
Third Award of $1,000