The Effect of N-methyl D-aspartate Receptor Shutdown on Neural Stem Cell Proliferation in Zebrafish Larvae

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Neurogenesis is highly crucial to the success of the nervous system, and perturbation of this process has the potential to elicit disease states. A better understanding has implications for discovering treatment opportunities for neurodevelopmental and neurodegenerative disorders. NMDA receptors are critical in mediating development and higher brain function, but much remains unknown regarding their role in neurogenesis. Therefore, by using a previously established zebrafish model to repress receptor function, I examined their effect on neuroepithelial cells and radial glial cells, which serve as the principal drivers of neurogenesis and can therefore paint a picture of the process upon receptor disruption. I quantified fluorescent images (provided by my mentor) derived via immunohistochemistry to determine cells marked positive for PCNA and/or S100ß. Multiple t-tests revealed few significant differences between the wild type and mutant zebrafish forebrains, however cell quantifications in the midbrain regions were significant; in the anterior midbrain of the mutant, more cells are present ($p=0.0122$) and actively proliferating ($p=0.0035$). The posterior midbrain of the mutant zebrafish did not contain a significantly greater amount of neural stem cells ($p=0.2104$), but mitotic activity was significantly upregulated ($p=0.0107$). The results of this study suggest that neurogenesis is regulated within a temporospatial gradient, along which the relative percentage of dividing neural stem cells increases caudally. This study contributes to the overarching goal of understanding neurogenesis within the zebrafish brain, as knowledge in this area allows us to better exploit the zebrafish model to yield information about the human brain.

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