ENRICHMENT-MEDIATED NEUROGENESIS IS IMPAIRED IN THE VENTRAL HIPPOCAMPUS IN A MOUSE MODEL OF FETAL ALCOHOL SPECTRUM DISORDER (FASD) AND POTENTIAL THERAPUETIC INTERVENTION

Authors: A.M. Rodriguez; L. Li; L.A. Cunningham

Affiliations:
University of New Mexico Medical School, Department of Neurosciences, Albuquerque, NM 87557, USA

Abstract:
Fetal alcohol spectrum disorder (FASD) is a leading cause of preventable intellectual disability and neural developmental disorders. Depression and anxiety are the most common mental illness in people with FASD. These disorders are related to ventral hippocampus function. The hippocampus is unique in its ability to produce new neurons throughout life. In fact, part of the therapeutic effect of some common antidepressants is to increase neurogenesis. Previous research conducted by our lab has shown that in a mouse model of FASD, enriched-environment (EE) mediated neurogenesis in the dorsal hippocampus is inhibited, this correlates with impaired pattern discrimination learning (Gustus et al., 2020). However, EE mediated neurogenesis of the ventral hippocampus has not been studied in a FASD model. Here, we tested the hypothesis that EE-mediated neurogenesis is impaired in the ventral hippocampus of prenatal alcohol exposed PAE mice. We utilized Nestin-CreER^{T2}:tdTomato mice as a means to label adult-generated hippocampal DGCs after PAE and placement in EE. tdTom+ DGCs in the ventral hippocampus were quantified histologically. We found that PAE had no significant (Tukey Post-Hoc, P=0.97) impact on neurogenesis under SH conditions (SAC-SH: M=93.0, SD = 56.91, N=5; PAE-SH: M=81.75, SD = 33.45, N=4), but significantly impaired (P= 0.01) the neurogenic response to EE (SAC-EE: M=173.9, SD = 21.44, N=5; PAE-EE: M=76.55, SD = 24.77, N=4). As ventral and dorsal EE mediated neurogenesis is impaired in PAE mice, we are currently studying if the use of the antidepressant fluoxetine will reinstate this neurogenesis.

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Non-expert Summary

The brain continues to produce new neurons in the area called the hippocampus. This area is involved in memory and learning, but also in depression and anxiety. People with FASD are more likely to experience depression and anxiety. We found that the area of the hippocampus involved in anxiety and depression doesn't produce neurons as it is supposed to when mice are placed in a cage with social and physical enrichment.