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Effects of Ethanol on Social Behavior & Brain Structure

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Honors Capstone Project in _____Biochemistry_____

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Abstract

Autism spectrum disorders are a developmental disorder characterized by abnormal social behavior. Those with autism have problems with social interactions, repetitive behaviors, and both verbal and non-verbal communication. While the cause of autism is not yet know, studies have shown that there are both genetic and environmental factors linked with autism. The amygdala is considered to be part of the "social brain", and atypical activation and morphology of the amygdala has been seen in those with autism.

For this research project, I utilized rats subjected to acute ethanol exposure during gestation and examined exposure effects on the anatomy and biochemistry of the brain. Acute ethanol exposure allows a more direct examination of vulnerable windows of neuronal development, and previous studies have shown that ethanol exposure on specific gestation dates results in abnormal social behavior and neurological alterations similar to those seen in those with autism. Therefore, for this research project it was hypothesized that the atypical behaviors are due to alterations in the amygdala structure and protein expression in synaptic terminals. The different gestation ages when the rats are exposed to ethanol were gestation days G12 and G15, which correspond to early part of development in the amygdala and peak neuronal development in the amygdala respectively. Testing of social behavior was conducted on the two different postnatal days P42 and P75, corresponding to late adolescence and adulthood respectively. The objective for this project is to compare and contrast the effect of timing of ethanol on anatomical and biochemical makeup of the amygdala.

To examine the anatomical structure of the amygdala, cytoarchitectonics was utilized on histochemically stained 12 mm sections of brain tissue collected following the social behavior tests. Sections containing the central nucleus of the amygdala were examined to determine the volume of the central nucleus, neuron packing density in the central nucleus, and the total number of neuron in the central nucleus of the amygdala. The biochemistry of the amygdala was analyzed using western blotting, in which a protein assay was run on excised punches of the central nucleus of the amygdala. The target proteins probed for were c-Fos, α-Synuclein, GABA-A receptor, and PSD-95 MAGUK scaffold protein to investigate the brain region activation and pre-synaptic & post-synaptic terminals.

The anatomical analysis results of the central nucleus for the G12 treated group indicated a significant age effect, with a lower number total number of neurons and lower neuron packing density at P75 than P42. The analysis of the expression of the alpha1 subunit of the GABA-A receptor in this project suggests that ethanol exposure causes a decrease in expression of the GABA-A receptor. These effects were seen at both early and peak neuronal development in the amygdala (G12 & G15), indicating that the GABA system is a target of prenatal ethanol exposure. Also, protein expression analysis of c-Fos for G15 treated animals resulted in a significantly higher expression at P42 than P75, expression in ethanol treated animals was lower than control, and a age/treatment interaction. In summary, the results from this research project indicated that the timed-ethanol exposure affected the anatomical and biochemical makeup of the central nucleus of the amygdala.

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