



COBRE Investigators

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Title of project: FAS Model: Structure and Function of Prefrontal Cortex

Summary:

Fetal alcohol spectrum disorder (FASD) encompasses a range of neurodevelopmental defects resulting from brain damage induced by prenatal alcohol exposure. Primary neuropsychological deficits in patients with FASD include impairments in memory, attention, reaction time, and executive functioning suggesting structural damage to the frontal lobes. Alterations in cell number and glia-neuronal ratio in cortex can contribute to lifelong psychiatric and learning disorders in patients with FASD. In animal models of FASD, such as the rat, it has been shown that the developing forebrain is vulnerable to the effects of alcohol during the period of synaptogenesis (which in humans begins in the third trimester of pregnancy). This vulnerability is signaled by a widespread increase in apoptosis in forebrain areas. It is not known, however, whether the majority of these apoptotic cells are neuronal or glial. Maintaining the proper ratio between the neuronal and glial phenotypes in the cortex is essential for its appropriate functioning. We have recently shown that neonatal alcohol exposure produced an increase in gliogenesis (NG2-expressing glia) in the adolescent motor cortex. We propose to investigate analogous changes in the prefrontal cortex. The proposed project will test the overall hypothesis that alcohol exposure in an animal model of binge drinking during the third trimester of pregnancy shifts glia-neuronal balance in the adolescent prefrontal cortex by increasing the proliferation of glia. Three specific aims will address this hypothesis: (1) we will investigate the effects of postnatal binge-like alcohol administration on neuronal and glial apoptosis in prefrontal cortex, (2) using injections of glutamate antagonist and GABA agonist during the same postnatal period, we will determine the possible mechanism by which postnatal alcohol causes cell death, and (3) we will evaluate the extended effects of neonatal alcohol on glial proliferation in adolescent PFC, where both grey and white matter continue to undergo significant developmental alterations in this critical period. The present study will document the phenotype of proliferating glia and confirm the persistence of new cells in adolescent prefrontal cortex. These data will provide a structural basis for behavioral alterations associated with FASD.