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Prenatal Alcohol Exposure and Placental Insufficiency Result in Altered Dendritic Complexity in Medial Frontal Cortical Neurons in Adult Rat Offspring

Prenatal Alcohol Exposure (PAE) results in deficits in executive functioning. PAE is also associated with placental abnormalities in function and perfusion, deemed placental insufficiency (PI). PI independently contributes to neurodevelopmental deficits. The impact on the combined effects of PAE and PI is unknown. We hypothesized that voluntary moderate PAE+PI would result in decreased neuronal complexity within the medial frontal cortex, a region critical to executive functioning, assessed through use of a three-dimensional (3D) Sholl analysis.

To establish a model of moderate PAE and PI, pregnant Long-Evans rats voluntarily drank 5% ethanol or saccharin water until embryonic day 18 (E18). On E19, an open laparotomy was performed to induce PI via occlusion of the uterine artery for 60 minutes. Pups delivered normally on E22 and weaned on postnatal day 24 (P24). At P100, brains were extracted, and Golgi-Cox staining conducted. Coronal sections of the medial frontal cortex (mFC) were imaged by confocal microscopy using z-stacking capabilities to render 3D images. 3D Sholl analysis was conducted with Imaris software to examine complexity between neurons in the mFC and area 25 of the cingulate cortex (A25).

Analysis of mFC neurons at P100 demonstrated increased proximal apical complexity after PI only, while PAE only and combined PAE+PI demonstrated diminished complexity compared to control. Basal projections of mFC neurons in PAE only and PI only offspring also showed increased complexity relative to controls. Analysis of A25 neurons demonstrated increased proximal apical branching complexity in PAE only compared to PI only and controls, and decreased complexity in PI only compared to combined PAE+PI. The basal dendritic complexity of A25 was not significantly different.

This paradigm demonstrated changes in dendritic complexity within the mFC and A25 that persist into adulthood. Abnormal dendritic arborization may impact the functional circuitry of these regions. Supported by K08 AA030080 and P50 AA22534.