Title: *Long-term effects of Prenatal Alcohol Exposure on GABAergic system in posterior parietal cortex*

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Fetal Alcohol Spectrum Disorders (FASDs) are a group of neurobehavioral deficits including physical, cognitive, learning and behavioral disabilities that persist throughout the lifespan. Our recent investigation showed that moderate prenatal alcohol exposure (PAE) during first and second-trimesters equivalent impairs cognitive control on a touchscreen continuous performance task accompanied by frontal and cortical power alterations. The literature to date had extensively investigated the molecular abnormalities underlying the PAE impairments in cognitive functions mediated by cortical areas, but there are no studies exploring the long-term effects of PAE in the posterior parietal cortex (PPC). The PPC represents one of the major cortical association areas involved in multiple cognitive processes. To address this knowledge gap, using behaviorally naïve control and PAE mice we characterized the GABAergic transmission in PPC. The triple immunostaining revealed that low PAE (BAC of dams ~ 30 mg/dl) induces a significant reduction of parvalbumin (PV^+) and calretinin (CR^+)-expressing GABAergic interneurons in adult animals (~ 3 months old). Next, in order to understand how this interneuronopathy modulates the GABAergic transmission, using a different set of littermates we conducted whole-cell patch clamp recordings in pyramidal neurons expressed in PPC layer 5. Spontaneous inhibitory postsynaptic currents (sIPSCs) were pharmacologically isolated using 50 μM AP5 and 10 μM CNQX to block NMDA and AMPA receptor-mediated currents. Surprisingly, the data collected revealed non-significant changes in sIPSCs measured in PAE animals. Since the PV^+ interneurons produce strong inhibition on pyramidal neurons generating large sIPSCs, we separated small and large events and the analysis did not show a significant treatment effect. Taken together, these findings suggest that the molecular mechanisms underlying the cognitive impairments observed in PAE mice might be mediated by the reduction of interneurons even though there is not a significant alteration in GABAA function measured in pyramidal neurons.

General Summary:

The cognitive deficits observed in Fetal Alcohol Spectrum Disorder (FASD) children can have catastrophic consequences across the lifespan, for this purpose, it is necessary to find targeted therapies. Posterior parietal cortex is a critical brain region involved in multiple cognitive processes including sensorimotor

integration, spatial navigation, decision-making, and movement planning. Investigating the effects of gestational alcohol exposure in this area could provide an important tool for developing new effective therapies.