3-O-E4-1 Oral Sessions

Hypo-serotonergic function is involved in the prenatal valproic acid-induced behavioral changes and hyper-excitation in the prefrontal cortex of mice

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Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder characterized by social deficit and stereotyped, repetitive patterns of behaviors and interests. Maternal use of valproic acid (VPA) during pregnancy is associated with an increased risk of ASD in the offspring. In the pathophysiological hypothesis of ASD, excitation/inhibition (E/I) imbalance is attracted. In this study, we investigated how VPA (500 mg/kg) at embryonic day 12.5 changes the emotional, cognitive and glutamatergic functions in the offspring of mice. Prenatal VPA exposure induced excessive repetitive self-grooming behavior, impairments of social behavior and object recognition memory, increased glutamatergic signaling [*i.e.* phospho-Ca²⁺/calmodulin-dependent protein kinase II (CaMKII) and phospho-protein kinase C (PKC) levels] and decreased serotonin contents in the prefrontal cortex. These results suggested that VPA-exposure induced ASD-like behaviors associated with hyper-excitation of glutamatergic and hypo-serotonergic functions in the prefrontal cortex. Activation of serotonergic system by fluoxetine (20mg/kg) attenuated the VPA-induced ASD-like behaviors and hyper-glutamatergic signaling in the prefrontal cortex. These results suggest that hypo-serotonergic function is involved in the prenatal VPA-induced ASD-like behaviors and hyper-excitation in the prefrontal cortex.