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CHARACTERIZATION OF THE HIPPOCAMPAL ACETYLCHOLINE SYSTEM IN A RODENT MODEL OF FETAL ALCOHOL SYNDROME

ABSTRACT

Fetal alcohol spectrum disorders (FASD) are a major public health concern, as it is estimated that 2-5% of children are exposed to alcohol at some point during prenatal development. FASD have been shown to cause damage to multiple brain regions, but research shows that the hippocampus is especially sensitive to alcohol exposure. This damage to the hippocampus explains, in part, deficits in learning and memory that are hallmark symptoms of FASD. The acetylcholine neurotransmitter system plays a major role in learning and memory, and the hippocampus is one of its main targets. This experiment used a rodent model of Fetal Alcohol Syndrome to examine neurochemical and behavioral changes as a result of developmental alcohol exposure, with a focus on the hippocampal acetylcholine system. Alcohol (3.0 g/kg) was administered via intragastric intubation to developing rat pups (PD 2-10). There were three treatment groups: ethanol-exposed (ET), intubated control (IC), and non-treated control (NC). In Experiment 1, in vivo microdialysis was used to measure acetylcholine release in adolescents (PD 32 and 34). During microdialysis, the effects of a high K⁺/Ca²⁺ aCSF solution (PD 32) and the effects of an acute galantamine (2.0 mg/kg; PD 34) injection on acetylcholine release were measured. Experiment 3 tested whether chronic administration of galantamine (2.0 mg/kg; PD 11-30), an acetylcholinesterase inhibitor, could attenuate alcohol-induced learning deficits in the context pre-exposure facilitation effect (CPFE; PD 30-32). Experiment 2 utilized brain tissue from Experiments 1 and 3 to measure the impact of developmental alcohol exposure and galantamine treatment on expression of choline acetyltransferase (ChAT; medial septum),
vesicular acetylcholine transporter (vAChT; ventral CA1) and the α7 nicotinic acetylcholine receptor (α7 nAChR; ventral CA1). We found that alcohol-exposed animals did not differ in acetylcholine release at baseline, but that alcohol exposure significantly decreased high K⁺/Ca²⁺-induced acetylcholine release while also significantly enhancing acetylcholine content following an acute injection of galantamine. Neither chronic galantamine nor alcohol exposure influenced performance in the CPFE task. Finally, the average number of ChAT+ cells was increased in alcohol-exposed animals that displayed the context-shock association (Pre), but not in the animals that did not learn the task (No Pre), indicating a significant effect of learning on this measure. Alcohol exposure did not significantly alter the density of vAChT or α7 nAChRs in the ventral CA1 region of the hippocampus. Taken together, these results indicate that the hippocampal acetylcholine system is significantly disrupted under conditions of pharmacological manipulations (e.g. high K⁺/Ca²⁺) in alcohol exposed animals. Furthermore, ChAT was up-regulated in alcohol-exposed animals that learned to associate the context and shock, which may account for their ability to perform this task. Developmental alcohol exposure may disrupt learning and memory in adolescence via a cholinergic mechanism.