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POSTNATAL ETHANOL EXPOSURE INDUCES CHRONIC NEUROINFLAMMATION AND IMPEDES HIPPOCAMPAL-DEPENDENT SYNAPTIC PLASTICITY AND LONG-TERM MEMORY IN ADOLESCENT RATS

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Offspring of women who drink while pregnant may suffer from fetal alcohol spectrum disorders (FASD), which includes pervasive and persistent alterations in behavior and cognition. FASD is modelled in rat pups via administration of ethanol (5 g/kg/day) over postnatal day 4 to 9, comparable to the human third trimester. Ethanol induces chronic neuroinflammation in the developing hippocampus, activating the COX-2 enzyme in microglia and the release of pro-inflammatory cytokines (e.g., IL-1β). We recently demonstrated a significant reduction in cytokine gene expression in ethanol-exposed (5E) rats given ibuprofen (COX-2 inhibitor) concurrent with ethanol and, as adolescents, amelioration of trace fear conditioning (TFC) memory deficits. Mast cells (MCs), a novel class of brain-resident immune cells, are also activated by postnatal ethanol. Indeed, postnatal ethanol induces a significant increase in the proportion of degranulated MCs and morphologically activated microglia in the hippocampus of male 5E rats. Both effects are blocked by central injections of cromolyn, a MC degranulation inhibitor, just prior to daily ethanol administration. Intriguingly, IL-1β plays a critical role in the maintenance of NMDA receptor-dependent long-term potentiation (LTP) and the consolidation of long-term memory. Ethanol-induced inflammation in the neonate brain of 5E rats was hypothesized to enhance hippocampal IL-1β release during TFC, impeding synaptic plasticity and memory formation. Our most recent findings confirm this prediction—IL-1β gene and protein expression is elevated in the hippocampus of male (but not female) 5E rats in the 24 hr period following TFC. Pre-training administration of Kineret, an IL-1 receptor antagonist, normalized IL-1β signalling and enhanced long-term memory and TFC test performance in male 5E rats. Collectively, results signify third trimester-equivalent ethanol exposure induces chronic hippocampal neuroinflammation leading, in later life, to aberrant learning-dependent synaptic plasticity and long-term memory in male, but not female, rodents.

Biography

Lindquist D H has received his PhD in Behavioral Neuroscience from Yale University in 2004. Following Postdoctoral Work at Indiana University and the University of Kansas, he joined the Psychology department at The Ohio State University in 2010. Over his career, he has published approximately 20 papers in reputed Neuroscience journals related to the neurobiology learning and memory, neurodevelopment and neuroinflammation.

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