RESVERATROL PREVENTS ALCOHOL-INDUCED COGNITIVE DEFICITS AND BRAIN DAMAGE BY BLOCKING INFLAMMATORY SIGNALING AND CELL DEATH CASCADE IN NEONATAL RAT BRAIN

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Human prenatal ethanol exposure that occurs during a period of increased synaptogenesis known as the “brain growth spurt” has been associated with significant impairments in attention, learning and memory. Recent studies have shown that administration of ethanol to infant rats during the synaptogenesis period (first 2 weeks after birth) triggers extensive apoptotic neurodegeneration throughout many regions of the developing brain and results in cognitive dysfunctions as the animal matures. The present study was designed with an aim to investigate the effect of resveratrol, a polyphenolic phytoalexin (trans-3,5,4-trihydroxy stilbene) present in red wine on alcohol-induced cognitive deficits and neuronal apoptosis in rat pups postnatally exposed to ethanol. Pups were administered ethanol (5g/kg, 12% v/v) by intragastric intubation on postnatal days 7, 8, and 9. Ethanol-exposed pups showed impaired memory in both the behavioral paradigms i.e. Morris water maze and elevated plus maze task. Behavioral deficit in ethanol-exposed pups was associated with enhanced acetylcholinesterase activity, increased oxidative-nitrosative stress, cytokine (TNF-α, IL-1β and TGF-β), NF-κβ and Caspase-3 levels in both cerebral cortex and hippocampus. Chronic treatment with resveratrol (10 and 20 mg/kg) significantly attenuated all the behavioral, biochemical and molecular changes in different brain regions of ethanol administered pups. The major finding of the study is that resveratrol blocks activation of NF-κβ pathway and apoptotic signaling and prevents cognitive deficits in rats postnatally exposed to ethanol.