Ethanol-induced epigenetic regulations at the Bdnf gene in C57BL/6J mice

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High ethanol intake is well known to induce both anxiolytic and anxiogenic effects, in correlation with chromatin remodeling in the amygdaloid brain region and deficits in cell proliferation and survival in the hippocampus of rodents. Whether only moderate but chronic ethanol intake in C57BL/6J mice could also have an impact on chromatin remodeling and neuroplasticity was addressed here. Chronic ethanol consumption in a free choice paradigm was found to induce marked changes in the expression of genes implicated in neural development and histone post-translational modifications in the mouse hippocampus. Transcripts encoding neural bHLH activators and those from Bdnf exons II, III and VI were upregulated, whereas those from Bdnf exon VIII and Hdacs were downregulated by ethanol compared with water consumption. These ethanol-induced changes were associated with enrichment in both acetylated H3 at Bdnf promoter PVI and trimethylated H3 at PII and PIII. Conversely, acetylated H3 at PIII and PVIII and trimethylated H3 at PVIII were decreased in ethanol-exposed mice. In parallel, hippocampal brain-derived neurotrophic factor (BDNF) levels and TrkB-mediated neurogenesis in the dentate gyrus were significantly enhanced by ethanol consumption. These results suggest that, in C57BL/6J mice, chronic and moderate ethanol intake produces marked epigenetic changes underlying BDNF overexpression and downstream hippocampal neurogenesis.

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