SIR2/SIRT1 DISINHIBITION OF GENE EXPRESSION BY ACUTE ALCOHOL LEADS TO PRESYNAPTIC CHANGES AND BEHAVIORAL PLASTICITY

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Acute ethanol inebriation causes neuroadaptive changes in behavior that favor increased intake. Ethanol-induced alterations in gene expression, through epigenetic and other means, are likely to change cellular and neural circuit function. Ethanol markedly changes histone acetylation, and the sirtuin Sir2/SIRT1 that deacetylates histones and transcription factors is essential for the rewarding effects of chronic cocaine use. We find that Sir2 in the mushroom bodies of Drosophila promotes acute ethanol-induced behavioral plasticity by allowing changes in the expression of presynaptic molecules. Our findings tie epigenetic effects of acute drug exposure to drug-induced behavioral plasticity. This occurs in a brain region that associates context with innate approach and avoidance responses. How these ethanol-induced molecular changes impact neuronal function and also interface with other molecular and cellular effects of acute ethanol will help define how circuits change to reinforce drug intake. These pathways may be used by other drugs of abuse.