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Effects of Social Isolation and Ethanol Drinking on the PFC Transcriptome

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Disruptions of cortical development by social isolation and/or binge ethanol during adolescence can lead to behavioral problems later in life including attention, social, and cognitive deficits, and can increase risk for alcohol use disorders. Our goal is to identify the mechanisms underlying the enduring behavioral and neurobiological consequences of social stress, and determine how these alterations may contribute to excessive alcohol drinking. Social stress was modeled by social isolation during adolescence and modulated using a novel neighbor housing environment as an interventional strategy that may alleviate addiction vulnerability associated with early-life social stress. Adolescent C57BL/6J mice were single or neighbor housed with or without access to intermittent ethanol. Prefrontal cortex tissue was collected from a subset of mice after adolescent drinking and used for transcriptomics profiling. As adults, remaining mice were tested for social, anxiety-like and cognitive behaviors and escalation of ethanol consumption. Most of our behavioral effects were more strongly modulated by housing than ethanol drinking. These data suggest that neighbor housing may partially ameliorate anxiety and cognitive deficits induced by social isolation, but does not change ethanol drinking behavior. Genomic profiling of the PFC identified a set of immediate early genes induced by housing which may underlie some of the behavioral phenotypes altered by social isolation. Ongoing analyses will continue to identify epigenetic and genomic targets modified by social stress and/or drinking and will further identify whether these behavioral alterations are mediated, in part, by dysregulation of myelin expression in the frontal cortex, or by dysregulation of the social circuit. *Supported by NIAAA P50AA022537 to MFM and JTW.*