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Opposite Epigenetic Modifications between Alcohol Use and Exercise Intervention

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Epigenetics is known to be influenced by both genetic predisposition and environmental exposures, reflecting integrated effects on molecular level dynamically. To elucidate molecular mechanisms underlying addiction development and intervention, we conducted a comparative study to explore associations of DNA methylation (DNAm) with alcohol use and exercise intervention. Three cohorts were profiled for DNAm, including a cross-sectional case-control cohort (81 hazardous drinkers and 81 age and sex matched controls), a binge drinking cohort (281 drinkers), and a longitudinal exercise cohort (53 healthy participants profiled at baseline and after a 12-month exercise intervention). Using regression analysis, we identified 906 CpG (Cytosine-Guanine dinucleotide) sites showing significant DNAm differences between drinkers and controls in the case-control cohort as well as associations with drinking behavior in the drinking cohort. In parallel, 341 CpG sites were identified for significant DNAm alterations between baseline and follow-up in the exercise cohort. Thirty-two CpG sites overlapped between the two sets of findings, of which 15 sites showed opposite directions of DNAm alterations between exercise and drinking. Associated genes of the 15 sites were enriched in signaling pathways related to synaptic plasticity. In addition, the identified methylation sites were significantly associated with impaired control over drinking, suggesting relevance to neural function. Collectively, the current findings provide preliminary evidence that exercise has the potential to partially reverse DNAm differences associated with drinking at some CpG sites, motivating rigorously designed longitudinal studies to better characterize epigenetic effects with respect to prevention and intervention of alcohol use disorders.