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Profiling epigenomic and transcriptomic alterations in postmortem prefrontal cortex of human alcoholics

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Abstract

Neuroadaptations underlying alcohol use disorders (AUDs) may be caused by alcohol consumption-induced brain epigenomic and transcriptomic alterations. Because of the inaccessibility of human brains, little is known about brain epigenomic and transcriptomic changes in AUD cases. This study profiled genome-wide DNA methylation and gene expression patterns in postmortem prefrontal cortex (PFC) of 23 AUD cases and 23 matched controls using Illumina HumanMethylation450 and HumanHT-12 Expression BeadChips, respectively. DNA methylation differences at individual CpGs and in different gene regions [promoter regions, gene bodies, and 3' untranslated regions (UTRs)] as well as gene expression differences between cases and controls were analyzed using multiple linear regression analysis, with sex, age, and postmortem interval as covariates. Correlations of CpG methylation and gene expression levels were examined by Pearson correlation analysis. Biological pathway analysis was performed using program IPA. 313 CpGs (mapped to 247 genes) were differentially methylated in AUD cases ($P_{nominal}$=2.6×10^{-7}-1.4×10^{-4}). AUDs-associated overall methylation changes mainly occurred in promoter regions and 3' UTRs. 734 genes showed differential expression in postmortem PFC of AUD cases ($P_{nominal}$=2.8×10^{-5}-0.05). 171 CpG (methylation)-gene (expression) pairs (i.e., methylation levels of CpGs and expression levels of respective genes were significantly correlated and both were significantly altered in AUD cases) were identified. Several biological pathways (e.g., the dopamine signaling pathway) potentially participating in the formation of neuroadaptations to alcohol were captured by 126 genes that were included in the above 171 pairs. Our findings suggest that the correlated DNA methylation and gene expression changes in the PFC may contribute to AUDs-associated neuroadaptations.

Biography

Dr. Huiping Zhang received his Ph.D. from Queen's University at Kingston in Canada in 2004. He worked as Postdoctoral Associate (2004-2006), Associate Research Scientist (2006-2009) and Assistant Professor (2009-present) at Yale University School of Medicine. He has published more than 30 peered-reviewed articles and is now serving as an editorial board member of PLOS ONE and the Journal of Addiction Research & Therapy.

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