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HIV-1 Tat and Cocaine Impact Astrocyte Energy Metabolism: Roles of microRNA in Epigenetic Regulation

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HIV infections and cocaine use are known to impact neuronal function. Clinical research has also proved that HIV positive (HIV+) with cocaine use show deteriorating brain metabolic functions such as behavioral and neurocognitive disorders. In the central nervous system (CNS), astrocytes are the primary regulators of energy metabolism, and if impaired, the astrocyte's energy resource may trigger neurodegeneration. HIV+ and cocaine use are known to interfere with this energy homeostasis and altered epigenetic modification, including miRNAs, which can target gene expression post-transcriptionally. Moreover, miRNAs can play an essential role in molecular level changes at several pathological dysfunctions in the CNS due to cocaine abuse and HIV infection. However, HIV+ and cocaine use could affect miRNA-mediated astrocyte's energy metabolism, and an essential epigenetic modification on miRNAs has not been elucidating yet. Here, we investigated the impact of HIV+ with cocaine exposure altered the expression of miRNAs derived from primary human astrocytes. We identified 1899 miRNAs expression analyzed by next-generation sequencing (NGS), and among 1899 transcripts, predominantly 115 were upregulated (miR4734, miR5580, miR548E, miR6799, miR6756, and miR4483), and 139 were downregulated (miR3133, miR551A, miR5580, miR155HG, and miR4426) in HIV+ with cocaine exposure. We also identified VAMP2, NFIB, PPM1H, MEIS1, and PSD93, which are significant gene targets of these miRNAs affected due to cocaine abuse and HIV-1 Tat exposure. Epigenetic changes in expression levels of these miRNAs' targets are associated with dysregulation of energy metabolism and neurodegeneration. These findings provide evidence that cocaine and HIV affect astrocyte energy metabolism, further leading to neurodegeneration.

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