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Cocaine enhances HIV infection, gene expression and replication by stimulating cell metabolism

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Background: Illicit drug users are at significant risk of contracting the Human Immunodeficiency Virus (HIV). A strong correlation exists between prohibited drugs use and an increase rate of HIV transmission.

Rationale/significance: Cocaine is one of the most widely abused drugs in the United States, which both impairs the normal functioning of brain cells and also augments HIV gene-expression in the central nervous system (CNS), even in the presence of effective antiretroviral therapy (ART).

Hypothesis: HIV replication depends primarily on the metabolic state of the host cell. Higher cell metabolisms allow the availability of required building blocks for viral progeny. We hypothesized that cocaine-induced signaling pathways leads to the stimulation of transcription factors, including NFAT, NF-kB and AP-1, which augments both overall cellular gene expression and metabolism; thus help HIV gene expression and replication.

Results and discussion: We discovered that cocaine enhances overall cell metabolism by co-stimulating transcription factors, primarily NFAT, NF-kB and AP-1, which enhance transcription of plethora of cellular genes. As anticipated, cocaine treatment besides enhancing HIV transcription and replication, augments overall cellular transcription resulted in enhanced cellular metabolism, confirmed by induced cell-activation markers. We also confirmed the higher recruitment of NFAT, NF-kB and AP-1 and presence of euchromatin structures at HIV LTR. The enhanced HIV and cellular transcription was also confirmed by increased recruitment of RNA polymerase via ChIP-Seq analysis following cocaine treatment. The obtained knowledge could be beneficial in designing novel highly specific therapies to counter cocaine and HIV effects in illicit drug-using population.