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Presentation Preference: Talk

Cocaine sensitizes the CD4+ T-cells for HIV infection by co-stimulating NF-kB, NFAT, and AP-1

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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 besides augmenting overall cell metabolism, promotes HIV gene expression and replication.

Results and discussion: In our previous findings, we established the important role of NF-KB in enhancing HIV gene expression and replication. Recently, we discovered that cocaine further augments HIV transcription by stimulating NFAT and AP-1. Results show that cocaine treatment besides enhancing HIV gene expression, augments overall cellular transcription. We noted higher recruitment of NFAT, NF-kB and AP-1 at HIV LTR following cocaine exposure. Subsequently, we noted that cocaine-induced AP-1 cooperates with both NFAT and NF-kB, for enhancing HIV transcription, besides enhanced RNA polymerase II C-terminal domain phosphorylation. We also confirmed the presence of euchromatin structures at HIV LTR. The obtained knowledge may be beneficial in designing novel highly specific therapies to counter cocaine and HIV effects in illicit drug-using population.