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# Cocaine promotes HIV gene expression and replication by co-stimulating NFAT, NF-kB and AP-1, as major transcription factors.

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**Background:** Illicit drug users are a high risk population for infection with 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:** Given the fact that HIV transcription depends primarily on the host cell transcriptional machinery, we hypothesize that cocaine-induced selective epigenetic changes and transcription factors (mainly NFAT, NF-kB and AP-1) cooperate in augmenting HIV gene expression and subsequently its 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. Subsequently, we noted that cocaine-induced AP-1 cooperates with both NFAT and NF-kB, for enhancing HIV transcription and replication. We found cocaine enhances HIV transcription by stimulating the specific isoforms of both NFAT and AP-1. We assessed the recruitment kinetics of the epigenetic -changes and -enzymes at LTR known to modulate HIV transcription, including histone phosphorylation, acetylation and methylation, following cocaine exposure. We noted the activation of certain reversible pathways, which counter each other's effect, but still found enhanced HIV transcription. The obtained knowledge may be beneficial in designing novel highly specific therapies to counter cocaine and HIV effects in illicit drug-using population.