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Methamphetamine promotes in macrophages stimulated with LTR mimic ssRNA40 expression of HIV-regulating lncRNA HEAL and pro-inflammatory factors but suppresses the interferon response

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Methamphetamine (METH) is frequently used by people living with human immunodeficiency virus-1 (PWH/HIV-1) and apparently compromises the anti-viral immune response. However, the underlying mechanisms are incompletely understood. We have recently identified the lncRNA HEAL as a promoter of HIV-1 infection (Chao et al. mBio 2019). Transfecting monocytic THP-1 cells with different concentrations of ssRNA40, a mimic of the HIV-1 long terminal repeat (LTR), recapitulating infection and using a scrambled ssRNA as control, we investigated the effects of METH (100 uM) on lncRNA HEAL and immune factors, including several implicated in HIV neurotoxicity. After 24 hours incubation the cells were collected for RNA analysis using quantitative RT-PCR. The ssRNA40 induced in a concentration-dependent fashion lncRNA HEAL and mRNA for IFNb and several pro-inflammatory factors at 2.5 and 5, but not at 1 ug/ml. METH alone triggered no significant changes of those RNAs. However, in combination with ssRNA40 at 1 ug/ml METH significantly increased expression of lncRNA HEAL and a subset of inflammatory factors. These METH effects were less pronounced or even reversed at ssRNA40 concentrations of 2.5 and 5 ug/ml. However, METH consistently down-regulated IFNb in combination with all ssRNA40 concentrations. In summary, METH appears to exert its strongest effect in promoting HIV via lncRNA HEAL at the lowest concentration of the LTR mimic while also inducing components of the pro-inflammatory arachidonic acid cascade and suppressing anti-viral IFNb. Therefore, METH apparently promotes HIV propagation, persistence and inflammatory factors implicated in macrophage-driven HIV neurotoxicity. (Supported by NIH R01 DA052209 to M.K.)