

HIV-1/gp120 protein and methamphetamine induce lasting alterations in four major neurotransmission systems of the central nervous system

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Individuals infected with human immunodeficiency virus type-1 (HIV-1) frequently use methamphetamine (METH). The combination of both HIV-1 and METH in the central nervous system (CNS) is suspected to exacerbate HIV-associated neurocognitive disorders (HAND). In addition, METH is a psychostimulant drug that compromises several neurotransmitter systems, ranging from the dopaminergic and serotonergic to glutamatergic and GABAergic networks. However, the combined effects of HIV-1 and METH on the brain remain incompletely understood at the molecular level.

We recently treated 3-4 months old HIV-1/gp120 transgenic (gp120tg) and wild type (wt) mice with an escalating METH binge regimen for 25 days. HIVgp120tg mice express the viral envelope protein in the central nervous system and share key pathological features with human AIDS brains. At 10-12 months of age, HIV-1/gp120tg and METH-exposed animals showed significant impairment in spatial learning and memory and neuropathology. METH-exposed and HIVgp120tg animals also displayed significant changes in components of the glutamatergic and GABAergic neurotransmission systems. METH-treated HIVgp120tg mice were the most severely affected. In order to further investigate underlying mechanisms in the brain, we used in the present study RT-qPCR arrays to assess expression of genes related to the dopaminergic and serotonergic neurotransmission systems. Six comparisons between the four experimental groups revealed significant differential gene regulation due to METH exposure and chronic HIV-1/gp120 expression, including *BDNF*, *CDK5*, *VMAT2*, *SERT1*, *GFAP*, *DRD5*, *HTR6*, *HTR1A/1D/2C/4/7*. In summary, histopathology and impaired spatial learning and memory due to METH exposure and HIV-1 gp120 expression are associated with significant alterations in the four major neurotransmission systems of the brain.

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