Neurotransmission-related gene expression reveals sexual dimorphism in long-term effects of methamphetamine and HIV-associated brain injury

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Methamphetamine (METH) use is common among individuals infected with human immunodeficiency virus type-1 (HIV-1) and aggravates HIV-associated neurocognitive disorders (HAND). However, the pathological mechanisms underlying the combined effects of HIV-1 and METH remain incompletely understood. Transgenic mice expressing a soluble viral envelope protein gp120 of HIV-1 in the brain (gp120tg) share characteristic neuropathological features with HIV/AIDS patients. We had previously treated gp120tg mice with an escalating METH binge regimen for 25 days and analyzed the animals after 7 months at about 12 months of age and found that prior METH treatment aggravated behavioral impairment, and METH-exposed gp120tg animals displayed reduced post-tetanic potentiation, while both gp120 expression and METH treatment diminished long-term potentiation and caused damage to neurites and synapses (Hoefer et al., Exp. Neurol. 2015). For this study, we investigated the expression of genes of the dopaminergic, serotonergic, GABAergic and glutaminergic neurotransmitter systems at RNA level using quantitative RT-PCR arrays. Cerebral cortex, hippocampus and striatum were analyzed in female and male samples separately and in combination. The results showed that METH treatment and HIV gp120 affected all neurotransmission systems, although with significant differences between females and males. Sexual dimorphism was most pronounced for the dopaminergic and serotonergic systems in all investigated brain structures. In summary, METH treatment and viral gp120 disturb learning and memory function and induce neuropathology in both sexes. However, our findings demonstrate significant sexual dimorphism and differences between brain regions at the RNA level in the long-term effects of METH exposure and HIV gp120 expression.