Submitter Name: Marcus Kaul
Submitted email: marcus.kaul@medsch.ucr.edu

Chronic, low dose methamphetamine reveals sexual dimorphism in memory performance impaired by exposure to HIV-1 Tat protein

Marcus Kaul[1,2,3], Ricky Maung[1,3], Daniel Ojeda-Juárez[1,3], Paloma Sanchez-Pavon[3], Ana B. Sanchez[2,3], Amanda Roberts[4], TMARC Group[2]

[1]Division of Biomedical Sciences, School of Medicine, University of California Riverside, Riverside, CA 92521, USA
[2]Translational Methamphetamine AIDS Research Center (TMARC), Department of Psychiatry, University of California San Diego, San Diego, CA 92093, USA
[3]Center for Infectious and Inflammatory Disease, Sanford Burnham Prebys Discovery Medical Institute, La Jolla, CA 92037, USA
[4]The Scripps Research Institute, Mouse Behavioral Assessment Core, 10550 North Torrey Pines Road, MB6, La Jolla, CA 92037, USA

We investigated the effects of chronic, low-dose methamphetamine (METH) use in the context of HIV infection of the brain. Therefore, we subjected transgenic mice that express a tetracycline-inducible viral protein Tat in the brain (iTat mice) at 4 months of age to a 12-week METH regimen starting week 1 at 0.5 mg/kg s.c., 1 x day, step-wise increase by 0.5 mg/kg with each injection over 5 days (Mon–Fri), followed by 11 weeks of 1 x 2.5 mg/kg/day. During week 4, the mice received Doxycyclin (Dox, 100 mg/kg, i.p.) for induction of Tat expression. The mouse cohort included rtTA-positive TRE-Tat-negative control animals, which cannot express Tat upon Dox injection, and comprised about 50 % females and males. Four months after METH exposure, at 11-12 months of age, all iTat-tg mice underwent behavioral testing, including optomotor test of vision (OPT), locomotor activity (LM), novel object recognition (NO) and Barnes maze test (BM; 4 day acquisition + probe trial). Tat compromised performance in the NO and BM paradigms but the combination of METH and Tat resulted unexpectedly in a virtually normal performance in the probe trial of the BM. However, the NO paradigm revealed a sexual dimorphism in that METH alone only compromised males, whereas females, in contrast to males, displayed no discrimination between familiar and novel object after exposure to Tat with or without METH. Thus, METH apparently compromises recognition but not spatial memory in a sex-dependent fashion.
Supported by NIH, MH087332, MH104131, MH105330, DA052209 and DA026306 (P5) to M.K.