Print this Page

NEUROSCIENCE 2014

Presentation Abstract

Program#/Poster#:	227.09/R1
Presentation Title:	Striatal dopaminergic neurotoxicity and neuroinflammation caused by methamphetamine are differentially affected by *in vivo* stressors versus corticosterone treatment
Location:	WCC Hall A-C
Presentation time:	Sunday, Nov 16, 2014, 1:00 PM - 5:00 PM
Presenter at Poster:	Sun, Nov. 16, 2014, 1:00 PM - 2:00 PM
Topic:	++C.11.g. Neurotoxicity and neurodegeneration
Authors:	***D. B. MILLER**, K. A. KELLY, J. P. O'CALLAGHAN; Ctr. Dis. Control & Prevention, CDC-NIOSH, MORGANTOWN, WV
Abstract:	In the mouse methamphetamine (METH) causes striatal dopaminergic nerve terminal damage accompanied by neuroinflammation as evidenced by a loss of dopamine (DA), tyrosine hydroxylase protein (TH), an increase in the astrogliosis marker GFAP and an increase in the mRNA of a number of proinflammatory cytokines and chemokines (e.g., IL-1B, LIF, CCL-2). Previously, we found exposure to corticosterone (CORT), a known anti-inflammatory agent, for 7 days in the drinking water prior to METH dosing unexpectedly enhanced the striatal damage and neuroinflammation. As CORT is released with *in vivo* stressor exposure, here we determined how METH neurotoxicity and neuroinflammation were affected by exposure to a different daily stressor for 4 days. Male C57Bl6J mice were exposed to a single s.c. injection of SAL or METH (20 mg/kg) ~ 22 hrs after the final stressor exposure and their rectal temperatures monitored at 0, 1, 3, 5, 7, 9, and 24 hrs post dosing. Striatum and cortex samples were collected 6 & 12 hrs after METH for cytokine gene expression and at 72 hrs for

neurotoxicity evaluation. On the 4 days prior to dosing, mice were weighed daily and the control group (No Stress: NS) remained in their home cage while the stressed groups (S) were exposed to the following stressors: (Day 1) damp bedding 6PM to 6AM; (Day 2) a strobe light 6PM to 6AM; (Day 3) restraint from 6AM to 6 PM in home cage; (Day 4) restraint and 1.0 mA inescapable 5 sec electric shock every 30 sec for 100 shocks. Surprisingly, stressor exposure reduced the mortality associated with METH. Stressor exposure reduced thymus weight by 39 & 82% in the S-SAL & S-METH indicating the stressor exposures caused CORT release. *In vivo* stressor exposure did not modify METH hyperthermia. In contrast to our previous work, *in vivo* stressor exposure did not exacerbate striatal neuroinflammation but rather reduced cytokine expression. Striatal astrogliosis was not exacerbated but greater striatal DA and TH reductions were observed. The differences in these neurotoxicity biomarkers may reflect an ability of the *in vivo* stressor protocol to down-regulate DA and TH rather than an increased neurotoxicity. (Supported by CDC-NIOSH intramural funds)

Disclosures: **D.B. Miller:** None. **K.A. Kelly:** None. **J.P. O'Callaghan:** None.

Keyword (s): METHAMPHETAMINE

STRESS

DOPAMINE