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Brain glutathione depletion as an animal model with relevance to schizophrenia: interaction with amphetamine and potential restoration by N-acetyl cysteine.

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Primary Theme and Topics
Disorders of the Nervous System
- Cognitive, Emotional and Behavioral State Disorders
  -- Schizophrenia: Animal models

Secondary Theme and Topics
Disorders of the Nervous System
- Behavioral Pharmacology
  -- Monoamines and behavior

Session: 557. Schizophrenia: Aminergic and Other Models
Poster

Presentation Time: Monday, November 14, 2005 2:00 PM-3:00 PM
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Oxidative stress has been implicated in schizophrenia where recent studies have demonstrated decreased glutathione (GSH) levels in cerebrospinal fluid (52% depletion). Treatment with 2-cyclohexene-1-one (CHX) has been used previously to deplete glutathione in various animal models. We observed that treatment of mice with CHX led to a dose-related decrease of GSH levels in the frontal cortex and striatum. Reductions were 54% and 38%, respectively, with 120 mg/kg. The current study aimed to investigate the behavioural effects of CHX-induced GSH depletion in combination with dopaminergic hyperactivity induced by amphetamine treatment. This study also aimed to assess if GSH depletion could be restored with N-acetyl cysteine (NAC) treatment. C57Bl/6 mice were treated with CHX (120 mg/kg, i.p.) and 60 mins later, NAC (300 or 1000 mg/kg i.p.) was injected and assessment of locomotor activity began. One hour later,amphetamine (5 mg/kg i.p.) was administered and behaviour assessed for another hour. Controls received saline injections. Total glutathione levels were assessed using an enzymatic-recycling assay and locomotion was assessed using video-tracking (Ethovision, Noldus). CHX-treated animals showed reduced locomotor activity as well as decreased habituation. Amphetamine treatment caused similarly marked locomotor hyperactivity in both saline and CHX-treated animals. NAC treatment reduced habituation but otherwise did not influence baseline or amphetamine-induced locomotor activity. These results suggest that, although CHX-induced GSH depletion in mice causes a reduction of baseline locomotor activity, the locomotor hyperactivity caused by amphetamine treatment, an animal model of psychosis, was not affected. NAC treatment did not reverse the behavioural effect of CHX or influence the action of amphetamine. Biochemical analysis is underway to assess if NAC treatment ameliorates the effect of CHX on GSH levels in the brain.