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P01.493 N-ACETYL-CYSTEINE TREATMENT INHIBITS DEPLETION OF BRAIN GLUTATHIONE LEVELS IN RATS: IMPLICATIONS FOR SCHIZOPHRENIA

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Statement of the Study: Reduced brain levels of glutathione and oxidative stress have recently been proposed as contributing factors in Schizophrenia. Glutathione is a free radical scavenger and its depletion, associated with the oxidative stress effects of altered dopamine release, may be implicated in the symptomatic process of the illness. Currently, a clinical trial is underway in which treatment with the antioxidant N-acetyl cysteine (NAC) is added to standard neuroleptic treatment. The aim of the present study was to investigate, in rats, possible biochemical mechanisms involved in the effects of this treatment.

Methods: Adult male Sprague-Dawley rats (ave. weight 420g) were treated with 2-Cyclohexene-1-one [CHX, 75 mg/kg, intraperitoneally (i.p.)]. NAC (1000 mg/kg, i.p.) was administered ninety minutes proceeding CHX treatment, and D-amphetamine sulphate (amphetamine, 2.5 mg/kg, i.p.) was injected 30 minutes later to induce dopaminergic hyperactivity. In all cases, control rats received saline injections (i.p.) in equal volumes to the treated rat. One hour following amphetamine treatment, striatal and frontal cortex samples were obtained for biochemical analysis.

Summary of Results: Results show that CHX induced a significant depletion of glutathione levels in both striatum and cortex of CHX-alone treated rats, but not in CHX-NAC treated rats. This effect occurred in both amphetamine-treated and saline-treated rats, although the effect appeared greater in the absence of amphetamine treatment.

Conclusion: These results demonstrate NAC treatment can restore depleted levels of cerebral glutathione. This predicts beneficial effects of this treatment in clinical conditions where brain glutathione levels are depleted, such as in schizophrenia.

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