

Effects of Manganese on the Developing Rat Brain: Oxidative-Stress Related Endpoints

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ABSTRACT

The purpose of this study was to evaluate biochemical endpoints related to oxidative stress in brains of neonatal rats exposed to manganese. Oral manganese chloride (MnCl₂) doses (0, 25, or 50 mg Mn/kg bw/day) were given daily to neonatal rats throughout lactation (i.e., from postnatal day [PND] 1 through 21). As previously reported by Dorman *et al.* (*J Appl Toxicol* 20:179-187, 2000), this treatment paradigm results in increased cerebral cortex (CTX) manganese concentrations in PND 21 rats from both manganese treatment groups. High dose manganese exposure also results in increased cerebellar (CB) manganese concentrations. This study determined whether lactational manganese exposure could affect the following end-points in CTX or CB tissues: metallothionein (MT) mRNA levels, glutamine synthetase (GS) activity, protein and mRNA levels, as well as reduced, oxidized, and total glutathione (GSH) levels. Manganese exposure did not affect CTX or CB: MT mRNA levels, GS activity, protein and mRNA levels, or amounts of reduced and total GSH. Statistically significant ($p < 0.05$) increases were noted by analysis of variance (ANOVA) in the following endpoints: GS mRNA levels (high Mn dose vs. control CB), reduced GSH levels (high Mn dose vs. control CTX and CB), and oxidized GSH levels (high and low Mn doses vs. control CTX). These results suggest that oral exposure to high levels of Mn in developing rats is associated with biochemical changes that might be indicative of oxidative stress (The study was supported by Ethyl Corporation, Richmond, VA).