Extracellular norepinephrine, norepinephrine receptor and transporter protein and mRNA levels are differentially altered in the developing rat brain due to dietary iron deficiency and manganese exposure.

Anderson JG, Fordahl SC, Cooney PT, Weaver TL, Colyer CL, Erikson KM.

Department of Nutrition, University of North Carolina at Greensboro, Greensboro, NC 27402-6170, USA.

BACKGROUND: Manganese (Mn) is an essential trace element, but overexposure is characterized by Parkinson's like symptoms in extreme cases. Previous studies have shown that Mn accumulation is exacerbated by dietary iron deficiency (ID) and disturbances in norepinephrine (NE) have been reported.

OBJECTIVE: Because behaviors associated with Mn neurotoxicity are complex, the goal of this study was to examine the effects of Mn exposure and ID-associated Mn accumulation on NE uptake in synaptosomes, extracellular NE concentrations, and expression of NE transport and receptor proteins.

METHODS: Sprague-Dawley rats were assigned to four dietary groups: control (CN; 35 mg Fe/kg diet), iron-deficient (ID; 6 mg Fe/kg diet), CN with Mn exposure (via the drinking water; 1 g Mn/L) (CNMn), and ID with Mn (IDMn).

RESULTS: (3)H-NE uptake decreased significantly (R=-0.753, p=0.001) with increased Mn concentration in the locus coeruleus, while decreased Fe was associated with decreased uptake of (3)H-NE in the caudate putamen (R=0.436, p=0.033) and locus coeruleus (R=0.86; p<0.001). Extracellular concentrations of NE in the caudate putamen were significantly decreased in response to Mn exposure and ID (p<0.001). A diverse response of Mn exposure and ID was observed on mRNA and protein expression of NE transporter (NET) and alpha(2) adrenergic receptor. For example, elevated brain Mn and decreased Fe caused an approximate 50% decrease in NET and alpha(2) adrenergic receptor protein expression in several brain regions, with reductions in mRNA expression also observed.

CONCLUSIONS: These data suggest that Mn exposure results in a decrease in NE uptake and extracellular NE concentrations via altered expression of transport and receptor proteins.

PMID: 19481535

FREE FULL TEXT