Effect of Manganese on Biogenic Amines in Mouse Brain (IV) Long-Term Exposure to Water-Insoluble Manganese Compounds

JUNKO KOMURA and MICHIKO SAKAMOTO

Department of Environmental Hygiene, Faculty of Pharmaceutical Sciences, Hokuriku University, Ho-3 Kanagawa-machi, Kanazawa 920-11, Japan

Chronic human exposure to relatively high levels of manganese (Mn) can culminate in psychosis, parkinsonian-like extrapyramidal symptoms, and other neuro-behavioral sequelae. Recently, neurotoxicity resulting from Mn has attracted attention because of the use of Mn as an antiknock ingredient in automobile fuels. There are various chemical forms of Mn, and each one has different physical, chemical and biological properties. Thus, we investigated the effects of relatively long-term exposure to some insoluble Mn compounds on the central nervous system (CNS) in the adult male mouse.

Male mice of ddY strain, aged 6 weeks, body weight about 30 g, were divided into 3 groups. Group 1 and 2 were fed diet containing Mn (2 g/kg) in the form of MnCO_3 or MnO_2 for 12 months. Group 3 served as the control and was fed standard laboratory mouse chow (Mn 14 mg/kg). Mean daily intake of diet was 3.7 g per mouse in all groups. Mice were sacrificed by decapitation at 24 h after the last feeding. Catecholamines in various brain regions were analyzed by using high-performance liquid chromatography with an ultraviolet detector (280 nm). Manganese in tissues was determined by atomic absorption spectrophotometry.

In the control group, Mn content was high in the cerebral cortex and corpus striatum, and low in the hypothalamus and cerebellum. In the manganese carbonate-exposed group (MnCO_3 group), the content of Mn was particularly increased in the hypothalamus and cerebral cortex; it was higher than in the control throughout the brain. In the manganese dioxide-exposed group (MnO_2

group), the Mn content was increased in the cerebral cortex compared to the control. Manganese carbonate and MnO_2 are virtually insoluble in water and alcohol, though MnO_2 is less soluble than MnCO_3 . Contents of Mn in the corpus striatum and hypothalamus were higher in the MnCO_3 group than in the MnO_2 group.

The level of dopamine (DA) was decreased in the corpus striatum of the MnO_2 group and in the hypothalamus of the manganese-exposed group (Mn group). On the contrary, the level of DA was increased in the cerebrum, cerebellum and medulla oblongata of the MnO_2 group. The level of norepinephrine was decreased in the corpus striatum, hypothalamus and hippocampus of the MnO_2 group, and in the cerebellum of the MnCO_3 group. The cerebrum is the center of the extrapyramidal system, the cerebellum and medulla oblongata are periphery, and the corpus striatum is the linking region. The above results suggest some disorder of the extrapyramidal system.

Further study was undertaken on the form of Mn in the brain. Brain striatum homogenate was fractionated by centrifugation, and the cytosol fraction was separated by the Sephadex G-75 gel filtration chromatography. The levels of Mn in striatum of the control group were similar in nuclei, mitochondria and cytosol, and low in microsomes. Manganese in nuclei of the MnCO_3 group was higher than that in the control group. The Mn levels were similar in the four subcellular fractions of the MnO_2 group. Manganese-exposed mice showed moderate increases of Mn in the fraction of about 10000 molecular weight in gel filtration chromatography of cytosol from the striatum.

Body weight gain was depressed in the Mn group for more than eight months. Spontaneous motor activity was low in the MnO_2 group for more than eight months. In conclusion, the physical and CNS effects of MnO_2 seemed to be similar to those of MnCO_3 .