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COMMENT

Manganese exposure is a risk for brain atrophy

Masaki Mogi[1]

Keywords Ambient manganese exposure · Neurotoxicity · Structural change of brain · Magnetic resonance imaging · Sex difference

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Although metals are essential for the maintenance of life and normal vital activities, there are also concerns about the harmful effects of overexposure. Manganese is one of the essential trace elements and is a component of pyruvate carboxylase, a glucose metabolizing enzyme, and superoxide dismutase (SOD), a scavenger of reactive oxygen species, and also acts as a catalyst to enhance enzyme activity [1]. Manganese deficiency is believed to cause bone lesions, abnormal blood coagulation, abnormal glucose metabolism, and reactive oxygen species (ROS)-induced disorders; however, the function of manganese in vivo is not yet fully understood.

Manganese is mainly taken into the body through oral intake and inhalation exposure, and manganese in the inhaled air is converted to trivalent cations by ceruloplasmin and bound to transferrin, and a portion is transferred to the brain [1]. Manganese is known to be neurotoxic because of reports of a younger age of onset of Parkinson's disease among welders [2] and a higher prevalence of Parkinson's disease among residents living near ferroalloy plants [3]. It has been suggested that manganese exposure may be associated with the development of neurodegenerative diseases such as Alzheimer's disease and Huntington's disease [4]. However, because the effects of manganese exposure on neurodegenerative diseases have been investigated mainly in Parkinson's disease, imaging analysis of the whole brain in subjects with manganese exposure has not been performed.

✉ Masaki Mogi
mmogi@m.ehime-u.ac.jp

[1] Department of Pharmacology, Ehime University, Graduate School of Medicine, Shitsukawa, Tohon, Ehime 791-0295, Japan

In the latest Hypertension Research, Woo et al. described the effects of ambient manganese exposure on organic changes in the brain, using brain imaging markers such as cortical thickness and white matter hyperintensities (WMH) evaluated by brain magnetic resonance imaging (MRI) [5]. The results showed that manganese concentration was correlated with cortical thinning in the parietal and occipital lobes in males, considering the concentration of manganese in the air based on their place of residence. It was also found that the amount of deep WMH was greater in areas with higher atmospheric manganese concentrations. On the other hand, no such correlation was observed in females. In conclusion, they suggested that atmospheric manganese concentration may induce brain atrophy (Fig. 1). They discussed the neurotoxicity of manganese, which crosses the blood-brain barrier and enters the brain, and proposed that manganese accumulation in the brain may promote autoxidation and conversion of various intracellular catecholamines such as dopamine, which are possible mechanisms of an increase in oxidative stress in the brain. Intracellular manganese ions accumulate predominantly in mitochondria and increase the degree of oxidative stress and mitochondrial damage [6].

Although an increase in oxidative stress by manganese accumulation may directly damage neurons, resulting in cortical thinning and increased WMH, blood pressure elevation also induces WMH and brain atrophy. Woo et al. did not investigate the effects of manganese exposure on blood pressure in this study; thus, we would like to know whether there is an association between manganese and blood pressure. There has been much discussion about the association of environmental exposure to trace elements including manganese, lead, zinc, cooper etc. with the risk of hypertension and elevated blood pressure in pregnant women. Blood manganese level was shown to be a potential risk factor for increased gestational blood pressure [7],

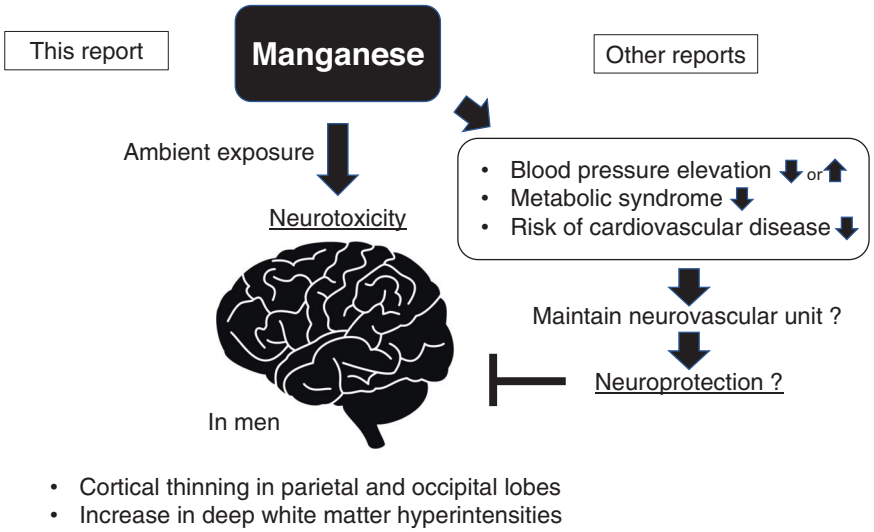

Fig. 1 Schematic presentation of effects of manganese on the brain. The present study by Woo et al. demonstrated the effects of ambient manganese exposure on structural change in the brain. They found that an increase in manganese exposure induced cortical thinning in the parietal and occipital lobes and an increase in deep white matter hyperintensities. However, previous reports indicated that an increase in serum or urine manganese level prevented blood pressure elevation and metabolic syndrome and reduced the risk of cardiovascular disease, which are related to maintenance of the neurovascular unit which plays an important role in neuron homeostasis. Thus, the actual effects of manganese on the brain are still unknown

although the results were less consistent in another study [8]. On the other hand, Wu et al. reported that there were significant negative associations between urinary manganese and both systolic and diastolic blood pressure [9]. Moreover, serum manganese level was reported to be negatively correlated with the risk of cardiovascular disease in older adults in the United States [10]. Furthermore, there has also been a focus on manganese exposure in the relation with metabolic syndrome. Recently, Riseberg et al. demonstrated that Mn exposure evaluated from urinary Mn concentration was associated with lower fasting glucose, indicating a possible beneficial effect on metabolic diseases [11]. Lo et al. also reported a U-shaped dose-response relationship between urinary Mn level and metabolic syndrome in a sex-specific manner [12]. Considering these reports, manganese may have a protective effect on endothelial damage via inhibiting blood pressure elevation or metabolic syndrome; thus, these beneficial effects of manganese may maintain the brain microcirculation, resulting in prevention of brain degeneration via inhibition of neurovascular uncoupling (Fig. 1). However, the actual effects of manganese on the brain are still an enigma.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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