

Current Challenges about Understanding of Manganese-Induced Neurotoxicity

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Editorial

Manganese (Mn) is found in three major biologically-relevant oxidation states Mn(II), Mn(III) and Mn(IV), and it is an essential trace metal that is involved for several pathway, in the normal cell function and metabolism. However, since XIX century, the Mn is well known as neuro (toxic) agent, during acute and chronic exposure for air, water or aliments containing either high- or low-level concentrations [1]. In addition to the exposure level and duration, other factors may contribute to Mn neuro (toxicity) such as cell target, developmental stage [2,3] gender, ethnicity, genetics, location, pre-existing medical conditions [1]; chemical speciation and fractionation of the metal [3].

Mn is homeostatically well-regulated and the knowledge about their transport across the cell have improved during last time; however, the studies of its mechanisms of action and toxicity are even incomplete as well as the established biomarkers to evaluate the effect of Mn exposure are not well defined [1,4]. Nevertheless, energy and mitochondrial dysfunction, oxidative stress, neurotransmitter impairment, metal homeostasis impairment, induction of protein aggregation and others are putative mechanisms linked to Mn neurotoxicity. And it are similar mechanisms for neurodegenerative effects (progressive loss of structure or function of neurons) causing irreversible consequences such as Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS) [4]. The inconsistency of these issues all together have complicated the comprehension of the mode of action of the manganese, and consequently the development of efficient therapeutic approaches to abolish the disturbance induced by this metal. Accordingly, from century XIX to century XXI, the society saw and increased its necessity of win the challenges about Mn neurotoxicity: How is controlled the homeostasis and the transport of the Mn in the brain? Which are the biomarkers of Mn-induced neuro (toxicity)? Which is the mechanism of Mn-induced neurotoxicity? Which is the Mn association with neuro degeneration and dementia? Why the therapeutic approaches for Mn neurotoxicity are not efficient?

Interestingly, during the last decades, the application of toxicogenomics approaches improved the toxicological sciences. It

combines toxicology with genomics or other high throughput molecular profiling technologies such as transcriptomics, proteomics and metabolomics, to study, *in vitro/in vivo* and cross-species the structure and function of the genome and its responds (pathways) to adverse xenobiotic exposure. Indeed, toxicogenomics have allowed the replacing, reduction and optimization of animal models, discover new biomarkers, and specially have permitted to study the underlying molecular mechanisms of toxicity that are difficult to overcome by conventional toxicology [5]. Despite, the manganese is a well-documented element in the Comparative Toxicogenomics Database (CTD), with 261 genes impaired from 10 organisms tested, and 24-curved diseases that showed a penchant for nervous system diseases [6], the current works have scarcely explored this information. Hence, the future projects to study the Mn-induced neurotoxicity must to consider the studies cross-species and whenever possible the use of toxicogenomics approach to help in the resolution of the challenges cited above.

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