Methylmercury and Brain Diseases: A Potential Connection with Vascular Diseases?

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Methylmercury (MeHg) is a highly neurotoxic environmental pollutant present in high concentrations in predatory fish. Although neurons and astrocytes have been recognized as main cellular targets involved in MeHg-induced neurotoxicity, the mechanisms mediating such toxicity are not completely understood. Based on experimental protocols with rodents and cultured cells, we have observed that glutamate dyshomeostasis and oxidative stress represent main events mediating MeHg-induced neurotoxicity. Of particular importance, selenoproteins, such as glutathione peroxidase, represent central molecular targets mediating MeHg-induced neurotoxicity and this event is related to the high affinity of MeHg for selenol groups of selenocysteine. On the other hand, adverse cardiovascular dysfunction has also been pointed as an important toxic consequence of MeHg exposure. Based on this evidence, we have developed in vivo studies to investigate whether MeHg exposure is able to change plasma biochemical parameters related to the vascular homeostasis, with a particular emphasis on cholesterol. Based on an animal model of MeHg-exposed mice, we observed, for the first time, that long-term MeHg exposure induced hypercholesterolemia. Additionally, hypercholesterolemic mice were more susceptible to MeHg-induced cerebellar glial activation. Based on in vitro experiments with cultured bovine aortic endothelial cells (BAECs), we observed that low concentrations of MeHg increased the production of superoxide anion and decreased the mitochondrial membrane potential (ΔΨₘ). Because superoxide anion production occurred in a NADPH oxidase-dependent manner, it is possible that the observed decreased ΔΨₘ represents a consequence of increased reactive oxygen species not necessarily generated in mitochondria. Our results indicate that increased plasma cholesterol levels and direct toxicity toward endothelial cells can represent important events mediating MeHg-induced changes on vascular homeostasis. Although both observed events (hypercholesterolemia and endothelial cell injury) support the concept of MeHg-induced cardiovascular toxicity, it is unclear if they contribute to MeHg-induced neurotoxicity (i.e., by disrupting the encephalic vasculature).

Keywords: Methylmercury, neurotoxicity, vascular dysfunction.