Astrocytes have been considered as mediators of methyl mercury (MeHg) and mercuric chloride (Hg\(^{2+}\)) neurotoxicity. Mercurials accumulate preferentially into astrocytes and inhibit glutamate and aspartate uptake by these cells. In this study we investigated the effects of ebselen, an anti-inflammatory and antioxidant seleno compound, and mercurials on glutamate uptake into rat cultured astrocytes and also into slices from adult mice exposed to MeHg in drinking water. In astrocytes, the inhibition of glutamate uptake by MeHg was partially prevented by ebselen, while for Hg\(^{2+}\) ebselen was totally preventive. MeHg increased the lipid peroxidation (measured by production of thiobarbituric acid reactive substances-TBARS), which was prevented by ebselen. We concluded that in vitro the protective effects of ebselen against the inhibitory effect of Hg\(^{2+}\) and methyl mercury on glutamate uptake by astrocytes are mediated by different mechanisms. Concerning Hg\(^{2+}\), ebselen acted by binding to the selenol derived from the open-ring metabolite of ebselen, whereas it blocked the lipoperoxidation induced by methyl mercury. In vivo exposure to MeHg caused a dose-dependent decrease on glutamate uptake by brain cortical slices and ebselen protected against this toxic effect of MeHg. MeHg exposure was also associated with an increase in oxidative stress (as determined by a decrease in antioxidant agents and by an increase in TBARS production) and these effects of MeHg were reversed by ebselen treatment. Our results indicate that glutamate transporters are in vivo targets for MeHg intoxication and strengthen the literature view that glutamate is an important factor in MeHg neurotoxicity. In view of the fact that ebselen is under clinical trials, our results could point to the possible use of ebselen in the treatment of mercury intoxication.

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