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学位論文題名	Effects of continuous exposure of mouse primitive neural stem cells to methylmercury in proliferation and differentiation stages 増殖期および分化期におけるマウス初期神経幹細胞に対する持続的メチル水銀暴露の影響
論文審査委員	主査 教授 木下 正信 委員 教授 菊池 吉晃 委員 客員教授 井上 順雄 (元首都大学東京教授)

【論文の内容の要旨】

Methylmercury (MeHg) is a potent neurotoxin that causes Minamata disease and is particularly harmful during pregnancy, causing abnormal pregnancy or various adverse effects including congenital Minamata disease. Neural stem cells (NSCs) can proliferate and differentiate into neurons and glia, playing a key role in the formation of the CNS. Here, we examined the effects of continuous exposure of homogeneous embryonic stem cell-derived primitive NSCs to MeHg in the proliferation and differentiation stages. Cultured without MeHg in the proliferation stage, NSCs showed an exponential increase in the number of the cells up to day 4. However, continuous exposure of NSCs to MeHg induced apoptosis and caused a decrease in the number of NSCs in a dose- and time-dependent manner. Continuous exposure of NSCs to MeHg in the differentiation stage also caused a decrease in the number of NSCs but had no or little effect on differentiation from surviving NSCs into neurons and glia. The NSCs were about 20 times more susceptible to MeHg in the proliferation stage than the differentiation stage. These effects of continuous MeHg exposure on NSCs may be valuable in elucidating the mechanisms by which MeHg exposure during pregnancy causes congenital Minamata disease and reproductive problems. In particular, the present results suggests that MeHg even at a very low concentration may decrease the number of proliferating NSCs in the early stages of development of central nervous system (CNS) and cause shortage of NSCs required for

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normal development of CNS.