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Developmental exposure to methylmercury alters neurotrophin expression in male mice

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Alterations in environmental conditions during development may produce long-lasting and often permanent changes in the function of the brain and in the expression of key genes involved in neuronal development and plasticity. We have investigated the effect of prenatal and early postnatal exposure to methylmercury (MeHg) by exposing pregnant mice to MeHg (0.5 mg/kg/day) via drinking water from gestational day 7 to day 7 after delivery. The offspring's behaviour was evaluated at different ages in acute tests for spontaneous motor functions, as well as with long-term monitoring of basic activities and learning abilities. We found decreased exploratory activity and reference memory impairment in the MeHg-exposed male mice. The forced swimming test revealed a predisposition to depressive behaviour in the MeHg-exposed males, and treatment with antidepressant reversed depressive-like changes. Neurotrophic factors, such as BDNF, are critical regulators of neuronal survival, synapse formation and connectivity in brain, and their mRNA levels are dynamically regulated by several factors that may produce long-term changes. We have analyzed the expression of BDNF mRNA in the brains of our experimental animals by using in situ hybridization and found a significant decrease in the limbic system of MeHg-exposed male mice. Interestingly, the treatment with antidepressant restores the mRNA expression to control levels. Preliminary findings indicate that exposure to MeHg produces long-lasting changes in the chromatin structure around BDNF promoter, which are consistent with reduced transcriptional activity of the BDNF gene. Our study provides novel evidence that developmental exposure to MeHg induces alteration in learning and long-lasting depression-like behaviour. Treatment with antidepressants not only normalizes behaviour but also the expression of BDNF mRNA. Considering that neurotrophic factors are present in blood and their levels appear to reflect changes at the central nervous system level, the analysis of their expression may be an excellent tool to study the molecular mechanisms of gene-environment interactions.