

Neonatal Administration of Thimerosal Causes Persistent Changes in Mu Opioid Receptors in the Rat Brain

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Abstract Thimerosal added to some pediatric vaccines is suspected in pathogenesis of several neurodevelopmental disorders. Our previous study showed that thimerosal administered to suckling rats causes persistent, endogenous opioid-mediated hypoalgesia. Here we examined, using immunohistochemical staining technique, the density of μ -opioid receptors (MORs) in the brains of rats, which in the second postnatal week received four i.m. injections of thimerosal at doses 12, 240, 1,440 or 3,000 $\mu\text{g Hg/kg}$. The periaqueductal gray, caudate putamen and hippocampus were examined. Thimerosal administration caused dose-dependent statistically significant increase in MOR densities in the periaqueductal gray and caudate putamen, but decrease in the dentate gyrus, where it was accompanied by the presence of degenerating neurons and loss of synaptic vesicle marker (synaptophysin). These data document that exposure to thimerosal during early postnatal life produces

lasting alterations in the densities of brain opioid receptors along with other neuropathological changes, which may disturb brain development.

Keywords Thimerosal · Mu opioid receptors · Rat · Brain · Development

Introduction

Thimerosal (THIM), an organomercury compound, which contains approximately 49% mercury (Hg) by weight, has been used for decades as a preservative in pediatric vaccines without adequate testing for its safety in developing organisms. THIM is metabolized in the body first into ethylmercury and subsequently into other organic and inorganic mercury forms [1]. Centuries of human experience and a large body of scientific data document that all forms of Hg are highly toxic. Considerable amounts of Hg have been found in the blood of human infants after the injection of THIM-containing vaccines [2, 3] and studies conducted with infant monkeys showed that Hg from THIM-vaccine injections accumulates in the brain at concentrations many times higher than those in the blood, and that it stays there for months or years [4]. Post vaccination levels of Hg in infant brains may reach medium nanomolar concentrations, which are neurotoxic and kill neurons in vitro [5]. THIM doses equivalent to those used in vaccines have been shown to harm the brains of developing mice [6].

Early life exposure to mercurials, including THIM, is suspected to be a pathogenic factor in several neurodevelopmental disorders [7–10]. We have previously shown that THIM administration to suckling rats in a mode similar to infant immunization and at doses analogous to those used in pediatric vaccines, or higher, persistently augments

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