

available at www.sciencedirect.comwww.elsevier.com/locate/brainres**BRAIN
RESEARCH****Research Report****Neonatal administration of a vaccine preservative, thimerosal, produces lasting impairment of nociception and apparent activation of opioid system in rats****Mieszko Olczak^a, Michalina Duszczyk^a, Pawel Mierzejewski^b, Maria Dorota Majewska^{a,*}**^aMarie Curie Chairs Program at the Department of Pharmacology and Physiology of the Nervous System, Institute of Psychiatry and Neurology, 02-957 Warsaw, Poland^bDepartment of Pharmacology and Physiology of the Nervous System, Institute of Psychiatry and Neurology, 02-957 Warsaw, Poland

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ABSTRACT

Thimerosal (THIM), an organomercury preservative added to many child vaccines is a suspected factor in pathogenesis of neurodevelopmental disorders. We examined the pharmacokinetics of Hg in the brain, liver and kidneys after i.m. THIM injection in suckling rats and we tested THIM effect on nociception. THIM solutions were injected to Wistar and Lewis rats in a vaccination-like mode on PN days 7, 9, 11 and 15 in four equal doses. For Wistar rats these were: 12, 48, 240, 720, 1440, 2160, 3000 µg Hg/kg and for Lewis: 54, 216, 540 and 1080 µg Hg/kg. Pharmacokinetic analysis revealed that Hg from THIM injections accumulates in the rat brain in significant amounts and remains there longer than 30 days after the injection. At the 6th week of age animals were examined for pain sensitivity using the hot plate test. THIM treated rats of both strains and sexes manifested statistically significantly elevated pain threshold (latency for paw licking, jumping) on a hot plate (56 °C). Wistar rats were more sensitive to this effect than Lewis rats. Protracted THIM-induced hypoalgesia was reversed by naloxone (5 mg/kg, i.p.) injected before the hot plate test, indicative of involvement of endogenous opioids. This was confirmed by augmented catalepsy after morphine (2.5 mg/kg, s.c.) injection. Acute THIM injection to 6-week-old rats also produced hypoalgesia, but this effect was transient and was gone within 14 days. Present findings show that THIM administration to suckling or adult rats impairs sensitivity to pain, apparently due to activation the endogenous opioid system.

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1. Introduction

Thimerosal (THIM; also known as thiomersal or sodium ethylmercurithiosalicylate), which contains about 49% of mercury (Hg) by weight, has been used as a vaccine preservative for decades without rigorous studies examining

its safety in developing mammalian organism, including infants. A vast body of scientific literature provides evidence that all forms of Hg are highly toxic to animals (rev. Díez, 2009; Clarkson and Magos, 2006). THIM is biotransformed in the body to ethylmercury and subsequently also into inorganic forms of Hg (Qvarnström et al., 2003). Significant amounts of

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Abbreviations: SIB, self injurious behaviors; THIM, thimerosal; Hg, mercury