Neurochem Res (2012) 37:436–447
DOI 10.1007/s11064-011-0630-z

ORIGINAL PAPER

Administration of Thimerosal to Infant Rats Increases Overflow of Glutamate and Aspartate in the Prefrontal Cortex: Protective Role of Dehydroepiandrosterone Sulfate

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Received: 11 August 2011 / Revised: 27 September 2011 / Accepted: 4 October 2011 / Published online: 21 October 2011

Abstract Thimerosal, a mercury-containing vaccine preservative, is a suspected factor in the etiology of neurodevelopmental disorders. We previously showed that its administration to infant rats causes behavioral, neurochemical and neuropathological abnormalities similar to those present in autism. Here we examined, using microdialysis, the effect of thimerosal on extracellular levels of neuroactive amino acids in the rat prefrontal cortex (PFC). Thimerosal administration (4 injections, i.m., 240 μg Hg/kg on postnatal days 7, 9, 11, 15) induced lasting changes in amino acid overflow: an increase of glutamate and aspartate accompanied by a decrease of glycine and alanine; measured 10–14 weeks after the injections. Four injections of thimerosal at a dose of 12.5 μg Hg/kg did not alter glutamate and aspartate concentrations at microdialysis time (but based on thimerosal pharmacokinetics, could have been effective soon after its injection). Application of thimerosal to the PFC in perfusion fluid evoked a rapid increase of glutamate overflow. Coadministration of the neurosteroid, dehydroepiandrosterone sulfate (DHEAS; 80 mg/kg; i.p.) prevented the thimerosal effect on glutamate and aspartate; the steroid alone had no influence on these amino acids. Coapplication of DHEAS with thimerosal in perfusion fluid also blocked the acute action of thimerosal on glutamate. In contrast, DHEAS alone reduced overflow of glycine and alanine, somewhat potentiating the thimerosal effect on these amino acids. Since excessive accumulation of extracellular glutamate is linked with excitotoxicity, our data imply that neonatal exposure to thimerosal-containing vaccines might induce excitotoxic brain injuries, leading to neurodevelopmental disorders. DHEAS may partially protect against mercurials-induced neurotoxicity.

Keywords Thimerosal · Glutamate · Amino acids · Microdialysis · DHEAS

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Introduction

Thimerosal, an organomercurial (THIM; sodium ethylmercurithiosalicylate), has been used as a preservative in liquid medicinal products, including pediatric vaccines, for decades without being adequately tested for safety in developing organisms. THIM, which contains approximately 49% mercury by weight and is composed of ethylmercury (EtHg) and thiosalicylic acid, is metabolized in the body to EtHg and further to inorganic forms of mercury [1]. Previous studies reported that THIM administration to rats leads to accumulation of mercury in the liver, kidneys and the brain, where it may produce toxic effects [2–6]. Although THIM was withdrawn from use in primary pediatric vaccines in most developed countries, it is still