



Perinatal multiple exposure to neurotoxic (lead, methylmercury, ethylmercury, and aluminum) substances and neurodevelopment at six and 24 months of age



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ABSTRACT

We studied neurodevelopment in infants from two communities. Children living in the vicinity of tin-ore kilns and smelters – TOKS; $n = 51$) were compared to children from a fishing village (Itapuã; $n = 45$). Mean hair-Hg (HHg) concentrations were significantly higher in Itapuã children which received significantly ($p = 0.0000001$) less mean ethylmercury ($88.6 \mu\text{g}$) from Thimerosal-containing vaccines (TCV) than the TOKS children ($120 \mu\text{g}$). Breast-milk Pb concentrations were significantly higher in the TOKS mothers ($p = 0.000017$; 10.04 vs. $3.9 \mu\text{g L}^{-1}$). Bayley mental development index (MDI) and psychomotor development index (PDI) were statistically significant (respectively $p < 0.0000001$, $p = 0.000007$) lower for the TOKS children only at 24 months of age. Multivariate regression analysis showed that MDI was negatively affected by breast-milk Pb and by HHg. PDI was positively affected by breastfeeding and negatively affected by ethylmercury. Milestone achievements were negatively affected by breast-milk Pb (age of walking) and by HHg (age of talking).

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1. Introduction

Early life neurodevelopmental challenges and resulting disabilities due to cumulative exposure to hazardous substances begin at pregnancy and/or during the post-natal period. Additionally, socio-economic disparities associated with psychological stimuli can modulate trajectories that influence mental and psychomotor outcomes. Exposure to environmental neurotoxic substances, *per se* or in combination, can burden the central nervous system (CNS) of the fetus and young child.

Due to the increased pollution or environmental contamination, children nowadays are exposed to more man-made toxic agents than in the past (Landrigan et al., 2005). The number of toxic molecules that are introduced with modern-day manufactured goods (including biocides) has increased considerably. As a result of CNS immaturity, the unborn fetus and infant have to deal with different kinds of toxic substances co-occurring from multiple

sources. Neurotoxic metals (e.g. lead, mercury, and aluminum) *per se* are known to negatively affect neurodevelopment even at low doses. Indeed, developmental effects have been demonstrated in animal models and have also been observed in children (Rice and Barone, 2000; Carpenter, 2001; Fox et al., 2012). As reviewed elsewhere (Rice and Barone, 2000; Fox et al., 2012), the effects of such substances can be developmental delays, transient or persistent neurological deficits, with neurobehavioral consequences in the individual and societal costs (Bellinger, 2004; Attina and Trasande, 2013). Worldwide, with the increase in manufactured goods and economic globalization, there is a high prevalence of exposure to neurotoxic chemicals *per se* or in combination.

Organic Hg compounds (methylmercury – MeHg, ethylmercury – EtHg) are comparably toxic and hazardous with demonstrable risks shown in animal and human studies (Dórea et al., 2013). While MeHg exposure is mainly through consumption of fish and seafood, EtHg exposure occurs only through Thimerosal-containing vaccines (TCV) widely used in pediatric populations of third-world countries. Additionally, besides EtHg, TCV contains adjuvant-Al (Dórea and Marques, 2010); individually, these substances are below the currently assumed toxicological threshold. However, cumulative

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