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Noninvasive biomarkers of manganese exposure and neuropsychological effects in environmentally exposed adults in Brazil

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HIGHLIGHTS

- Noninvasive biomarkers evaluate Mn exposure to metallurgical emissions.
- An inverse gradient of exposure is observed in those living relatively further.
- Scalp hair, fingernail and axillary hair are useful matrices to assess Mn exposure.
- The levels observed are associated with detrimental neuropsychological effects.

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ABSTRACT

Manganese (Mn), an essential element to humans, in excess can cause neurotoxic damage. So far, Mn exposure assessment has no ideal biomarker. This study aims to investigate the association between Mn exposure, using noninvasive biomarkers, and neuropsychological effects in environmentally exposed adults. The residents of two communities near to a ferromanganese refinery in Bahia, Brazil were evaluated. Volunteers aged 15–55 of both sexes provided scalp hair, axillary hair, fingernail and saliva specimens for Mn determination by electrothermal absorption spectrometry. Several neuropsychological tests were used to evaluate cognitive, attention, memory, motor and executive functions. Significant correlations were observed between Mn in hair (MnH, median 8.95 μg/g), axillary hair (MnAxH,18.49 μg/g) and fingernail (MnFN, 6.91 μg/g) with the performances in several neuropsychological tests. No association was observed between manganese levels in saliva (MnSal, 4.2 μg/L) and any neuropsychological function. Multiple regression analysis detected an inverse association between Log MnH and IQ (β = −4.76 [CI 95% −9.17 to −0.36]) and between Log MnFN and visual working memory (β = −3.33 [CI 95% −6.15 to −0.52]). Direct association was observed between Log MnFN and time of completion in the cognitive flexibility task (β = 56.29 [CI 95% 2.41–110.18]). The Mn biomonitoring using noninvasive biomarkers was able to detect high exposure levels, which were associated with detrimental neuropsychological effects in adults exposed to industrial emissions.

1. Introduction

Manganese (Mn) is an essential mineral (Aschner and Aschner, 2005), that when present in excess in the body, can cause damage to the central nervous system (Aschner et al., 2007). The accumulation of this element in the basal ganglia and cerebral frontal cortex (Reaney et al., 2006; Rivera-Mancía et al., 2011; Sen et al., 2011), as well as its correlation with poor performance on neuropsychological tests (Sen et al., 2011) have been demonstrated in animals and humans.

The action of Mn on neurotransmitters can cause changes in synaptic mechanisms mediated by dopamine, glutamate and γ-aminobutyric acid (GABA) (Burton and Guilarte, 2009), which can trigger poor performance on neuropsychological tests assessing motor, cognitive and behavioral functions. Studies with

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non-human primates exposed to Mn showed behavior similar to Parkinson's disease and impairment of cognitive and motor functions (Burton and Guilarte, 2009; Schneider et al., 2009). Occupational and environmental exposures to Mn have also been correlated with motor impairment (Lucchini et al., 2012; Mergler et al., 1994), working memory (Park et al., 2009), low cognitive performance (Bouchard et al., 2011; Menezes-Filho et al 2011; Riojas-Rodríguez et al 2010; Wasserman et al., 2006), low academic performance (Khan et al., 2012), hyperactivity (Bouchard et al., 2007), externalizing behaviors (Khan et al., 2011), negative effects on attention (Laohaudomchok et al., 2011) and memory(Torres-Agustín et al., 2013).

Communities located nearby mine ore extraction (Riojas-Rodríguez et al., 2010), metal alloys plants (Menezes-Filho et al., 2009a) and near agricultural areas spraying with fungicides such as maneb and mancozeb (Geissen et al., 2010; Mora et al., 2014), among others, are groups at risk of excessive Mn exposure. Epidemiological studies on communities environmentally exposed to this metal have successfully used scalp hair Mn (MnH) and air Mn as biological and environmental markers of exposure (Menezes-Filho et al., 2009a; Riojas-Rodríguez et al., 2010; Rodríguez-Agudelo et al., 2006). In general, the usefulness of a biomarker of exposure should be evaluated by its ability to characterize and differentiate exposed and non-exposed groups, as well as by its ability to predict health disturbances; it should also be able to anticipate neuropsychological impairment as a consequence of short or long term exposure.

Conflicting results in the literature do not contribute to the selection of the ideal biomarker to assess Mn exposure, which would be the one that best correlates biological levels of Mn with environmental Mn concentrations. Blood and hair Mn levels have been widely used in environmental and occupational studies in which neuropsychological outcomes resulting from exposure to this metal were evaluated (Bader et al., 2000; Rodríguez-Agudelo et al., (2006); Bowler et al., 2007; Menezes-Filho et al., 2009b; Zheng et al., 2011). However, Mn blood levels have rarely been associated with performance on neuropsychological tests (Roels et al., 2012; Bhang et al., 2013). Mn levels in saliva, axillary hair and nails, on the other hand, have been used only in exposure assessment studies. None used these biomarkers to investigate their associations with neuropsychological effects (Bader et al., 1999; Cowan et al., 2009; Gil et al., 2011; Laohaudomchok et al., 2011; Mehra and Juneja, 2005; Menezes et al., 2004; Wang et al., 2008; Wongwit et al., 2004).

The authors have been gathering evidences about excessive Mn exposure of children and their mothers who live in communities near a metallurgical plant. It was found negative associations between internal dose of Mn, measured in hair, and intellectual functions, working memory and attention (Menezes-Filho et al., 2011; Carvalho et al., 2013), and direct association with behavioral changes, specially externalizing behavior (Menezes-Filho et al., 2013). In these studies, it was found that only MnH levels were associated with neuropsychological function scores when adjusted for social–economic covariables, like gender, age, height-age z-score and maternal education. Blood Mn levels were not associated

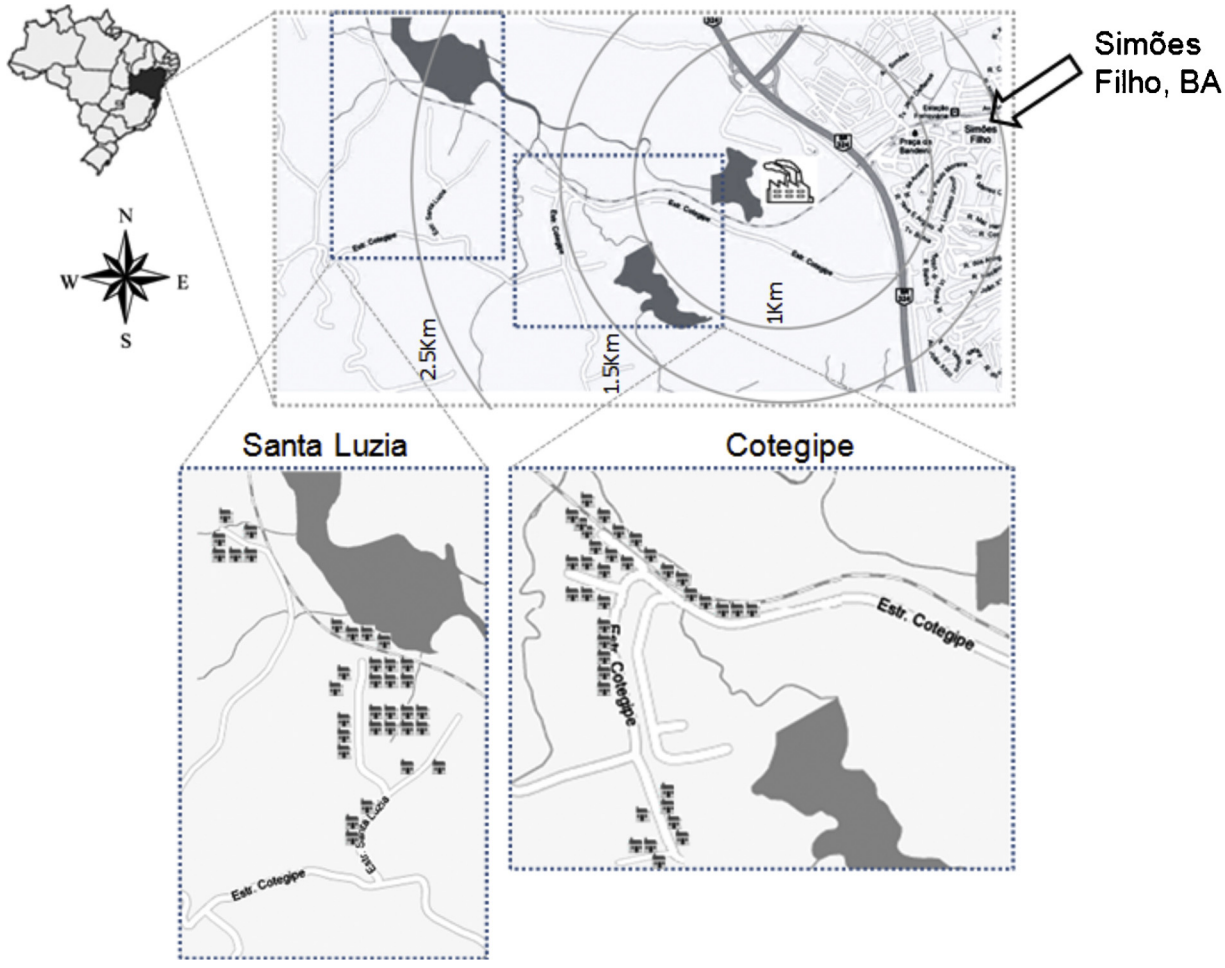

Fig. 1. Schematique map of the study location in the district of Simões Filho, Bahia, Brazil.