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Changes in water manganese levels and longitudinal assessment of intellectual function in children exposed through drinking water

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ABSTRACT

Background: Manganese is commonly found in water but potential neurotoxic effects from exposure through drinking water are poorly understood. We previously reported a cross-sectional study showing that drinking water Mn concentration was associated with lower IQ in children aged 6 to 13 years.
Objective: For this follow-up study, we aimed to re-assess the relation between exposure to Mn from drinking water and IQ at adolescence. In addition, we aimed to examine whether changes in drinking water Mn concentration was associated with changes in IQ scores.
Methods: From the 380 children enrolled in the baseline study, 287 participated to this follow-up study conducted in average 4.4 years after. Mn concentration was measured in home tap water and children's hair. The relationships between these Mn exposure indicators and IQ scores (Weschsler Abbreviated Scale of Intelligence) at follow-up were assessed with linear regression analysis, adjusting for potential confounders. Intra-individual differences in IQ scores between the two examinations were compared for children whose Mn concentration in water remained stable between examinations, increased or decreased.
Results: The mean age at follow-up was 13.7 years (range, 10.5 to 18.0 years). Geometric mean of Mn concentration in water at follow-up was 14.5 μg/L. Higher Mn concentration in water measured at follow-up was associated with lower Performance IQ in girls (β for a 10-fold increase = −2.8, 95% confidence intervals [CI] −4.8 to −0.8) and higher Performance IQ in boys (β = 3.9, 95% CI 1.4 to 6.4). IQ scores were not significantly associated with Mn concentration in hair, although similar trends as for concentration in water were observed. For children whose Mn concentration in water increased between baseline and follow-up, Performance IQ scores decreased significantly (intra-individual difference, −2.4 points).
Conclusion: Higher levels of Mn in drinking water were associated with lower Performance IQ in girls, whereas the opposite was observed in boys. These findings suggest long-term exposure to Mn through drinking water is associated differently with cognition in boys and girls.

1. Introduction

Manganese (Mn) is an essential element that occurs naturally in soil, air, as well as in all living organisms. This metal is also commonly present in groundwater, sometimes in high concentrations, due to local geological characteristics. High Mn concentration have been reported in drinking water in many countries around the world where groundwater is used for human consumption (Frisbie et al., 2012), including Canada (Barbeau et al., 2011). Mn is an essential nutrient, but in large dose can also be a potent neurotoxicant, with effects on cognition, behavior, and neuromotor function (Dobson et al., 2004). Early studies depicting the neurotoxic effects of Mn were conducted in occupationally exposed groups (Mergler et al., 1994; Rodier 1955; Roels et al.,

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1987), and more recently increased efforts were made to investigate Mn neurotoxicity in environmentally exposed children (O'Neal and Zheng, 2015).

Epidemiological evidence suggests that Mn exposure from drinking water could be associated with lower intelligence quotient (IQ) scores in children (Bouchard et al., 2011; Wasserman et al., 2006). Drinking water Mn concentrations has also been associated with poorer memory, attention, motor functions (Oulhote et al., 2014a), mathematics achievement scores (Khan et al., 2012), perceptual reasoning, working memory (Nascimento et al., 2016; Rahman et al., 2016; Wasserman et al., 2011, 2016), as well as behavior problems (Bouchard et al., 2007; Khan et al., 2011; Rahman et al., 2016). Although these studies vary greatly in terms of levels of exposure, they support the hypothesis that Mn exposure might adversely affect the developing brain.

We previously reported that elevated water Mn concentration (MnW) was associated with lower IQ in a group of school-age children aged 6–13 years (Bouchard et al., 2011). In this study, children in the highest quintile of Mn concentration had IQ scores 6 points lower than those in the lowest quintile. The association between MnW and IQ was stronger for girls than for boys. Hair Mn concentrations were also associated with lower IQ scores. Importantly, these results were observed at levels of exposure currently considered low and safe since and only 3% of participants had drinking water exceeding the World Health Organization guideline of 400 μg Mn/L (World Health Organization, 2004) (before this guideline it was discontinued altogether in 2011; World Health Organization, 2011).

The present study follows up the above cohort, and was conducted approximately four years after the initial study, depending on participants. The first objective was to re-assess the relation between water Mn concentration and cognition in this cohort around adolescence. The second objective was to monitor changes in Mn concentration in participants' drinking water and to investigate how it might relate to change in IQ scores.

2. Methods

2.1. Study design and recruitment

Participants of the baseline epidemiological study in southern Quebec (Canada) carried out by Bouchard et al. in 2007–2009 were contacted for the present follow-up study, conducted in 2012–2013. Details on selection and recruitment of the baseline study participants are reported elsewhere (Bouchard et al., 2011). Of the initial 380 participants (mean age, 9.3 years; standard deviation [SD], 1.8), 287 children (mean age, 13.7 years; SD, 1.8) participated in the follow-up study. Mean time elapse between baseline and follow-up examinations was 4.4 years (range, 4.0-5.2 years). The main reason for attrition was loss of contact with participants (11%). Among participants with whom we maintained contact, participation rate was 85%. For each participant, an informed written consent was obtained from a parent, as well as written assent from the adolescent. The research procedures were approved by the Sainte-Justine Hospital and Université du Québec à Montréal research ethics committees.

2.2. Mn measurements

The same procedures as in Bouchard et al. (2011) were used for collecting water and hair samples to ensure comparability of results between baseline and follow-up examinations.

A water sample from the kitchen tap was collected for every child enrolled in the study, using a standardized sampling procedure: 1) open the tap for 5 min, 2) close and leave untouched for 30 min, and 3) collect first draw (Van den Hoven and Slaats, 2006). We added 0.15 mL nitric acid (50%) to the 50-mL water sample, which was then stored at 4 °C. Mn and other metals (iron, arsenic, and lead) were measured by inductively coupled plasma mass spectrometry (ICP-MS) at the Department of Chemistry, Université de Montréal.

Mn concentration was measured in a hair sample (MnH) collected from the occiput of each child, cutting as close as possible to the root with surgical stainless steel scissors. The 2 cm closest to the scalp was used for analysis. Hair samples were washed and digested following the procedure described in Wright et al. (2006) and analysed by ICP-MS. A certified reference material was used to control the quality of analysis with every batch of digestions. Missing data ($n = 13$) occurred for the following reasons: participant's refusal to give sample, short hair length, recently dyed hair and problems in laboratory analysis.

2.3. Time-averaged water Mn exposure

For each participant, one parent was interviewed to collect information on water supply to the house, including changes that occurred between the baseline and this follow-up study. For 31% of participants (n = 88), changes had occurred in their water supply since the baseline study: some moved (44%, n = 39), some reported a change in their domestic water treatment system (41%, n = 36), and some were drawing water supply from a municipality that changed the water treatment system (15%, n = 13). In our analyses, we used Mn water concentrations measured at baseline and follow-up examinations and calculated a time-averaged MnW (TAWMn), taking into consideration changes to water supply made in-between studies. TAWMn could not be calculated for only one

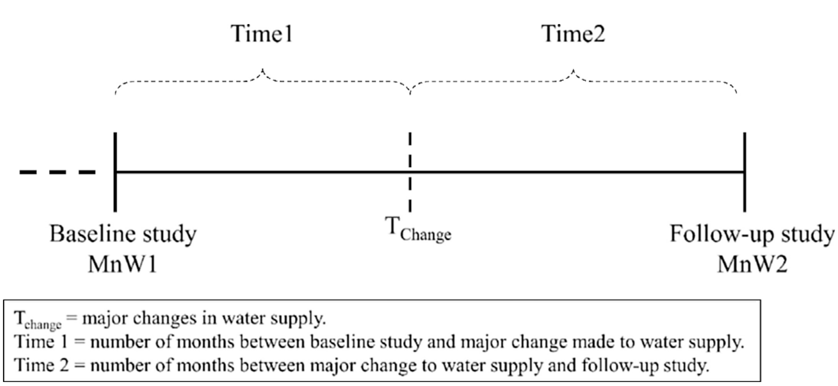

Fig. 1. Calculation of the TAWMn. MnW1, Mn concentration at baseline; MnW2, Mn concentration at follow-up; T_{Change}, major change in water supply; Time 1, number of months between baseline examination and major change made to water supply; Time 2, number of months between major change to water supply and follow-up examination.