



## Manganese exposure from drinking water and children's academic achievement

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### ABSTRACT

Drinking water manganese (WMn) is a potential threat to children's health due to its associations with a wide range of outcomes including cognitive, behavioral and neuropsychological effects. Although adverse effects of Mn on cognitive function of the children indicate possible impact on their academic achievement little evidence on this issue is available. Moreover, little is known regarding potential interactions between exposure to Mn and other metals, especially water arsenic (WAs). In Araihaazar, a rural area of Bangladesh, we conducted a cross-sectional study of 840 children to investigate associations between WMn and WAs and academic achievement in mathematics and languages among elementary school-children, aged 8–11 years. Data on As and Mn exposure were collected from the participants at the baseline of an ongoing longitudinal study of school-based educational intervention. Annual scores of the study children in languages (Bangla and English) and mathematics were obtained from the academic achievement records of the elementary schools. WMn above the WHO standard of 400  $\mu\text{g/L}$  was associated with 6.4% score loss (95% CI =  $-12.3$  to  $-0.5$ ) in mathematics achievement test scores, adjusted for WAs and other sociodemographic variables. We did not find any statistically significant associations between WMn and academic achievement in either language. Neither WAs nor urinary As was significantly related to any of the three academic achievement scores. Our finding suggests that a large number of children in rural Bangladesh may experience deficits in mathematics due to high concentrations of Mn exposure in drinking water.

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### 1. Introduction

Health effects of chronic manganese (Mn) exposure in both occupational (e.g. welding) and environmental settings are reported in adults. In children, exposure to Mn is likely from environmental sources with exposure levels lower than in adults. Despite lower levels of exposure, several studies report cognitive, neurobehavioral and neuropsychological health effects in children (Bouchard et al., 2007, 2011; Ericson et al., 2007; Khan et al., 2011; Kim et al., 2009; Menezes-Filho et al., 2009; Takser et al., 2003; Wasserman et al., 2006; Wright et al., 2006). The memory deficits

that often accompany exposure in both children (He et al., 1994; Wasserman et al., 2006) and adults (Bowler et al., 2007; Chang et al., 2009, 2010; Lucchini et al., 1995; Lucchini and Zimmerman, 2009) suggest consequences for children's academic achievement. While cognitive ability is certainly related to academic achievement, early-school academic achievement may be more predictive of functional capacity such as success in later stages in school (Duncan et al., 2007; Hooper et al., 2010; Romano et al., 2010).

Although lowered academic achievement in languages, math, science and other disciplines has been related to children's exposure to lead (Chandramouli et al., 2009; Miranda et al., 2007; Zahran et al., 2009) associations between Mn exposure and measures of children's school performance have less often been reported. In an ecological study in China, Mn-exposed children were found to have significantly lower school performance in mathematics and language (Zhang et al., 1995) compared to children in a non-exposed village.

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In Bangladesh, especially in rural areas, people rely on groundwater as the only source of fresh drinking water. However, both naturally occurring Mn and arsenic (As) in groundwater have been recognized as threats to rural public health. Since 2000, a team of health, earth and social scientists at Columbia University has carried out a large collaborative projects in Araihaazar, Bangladesh. In this region, independent health effects of both Mn and As on children's intelligence have been documented (Wasserman et al., 2004, 2006, 2007).

This study examines the associations between Mn and/or As and academic achievement among 8–11 year old children with wide ranges of As and Mn exposures. We also examine the joint effect of Mn and As on children's academic achievement to explore possible effect modification (Kim et al., 2009; Wright et al., 2006).

## 2. Methods

### 2.1. Overview

This cross-sectional study is a component of an ongoing, prospective elementary school-based intervention study for lowering arsenic exposure from drinking water in Araihaazar, Bangladesh. The study area is adjacent to a previously described study area for a larger cohort study of adults (Ahsan et al., 2006) consisting of three unions of Araihaazar upazilla located about 25 km southeast of the capital city Dhaka. Araihaazar has an area of 183 km<sup>2</sup> and contains 12 unions, the smallest administrative units in Bangladesh, which each consists of 10–15 villages. Every family in Araihaazar typically lives in a house made of tin, mud, hay and in some cases concrete. Several houses are clustered together to form a bari representing a small segment of the community (sometimes an extended family). Every family generally relies on a household well (also known as tubewell) to get groundwater and uses it for drinking and cooking. We report on 840 children enrolled in an ongoing school intervention study at 14 elementary schools.

### 2.2. Selection of schools and participants

We initially identified 27 elementary schools in three unions (Haizadi, Uchitpur and Khagkanda) of Araihaazar within reasonable travel distance to the field clinic where our project offices are located. Schools were selected for participation based on three eligibility criteria: (1) ten or more age-appropriate children (8–11 years) in each classroom, (2) all teachers agreed to participate in an ongoing intervention study and (3) schools agreed to provide us with the academic performance records of the participating children. We identified 14 schools in the three unions that met the selection criteria and subsequently recruited children from these schools.

To begin the recruitment, our field staff first visited each of the 14 schools and obtained a list of all 1925 enrolled students with their addresses. Children of these 14 schools came from 30 different villages of three unions. We conducted home visits to enroll the children in the study. We also made sure that we recruited a minimum of 9–12 children from each of these 30 villages. Homes of 952 potential participants were visited, continuing until our targeted sample size of roughly 800 children was enrolled. Inclusion criteria restricted enrollment to children aged 8–11 years who attended school in an age-appropriate grade, had no known physical disability or chronic illness, and were not twins. Of the 952 children whose families were visited for eligibility review, we were unable to locate 75, either because the family had moved ( $n = 12$ ) or because no one was available at the time of the visit ( $n = 63$ ). Twenty-seven children were older than the specified age, and 10 attended school only infrequently.

Altogether, 840 children agreed to participate. By design, measures of urinary As (UAs) were available on half the sample ( $n = 420$ ), whereas measures of water As and Mn (WAs, WMn) from the home well were available on all.

### 2.3. Procedure

Prior to conducting this study, we secured approval from Institutional Review Boards at Columbia University Medical Center and the Bangladesh Medical Research Council, and obtained written informed consent from parents and school-teachers, as well as child assent. Once parental consent and child assent were obtained, the field team collected socio-demographic information during a structured interview and observation in home visits. At this time, we also identified the home well for each child that was the source of primary drinking water for the child's family. Water sample from this home well and child's urine sample were collected. Height, weight, head and arm circumferences of each child were also measured during this visit. The field team visited the schools and subsequently met with teachers to obtain the performance records of each child in the most recent annual school-wide district tests in both language (Bangla and English) and mathematics. Teachers were blind to children's household well As and Mn status.

### 2.4. Measures

#### 2.4.1. Teacher characteristics

Teachers were asked questions related to their experience, including their age, number of years teaching and their educational qualifications.

#### 2.4.2. Child characteristics

Socio-demographic measures included information on paternal and maternal education and father's occupation. Characteristics of the physical home environment were measured by noting the type of construction (roof, wall and floor) of the house and availability of television and radio.

#### 2.4.3. Well water measurement

As previously described (Cheng et al., 2004; Hafeman et al., 2005) well water samples from each participant's household drinking water source were collected in 20-mL polyethylene scintillation vials. Water samples were acidified with high-purity Optima HCl for at least 48 h before analysis to ensure redissolution of any iron oxides that might have precipitated (van Geen et al., 2007). Water samples were then diluted 1:10 in a solution spiked with 73Ge and 74Ge for internal drift correction and analyzed for As and Mn by high-resolution inductively coupled plasma mass spectrometry (HR ICP-MS). Further details on field sampling and laboratory analysis procedures are described elsewhere (Cheng et al., 2004; van Geen et al., 2005). For As, the detection limit of the method was typically  $<0.02 \mu\text{g/L}$ , estimated by multiplying the As concentration corresponding to the blank by a factor of 3. The long-term reproducibility determined from consistency standards included with each run averaged 4% (1-sigma) in the 40–500  $\mu\text{g/L}$  range. For Mn, the detection limit of the method is typically  $<0.02 \text{mg/L}$  and the long-term reproducibility averaged 6% in the 0.2–2.0  $\text{mg/L}$  range.

#### 2.4.4. Urinary measurements

As previously described (Wasserman et al., 2006), UAs was measured by graphite furnace atomic absorption spectrophotometry (GFAA) using a Perkin-Elmer Analyst 600 system (Nixon et al., 1991). UAs levels were adjusted for creatinine concentrations,

which were analyzed by a colorimetric method based on Jaffe's reaction (Heinegard and Tiderstrom, 1973).

### 2.5. Outcome assessment: academic achievement

Elementary school children are evaluated in three disciplines in Bangladesh: Bangla, English as a second language, and mathematics. We obtained the annual scores from the academic achievement records of the schools. These scores are based on national uniform tests given to students in participating public and private schools. Scores are reported as percent correct and range from 0 to 100. Language tests evaluate children's memory skills; for example, "Write the first four sentences of rhyme 'X'", "Translate the following sentences into English", and "When was Mr. Y (a famous writer) born?" In contrast, mathematics test questions evaluate analytical skills and problem solving abilities, for example, calculations relying on addition and subtraction, or word problems.

### 2.6. Statistical analyses

Preliminary analyses found the distributions of both WMn and WAs to be skewed and the logarithmic transformations were used in the analyses. Summary statistics were calculated to describe the sample. Spearman correlation coefficients were used to estimate bivariate association between markers of exposures. To account for correlations in children's academic achievement scores when they were with the same primary class teacher, we employed linear models using repeated measures. Models were estimated both with and without adjustment for potential confounders. Children's academic achievement test scores with the same primary class teacher tended to be correlated (because of the clustering of children within each class teacher) and the GEE models accounted

for within teacher correlations. To identify the control variables, we first identified variables from the literature associated with child's academic achievement. Second, we examined whether the estimated regression coefficient relating exposure to outcome changed by more than 0.5 standard error after excluding the potential confounder from the model. The final model included covariates which met this criterion.

WMn was also categorized into five categories, one below WHO standard (i.e. 400  $\mu\text{g/L}$ ) and four for higher exposure levels with approximately equal numbers of subjects in each. We repeated the models using dummy variables to describe the categorization. When the coefficients of adjacent categories were similar, the categories were collapsed to yield parsimonious models. We also tested for WAs by WMn interaction by including an interaction term between WAs and WMn in the full model. Finally, we estimated a piece-wise linear function with an *a priori* knot at WMn of 400  $\mu\text{g/L}$  to examine the associations below and above the safe water standard.

## 3. Results

### 3.1. Sample characteristics

Characteristics of included children are described in Table 1. More female students than male students were included. On average, children had attended school for approximately a lifetime total of 30 months, although they were currently attending classes as second through fifth graders. About half the parents had no formal education. Participants were exposed to expectably high levels of As and Mn in drinking water: mean WAs and WMn concentrations were 13 and 3 times the WHO standards of 10 and 400  $\mu\text{g/L}$ , respectively. On average, teachers had 10 years of

**Table 1**  
Sample characteristics of study population ( $N=840$ ).

Variables	% (n)	Mean (SD)	Median	Range
Male	47.1 (396)			
House construction				
Biomass/Hay/Mud	2.3 (19)			
Corrugate	91.4 (768)			
Concrete	6.3 (53)			
School-grade				
Second	160 (19.0)			
Third	397 (47.3)			
Fourth and fifth	283 (33.7)			
Maternal education				
No education	53.6 (450)			
Elementary	31.8 (267)			
Middle school and higher	14.6 (123)			
Paternal education				
No education	48.7 (409)			
Elementary	29.3 (246)			
Middle school and higher	22.0 (185)			
Child age (years)		9.3 (0.8)	9.3	8.0–11.0
Months attending school		32.8 (8.3)	31.0	16.0–48.0
BMI ( $\text{kg/m}^2$ )		14.2 (1.2)	14.2	10.8–19.1
Head circumference (cm)		49.2 (1.5)	49.3	45.3–55.0
Teachers' experience (years)		13.0 (7.9)	15.0	2.0–34.0
Teachers' age (years)		36.7 (7.6)	37.0	23.0–56.0
Water As ( $\mu\text{g/L}$ )		119.5 (147.5)	81.9	0.1–1263.2
Water Mn ( $\mu\text{g/L}$ )		1387.9 (866.3)	1301.6	10.0–5710.1
Urine As ( $\mu\text{g/L}$ )		138.9 (133.0)	93.0	6.0–910.0
Urine creatinine (mg/dL)		44.3 (34.0)	35.1	4.1–251.3
Urine As (mg/g creatinine)		368.0 (307.9)	271.9	47.4–2589.7
Bangla language score ( $n=830$ )		45.1 (19.1)	44.0	0.0–93.0
English language score ( $n=831$ )		45.9 (20.3)	46.0	0.0–96.5
Mathematics score ( $n=830$ )		48.4 (21.0)	47.0	0.0–99.0

**Table 2**  
Model covariates and academic achievement scores (N=840).

	Bangla language score b (95% CI)	English language score b (95% CI)	Math score b (95% CI)
School-grade			
Fourth/fifth vs. second grade	-7.87 (-13.26 to -2.46)**	-4.90 (-10.71 to 0.92)	-19.84 (-25.50 to -14.17)****
Third vs. second grade	-3.41 (-8.06 to 1.25)	-3.70 (-9.81 to 2.40)	-10.33 (-15.29 to -5.38)****
Maternal education			
Middle-school or higher vs. No education	5.80 (2.59 to 9.01)**	7.61 (3.62 to 11.61)***	6.24 (2.72 to 9.77)***
Elementary vs. No education	1.36 (-1.52 to 4.23)	-0.78 (-3.37 to 1.80)	1.51 (-1.17 to 4.19)
Paternal education			
Middle-school or higher vs. No education	4.20 (0.57 to 7.81) <sup>†</sup>	4.74 (0.33 to 9.61) <sup>†</sup>	4.28 (-0.46 to 9.03) <sup>†</sup>
Elementary vs. No education	1.63 (-1.06 to 4.32)	2.35 (-0.57 to 5.28)	1.77 (-0.72 to 4.26)
Head circumference (cm)	1.51 (0.79 to 2.22)****	0.79 (-0.05 to 1.62) <sup>†</sup>	1.18 (0.40 to 1.96)**

<sup>†</sup>  $p < 0.08$ .

<sup>\*</sup>  $p < 0.05$ .

<sup>\*\*</sup>  $p < 0.01$ .

<sup>\*\*\*</sup>  $p < 0.001$ .

<sup>\*\*\*\*</sup>  $p < 0.0001$ .

teaching experience. The average test percentage scores for each of the three academic areas were approximately 50%.

### 3.2. Correlations among measures of exposure and outcomes

We found the correlation between WAs and urinary As (UAs) positive and statistically significant (Spearman correlation coefficient  $r = 0.68$ ,  $p < 0.0001$ ). The correlation between WAs and WMn was also statistically significant ( $r = 0.22$ ,  $p < 0.0001$ ). The three measures of academic achievement were also positively correlated ( $r$ 's between 0.70 and 0.75, all  $p < 0.0001$ ).

### 3.3. Associations between sociodemographic factors and academic achievement

Associations between sociodemographic factors (i.e. school-grade, head circumference, maternal education and paternal education) and all academic outcomes were in the expected directions (Table 2). Fourth and fifth grade students had lower

academic scores than second graders and the difference was statistically significant. Achievement test scores increased as head circumference increased. Children whose mothers and fathers attended middle school or beyond had significantly higher achievement test scores than those whose parents had no formal schooling. No other sociodemographic variables were associated with the outcomes when added to the models.

### 3.4. Associations between exposure markers and academic achievement

The covariate and WAs adjusted mean test scores by WMn categories were similar for WMn  $> 400 \mu\text{g/L}$ , suggesting a threshold effect (Table 3). High exposure categories of WMn were therefore combined. Covariates and WMn adjusted mean test scores in all WAs categories were similar indicating that WAs was not related to any of the three test scores. The results also suggested a dichotomization of the exposure variables on the basis of the WHO standards. Table 4 presents the associations between

**Table 3**  
Adjusted mean academic achievement scores<sup>a</sup> for the categories (pentiles) of water manganese (N=840).

WMn categories ( $\mu\text{g/L}$ )	Bangla language score Adjusted mean (se)	English language score Adjusted mean (se)	Math score Adjusted mean (se)
$\leq 400$	49.8 (3.1)	51.4 (3.2)	58.9 (3.7)
401–1000	48.1 (2.1)	46.9 (1.9)	51.7 (1.9)
1001–1440	49.0 (2.1)	49.3 (2.4)	52.8 (2.1)
1441–2000	48.1 (1.6)	49.3 (1.7)	53.5 (1.7)
2001–6000	48.8 (2.1)	48.8 (2.4)	53.0 (2.1)

<sup>a</sup> Means adjusted for log-transformed WAs, school-grade, maternal education, paternal education and head circumference and controlling for within-teacher correlations in rating the children.

**Table 4**  
Unadjusted and adjusted associations between water arsenic and water manganese and children's academic achievement scores (N=840).

Exposure variables ( $\mu\text{g/L}$ )	Bangla language score b (95% CI)	English language score b (95% CI)	Math score b (95% CI)
	<i>Adjusted only for the other element</i>		
Water As (dichotomized)	-2.33 (-5.23 to 0.61)	-1.57 (-5.11 to 1.98)	0.38 (-3.75 to 4.50)
Water Mn (>400 vs. $\leq 400$ )	-0.16 (-5.45 to 5.12)	-2.33 (-6.93 to 2.24)	-6.67 (-13.42 to 0.25) <sup>†</sup>
	<i>After adjustment for additional socio-demographic features<sup>a</sup></i>		
Water As (dichotomized)	-1.71 (-4.77 to 1.34)	-0.73 (-4.32 to 2.86)	0.56 (-2.98 to 4.10)
Water Mn (>400 vs. $\leq 400$ )	-1.01 (-6.14 to 4.12)	-2.66 (-7.16 to 1.83)	-6.37 (-12.27 to -0.46) <sup>†</sup>

<sup>a</sup> Models additionally adjusted for school-grade, maternal education, paternal education and head circumference and controlling for within-teacher correlations in rating the children.

<sup>†</sup>  $p < 0.06$ .

<sup>\*</sup>  $p < 0.05$ .

the exposures and the children's academic achievement test scores with dichotomized WAs and WMn.

#### 3.4.1. Mathematics achievement score

When WMn is modeled categorically, the adjusted regression model showed that children in all four high WMn categories lost points in their math test scores when compared with the children of the lowest exposure category (WMn  $\leq$  400  $\mu\text{g/L}$ ). In this model, estimated adjusted  $b$  values for the four high exposure categories were  $-7.1$ ,  $-6.4$ ,  $-5.5$  and  $-5.9$  ( $p = 0.03$ – $0.10$ ). When dichotomized WMn was put in the model WMn above 400  $\mu\text{g/L}$  was associated with 6% loss, 95% CI = ( $-12.27$  to  $-0.47$ ) in mathematics achievement test score, adjusted for WAs and other variables. When we put WMn as a continuous variable in a similar model log-transformed WMn also predicted loss of mathematics score ( $b = -1.7$ ,  $p = 0.07$ ). Neither WAs nor UAs were significantly related to mathematics achievement score ( $p < 0.05$ ), with or without adjustment for other covariates. The results from the spline regression models confirmed these associations.

#### 3.4.2. Language achievement scores

High WMn ( $>400 \mu\text{g/L}$ ) was also associated with a 1 and 3% reductions in Bangla and English mean test scores after adjustment for covariates, respectively, but these losses were not statistically significant ( $p > 0.24$ ). Both WAs and UAs were unrelated to language test scores, before or after adjustment (data not shown). Results from the spline regression models confirmed these results.

A linear model with repeated measures was used to test whether the points lost in mathematics and language achievement due to WMn exposure were different. For these analyses, within child correlations in the test scores were modeled as nuisance parameters. The point loss in mathematics test scores due to high WMn ( $>400 \mu\text{g/L}$ ) was greater than the loss in either language test scores ( $p < 0.01$ ) and this difference was statistically significant. No statistically significant interactions between WMn and WAs and any outcome measure was found.

## 4. Discussion

We found a statistically significant negative association between WMn (dichotomized at the WHO standard) and mathematics achievement test scores that persisted upon adjustment for sociodemographic variables, such as parental and maternal education. WMn was negatively associated with language scores although the associations were not statistically significant. High WMn ( $>400 \mu\text{g/L}$ ) was more strongly associated with mathematics achievement as compared with language achievement and this difference was statistically significant. Neither UAs nor WAs were associated with any of the three achievement scores.

In Bangladesh, the teaching of Bangla and English is not based on classroom interactions. A reading–memorization–writing approach is traditionally practiced, especially in rural areas. Teachers and students read and recite stories, poems and essays in the classroom throughout the year. At the end of the school-year, students are tested on their memorization skills by answering both short and descriptive questions about these rhymes, poems and essays. Students do not need to think critically, rather they are asked to remember specific parts of the materials they have read and to reproduce that content during testing. Therefore, language tests contain few questions that require working memory. This process of memory retrieval is much faster, automatic and has very little or no dependence on working memory (Ashcraft and Krause, 2007). In contrast, in teaching mathematics children are required to make greater use of analytical skills, abilities that are necessary for solving the types of problems that appear in the annual

mathematics test. Mathematics test problems require strategy-based solutions which are heavily dependent on working memory (Ashcraft and Krause, 2007). Our study results are consistent with the literature that showed poor working memory as a predictor of mathematics achievement (Bull and Scerif, 2001; Bull et al., 2008; Geary et al., 2004). More specifically working memory is a strong predictor of arithmetic skills (Andersson, 2008), which are the predominant forms of mathematics learning in Bangladeshi elementary school system. Although working memory predicts other types of academic achievements such as language skills (Bull et al., 2008) differences in the way language and mathematics contents are taught and assessed may explain the greater impact of WMn exposure on mathematics achievement.

#### 4.1. Mn neurotoxicity and working memory

Animal studies suggest that certain neurotransmitters have particular impact on memory and learning, including glutamate,  $\gamma$ -amino butyric acid (GABA), dopamine, acetylcholine, serotonin and norepinephrine (Myhrer, 2003). Animal models suggest that Mn affects neurotransmitters in the dopaminergic and glutamatergic systems (Tran et al., 2002) as well as serotonin binding (Velez-Pardo et al., 1995). For example, animals dosed with various concentrations of Mn postnatally commit more errors and exhibit learning deficiencies in radial arm mazes compared to control animals (Kern et al., 2010). Animal studies also support the view that brains of young animals have the ability to achieve higher Mn concentrations than those of adults (Dorman et al., 2000; Moreno et al., 2009). Animal studies have identified brain compartments, such as basal ganglia, prefrontal cortex, cerebellum and hippocampus where Mn primarily accumulates (Bock et al., 2008; Guilarte et al., 2006; Rose et al., 1999; Schneider et al., 2009; Yamada et al., 1986) resulting in detrimental effects on working memory processes and learning. Other research with non-human primates has documented similar impact of Mn on both spatial and non-spatial working memory (Schneider et al., 2006, 2009).

Importantly, Mn exposure results in similar types of deficits in occupational epidemiological studies of welders, where multiple investigations consistently demonstrate detrimental effects on immediate, short-term and long-term memory functions (Bowler et al., 2007; Chang et al., 2009, 2010; Lucchini et al., 1995, 1999). Working memory contributes to children's learning capacity. Compared to IQ measures, working memory better predicts academic achievement and overall learning (Alloway and Alloway, 2010). In a longitudinal study, poorer working memory skill in kindergarten children was associated with lower academic attainment in reading, spelling, mathematical reasoning and number operations at age 10–11 years (Alloway and Alloway, 2010). Recently, in a separate cohort of Bangladeshi children, we observed decreased WISC-IV working memory scores in 10 year old children drinking from household wells with elevated levels of WMn (Wasserman et al., 2011).

#### 4.2. As and academic achievement

We did not observe associations between measures of As exposure and academic achievement. Toxicity of As occurs through oxidative stress leading to neuronal injury (Larochette et al., 1999), changes of neurotransmitter levels by affecting basal ganglia (Rodriguez et al., 2003), decreases of superoxide dismutase (Modi and Flora, 2007) and glutathione-related enzyme activities (Kannan and Flora, 2004). Recent work has also proposed detrimental effects of As through disruption of neuron cytoskeletal network (Giasson et al., 2002; Vahidnia et al., 2008). Our own research group at Columbia University has also reported lower scores on intelligence tests in children in relation to As exposure

(Wasserman et al., 2004, 2007). However, evidence of the effect of As on working memory of children, a stronger predictor of academic achievement at later stage in life is not convincing in the literature. Our group has recently found significant effect of As on working memory of the Bangladesh children in statistical models before adjustment for important sociodemographic variables known to be related to intelligence scores; this association became non-statistically significant after adjustment (Wasserman et al., 2011). Thus, we anticipated that the effect of As on a functional outcome like academic achievement is less likely to be observed at this age group even though As is considered as a potential neurotoxicant. In addition, to the best of our knowledge, no systematic laboratory study has been done to show the effect of As on different brain compartments that are associated with learning. We therefore propose that As alters cognitive and neurological functions but has minimal impact on learning capacity and academic achievement. Alternatively, As toxicity may show latent effects on learning.

#### 4.3. Limitations of the study

Our study results may have encountered limited “geographic generalizability” since the study population may represent only comparable communities with similar sociodemographic characteristics. Our findings may not be generalizable to children living in urban communities. The cross-sectional design of this study can be considered as another limitation as it can hinder cause and effect inferences. The lack of tests for working memory is another limitation with respect to interpreting the results.

The design of the prospective educational intervention study from which this cross-sectional study evolved allowed collection of urine and water samples for measuring exposures among participants. Therefore, no Mn biomarker of dose except WMn was available. Blood manganese (BMn) reflects only recent exposure and therefore, may not reliably indicate total body burden of Mn (Bouchard et al., 2011). Although two recent studies reported associations between hair manganese (HMn) and child intelligence (Bouchard et al., 2011; Menezes-Filho et al., 2011) a recent study found significant association in girls only (Riojas-Rodriguez et al., 2010). Thus literature indicates that defining optimal Mn biomarker of dose remain an open question.

#### 5. Conclusions

In Bangladesh, the problem of groundwater contaminated with As has received enormous public health attention because of the diversity of adverse health effects associated with such exposure. It is now clear that many of these same regions have excessive concentrations of Mn in the well water. However, elevated levels of Mn have received very little attention from the government and development agencies. The British Geological Survey found 35% of the samples collected from various parts of the country exceeding the former WHO Mn guideline of 500  $\mu\text{g/L}$  (BGS/DPHE, 2001). In Araihaazar, where we conducted our study, the proportion of high Mn wells exceeding the WHO standard is even higher (80%) (Cheng et al., 2004). Selection of 400  $\mu\text{g/L}$  as a cut off was based on the current WHO guideline. However, the objective of our statistical analyses was not to establish whether this value is effectively protective. We cannot rule out possible effects of WMn on math achievement below the level of 400  $\mu\text{g/L}$ . In a recent epidemiological study in the same region, Hafeman et al. (2007) observed an elevated mortality risk during first year of life in the infants exposed to high WMn ( $>400 \mu\text{g/L}$ ) (OR = 1.8 and 95% CI = 1.2–2.6) compared to infants with lower exposures. Added to our new finding of a significant association between WMn and mathematics achievement, we hope this will motivate stakeholders in

Bangladesh to seriously consider measures for reducing WMn exposure in the near future. The task may be even more arduous than reducing WAs exposure. In only 4 of the 26 villages where the children in this study live was at least one household well identified with no more than 10  $\mu\text{g/L}$  As and no more than 400  $\mu\text{g/L}$  Mn. Using arsenic as the only criterion, there is at least one household well in 16 of the 26 villages that could be shared as a source of drinking water. An additional complication is that deeper aquifers, which have successfully been tapped to install deep community well throughout Araihaazar to dramatically lower As exposure do not necessarily meet the current WHO guideline for Mn (van Geen et al., 2007).

Elevated groundwater Mn can be a significant source of human exposure in developing countries like Bangladesh. Even in a developed country such as the US, where 5.2% of household wells contain more than 300  $\mu\text{g/L}$  of Mn (DeSimone et al., 2009), a large number of children may be at risk for deficits in academic achievement. Our findings add to the growing concern about the impact of water-borne Mn exposure on children's health.

#### Conflict of interest statement

The authors declare that they have no actual or potential competing financial interests.

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