Proximity to point sources of environmental mercury release as a predictor of autism prevalence

Raymond F. Palmer[a],*, Stephen Blanchard[b], Robert Wood[a]

[a]*University of Texas Health Science Center, San Antonio Department of Family and Community Medicine, 7703 Floyd Curl Drive, San Antonio Texas, Mail Code 7794, TX 78229-3900, USA*
[b]*Department of Sociology, Our Lady of the Lake University, San Antonio Texas, TX, USA*

Abstract

The objective of this study was to determine if proximity to sources of mercury pollution in 1998 were related to autism prevalence in 2002. Autism count data from the Texas Educational Agency and environmental mercury release data from the Environmental Protection Agency were used. We found that for every 1000 pounds of industrial release, there was a corresponding 2.6% increase in autism rates ($p < .05$) and a 3.7% increase associated with power plant emissions($P < .05$). Distances to these sources were independent predictors after adjustment for relevant covariates. For every 10 miles from industrial or power plant sources, there was an associated decreased autism Incident Risk of 2.0% and 1.4%, respectively ($p < .05$). While design limitations preclude interpretation of individual risk, further investigations of environmental risks to child development issues are warranted.
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Introduction

Mercury is a heavy metal found naturally in trace amounts in the earth's atmosphere in differing forms—as elemental vapor, reactive gaseous compounds, or particulate matter. Studies show that background levels of environmental mercury deposition have steadily increased several fold since the pre-industrial era (Schuster et al., 2002), with the largest source of potentially adverse exposures coming primarily from coal-fired utility plants (33%), municipal/medical waste incinerators (29%) and commercial/industrial boilers (18%)—estimated to be responsible for 158 tons of environmental mercury released per year in the US (Environmental Protection Agency, Report to Congress, 1997). Other sources include hazardous waste sites, cement factories, and chlorine production plants. According to the Agency for Toxic Substances and Disease Registry (ATSDR), next to arsenic and lead,

mercury is the third most frequently found toxic substance in waste facilities in the United States (ATSDR, 2001).

Mercury is now widespread in the environment (EPA, 1997; ATSDR, 2001). The long-range atmospheric transport of mercury (Ebinghaus et al., 2001), and its conversion to organic forms through bio-accumulation in the aquatic food chain has been known for some time (MacGregor, 1975; Mahaffey, 1999). Notwithstanding, there are emerging concerns over the potential adverse effects of ambient levels of environmental mercury during early childhood development. There is sufficient evidence that children and other developing organisms are particularly susceptible to the adverse neurological effects of mercury (Landrigan and Garg, 2002; Grandjean et al., 1995; Ramirez et al., 2003; Rice and Barone, 2000).

Evidence from animal studies suggests that neonates lack the ability to efficiently excrete both methylmercury (Rowland et al., 1983) and inorganic mercury (Thomas and Smith, 1979), and that there is a higher lactational transfer of inorganic mercury than methylmercury (Sundberg et al., 1991a, b). Correspondingly, it has been shown that infants exposed via milk from mothers who were accidentally

*Corresponding author. Tel.: +1 210 827 7681.
E-mail address: palmerr@uthscsa.edu (R.F. Palmer).

poisoned by methylmercury-contaminated bread in Iraq accumulated higher mercury concentrations in their blood than did their mothers (Amin-Zaki et al., 1988) and the Faroe Island studies show that hair mercury concentrations in infants increased with the duration of the nursing period (Grandjean et al., 1994). It has also been shown that maternal dental amalgams have been linked to higher body burdens in infants (Oskarsson et al., 1996).

A 10-year longitudinal cohort monitoring study in Finland demonstrated that median hair total mercury concentrations increased in individuals who lived 2 km from a mercury polluting power plant compared to unexposed reference groups living further away (Kurttio et al., 1998). A study performed in China demonstrated that higher mercury concentrations are present in soil sediments and rice fields that are in close proximity to mercury emitting industrial plants and mining operations compared to areas that are more distant (Wang et al., 2003). A variety of similar investigations involving human, plant, and animal studies performed in different global locations consistently demonstrate that mercury concentrations are inversely associated with distance to the environmental source (Ordonez et al., 2003; Fernandez et al., 2000; Hardaway et al., 2002; Navarro et al., 1993; Kalac et al., 1991; Moore and Sutherland, 1981).

A 2000 report by the National Academy of Sciences' National Research Council estimates that approximately 60,000 children per year may be born in the US with neurological problems due to in utero exposure to methylmercury (NAS, 2000). The neurotoxicity of low-level mercury exposure has only recently been documented (NAS, 2000; EPA, 1997) and little is known about persistent low-dose ambient exposures coming from environmental sources or its influence on childhood developmental disorders such as autism—a condition affecting impairments in social, communicative, and behavior development typically present before age 3 years manifested by abnormalities in cognitive functioning, learning, attention, and sensory processing (Yeargin-Allsopp et al., 2003; CDC, 2007).

One hypothesis, which has been advanced to explain the recently observed increases in autism in the US and Europe, is that biological damage from neurotoxic substances such as mercury may play a causal role (Bernard et al., 2002). Holmes et al. (2003) found that mercury levels in the hair of autistic children were significantly lower than non-autistic controls indicating, according to the authors, that autistic children retain mercury in their body due to impairments in detoxification pathways. After the administration of a heavy metal chelating agent, Bradstreet et al. (2003) demonstrated that autistic children, relative to controls excreted more mercury in urine than non-autistic controls. Two recent studies have shown that body burden of mercury, as indicated by increased levels of urinary porphyrins specific to mercury exposure, are significantly higher in autistic children than in non-autistic children (Nataf et al., 2006; Geier and Geier, 2006).

While the association between autism and thimerisol (a mercury-based preservative formerly used in the childhood vaccination schedule during the 1990s) has not been scientifically established (Freed et al., 2002; Schechter and Grether, 2008), two studies have demonstrated an association with environmental sources of mercury and autism. Windham et al. (2006) demonstrated that ambient air mercury was associated with elevated autism risk in a case–control study in California, and Palmer et al. (2006) demonstrated that environmental mercury pollution was associated with point prevalence estimates of autism using EPA reported mercury release data from 254 counties in Texas. A major limitation to this study was that the cross-sectional design precluded any causal inferences. In addition, exposure was inferred from total pounds of environmentally released mercury aggregated at the county level at a specific point in time. Using distance to potential exposure sources may be a more reasonable proxy for exposure than one defined by total amount contained within artificial county boundaries. Given the literature on the relevance of proximity to the source of mercury and body burden, we suspect that distance to the source of mercury exposure may actually explain, at least in part, the association between increased autism rates and environmental mercury pollution found in both the Palmer et al. (2006) and Windham et al. (2006) studies.

The objective of the current study is to determine if proximity to major sources of mercury pollution is related to autism prevalence rates.

Methods

Data source and sample

Data for environmentally released mercury were obtained from the *United State Environmental Protection Agency Toxics Release Inventory* (TRI) (USEPA-TRI, 2006). TRI collects information about chemical releases and waste management reported by major industrial facilities in the US. The TRI database was established by Section 313 of the Emergency Planning and Community Right-To-Know Act of 1986 (EPCRA). Under EPCRA, industrial facilities in specific sectors are required to report their environmental releases and waste management practices annually to the EPA. Facilities covered by this act must disclose their releases to air, water, and land of approximately 650 toxic chemicals, as well as the quantities of chemicals they recycle, treat, burn, or otherwise dispose of on-site and off-site. The current analysis used the 1998 county pollution report that industrial facilities provided to TRI. Data for environmentally released mercury by coal-fired power plants were obtained from TRI and from the Texas Commission for Environmental Quality. In all, 39 coal-fired power plants and 56 industrial facilities in Texas were used in the analysis.

Measure of distance from mercury sources

The address location of coal-fired power plants and industrial facilities were entered into Arc-view V 9.0 Geographic Information Systems software along with polygonal shapes or boundaries of the school districts of Texas. GIS was then used to assign the *XY* location coordinates (latitude and longitude) of each plant and facility as well as to locate the centroid or *XY* geographical center of each school district. The amount of mercury emitted by each plant and by each facility was weighted on the *XY* coordinate of each plant's and facility's location. Using SPSS version 14 software, the distances between the *XY* coordinate of each source of emission and the *XY* coordinate of each school district centroid were calculated. As a result, each school district received a distance-in-miles measurement calculated separately for power plants and industrial facilities.

School district data

Administrative data from the Texas Education Agency (TEA) were analyzed. In compliance with the Texas Education Code, the Public Education Information Management System (PEIMS) contains data necessary for the legislature and the TEA to perform their legally authorized functions in overseeing public education. The database consists of student demographic, personnel, financial, and organizational information. Data descriptions are available at the TEA website http://www.tea.state.tx.us/data.html. Autism counts per school district were obtained by special request from the TEA. Data were from 1040 school districts in 254 counties in Texas. Diagnoses of autistic disorder are abstracted from the school records and are made by qualified special education psychologists employed by the TEA or from psychologists or medical doctors outside the TEA system. While diagnoses were not standardized, there is considerable evidence that diagnoses of autistic disorder are made with good reliability and specificity in the field (Eisenmajer et al., 1996; Hill et al., 2001; Mahoney et al., 1998). Autism prevalence rates from 2002 were used as the outcome and 1997 rates were used as a covariate in multivariate regression models.

We have identified the key covariates from prior work (Palmer et al., 2005, 2006), which were used in this study to adjust for potential confounding. *Urbanicity* and *School District Resources* have been demonstrated to be important covariates as they relate to greater identification of autism spectrum disorders. We also include a measure of ethnicity (percent white in school district).

Urbanicity

Eight separate demographically defined school district regions were used in the analysis as defined by the TEA: major urban districts and other central cities (1) major suburban districts and other central city suburbs (2) non-metropolitan and rural school districts (5).

In the current analysis, dummy variables were included in the analysis coding urban (dummy variable 1, and suburban (dummy variable 2), contrasted with non-metro and rural districts which were the referent group. Details and specific definitions of urbanicity categories can be obtained at the TEA website http://www.tea.state.tx.us/data.html.

Racial composition was accounted for by the proportion of White children enrolled in schools within each district.

Total number of students reflects all enrolled students in the districts 2002 school year and was used as the denominator in calculating autism rates.

District population wealth was calculated as the district's total taxable property value in 1998 as determined by the Comptroller's Property Tax Division (CPTD), divided by the total number of students in the district in 1998. Property value was determined by the CPTD as part of its annual study, which attempts to present uniformly appraised property valuations statewide. The CPTD value is calculated by applying ratios created from uniform independent appraisals to the district's assessed valuations.

Statistical methods

District autism data in 2002 were treated as event counts and used as the outcome in a Poisson regression model predicted by pounds of environmental mercury release in 1998, distance to sources of the release, and the relevant covariates. Total number of students enrolled in each district for 2002 defined the rates for each district. An over dispersion correction was applied due to the mean and variance not being equal. Due to the hierarchical structure of the data (e.g. districts nested within counties), the Poisson model was fit using MlWin multilevel modeling software (Rasbash et al., 1999) to obtain unbiased standard errors. Polynomials were added to the model to determine if a non-linear association was present between pounds of mercury, distance and autism rates. Regression coefficients of the models are reported as incident rate ratios by exponentiating the Poisson model coefficients.

Modeling strategy

Pounds of mercury release were first entered into the model followed by polynomial functions to access non-linear associations with autism rates. Next, *distance* was entered into the model to determine if it decreased the effect of *pounds*. Finally all covariates were entered: baseline *autism rates in 1997*, *urbanicity*, *racial composition*, *proportion of economically disadvantaged students,* and *district population wealth.* Note that mercury release data from 1998 are used to predict autism rates in 2002; it is plausible to postulate that releases during 1998 would have exposure potential for a cohort who was in utero in 1997. If an effect was present, this would be reflected in the 2002 school district records—the age (5 years old) this cohort would be entering the system.

Results

Table 1 shows the descriptive statistics of the study variables. Note that there is considerable variation in each variable. Table 2 shows the Poisson regression coefficients and the corresponding Incident Risk Ratio (IRR) for the models exploring the linear and non-linear association between 1998 mercury release from industrial sources, distance, and 2002 autism rates. Model 1a shows that environmentally released mercury in 1998 is significantly associated with autism rates in 2002. We multiplied the coefficient by 1000 to reflect increases in autism rates per 1000 pounds. The coefficient yields an IRR of 1.026, indicating that for every 1000 pounds of release in 1998, there is a corresponding 2.6% increase in 2002 autism rates. In model 1b, the squared term for pounds was entered into the model. Note that the linear coefficient is no longer significant and the polynomial term is. This indicates that the association between industrial sources of mercury release is non-linear—e.g. for every 1000 pounds there is an associated 1.1% accelerated risk. Adding distance to the equation in model 1c shows that

Table 1
Descriptive statistics of study variables

	Mean or percent	Standard deviation	Range
Predictor variables			
Total number pounds of mercury per year for power plants	1225 lb	946	8–2516
Total number pounds of mercury per year for industrial facilities	1526 lb	1909	3–6685
Minimum distance to industrial facilities	39.7 miles	29.3	0.34–170.4
Minimum distance to power plants	71.7 miles	53.2	0.74–305.8
Relevant demographic covariates			
Value of taxable property	$265,148	$328,631	0–$3,481,369
Percent urban	4%	–	–
Percent suburban	15%	–	–
Percent White	61.5%	–	0–100%
Proportion autism 1997 (rate per 1000)	0.85	2.1	0–26.3
Outcome variable			
Proportion autism 2002 (rate per 1000)	2.0	3.2	0–39.5

Table 2
2002 Autism rates as a function of industrial release of mercury in 1998

Model 1: 2002 autism rates as function of 1998 pounds of mercury emission from industrial sources	Amount of Hg (per 1000 lb)	Amount of Hg (per 1000 lb)^2	Distance to industrial sources per 10 miles	1997 autism rates	District Wealth (per $100,000)	Urban vs. rural	Suburban vs. rural	Percent White
Model 1a								
Regression coefficient (standard error)	**.026 (.010)***	–	–	–	–	–	–	–
Incident Risk Ratio	**1.026**	–	–	–	–	–	–	–
Model 1b								
Regression coefficient (standard error)	−.007 (.014)ns	**.018 (.006)****	–	–	–	–	–	–
Incident Risk Ratio	–	**1.018**	–	–	–	–	–	–
Model 1c								
Regression coefficient (standard error)	.021 (.015)ns	**.02 (.006)****	**−.014 (.006)***	–	–	–	–	–
Incident Risk Ratio	–	**1.020**	**0.986**	–	–	–	–	–
Model 1d								
Regression coefficient (standard error)	.003 (.011)ns	**.018 (.005)****	**−.02 (.008)***	**.16 (.01)*****	**.047 (.01)****	**.29 (.04)*****	**.33 (.04)*****	**.004 (.001)****
Incident Risk Ratio	–	**1.018**	**.980**	**1.170**	**1.048**	**1.33**	**1.39**	**1.004**

Note: Second column reflects the amount of mercury squared, the non-linear polynomial term.
ns: not significant
  *p<.05.
  **p<.01.
  ***p<.001.

Table 3
2002 Autism rates as a function of power plant release of mercury in 1998

Model 2: 2002 autism rates as function of 1998 pounds of mercury emission from power plant sources	Pounds of Hg per 1000	Non-linear term (Pounds of Hg per 1000)^2	Distance to industrial sources per 10 miles	1997 autism rates	District Wealth (per $100,000)	Urban vs. rural	Suburban vs. rural	Percent White
Model 2a								
Regression coefficient (standard error)	.037 (.018)*	—	—	—	—	—	—	—
Incident Risk Ratio	1.037	—	—	—	—	—	—	—
Model 2b								
Regression coefficient (standard error)	.044 (.020)*	.050(.030)^{ns}	—	—	—	—	—	—
Incident Risk Ratio	1.044	—	—	—	—	—	—	—
Model 2c								
Regression coefficient (standard error)	.017 (.022)^{ns}	—	.011 (.040)*	—	—	—	—	—
Incident Risk Ratio	—	—	.989	—	—	—	—	—
Model 2d								
Regression coefficient (standard error)	.003 (.011)^{ns}	—	.014 (.045)*	.161 (.01)***	.045 (.01)**	.290 (.04)***	.330 (.04)***	.005 (.001)**
Incident Risk Ratio	—	—	.986	1.170	1.056	1.33	1.39	1.005

Note: Second column reflects the amount of mercury squared, the non-linear polynomial term.
ns: not significant
*$p<.05$.
**$p<.01$.
***$p<.001$.

for every 10 miles away from the source there is a decreased autism Incident Risk of 1.4%. Adding non-linear terms for distance (distance squared and the square root of distance) (not depicted) was not significant and therefore not utilized in other models. Model 1d is the fully adjusted model depicting that the positive non-linear term for pounds, and the inverse association for distance, remain independently associated with 2002 autism rates after adjustment for 1997 autism rates, urbanicity, racial composition, and district wealth. Urbanicity and 1997 autism rates demonstrate to be the strongest predictors of 2002 autism rates in the final model.

Table 3 shows the Poisson regression coefficients and the corresponding IRR for the models exploring the linear and non-linear association between 1998 mercury release from power plant sources, distance to these sources, and 2002 autism rates.

Model 2a shows that environmentally released mercury from power plants in 1998 is significantly associated with autism rates in 2002. For every 1000 pounds of release there is a corresponding 3.7% increase in autism rates. In model 2b, the squared term for pounds was entered into the model and was not significant and therefore, not used in the subsequent models. Adding distance to the equation in model 2c shows that for every 10 miles away from the source, there is a significant 1% decrease in the autism Incident Risk. A 20-mile distance would yield a 2.2% decreased risk. Adding non-linear distance terms (distance squared and the square root of distance) (not depicted) was not significant and therefore not utilized in the next model. Most importantly however, in model 2c, the coefficient for pounds is no longer significant. This suggests that the direct effect between pounds of release in 1998 and 2002 autism rates are fully explained by distance to the source of release. The fully adjusted model 2d shows that this effect remains independent after adjustment for the covariates.

Discussion

These results build upon two prior studies demonstrating an association between environmental mercury release and autism rates (Palmer et al., 2006; Windham et al., 2006). The current study shows that environmental mercury in 1998 is associated with autism rates in 2002 after adjusting for other relevant sociodemographic covariates including autism rates in 1997. This is consistent with the prior reports. The novel findings in this study are that distance to the sources of mercury release was independently related to autism rates. In the separate analysis of power plant emissions, distance to the source fully explained the association between total pounds of mercury release and autism rates.

We also found that the association between releases from industrial rather than power plant sources was non-linear—e.g. increases in pounds from industrial sites were associated with an accelerated risk function. This difference in the shapes of the exposure-response curve for industrial

release (exponential increase) versus release from power plants (linear) might be explained by the fact that pollution from industrial sources are relatively more localized and not as far spreading as pollution from power plants. It is reasonable to suspect that greater local release could cause exponential effects as compared to more widely distributed releases.

On the other hand, the non-linear functions for distance were not significantly related to the outcome. It is plausible to suspect that exposure mediated by distance from the source depends more on other factors such as characteristics of the physical environment and predominant wind or rain patterns rather than simply distance alone. Exposure from power plants can potentially span thousands of miles and modeling the kinds of factors that affect exposure over time would require data that are not readily available. Notwithstanding, the results demonstrate an overall inverse association between distance to the source of release and subsequent autism rates. While these effects are relatively small, they are significant and demonstrate potential public health risks.

Although a major limitation to this study is that we cannot verify exposure at the individual level, a host of other plant, animal and human studies have demonstrated that distance to sources of environmental mercury exposure are related to increased body burdens of mercury (Ordonez et al., 2003; Fernandez et al., 2000; Hardaway et al., 2002; Navarro et al., 1993; Kalac et al., 1991; Moore and Sutherland, 1981). However, the effects of duration and dose amounts of environmental exposures are not currently known—and we do not know that body burden of mercury is in fact related to the potential exposure measures used in these analyses.

Mercury is a known immune modulator (Moszczynski, 1997). These effects include the production of autoantibodies to myelin basic protein (El-Fawal et al., 1999) and effects on the ratio of Th1/Th2 immunity factors (Kroemer et al., 1996). This is consistent with the literature demonstrating similar types of altered immune function in autistic children (Singh et al., 1997; Singh and Rivas, 2004; Krause et al., 2002; Cohly and Panja, 2005; Vojdani et al., 2003). However, unlike the specific vector known about exposure through fish consumption, very little is known about exposure routes from seemingly randomly distributed ambient exposures in the environment—particularly in air.

Even if ambient air, ground exposure routes, and low-level toxic thresholds can be identified by researchers, differential genetic susceptibilities in the ability to metabolize heavy metals and other pollutants would still need to be considered in future research (Herbert et al., 2006). While inconclusive to date, the existing studies warrant the need for further investigation on environmental mercury pollution and the developmental health of children.

There are some important limitations to this manuscript that should be addressed. First, these data do not reflect the true community prevalence rates of autism, largely because children who are not of school age are not counted

in the TEA data system. This is reflected in the $\frac{1}{500}$ autism rates for 2002 present in Table 1—which are lower than the current CDC reports of $\frac{1}{150}$ (CDC, 2007).

Further, individual risk cannot be inferred from population-based ecological studies such as this. Further, conclusions about exposure are limited, because distance was not calculated from individual homes to the pollution source, but from school district centroids of varying sizes. Rural school districts are usually larger in size than urban school districts and are one good reason to include urbanicty as covariates in these models.

This study should be viewed as hypothesis generating—a first step in examining the potential role of environmental mercury and childhood developmental disorders. Nothing is known about specific exposure routes, dosage, timing, and individual susceptibility. We suspect that persistent low-dose exposures to various environmental toxicants, including mercury, that occur during critical windows of neural development among genetically susceptible children (with a diminished capacity for metabolizing accumulated toxicants) may increase the risk for developmental disorders such as autism. Successfully identifying the specific combination of environmental exposures and genetic susceptibilities can inform the development of targeted prevention intervention strategies.

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