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Adult neuropsychological performance following prenatal and early postnatal exposure to tetrachloroethylene (PCE)-contaminated drinking water

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ABSTRACT

This population-based retrospective cohort study examined adult performance on a battery of neuropsychological tests in relation to prenatal and early postnatal exposure to tetrachloroethylene (PCE)-contaminated drinking water on Cape Cod, Massachusetts. Subjects were identified through birth records from 1969 through 1983. Exposure was modeled using pipe network information from town water departments, a PCE leaching and transport algorithm, EPANet water flow modeling software, and a Geographic Information System (GIS). Results of crude and multivariate analyses among 35 exposed and 28 unexposed subjects showed no association between prenatal and early postnatal exposure and decrements on tests that assess abilities in the domains of omnibus intelligence, academic achievement or language. The results were suggestive of an association between prenatal and early postnatal PCE exposure and diminished performance on tests that assessed abilities in the domains of visuospatial functioning, learning and memory, motor, attention and mood. Because the sample size was small, most findings were not statistically significant. Future studies with larger sample sizes should be conducted to further define the neuropsychological consequences of early developmental PCE exposure.

1. Introduction

Tetrachloroethylene (PCE, Perc or perchloroethylene) is a manufactured colorless liquid most commonly used for fabric dry cleaning and metal degreasing. PCE is one of the most frequently detected solvents in groundwater (Moran et al., 2007) and at United States Environmental Protection Agency (USEPA) Superfund sites (EPA, 2008). PCE and its main metabolite dichloroacetylene (DCA) are recognized human and animal neurotoxicants (TOXICS OOPPA, 1994a, 1994b; Stevens and Eisenmann, 1997; Feldman, 1999; Klaassen, 2001; Brown Dzubow et al., 2010; Bale et al., 2011). These fat soluble substances have a high affinity for the lipophilic tissues of the central nervous system (Altmann et al., 1995; Brown Dzubow et al., 2010). PCE also readily crosses both the placental and blood brain barriers (Klaassen, 2001).

Most of the epidemiological literature on the neurotoxic effects of solvents such as PCE has focused on sequelae among adults with occupational exposures to mixtures of organic solvents. Impairments in cognition and vision have been observed, as have mood changes (White et al., 1995; Grosch et al., 1996; Pauling and Ogden, 1996; Morrow et al., 1997; Tsai et al., 1997; Daniell et al., 1999; Condray et al., 2000; Morrow et al., 2000; Bowler et al., 2001; Klaassen, 2001; Bockelmann et al., 2002; Kilburn, 2002; Morrow and Scott, 2002; Rosenberg et al., 2002; Fiedler et al., 2003; Reif et al., 2003; Ichihara et al., 2004; Wood and Liossi, 2005). The cognitive sequelae observed following mixed organic solvent exposures included diminished performance on measures of memory, attention/executive function, and motor skills. The few studies examining adult occupational exposures to PCE alone have produced mixed results. Some studies found diminished performance on measures of attention/executive function (TOXICS OOPPA, 1994a, 1994b; Grosch et al., 1996), while other studies have not found any adverse neurological effects (Grosch et al., 1996; Daniell et al., 1999). All studies that examined visuospatial abilities have found a diminished performance associated with PCE exposure (TOXICS OOPPA, 1994a, 1994b; Echeverria et al., 1995; Daniell et al., 1999).

Three prior studies have examined effects of maternal occupational mixed solvent exposure during the prenatal period on neurodevelopment. A study by Eskenazi et al. (1988) showed no significant impact on general mental abilities assessed by the McCarthy Scales of

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Children's Abilities among children at ages 3–4 years. Domain-specific functions such as memory and language tests were not examined.

In contrast, Till et al. (2001) found that prenatal maternal exposure to organic solvent mixtures was associated with worse performance on measures of expressive and receptive language and reduced graphomotor skills using NEPSY tests among children at ages 3–7 years. Study parents also rated exposed children as having more behavioral problems on a child behavior checklist than unexposed children. Laslo-Baker et al. (2004) also found that children exposed to organic solvent mixtures during the prenatal period scored lower on neurobehavioral tests of general intelligence, language and motor abilities at ages 3–7 years.

One study examined postnatal exposure to PCE and subsequent neurobehavioral function among children who attended a day care facility adjacent to a dry cleaning establishment using PCE. Behavioral assessment took place when children were between the ages of 4–5 years (NYSDOH, 2005b) and 4–5 years later (NYSDOH, 2005a, 2005c). No behavioral effects were found at either assessment.

The present study examined environmental PCE exposure in an unusual scenario. In early 1980 elevated levels of PCE were discovered in the drinking water supplies of many New England towns. Investigations revealed that the public water distribution systems in these towns had installed vinyl-lined asbestos-cement (VL/AC) pipes to address alkalinity problems. Approximately 660 miles of VL/AC pipes were installed in Massachusetts from 1968 through early 1980; a large proportion was installed in eight towns in the Cape Cod region (Larson et al., 1983). These towns were Barnstable, Brewster, Bourne, Chatham, Falmouth, Mashpee, Provincetown, and Sandwich. The pipe manufacturing process involved spraying a mixture of vinyl toluene resin and PCE onto the interior of the pipe. It was believed that the PCE would volatilize before the pipes were installed; however, substantial quantities remained. PCE measurements taken in 1980 from Cape Cod public drinking water supplies ranged from 1.5 μg/L to 7750 μg/L (Demond, 1982). State officials decided to flush and bleed the VL/AC pipes in order to reduce the PCE concentrations to 40 μg/L, the action level determined to be safe at the time (Commonwealth of Massachusetts Department of Environmental Quality Engineering, Division of Water Supply, 1982). The current United States Environmental Protection Agency (USEPA) maximum contaminant level (MCL) is 5 μg/L (TOXICS OOPPA, 1994a, 1994b).

These unique circumstances presented a valuable setting for examining the neurodevelopmental impact of prenatal and early postnatal exposure to PCE because thousands of pregnant Cape Cod residents were exposed to a large range of levels, and other water contaminants were rare (Aschengrau and Ozonoff, submitted for publication). Furthermore, the VL/AC pipes were irregularly distributed according to the replacement and expansion needs of the towns, leading to little confounding by environmental and population characteristics. The irregular distribution of VL/AC pipes also meant that specific subjects could be identified as having water supplied through VL/AC pipes while others could be identified as unexposed. The current paper describes an evaluation of the associations between early PCE exposure and neurobehavioral function in this population. We predicted that young adults with prenatal and early childhood PCE exposure would show decrements in performance on neuropsychological outcomes measures relative to unexposed controls, particularly in the domains of visuospatial abilities, attention and executive function, short-term memory and mood.

2. Material and methods

2.1. Study population selection

Subjects were eligible if they were born between 1969 and 1983 to mothers who lived in one of eight Cape Cod towns with VL/AC water distribution pipes. Over 13,000 birth certificates were manually reviewed and the maternal addresses on the certificate were cross-matched with a database of all street locations with VL/AC pipes. The database also contained information on the installation year, and diameter of the pipes. This tentative designation was based on visual inspection of the maps of water pipes in the immediate vicinity of the birth residence.

Based on the initial exposure assessment, two groups of children were selected, those tentatively labeled as exposed and those tentatively labeled unexposed. The initial exposed group included 1910 individuals. A total of 1928 "unexposed" children were randomly selected and frequency matched to exposed children on the month and year of birth. More extensive exposure assessments were conducted following the return of self-administered questionnaires which included residential histories as well as information on the drinking water source. For a more detailed explanation see Janulewicz et al. (2008).

The study was approved by the Institutional Review Boards (IRB) of the Massachusetts Department of Public Health and Boston University Medical Center and the 24A/B/11B Review Committee at the Massachusetts Department of Public Health.

2.2. Follow-up and enrollment

Follow-up and enrollment of subjects took place between 2006 and 2010. Subjects were traced to obtain their current addresses and telephone numbers using Massachusetts residence lists; death, marriage, divorce, credit bureau and alumni records; and telephone books, directory assistance, and the Internet White Pages. Recruitment letters explaining the purpose of the study and accompanying self-administered questionnaires were sent to all traced subjects. Two percent of the selected population were deceased, 6.8% were not located, 45.8% were located but never responded to any contact attempts (4 attempts were made by mail and telephone), and 3.9% refused to participate (Table 1). In addition, the Massachusetts Department of Public Health did not allow us to contact 9.0% of the subjects whose mothers refused to participate in our prior cohort study of reproductive and developmental outcomes (Janulewicz et al., 2008). These percentages were similar for both the exposed and unexposed groups. In all, 619 exposed and 626 unexposed subjects returned the study questionnaire. Of those who returned the survey, 2.5% were

Table 1
Selection, enrollment, exposure status and exclusions of study population.

	Initial exposure status		Total
	Exposed	Unexposed	
Selected for neuropsychological testing	619[a]	626[a]	1245[a]
Excluded from neuropsychological testing[a]			
Outside geographic area	167	179	346
No maternal questionnaire data	126	157	283
Only postnatal exposure	44	34	78
Multiple birth	7	16	23
Other[c]	153	132	285
Eligible for neuropsychological testing	112[a]	107[a]	219[a]
Unable to contact	63	65	128
Refused	17	9	26
Underwent neuropsychological testing			
Final exposure status[b]			
Exposed during pre and postnatal period	31	4	35[b]
Unexposed	0	28	28[b]

[a] Based on initial exposure assessment.
[b] Based on questionnaire data and in depth exposure assessment.
[c] Reported use of 2 or more illicit drugs, N = 168; reported excessive alcohol use (e.g. average daily volume > 3 drinks), N = 162; history of neurological disease, N = 123; possible occupational exposure to solvents, N = 121; severe hearing or vision problems, N = 20; Other environmental exposure to solvents, N = 14; other, N = 4). Exclusions do not add up to the total number excluded because some subjects are counted in multiple categories.