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Environmental styrene exposure and neurologic symptoms in U.S. Gulf coast residents☆

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ABSTRACT

Background: Styrene is an established neurotoxicant at occupational levels, but effects at levels relevant to the general population have not been studied. We examined the neurologic effects of environmental styrene exposure among U.S. Gulf coast residents.

Methods: We used National Air Toxics Assessment (NATA) 2011 estimates of ambient styrene concentrations to assign exposure levels for 21,962 non-diabetic Gulf state residents, and additionally measured blood styrene concentration in a subset of participants (n = 874). Neurologic symptoms, as well as detailed covariate information, were ascertained via telephone interview. We used log-binomial regression to estimate prevalence ratios (PR) and 95% confidence intervals (95% CI) for cross-sectional associations between both ambient and blood styrene levels and self-reported neurologic symptoms. We estimated associations independently for ten unique symptoms, as well as for the presence of any neurologic, central nervous system (CNS), or peripheral nervous system (PNS) symptoms. We also examined heterogeneity of associations with estimated ambient styrene levels by race and sex.

Results: One-third of participants reported at least one neurologic symptom. The highest quartile of estimated ambient styrene was associated with one or more neurologic (PR, 1.12; 95% CI: 1.07,1.18), CNS (PR, 1.17; 95% CI: 1.11,1.25), and PNS (PR, 1.16; 95% CI: 1.09,1.25) symptom. Results were less consistent for biomarker analyses, but blood styrene level was suggestively associated with nausea (PR, 1.78; 95% CI: 1.04, 3.03). In stratified analyses, we observed the strongest effects among non-White participants.

Conclusions: Increasing estimated ambient styrene concentration was consistently associated with increased prevalence of neurologic symptoms. Associations between blood styrene levels and some neurologic symptoms were suggestive. Environmental styrene exposure levels may be sufficient to elicit symptomatic neurotoxic effects.

1. Introduction

Styrene is a hydrocarbon used in the production of plastics, fiberglass laminates, rubber, and resins found in consumer products and commercial and residential building materials. Manufactured styrene products include insulation, fiberglass boats, automotive parts, car tires, Styrofoam, and plastic drinking glasses (ATSDR, 2010). Styrene is an established neurotoxicant at occupational levels (ATSDR, 2010; CDC, 1978; IARC, 2002), but has not been studied at environmental levels experienced outside of occupational contexts. Epidemiologic studies to date have focused on highly exposed workers, whose average blood concentrations are 25 times higher than those of the general population (Brugnone et al., 1993; Coggon, 1994; Cherry and Gautrin, 1990; Papaleo et al., 2011; Seeber et al., 2009; Toppila et al., 2006; Triebig et al., 1989; Vodička et al., 1995).

Inhalation of tobacco smoke, off-gassing of building materials and consumer products, and vehicle and industrial emissions accounts for over 90% of styrene exposure in the general population (ATSDR, 2011; USEPA, 1994; IARC, 2002; CDC, 2013). Exposure via dermal contact is typically limited to occupational settings, and internal dose due to

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ingestion from food and water is considered negligible. Among smokers, cigarettes are considered the dominant source of styrene exposure, and smoking is the single most important individual predictor of human exposure to styrene (ATSDR, 2010; Adgate et al., 2004; Ashley et al., 1994, 1995; Cohen et al., 2002; Wallace, 1986; Wallace et al., 1987; Chambers et al., 2011). Styrene is released into the air from automobile exhaust, cigarette smoke, photocopiers and printers, and industries using or manufacturing styrene. The Gulf region is home to a prolific petrochemical industry, many styrene-emitting industries, and over half of all U.S. styrene production (ATSDR, 2010; NTP, 2014), potentially exposing Gulf residents to a high intensity of environmental styrene emissions.

Styrene is commonly detected in urban air, near industrial sites and landfills, and in high traffic areas, although typically at levels substantially lower than in occupational settings. Rural and suburban air generally contains lower concentrations of styrene than urban air (Miller et al., 1994). In the U.S. general population, daily exposure to styrene in air is estimated to be 18–54 μg/person (ATSDR, 2010), and indoor air usually contains higher levels of styrene than outdoor air. Because the half-life of styrene in blood is approximately 13 h (CDC, 1978), blood styrene measurements reflect recent exposure.

The Agency for Toxic Substances and Disease Registry (ATSDR) has identified the central nervous system (CNS) as the primary target for styrene toxicity, with less marked effects in the peripheral nervous system (PNS) (ATSDR, 2011; Gobba et al., 1995). Like many other volatile organic compounds, styrene monomer is a CNS depressant with anesthesia-like properties (IARC, 2002; Tormoehlen et al., 2014). Acute solvent-induced neurotoxicity, including that caused by styrene, is characterized by symptoms of acute intoxication, commonly described as a feeling of drunkenness. Long term exposures at levels found in occupational settings have been associated with chronic adverse neurotoxic effects. Occupational studies demonstrate styrene-induced neurotoxicity, from both acute and chronic inhaled exposure among highly-exposed workers. Symptoms include feeling “drunk” and tiredness (Checkoway et al., 1992), impaired vision (Gobba et al., 1995; Kishi et al., 2001), vestibular dysfunction (Toppila et al., 2006), headaches (Edling et al., 1993), delayed reaction time (Jegaden et al., 1993; Tsai and Chen, 1996), impaired attention and memory (Cherry and Gautrin, 1990), hearing deficits (Johnson et al., 2006), diminished nerve conduction velocity (Cherry and Gautrin, 1990; Murata et al., 1994; Rosén et al., 1978; Stetkarova et al., 1993; Matikainen et al., 1993), and abnormal electroencephalogram results (Matikainen et al., 1993; Seppäläinen and Härkönen, 1976). Similar effects have been observed at lower occupational airborne exposure levels, ranging from 10 to 30 ppm, in most (Papaleo et al., 2011; Gobba et al., 1995; Edling et al., 1993; Jegaden et al., 1993; Tsai and Chen, 1996; Mutti et al., 1984; Flodin et al., 1989; Tsai et al., 1997; Viaene, 2001), though not all (Triebig et al., 1989; Rebert and Hall, 1994), studies.

The human health effects of chronic styrene exposure at typical environmental levels remain largely unknown (Cohen et al., 2002). We set out to assess the associations between two metrics of styrene exposure - estimated ambient concentrations and measured blood levels - and self-reported neurologic symptoms among Gulf state residents. Quantifying the association between environmental styrene exposure and highly sensitive, but non-specific, neurologic symptoms may lend insight into early manifestations of environmentally induced neurotoxicity due to chronic exposures at levels insufficient to cause clinically apparent toxicity.

2. Methods

2.1. Study design and participants

We used data from the Gulf Long-term Follow-up Study (GuLF STUDY), a prospective cohort of adults (ages 21 and older) who participated in oil spill response activities and others who received safety training, but were not hired, following the 2010 *Deepwater Horizon* disaster. A detailed description of this study is available elsewhere (Kwok et al., 2017). Of the 25,848 English- or Spanish-speaking GuLF STUDY participants living in the Gulf region (Alabama, Florida, Louisiana, Mississippi, and Texas) at enrollment, 24,903 reported addresses that were successfully geocoded to a 2010 U.S. Census tract. From this sample of participants with known residential locations, we excluded participants with any missing neurologic symptom information (n = 304), missing demographic characteristics (n = 573), and missing covariate information (n = 201), leaving 23,825 eligible participants. Because autonomic and peripheral neuropathy are known complications of diabetes (Freeman, 2014), we further restricted the study sample to participants with no self-reported physician diagnosis of diabetes (exclude 1825 diabetics and 38 with missing diagnosis information), resulting in a final analytic sample of 21,962.

Approximately 2–3 years after the oil spill (May 2012–July 2013), a subset of GuLF STUDY participants living in the Gulf region (N = 1055) were enrolled in the Chemical Biomonitoring Study (CBS) (Engel et al., 2017; Werder et al., 2018). CBS participants provided an extra blood sample for measuring styrene and other compounds and completed a questionnaire about usual and recent exposures and exposure opportunities.

Ultimately, 994 participants provided blood samples sufficient for quantification of styrene levels. Of those, we excluded 20 participants missing neurologic symptom information, nine with incomplete demographic characteristics, and four individuals missing other covariate information, leaving 961 eligible participants. We then excluded known diabetics (n = 86 of the 1825 diabetics from the parent study) or those missing diagnosis information (n = 1), for a final analytic sample of 874.

Participants provided written informed consent, and the Institutional Review Board of the National Institute of Environmental Health Sciences approved this study.

2.2. National Air Toxics Assessment

The United States Environmental Protection Agency (EPA) 2011 National-scale Air Toxics Assessment (NATA) (USEPA, 2011a) evaluates 180 air toxics across the United States using emissions inventories, dispersion modeling, photochemical modeling, exposure modeling, and toxicity analyses. NATA generates annual average ambient air toxic concentrations (μg/m^3) for each U.S. census tract. We employed NATA styrene estimates as indicators of typical environmental exposure by mapping each participant's geocoded home location to a corresponding 2010 U.S. census tract. Geocodes were based on self-reported home address at enrollment. The 2011 NATA estimated annual average ambient styrene concentration corresponding to an individual's home census tract was applied as a surrogate of usual ambient styrene exposure for each cohort member residing in the Gulf region.

2.3. Blood styrene measurement

Blood collection tubes containing potassium oxalate and sodium fluoride anticoagulant were used to collect 10 mL of blood for styrene measurement. Tubes and stoppers were pre-treated by the Centers for Disease Control and Prevention (CDC) laboratory to remove VOC residues to minimize pre-collection contamination (Chambers et al., 2008; Chambers et al., 2005). Samples were stored in a 4 °C refrigerator prior to being shipped overnight on cold packs in biweekly batches to the Division of Laboratory Sciences, National Center for Environmental Health, CDC in Atlanta, Georgia, for analysis of VOCs. Analysis of styrene followed standard CDC procedures, using equilibrium headspace solid-phase micro-extraction with benchtop gas chromatography/mass spectrometry (Blount et al., 2006; Chambers et al., 2006). The laboratory provided actual measured values below the limit of detection (LOD) (0.03 ng/mL).