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Components of air pollution and cognitive function in middle-aged and older adults in Los Angeles

Nicole M. Gatto [a,*], Victor W. Henderson [e,f], Howard N. Hodis [b,c], Jan A. St. John [b,c], Fred Lurmann [d], Jiu-Chiuan Chen [b], Wendy J. Mack [b,c]

[a] Department of Epidemiology, Biostatistics & Population Medicine, School of Public Health, Loma Linda University, Loma Linda, CA, USA
[b] Department of Preventive Medicine, Keck School of Medicine, USC, Los Angeles, CA, USA
[c] Atherosclerosis Research Unit, Department of Medicine, Keck School of Medicine, USC, Los Angeles, CA, USA
[d] Sonoma Technology, Inc., Petaluma, CA, USA
[e] Department of Health Research & Policy (Epidemiology), Stanford University, Stanford, CA, USA
[f] Department of Neurology & Neurological Sciences, Stanford University, Stanford, CA, USA

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ABSTRACT

While experiments in animals demonstrate neurotoxic effects of particulate matter (PM) and ozone (O_3), epidemiologic evidence is sparse regarding the relationship between different constituencies of air pollution mixtures and cognitive function in adults. We examined cross-sectional associations between various ambient air pollutants [O_3, $PM_{2.5}$ and nitrogen dioxide (NO_2)] and six measures of cognitive function and global cognition among healthy, cognitively intact individuals ($n = 1496$, mean age 60.5 years) residing in the Los Angeles Basin. Air pollution exposures were assigned to each residential address in 2000–06 using a geographic information system that included monitoring data. A neuropsychological battery was used to assess cognitive function; a principal components analysis defined six domain-specific functions and a measure of global cognitive function was created. Regression models estimated effects of air pollutants on cognitive function, adjusting for age, gender, race, education, income, study and mood. Increasing exposure to $PM_{2.5}$ was associated with lower verbal learning ($\beta = -0.32$ per 10 $\mu g/m^3$ $PM_{2.5}$, 95% CI = −0.63, 0.00; $p = 0.05$). Ambient exposure to NO_2 >20 ppb tended to be associated with lower logical memory. Compared to the lowest level of exposure to ambient O_3, exposure above 49 ppb was associated with lower executive function. Including carotid artery intima-media thickness, a measure of subclinical atherosclerosis, in models as a possible mediator did not attenuate effect estimates. This study provides support for cross-sectional associations between increasing levels of ambient O_3, $PM_{2.5}$ and NO_2 and measures of domain-specific cognitive abilities.

1. Introduction

Increasing numbers of US adults are living longer (Wood and Walker, 2005) and population growth continues to shift to urban metropolitan areas (Perry et al., 2000). There is thus a growing need to direct efforts to understand adverse cognitive health outcomes relevant to aging populations, including cognitive impairment (CI) and dementia (Comas-Herrera et al., 2007), as well as potential health risks from environmental exposures such as air pollution that are prevalent in urban areas (National Atlas of the United States, 2009). Cognitively impaired persons require nursing home care at twice the rate of cognitively intact persons, and incur significantly greater mental healthcare costs (Anon., 2009; Coughlin and Liu, 1989; Mackin et al., 2011), making prevention an important priority (Plassman et al., 2008). In urban areas, ambient air pollution is a mixture of gaseous pollutants and particulate matter (PM) that derive from sources mostly related to burning fuel of motor vehicles, diesel-powered transport and equipment and local industrial processes (Dickey, 2000; Lewtas, 2007; Valavanidis et al., 2008). While the aging brain is vulnerable to many environmental insults including urban air pollution, investigations in this emerging field are limited despite the potentially modifiable nature of this exposure.

The association between air pollution and both respiratory and cardiovascular morbidity and mortality has been extensively studied for both acute and chronic ambient PM exposure

* Corresponding author at: Department of Epidemiology, Biostatistics & Population Medicine, Loma Linda University, School of Public Health, 24951 North Circle Drive, Nichol Hall 2025, Loma Linda, CA 92350, USA. Tel.: +1 909 558 7597.
E-mail address: ngatto@llu.edu (N.M. Gatto).

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(Chen et al., 2008; Franchini and Mannucci, 2009; Ghio et al., 2012; Gotschi et al., 2008; Pelucchi et al., 2009), with hypothesized biological pathways including systemic as well as tissue-specific inflammation (Block and Calderon-Garciduenas, 2009; Calderon-Garciduenas et al., 2008b; Kunzli et al., 2005). Cardiovascular disease (CVD) is known to impact cognitive function in later years (O'Brien, 2006), and vascular and metabolic risk factors including high blood pressure, overweight and obesity, diabetes and stroke (Rosamond et al., 2007) have been shown to be inversely associated with cognitive function among middle-aged and older adults (NIH, 2007). Subclinical atherosclerosis measured by carotid artery intima-media thickness (CIMT) has been associated with lower cognitive function (Gatto et al., 2009; Johnston et al., 2004; Muller et al., 2007), and long-term exposure to ambient air pollution has been associated with CIMT (Kunzli et al., 2005). Many animal studies have reported the effects of air pollutants on the central nervous system (CNS) likely via inflammatory and oxidative stress pathways (Block and Calderon-Garciduenas, 2009; Genc et al., 2012; Gonzalez-Flecha, 2004). Studies of experimental particles simulating $PM_{2.5}$ from tailpipe emissions of motor vehicles raise the question as to whether the blood–brain barrier (BBB) may be breached (Lockman et al., 2004; MohanKumar et al., 2008; Muhlfeld et al., 2008). In vivo studies with acute and chronic low-level exposures to ozone (O_3), PM, or PM-O_3 mixtures have demonstrated neurotoxic effects in different animal models (Dorado-Martinez et al., 2001; Rivas-Arancibia et al., 1998; Sirivelu et al., 2006; Sorace et al., 2001). Suggested neuropathological evidence of accelerated brain aging has been described in the olfactory and respiratory nasal mucosae, olfactory bulb, and cortex of experimental dogs raised in Mexico City where air pollution is a mixture of O_3, aldehydes, PM, and other components (Calderon-Garciduenas et al., 2008a).

Studies of air pollution and cognitive dysfunction in humans have previously focused on acute exposure in human volunteers. Short-term exposure to a mixture of diesel exhaust and gaseous pollutants in a chamber study increased the median power frequency in the frontal cortex measured by quantitative EEG (Cruts et al., 2008). Healthy college students with short-term exposure to carbon monoxide (CO) from kerosene heating stoves used indoors had lower scores on neuropsychological tests indicating dysfunction in multiple areas of cognition (Amitai et al., 1998).

Population-based epidemiologic studies are sparse and limited mainly to examinations of PM pollution among elderly adults (Power et al., 2011; Ranft et al., 2009; Weuve et al., 2012). None of these studies simultaneously examined putative associations between gaseous pollutants and PM with cognitive function. One study using NHANES-III data collected in younger US adults reported associations between O_3 and reduced performance on cognitive tasks requiring attention, short-term memory and coding abilities; associations with PM_{10} and these tasks were not present after taking into account race/ethnicity and socioeconomic status (Chen and Schwartz, 2009). To the best of our knowledge, previous studies have only reported associations between air pollution exposure and assumed cognitive constructs suggested by neuropsychological tools without performing comprehensive psychometric analyses to assist in the interpretation of possibly heterogeneous results.

We investigated cross-sectional associations between components of ambient urban air pollution [O_3, $PM_{2.5}$ and nitrogen dioxide (NO_2)] from residential exposure, global cognition and six domains of cognitive function in healthy, cognitively intact middle-aged and older adults in the greater Los Angeles area, California. Given the previously-documented strong associations between PM exposure and cardiovascular disease (CVD) (Breton et al., 2012; Kunzli et al., 2005, 2010), this study also assessed whether and to what extent the association between air pollution and cognition may be mediated by subclinical atherosclerosis.

2. Materials and methods

2.1. Study population

Analyses used baseline data obtained prior to randomization from 1496 healthy, cognitively intact adult participants enrolled in three randomized, double-blind, placebo-controlled clinical trials conducted during 2000–2006 at the University of Southern California (USC) Atherosclerosis Research Unit [B-Vitamin Atherosclerosis Intervention Trial (BVAIT; ClinicalTrials.gov identifier NCT00114400), Women's Isoflavone Soy Health (WISH; NCT00118846) Trial, and Early Versus Late Intervention Trial With Estradiol (ELITE; NCT00114517)] (Henderson et al., 2012; Hodis et al., 2009, 2011). Briefly, postmenopausal women without clinical evidence of CVD were eligible for WISH and ELITE; otherwise healthy men and postmenopausal women with fasting plasma homocysteine levels $\geq$8.5 μmol/L were eligible for BVAIT. Recruitment occurred over the entire Los Angeles Basin, covering a geographic area of approximately 64,000 km^2. A total of 5698 individuals were screened via telephone or in person. Exclusions were made for any clinical signs or symptoms of CVD (n = 165), diabetes mellitus or fasting serum glucose $\geq$126 mg/dL (n = 137), triglyceride (TG) levels $\geq$500 mg/dL (n = 3), hypertension [systolic blood pressure (SBP) $\geq$160 mmHg and/or diastolic blood pressure (DBP) $\geq$100 mmHg] (n = 13), untreated thyroid disease (n = 4), creatinine clearance $<$70 mL/min or serum creatinine $>$2.0 mg/dL (n = 6), a life threatening disease with prognosis $<$5 years (n = 124), alcohol intake $>$5 drinks per day/substance abuse (n = 4), unwillingness to stop taking vitamin supplements (n = 626), current use of hormone therapy (WISH or ELITE) (n = 212), hysterectomy and no oophorectomy (ELITE) (n = 132), or 6–9 years postmenopausal (ELITE) (n = 190). A total of 1499 subjects were randomized; all participants signed written informed consent approved by the USC Institutional Review Board.

2.2. Measurements

2.2.1. Air pollution exposure assignment

Employing a GIS-based system, yearly air pollution exposure assignments were derived from measured ambient air quality data spatially mapped to subjects' geocoded residence addresses at year of randomization (2000–2006). These data were initially automatically geocoded to TigerLine files (Navteq, 2006), then manually resolved in a multi-step process similar to that described by McElroy et al. (2003). Ambient air quality data were primarily extracted from the Air Quality System (AQS), maintained by the US Environmental Protection Agency (http://www.epa.gov/ttn/airs/airsaqs/). A database of O_3 (8 h maximum), NO_2 (24 h) and $PM_{2.5}$ (mass, 24 h) concentrations at monitoring stations was compiled from a June 2008 AQS version. Measurements obtained using Federal Reference Methods and Federal Equivalent Methods were included and supplemented with monthly average O_3, NO_2, and $PM_{2.5}$ concentrations measured in the Southern California Children's Health Study (Peters et al., 2004). Daily, monthly, and annual average concentrations were calculated using a 75% data completeness criterion. The database included measurements from California and border areas of nearby states for calendar years 2000–2006. The density of measurement stations in this regional air monitoring network is every 20–40 km in urban areas and 50–150 km in rural areas (ARB, 2008).

Annual average concentrations for 2000–2006 from monitoring stations were spatially interpolated to subjects' residential addresses using inverse-distance-squared weighting in a GIS.