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# Fine particulate matter exposure and olfactory dysfunction among urban-dwelling older US adults

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ABSTRACT

*Objectives:* The olfactory nerve is anatomically susceptible to injury from pollution in inspired air, but there are no large-scale epidemiologic studies investigating this relationship.

*Methods:* Cross-sectional study using data from the National Social Life, Health, and Aging Project, a representative sample of home-dwelling US adults age 57–85 years. Olfactory function was tested using a validated 5-item odor identification test (Sniffin' Sticks). Exposure to fine particulate matter ($PM_{2.5}$) at each respondent's home was estimated as 1–12 month moving averages prior to olfactory assessment using validated spatio-temporal models.

*Results:* Olfactory dysfunction was significantly associated with $PM_{2.5}$ exposures averaged over 3–12 months in urban-dwelling respondents. The strongest effect was for 6 month average exposure (per 1-IQR increase in $PM_{2.5}$: OR 1.28, 95% CI 1.05, 1.55) adjusting for age, gender, race/ethnicity, education, cognition, comorbidity, smoking, and the season. Interestingly, the most deleterious effects were observed among the youngest respondents, 57–64 years old, and those living in the northeast and south.

*Conclusions:* We show for the first time that air pollution exposure is associated with poor olfaction among urban-living, older US adults.

## 1. Introduction

Loss of olfactory function poses a huge burden to older adults, with a prevalence of approximately 24% (Murphy et al., 2002; Pinto et al., 2014a; Schubert et al., 2009). Olfactory dysfunction has a major human impact, in terms of decreased quality of life (Smeets et al., 2009), impaired nutrition and enjoyment of foods (Schiffman and Graham, 2000), a decreased ability to detect hazards (e.g., gas leaks or fires) (Santos et al., 2004), decreased sex drive (Toller, 1999), and increased feelings of depression and distress (Smeets et al., 2009). Olfactory dysfunction may also be an indicator of the development of neurodegenerative conditions, such as Parkinson's (Ross et al., 2008) or Alzheimer's diseases (Devanand et al., 2000), and a predictor of mortality (Wilson et al., 2011; Pinto et al., 2014b; Devanand et al., 2015). Loss of olfactory function therefore represents a significant public health problem, particularly among older adults.

Anatomically, the olfactory neurons comprise the first cranial nerve, which is directly exposed to the outside environment due to its position in the roof of the nasal cavity (Cullen and Leopold, 1999; Pinto, 2011). Harmful airborne pollutants may come into direct contact with olfactory neurons and may thus play a role in olfactory decline. Additionally, air pollution may explain mechanisms through which loss of olfaction serves as an indicator of future neurocognitive decline; the olfactory nerve can serve as a route of transportation for inhaled particles between the environment and the brain that bypasses the blood-brain barrier (Lucchini et al., 2012; Oberdörster et al., 2004). While occupational exposures have also been associated with impaired olfaction (Doty, 2006; Gobba, 2006), few (if any) large-scale studies have examined the impact of air pollution on olfactory loss in the general population.

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Of the common air pollutants, the impacts of fine particulate matter ($PM_{2.5}$, diameter $< 2.5$ μm) on olfactory function may be particularly important to examine. $PM_{2.5}$ is a class of pollutant with well-documented impacts on mortality, cardiovascular disease, and to a lesser extent cognitive health (Ailshire and Crimmins, 2014; Brunekreef and Holgate, 2002). Exposure to $PM_{2.5}$ has also been linked to poor olfaction in studies of younger adults in Mexico City, a city with substantially elevated $PM_{2.5}$ concentrations, compared to those living in nearby cities with lower pollution levels (Hudson et al., 2006; Calderon-Garciduenas et al., 2010). Indirect support for these findings was provided by a study of older German women (ages 68–79 years), which found olfactory dysfunction to be associated with distance to the nearest roadway, a proxy for $PM_{2.5}$ exposure (Ranft et al., 2009).

To examine the relationship between olfaction and $PM_{2.5}$ in the general population, we used data from the National Social Life, Health and Aging Project (NSHAP), a nationally representative sample of older US adults (age 57–85) living at home (Suzman, 2009). In 2005-06, NSHAP performed olfactory testing and collected information on a wide range of health conditions and social measures (Schumm et al., 2009). We linked data for each NSHAP respondent to monthly $PM_{2.5}$ exposures estimated for each respondent at his/her home address using previously validated GIS-based spatio-temporal models (Yanosky et al., 2014). Using these data, we examined the association between individual-specific $PM_{2.5}$ exposures and olfactory function in an effort to explore pollution exposure as a risk factor for olfactory decline.

## 2. Methods

### 2.1. Study population

In 2005-06, professional interviewers from NORC at The University of Chicago conducted in-home interviews with 3005 community-dwelling older adults (1454 men and 1551 women), a representative sample of the US community-dwelling population 57–85 years of age (O'Muircheartaigh et al., 2009; Suzman, 2009). Numerous measures were obtained for each respondent, including olfactory, demographic, social, psychological, and biological measures, as described below. Our main analyses was restricted to respondents who were determined to live in urban areas based on rural-urban commuting area (RUCA) codes, given that a majority of previous work on pollution and olfaction has centered on residents of Mexico City, a highly exposed urban group (Calderon-Garciduenas et al., 2010; Calderón-Garcidueñas et al., 2003). Others have compared the olfactory ability of residents of major European urban centers to that of people dwelling in entirely non-industrialized regions (Sorokowska et al., 2015, 2013). RUCA codes 1–3 were considered urban areas and codes 4–10 were considered rural (Hall et al., 2006). To evaluate whether any observed association between $PM_{2.5}$ and olfaction in urban respondents was different in rural respondents, we separately expanded our analyses to all NSHAP respondents and treated urban/rural dwelling as a potential modifier.

The Institutional Review Boards of The University of Chicago and NORC approved this study and all respondents provided written, informed consent.

### 2.2. Olfactory Assessment

Olfactory function was measured using a validated, odor identification test comprising a shortened version of the Sniffin' Sticks (Mueller and Renner, 2006; Schumm et al., 2009). Robust associations have been identified using the data obtained from this 5-item test (Pinto et al., 2014a, 2014b). Five felt-tipped pens containing different odorants were presented one at a time to respondents. After smelling the tip of the pen, respondents were given a card with four labeled pictures and asked to identify the odorant via a forced choice protocol. The odorant response sets were as follows (*correct odor in italics*): (1) chamomile, raspberry, *rose*, cherry; (2) smoke, glue, *leather*, grass; (3) *orange*, blueberry, strawberry, onion; (4) bread, *fish*, cheese, ham; and (5) chive, *peppermint*, pine, onion. Refusals to provide an answer to a given odorant were treated as incorrect.

A score of four or five correct answers was classified as normosmic, and a score of three or fewer correct answers was classified as olfactory dysfunction, a standard threshold (Pinto et al., 2014a; Schumm et al., 2009) which yields a prevalence of olfactory dysfunction consistent across studies (Murphy et al., 2002; Schubert et al., 2009). Changing the cutoff for olfactory dysfunction to ≤2 or ≤4 odors correct yielded similar results (data not shown).

### 2.3. Air pollution exposure assessment

Geographic Information Systems **(**GIS)-based spatio-temporal models predicting monthly $PM_{2.5}$ concentrations have been previously developed and validated for the conterminous US with high accuracy ($R^2$=0.77) (Yanosky et al., 2014). Models used measured $PM_{2.5}$ concentrations, monitoring site locations, location-specific site characteristics, location- and month-specific meteorology data, and spatial smoothing of monthly- and long-term average levels to describe small and large-scale spatial and temporal variability in these concentrations. From these models, 1, 3, 6, 9, and 12 month $PM_{2.5}$ exposures were estimated for each respondent as moving averages based on their home address and date of olfactory assessment.

### 2.4. Other covariates

Our analyses controlled for numerous potential confounders, including age and gender due to their previously observed, consistent associations with olfactory function (Brämerson et al., 2004; Murphy et al., 2002; Pinto et al., 2014a; Schubert et al., 2009); race/ethnicity; cognitive function; education, as a proxy for socioeconomic status; smoking; comorbidity; and season. Race/ethnicity was coded by self-report using standard categories: White, Black, Hispanic (non-Black), and Other. Education was defined as the highest degree or certification completed. These basic demographic factors were also considered as potential modifiers of any pollution-olfaction association, to identify potentially vulnerable subgroups of the population. For this interaction analysis only, age was treated as a categorical variable with respondents grouped into ages 57–64 years, 65–74 years, and 75–85 years, as in prior work.

Cognitive function was measured using the Short Portable Mental Status Questionnaire (SPMSQ, scores from 0 to 10) (Pfeiffer, 1975). Although smoking has an unclear association with olfactory dysfunction (Brämerson et al., 2004; Frye et al., 1990; Ranft et al., 2009; Vennemann et al., 2008), current smoking (based on either positive self-report or a salivary cotinine ≥15 ng/mL) was included as a potential confounder because of its mechanistic relevance to air pollution exposure. Further, smoking was evaluated as a potential modifier of the associations between $PM_{2.5}$ exposure and olfaction. A modified Charlson comorbidity index was calculated for each respondent based on occurrence of mortality-associated conditions (Charlson et al., 1987; Pham-Kanter, 2009) and also considered as a potential modifier. Because of known seasonal variation in PM levels (Bell et al., 2007) and plausible seasonal differences in olfaction, we also included a season variable to compare cooler (October–March) versus warmer (April–September) months.

Additional variables evaluated as potential modifiers included: physical activity, considered as either high activity (1+ times per week) or low activity ($< 1$ time per week); region of the country (West, Midwest, South, or Northeast; states included in each region are listed in Supplemental Material, Table S1); and current employment status.

### 2.5. Statistical analysis

Multivariate logistic regression was used to estimate the relation-