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Short-term exposures to ambient air pollution and risk of recurrent ischemic stroke

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Abbreviations:
$PM_{2.5}$particulate matter less than 2.5μm in aerodynamic diameter
O_3Ozone

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ABSTRACT

Objective: To investigate the association between short-term changes in ambient pollution (particulate matter < 2.5 μm in aerodynamic diameter ($PM_{2.5}$) and ozone (O_3)) and the risk of recurrent ischemic stroke among individuals living in a bi-ethnic community.

Methods: We identified recurrent ischemic stroke cases from the population-based Brain Attack Surveillance in Corpus Christi (BASIC) project between 2000 and 2012. Associations between $PM_{2.5}$ (mean 24-h) and O_3 (maximal 8-h) levels, measured on the previous day, and odds of ischemic stroke were assessed using a time-stratified case-crossover design and modeled using conditional logistic regression.

Results: There were 317 recurrent ischemic strokes after excluding 41 strokes that occurred on days with missing air pollution data. Mean age was 72 years (SD=12) and median time to stroke recurrence was 1.1 years (IQR: 0.2–2.8 years). Median levels of $PM_{2.5}$ and O_3 over the study period were 7.7 μg/m^3 (IQR: 5.6–10.7 μg/m^3) and 35.2 ppb (IQR: 25.0–46.1 ppb), respectively. We observed no associations between previous-day $PM_{2.5}$ and O_3 and odds of recurrent stroke (OR=0.95 per 10 μg/m^3 of $PM_{2.5}$, 95% CI: 0.71–1.28 and OR=0.97 per 10ppb of O_3, 95% CI: 0.87–1.07) after adjusting for ambient temperature and relative humidity. Co-adjustment of both pollutants did not change the results.

Conclusion: We found no evidence of associations between previous-day air pollution levels and recurrent ischemic stroke. Research on the influence of air pollutants on risk of stroke recurrence is still in its infancy, and more research is necessary in studies that are adequately powered to understand the relation.

1. Introduction

Recurrent strokes are associated with worse outcomes and greater mortality relative to first strokes (Jerrgensen et al., 1997; Pettersen et al., 2002; Weimar et al., 2002). Short-term ambient air pollution as a risk factor for stroke has been gaining attention (Henrotin et al., 2010; Lisabeth et al., 2008; O'Donnell et al., 2011; Wellenius et al., 2012; Wing et al., 2015). Although associations between air pollution and risk of stroke have been observed, the evidence for short-term effects of air pollution on risk of stroke recurrence is in its infancy with only a few studies reported to date (Henrotin et al., 2010; O'Donnell et al., 2011; Suissa et al., 2013; Wellenius et al., 2012). While there is little evidence, it is a plausible that individuals with prior stroke may be more vulnerable to the effects of air pollution on stroke given they are likely to have systemic or more severe atherosclerosis in the vessels of the brain (Suissa et al., 2013; Villeneuve et al., 2012). Recently, there has been a call by researchers to further investigate the susceptibility of persons with a history of stroke to the effects of air pollution (Oudin et al., 2012). Our objective was to investigate the association between daily variations in ambient air pollutant ($PM_{2.5}$ and O_3) levels and risk of recurrent stroke.

2. Material and methods

2.1. Study population

Data are from the Brain Attack Surveillance in Corpus Christi (BASIC) Project, which is an ongoing population-based stroke surveillance study in Nueces County, Texas. Nueces County is located on the Gulf Coast and has a large petroleum and petrochemical industry

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presence (Lisabeth et al., 2008). The topography of the county is flat, with elevation varying from sea level to a maximum elevation of 180 feet (TNRIS (Texas Natural Resources Information System), 2013). Approximately, 340,000 people live in Nueces County with the majority of the population (95%) residing in the urban city of Corpus Christi. Based on the 2010 Census, 61% of the population is Mexican American and 33% is non-Hispanic white (US Census Bureau, 2012).

A combination of active and passive surveillance techniques were used to identify ischemic stroke cases between January 2000 and June 2012, as has been previously described (Morgenstern et al., 2013). Ischemic strokes were defined clinically as a focal neurologic deficit of acute onset specifically attributable to cerebrovascular distribution lasting longer than 24 h. Recurrent strokes were defined as the first recurrent ischemic stroke (one per individual) following an incident ischemic stroke identified in BASIC. Recurrent strokes that occurred on the same calendar day as the first stroke were excluded. Per the BASIC protocol, patients were excluded if they were younger than 45 years of age, lived outside of Nueces County, or if their strokes were the result of trauma. The BASIC project was approved by the University of Michigan Institutional Review Board and each of the Nueces County hospital systems.

2.2. Study design

A time-stratified case-crossover design was used to assess the association between air pollution and odds of recurrent stroke among individuals with ischemic stroke. This study design effectively controls for all time-invariant individual level characteristics, while comparing each subject's exposure to air pollution prior to the recurrent stroke event with his or her own exposure during referent control periods where he/she did not have a recurrent stroke (Lumley and Levy, 2000). Control periods were selected on the same day of the week, falling in the same month, and the same year as the recurrent stroke (Janes et al., 2005).

2.3. Air pollutant and meteorology data

Data for $PM_{2.5}$, O_3 and meteorological data from 2000 to 2012 were obtained from the Texas Commission on Environmental Quality's Texas Air Monitoring Information System from a centrally located monitor. Data from this monitor were highly correlated with others in the county ($\rho > 0.8$) (TCEQ (Texas Commission on Environmental Quality), 2012). $PM_{2.5}$, temperature and relative humidity were averaged daily (midnight to midnight) and O_3 was summarized as the maximal 8-h average. Each air pollutant was examined 1-d prior to recurrent stroke onset based on associations from other studies and the belief that this time period includes the appropriate window for triggering a recurrent stroke (Henrotin et al., 2010; Suissa et al., 2013; Wellenius et al., 2012). We also examined exposures on the same-day, 2-days prior and 3-days prior to onset of recurrent stroke in secondary analyses.

2.4. Statistical methods

Descriptive statistics were calculated for the study population, air pollution exposures and meteorological data and summarized using means/medians and frequencies/percents. Conditional logistic regression models, stratifying on each recurrent stroke (limited to one recurrent stroke per individual), were used to calculate odds ratios (ORs) for a 10 $\mu g/m^3$ or 10 ppb change in $PM_{2.5}$ or O_3, respectively, and corresponding 95% confidence intervals (CI). Unadjusted models were run for each pollutant on each lag day separately. Models were then repeated adjusting for ambient temperature and relative humidity measured on the same day as pollutant exposure. Functional forms of air pollutant and meteorological variables were assessed using penalized polynomial splines and found linear functional forms to be appropriate. The association between each pollutant and recurrent stroke was first examined separately and then in two-pollutant models. All analyses were conducted using SAS version 9.3 (SAS Institute Inc, Cary, NC) and the R statistical package, version 3.0.1.

Table 1
Baseline characteristics (N (%)) for recurrent ischemic strokes between January 2000 and June 2012.

Characteristic	n=317
Age group	
45–59	69 (22)
60–74	108 (34)
75+	140 (44)
Sex	
Female	169 (53)
Male	148 (47)
Ethnicity	
Non-Hispanic white	115 (36)
Mexican American	202 (64)
Atrial fibrillation	67 (21)
Coronary artery disease	122 (38)
Diabetes	166 (52)
Hypertension	266 (84)
NIH Stroke Scale (Index)	
≥ 6	97 (31)
< 6	220 (69)
Smoking status	
Never	233 (74)
Former	38 (12)
Current	42 (13)
Within 1 year of index stroke	147 (46)
Within 5 km of monitor	154 (48)
Within 90 days of index stroke	86 (27)
Discharged Home (Index)[a]	
Yes	126 (61)
No	80 (39)

NIH = National Institute of Health.
[a] Only available for a subset of the cases.

3. Results

A total of 3216 first-ever ischemic strokes were identified; 388 of these individuals had a recurrent stroke. Restricting to the first recurrent ischemic stroke and excluding those events that occurred on the same calendar day as the index stroke, reduced our sample to 358. Our analytic sample was further reduced to 317 recurrent ischemic strokes after excluding 41 strokes that occurred on days with missing air pollution data. Mean age of the 317 recurrent stroke cases was 72 years (SD=12) (Table 1). Sixty-four percent of cases were Mexican American (n=202) and 53% (n=169) were female. The median time to stroke recurrence was 1.1 years with an interquartile range (IQR) of 0.2–2.8 years. Median levels of $PM_{2.5}$ and O_3 over the study period were 7.7 $\mu g/m^3$ (IQR: 5.6–10.7 $\mu g/m^3$) and 35.2 ppb (IQR: 25.0–46.1 ppb), respectively.

We observed no associations between previous-day $PM_{2.5}$ and O_3 and odds of recurrent ischemic stroke in either unadjusted models or models adjusted for ambient temperature and relative humidity (Figs. 1 and 2). Associations between air pollutants and recurrent stroke were consistently null for other lagged exposure days (lag 2 and lag 3 days), but there was a suggestive protective effect for same-day levels of both pollutants (Figs. 1 and 2). Neither ambient temperature nor relative humidity were associated with recurrent stroke in the adjusted models for $PM_{2.5}$ or O_3, with the exception of ambient temperature in the Lag 2 model. Temperature two days prior to recurrent stroke was suggestive of an association, but did not reach