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Research Letter

Title: Exposure to particulate air pollution triggers recurrent, but not first-ever, ischemic stroke

Authors: Anna Oudin^{1,2*}, Bertil Forsberg¹, Kristina Jakobsson²

¹Department of Public Health and Clinical Medicine, Umeå University, Sweden

²Department of Laboratory Medicine, Lund University, Sweden

*Corresponding author

Address of corresponding author:

Anna.oudin@envmed.umu.se

Anna Oudin

Occupational and Environmental Medicine

901 87 Umeå

Sweden

Telephone: 0046 90 785 08 73

Fax: 0046 90 785 24 56

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It is quite well known that exposure to elevated concentrations of ambient particulate air pollution increase the number of stroke events the following days.¹⁻³ Susceptible groups has so far received little attention in the literature although there are some evidence for disease history to influence susceptibility to air pollution; Pope and colleagues observed that patients with underlying coronary artery disease had an increased susceptibility to short-term particulate exposure,⁴ whereas Henrotin et al. reported that the trigger effect of ozone on stroke events was much more pronounced in individuals with a history of cardiovascular disease than in individuals without such a history.⁵

In a previous study the authors observed that increased levels of ambient particulate matter (PM₁₀) resulted in an increase in the number of patients admitted for ischemic stroke the next day.² In the present study, we aimed at investigating if the effect in the previous study was modified by stroke history, in line with what Henrotin et al.⁵ and Pope et al.⁴ reported.

The study material was collected in 2008 in order to investigate effects of air pollution on stroke risk and has so far resulted in three publications where the data collection and the original study are described in detail.^{2,6,7} In the present study we used the time-stratified case-crossover method. A brief description of material and methods are given in the Supplementary File.

The median number of ischemic strokes per day was 6 with an interquartile range (IQR) of 4-8. The median daily concentration of PM₁₀ was 16.3 µg/m³ and the IQR was 12.8-21.1 µg/m³. The multi-pollutant model effect estimates for ischemic stroke in association with an IQR increase in PM₁₀ are presented in Table 1. The estimated increase in ischemic stroke events was 2.3% (95% Confidence Interval (CI): -0.003-5.1), for an IQR increase in PM₁₀ lag01. The results suggested that the effect of PM₁₀ on ischemic stroke events solely was present in persons with a previous stroke, the increase in that group being 4.3% (95% CI: -0.004-9.3), whereas the estimated change was -0.003% (95% CI: -3.2-2.6), in persons with no previous stroke, p for interaction 0.044.

The results indicate that susceptibility to short-term exposure to air pollution exposure depends on disease history: that elevated levels of PM₁₀ increase the number of ischemic stroke events the same and following day in patients with a history of stroke but not in persons without a previous stroke. The evidence for interactions between air pollution and comorbid factors on stroke risk is growing; recent research suggest that the diabetes induced risk of first-time ischemic stroke depends on air pollution levels in the neighborhood of the patient ⁷ and that diabetics are more sensitive to trigger effects of fine particulate air pollution than non-diabetics. ⁸ Henrotin and colleagues reported that the amount of cardiovascular risk factors was of interest.⁵ The results of the present study support previous indications that short-term trigger effects of air pollution on cardiovascular events is mainly attributed to patients with a history of cardiovascular disease. The pathways for such an increased susceptibility are unknown and should be studied in future studies. A finer description of disease history than available in the present study, for example information on type of stroke/cardiovascular disease and number of previous events might help to understand potential pathways in future studies.

Overall we observed trigger effects of particulate air pollution on ischemic recurrent stroke but not on first-ever ischemic stroke.

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Table 1. Odds Ratios (ORs) and 95 % Confidence Intervals (CIs) for ischemic stroke associated with an interquartile range increase in PM₁₀ obtained with the case-crossover method, adjusted for day of week (by design) and for temperature and ozone.

All ischemic strokes		First-time strokes		Recurrent strokes	
OR	95% CI	OR	95% CI	OR	95% CI
1.023	0.996-1.051	0.997	0.968-1.026	1.043	0.996-1.093
p-value for interaction by first-ever or recurrent stroke, p = 0.044					

Material and Methods

The study material was collected in 2008 in order to investigate effects of air pollution on stroke and has so far resulted in three publications where the data collection and original study are described in detail.¹⁻³ Briefly, data on hospital admitted strokes between the years 2001 and 2005 in the southernmost region in Sweden (Scania) were obtained from The national stroke register (Riks-stroke) which collects data on hospital admitted strokes directly from Swedish hospitals, capturing around 85% of all hospital admitted strokes. Riks-stroke has high quality stroke assessment with computer tomography assessed diagnoses, and importantly for the present study; data is collected on stroke history. The data file from Riks-stroke consisted of 11 267 patients with ischemic stroke of which 2982 (27%) had a history of stroke and 8142 (72%) did not have a history of stroke. For 143 (1%) patients, information on stroke history was missing. The median age was, somewhat surprisingly, rather similar in both groups: 78 years at diagnosis in patients with a history of stroke history and 76 years in patients without a previous stroke. Data on daily levels of particulate air pollution (PM₁₀) and daily maximum ozone were obtained from a measuring station in a rural area, representing rural background levels. Daily average temperature was available from another measuring station which was located in an urban area. Out of the N = 1826 days in the time period 65 (4%) had a missing value on PM₁₀, daily maximum ozone or temperature. Missing values were imputed with a standard imputation technique by replacing the missing value with an average of the two days closest to the missing value. All analyses were run both with and without the missing and imputed values.

Statistical analysis

We used the time-stratified case-crossover method ⁴⁻⁷ and analyzed data with conditional logistic regression analysis. The case-crossover design can be assumed to produce bias-free estimates, but if strong time trends are present the method might be biased.⁸ According to convention, we defined cases as the days the ischemic strokes had occurred: if for example three ischemic stroke happened the same day, three cases were defined that day. We selected the matched controls as the weekdays within the same month as the cases occurred. For example, if the 11th of July 2005 was a case, the controls were selected as the 4th, 18th and 25th of July 2005. The idea with selecting the days like that is to create a built-in control for season, time-trends and day-of-week effects. We produced both single- and multi-(PM₁₀) models as well as models adjusted and not adjusted for influenza. A p-value for interaction was calculated with logistic regression analysis.

The previous study indicated that the effect was strongest for the previous day PM₁₀ (lag 1). No effect was observed for later lags. Here, the lag01 (average of the levels on the same day and the day before) was used for the air pollution variables, but all analyses were repeated with lag1 variables in single-lag models. We did all analyses with SAS v 9.2.

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