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Combined effects of road traffic noise and ambient air pollution in relation to risk for stroke?

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ABSTRACT

Exposure to road traffic noise and air pollution have both been associated with risk for stroke. The few studies including both exposures show inconsistent results. We aimed to investigate potential mutual confounding and combined effects between road traffic noise and air pollution in association with risk for stroke. In a population-based cohort of 57,053 people aged 50–64 years at enrollment, we identified 1999 incident stroke cases in national registries, followed by validation through medical records. Mean follow-up time was 11.2 years. Present and historical residential addresses from 1987 to 2009 were identified in national registers and road traffic noise and air pollution were modeled for all addresses. Analyses were done using Cox regression. A higher mean annual exposure at time of diagnosis of 10 $\mu g/m^3$ nitrogen dioxide (NO_2) and 10 dB road traffic noise at the residential address was associated with ischemic stroke with incidence rate ratios (IRR) of 1.11 (95% CI: 1.03, 1.20) and 1.16 (95% CI: 1.07, 1.24), respectively, in single exposure models. In two-exposure models road traffic noise (IRR: 1.15) and not NO_2 (IRR: 1.02) was associated with ischemic stroke. The strongest association was found for combination of high noise and high NO_2 (IRR = 1.28; 95% CI = 1.09–1.52). Fatal stroke was positively associated with air pollution and not with traffic noise. In conclusion, in mutually adjusted models road traffic noise and not air pollution was associated ischemic stroke, while only air pollution affected risk for fatal strokes. There were indications of combined effects.

1. Introduction

Long-term exposure to road traffic noise and ambient air pollution are both suspected of increasing the risk for cerebrovascular events (Andersen et al., 2012; Floud et al., 2013; Maheswaran et al., 2012; Miller et al., 2007; Sorensen et al., 2011). However, as road traffic is an important source of both noise and ambient air pollution, the two exposures are correlated, raising questions about the extent of mutual confounding and combined effects.

A number of studies have investigated associations between short-term exposure to air pollution and stroke, and they generally report that elevated air pollution levels can trigger hospitalization and death from stroke within few days (Andersen et al., 2010; Oudin et al., 2010; Wellenius et al., 2012). Studies on long-term exposure to air pollution and incidence and mortality of stroke are less consistent, as some find or indicate positive associations (Andersen et al., 2012; Lipsett et al., 2011; Maheswaran et al., 2012; Miller et al., 2007; Raaschou-Nielsen et al., 2012) whereas others report no associations (Atkinson et al., 2013; Nafstad et al., 2004; Oudin et al., 2009). Only the Danish mortality study on air pollution adjusted analyses for road traffic noise, which lowered estimates slightly (Raaschou-Nielsen et al., 2012). Three studies have investigated the relationship between road traffic noise and cerebrovascular disease with inconsistent results. A Dutch cohort study reported no associations between road traffic noise and cerebrovascular mortality neither before nor after adjustment for

Abbreviations: NO_2, nitrogen dioxide; NO_x, nitrogen oxides; IRR, incidence rate ratios; L_{den}, noise level day–evening–night; SES, socioeconomic status; MET, metabolic equivalent

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air pollution (Beelen et al., 2009); we previously reported a significant association between road traffic noise and incident stroke, both before and after adjustment for air pollution in a Danish cohort (Sorensen et al., 2011); and a recent cross-sectional multi-center study using a joint category of self-reported heart disease and stroke, indicated that road traffic noise increase risk only before adjustment for air pollution (Floud et al., 2013). Two recent studies found aircraft noise to be positively associated with risk for stroke hospitalization (Correia et al., 2013; Hansell et al., 2013). One of these studies adjusted for air pollution, which did not confound the results (Correia et al., 2013), potentially because aircraft noise is only weakly to moderately correlated with air pollution (Clark et al., 2012; Floud et al., 2013), indicating an association between aircraft noise and risk for stroke independent of air pollution.

Some of the overall biological mechanisms believed to link exposure to risk for stroke are similar for road traffic noise and ambient air pollution, including effects on the vascular system such as endothelial dysfunction, increased blood pressure and atherosclerosis (Auchincloss et al., 2008; Briet et al., 2007; Kalsch et al., 2013; Schmidt et al., 2013; Schneider et al., 2008; van Kempen and Babisch, 2012; Wellenius et al., 2013). Both exposures are also suspected of increasing oxidative stress and affecting the immune system (Miller et al., 2012; Prasher, 2009; Schmidt et al., 2013). However, the pathways through which the two exposures act are very different; particulate air pollution through inhalation and translocation to the blood, whereas traffic noise exerts more indirect effects through stress and disturbance of sleep (Donaldson et al., 2005; Miedema and Vos, 2007; Selander et al., 2009a).

The aim of the present study was to investigate mutual confounding and combined associations between residential exposure to road traffic noise and ambient air pollution in relation to risk for incident stroke in a large prospective cohort. We used NO_x and NO_2 as indicators of air pollution, because they have been shown to be good markers of traffic-related air pollution and correlate closely with particulate matter. We also aimed to investigate associations between the two exposures and fatal incident stroke and subtypes of strokes: subarachnoid hemorrhage, intracerebral hemorrhage and cerebral infarction.

2. Methods

2.1. Study population

The study was based on the Danish Diet, Cancer and Health cohort (Tjønneland et al., 2007). In total, 57,053 of 160,725 residents of Copenhagen or Aarhus aged 50–64 years without a history of cancer were enrolled into the cohort between 1993 and 1997. Participants had to be born in Denmark. At enrollment, each participant completed self-administered, interviewer-checked, questionnaires covering food intake, lifestyle habits including detailed information on present and previous smoking and physical activity, health status, and social factors. Participants reported frequency of daily smoking of four types of tobacco as well as previous smoking. The average amount of tobacco smoked each day (smoking intensity) was calculated by equating a cigarette to 1 g, a cheroot or a pipe to 3 g, and a cigar to 5 g of tobacco. Information on physical activity was based on 12 questions covering average number of hours per week spent in the past year on different types of leisure time physical activity. The total energy per week spent on leisure time physical activity was evaluated using the MET-score. In a food frequency questionnaire participants were asked how often on average they had consumed different types of foods during the preceding 12 months. A mean daily intake of foods (g/day) was calculated by multiplying the frequencies of intake by a gender specific portion size using the software Foodcalc version 1.3 (Lauritsen, 2004). Participants also reported their average amount of alcohol consumption as the intake of specific amounts of each beverage type: light, normal, and fortified beer; red, white, and fortified wine; and spirits, which were converted into number of standard drinks (12 g alcohol) and added to yield a measure of average g alcohol per day. Coffee consumption was defined in four categories: ≤ 1, 2–3, 4–5 and ≥ 6 cups of coffee per day. Height and weight were measured by trained staff members according to standardized protocols, from which BMI was calculated (kg/m^2).

The study was conducted in accordance with the Helsinki Declaration, approved by local ethical committees (Copenhagen and Frederiksberg) and all participants provided written informed consent.

2.2. Identification of outcome

The endpoint was incident stroke (International Classification of Disease (ICD) 10: I60, I61, I63 and I64), and potential cases were identified by linkage to the nationwide Danish National Hospital Registry and the Danish Causes of Death Registry. We considered both primary and secondary discharge stroke diagnosis as possible stroke cases. All these potential cases were validated by direct review of medical records by a physician with neurological experience. Stroke cases were defined as rapid onset of focal or global neurological deficit of vascular origin that persisted beyond 24 h, leading to either death or confirmed by CT or MRI scan. Based on CT, MRI, autopsy records and lumbal punctures, we subsequently categorized strokes in following sub-diagnoses: subarachnoid hemorrhage, intracerebral hemorrhage and ischemic stroke (cerebral infarction) as well as fatal strokes, defined as death within 30 days of hospitalization for stroke.

2.3. Exposure assessment

2.3.1. Road traffic noise

Road traffic noise exposure was calculated for the years 1990, 1995, 2000, 2005 and 2010 using SoundPLAN (version 6.5, http://www.soundplan.dk/) for all residential addresses at which cohort members had lived between 1987 and diagnosis/censoring. This noise calculation program is based on the Nordic prediction method for road traffic noise (Bendtsen, 1999). The input variables for the noise model were: point for noise estimation (geographical coordinates and height); road links with information on annual average daily traffic, vehicle distribution (of light and heavy vehicles), travel speed, and road type (motorway, express road, road wider than 6 m, road less than 6 m and more than 3 m, and other road); and building polygons for all buildings. We obtained traffic data for all Danish roads with more than 1000 vehicles per day from a national road and traffic database (Jensen et al., 2009), based on different traffic data sources, including: (1) data from the 140 Danish municipalities with most residents, covering 97.5% of the addresses included in the present study; (2) a central database covering all the major state and county roads and (3) database on all major roads in the Greater Copenhagen Area. We assumed a flat terrain, which is a reasonable assumption in Denmark, and that urban areas, roads, and areas with water were hard surfaces, whereas all other areas were acoustically porous. No information was available on noise barriers or road surfaces. Road traffic noise was calculated as the equivalent continuous A-weighted sound pressure level (L_{Aeq}) at the most exposed facade of the dwelling at each address for day (L_d; 07:00–19:00 h), evening (L_e; 19:00–22:00 h) and night (L_n; 22:00–07:00 h), and expressed as L_{den} (den = day, evening, night) by applying a 5-dB penalty for the evening and a 10-dB penalty for the night as follows:

$$L_{den} = 10 \times \log(1/24 \times (12 \times \exp(L_d/10) + 3 \times \exp((L_e+5)/10) + 9 \times \exp((L_n+10)/10)))$$

Similar to a previous study, all values below 42 dB was considered as a lower limit of ambient noise and set to 42 dB (Selander et al., 2009b).

2.3.2. Air pollution

Ambient concentrations of NO_x and NO_2 were calculated with the Danish AirGIS dispersion modeling system for each year (1987–2009) at each address at which the cohort members had lived, including the Operational Street Pollution Model (OSPM). AirGIS allows calculation of air pollution at a location as the sum of: local air pollution from traffic in the streets; the urban background contribution; and a regional background contribution (Berkowicz et al., 2008). Input data for the AirGIS system included traffic data for individual road links (same input data as described for the noise modeling), emission factors for the Danish car fleet, street and building geometry, building height and meteorological data (Jensen et al., 2001). The AirGIS system and the OSPM model have been successfully validated and applied in several studies (Ketzel et al., 2011, 2012; Raaschou-Nielsen et al., 2011). As an example, AirGIS modeled and measured 1-month mean concentrations of NO_x and NO_2 over an 8-year period (1998–2005) in a busy street in Copenhagen (Jagtvej, 25,000 vehicles/day, street canyon) showed a correlation coefficient of 0.88 and 0.67, respectively (Ketzel et al., 2011).

2.4. Statistical analyses

Analyses were based on Cox proportional hazards model with age as underlying time, ensuring comparison of individuals of the same age. We used left truncation at age at 1st July 1997 (to ensure at least 10 years of exposure history for all cohort participants), and followed participants until age of stroke, death, emigration, or 30 November 2009, whichever came first. Exposure to road traffic noise and air pollution were modeled as exposure at the address at the time of diagnosis, exposure at the address at the time of enrolment into the cohort, and as time-weighted averages for the 1-, 5- and 10- year periods preceding the diagnosis, taking all present and historical addresses in that period into account. The time-