Exposure to traffic noise and risk for febrile seizure: a cohort study

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ABSTRACT

Traffic noise stresses and disturbs sleep, which are mechanisms that may affect risk of febrile seizures. We aimed to investigate whether road traffic noise increased risk for febrile seizures in children.

In a population of 57,282 children from the Danish National Birth Cohort we identified 2,175 children diagnosed with incident febrile seizure before 6 years of age. Residential address history from conception to 6 years of age was found in national registers, and road traffic noise (L_{den}) and air pollution (NO_2) were modeled for all addresses. Analyses were done using Cox proportional hazard model.

An interquartile range increase in childhood road traffic noise exposure (9.5 dB) was associated with an incidence rate ratio (IRR) of 1.11 (1.04-1.19) higher risk of febrile seizures after adjustment for gender, maternal lifestyle and socioeconomic status. After further adjustment for air pollution, the IRR was 1.08 (1.00-1.16). In these mutually adjusted models air pollution also seemed associated with febrile seizures (IRR: 1.03 (0.99-1.06)).

In conclusion, road traffic noise increased risk of febrile seizures in children, both before and after air pollution adjustment.

INTRODUCTION

Febrile seizures are the most common seizure disorder in early childhood, affecting 2-5% of the pediatric population [1]. The cause of febrile seizures is unknown, although an attack always involves high fever, with major upper airway infections, mainly viral, representing the most common provoking factors.

Road traffic noise and air pollution are common environmental exposures that co-exist. Traffic noise is believed hazardous through stress response and disturbance of sleep. Studies have indicated that both stress and disturbance of sleep impairs the immune system, which may increase susceptibility to viral infections [2-4]. Also, outdoor air pollution has been associated with higher risk for ear infections and respiratory infections in children [5, 6].

Believed mechanisms include that air pollution induces oxidative stress and affects inflammatory responses.

The aim of this study was to investigate whether residential exposure to road traffic noise during early life are associated with risk for febrile seizures in childhood, both before and after adjustment for air pollution, using data from a large population based cohort.

METHODS

The study was based on the Danish National Birth Cohort (DNBC), which consecutively recruited pregnant women from March 1996 to November 2002 from all over Denmark [7]. After providing written informed consent, the women participated in two prenatal computer-assisted telephone interviews around gestational week 16 and 31, including questions on smoking habits, alcohol intake and parity. When the child was 7 years of age, a follow-up questionnaire was mailed to the parents, in which 57,282 children participated. For these 57,282 children we had gained information on childhood addresses and traffic exposures, and these children therefore constituted the study base of the present study.

Children with febrile seizures were identified in the nationwide Danish National Patient, using International Classification of Diseases, 10th revision (ICD10) code R56. Only children with a diagnosis in the period between 3 months and 5 years of age (until the day before their 6 years birthday) were included as cases as febrile seizures occurs within this age span. We only included the first diagnosis of febrile seizures.

Residential address history for all children participating in the 7-years follow-up questionnaire between conception and end of follow-up (event, death, emigration or 5-years of age) were collected from the Danish Civil Registration System. All addresses were geocoded. Annual levels of road traffic noise were estimated using SoundPLAN, which is a calculation program that implements the joint Nordic prediction method for road traffic noise [8]. The noise model requires information on a number of variables: geocode and height for each address (at most exposed façade); information on annual average daily traffic for all Danish road links, distribution of light and heavy vehicles for all road links, travel speed and road type for all road links (motorway, express road, road wider than 6 m, road less than 6 m and more than 3 m, and other road); and polygons (3D) for all buildings in Denmark, obtained from the Danish Geodata Agency. We did not have information on noise barriers and road surface. We calculated road traffic noise as the equivalent continuous A-weighted sound pressure levels at the most exposed facade of each residence during day, evening and night, and expressed noise exposure as L_{den}.

We used an dispersion modelling system (AirGIS) to calculate exposure to annual levels of ambient NO_2 for all addresses [9]. This modelling system calculates air pollution at each address as the sum of: a) air pollution from the nearest street, calculated using information on traffic, car fleet emission factors, geometry of streets and buildings as well as daily information on meteorology; b) urban background, which is calculated using information on emission density, city dimensions and heights of buildings; and c) regional background, estimated from rural monitoring data and national vehicle emissions [9]. For traffic input data, the information used were the same as described above for noise. NO_2 is a surrogate for a mix of traffic-related air pollutants.

Analyses were based on Cox proportional hazard models, using age as the underlying time. We used left truncation at 3 months of age (delayed entry), and right censoring at the age of febrile seizure (event), death, emigration or until the day before they reached 6 years of age. We analyzed two exposure windows: pregnancy and childhood. Exposure to road traffic noise and air pollution during pregnancy was modelled as mean exposure, taking all

addresses during pregnancy into account. Childhood exposures were modelled as the yearly mean exposure at the diagnosis address, and entered as time-dependent variables into the statistical risk model.

Incidence rate ratios (IRR) for febrile seizure per interquartile range (IQR) increase in exposure to road traffic noise and air pollution were analysed in three models. Model 1 with adjustment for age (by design); Model 2 with further adjustment for sex of the child, maternal age at birth, parity, smoking and alcohol intake during 1st trimester, level of education, disposable income. In Model 3, we adjusted road traffic noise for air pollution and *vice versa*, (for same exposure time-windows).

RESULTS

Among the 57,282 children participating in the 7-years follow-up questionnaire we excluded 2,374 that were not singletons, 949 with missing exposure information, 2,494 with missing information on one or more potential confounders, leaving a study population of 51,465 children of whom 2,175 were diagnosed with febrile seizures during the follow-up period.

Children with febrile seizures were more likely to be boys and to be the first-born child, whereas only small differences were seen between the cases and the cohort with regard to maternal age, maternal education, household disposable income, maternal smoking and maternal alcohol consumption. Residential exposure to air pollution and road traffic noise were correlated (pregnancy: Spearman correlation = 0.47).

In adjusted analyses (Model 2), exposure to childhood noise and air pollution was statistically significant associated with a higher risk for febrile seizures (Table 1). Same tendencies were seen for pregnancy exposure, but the estimates were statistically insignificant. In two-pollutant models the estimates were lower, but there was still a statistically significant association with childhood exposure to road traffic noise (IRR: 1.08; 95% CI: 1.00-1.16) and an insignificant association for air pollution (IRR: 1.03; 0.99-1.06).

Table 1 Associations between pregnancy and childhood exposure to road traffic noise and air pollution and risk for febrile seizures.

	Model 1 **IRR (95% CI)**	**Model 2** **IRR (95% CI)**	**Model 3** **IRR (95% CI)**
Pregnancy exposure			
L_{den}, per IQR (9.5 dB)	1.09 (1.02-1.16)	1.06 (0.99-1.13)	1.06 (0.98-1.14)
NO_2, per IQR (5.5 µg/m^3)	1.03 (0.99-1.06)	1.02 (0.98-1.06)	1.00 (0.96-1.05)
Childhood exposure (diagnosis)			
L_{den}, per IQR (9.5 dB)	1.13 (1.06-1.21)	1.11 (1.04-1.19)	1.08 (1.00-1.16)
NO_2, per IQR (4.0 µg/m^3)	1.06 (1.03-1.09)	1.05 (1.02-1.07)	1.03 (0.99-1.06)

Model 1: Adjusted for age; Model 2: further adjusted for sex, maternal age at birth, household income at birth, maternal education at birth, parity at birth, smoking and alcohol consumption during pregnancy, calendar-year; Model 3: Further mutual exposure adjustment.

DISCUSSION

We found residential exposure to road traffic noise and air pollution during childhood to be associated with a higher risk for febrile seizures. In analyses with mutual exposure adjustment, the estimates were lowered, but still statistically significant for childhood exposure to road traffic noise and borderline significant for childhood exposure to air pollution.

We have not been able to identify other studies investigating the association between exposure to road traffic noise and air pollution and risk for febrile seizures. However, our finding of a positive association with risk for febrile seizures are supported by a number of studies showing that exposure to air pollution is associated with upper airway and ear infections, which are the most common provoking factors for febrile seizures [5, 6]. Similarly, studies have found that both stress and disturbance of sleep, which are the believed mechanisms behind the hazardous effects of noise, may increase susceptibility to viral infections [2-4].

Road traffic noise and air pollution were correlated in the present study, reflecting that road traffic is a source of both exposures. In analyses with mutual exposure adjustment, the estimates for both noise and air pollution were slightly lowered, indicating a small confounding effect. However, the estimates remained statistically significant for childhood exposure to road traffic noise and borderline significant for childhood exposure to air pollution, indicating that both of these co-existing traffic pollutants affects the risk for febrile seizures.

The strengths of our study include its size, access to residential address histories, information on various potential confounders obtained from questionnaires and nationwide registers. Furthermore, a validation study found that registration of febrile seizures in the Danish National Patient Register were generally good [10]. Also, road traffic noise and air pollution were estimated using good input data and state-of-the art exposure models. The present study also has some limitations. Estimation of air pollution and road traffic noise were based on exposure models, and although both models are state-of-the-art models, estimation of exposure is inevitably associated with some degree of uncertainty. As the exposure model does not distinguish between cases and non-cases, such misclassification is likely to be non-differential. We also lacked information on factors that influence the personal exposure to air pollution and road traffic noise, including time spend at home, information on commuting and occupational exposure, and direction of the bedroom, which may result in exposure misclassification. We would expect such misclassification to be unrelated to our outcome of interest and, therefore, draw the estimates towards the null. Residual confounding by unmeasured characteristics is always a risk, although only few risk factors for febrile seizures are known.

In conclusion, the present study indicates that exposure to residential road traffic noise and air pollution may be associated with higher risk for febrile seizures, but further studies are needed.

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