Road traffic noise and risk for non-Hodgkin lymphoma among adults

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Summary
Exposure to traffic noise may result in stress and sleep disturbances, which may impair the immune system. People with weakened immune systems are known to have a higher risk for non-Hodgkin lymphoma (NHL). We aimed to determine whether traffic noise was associated with risk for NHL. We identified 2,753 cases aged 30-84 years with a primary diagnosis of NHL in Denmark between 1992 and 2010. For each case we selected two random population controls, matched on sex and year of birth. Road traffic noise was calculated for all present and historical residential addresses of cases and controls from 1987 to 2010. Associations between traffic noise and risk for NHL were estimated using conditional logistic regression, adjusted for socioeconomic position. We found a 5-year time-weighted mean of road traffic noise above 65 dB to be associated with an 18% higher risk for NHL (95% confidence interval (CI) 1.01-1.37) when compared to road traffic noise below 55 dB, whereas for exposure between 55 and 65 dB no association was found. In analyses of NHL subtypes, we found no association between road traffic noise and risk for T-cell lymphoma, whereas increased risks for B-cell lymphoma and unspecified lymphomas were observed at exposures above 65 dB. In conclusion, our nationwide study may indicate that high exposure to traffic noise is associated with higher risk for NHL

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1. Introduction

Non-Hodgkin lymphoma (NHL) is a diverse group of malignancies originating from lymphoid tissue. The etiology of most NHL types remains largely unknown. A well-established risk factor is suppression of the immune system, and several studies have shown an increased risk of NHL among HIV patients and organ recipients receiving immunosuppressive drugs [1, 2]. Due to the strong relationship between the immune system and development of NHL, it is possible that also more moderate immune system disturbances may affect the risk for NHL.

Exposure to traffic noise has been associated with impaired human health [3]. One proposed mechanism is disturbance of sleep, as nighttime exposure to traffic noise at normal urban levels has been associated with sleep disturbances, including short sleep duration and reduced sleep quality [4]. Sleep is known to have a strong regulatory influence on the immune system [5], and deprivation of sleep has been associated with impairment of the immune system [6-8].

Another potential adverse health effect of noise is trigger of a stress response, with hyperactivity of the sympathetic autonomic nervous system, activation of the hypothalamus-pituitary-adrenal axis and increased levels of cortisol [9, 10]. Noise-induced stress may affect the immune system. Some studies have indicated that exposure to various acute and chronic stressors, e.g. exams and stressful life events, is associated with an impaired immune system [11].

In the present nationwide case-control study, we aimed to investigate the association between exposure to traffic noise and risk for NHL within the adult population of Denmark.

2. Methods

2.1. Study population

Since 1968, all Danish citizens have been assigned a unique personal identification number that encodes the date of birth and sex. This number is maintained by the Danish Civil Registration System, which also keeps continuously updated records on migration to and from Denmark, dates of death (if any) and changes in addresses (complete since 1971). The personal identification number is a key identifier that enables linkage across all Danish healthcare registries.

Cases were identified using the Danish Cancer Registry, which is considered close to complete and contains information on all cancer cases in Denmark since 1943 [12]. Eligible cases were Danes between 30 and 84 years of age with a primary diagnosis of NHL between 1992 and 2010. The NHL cases were defined as cancer diagnoses with morphology codes 9590-9596 and 9670-9729 according to the third edition of International Classification of Diseases for Oncology (ICD-O-3). We further required that cases were born in Denmark, had no previous diagnosis of cancer (except non-melanoma skin cancer), and lived at a geocodable address in Denmark at the time of diagnosis.

For each case two random controls, matched on sex and year of birth, were selected from the Civil Registration System. Controls which were dead, emigrated or diagnosed with cancer (except non-melanoma skin cancer) before the date of diagnosis of their matched case where excluded and substitute controls, matched on sex and year of birth, and under risk at age at diagnosis of the matched case, where sampled from surplus controls from the present study as well as from random population controls sampled for other ongoing studies. All controls in the final sample where required to be alive, free of cancer (except non-melanoma skin cancer), born in Denmark and living at a geocodable address in Denmark at time of diagnosis of matched case.

2.2. Exposure

Residential address history for all cases and controls between 1st of January 1987 and index date was collected using the Civil Registration System. Road traffic noise exposure was calculated for all present and historical addresses using SoundPLAN, which implements the joint Nordic prediction method for road traffic noise [13]. The equivalent noise level was calculated for each address at the most exposed facade of the actual building, in each of the time periods: day (07–19), evening (19–22) and night (22–07). Input variables for the model were: point of noise estimation (geographical coordinate and height (floor) for each address), road links with information on annual average daily traffic, vehicle distribution (light, heavy), travel speed and road type; and building polygons for all Danish buildings.

Table I. Associations between exposure to residential traffic noise and risk for non-Hodgkin lymphoma

	N cases	Crude OR (95% CI) [a,b]	Adjusted OR (95% CI) [a,c]
1-year exposure [d]			
< 55 dB	1,133	1.00	1.00
55-65 dB	1,221	0.99 (0.90-1.10)	1.00 (0.90-1.10)
≥ 65 dB	399	1.21 (1.04-1.40)	1.22 (1.05-1.42)
5-year exposure [d]			
< 55 dB	1103	1.00	1.00
55-65 dB	1256	0.97 (0.88-1.08)	0.98 (0.88-1.08)
≥ 65 dB	394	1.16 (1.00-1.35)	1.18 (1.01-1.37)

[a]OR, odds ratio; CI, confidence interval, [b]Crude (match on sex and year of birth) [c] Model I plus adjustment for disposable income, level of education, cohabiting status, comorbidity, railway noise and airport noise, [d]Time-weighted mean exposure preceding the index date, taking all addresses in that period into account

We obtained traffic counts for all Danish roads with more than 1,000 vehicles per day from a national road and traffic database [14]. This database is based on a number of different traffic data sources ranked as follows: 1) Collection of traffic data from Danish municipalities; 2) Traffic data from a central database covering all the major state and county roads; 3) Traffic data for 1995–2000 for all major roads in the Greater Copenhagen Area; 4) Smoothed traffic data [14]. We assumed 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 assumed to be acoustically porous. No information was available on noise barriers or type of asphalt. Road traffic noise was expressed as L_{den} (day, evening and night).

2.3. Potential confounders

Information on individual socioeconomic position (SEP) of study participants was obtained by linking cases and controls to various population-based administrative registers operated by Statistics Denmark that since 1980 contain annually updated data from the Civil Registration System, the taxation authorities and the Register for Education Statistics. We received information on: highest attained education (basic school/high school education (7–12 years of primary, secondary and grammar-school education), vocational education (10–12 years) and higher education (⩾13 years)); cohabiting status (married/cohabiting, single, widow/widower or divorced); and individually disposable income determined as the household income after taxation and interest per person, adjusted for number of persons in the household and divided into quintiles based on Danish background population (age-standardized).

Information on comorbidity was obtained from the Danish National Patient Registry, which holds information on all non-psychiatric hospital admissions and on all outpatient and psychiatric hospital contacts since 1995. The data include medical diagnoses (ICD-8 until 1993 and ICD-10 from 1994 onwards), surgical procedures, and date of activity. Using this register we generated Charlson Comorbidity index (0, 1 and ≥2) for all cases and controls based on all relevant diagnosis until one year before the index date.

Exposure to railway noise was calculated for all addresses using SoundPLAN, with implementation of NORD2000, which is a Nordic calculation method for prediction of noise propagating for railway traffic noise. The noise impact from all Danish airports and airfields was determined from information about noise zones (5 dB categories) obtained from local authorities. The concentration of ambient air pollution (NO_2) was calculated using the Danish AirGIS modelling system for each year (1987-2010) at each address [15].

3. Results

From an initial study population of 7,722 individuals, we excluded 124 with missing exposure information and five with missing information on potential confounders. After these exclusions, 33 cases had no matching controls and64 controls had no matching case, and were excluded.

Table II. Associations between 5-year exposure to residential road traffic noise and risk for subtypes of non-Hodgkin lymphoma

Subtype of NHL	Road traffic noise, 5-years	N cases	OR (95% CI) [a,c]
B-cell lymphoma	< 55 dB	815	1.00
	55-65 dB	922	0.95 (0.84-1.67)
	≥ 65 dB	290	1.16 (0.97-1.38)
T-cell lymphoma	< 55 dB	96	1.00
	55-65 dB	107	0.95 (0.67-1.37)
	≥ 65 dB	26	0.82 (0.46-1.45)
Lymphomas, NOS [b]	< 55 dB	192	1.00
	55-65 dB	227	1.08 (0.84-1.39)
	≥ 65 dB	78	1.34 (0.94-1.91)

[a]Odds ratio with 95% confidence interval with match on sex and year of birth and adjustment for disposable income, level of education, cohabiting status and comorbidity, [b]NOS: Not Otherwise Specified

After exclusions, the final study population comprised of 7,496 individuals; 2,753 NHL cases and 4,743 controls.

Cases had slightly more comorbidity than controls, whereas SEP was similar between cases and controls. Cases were more often cohabiting as compared with the controls. Spearman's correlations were 0.95 for 1-year and 5-years exposure to road traffic noise.

A 5-year time-weighted mean of road traffic noise above 65 dB was associated with an 18% higher risk for NHL (95% CI: 1.01-1.37), compared with road traffic noise below 55 dB, whereas for exposure between 55 and 65 dB no association was found (OR: 0.98; 95% CI: 0.88-1.08) (Table I). Additional adjustment for air pollution (NO_2) yielded slightly higher risk estimates: mean 1-year and 5-years road traffic noise exposure above 65 dB were associated with ORs of 1.26 (95% CI: 1.05-1.52) and 1.23 (95% CI: 1.02-1.48), respectively (results not shown).

In analyses of NHL subtypes, B-cell lymphoma and unspecified lymphoma seemed associated with road traffic noise above 65 dB, whereas no associations were found for T-cell lymphoma (Table II).

4. Discussion

In our nationwide study we found that exposure to road traffic noise above 65 dB was associated with a higher risk for NHL compared with road traffic noise exposures below 55 dB. Road traffic noise exposures above 65 dB seemed associated with increased risk for B-cell lymphoma and unspecified lymphomas in subtype analyses.

We are not aware of other studies examining the association between traffic noise and NHL. Instead, a number of studies have reported associations between exposures to traffic noise and cardiovascular disease [3], with proposed mechanisms through disturbance of sleep, annoyance and stress [4, 9], followed by rise in cardiovascular risk factors, including blood pressure, blood lipids and blood glucose [10]. Since disturbance of sleep and stress have also been associated with a weakened immune system [6, 7, 11], it appears biologically plausible that long-term exposure to traffic noise, through stress and disturbance of sleep, may also affect diseases in which the immune system plays a central role, e.g. NHL. A few epidemiological studies have reported that night shift work, representing a massive disturbance of sleep and the circadian rhythm, is associated with an increased risk for NHL [16, 17]. Also, three studies have examined associations between various noise exposures and inflammatory biological markers [18-20]. These studies indicated no or only weak associations. However, only a very limited number of inflammatory markers were investigated and the

definition of noise exposure differed markedly. Thus, additional studies are warranted.

The present study indicated a non-linear association, where only people exposed to high levels of road traffic noise were at increased risk for NHL. This pattern, together with the explorative character of our study, dictates that our results should be treated with caution.

The present study suggested that road traffic noise was associated with both B-cell lymphoma and unspecified lymphoma, whereas for T-cell lymphomas no association was found. The lack of association for T-cell lymphomas may be a result of the small numbers and chance. It is, however, in line with many other studies showing etiologic heterogeneity among subtypes of NHL [21].

The strengths of this study include its size and design. The study was a register-based approach based on the entire Danish population, using national registries of high quality with nearly complete coverage of all Danish residents. The exposure to road traffic noise covered a 5-year period before a diagnosis of NHL and was based on register information on historical addresses, together with information on road lines, buildings and traffic collected from national registers and municipalities. This approach minimized the risk for selection bias and differential misclassification. The register-based nature of the study, however, restricts the available data on potential confounders. There are, however, only few established risk factors for NHL. A potential confounder is exposure to air pollution, as air pollution and road traffic noise are correlated and air pollution has been suggested to be associated with NHL [22]. However, the association between air pollution and NHL has not been established, and the additional adjustment for air pollution in the present study resulted in only minor changes in risk estimates.

Another limitation was that we had information on exposure only five years preceding a diagnosis of NHL. However, studies of lymphoproliferative diseases after organ transplantation followed by immunosuppressive medication have observed an excess risk of lymphoma occurring already in the second or third year after transplantation, indicating that the latency period of NHL is shorter than for most other types of cancer [23]. Also, we found a strong correlation between 1- and 5-years' time-weighted means of road traffic noise, which suggests that the 5-year mean is also a good proxy for longer term exposure to road traffic noise.

During the last four decades increasingly accurate and reliable prediction methods for traffic noise have been developed. Although the Nordic prediction method has been used for many years, estimation of noise is inevitably associated with some degree of uncertainty. One reason could be inaccurate input data, e.g., we lacked information on noise barriers and asphalt type in the modeling of road traffic noise. This could have resulted in exposure misclassification, though such misclassification would conceivably be non-differential. Another limitation was that we had no information on individual factors associated with the experience of noise, such as bedroom location, window opening habits or hearing impairment. Studies of traffic noise and cardiovascular diseases have found stronger associations with road traffic noise when these factors are considered, indicating that an effect of noise might be underestimated in the present study.

5. Conclusions

In conclusion, our nationwide study indicates that exposure to road traffic noise at high levels may be associated with NHL among adults. However, as the first study of traffic noise and risk for NHL, our results should be interpreted with caution.

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