Environment International 158 (2022) 106946

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Environmental noise exposure and emotional, aggressive, and attention-deficit/hyperactivity disorder-related symptoms in children from two European birth cohorts

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ARTICLE INFO

Handling Editor: Zorana Andersen

Keywords:
Noise pollution
Transportation noise
Anxiety
Aggression
Behavioral symptoms
Longitudinal studies

ABSTRACT

Background: Environmental noise exposure is increasing but limited research has been done on the association with emotional, aggressive, and attention-deficit/hyperactivity disorder (ADHD)-related symptoms in children.
Objective: To analyze the association between prenatal and childhood environmental noise exposure and emotional, aggressive, and ADHD-related symptoms in children from two European birth cohorts.
Methods: We included 534 children from the Spanish INMA-Sabadell Project and 7424 from the Dutch Generation R Study. Average 24 h noise exposure at the participants' home address during pregnancy and childhood periods were estimated using EU maps from road traffic noise and total noise (road, aircraft, railway, and industry). Symptom outcomes were assessed using validated questionnaires: Strengths and Difficulties Questionnaire, Child Behavioral Checklist, ADHD Criteria of Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition List, and Conner's Parent Rating Scale-Revised at 4, 7 and 9 years (INMA-Sabadell cohort) and 18 months, 3, 5, and 9 years (Generation R Study). Adjusted linear mixed models of prenatal and repeated childhood noise exposure with repeated symptom outcomes were run separately by cohort and overall estimates were combined with random-effects meta-analysis.
Results: Average prenatal and childhood road traffic noise exposure levels were 61.3 (SD 6.1) and 61.7 (SD 5.8) for INMA-Sabadell and 54.6 (SD 7.9) and 51.6 (SD 7.1) for Generation R, respectively. Prenatal and childhood road traffic noise exposure were not associated with emotional, aggressive, or ADHD-related symptoms. No heterogeneity was observed between cohorts and results were comparable for total noise exposure.
Conclusions: No association was observed between prenatal or childhood road traffic or total noise exposure and symptom outcomes in children. Future studies should include a more comprehensive noise exposure assessment considering noise sensitivity and noise exposure at different settings such as work for pregnant women and school for children.

1. Introduction

The continuously growing world population is accompanied by a rapid increase in urbanization, with a projected growth of 55% to 70% living in urban areas by 2050 (The World Bank, 2019; United Nations: Department of Economic and Social Affairs, 2019). Within our urbanized world, exposure to noise has become unavoidable due to a growing demand of transport (Erickson and Newman, 2017; European Environmental Agency, 2020). Transportation noise exposure from road traffic, railway, and aircraft is considered the second most significant

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https://doi.org/10.1016/j.envint.2021.106946
Received 3 June 2021; Received in revised form 23 September 2021; Accepted 18 October 2021
Available online 27 October 2021

environmental cause of ill-health in Western Europe (European Environmental Agency, 2020). Evidence of increased risk in negative physiological and psychological health due to prolonged exposure to environmental noise is the driving force behind the guidelines and recommendations that the World Health Organization sets in an attempt to limit the levels of noise exposure and protect human health (World Health Organization, 2018).

Children specifically are more vulnerable and susceptible to the potential harmful effects of environmental noise exposure (Erickson and Newman, 2017; Gupta et al., 2018). A suggested biological mechanism highlights how environmental noise exposure during pregnancy can increase the levels of maternal stress hormones and influence the hypothalamic–pituitary adrenal axis, ultimately impacting the brain development of the child (Beijers et al., 2014; Gitau et al., 1998; Graignic-Philippe et al., 2014; Jafari et al., 2017; Lautarescu et al., 2020). Children also have less developed coping strategies than adults and less control over the levels of noise they are exposed to (Evans et al., 1991; Gupta et al., 2018; Stansfeld and Matheson, 2003). Studies investigating the association between environmental noise exposure, mainly residential road traffic and aircraft noise, and emotional, aggressive, and attention-deficit/hyperactivity disorder (ADHD)-related symptoms in children often show heterogenous results (Clark et al., 2020; Clark and Paunovic, 2018a, 2018b; Stansfeld and Clark, 2015; Zijlema et al., 2021). Studies mainly assessed ADHD-related symptoms and very few include emotional and aggressive symptoms. Further, most studies focused primarily on the exposure during childhood, while pregnancy exposure could also be a relevant window since the developmental processes of the fetus might be influenced by noise exposure-induced maternal stress. Also, studies usually assessed the transportation noise sources separately, while an individual can be exposed to more than one source, and thus the overall effect of exposure to multiple noise sources should also be investigated.

Therefore, this study aims to evaluate the association between prenatal and childhood exposure to road traffic and overall transportation noise with emotional, aggressive, and ADHD-related symptoms in children from two European birth cohorts.

2. Methods

2.1. Population and study design

This study was embedded in two population-based prospective cohort studies: the Spanish INMA Project (Guxens et al., 2012) and the Dutch Generation R Study (Hofman et al., 2004; Kooijman et al., 2016). The INMA Project is a network of birth cohorts set up in several regions of Spain following a common protocol, and for this analysis we only included the INMA-Sabadell cohort due to availability on noise exposure data. The cohort includes 778 pregnant women and their children resident in the city of Sabadell (Catalonia, Spain) who visited the public health center of Sabadell between July 2004 and July 2006 for an ultrasound in the first trimester. Inclusion criteria were 16 years or older, singleton pregnancy, no assisted reproduction program, intention to deliver in the reference hospital, and no communication problems. The Generation R Study is a cohort study that recruited 9749 pregnant women living in the city of Rotterdam, the Netherlands, with an expected delivery date between April 2002 and January 2006. Inclusion criterium was being resident in Rotterdam when the child was born. In our study, we included children with at least one noise exposure value and one symptom outcome measurement (n = 534 for INMA-Sabadell and 7424 for Generation R, Fig. S1). Ethical approval was obtained prior to recruitment from the Clinical Research Ethical Committee of the Municipal Institute of Healthcare (CEIC-IMAS) for the INMA-Sabadell cohort and from the Medical Ethical Committee of Erasmus MC, University Medical Centre Rotterdam, in accordance with Dutch law for the Generation R Study. Informed consent was obtained from parents in both studies.

2.2. Noise exposure

Existing noise maps developed in 2012 for Rotterdam and 2006 and 2012 for Sabadell were used to assess the annual levels of outdoor noise exposure at each participant's home address. We did not use an earlier noise map for Rotterdam (i.e., the one of 2007) because the methodology used to develop that earlier map differed to the one of 2012, making the estimations incomparable. The noise maps meet the requirements of the European Environmental Noise Directive (European Environmental Noise Directive, 2002). The noise maps for Sabadell were based on a model at street level that covered the entire municipal surface and the noise map for Rotterdam was solely based on residential buildings. Accuracy of the noise models was assured because they were developed to assess exposure at the residential addresses. Noise maps were available for exposure levels of residential road traffic, railway, aircraft, and industry noise. However, in the INMA-Sabadell cohort, children were not exposed to railway, aircraft, or industry noise, so data solely from residential road traffic was used. Noise exposure levels for the Generation R Study consisted of data from residential road traffic, railway, aircraft, and industry.

For each noise exposure source, the day-evening-night noise indicator (L_{DEN}) was calculated as the A-weighted average sound levels over the entire 24 h of a day with penalties for the evening (+5 decibel (dB)) and night (+10 dB) (European Environmental Noise Directive, 2002). The L_{DAY}, $L_{EVENING}$ and L_{NIGHT} indicators were respectively the A-weighted average sound levels assessed during the day (12 h for Generation R, 07:00–19:00 and 14 h for INMA-Sabadell, 07:00–21:00), the evening (4 h for Generation R, 19:00–23:00 and 2 h for INMA-Sabadell, 21:00–23:00), and the night (8 h for both cohorts, 23:00–07:00), and were calculated using the formulas detailed in Methods S1 (European Environmental Noise Directive, 2002). Total noise exposure levels for the Generation R Study were calculated using the formula detailed in Methods S1. The levels of L_{DEN} of each noise exposure source were applied to each geocoded participant's address during the period of interest. In one address where L_{DEN} was below the threshold of 40 dB, considered as the minimum reliable value, we changed the value of that address to 40 dB. Considering the number of days that the participant spent at each address and weighting the noise levels accordingly, we calculated the mean levels of L_{DEN} for each participant for the pregnancy period (from conception until birth), and for different periods during childhood, depending on the assessment of the outcomes. For the INMA-Sabadell cohort these periods were: from birth to 4 years old, from 4 to 7 years old, and from 7 to 9 years old, and for the Generation R Study: from birth to 18 months old, from 18 months to 3 years old, from 3 to 5 years old, and from 5 to 9 years old. In both cohorts, we considered the mean level of L_{DEN} during a period of interest as missing if the child had lived outside of the study area for more than 50% of the time. A subject was included in the analysis if they had at least one noise exposure measurement (Fig. S1).

2.3. Emotional, aggressive, and ADHD-related symptom assessment

Validated questionnaires were used throughout childhood to assess emotional, aggressive, and ADHD-related symptoms in both cohorts (Methods S2). The questionnaires used varied between cohorts and measurement time points (Fig. S2). In the INMA-Sabadell cohort, emotional and aggressive symptoms were assessed using the Strength and Difficulties Questionnaire (SDQ) (Goodman et al., 2003) at 7 years of age and the Child Behavioral Checklist 6–18 (CBCL 6–18) (Achenbach and Rescorla, 2001) at 9 years of age. ADHD-related symptoms were reported using the ADHD Criteria of Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (ADHD-DSM-IV) list at 4 years of age (American Psychiatric Association, 2000) and the Conner's Parent Rating Scale-Revised (CPRS) at 7 and 9 years of age (Conners, 1997). In the Generation R Study, emotional, aggressive, and ADHD-related symptoms were reported at 18 months, 3, and 5 years of age using the CBCL

1.5–5 questionnaire and at 9 years of age using the CBCL 6–18 questionnaire (Achenbach and Rescorla, 2001). All questionnaires were completed by the mother, except for the ADHD-DSM-IV list, which was done by the teacher. To make the results from the questionnaires comparable across cohorts, sum scores of the symptom categories were square root transformed to reach normal distribution and then standardized by calculating the Z-score of the raw scores. A higher score indicates more symptoms.

2.4. Potential confounding variables

Potential confounding variables for both cohorts were defined a priori based on previous scientific literature, available data, and using a direct acyclic graph (Hernán et al., 2002). Information for both cohorts on parental age at enrollment (in years), parental ethnicity (Spanish or Others for the INMA-Sabadell cohort, and Dutch, Surinamese, Turkish, Moroccan or Others for the Generation R Study), parental education level (low: no education, unfinished primary or primary; medium: secondary; high: university degree), parental social class based on occupation (low: unskilled or (partly) skilled manual workers; medium: financial management, administrative and other support staff, other self-employed professionals, supervisors of manual workers, and skilled non-manual workers; high: managers of companies, and intermediate or higher level professionals), family status (dual or single parent), maternal parity (nulliparous, one child, two or more children), maternal smoking during pregnancy (yes or no), maternal alcohol use during pregnancy (yes or no) and monthly household income (only for the Generation R Study, (<€900, €900–1600, €1600–2220 or >€2200) was collected by questionnaires during pregnancy. Parental psychological distress was measured during pregnancy using the Brief Symptom Inventory for the Generation R Study and at child's 14 months using the General Health Questionnaire for the INMA-Sabadell cohort (Derogatis, 1993; Goldberg et al., 1997). Child sex was obtained from hospital records, and parental height (cm) and weight (kg) was measured or self-reported in the 1st trimester of pregnancy and subsequently used to calculate the pre-pregnancy body mass index (in kg/m^2) for both cohorts. Traffic-related air pollution was not explored as co-exposure because we did not find associations between air pollution and our symptom outcomes in either cohort (Forns et al., 2018; Jorcano et al., 2019).

2.5. Statistical analyses

To increase validity of results and limit attrition bias, missing values of the potential confounding variables were 25 times imputed for all subjects using standard procedures for multiple imputation (Table S1) (Spratt et al., 2010; Sterne et al., 2009). The percentage of missing values for the confounding variables was low, except for paternal characteristics in the Generation R Study which were between 30.4% and 48.5%. Distributions in imputed datasets were similar to those in observed datasets (Table S2).

Children included in the analysis (534 for INMA-Sabadell cohort and 7424 for Generation R Study, Fig. S1) were more likely to have parents with a national origin from the cohort site (Spanish or Dutch), have a higher education level and social class, and have mothers that are older, nulliparous, and did not smoke during pregnancy than those not included (Table S3). Thus, inverse probability weighting was used to correct for selection bias (Weisskopf et al., 2015; Weuve et al., 2012). In brief, we used information available for all participants at recruitment to predict the probability of participation in the current study and used the inverse of those probabilities as weights in the analyses so that results would be representative for the initial population. The variables used to create the weights can be found in Table S4.

First, linear mixed models (LMM) were run separately per cohort to examine the association between average prenatal noise exposure in relation to the repeated measures of emotional, aggressive, and ADHD-related symptoms at 4, 7, and 9 years old for INMA-Sabadell and at 18 months, 3, 5 and 9 years for Generation R (Fig. S2). Overall estimates of each cohort were then combined using random effects meta-analysis and the heterogeneity of the estimates was assessed using Cochran Q test and the I^2 statistic.

Second, LMM were run separately per cohort to examine the association between the repeated estimates of noise exposure during childhood in relation to the repeated measures of emotional, aggressive, and ADHD-related symptoms. Thus, for INMA-Sabadell, LMM for emotional and aggressive symptoms included noise exposure estimations between birth and 7 years and between 7 and 9 years, and symptom outcome data at 7 and 9 years. LMM for ADHD-related symptoms included noise exposure estimations between birth and 4 years, between 4 and 7 years, and between 7 and 9 years, and symptom outcome data at 4, 7, and 9 years. For Generation R, all LMM included noise exposure estimations between birth and 18 months, between 18 months and 3 years, between 3 and 5 years, and between 5 and 9 years, and symptom outcome data at 18 months, 3, 5, and 9 years. Each LMM resulted in one overall childhood effect estimate. Overall estimates of each cohort were then combined using random effects meta-analysis and the heterogeneity of the estimates was assessed using Cochran Q test and the I^2 statistic.

Third, to examine the association between each lifetime period of childhood noise exposure and the repeated emotional, aggressive, and ADHD-related symptoms at each time point, LMM detailed in the previous paragraph were re-run including an interaction term between noise exposure and the age at the assessment of the symptom outcome. These models could not be combined into random effects meta-analysis because each cohort assessed the outcomes at different ages. Thus, effect estimates at each age of the assessment of the symptom outcome are presented separately per cohort.

All LMM included a random intercept to account for the non-independence due to repeated measures of exposure and outcome per subject. All models were first unadjusted, and then adjusted for all potential confounding variables described above. We conducted a sensitivity analysis where we performed all LMM with only the children that had complete childhood noise exposure measurements. Statistical analyses were carried out using STATA (version 14.0; StataCorporation, College Station, TX) and R (version 4.0.0; R Core Team (2020)).

3. Results

Participant characteristics of the study population from both cohorts are shown in Table 1. The average age of mothers was 31.8 and 30.7 years in the INMA-Sabadell cohort and Generation R Study, respectively. In the INMA-Sabadell cohort, most mothers were Spanish (90.5%), had a medium education (43.8%), and were from a low social class (44.5%). In the Generation R Study, the household income was mostly high (59.9%), and most mothers were Dutch (56.2%), had a high education (48.9%), and were from a high social class (63.9%).

Average prenatal road traffic noise exposure levels were 61.3 (standard deviation (SD) 6.1) and 54.6 (SD 7.9), whereas average childhood road traffic noise exposure levels were 61.7 (SD 5.8) and 51.6 (SD 7.1) in the INMA-Sabadell cohort and the Generation R Study, respectively. Average total noise exposure levels in the Generation R Study were 55.8 (SD 7.1) during pregnancy and 52.8 (SD 6.8) during childhood. Distribution of the noise exposure levels can be found in Table S5 and Fig. S3. Road traffic noise exposure levels throughout the different lifetime periods were moderately to strongly correlated (between 0.69 and 0.94 in the INMA-Sabadell cohort and between 0.48 and 0.91 in the Generation R Study, respectively). In the Generation R Study, total noise exposure during pregnancy and childhood was moderately to strongly correlated (between 0.49 and 0.91) and traffic and total noise exposure were strongly correlated (between 0.95 and 0.97, Table S6).

Prenatal road traffic noise exposure was not associated with emotional, aggressive, or ADHD-related symptoms in the unadjusted and adjusted models for the INMA-Sabadell cohort and Generation R

Table 1
Population characteristics of the INMA-Sabadell cohort and Generation R Study.

Characteristics		INMA-Sabadell (n = 534)	Generation R (n = 7,424)
Noise Exposure (decibels)			
Road	Prenatal	61.3 (6.1)	54.6 (7.9)
	Childhood	61.6 (6.1)	53.7 (7.5)
Total	Prenatal	–	55.8 (7.1)
	Childhood	–	55.2 (6.7)
Maternal Characteristics			
Age at enrolment (years)		31.8 (4.2)	30.7 (5.0)
Pre-pregnancy body mass index (kg/m^2)		22.7 (21.1; 25.4)	22.6 (20.8; 25.2)
Ethnicity			
Spanish		90.5	–
Dutch		–	56.2
Surinamese		–	7.3
Turkish		–	8.1
Moroccan		–	5.1
Others		9.5	23.3
Education during pregnancy			
Low		24.1	8.3
Medium		43.8	42.8
High		32.1	48.9
Social Class during pregnancy			
Low		44.5	3.9
Medium		32.4	32.2
High		23.1	63.9
Psychological distress[1]		9.0 (7.0; 12.0)	0.2 (0.1; 0.3)
Parity			
0		56.1	56.7
1		37.3	30.5
2+		6.6	12.8
Smoking during pregnancy (no vs. yes)		73.2	84.0
Alcohol during pregnancy (no vs. yes)		77.9	59.2
Paternal Characteristics			
Age at enrolment (years)		33.6 (4.8)	33.2 (5.5)
Body mass index during pregnancy (kg/m^2)		25.4 (23.5; 27.7)	24.9 (22.9; 27.2)
Ethnicity			
Spanish		89.8	–
Dutch		–	64.8
Surinamese		–	5.6
Turkish		–	5.6
Moroccan		–	3.2
Others		10.2	20.8
Education during pregnancy			
Low		36.7	6.7
Medium		42.0	39.4
High		21.2	53.9
Social Class during pregnancy			
Low		57.4	8.5
Medium		18.7	22.7
High		23.9	68.8
Psychological distress[1]		9.0 (7.0; 11.0)	0.1 (0.0; 0.2)
Household Characteristics			
Family status (dual vs. single parent)		98.8	89.0
Monthly income during pregnancy			
<900€		–	9.0
900–1600€		–	15.7
1600–2200€		–	15.4
>2200€		–	59.9

Values are percentages for categorical, mean (standard deviation) for continuous variables, and median (25th; 75th percentile) for body mass index and psychopathological distress.
[1] Score range 0–36 for the INMA-Sabadell cohort (assessed at child's 14 months) and 0–4 for the Generation R Study (assessed during pregnancy).

Study, separately or combined in the meta-analysis (Fig. 1A, Table S7). Similarly, overall childhood road traffic noise exposure showed no association with emotional, aggressive, or ADHD-related symptoms (Fig. 1B, Table S7). When analyzing the associations per childhood lifetime period, there were no associations between road traffic noise exposure and emotional, aggressive, or ADHD-related symptoms at 4, 7 or 9 years of age for the INMA-Sabadell cohort (Fig. 2A, Table S8). In the Generation R Study, higher road traffic noise exposure was not associated with any symptoms at 18 months, 3 years, or 5 years. However, higher road traffic noise exposure was associated with lower emotional, but not aggressive or ADHD-related, symptoms at 9 years (Fig. 2B, Table S8). Effect estimates were materially unchanged when looking at prenatal and childhood total noise exposure in the Generation R Study (Fig. S4 and Tables S7-S8). Effect estimates were also unchanged in children with complete childhood noise exposure levels or in children with no missing values for potential confounding variables (Tables S9 and S10).

4. Discussion

In this study, we found no evidence of an association of residential road traffic noise exposure during pregnancy or childhood with emotional, aggressive, and ADHD-related symptoms in children from two European birth cohorts. Associations were also absent for total noise

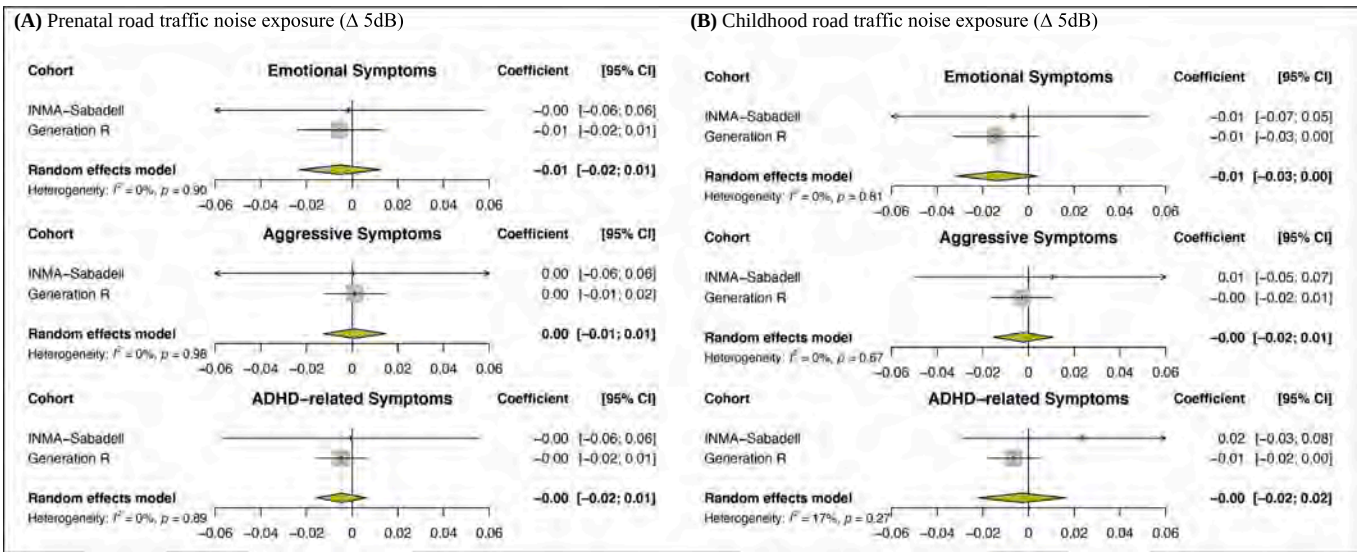

Fig. 1. Fully adjusted associations of a 5 dB increase in prenatal (A) or childhood (B) road traffic noise exposure and standardized emotional, aggressive, or attention-deficit/hyperactivity disorder (ADHD)-related symptom scores in the INMA-Sabadell cohort and Generation R Study. Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; dB, decibels; I^2, percentage of the total variability due to between-cohort heterogeneity; p; p-value of heterogeneity using the Cochran's Q test. Coefficients and 95% confidence intervals were obtained by random-effects meta-analysis. Within each cohort, linear mixed models were adjusted for child sex, parental age, body mass index, ethnicity, education, social class and psychological distress, parity, smoking and alcohol during pregnancy, and family status. Generation R Study models were additionally adjusted for monthly household income.

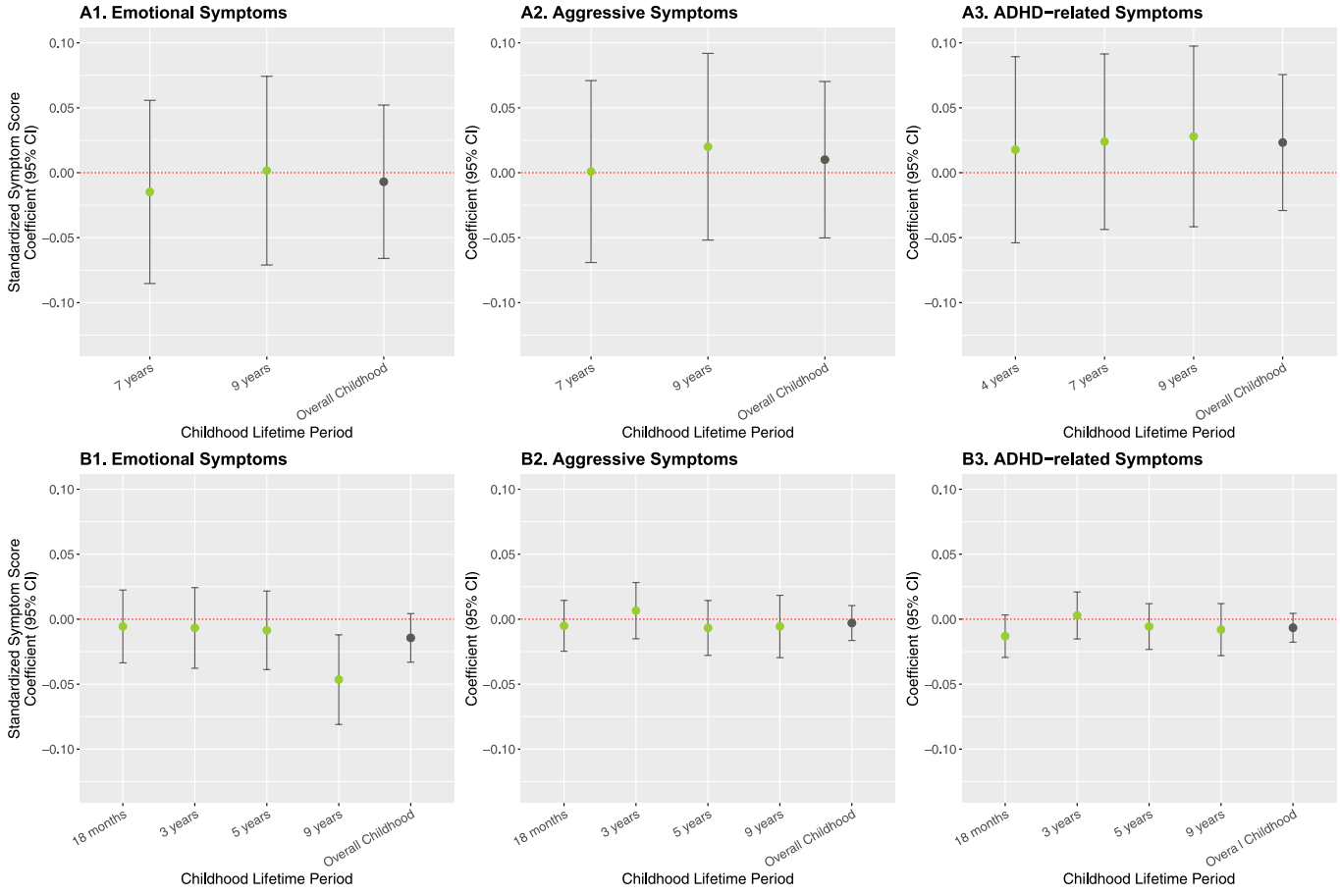

Fig. 2. Fully adjusted associations of a 5 dB increase in road traffic noise exposure in the INMA-Sabadell cohort (A) and the Generation R Study (B) during childhood lifetime periods and overall childhood, and standardized emotional, aggressive, or attention-deficit/hyperactivity disorder (ADHD)-related symptom scores. Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; dB, decibels. Coefficients and 95% confidence intervals were obtained by linear mixed models. Linear mixed models were adjusted for child sex, parental age, body mass index, ethnicity, education, social class and psychological distress, parity, smoking and alcohol during pregnancy, and family status. Generation R Study models were additionally adjusted for monthly household income.

exposure in which railway, aircraft, and industry noise exposure were additionally assessed.

Regarding emotional and aggressive symptoms, the absence of associations with environmental noise exposure during pregnancy is consistent with a study looking at these relationships. They found no indication of an association between prenatal road traffic noise and emotional or aggressive symptoms (Hjortebjerg et al., 2016). Similarly, no associations between childhood road traffic noise exposure and emotional and aggressive symptoms were found, which is in line with results from a few studies (Crombie et al., 2011; Forns et al., 2016; Hjortebjerg et al., 2016; Stansfeld et al., 2009). However, two studies observed that road traffic noise exposure at schools in the Netherlands, Spain, and United Kingdom were related to less aggressive symptoms in children aged 9–10 years (Crombie et al., 2011; Stansfeld et al., 2009). They attributed their counterintuitive findings to chance, difficulties experienced in accurately measuring road traffic noise exposure, or to exposure misclassification (Crombie et al., 2011; Stansfeld et al., 2009). In our study, we also found an unexpected protective association between road traffic and total noise exposure and emotional symptoms at 9 years in children from the Generation R Study. Of our population at 18 months, around 26% had missing noise exposure levels at 9 years, because they moved outside Rotterdam and noise exposure could not be estimated. These children had parents with a higher socio-economic status and reported less emotional symptoms at younger ages and more symptoms at 9 years old compared to those children who continued living in Rotterdam. Thus, our unexpected results were most probably due to selection bias. With limited literature available on the association between environmental noise exposure and emotional and aggressive symptoms, it is important that future studies include these outcomes to better understand the possible impact on children, especially at older ages.

The relationship between environmental noise exposure and ADHD-related symptoms has been studied more intensively. No associations were found between prenatal environmental noise exposure and ADHD-related symptoms in previous literature (Hjortebjerg et al., 2016; Weyde et al., 2017). However, with relation to environmental noise exposure throughout childhood, two cross-sectional and two longitudinal studies in different European cities showed an association of higher road traffic noise exposure at home or at school with higher hyperactivity or inattention problems in children aged 7–11 years (Forns et al., 2016; Hjortebjerg et al., 2016; Tiesler et al., 2013; Weyde et al., 2017). Further, three other cross-sectional studies found that higher aircraft noise exposure at school was associated with higher hyperactivity or inattention problems in children from the Netherlands, United Kingdom, and Spain aged 8–11 years (Crombie et al., 2011; Haines et al., 2001; Stansfeld et al., 2009). In contrast, Zijlema et al. also found no association between residential and school road traffic noise exposure and ADHD-related symptoms in Dutch children aged 10–12 years, rather, they observed a protective association with ADHD clinical diagnosis (Zijlema et al., 2021). Most previous studies focused on noise exposure at school instead of at the residential address, which could explain the discrepancies between their results and ours (Crombie et al., 2011; Forns et al., 2016; Haines et al., 2001; Stansfeld et al., 2009; Zijlema et al., 2021). Noise exposure at school might become especially relevant during the older lifetime periods of our study (compulsory age to attend school in the Netherlands is 5 years and in Spain is 6 years), since they spend more time at school when overall road traffic flow is higher. In line with this idea, mothers likely spend a large portion of their pregnancy at their place of work, thus noise exposure at work can be relevant to include for the estimations during the pregnancy period. Having information on noise exposure at school, work, and residential address would give a more accurate and comprehensive estimation of the noise levels that children are exposed to. Lastly, noise sensitivity has been shown to be associated with more behavioral problems and ADHD-related symptoms (Lim et al., 2018; Zijlema et al., 2021). It is defined as lower tolerance to everyday environmental sounds, and an increased sensitivity is normal in younger children, while they become more desensitized as the auditory system matures (NHS Foundation Trust, 2021; Potgieter et al., 2020). It can contribute to how children cope with negative effects of noise, potentially moderating the association between noise exposure and symptom outcomes (Eze et al., 2020; Lim et al., 2018; Zijlema et al., 2021). Evaluating noise sensitivity as a possible effect modifier of the association between environmental noise exposure and symptom outcomes can also help to give a more comprehensive idea of the potential impact of noise exposure.

The main strength of our study is the inclusion of two population-based birth cohorts from two different areas in Europe, and the prospective nature of these studies. Also, noise exposure estimations accounted for the time a child spent at each address. We also used multiple imputation and inverse probability weighting to account for selection bias, which increases the validity of our results (Sterne et al., 2009). We included the symptom outcome scores as continuous scales, allowing us to examine whether an association was present on a wide spectrum, improving the statistical power of the study and reducing outcome misclassification. Furthermore, the assessment of repeated exposure and outcome measurements using a LMM approach is another strength of our study. Using this approach increased the statistical power of the analysis, allowed for a correct modelling of the non-independence in the longitudinal data, and ensured the proper handling of missing data (Harrison et al., 2018).

Our study also has some limitations that merit discussion. The first is the possibility of information bias. Non-uniformity could be present in the data, since we used different questionnaires to assess symptoms outcomes at different ages completed by different reporters. However, we standardized the symptoms scales and results were similar across questionnaires and reporters. Also, even though multiple imputation was performed, some potential confounding variables had high percentage of missingness (30.4 – 48.5%). To ensure validity of the results based on the imputed datasets, in the multiple imputation procedure we applied models that used predictor variables that were moderately to strongly correlated with the missing potential confounding variables and explored the plausibility of the imputation data. Further, effect estimates were unchanged in children with no missing values for potential confounding variables. The possibility of non-differential exposure misclassification should be addressed. Measurement error in the noise estimations and including children in the analysis that lived at least 50% of the time in the study area may have resulted in incorrect assignment of the noise exposure levels of some participants. Thus, our effect estimates may be biased towards the null and lead to incorrect estimations of the true association. However, we aimed to improve the noise estimations as much as possible by assessing them as a continuous exposure variable and accounting for the changes in residential address. Also, we used the L_{DEN} indicator instead of the L_{NIGHT} indicator because it includes the noise exposure during the evening (i.e., between 19:00 and 23:00) which is also a relevant exposure time for children and the exposure during both the evening and the night has a greater weight than the exposure during the day. Nevertheless, L_{DEN} and L_{NIGHT} were highly correlated (rho = 0.90). Further, we could not investigate whether our results were influenced by two potential effect modifiers such as noise sensitivity and location of the child's bedroom. Having information on the location of the child's bedroom (e.g., if the bedroom has windows facing the street where the noise exposure is estimated or the floor where the bedroom is located) would have reduced the measurement error on the noise estimation and could have provided more valid effect estimates of the association (Eze et al., 2020; Grelat et al., 2016; Hjortebjerg et al., 2016; Pujol et al., 2012). Even though we were able to assess multiple noise sources (road traffic, aircraft, railway, and industry) for the Generation R Study, there were too few children exposed to the separate noise sources to conduct source-specific analyses. Future studies should include populations where the prevalence of these exposure sources is higher, include a more exhaustive noise exposure assessment, and determine the overall effect on symptom outcomes.

5. Conclusion

In conclusion, in this study no association was observed between prenatal and childhood environmental noise exposure and emotional, aggressive, and ADHD-related symptoms in children in two European birth cohorts. Our analyses using longitudinal data and information from multiple noise sources showed absence of associations in line with previous research that found no association with emotional or aggressive symptoms, but not with research that more consistently showed associations with higher ADHD-related symptoms. Further longitudinal studies including a more comprehensive noise exposure assessment considering noise sensitivity, exposure at work for pregnant women or at school for children are warranted to fully understand how environmental noise exposure can affect children's health.

Funding

The Generation R Study is conducted by the Erasmus Medical Center in close collaboration with the School of Law and Faculty of Social Sciences of the Erasmus University Rotterdam, the Municipal Health Service Rotterdam area, Rotterdam, the Rotterdam Homecare Foundation, Rotterdam and the Stichting Trombosedienst & Artsenlaboratorium Rijnmond (STAR-MDC), Rotterdam. We gratefully acknowledge the contribution of children and parents, general practitioners, hospitals, midwives, and pharmacies in Rotterdam. The general design of Generation R Study is made possible by financial support from the Erasmus Medical Center, Rotterdam, the Erasmus University Rotterdam, the Netherlands Organization for Health Research and Development (ZonMw), the Netherlands Organization for Scientific Research (NWO), and the Ministry of Health, Welfare and Sport. The work of Henning Tiemeier was supported by the NWO (NWO-grant 016 VICI.170.200). The geocodification of the addresses of the study participants was done within the framework of a project funded by the Health Effects Institute (HEI) (Assistance Award No. R-82811201). Mònica Guxens received funding from the Spanish Institute of Health Carlos III (CPII18/00018, PI17/01340). We thank DCMR Milieudienst Rijnmond for providing the noise data. We acknowledge support from the Spanish Ministry of Science and Innovation and State Research Agency through the "Centro de Excelencia Severo Ochoa 2019–2023" Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the CERCA Program".

CRediT authorship contribution statement

Esmée Essers: Conceptualization, Formal analysis, Methodology, Writing – original draft, Visualization. **Laura Pérez-Crespo:** Conceptualization, Formal analysis, Methodology, Writing – review & editing, Visualization, Supervision. **Maria Foraster:** Methodology, Writing – review & editing. **Albert Ambrós:** Methodology, Writing – review & editing. **Henning Tiemeier:** Writing – review & editing, Funding acquisition. **Mònica Guxens:** Conceptualization, Methodology, Writing – review & editing, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

None.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106946.

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