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Abstract

Background: Studies revealed long-term associations between noise exposure and cardiovascular health, but the underlying short-term mechanisms remain uncertain.

Objectives: To explore the concomitant and lagged short-term associations between personal exposure to noise and heart rate variability (HRV) in a real life setting in the Île-de-France region.

Methods: The RECORD MultiSensor Study collected between July 2014 and June 2015 noise and heart rate data for 75 participants, aged 34 to 74 years, in their living environments for 7 days using a personal dosimeter and electrocardiography (ECG) sensor on the chest. HRV parameters and noise levels were calculated for 5-minute windows. Short-term relationships between noise level and log-transformed HRV parameters were assessed using mixed effects models with a random intercept for participants and a temporal autocorrelation structure, adjusted for heart rate, physical activity (accelerometry), and short-term trends.

Results: An increase by one dB(A) of A-weighted equivalent sound pressure level (Leq) was associated with a 0.97% concomitant increase of the Standard deviation of normal to normal intervals (SDNN) (95% CI: 0.92, 1.02), of 2.08% of the Low frequency band power (LF) (95% CI: 1.97, 2.18), of 1.30% of the High frequency band power (HF) (95% CI: 1.17, 1.43), and of 1.16% of the LF/HF ratio (95% CI: 1.10, 1.23). The analysis of lagged exposures to noise adjusted for the concomitant exposure illustrates the dynamic of recovery of the autonomic nervous system. Non-linear associations were documented with all HRV parameters with the exception of HF. Piecewise regression revealed that the association was almost 6 times stronger below than above 65 Leq dB(A) for the SDNN and LF/HF ratio.

Conclusion: Personal noise exposure was found to be related to a concomitant increase of the overall HRV, with evidence of imbalance of the autonomic nervous system towards sympathetic activity, a pathway to increased cardiovascular morbidity and mortality.

Keywords: Noise, Heart Rate Variability, Sensors, Autonomic nervous system.

INTRODUCTION

Previous literature has established the effects of noise exposure on health [1-3]. In addition to hearing impairment after repeated exposure to high noise levels, there are effects of noise on sleep quality, hypertension, and the development of cardiovascular disease [4]. WHO estimates that the number of healthy life years lost due to noise exposure is between 1 and 1.6 million years for the Western Europe population each year [5]. This quantification takes into account the impact of ischemic heart disease, cognitive disorders in children, sleep disorders, and of "noise annoyance" caused by long-term exposure to noise.

The general theory of stress [6] serves as a basis for the hypothesis linking noise exposure, the autonomic nervous system and the endocrine system, the homeostasis of the human body [7], and in the long run the development of cardiovascular diseases [8]. Babisch et al. [9] distinguished an indirect effect of noise mediated by the subjective perception and cognitive interpretation of sounds and a direct effect based on the interaction of the acoustic nerve with other parts of the central nervous system, the two of which are expected to affect the autonomic nervous system.

The autonomic nervous system regulates different functions of the body including heart rate. The study of heart rate variability (HRV) thus enables to explore whether and how the autonomic nervous system is disrupted by noise levels. In addition, HRV has also been identified as a risk factor with a reduced HRV being associated with the occurrence of cardiovascular events [10].

Several studies have documented associations between noise exposure and an increased heart rate [11-13]. However, few studies have examined the link between exposure to noise and HRV. In an experimental setting, an increase of sympathetic activity was observed in subjects exposed to a noise level of 95 dB(A) Leq during 135 minutes [14]. Another experiment showed that a noise level as low as 45 dB(A) affected HRV parameters [15].

To our knowledge, only three studies were carried out with a non-simulated exposure. One study asked 40 healthy participants to sit for 2 hours either in a traffic area or in a park [16]. Associations between short-term exposure to noise and decreased HRV were found as well as associations with the sympathovagal balance with an increased sympathetic activity and decreased parasympathetic activity. A similar imbalance was found in the second study, in which 36 healthy participants were instructed to follow a pre-determined route covering various sites in the city of Tel Aviv for two sequential days [17]. In the third study [18], the only one in a non-experimental setting we are aware of, 110 individuals underwent personal noise monitoring and continuous electrocardiography (ECG) 4 times every 4 to 6 weeks during their daily activities. Associations were documented between noise exposure and HRV parameters in concomitant windows.

Overall, previous literature is scarce and primarily based on controlled settings or experimental designs, raising the question of the generalizability of the findings. Thus the objective of this study was to explore the concomitant and lagged short-term associations between personal exposure to noise and HRV in a real life setting in the Île-de-France region.

METHODS

Data collection and processing

<u>Population</u>

Participants came from the RECORD Cohort Study [19], and more particularly from the RECORD MultiSensor sub-study, which aimed at investigating the relationships between transport and health using sensor-based measurement. Participants of the RECORD Cohort were born between 1928 and 1978, were residing at baseline in 10 districts of Paris and 111 other municipalities of the Ile-de-France region, and were recruited without a priori sampling during preventive checkups performed by the IPC Medical Centre between 2007 and 2008.

During the second wave of the RECORD Study, a fraction of the participants were invited to enter the RECORD MultiSensor Study, between July 2014 and June 2015. After completing their health checkups, these participants were asked to wear an accelerometer and an ECG sensor during their waking hours, from the day of completion of the checkup D0 up to D8. Since the checkup could happen at different hours during D0, only measurements between D1 (3 am) and D8 (3 am) were taken into account, i.e., 7 days of data collection. Among the 129 participants of this group, 78 also carried a personal noise dosimeter. The inner clock of each ECG sensor, accelerometer, and noise dosimeter was synchronized with the Internet Time of the computer before giving it to the participants. Participants wearing a pacemaker or with hearing problems were not included. Written informed consent was obtained from all participants. The RECORD Multisensor Study was approved by the French Data Protection Authority (CNIL).

HRV parameters

The participants wore a BioPatch BHM 3 (Zephyr Technology, Annapolis, MD) on the chest, an ECG with two electrodes, a technology which was validated against a 12-lead ECG for HRV measurement [20]. They were instructed to keep it on from the moment they woke up until they went to bed since they had to charge it overnight. The two electrodes were changed every day. From the ECG sampled at 1 kHz, inter-beat (RR) intervals were generated by the BioPatch at an 18Hz frequency. HRV parameters were calculated based on these RR intervals. The entire signal processing was carried out under R version 3.4.0 [21] and the calculation of HRV parameters through the RHRV package version 4.2.3 [22].

Data selection. The raw data of RR intervals extracted from the BioPatch were cut into continuous observation sequences of any length, corresponding to the sequences remaining after excluding periods where the sensor was not worn or where the sensor had lost contact with the skin. The continuous sequences of less than 20 beats were excluded at this stage.

Filtering. Based on the RHRV package, two types of filters were applied to RR intervals: a fixed filter retaining the physiologically acceptable values [25-200 bpm] and a dynamic filter comparing the value of the RR interval with the value of the preceding interval, the value of the following interval, and with an average of the values of the 50 preceding intervals [23]. If the absolute difference in percentage was lower than a given threshold for at least one of the comparisons, the interval was retained. The threshold was computed every 50 intervals, taking into account the standard deviation of these intervals, but is bounded between 12% and 20%.

Interpolation. After filtering, the remaining RR intervals were interpolated at a frequency of 4Hz [24] using a cubic spline function [25] in order to produce a uniformly sampled signal. Empty sequences with more than 30s of continuous filtered RR intervals were not interpolated. Interpolation had a dual function. On one hand, producing a uniformly sampled signal enabled us to meet the prerequisites of frequency analysis. On the other hand, it generated values for the filtered RR intervals.

Windowing. Each day (24h) was cut into successive and mutually exclusive windows of 5 minutes for a theoretical maximum of 288 windows per day. Windows having less than 200 beats or with more than 20% of RR interval removed during the filtering step (even if subsequently re-interpolated) were excluded [26].

HRV parameters calculation. The standard deviation of normal to normal RR intervals (SDNN) was computed for each window. It was expressed in milliseconds. The frequency domain parameters were extracted through a Daubechie Least Asymetric(8) wavelet transform [27]. This method was selected for its ability to decompose non-stationary signals, unlike the Fourier transform [28]. The frequency bands were defined according to the recommendations [29]:

- Low Frequencies (LF): 0,04 – 0,15 Hz
- High Frequencies (HF): 0,15 – 0,40 Hz

The power of each band (in ms²) was computed, as well as the LF/HF ratio. Total Power (TP), and normalized LF (LFnu) and HF (HFnu) bands powers (each divided by the sum of HF and LF bands powers) were also computed, but not considered in the models because of the mathematical redundancy of HFnu and LFnu with the LF/HF ratio [30, 31] and TP with SDNN, since the first one represents the variance of HRV, while the second represents its standard deviation [29].

The four parameters (SDNN, LF and HF bands, and LF/HF ratio) were expressed as continuous variables in descriptive statistics and were log-transformed in the models in order to correct for heteroscedasticity.

<u>Individual noise exposure</u>

The assessment of individual noise exposure was performed with a wearable Class II dosimeter Wed007 - 01dB (ACOEM Limonest, France) allowing noise level measurements between 40 and 120 dB(A) (tolerance ± 1.0 dB) every second. The measurement was A-weighted [dB(A)], a weighting that corresponds to the sensitivity of the human ear. During the day, participants were instructed to wear the dosimeter on the belt while placing the microphone near the ear and above the clothing and charge the device overnight.

Similarly to HRV parameters, noise data were aggregated in 5-minute windows. This aggregation used the notion of equivalent sound level (Leq). The Leq is a representation of the constant noise level that would have been produced with the same energy than the noise actually perceived during the given period. It is expressed in dB and is calculated as follows:

$$\boldsymbol{L_{eq}} = 10 \log \times \frac{1}{T} \int_{0}^{T} 10^{\frac{L(t)}{10}}\, dt$$

$\boldsymbol{L_{eq}}$: *equivalent sound level*

$\boldsymbol{L(t)}$: *noise level at time t*

$\boldsymbol{T}$: *period's length in seconds*

The noise level was used in its continuous form and expressed in Leq dBA. For each 5-minute window, the noise level of the three preceding windows was also computed in order to represent lagged noise at -5 minutes, -10 minutes, and -15 minutes.

Individual exposure to sound level was assessed with a wearable Class II dosimeter Wed007 -01dB (ACOEM Limonest, France) allowing for A-weighted measurements - a weighting that corresponds to the sensitivity of the human ear - between 40 and 120 dB(A) (tolerance ± 1.0 dB) every second (LAeq,1s). During the day, participants were instructed to place the microphone near the ear and over the clothing, to wear the dosimeter on the belt and to charge the device overnight. All of the dosimeters were calibrated at the beginning of the study following the manufacturer's instructions using a standard acoustic calibrator (1 KHz sine wave at 94 dB).

Based on the A-weighted Leq,1s (LAeq,1s), the equivalent sound level (LAeq) was computed within each time window. The LAeq is a representation of the constant sound level that would have been produced with the same energy than the varying sound level actually produced during the given period. It is one of the main sound level indicators used in environmental noise assessment [32].

Accelerometer data

Participants wore an Actigraph wGT3X+ tri-axial accelerometer on the right hip with a dedicated elastic belt for the recruitment day and 7 additional days. They were asked to remove the belt only when sleeping and when they were in contact with water. Accelerometry was collected for 5 second epochs and aggregated over the 5-minute windows. Vector magnitude was used as an indicator of physical activity in the regression analysis and was computed as follows:

$$VM = \sqrt{Axis\ 1^2 + Axis\ 2^2 + Axis\ 3^2}$$

Other covariates

Sociodemographic and health variables were collected from the IPC medical questionnaire and RECORD questionnaire filled in during the health checkup. Age, sex, medical histories (of hypertension, myocardial infarction, angina, and angioplasty), occupation, and educational level were considered. Age was coded as a continuous variable and the 4 medical history variables as separate binary variables.

Education was coded in 4 categories: low (no education, primary education, or lower secondary education); medium-low (higher secondary education and lower tertiary education, i.e., 1 or 2 years); medium-high (intermediate tertiary education: 3 or 4 years); and high (upper tertiary education: 5 years or more). Employment status was divided into employed, unemployed, retired, and other employment statuses.

Statistical analysis

Linear mixed models applied to the 5-minute measurement windows were used to estimate associations between individual exposure to noise and HRV parameters. To take the repeated measures into account, a mixed model with a random intercept at the individual level was used. Short-term trends over the day were taken into account with smoothing splines estimated for each participant. Preliminary analyses showed no long term-trend at the scale of the week or the year.

We successively estimated models with linear associations including only the concomitant noise exposure variable and models including together the concomitant and progressively added lagged noise variables before adjusting for time-varying variables (heart rate and accelerometer vector magnitude). We conducted sensitivity analyses limiting the dataset to windows with no filtered RR intervals and to windows with stationary RR sequences. Stationarity within each 5-minute window was assessed with the augmented Dickey–Fuller test [33].

Non-linear associations were then considered including second to third degree polynomials and natural cubic splines separately for concomitant noise and lagged noise. The linear or non-linear associations minimizing the Bayesian information criterion (BIC) were selected for the final models. In addition to the non-linear associations, piecewise regressions were considered in order to produce interpretable coefficients. A common breakpoint value was chosen for all the HRV parameters for ease of interpretation by looking at the breakpoints minimizing the BIC for each HRV parameter.

In the nonlinear association models and the piecewise regression, temporal autocorrelation between the repeated measurements of each participant was taken into account by an autoregressive model of order 1 AR(1) [34, 35]. This covariance structure assigns to each pair of measures of a participant a correlation that decreases with the increase of the time interval separating the measures. The correlation is expressed as ρ^k, where k is the time interval separating each pair of observations (number of 5-minute windows) and ρ the correlation of a pair of successive observations (range between 0 and 1) [36]. All analyses were performed in

R version 3.4.0 [21]. Mixed models were estimated with the nlme package version 3.1-131 [37] and smoothing splines with the lmeSplines package version 1.1-10 [38].

RESULTS

Sample description

From the initial sample of 78 individuals, 14 129 and 6381 hours of measurements were collected by the noise dosimeter and ECG sensor respectively (unlike the noise sensor, the ECG sensor did not collect data during sleep). Three participants were excluded because either the ECG sensor, the noise dosimeter, or the accelerometer did not work or was not worn. Only windows with concurrent measures of noise level, HRV, and accelerometry were retained. Afterwards, windows with any missing noise data were removed (n = 60), as were those where more than 20% of the RR intervals stemmed from the interpolation and / or those with less than 200 beats (n = 592). In the end, the study sample considered in this work comprised 53 969 windows of 5 minutes (4497.4 hours in total) of concomitant noise, HRV, and accelerometry measurements for 75 individuals over 7 days. *Table 1* summarizes the participants' main characteristics.

The sample included individuals aged 34 to 74 years with an average age of 51.5 years (SD: 10.4). It was mainly composed of men (64%), employed people (65.3%), and people with a high level of education (52% of the participants had 3 or more years of tertiary education). Of the participants, 21 (28%) had a history of hypertension defined as "self-reported blood pressure equal to or greater than 140 mmHg repeatedly", while 12 participants (16%) were taking blood pressure lowering medications. None of the participants had a history of myocardial infarction or angina pectoris.

Measurement windows and noise levels

As shown in *Table 2*, the distribution of the number of measurement windows was equivalent across the days (ANOVA test, p = 0.25), with a decline at the end of the week. *Figure 1* shows the distribution of measurement windows by time across the day (average of all days). Most of the measures were taken between 8am and 10pm, an interval covering 87% of the observations.

Figure 2 shows the histogram of measured noise levels, ranging from 32.6 to 113.7 Leq dB(A) with an average of 66.1 and a standard deviation of 10.9 Leq dB(A).

Correlations between the cardiovascular parameters

Figure 3 represents the correlation between the different cardiovascular parameters. TP and SDNN are highly correlated (r = 0.94) as the first one represents the variance of HRV and the second one its standard deviation. HFnu and LFnu have a perfect correlation of -1, while they both share with LF/HF a correlation of 0.79, positive for LFnu and negative for HFnu. LF and HF are correlated between them (r = 0.80) as well as with both TP and SDNN, with correlations ranging from 0.59 to 0.79. Heart rate is mildly correlated with most of the HRV parameters with the exception of HF.

Concomitant measures of noise and HRV

Table 3 provides the average values of heart rate and HRV parameters over four increasing noise level categories. The mean values of all parameters showed an increasing trend confirmed by the Jonckheere-Terpstra trend test.

Mixed-effects models: linear associations

Table 4 reports the linear relationships of HRV parameters with (A) concomitant and progressively added lagged noise, (B) adjusted for heart rate and accelerometer vector magnitude. Since the HRV parameters were log-transformed, the associations in the Table represent changes in percentage of the mean outcome for an increase of one Leq dB(A). In the models including only concomitant noise, positive associations were documented with all four HRV parameters. When adding lagged noise, these associations were pulled towards higher values, while lagged noise was systematically negatively associated with all HRV parameters, with however smaller magnitudes than the concomitant noise. When adjusted for heart rate and accelerometer vector magnitude, SDNN and LF and HF powers associations with concomitant and lagged noise were pulled towards the positive while the association of LF/HF with noise was pulled towards the negative. The variance inflation factor of the independent variables for every HRV parameter remained below 3 (Supplementary material I).

Models C and D in Table 4 report also the associations for (C) windows including no filtered RR intervals and (D) for windows with stationary RR sequences as a sensitivity analysis. There are no noticeable changes in term of direction of the associations. The coefficients were also quite stable between the different models, with two exceptions: (i) the reduction of the association of HF power with concomitant noise between models (B) and (C), moving from 1.30% to 0.86%, the effects of which are also observable on LF/HF; (ii) the reduction in the association between concomitant noise and SDNN between models (B) and (D), moving from 0.97% to 0.72%.

History of hypertension, blood pressure lowering medication intake, educational level, and employment status were not associated with any of the HRV parameters and were therefore not included in the models.

Mixed-effects models: non-linear associations and piecewise regression

Figure 4 represents both the non-linear associations between concomitant noise and the HRV parameters, as well as the piecewise regression with concomitant and lagged noise for models adjusted for heart rate, accelerometer vector magnitude, and short-term trend with a temporal autocorrelation structure. The specifications of each model are available in the supplementary material II.

The best association, based on the BIC, between noise and the different HRV parameters was the natural cubic spline with the exception of HF power, for which it was the linear association. Regarding piecewise regression (numerical values shown in supplementary material III), a breakpoint at 65 Leq dB(A) was chosen based on the examination of which breakpoint ranging from 61 to 66 Leq dB(A) gave the best BIC for each HRV parameter.

For concomitant noise levels below 65 Leq dB(A), a quasi-linear increase was documented for all HRV parameters, starting at the lowest measured noise levels. Piecewise regression showed that that the slope of the association was much weaker above 65 Leq dB(A) than below this noise level, at the most 6 times weaker for the SDNN and LF/HF ratio.

As shown in Supplementary material III, the piecewise regression associations between lagged noise exposure variables and the HRV parameters were either negative or null (after mutual adjustment and adjustment for concomitant noise). Below 65 Leq dB(A), the different lagged noises were all negatively associated, with the exception of the 5 min lagged noise with LF and HF powers which did not show any association. Above 65 Leq dB(A), the lagged noise variables did not show any association with the HRV parameters, with the exception of the 5 min lagged noise associations with SDNN and LF/HF. In this piecewise regression analysis, there was no identifiable pattern of associations with increasing lag.

DISCUSSION

Summary of results

This study aimed to explore the relationship between individual acute exposure to noise and 4 HRV parameters (SDNN, LF, HF, LF/HF ratio). Concomitant noise was positively associated with all 4 HRV parameters, after adjustment for heart rate, accelerometry, short-term trend, and even after controlling for the lagged noise variables. After mutual adjustment for the concomitant and lagged exposures, the lagged noise exposures were negatively associated with all 4 HRV parameters. Analyses restricted to sequences without removed RR intervals or to stationary RR sequences supported the same conclusions. Piecewise regression with a breakpoint at 65 Leq dB(A) demonstrated that the association was stronger below this threshold.

Strengths and limitations

First, the use of wearable sensors enabled to accurately measure continuously over time the personal noise exposure, HRV parameters, and physical activity as a confounder. We could reduce misclassification biases that would have resulted from the use of proxy indicators of noise exposure derived from interpolated measurements or modeling work. Similarly, this approach allowed us to escape from controlled laboratory environments and permitted observation in a “real life” context. This non-constrained observation over a week in various living environments yielded a wide range of situations of exposure to noise and related reactions of the autonomic nervous system.

A related strength of this study lies in the large number of observations that were collected. Indeed, a total of 4497.4 hours of concomitant noise, HRV, and accelerometry measurements from 75 individuals were analyzed in this study. This is considerably more than in the three other studies that have addressed the problem, that relied on 156 hours (n = 40), approximately 100 hours (n = 36), and 1785 hours (n = 110) of observation, respectively [16-18], although the third one had a larger number of participants.

However, as a weakness resulting from this strength, this considerable amount of data could only be handled by automated processes, made of filtering and calculation rules. Thus, each of the signal processing steps leading to the calculation of the HRV parameters may be a source of measurement bias [39]. First, the identification of beats and RR intervals from the ECG was performed by the internal algorithm of the BioPatch. Although its ability to correctly measure heart rate at different levels of physical activity has been verified by the manufacturer, the specificity and sensitivity of the algorithm are unknown, as well as their variation according to the wearer's activity. The filtering of ectopic and abnormal beats can also be a source of bias. Filtering was performed on the sequences of intervals, which provide limited information for the identification and selection of valid heartbeats. The filtering step is crucial for calculating the HRV parameters, since even a small proportion of ectopic beats can seriously affect the measurements [40]. While the approach to retain only sequences without removed RR intervals was explored in this study, it could however introduce problematic selection biases [29]. The same statement applies to restricting data to stationary sequences.

The subsequent signal processing steps can also be a source of heterogeneity between studies, affecting their comparability. The latest recommendations related to the measurement of HRV were drafted in 1996 [29]; they do not cover all processing stages and do not include methods introduced since then (e.g., wavelet transformation for calculating HRV frequency domain parameters). Various software are available for the calculation of HRV parameters, but it seems that no clear consensus has been reached as to the exact sequence of signal processing steps needed from the recording to the calculation of HRV parameters [39].

Another limitation of the study pertains to the lack of information about confounders like tobacco and alcohol consumption during the observation week, or personal air pollution measurements which effects on HRV have been previously described [16]

Finally, the study design allowed us to analyze a large number of 5-min windows, but the small number of participants in this study (n = 75) limits the use of individual-level variables as stratifiers (the association estimated in each stratum would likely not represent the true association in this stratum).

Interpretation of findings

<u>General framework</u>

Through the complementary HRV parameters, it is the state of the autonomic nervous system that is being assessed. The SDNN is a global measure of HRV, reflecting the combined state of the two branches of the autonomic nervous system. It thus masks the modulations of HRV caused by each branch of the autonomic nervous system. This decomposition of HRV is however possible through frequency domain parameters breaking down HRV according to the frequencies of heart rate modulations. Two of these frequency bands were considered in this study: the low frequency band LF (0.04 to 0.15 Hz) and the high frequency band HF (0.15 to 0.40 Hz). The HF band reflects parasympathetic activity [41] while the LF band, which was initially described as a reflection of the sympathetic system [42], is currently considered as the result of the combined effects of the two branches of the autonomic nervous system [43]. The LF/HF ratio is in turn an index of the sympathetic / parasympathetic balance.

Several studies have shown that a reduction of the SDNN is associated with the occurrence of cardiovascular events and with cardiovascular mortality [10, 44-46]. The Framingham Heart study [47] has found, of numerous HRV parameters, the SDNN to be the best predictor of new cardiac events with a reduction of one standard deviation being linked with a 50% increase in the risk of cardiovascular events over 3.5 years.

<u>Concomitant associations</u>

In this study, an increase in noise level was associated with a concomitant increase in SDNN, in the power of the LF band and the HF band, and in the LF/HF ratio. The concomitant increase in SDNN with noise stems from the association of noise with both the LF band power and HF band power, suggesting that noise exposure increased both the low frequency and high frequency modulations of heart rate. Thus in this study, a higher exposure to noise was not associated with an overall concomitant reduction in HRV, which was also observed in other studies [18, 48]. An increase in personal noise exposure was also associated with a concomitant increase in the LF/HF ratio. Together with the observed increases with noise of LF and HF band powers, this higher LF/HF ratio reflects a comparatively larger increase in sympathetic activity than parasympathetic activity, implying an imbalance of the autonomic nervous system associated with noise exposure. These results are in line with the reaction scheme formalized by Babisch and colleagues [9], as noise acts as a stressor triggering the fight or flight response with an activation of the sympathetic branch of the autonomic nervous system. This was documented by several studies with either simulated [49, 50] or non-simulated [17, 18] noise exposure. It is this imbalance that is conceptualized as a bridge between noise exposure and the subsequent development of cardiovascular diseases [9]. In terms of heart rate, this sympathetic dominance over the parasympathetic system leads to high heart rate values, as the first increases heart rate and the role of the second is to decrease it. This is consistent with our finding that higher noise levels were also associated with an increased heart rate in adjusted models (data not shown).

Mutually adjusted lagged and concomitant associations

When associations with concomitant and lagged noise were mutually adjusted, the associations of concomitant noise with HRV parameters were slightly pulled towards the positive while lagged noise showed negative associations with HRV parameters. The negative association between lagged noise and SDNN might express a recovery of the autonomic nervous system, after the increase in SDNN with a concomitant exposure to noise, which was of much larger magnitude. Kraus and colleagues reported somewhat comparable patterns of associations with, e.g., a positive association of concomitant noise with SDNN but negative associations of lagged noise variables with SDNN when such exposure variables were mutually adjusted for [18]. As speculated by Kraus and colleagues, this positive and negative associations of, respectively, concomitant and lagged noise with HRV parameters may be attributable to an overreaction and self-regulation of the autonomic nervous system but further research is needed in order to better understand those short-term dynamics.

Non-linear and piecewise regression

With the exception of the HF band power, non-linear associations were documented between concomitant noise level and the HRV parameters. These associations shared a similar shape, with a decreasing slope as the noise level increased. This was explicitly reflected with the piecewise regression showing that the slope was much steeper below then above 65 Leq dB(A), mainly for the SDNN and the LF/HF ratio.

In our study, the associations of concomitant and lagged noise levels with HRV started at the lowest observed noise levels (around 40 Leq dB(A)) and reached a maximum after 65 Leq dB(A). Kraus and colleagues reported similar results in the case of the SDNN and the LF/HF ratio with a similarly chosen breakpoint at 65 Leq dB(A).

This threshold is however of limited clinical significance as it hides individual variations. It was slightly different depending on the HRV parameter, may have been influenced by the distribution of noise values, and does not strictly identify the beginning of the plateau but is close to where the biggest shift in slope occurs.

Conclusion

In this study, a higher exposure to noise in real life settings was associated with increases in the LF and HF band powers, thus with an increase in the overall HRV (as expressed with the SDNN). Our analysis of the lagged noise exposures adjusted for the concomitant exposure showed evidence of a recovery starting after a 5-minute lag. Non-linear and piecewise regressions allowed us to identify a breakpoint at 65 dB(A) Leq, below which the reported association was much stronger. Future research will be needed to better understand the dynamics through which and timescales over which noise exposure influences the autonomic nervous system. Perspectives for this work include a better characterization of the daily activity of the participants during the observation windows in order to contextualize the reported association, the use of different summary measures for noise, and the consideration of the effects of air pollution in conjunction with those of noise to assess both their potential for reciprocal confounding and their synergistic effects on cardiovascular health.

References

1. Ising, H. and B. Kruppa, *Health effects caused by noise: evidence in the literature from the past 25 years.* Noise and Health, 2004. **6**(22): p. 5.
2. Basner, M., et al., *Auditory and non-auditory effects of noise on health.* The Lancet, 2014. **383**(9925): p. 1325-1332.
3. Münzel, T., et al., *Cardiovascular effects of environmental noise exposure.* European heart journal, 2014. **35**(13): p. 829-836.
4. Stansfeld, S.A. and M.P. Matheson, *Noise pollution: non-auditory effects on health.* British medical bulletin, 2003. **68**(1): p. 243-257.
5. Organization, W.H., *Burden of disease from environmental noise-Quantification of healthy life years lost in Europe.* WHO Regional Office for Europe, Bonn, 2011.
6. Selye, H., *The general adaptation syndrome and the diseases of adaptation 1.* The Journal of Clinical Endocrinology & Metabolism, 1946. **6**(2): p. 117-230.
7. Babisch, W., *Cardiovascular effects of noise.* Noise and Health, 2011. **13**(52): p. 201.
8. Babisch, W., et al., *Traffic noise and risk of myocardial infarction.* Epidemiology, 2005. **16**(1): p. 33-40.
9. Babisch, W., *The noise/stress concept, risk assessment and research needs.* Noise and health, 2002. **4**(16): p. 1.
10. Thayer, J.F., S.S. Yamamoto, and J.F. Brosschot, *The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors.* International journal of cardiology, 2010. **141**(2): p. 122-131.
11. Croy, I., M.G. Smith, and K.P. Waye, *Effects of train noise and vibration on human heart rate during sleep: an experimental study.* BMJ open, 2013. **3**(5): p. e002655.
12. Mahmood, R., et al., *Effect of noise on heart rate.* Journal of Postgraduate Medical Institute (Peshawar-Pakistan), 2011. **20**(1).
13. Smith, M.G., et al., *On the influence of freight trains on humans: a laboratory investigation of the impact of nocturnal low frequency vibration and noise on sleep and heart rate.* PloS one, 2013. **8**(2): p. e55829.
14. Tzaneva, L., S. Danev, and R. Nikolova, *Investigation of noise exposure effect on heart rate variability parameters.* Central European journal of public health, 2001. **9**(3): p. 130-132.
15. Sim, C.S., et al., *The Effects of Different Noise Types on Heart Rate Variability in Men.* Yonsei medical journal, 2015. **56**(1): p. 235-243.
16. Huang, J., et al., *The impacts of short-term exposure to noise and traffic-related air pollution on heart rate variability in young healthy adults.* Journal of Exposure Science and Environmental Epidemiology, 2013. **23**(5): p. 559-564.
17. Schnell, I., et al., *Human exposure to environmental health concern by types of urban environment: The case of Tel Aviv.* Environmental Pollution, 2016. **208**: p. 58-65.
18. Kraus, U., et al., *Individual daytime noise exposure during routine activities and heart rate variability in adults: a repeated measures study.* Environmental health perspectives, 2013. **121**(5): p. 607.
19. Chaix, B., et al., *Cohort Profile: Residential and non-residential environments, individual activity spaces and cardiovascular risk factors and diseases—The RECORD Cohort Study.* International journal of epidemiology, 2011: p. dyr107.
20. Nunan, D., et al., *Validity and reliability of short-term heart-rate variability from the Polar S810.* Medicine+ Science in Sports+ Exercise, 2009. **41**(1): p. 243.
21. Team, R.C., *R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria, 2012*. 2012, ISBN 3-900051-07-0.
22. Rodríguez-Liñares, L., et al., *An open source tool for heart rate variability spectral analysis.* Computer methods and programs in biomedicine, 2011. **103**(1): p. 39-50.
23. Vila, J., et al., *Time-frequency analysis of heart-rate variability.* Engineering in Medicine and Biology Magazine, IEEE, 1997. **16**(5): p. 119-126.

24. Singh, D., K. Vinod, and S. Saxena, *Sampling frequency of the RR interval time series for spectral analysis of heart rate variability.* Journal of medical engineering & technology, 2004. **28**(6): p. 263-272.
25. Daskalov, I. and I. Christov, *Improvement of resolution in measurement of electrocardiogram RR intervals by interpolation.* Medical engineering & physics, 1997. **19**(4): p. 375-379.
26. Salo, M.A., H.V. Huikuri, and T. Seppanen, *Ectopic beats in heart rate variability analysis: effects of editing on time and frequency domain measures.* Annals of noninvasive electrocardiology, 2001. **6**(1): p. 5-17.
27. García, C.A., et al., *A new algorithm for wavelet-based heart rate variability analysis.* Biomedical Signal Processing and Control, 2013. **8**(6): p. 542-550.
28. Mallat, S.G., *A theory for multiresolution signal decomposition: the wavelet representation.* Pattern Analysis and Machine Intelligence, IEEE Transactions on, 1989. **11**(7): p. 674-693.
29. Cardiology, T.F.o.t.E.S.o., *Heart rate variability standards of measurement, physiological interpretation, and clinical use.* Eur Heart J, 1996. **17**: p. 354-381.
30. Burr, R.L., *Interpretation of normalized spectral heart rate variability indices in sleep research: a critical review.* SLEEP-NEW YORK THEN WESTCHESTER-, 2007. **30**(7): p. 913.
31. Heathers, J.A., *Everything Hertz: methodological issues in short-term frequency-domain HRV.* Frontiers in physiology, 2014. **5**.
32. Ricciardi, P., et al., *Sound quality indicators Night noise guidelines for urban places in Paris cross-validated by Milan dataEurope.* The Journal of the Acoustical Society of America, 20152009. **138**(4): p. 2337-2348.
33. Banerjee, A., et al., *Co-integration, error correction, and the econometric analysis of non-stationary data.* OUP Catalogue, 1993.
34. Kincaid, C. *Guidelines for selecting the covariance structure in mixed model analysis*. in *Proceedings of the Thirtieth Annual SAS Users Group International Conference*. 2005. SAS Institute Inc Cary, NC.
35. Pinheiro, J. and D. Bates, *Mixed-effects models in S and S-PLUS*. 2006: Springer Science & Business Media.
36. Fitzmaurice, G.M., N.M. Laird, and J.H. Ware, *Applied longitudinal analysis*. Vol. 998. 2012: John Wiley & Sons.
37. Pinheiro, J., et al., *R Development Core Team (2015) nlme: linear and nonlinear mixed effects models. R package version 3.1-131.* R Foundation for Statistical Computing, Vienna, 2015.
38. Ball, R. and M.A. Galecki, *Package 'lmeSplines'.* 2015.
39. Jarrin, D.C., et al., *Measurement fidelity of heart rate variability signal processing: the devil is in the details.* International Journal of Psychophysiology, 2012. **86**(1): p. 88-97.
40. Storck, N., et al., *Automatic computerized analysis of heart rate variability with digital filtering of ectopic beats.* Clinical Physiology, 2001. **21**(1): p. 15-24.
41. Montano, N., et al., *Power spectrum analysis of heart rate variability to assess the changes in sympathovagal balance during graded orthostatic tilt.* Circulation, 1994. **90**(4): p. 1826-1831.
42. Malliani, A., et al., *Cardiovascular neural regulation explored in the frequency domain.* Circulation, 1991. **84**(2): p. 482-492.
43. Billman, G.E., *Heart rate variability–a historical perspective.* Frontiers in physiology, 2011. **2**.
44. La Rovere, M.T., et al., *Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction.* The Lancet, 1998. **351**(9101): p. 478-484.
45. Nolan, J., et al., *Prospective study of heart rate variability and mortality in chronic heart failure results of the United Kingdom heart failure evaluation and assessment of risk trial (UK-Heart).* Circulation, 1998. **98**(15): p. 1510-1516.
46. Ponikowski, P., et al., *Depressed heart rate variability as an independent predictor of death in chronic congestive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy.* The American journal of cardiology, 1997. **79**(12): p. 1645-1650.
47. Tsuji, H., et al., *Impact of reduced heart rate variability on risk for cardiac events The Framingham Heart Study.* Circulation, 1996. **94**(11): p. 2850-2855.

48. Björ, B., et al., *Acute effects on heart rate variability when exposed to hand transmitted vibration and noise.* International archives of occupational and environmental health, 2007. **81**(2): p. 193-199.
49. Valenti, V.E., et al., *Auditory stimulation and cardiac autonomic regulation.* Clinics, 2012. **67**(8): p. 955-958.
50. Lee, G.-S., M.-L. Chen, and G.-Y. Wang, *Evoked response of heart rate variability using short-duration white noise.* Autonomic Neuroscience, 2010. **155**(1): p. 94-97.

Table 1 Descriptive statistics for the sample (N = 75)

Variable	**n (%)**
Men	48 (64%)
History of hypertension	21 (28%)
Intake of antihypertensive medications	12 (16%)
Employment status	
Employed	49 (65.3%)
Unemployed	11 (14.7%)
Retired	13 (17.3%)
Other	2 (2.7%)
Educational level	
No education, primary, lower secondary	13 (17.3%)
Higher secondary, lower tertiary	23 (30.7%)
Intermediate tertiary	19 (25.3%)
Upper tertiary	20 (26.7%)

Table 2 Distribution of the 5-minute windows per participant over the week* (n = 53969)

Day	**Mean** ± **σ**
Monday	103.1 ± 70.1
Tuesday	105.3 ± 64.0
Wednesday	111.9 ± 61.8
Thursday	111.4 ± 60.2
Friday	103.3 ± 61.4
Saturday	95.9 ± 57.7
Sunday	88.7 ± 60.7
ANOVA	p = 0.25

*Number of follow-up days = 6.0 ± 1.5; number of windows per participant = 719.6 ± 268.3

Table 3 Mean and standard deviation of HRV parameters and heart rate according to four increasing categories of noise level

		HR (bpm)		SDNN (ms)		LF/HF (w.u)		LF power (ms^2)		HF power (ms^2)	
Noise Leq [dB(A)]	**n**	**Mean**	**σ**	**Mean**	**σ**	**Mean**	**σ**	**Mean**	**σ**	**Mean**	**σ**
[30,45]	2395	71.0	±11.7	50.5	±26.6	12.8	±9.4	1119.9	±1516.0	447.3	±753.1
(45,65]	19767	75.6	±13.0	61.0	±29.0	15.7	±9.9	1453.5	±1666.5	477.1	±721.4
(65,80]	27560	82.4	±14.3	62.7	±28.3	17.4	±10.2	1603.9	±1816.5	545.0	±850.5
(80,110]	4246	86.3	±15.1	59.5	±27.7	16.9	±10.0	1650.3	±1887.8	627.4	±941.9
Trend		$p < 0.0001$		$p < 0.0001$		$p < 0.0001$		$p < 0.0001$		$p < 0.0001$	

Abbreviations: HR: Heart rate; Leq [dB(A)]: A-weighted equivalent sound pressure level in dB; bpm: beats per minute; ms: milliseconds; w.u: without unit

Trend tested using Jonckheere-Terpstra test with the alternative hypothesis being “increasing”

Table 4 Linear associations between concomitant and lagged noise exposure variables and log-transformed HRV parameters

	SDNN				LF/HF				LF				HF			
	0 min	**5 min**	**10 min**	**15 min**	**0 min**	**5 min**	**10 min**	**15 min**	**0 min**	**5 min**	**10 min**	**15 min**	**0 min**	**5 min**	**10 min**	**15 min**
A	+0.52				+1.23				+1.01				+0.37			
	+0.83	−0.45			+1.33	−0.15			+1.41	−0.59			+0.74	−0.53		
	+0.88	−0.23	−0.37		+1.35	−0.08	−0.12		+1.51	−0.21	−0.65		+0.83	−0.17	−0.62	
	+0.90	−0.21	−0.22	−0.25	+1.35	−0.08	−0.08	−0.07	+1.54	−0.17	−0.41	−0.41	+0.86	−0.13[ns]	−0.39	−0.39
B	+0.97	−0.16	−0.17	−0.19	+1.16	−0.14	−0.12	−0.12	+2.08	+0.01[ns]	−0.31	−0.30	+1.30	+0.04[ns]	−0.28	−0.25
C	+0.95	−0.12	−0.21	−0.12	+1.41	−0.06[ns]	−0.14	−0.15	+2.08	+0.03[ns]	−0.33	−0.25	+0.86	−0.03[ns]	−0.25	−0.15
D	+0.72	+0.03[ns]	−0.19	−0.17	+1.11	−0.03[ns]	−0.10[ns]	−0.10[ns]	+1.92	+0.01[ns]	−0.25	−0.34	+1.23	−0.10[ns]	−0.23[ns]	−0.35

For each HRV parameter, each line represents a different model. Associations represent changes in percentage of the mean outcome for an increase of one Leq [dB(A)]. They were estimated from models with a random effect at the individual level and adjusted for short-term trends. Models A include only concomitant and progressively added lagged noise, while models B are additionally adjusted for heart rate and accelerometer vector magnitude. Models C include only windows without filtered RR (n = 17 321). Models D include only stationary RR sequences (n = 14 350).

The associations are statistically significant ($p < 0.05$) unless stated otherwise.

Abbreviations: Leq [dB(A)]: A-weighted equivalent sound pressure level in dB; SDNN: Standard deviation of RR intervals; LF/HF: Low frequency to high frequency ratio; LF: Low frequency band power in ms^2; HF: High frequency band power in ms^2; ns: not significant.

Fig. 1 Distribution of the analyzed 5-minute windows over the day

Fig. 2 Histogram of measured noise levels in Leq dB(A)

Fig. 3 Correlations between the cardiovascular parameters

Fig. 4 Plot of the nonlinear and piecewise associations between concomitant or lagged noise and the 4 HRV parameters, estimated from models with a random effect at the individual level and a temporal autocorrelation structure, adjusted for heart rate, accelerometer vector magnitude, and short term trend

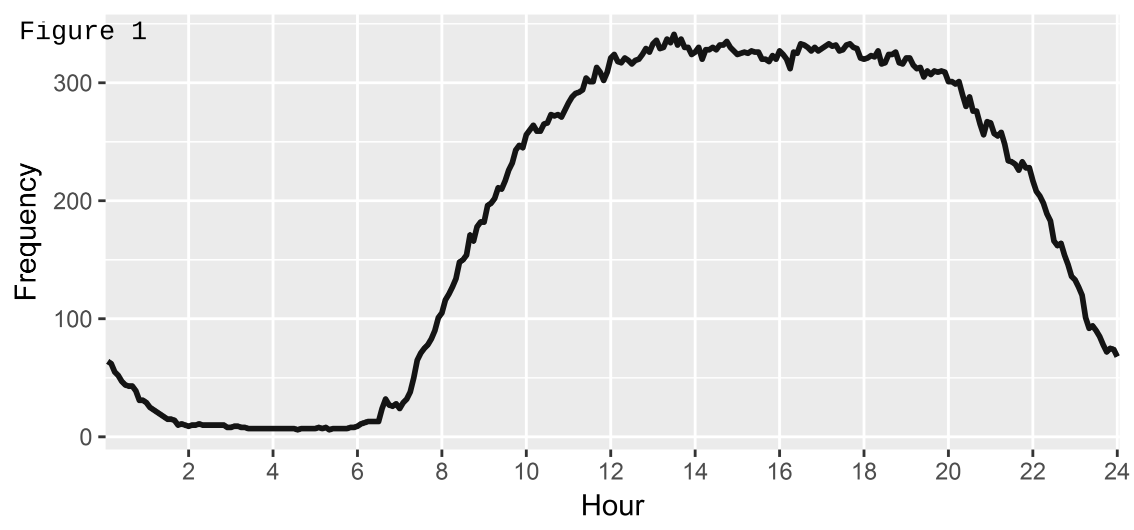
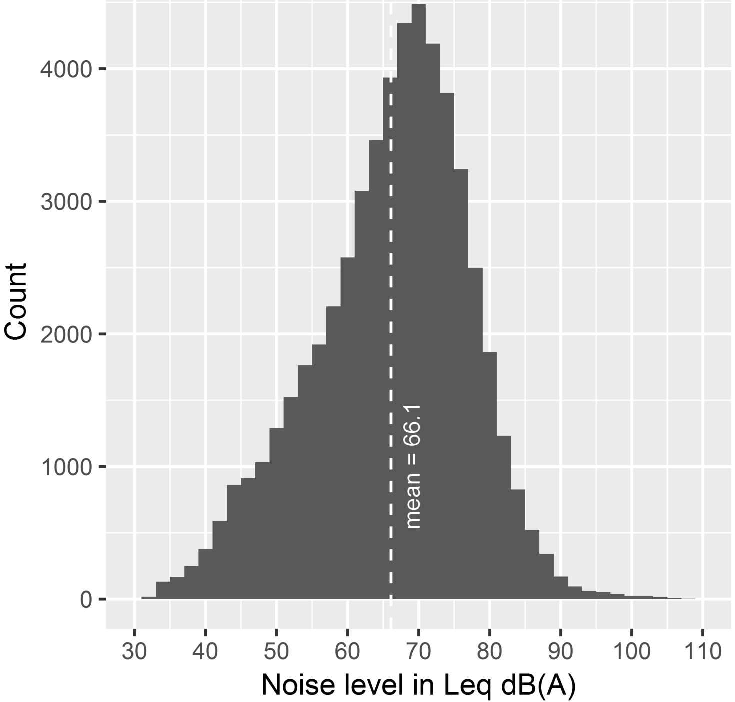


Figure 1
Frequency
0
100
200
300
2
4
6
8
10
12
14
16
18
20
22
24
Hour

Figure 2



Count
4000
3000
2000
1000
0
mean = 66.1
30
40
50
60
70
80
90
100
110
Noise level in Leq dB(A)

Figure 3

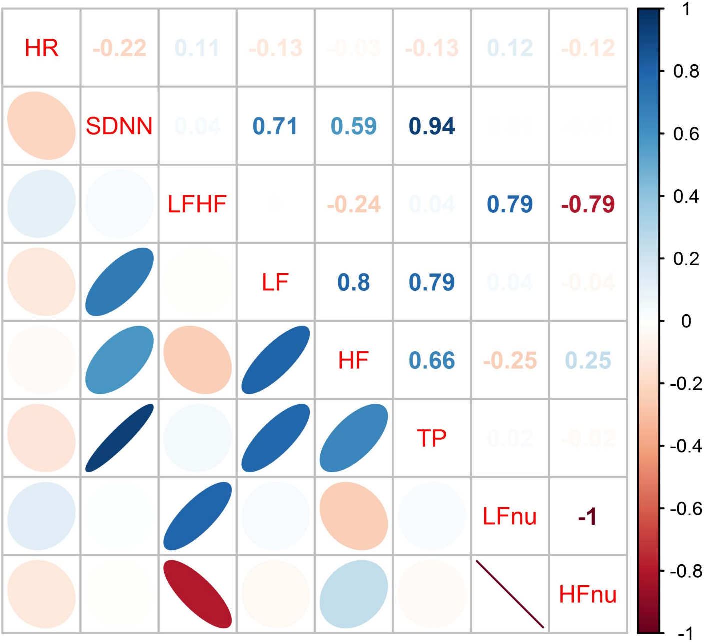
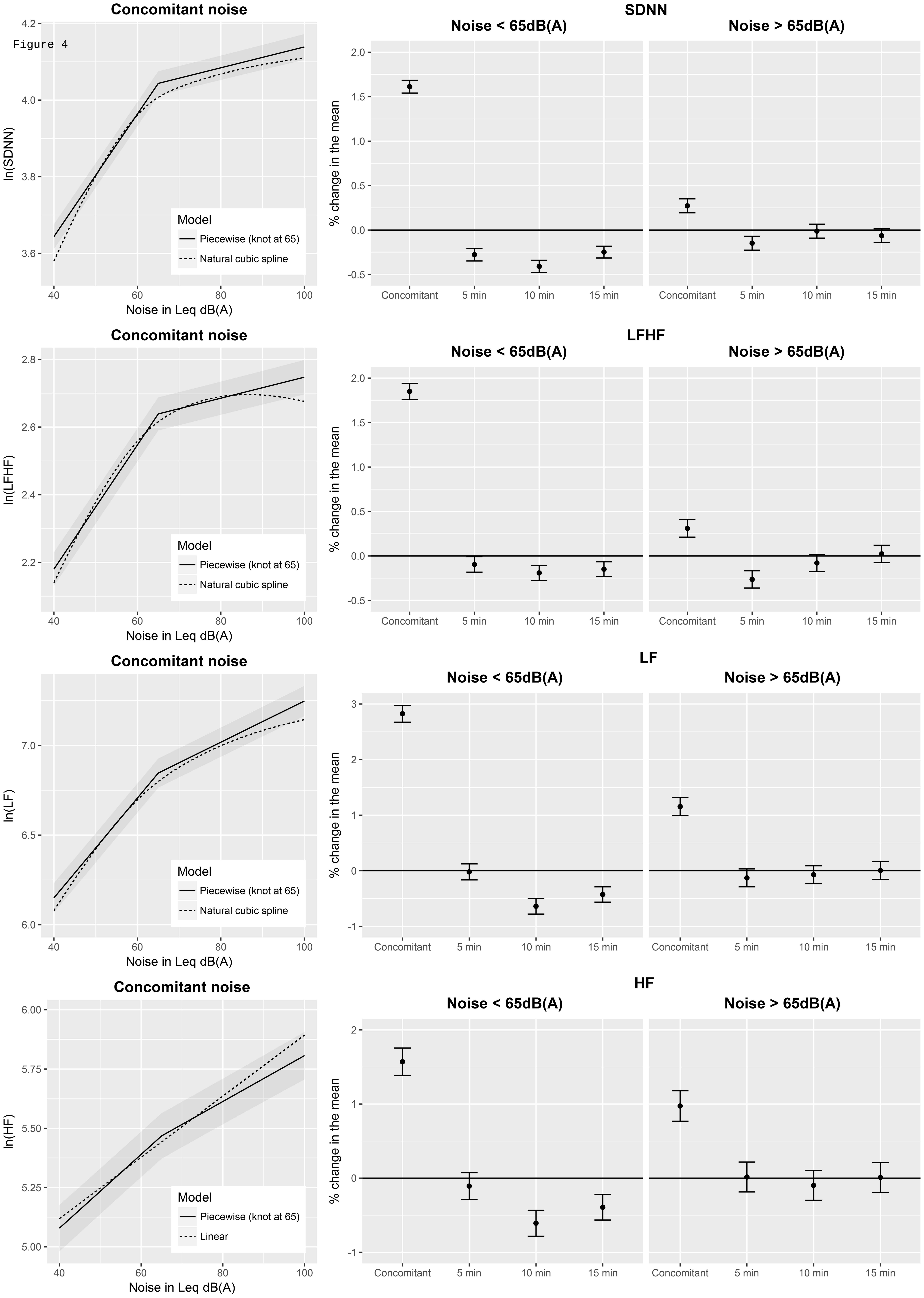

HR
-0.22
0.11
-0.13
-0.13
0.12
-0.12
SDNN
0.71
0.59
0.94
LFHF
-0.24
0.79
-0.79
LF
0.8
0.79
HF
0.66
-0.25
0.25
TP
LFnu
-1
HFnu
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1

Figure 4



Concomitant noise
ln(SDNN)
Noise in Leq dB(A)
Model
Piecewise (knot at 65)
Natural cubic spline
SDNN
Noise < 65dB(A)
Noise > 65dB(A)
% change in the mean
Concomitant
5 min
10 min
15 min
Concomitant noise
ln(LFHF)
Noise in Leq dB(A)
Model
Piecewise (knot at 65)
Natural cubic spline
LFHF
Noise < 65dB(A)
Noise > 65dB(A)
% change in the mean
Concomitant noise
ln(LF)
Noise in Leq dB(A)
Model
Piecewise (knot at 65)
Natural cubic spline
LF
Noise < 65dB(A)
Noise > 65dB(A)
% change in the mean
Concomitant noise
ln(HF)
Noise in Leq dB(A)
Model
Piecewise (knot at 65)
Linear
HF
Noise < 65dB(A)
Noise > 65dB(A)
% change in the mean

Supplementary material

I. Variance inflation factor of the linear association models

	SDNN	LF/HF	LF	HF
Noise - 0 min	2.07	2.03	2.05	2.05
Noise - 5 min	2.65	2.59	2.63	2.62
Noise - 10 min	2.65	2.59	2.62	2.62
Noise - 15 min	1.99	1.95	1.97	1.97
Heart rate	1.74	1.74	1.74	1.74
Vector magnitude	1.67	1.67	1.67	1.67

II. Models' specification for the non-linear association models

ln(SDNN) = ncs(Concomitant noise) + poly2(Lagged noise (5 min)) + poly2 (Lagged noise (10 min)) + poly2 (Lagged noise (15 min)) + Heart Rate + Vector magnitude

ln(LFHF) = ncs(Concomitant noise) + poly1(Lagged noise (5 min)) + poly1 (Lagged noise (10 min)) + poly1(Lagged noise (15 min)) + Heart Rate + Vector magnitude

ln(LF) = ncs(Concomitant noise) + poly2(Lagged noise (5 min)) + poly2(Lagged noise (10 min)) + poly2(Lagged noise (15 min)) + Heart Rate + Vector magnitude

ln(HF) = poly1(Concomitant noise) + poly1(Lagged noise (5 min)) + poly1 (Lagged noise (10 min)) + poly1(Lagged noise (15 min)) + Heart Rate + Vector magnitude

All the models included a temporal autocorrelation structure and were adjusted for short term trends.

Abbreviations:

ncs = natural cubic spline with two boundary knots and two internal knots at the 33^{rd} and 66^{th} quantiles.
Polyx = x^{th} degree polynomial

III. Piece-wise regression: Numerical values

	SDNN	
	<65 dB(A)	>65 dB(A)
Noise - 0 min	+1.61 [+1.54 to +1.68]	+0.27 [+0.19 to +0.35]
Noise - 5 min	−0.28 [−0.35 to −0.21]	−0.15 [−0.23 to −0.07]
Noise - 10 min	−0.41 [−0.48 to −0.34]	−0.01 [−0.09 to +0.07]
Noise - 15 min	−0.25 [−0.31 to −0.18]	−0.06 [−0.14 to +0.01]
	LF/HF	
	<65 dB(A)	>65 dB(A)
Noise - 0 min	+1.85 [+1.76 to +1.94]	+0.31 [+0.21 to +0.41]
Noise - 5 min	−0.10 [−0.18 to −0.01]	−0.26 [−0.36 to −0.17]
Noise - 10 min	−0.19 [−0.28 to −0.11]	−0.08 [−0.18 to +0.02]
Noise - 15 min	−0.15 [−0.23 to −0.07]	+0.02 [−0.07 to +0.12]
	LF	
	<65 dB(A)	>65 dB(A)
Noise - 0 min	+2.82 [+2.67 to +2.97]	+1.15 [+0.99 to +1.32]
Noise - 5 min	−0.02 [−0.16 to +0.12]	−0.13 [−0.29 to +0.03]
Noise - 10 min	−0.64 [−0.78 to −0.50]	−0.07 [−0.23 to +0.09]
Noise - 15 min	−0.43 [−0.56 to −0.29]	+0.01 [−0.16 to +0.17]
	HF	
	<65 dB(A)	>65 dB(A)
Noise - 0 min	+1.57 [+1.38 to +1.76]	+0.97 [+0.77 to +1.18]
Noise - 5 min	−0.11 [−0.29 to +0.07]	+0.02 [−0.19 to +0.22]
Noise - 10 min	−0.61 [−0.78 to −0.43]	−0.10 [−0.30 to +0.10]
Noise - 15 min	−0.39 [−0.57 to −0.22]	+0.01 [−0.19 to +0.21]

The coefficients represent changes in percentage of the mean outcome for an increase of one Leq dB(A). 95% confidence interval are reported.