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The short-term association between exposure to noise and heart rate variability in daily destinations and mobility contexts

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Phone: +33 1 44 73 89 54 Fax: +33 1 44 73 84 62 Abstract

Background: Personal exposure to noise has been shown to be associated with concomitant

increases and lagged decreases of short-term heart rate variability (HRV). It is however unknown

whether this association differs between contexts defined by visited places or mobility as both

exposure sources and expectations may be different between these contexts.

Method: Between July 2014 and June 2015, the RECORD MultiSensor Study collected sound level and

heart rate data for 75 participants, aged 34-74 years, in their living environments for 7 days using a

personal dosimeter and electrocardiography sensor on the chest. Their whereabouts were collected

using a GPS receiver and a mobility survey. Short-term concomitant and lagged associations

between sound level and HRV parameters were assessed within types of visited places and transport

modes using mixed effects models with a random intercept for participants.

Results: Increases in sound level were associated with a concomitant increase in all HR/HRV

parameters, and delayed decreases in the overall HRV. Interactions between the sound level and the

visited place/mobility context were documented. Compared with home, the concomitant association

of sound level with HR and rMSSD was doubled within active and private motorized transport modes

respectively.

Conclusion: The association of sound level with HR/HRV varies between visited places/mobility

contexts. Future studies investigating these context-dependent associations in ambulatory settings

will need to assess additional acoustical factors relating to the visited environments as well as non-

acoustical factors impacting the perception of noise.

Keywords: Noise; Heart rate variability; Autonomic nervous system; Mobility; Sensors

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1 Introduction

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Noise is an environmental stressor ubiquitous to our urbanized modern lives, from traffic related noise to occupational noise, and noise in the household. Auditory health effects of noise are well known (1), with an average of 16% of the adult-onset hearing loss around the world being related to occupational noise (2). There is however increasing evidence on the non-auditory effects of noise on health (3), linking noise exposure with an increased risk of developing coronary heart disease as well as hypertension. The noise reaction model introduced by Babisch (4) links noise exposure and the later development of cardiovascular diseases through the activation of the autonomic nervous system and endocrine systems as noise acts as a psychosocial stressor. In a previous study (5), we assessed the short-term association between personal exposure to sound level and heart rate variability (HRV) parameters as a proxy for the state of the autonomic nervous system. We observed a concomitant increase of HRV parameters with the sound level. The use of wearable sensors allowed us to assess this association in a real life setting, therefore avoiding the limitations of modelled exposure or of exposure measured only at home or work, which ignores exposure in different visited places or during trips. However, the reaction of the autonomic nervous system to an elevated sound level is likely to vary depending on the context. Indeed, first, the sources of elevated sound levels obviously vary depending on the context, and the perception of sounds as noise may depend on the source. Second, the expectations of people regarding the appropriate sound level may vary from one context to the other (e.g. home compared to the workplace or trips) as was underlined in the rationale for the development of a noise sensitivity questionnaire in different situations in daily life (6). Thus, an elevated sound level may be differentially interpreted as noise, and therefore may elicit different physiological reactions. Overall, the aim of this study is to assess how the context, as defined by

- visited places or mobility (modes of transport), interacts with sound level in its short term
- 26 concomitant or lagged association with heart rate and heart rate variability.

Method

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- 28 Population
- 29 Participants came from the RECORD Cohort Study (7, 8), and more particularly from the RECORD 30 MultiSensor sub-study, which aimed at investigating the relationships between transport and health 31 using sensor-based measurement. Details regarding the study sample as well as the data collection 32 protocol have been published elsewhere (5, 9). In summary, participants of the RECORD study were 33 born between 1928 and 1978 and were residing in the Ile-de-France region. They were recruited 34 between 2007 and 2008 without a priori sampling during preventive checkups performed by the IPC 35 Medical Centre on behalf of the French social security. During the second wave of the RECORD Study 36 in which new participants were also recruited, a fraction of the participants joined the RECORD 37 MultiSensor Study between July 2014 and June 2015 in which they underwent a physiological and 38 environmental sound monitoring. For a period of 7 days during their waking hours, participants were 39 instructed to wear an electrocardiography (ECG) sensor, a dosimeter, a GPS receiver, and an 40 accelerometer. Participants wearing a pacemaker or with hearing problems were not included. 41 Written informed consent was obtained from all participants. The RECORD Multisensor Study was 42 approved by the French Data Protection Authority (CNIL) regarding both the ethical and data 43 security aspects (No: DR-2013-568).
- 44 Mobility survey
- The data extracted from the BT-Q1000XT GPS receiver (Qstarz International, Taipei, Taiwan) were pre-processed after the 7-day data collection (10) in order to identify the visited places as well as the
- 47 start and end times of each trip stage, defined as a segment of a trip using a unique transport mode.
- 48 These data were in turn consolidated during a phone mobility survey with the participants, producing

- in the end a detailed timetable covering the 7-day observation period. This timetable consisted of a
- 50 time-stamped list of the visited places and trip stages between them.
- For the present analysis, visited places were recoded to "Home" and "non-Home" while transport
- 52 modes were divided into "Active transport modes" (i.e., walking and biking), "Private motorized
- vehicles" (i.e., cars and motorcycles as a driver or as a passenger) and "Public transport" (i.e., bus,
- tramway, metro and train).
- Each visit at a place and trip stage was cut into contiguous time windows for which summaries of
- heart rate variability, sound level, and physical activity were computed. Two time scales were used in
- 57 this study: (i) 5-minute windows as they correspond to the recommended duration for the
- 58 measurement of short-term HRV (11) and (ii) 1-minute windows in order to assess HRV dynamics
- that may be masked within 5-min windows. These windows represented the statistical units of this
- study. The definition of windows uses as a starting time point the beginning of each visit at a place
- 61 and each trip stage. Offcuts at the end of each segment were excluded from the analysis as they had
- a duration shorter than 5 minutes or 1 minute.
- 63 Sound level measurement/indicators
- 64 Individual exposure to sound level was assessed with a wearable Class II dosimeter Wed007 01dB
- 65 (ACOEM Limonest, France) allowing for A-weighted measurements a weighting that corresponds to
- 66 the sensitivity of the human ear between 40 and 120 dB(A) (tolerance ± 1.0 dB) every second
- 67 (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
- 70 using a standard acoustic calibrator (1 KHz sine wave at 94 dB).
- 71 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
- 74 period. It is one of the main sound level indicators used in environmental noise assessment (12).
- 75 Heart rate variability
- 76 The participants wore a BioPatch BHM 3 (Zephyr Technology, Annapolis, MD, USA) on the chest, an
- easy to set-up two electrodes ECG that collects data only if it is correctly worn. The use of a similar
- 78 two electrodes ECG has been validated against a 12 lead ECG for the measurement of HRV (13).
- 79 Participants were instructed to put it on when they woke up using new electrodes every day and
- 80 to remove it when they went to bed as they had to charge it overnight. Files containing the inter-beat
- 81 (RR) intervals were generated by the BioPatch and then processed in order to compute HRV
- parameters for which the specific signal processing steps are detailed elsewhere (5). Heart rate (HR)
- in bpm, the standard deviation of normal to normal RR intervals (SDNN) in ms as well as the root
- 84 mean square of the successive differences (rMSSD) in ms were computed for each time window
- 85 following the standard definitions (11). Both the high frequency (HF: 0.15 to 0.4 Hz) band power and
- the rMSSD represent vagal cardiac influence (i.e., the influence of the parasympathetic branch of the
- autonomic nervous system on heart rate) (14), but the latter was selected as it is less affected by
- 88 breathing (15). The low frequency (LF: 0.04 to 0.15 Hz) band power as well as the LF/HF ratio were
- 89 not considered in this study as their physiological interpretation is regarded to be unclear in the
- 90 latest literature (16). All of the outcomes were log transformed in order to correct for
- 91 heteroscedasticity. The entire signal processing was carried out under R version 3.4.3 (17) and the
- 92 calculation of HRV parameters through the "RHRV" package version 4.2.3 (18).
 - Accelerometry

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- In addition to the aforementioned sensors, the participants wore an Actigraph wGT3X+ tri-axial
- 95 accelerometer (ActiGraph LLC, Pensacola, FL, USA) on the right hip with a dedicated elastic belt. They
- 96 were asked to remove the belt only when sleeping and when they were in contact with water.
- 97 Accelerometry was collected in 5-second epochs. The count values of each of the three axes were

combined to produce the vector magnitude which in turn was summed up over the 5-minute and 1-minute windows. Additionally the coefficient of variation of the vector magnitude within each window was computed by dividing its standard deviation by its mean. Windows with a mean vector magnitude equal to zero were given a coefficient of variation of zero.

Socio-demographic variables

Age, sex, level of education, and employment status (only used for descriptive purposes) were collected from the IPC administrative database and medical questionnaire and the RECORD questionnaire filled in during the health checkup.

Statistical analysis

Linear mixed models applied separately to the 5-minute and 1-minute measurement windows were used to estimate associations between individual sound level exposure and HRV parameters. To take the clustering of the repeated measures into account as well as the imbalanced number of windows between participants, a mixed model with a random intercept at the individual level was used (19). Short-term trends of HRV parameters over the day were taken into account with smoothing splines estimated for each participant. The temporal autocorrelation between the repeated measurements of each participant was taken into account using an autoregressive model of order 1 AR(1) (20). This covariance structure assigns to each pair of measurements, within a participant, a correlation that decreases as the time interval separating the measurements increases. The correlation is expressed as ρ^k , where k is the time interval (in minutes) separating each pair of observations and ρ the correlation (ranging between 0 and 1) of a pair of observations separated by a one minute interval (19).

Separate models were built for each electrocardiographic outcome in two stages: (1) with the concomitant and lagged sound levels and (2) with an additional interaction term between the context and both the concomitant and lagged sound levels. All models were adjusted for the context (as defined by the mobility survey, with "Home" as the reference value), for heart rate (when the

outcome was HRV), and for the accelerometer vector magnitude and its coefficient of variation. Since the outcomes were log transformed, the regression coefficients were back transformed [using the formula: $(\exp(\beta) - 1) \times 100$], representing percent changes in the mean outcome for a one unit increase. In order to correctly assess the interaction between sound level and context, lagged sound level was defined as the sound level in the preceding time window(s) within the same context. For the 5minute windows a single lag (-5min) was considered in order to limit the exclusion of short trips. For the 1-minute windows four lags were considered (-1min, -2min, -3min and -4min) and the interaction with the lagged exposure was assessed using the furthest lag. Observations for which such lagged variables could not be defined (e.g., the first 5-minute window within a context episode) were discarded. To assess the degree of multicollinearity within the models, particularly with the addition of lagged sound levels, the generalized variance inflation factor (GVIF) was computed using the vif.lme function implemented in the "car" package (21). The GVIF is a generalization of the variance inflation factor (VIF) that can be applied to categorical explanatory variables (22). Values of VIF < 4 are usually considered to be acceptable (23). As the high number of observations in the 1-minute windows based dataset (more than 250 000 data points) rendered model fitting impossible with our current equipment (due to the autocorrelation structure), the dataset was under-sampled by selecting 20% of the 1-minute windows spent at activity places ("Home" and "non-Home"). Observations within trips were all included. Statistical analysis was done in R version 3.4.3 (17) using the "nlme" package version 3.1-131 (24) and the "ImeSplines" package version 1.1–10 (25). The calculation of confidence intervals of the association within each context, based on linear combinations, was done using the "multcomp" package version 1.4-8 (26). Plots were created using the "ggplot2" package version 2.2.1 (27).

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Descriptive statistics

Of the initial 78 participants, three were excluded as either their accelerometer, noise dosimeter or ECG sensor did not work or was not worn. Consequently, the study sample consisted of 75 participants whose characteristics are presented in Table 1 (additional information regarding the distribution of contexts relative to the socio-demographic characteristics are available in Table S1 of the supplementary material). For the 75 participants the collected raw measurements consisted of 6 329 hours of RR intervals, 13 843 hours of sound level measurements and 11 825 hours of accelerometer data. Merging the three data sources with the timetable of the mobility survey, based on the timestamps, produced 5 221 hours of simultaneous measurements. After quality check (e.g., excluding periods of non-wear for the accelerometer, or missing data for sound level and RR intervals), 4 253 hours of measurement were selected. Finally, when considering only the 5-min windows with an available lagged exposure, 3 994 hours were available for analysis, representing 47 933 windows of 5-min. The final sample of 1-min windows had 251 110 observations which was reduced to 65 502 after under-sampling. Table 2 shows descriptive statistics on sound level and HR/HRV parameters within the different contexts considered, while Figure 1 shows the density plots of measured sound levels within each context. Visited places ("Home" and "non-Home") had the lowest mean values and the largest standard deviations, while "Private motorized vehicles" had the highest mean value. The overall sound level had a mean value and standard deviation of 65.7 dB(A) (SD: 11.0) with values ranging from 32.6 dB(A) to 112.0 dB(A). Mean sound level values were higher in transport modes [72.5 dB(A) (SD: 7.7)] than in visited places [65.3 dB(A) (SD: 11.1)] with a statistically significant difference (p < 0.0001).

Linear mixed effects models

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Mixed effects models were fitted for each combination of sound level and HRV indicators, adjusted for the visited place or mobility context in addition to the accelerometer vector magnitude and its coefficient of variation, heart rate (when the outcome was HRV), and short-term trend. All models included the temporal autocorrelation structure as it improved the model fit, assessed using the likelihood ratio test (p < 0.0001) (see **Tables S2** and **S3** of the supplementary material). Based on the 5-minute windows, **Table 3**, shows the change in percentage in the outcome for a one dB(A) increase for models including concomitant and lagged sound levels. Sound level was positively associated with a concomitant increase in HR, SDNN and rMSSD. Lagged associations (-5min) differed between the outcomes as it was positive for HR and negative for SDNN and rMSSD, with a 95% CI for the latter that overlapped zero. Similar patterns were observed when using 1-minute windows (Table 4) i.e. all concomitant and lagged (-1min) associations were positive while lagged associations starting at -2min were negative for SDNN and rMSSD with a 95% CI for the latter that overlapped zero. No multicollinearity issues were detected in the models as the generalized variance inflation factors were below 1.71 and 2.62 in the models based on 5-minute and 1-minute windows respectively (Table S6 and S7 of the supplementary material). The same models were then fitted with the addition of an interaction between the mobility context variable and both the concomitant and lagged sound level variables, using "Home" as the reference level. Figure 2 shows the estimated associations within each context based on the 5-minute windows while the coefficients are available in the supplementary material **Table S8**. For HR, the overall interactions between the context and the concomitant and lagged sound levels were statistically significant (p < 0.0001 and p = 0.0016 respectively). Compared with the concomitant positive association documented between sound level and HR at home, the

concomitant associations with HR was slightly stronger in non-Home (difference: +0.024, 95% CI:

+0.011 to +0.038) and twice as high during active transport modes (difference: +0.146, 95% CI: +0.082 to +0.210) while the 95% CI of the association within Public transport modes overlapped zero (estimate: 0.066, 95% CI: -0.080 to 0.211). Regarding lagged associations, the only statistically significant difference compared with Home was in non-Home which was slightly lower. The 95% CI of the lagged associations within all three transport mode contexts overlapped zero, with a point estimate for private motorized transport modes close to the null and a point estimate for public transports close to its concomitant association estimate. For SDNN, the overall interaction between the context and the concomitant and lagged sound levels was statistically significant only for the latter (p = 0.1562 and p < 0.0001 respectively). Concomitant associations were positive in all contexts with a 95% CI overlapping zero only in the case of public transports (estimate: 0.452, 95% CI: -0.511 to 1.423). Lagged associations were negative across contexts, with the exception of public transports for which the point estimate remained close to that of its concomitant association. The 95% CI of lagged associations with SDNN overlapped zero for the three transport mode contexts. Compared with home, the lagged associations in non-home was significantly more negative. Regarding rMSSD, the overall interaction between the context and the concomitant and lagged sound levels were both statistically significant (p = 0.0002 and p = 0.0245 respectively). Concomitant associations were positive across contexts with the exception of public transports for which the association was negative, with a 95% CI overlapping zero (estimate: -0.137, 95% CI: -1.294 to 1.034). Compared to home, the concomitant association within private motorized transport modes was doubled (difference: +0.756, 95% CI: +0.290 to +1.224) while the lagged association was slightly lower – and therefore negative – in non-home. Lagged associations were close to the null across contexts with a 95% CI overlapping zero for the three transport modes.

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Similar patterns were observed when using 1-min windows, both for the concomitant and lagged

associations (Supplementary Material Figure S1 and Table S9). The only notable exception was the

concomitant association between sound level and HR within active transport modes which was lower

(but still positive with a 95% CI excluding zero) than the one observed at home (as opposed to higher

when considering 5-min windows).

Discussion

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Summary of results

In this study, we assessed the concomitant and lagged short-term associations between sound level and HR and HRV across different contexts of daily life exposure (visited places/transport modes). We documented positive concomitant associations with HR, SDNN and rMSSD as well as lagged associations of smaller magnitude, that were positive with HR and negative with both SDNN and rMSSD, (however the confidence interval of the latter association overlapping zero). These associations were documented for 5-min windows and similar patterns were observed when using smaller windows (1-min) with a positive concomitant and lagged (-1min) association with the three outcomes and starting at lag -2min a negative association with SDNN and rMSSD. When considering the interaction between the sound level and the context in their concomitant effects on HR and HRV, some differences were documented within transport modes. While the concomitant associations were positive across contexts and outcomes (with the exception of public transport modes in the model for rMSSD), a stronger association of sound level with HR within active transport modes and a stronger association with rMSSD within private motorized transport modes were documented, both doubled compared to the effect observed at home. Regarding lagged associations, they had a smaller magnitude across contexts, with the exception of public transport modes for which the point estimates remained close to those of the concomitant associations. The overall positive concomitant and lagged associations between sound level and HR may be explained by sounds acting as stressors triggering the fight-or-flight response with the activation of the sympathetic branch of the autonomic nervous system leading to an increased HR (28). This association have been documented in various studies, both in controlled and ambulatory settings as was underlined by Idrobo Avila et al. in a review on the relationship between sound and electrocardiographic signals (29). In a study by Holand et al. (30) participants were exposed to an auditory startle stimulus while HR and blood pressure (BP) were continuously monitored. Their

results showed an increase followed by a decrease towards the baseline in both HR and BP in the 30s following the stimulus. The results of our study additionally suggest that sound stimuli may have measurable delayed effects on HR lasting at least 5 minutes. In a study by Kraus et al. (31) similar positive concomitant and lagged (up to 15 min) short-term associations between sound level and HR were documented during daily life activities.

The SDNN represents the overall HRV. A reduced SDNN has been linked to an increased risk of cardiovascular morbidity and mortality in populations with (32) and without known cardiovascular diseases (33). The short-term association between sound stimuli and SDNN has been explored in previous studies, with inconsistent results. Sim et al. (34) and Oh et al. (35) found no significant changes in SDNN in participants exposed to different types of noise. Björ et al. (36) found an increased total power (another measurement of overall HRV) in participants during exposure to an 85 dB(A) white noise (i.e., a sound containing all audible frequencies at equal intensities). Conversely, Walker et al. (37) documented a reduced SDNN during exposure to low frequency noise (31.5 to 125 Hz), but not to high frequency noise (500 Hz to 2 kHz), while Huang et al. (38) reported a decreased SDNN with increasing sound levels only for the cumulative lagged exposure over 30 min (among 5 min, 15 min, 30 min and 1 h).

The rMSSD represents the vagally mediated HRV (parasympathetic branch of the autonomic nervous system) with some studies suggesting that a reduced vagal tone is an independent risk factor for all-cause mortality (39). Similarly to SDNN, previous studies assessing the associations between sound stimuli and vagal tone have documented discrepant results. In the studies by Björ et al. (36), Lee et al. (40) and Sim et al. (34), which used HF power as a proxy for vagal tone, no changes were associated with exposure to white noise (for the first two studies) and to traffic and speech noise (for the third study). The study by Oh et al. (35) found a significant increase in vagal tone when exposed to a car horn sound, but only for HF power and not for rMSSD. Cho et al. (41) documented a decrease in HF power during exposure to low frequency (100 Hz) and high frequency (10 kHz) white noise but

not during 1 kHz white noise, while Walker et al. (37) found a significant decrease in HF power during exposure to low frequency noise (31.5 to 125 Hz) but not during high frequency noise (500 Hz to 2 kHz) and no changes in rMSSD. Regarding the two studies with a non-simulated sound exposure, Kraus et al. (31) reported a concomitant decrease in HF power for sounds below 65 dB(A) (and an increase for sounds above), and Huang et al. (38) reported a decrease in HF power with both concomitant and cumulative lagged sound levels, up to 15 min.

The diverging results between the studies may be explained by differences in study design (type and duration of exposure, controlled or real life setting, measurement during or before and after exposure) as well as differences in the specific parameter used to assess the vagal tone, which limits the comparability of the results.

The concomitant increase in SDNN and rMSSD with increasing sound levels remains difficult to explain. However, one potential explanation could be that this increase is driven by peaks in the sound level which repeatedly trigger startle responses characterized by a peak in HR within few seconds (30), therefore momentarily increasing SDNN. As these quick responses are driven by the inhibition and reactivation of the parasympathetic branch (42), this would also explain the concomitant increase in rMSSD. As observed when assessing the concomitant and lagged associations using 1-min windows, this increase lasted 2 minutes before being counterbalanced. This is suggested by the lagged negative associations between sound level and both SDNN and rMSSD which were however not statistically significant for the latter. Kraus et al. (31) found patterns of association similar to those documented in this study, i.e. a positive concomitant and negative lagged associations between sound level and SDNN using 5-min windows. In both the study by Kraus et al. and in a previous study by our team on the same dataset (5), this delayed reduction in SDNN was still statistically significant after 15 minutes (maximum lag explored in both studies).

Regarding the interactions between the context of exposure and the sound level in their effects on HR and HRV parameters, few differences were documented in this study. Compared with home, the

concomitant association in other visited places was slightly stronger for HR while the lagged associations were slightly weaker for the three outcomes in this context. Within transport modes, a doubled concomitant association of sound level with HR within active transport modes and with rMSSD within private motorized transport modes were observed while associations within public transport modes were statistically non-significant. These differences may be related with differences in both the nature of the sounds as well as the perceived control over them associated with each of these contexts. Indeed, compared to home, active and private motorized transport modes are dominated by road traffic noises while offering less control over the sound environments. Lagged associations within all transport modes contexts were statistically non-significant with higher confidence intervals compared to the estimates within visited places. This stems from the relatively low number of observations within transport modes (6.0% of the sample) particularly for public transport modes (1.4% of the sample).

Strengths and limitations

Strengths:

The use of wearable sensors in combination with the mobility survey allowed us to assess precisely and objectively both the exposure (sound level) and the outcome (HR and HRV) as well as the transport modes/visited places in a "real life" setting. The analyzed time windows were defined according to the mobility survey, allowing us to slice the continuous sensor measurements into 5-min and 1-min windows within each defined context. This method allowed us in turn, to contextualize the association between sound level and HRV by looking at the interaction between sound level and mobility contexts. This approach allowed us also to assess the associations in "real life" situations which seems necessary since an experiment on stress effects of noise by Ising et al (43) comparing a field and a laboratory experiment found no correlation between both setups, underlining the necessity for field measurements. Finally, another strength of this study lies in the large number of

observations (i.e., n=47 933 windows at the 5-min window level), with however a limited number of participants (n=75).

Limitations and potential explanations for observed differences:

The observed differences between the mobility contexts are however difficult to interpret. First, the comparability with other studies is limited by differences in study design (29) (controlled or ambulatory setting, concomitant or lagged association), and in the signal processing steps for the calculation of HRV indicators (44). Second, the physiological correlates of HRV indicators have been criticized lately, in particular their ability to measure changes in the sympathetic branch activity and therefore, their ability to represent the balance of the autonomic nervous system (45). These limitations could be overcome by complementing the HRV assessment with that of galvanic skin response which is modulated by sympathetic activity and proved to be feasible in an ambulatory setting if confounders are taken into account (46). As for the comparability with other studies, this would require the standardization of the processing and reporting of HRV indicators across studies, which could be achieved by an update of the recommendations for HRV measurement and interpretation which date back to 1996 (11).

Another limitation of this study, which is related to the ambulatory "real life" assessment approach, lies in the unmeasured confounders that may impact HRV, namely air pollution (47), vibrations (48), body posture (49), and other psychological stressors (50). These confounders could be taken into account in future studies either with the use of additional sensors, or questionnaires on mobile phones. This approach would prove useful in order to disentangle the effects of various environmental stressors. Another confounder which was taken into account in this study is physical activity (51). Although we measured it objectively with accelerometry, the use of a single accelerometer placed at the hip may underestimate upper body movements and as well as total physical activity while cycling (52).

The observed differences between contexts could also be related to differences in the sound environments within each context that a single indicator cannot encompass. Three distinct components could be used to describe the acoustical characteristics of a sound environment: the energetic, temporal, and spectral dimensions (53). The Leq, the traditionally used indicator in environmental noise assessment, represents the energetic dimension, but it does not encompass temporal variations (in this case within the 5-minute and 1-minute windows) and the spectral components of the sound environments. Regarding the spectral dimension, in our study the measurements were A-weighted, a weighting that accounts for the human ear sensibility as it is less sensitive to low frequencies. As a consequence low frequency noises are underestimated even though they have been shown to impact HRV (37) and are recognized as a special environmental noise issue (54). The three dimensions of sound environments (energetic, temporal, and spectral) can be accounted for in future studies by using sound level dosimeters with octave band filters (or 1/3 octave band filters) allowing for the concomitant measurement of sound level over split frequency bands. This would allow to encompass the spectral dimension, while the temporal and energetic dimensions could be taken into account by using different noise indicators, e.g., the range of noise levels (53). Additionally, as the distinction between sound and noise lies in its subjective assessment, different non-acoustical factors may modify the perception of a specific sound and the resulting physiological reactions. These factors include the level of mental arousal, the meaning and predictability of the sounds, and the perceived control over the sound source (55, 56). These non-acoustical factors (perception) as well as the ongoing task during the real life assessment could be collected using two complementary approaches, i.e., an enhanced version of our mobility survey and ecological momentary assessment (57) with questionnaires on mobile phones. On one hand, this would allow one to ask participants questions about their perception of current sound environments, on the

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other hand this would also allow researchers to assess the participants' subjective stress in order to bridge the gap between subjective and objective stress (HRV).

This study attempted to evaluate the interactions between visited place/mobility contexts and sound levels in their association with HRV parameters. Interpretation of the results is however limited by the aforementioned factors which could be overcome by future studies aiming at assessing the effects of environmental stressors in an ambulatory unrestricted setting. Such will be the case of our ongoing Mobilisense project, for which sound level meters with 1/3 band octave filters will be used in combination with personal air pollution sensors as well as questionnaires on mobile phone.

Conclusion

In conclusion, in this study there was some evidence of differences in the association of sound level with HR and HRV parameters across visited places and mobility contexts. While the overall concomitant association between sound level and HR and HRV parameters was positive, some mobility contexts showed stronger positive associations. While our work represents an advance in the understanding of noise effects in real-life settings, the interpretation of those differences will have to be improved by the assessment of currently unmeasured factors. Overall, future studies assessing the effects of noise on the autonomic nervous system should supplement HRV monitoring with additional physiological measurements (e.g. Galvanic skin response) and environmental measurements (air pollutants) as well as complementary noise indicators while simultaneously assessing subjective factors on both the sound level exposure and related perceived stress.

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Figure legends

Figure 1: Density plots of LAeq sound levels within visited places and transport modes. Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes.

Figure 2: Estimated associations (and their 95% CI) between concomitant and lagged sound levels and HR/HRV parameters in different mobility defined contexts using 5-min windows. Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes. Asterisks denote a statistically significant difference with Home (reference level) *p<0.05, **p<0.01, ***p<0.001.

Table 1 Descriptive statistics of the participants characteristics (N = 75)

Variable	n (%)
Men	48 (64%)
Age	
[34-40]	16 (21.3%)
]40-50]	19 (25.3%)
]50-60]	23 (30.7%)
]60-74]	17 (22.7%)
Employment status	
Employed	49 (65.3%)
Unemployed	11 (14.7%)
Retired	13 (17.3%)
Other	2 (2.7%)
Annoyed by noise during work	17 (22.7%)
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: Number of 5-min windows and summary statistics of sound level, heart rate and heart rate variability measurements per context (n = 47 933)

Contoxt n		Le	eq [db(A)]	F	HR (bpm)		SDNN (ms)		rMSSD (ms)	
Context	n	mean (sd)	median (range)	mean (sd)	median (range)	mean (sd)	median (range)	mean (sd)	median (range)	
Home	25589	64.4 (11.3)	65.5 (32.6-107.0)	77.9 (13.0)	77.3 (44.8-143.4)	60.8 (30.1)	54.7 (6.2-270.9)	35.7 (24.9)	28.6 (1.8-261.2)	
non-Home	19466	66.5 (10.6)	67.4 (34.3-102.4)	78.9 (13.5)	77.8 (46.6-171.1)	63.4 (29.7)	57.3 (7.8-258.5)	36.9 (26.2)	29.6 (2.1-238.1)	
Active	791	70.4 (8.3)	71.4 (33.6- 91.9)	96.2 (19.0)	94.8 (52.3-164.2)	53.1 (33.4)	45.4 (8.8-242.3)	29.8 (29.0)	21.6 (2.2-201.8)	
Priv.Mot	1434	73.7 (7.6)	72.8 (49.2-112.0)	78.8 (13.4)	77.1 (50.7-142.6)	48.1 (25.3)	43.0 (7.7-188.1)	31.1 (24.4)	23.7 (1.8-186.2)	
Public	653	72.6 (6.6)	72.6 (40.8-89.3)	78.6 (11.3)	77.6 (54.1-118.1)	51.3 (28.9)	43.7 (9.5-184.4)	27.9 (23.4)	22.0 (3.7-167.8)	

Leq: Equivalent continuous sound level of A-weighted Leq,1s, HR: Heart rate in beats per minute, SDNN: Standard deviation of normal to normal RR intervals in milliseconds, rMSSD: Root mean square of the successive differences in milliseconds.

Table 3: Coefficients and 95% confidence intervals of the percentage change in the mean outcome associated with a one dB(A) increase in the sound level in the 5-minute windows.

	HR (bpm)			SDNN (ms)	rMSSD (ms)		
	β	95% CI	β	95% CI	β	95% CI	
Concomitant	+0.141	[+0.135 to +0.148]	+0.894	[+0.849 to +0.939]	+0.600	[+0.546 to +0.655]	
Lagged (-5min)	+0.033	[+0.026 to +0.039]	-0.315	[-0.358 to -0.272]	-0.050	[-0.102 to +0.002]	

Models were adjusted for accelerometer vector magnitude and its coefficient of variation, heart rate (only for HRV outcomes), short-term trend and context. Complete models are available in the Table S3 of the supplementary material.

Abbreviations: HR: Heart rate, SDNN: Standard deviation of normal to normal RR intervals, rMSSD: Root mean square of the successive differences.

Table 4: Coefficients and 95% confidence intervals of the percentage change in the mean outcome associated with a one dB(A) increase in the sound level in the 1-minute windows.

		HR (bpm)		SDNN (ms)	rMSSD (ms)		
	β	95% CI	β	95% CI	β	95% CI	
Concomitant	+0.112	[+0.105 to +0.119]	+0.755	[+0.698 to +0.813]	+0.526	[+0.460 to +0.592]	
Lagged (–1min)	+0.076	[+0.069 to +0.083]	+0.180	[+0.119 to +0.241]	+0.141	[+0.072 to +0.210]	
Lagged (-2min)	+0.016	[+0.009 to +0.023]	-0.129	[-0.190 to -0.068]	-0.067	[-0.136 to +0.002]	
Lagged (-3min)	+0.016	[+0.009 to +0.023]	-0.060	[-0.122 to +0.001]	-0.025	[-0.094 to +0.045]	
Lagged (-4min)	+0.016	[+0.008 to +0.022]	-0.160	[-0.217 to -0.104]	-0.059	[-0.124 to +0.006]	

Models were adjusted for accelerometer vector magnitude and its coefficient of variation, heart rate (only for HRV outcomes), short-term trend and context. Complete models are available in the Table S3 of the supplementary material.

Abbreviations: HR: Heart rate, SDNN: Standard deviation of normal to normal RR intervals, rMSSD: Root mean square of the successive differences.

Figure 1 **Context** Home non-Home Active Priv.Mot 0.06-Public 0.04 density 0.02-0.00-35 45 55 65 75 85 95 105 Sound level in Leq dB(A)

Figure 2

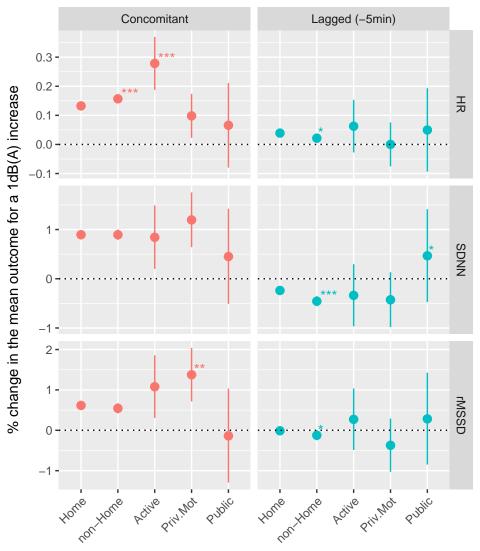


 Table S1: Distribution of individual characteristics across contexts. Percentages are relative to each line.

		N (participants)	N (5-min windows)	Home	non-Home	Active	Priv.Mot	Public
Enople: moont	Employed	49	31601	43.7%	50.4%	1.6%	2.5%	1.7%
Employment	Unemployed	26	16332	72.2%	21.6%	1.7%	3.9%	0.7%
Sex	Women	27	17301	59.8%	34.8%	1.5%	2.8%	1.1%
Sex	Men	48	30632	49.8%	43.9%	1.8%	3.1%	1.5%
Education	<3y tertiary	36	22672	54.0%	41.1%	1.2%	2.7%	1.1%
Education	≥3y tertiary	39	25261	52.9%	40.2%	2.1%	3.2%	1.6%
Age	<52y	36	24215	51.1%	44.0%	1.5%	2.1%	1.4%
	≥52y	39	23718	55.8%	37.2%	1.9%	3.9%	1.3%

Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes.

Table S2: Model fit indices and likelihood ratio test between models with and without the autoregressive covariance structure of order 1 (for models based on 5-min windows)

Models	df	AIC	BIC	logLik	L.Ratio	p-value
SDNN: model without interaction, with AR	14	34083.59	34206.47	-17027.79	5735.237	<.0001
SDNN: model without interaction, without AR	13	39816.82	39930.93	-19895.41	3/33.23/	<.0001
rMSSD: model without interaction, with AR	14	51862.88	51985.77	-25917.44	11467.62	<.0001
rMSSD: model without interaction, without AR	13	63328.50	63442.61	-31651.25	11407.02	<.0001
HR: model without interaction, with AR	13	-147971.64	-147857.53	73998.82	60916.62	<.0001
HR: model without interaction, without AR	12	-87057.02	-86951.69	43540.51	00910.02	<.0001
SDNN: model with interaction, with AR	22	34064.56	34257.67	-17010.28	F707 41F	1 0001
SDNN: model with interaction, without AR	21	39769.98	39954.31	-19863.99	5707.415	<.0001
rMSSD: model with interaction, with AR	22	51849.03	52042.13	-25902.51	11425.56	<.0001
rMSSD: model with interaction, without AR	21	63272.59	63456.92	-31615.30	11425.50	<.0001
HR: model with interaction, with AR	21	-148007.85	-147823.52	74024.93	C0700 FC	< 0001
HR: model with interaction, without AR	20	-87300.29	-87124.74	43670.14	60709.56	<.0001

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, df: degrees of freedom

Table S3: Model fit indices and likelihood ratio test between models with and without the autoregressive covariance structure of order 1 (for models based on 1-min windows)

Models	df	AIC	BIC	logLik	L.Ratio	p-value
SDNN: model without interaction, with AR	17	84607.52	84762.05	-42286.76	5460.509	<.0001
SDNN: model without interaction, without AR	16	90066.03	90211.47	-45017.01	3460.309	<.0001
rMSSD: model without interaction, with AR	17	105873.3	106027.9	-52919.67	9518.862	<.0001
rMSSD: model without interaction, without AR	16	115390.2	115535.6	-57679.10	9316.602	<.0001
HR: model without interaction, with AR	16	-164894.7	-164749.3	82463.36	C1740 C	<.0001
HR: model without interaction, without AR	15	-103148.1	-103011.8	51589.06	61748.6	<.0001
SDNN: model with interaction, with AR	25	84583.56	84810.80	-42266.78	F 4 4 1 77 F	<.0001
SDNN: model with interaction, without AR	24	90023.33	90241.49	-44987.67	5441.775	<.0001
rMSSD: model with interaction, with AR	25	105852.7	106080.0	-52901.36	9477.673	<.0001
rMSSD: model with interaction, without AR	24	115328.4	115546.5	-57640.19	9477.075	<.0001
HR: model with interaction, with AR	24	-164960.9	-164742.7	82504.44	61240.0	< 0001
HR: model with interaction, without AR	23	-103622.0	-103412.9	51833.99	61340.9	<.0001

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, df: degrees of freedom

Table S4: Coefficients and 95% CI of the percent change in the mean outcome associated with a one unit increase for the 5-min windows. The intercept represents the geometric mean of the outcome at home when all variables are set to zero.

		HR (bpm)		SDNN (ms)		rMSSD (ms)		
	β	95% CI	β	95% CI	β	95% CI		
Intercept	+69.870	[+68.158 to +71.625]	+93.939	[+86.973 to +101.464]	+83.936	[+75.002 to +93.934]		
LAeq	+0.141	[+0.135 to +0.148]	+0.894	[+0.849 to +0.939]	+0.600	[+0.546 to +0.655]		
LAeq(-5min)	+0.033	[+0.026 to +0.039]	-0.315	[-0.358 to -0.272]	-0.050	[-0.102 to +0.002]		
Context(non-Home)	-0.330	[-0.896 to +0.240]	-0.198	[-1.482 to +1.102]	+2.202	[+0.271 to +4.169]		
Context(Active)	+3.389	[+2.592 to +4.191]	-35.825	[-38.028 to -33.544]	-25.895	[-29.303 to -22.323]		
Context(Priv.Mot)	-3.633	[-4.336 to -2.925]	-21.689	[-23.816 to -19.504]	-13.034	[-16.317 to -9.623]		
Context(Public)	-2.010	[-3.046 to -0.964]	-15.721	[-18.848 to -12.474]	-14.460	[-18.818 to -9.867]		
VM	+4.616	[+4.551 to +4.682]	+14.438	[+13.879 to +15.001]	+11.031	[+10.357 to +11.710]		
CV(VM)	-0.160	[-0.180 to -0.139]	-0.404	[-0.574 to -0.234]	-0.557	[-0.753 to -0.360]		
HR	-	-	-1.150	[-1.200 to -1.099]	-1.783	[-1.851 to -1.715]		

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, LAeq: equivalent continuous sound level of A-weighted Leq,1s, Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes, VM: Vector magnitude (standardized), CV: Coefficient of variation (range: 0-1).

Table S5: Coefficients and 95% CI of the percent change in the mean outcome associated with a one unit increase for the 1-min windows. The intercept represents the geometric mean of the outcome at home when all variables are set to zero.

		HR (bpm)		SDNN (ms		rMSSD (ms)
	β	95% CI	β	95% CI	β	95% CI
Intercept	+67.297	[+65.588 to +69.051]	+77.473	[+71.590 to +83.841]	+94.925	[+85.436 to +105.468]
LAeq	+0.112	[+0.105 to +0.119]	+0.755	[+0.698 to +0.813]	+0.526	[+0.460 to +0.592]
LAeq(-1min)	+0.076	[+0.069 to +0.083]	+0.180	[+0.119 to +0.241]	+0.141	[+0.072 to +0.210]
LAeq(-2min)	+0.016	[+0.009 to +0.023]	-0.129	[-0.190 to -0.068]	-0.067	[-0.136 to +0.002]
LAeq(-3min)	+0.016	[+0.009 to +0.023]	-0.060	[-0.122 to +0.001]	-0.025	[-0.094 to +0.045]
LAeq(-4min)	+0.016	[+0.008 to +0.022]	-0.160	[-0.217 to -0.104]	-0.059	[-0.124 to +0.006]
Context(non-Home)	-0.360	[-0.902 to +0.185]	+1.646	[+0.338 to +2.971]	+4.532	[+2.773 to +6.320]
Context(Active)	+7.239	[+6.471 to +8.013]	-20.314	[-22.116 to -18.471]	-5.093	[-7.947 to -2.152]
Context(Priv.Mot)	-2.804	[-3.555 to -2.048]	-17.553	[-19.155 to -15.920]	-8.248	[-10.678 to -5.752]
Context(Public)	-0.979	[-2.001 to +0.052]	-17.343	[-19.447 to -15.184]	-12.427	[-15.465 to -9.279]
VM	+5.152	[+5.067 to +5.237]	+8.087	[+7.446 to +8.732]	+8.534	[+7.743 to +9.330]
CV(VM)	+0.198	[+0.160 to +0.236]	+4.914	[+4.573 to +5.256]	+1.682	[+1.300 to +2.065]
HR	-	-	-1.329	[-1.372 to -1.286]	-2.102	[-2.156 to -2.047]

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, LAeq: equivalent continuous sound level of A-weighted Leq,1s, Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes, VM: Vector magnitude (standardized), CV: Coefficient of variation (range: 0-1).

Table S6: Generalized variance inflation factors associated with each independent variable for the models based on the 5-min windows. Columns represent separate models.

	HR	SDNN	rMSSD
LAeq	1.12	1.29	1.17
LAeq (-5min)	1.06	1.21	1.08
Context	1.09	1.23	1.20
VM	1.23	1.71	1.69
CV(VM)	1.10	1.16	1.13
HR	-	1.55	1.57

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, VM: Vector Magnitude, CV: Coefficient of variation, LAeq: equivalent continuous sound level of A–weighted Leq,1s

Table S7: Generalized variance inflation factors associated with each independent variable for the models based on the 1-min windows. Columns represent separate models.

	HR	SDNN	rMSSD
LAeq	1.05	2.25	1.91
LAeq (-1min)	1.04	2.58	2.11
LAeq (-2min)	1.04	2.62	2.12
LAeq (-3min)	1.04	2.60	2.11
LAeq (-4min)	1.03	2.24	1.89
Context	1.10	1.49	1.42
VM	1.12	1.67	1.61
CV(VM)	1.04	1.07	1.06
HR	-	1.56	1.52

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, VM: Vector Magnitude, CV: Coefficient of variation, LAeq: equivalent continuous sound level of A–weighted Leq,1s

Table S8: Coefficients and 95% confidence intervals of the percentage change in the mean outcome associated with a one dB(A) increase in the sound level in the 5-minute windows. The coefficients for the main effect represent the association in the reference level (Home) while the coefficients of the interaction terms represent differences relative to the reference level. The total effect within each context is obtained by summing up the coefficients for the main and interaction effects.

	HR			SDNN		rMSSD
	β	95% CI	β	95% CI	β	95% CI
LAeq (ref : Home)	+0.132	[+0.124 to +0.141]	+0.895	[+0.838 to +0.951]	+0.616	[+0.548 to +0.684]
LAeq (-5min) (ref : Home)	+0.039	[+0.031 to +0.047]	-0.238	[-0.292 to -0.184]	-0.012	[-0.078 to +0.054]
LAeq*non-Home	+0.024	[+0.011 to +0.038]	-0.000	[-0.090 to +0.090]	-0.070	[-0.179 to +0.038]
LAeq*Active	+0.146	[+0.082 to +0.210]	-0.052	[-0.503 to +0.402]	+0.460	[-0.083 to +1.006]
LAeq*Priv.Mot	-0.034	[-0.088 to +0.019]	+0.298	[-0.093 to +0.691]	+0.756	[+0.290 to +1.224]
LAeq*Public	-0.067	[-0.169 to +0.036]	-0.439	[-1.114 to +0.240]	-0.748	[-1.560 to +0.070]
LAeq (-5min)*non–Home	-0.017	[-0.031 to -0.004]	-0.218	[-0.308 to -0.129]	-0.112	[-0.220 to -0.003]
LAeq (-5min)*Active	+0.024	[-0.040 to +0.087]	-0.100	[-0.547 to +0.350]	+0.283	[-0.254 to +0.823]
LAeq (-5min)*Priv.Mot	-0.039	[-0.092 to +0.014]	-0.189	[-0.585 to +0.209]	-0.359	[-0.826 to +0.110]
LAeq (-5min)*Public	+0.011	[-0.090 to +0.111]	+0.707	[+0.042 to +1.376]	+0.296	[-0.503 to +1.101]

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, LAeq: equivalent continuous sound level of A-weighted Leq,1s, Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes.

Table S9: Coefficients and 95% confidence intervals of the percentage change in the mean outcome associated with a one dB(A) increase in the sound level in the 1-minute windows. The coefficients for the main effect represent the association in the reference level (Home) while the coefficients of the interaction terms represent differences relative to the reference level. The total effect within each context is obtained by summing up the coefficients for the main and interaction effects.

	HR		SDNN		rMSSD	
	β	95% CI	β	95% CI	β	95% CI
LAeq (ref : Home)	+0.112	[+0.102 to +0.122]	+0.791	[+0.718 to +0.864]	+0.534	[+0.448 to +0.619]
LAeq (-4min) (ref : Home)	+0.017	[+0.007 to +0.027]	-0.103	[-0.174 to -0.031]	+0.000	[-0.084 to +0.085]
LAeq*non-Home	+0.040	[+0.024 to +0.056]	-0.033	[-0.137 to +0.071]	-0.067	[-0.191 to +0.058]
LAeq*Active	-0.049	[-0.074 to -0.025]	-0.157	[-0.354 to +0.041]	+0.113	[-0.118 to +0.344]
LAeq*Priv.Mot	-0.029	[-0.055 to -0.004]	+0.071	[-0.130 to +0.272]	+0.326	[+0.088 to +0.563]
LAeq*Public	-0.077	[-0.112 to -0.042]	-0.551	[-0.841 to -0.260]	-0.511	[-0.849 to -0.172]
LAeq (-4min)*non-Home	+0.000	[-0.016 to +0.017]	-0.191	[-0.295 to -0.088]	-0.171	[-0.296 to -0.046]
LAeq (-4min)*Active	-0.003	[-0.028 to +0.021]	+0.024	[-0.174 to +0.222]	+0.051	[-0.180 to +0.283]
LAeq (-4min)*Priv.Mot	-0.010	[-0.034 to +0.015]	-0.105	[-0.302 to +0.093]	-0.176	[-0.408 to +0.056]
LAeq (-4min)*Public	-0.002	[-0.036 to +0.032]	+0.198	[-0.088 to +0.485]	+0.085	[-0.246 to +0.418]

HR: heart rate, SDNN: standard deviation of normal to normal RR intervals, rMSSD: root mean square of the successive differences, LAeq: equivalent continuous sound level of A-weighted Leq,1s, Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes.

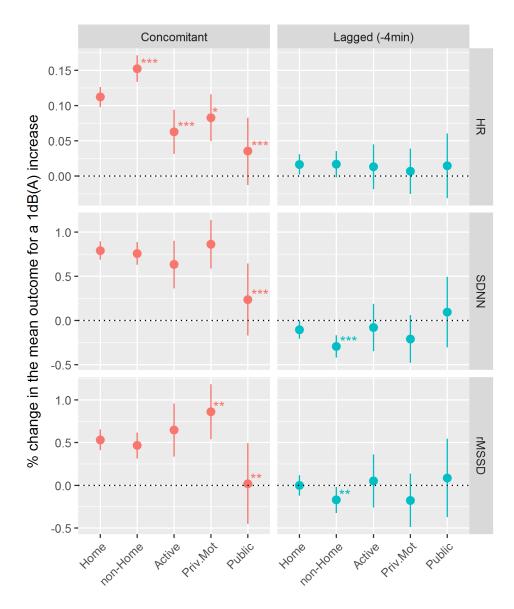


Figure S1: Estimated associations (and their 95% CI) between concomitant and lagged sound levels and HR/HRV parameters in different mobility defined contexts using 1-min windows. Active: active transport modes, Priv.Mot: private motorized transport modes, Public: public transport modes. Asterisks denote a statistically significant difference with Home (reference level) *p<0.05, **p<0.01, ***p<0.001.