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## **Transportation noise impairs cardiovascular function without altering sleep: The importance of autonomic arousals**

Laurie Thiesse, Franziska Rudzik, Jan Kraemer, Karine Spiegel, Rachel Leproult, Niels Wessel, Reto Pieren, Harris Héritier, Ikenna Eze, Maria Foraster, et al.

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1 Transportation noise impairs cardiovascular function without altering sleep: the  
 2 importance of autonomic arousals

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**35 ABSTRACT****36 Aims**

37 Chronic exposure to nocturnal transportation noise has been linked to cardiovascular disorders with  
38 sleep impairment as the main mediator. Here we examined whether nocturnal transportation noise  
39 affects the main stress pathways, and whether it relates to changes in the macro and micro structure  
40 of sleep.

**41 Methods and results**

42 Twenty-six young healthy participants (12 women,  $24.6 \pm 0.7$  years, mean  $\pm$  SE) spent five  
43 consecutive 24-h days and one last morning in the laboratory. The first (baseline) and last (recovery)  
44 nights comprised a quiet ambient scenario. In-between, four different noise scenarios  
45 (low/medium/high intermittent road or rail scenarios with an identical equivalent continuous sound  
46 level of 45dB) were randomly presented during the 8-h nights. Participants felt more annoyed from  
47 the transportation noise scenarios compared to the quiet ambient scenario played back during the  
48 baseline and recovery nights ( $F_{5,117}=10.2$ ,  $p<0.001$ ). Nocturnal transportation noise did not  
49 significantly impact polysomnographically assessed sleep macrostructure, blood pressure, nocturnal  
50 catecholamine levels and morning cytokine levels. Evening cortisol levels increased after sleeping  
51 with highly intermittent road noise compared to baseline ( $p=0.002$ , noise effect:  $F_{4,83}=4.0$ ,  $p=0.005$ ), a  
52 result related to increased cumulative duration of autonomic arousals during the noise nights  
53 ( $F_{5,106}=3.4$ ,  $p<0.001$ ; correlation:  $r_{\text{pearson}}=0.64$ ,  $p=0.006$ ).

**54 Conclusion**

55 Under controlled laboratory conditions, highly intermittent nocturnal road noise exposure at 45dB  
56 increased the cumulative duration of autonomic arousals during sleep and next-day evening cortisol  
57 levels. Our results indicate that, without impairing sleep macrostructure, nocturnal transportation  
58 noise of 45dB is a physiological stressor that affects the hypothalamic-pituitary-adrenal axis during  
59 the following day in healthy young good sleepers.

60

61 **Keywords** Traffic noise, Intermittency, Blood pressure, Heart rate variability, Stress hormones,  
62 Inflammation

63

64

65

**66 INTRODUCTION**

67 Epidemiological evidence for harmful effects of transportation noise on the cardiovascular system is  
68 rapidly growing (1). Populations exposed to high levels of noise from roads, railways or airports are at  
69 higher risk for cardiovascular diseases (1), also when adjusting for air pollution (2). It is assumed that  
70 acute exposure to noise activates the two main stress pathways, the sympatho-adrenal-medullary  
71 pathway and the hypothalamic–pituitary–adrenal axis (3). In response to an acute stressor, the  
72 sympatho-adrenal-medullary axis is activated and releases catecholamines while the hypothalamic–  
73 pituitary–adrenal axis sustains the response via the secretion of glucocorticoids (e.g. cortisol) (4). The  
74 repetitive activation of these two stress pathways may lead to higher blood pressure (BP),  
75 dyslipidemia, impaired glucose regulation, altered heart rate variability (HRV) or even endothelial  
76 dysfunction through induction of oxidative stress and vascular inflammation (5); all of these  
77 conditions may contribute to the development of cardiovascular diseases.

78 Nocturnal hours are particularly relevant for transportation noise induced cardiovascular diseases  
79 and mortality (6, 7). Noise may disturb sleep and impair its restorative function on the stress system  
80 (8). Therefore, several field and laboratory studies investigated the effect of nocturnal transportation  
81 noise on sleep or cardiovascular outcomes (9-13). To our best knowledge, the potential role of  
82 polysomnographically assessed sleep variables as a proxy of the effect of nocturnal transportation  
83 noise on both stress pathways has not yet been investigated together in a single setting. Thus, our  
84 combined analysis aimed at obtaining an overall picture of the nocturnal noise-cardiovascular  
85 impairment pathway.

86 Here, we explored the impact of short-term effects of nocturnal transportation noise exposure on  
87 sleep and cardiovascular outcomes. The main goal was to determine the role of sleep, and more  
88 precisely of cortical and autonomic arousals (CA and AA, respectively), in the complex noise-  
89 cardiovascular system pathway. We hypothesized that nocturnal transportation noise exposure  
90 deteriorates sleep by increasing CA and AA, impairing hemodynamic variables (heart rate (HR) and  
91 BP), increasing sympathetic or decreasing parasympathetic nervous activity and increasing nocturnal  
92 catecholamine levels. Additionally, daytime cortisol levels and inflammatory markers were expected  
93 to increase after nocturnal noise exposure. Since our noise scenarios differed according to their  
94 intermittency ratio (IR), a new acoustical metric that has been recently associated with arterial  
95 stiffness, glucose tolerance and cardiovascular mortality (14-16), we hypothesized that higher IR  
96 would have a stronger impact on the above mentioned outcomes than scenarios with lower IR.

97

98

99 **METHODS**100 **Study participants**

101 Participants were healthy non-smokers free of any medication as assessed by the clinical history,  
102 physical examination, routine blood and toxicological urine screening. Participants habitually slept 7  
103 to 9 hours per night and reported good sleep quality (Pittsburgh Sleep Quality Index, (17) PSQI  $\leq$  5)  
104 and no daytime sleepiness (Epworth Sleepiness Scale, (18) ESS  $\leq$  10). Volunteers with sleep disorders  
105 (diagnosed during an adaptation night), shift work, extreme chronotypes (Munich Chronotype  
106 Questionnaire, [34] MCTQ  $<$  2 or MCTQ  $\geq$  7) or hearing loss were excluded. Noise sensitivity was  
107 assessed using the short version of the German *Lärmempfindlichkeitsfragebogen* (LEF-K) (19) and the  
108 *Noise Sensitivity Questionnaire* (NoiSeQ) (20) but was not part of the selection criteria.

109 All participants gave written informed consent. The protocol was approved by the local ethics  
110 committee (EKNZ/Ethikkommission Nordwest- und Zentralschweiz, Switzerland), and conformed to  
111 the Declaration of Helsinki.

112

113 **Procedure**

114 One week prior to the study, participants were asked to follow their habitual bedtimes within  $\pm$  30  
115 minutes, spending 8 hours in bed and not taking naps. Compliance was assessed via actigraphy  
116 (Actiwatch L, Cambridge Neurotechnologies, Cambridge, UK). Additionally, participants were asked  
117 to avoid stimulating substances (coffee, tea, chocolate) and alcohol.

118 Participants spent five consecutive 24-h days and one last morning in the laboratory in individual  
119 windowless and soundproof bedrooms. Two identical bedrooms were specially equipped for this  
120 study design with loudspeakers and microphones to playback the noise scenarios over the night  
121 period. Light intensity during the daytime was kept constant (between 50 and 150 lux at participant's  
122 eye) and room temperature was set at 22°C. Participants had an 8-h sleep opportunity per night  
123 scheduled at their habitual bedtimes. The study protocol is illustrated in Figure 1.

124

125 **Nocturnal noise exposure**

126 Noise exposure characteristics were extensively described in previous publications with this dataset  
127 (15, 21). In short, all participants started and ended the study respectively with a baseline and a  
128 recovery night during which a quiet ambient scenario (30-Ambient-IR30) was applied to reproduce a  
129 tilted window situation (Figure 1). In between, participants were randomly exposed to four different  
130 noise scenarios which had eight identical hourly equivalent continuous sound pressure levels  
131 ( $L_{Aeq,1h}=45$ dB at the ear of the sleeper) during lights-OFF to lights-ON. The noise scenarios differed  
132 with respect to the noise source (road or railway) and IR, a metric which describes the share of  
133 individual noise events compared to the overall sound exposure (22) - for details see Table 1. During  
134 the last morning of the study, participants were asked to retrospectively evaluate noise annoyance

135 during each night on a scale of 0 to 100 with the question “How annoyed were you during the night  
136 by the noise”?

### 137 **Sleep measurement**

138 *Subjective sleep quality* was assessed 5-10 min upon awakening with the LEEDS Sleep Evaluation  
139 Questionnaire (23).

140 *Polysomnographic sleep recordings* (PSG) included 12 electroencephalographic, 2 electro-  
141 oculographic and 2 electromyographic derivations (Vitaport-3 digital recorder). Rapid eye movement  
142 (REM) and Non-REM (NREM1, NREM2 and low wave sleep) sleep, sleep efficiency (percentage of  
143 total sleep time (TST: time spent in REM and Non-REM sleep) between lights-OFF and lights-ON),  
144 sleep latency (time between lights-OFF and NREM2 onset) and CA were scored according to standard  
145 criteria (24). Further details on sleep measurements are described in (21).

### 146 **Salivary cortisol**

147 Saliva samples were obtained every 30 min during the first 3h after wake-up, 4h30 before lights-OFF  
148 and every 2h in-between. Samples were kept at -20°C until assay. Cortisol was measured using a  
149 direct salivary enzyme-linked immunosorbent assay (ELISA) with a limit of sensitivity of 1.0 ng/mL  
150 and a mean intra-assay coefficient of variation (CV) <10% (ALPCO Diagnostics, Salem, NH, USA).  
151 Cortisol awakening response was calculated as the absolute change between the first and the second  
152 morning sample (25). The daytime trend in salivary cortisol was quantified using the best-fit curve  
153 based on periodogram calculations (26). The rate of decrease of the cortisol profile was calculated as  
154 the absolute change “acrophase–nadir” divided by the time interval. The area under the curve during  
155 the last 2h before lights-OFF was calculated to assess evening cortisol levels.

156

### 157 **Urinary catecholamines**

158 Before bedtime, participants were instructed to use the toilet. Overnight urine was then collected  
159 until wake-up time in an acidified urine container (HCL 5M, pH<4.0). The light-protected samples  
160 were stored at -80°C until analysis. The catecholamines, epinephrine and norepinephrine, were  
161 measured by high-performance liquid chromatography (Recipe, Munich, Germany). Epinephrine and  
162 norepinephrine concentrations were normalized to creatinine, assessed in the same samples (Roche  
163 / Hitachi cobas c systems) with a limit of sensitivity of 100 µmol/L.

164

### 165 **Serum inflammatory markers**

166 A fasting blood sample was obtained one hour after scheduled wake-up time following baseline, the  
167 last noise night (NN5) and recovery nights. Serum was obtained after 30 min clotting at room  
168 temperature and centrifugation at 4°C for 10 min at 3500rpm. IL-6, TNFα, adiponectin and CRP were  
169 measured by a commercially available multiplex beads immunoassay with intra-assay CV <8%

170 (Luminex Performance assay, Human Obesity Panel, R&D Systems, Minneapolis, USA). Leptin was  
171 measured with an ELISA test (11-LEPHU-E01) with a limit of detection of 0.50 ng/mL and an intra-  
172 assay CV <5.5%.

173

#### 174 **Heart rate variability (HRV)**

175 An electrocardiogram was recorded continuously throughout the laboratory study. Data acquisition  
176 and post-acquisition analyses were carried out in accordance with established standards (27).  
177 Accordingly, analyses were carried out on the shortest time window, i.e. 5 min, over the 8h sleep  
178 opportunity. Segments occurring during more than 2.5 min of wakefulness were excluded. Heart rate  
179 was derived from the mean normal beat-to-beat interval (N-N,  $HR=60/N-N$ ). Global HRV was  
180 obtained from the standard deviation over the whole time series (SDNN) and vagal activity was  
181 indirectly measured with the root mean square of successive N-N intervals (RMSSD) and the  
182 percentage of N-N interval differences greater than 50 ms (pNN50). Spectral analysis was based on  
183 the Fast Fourier transform with low-frequency (LF, 0.04-0.15 Hz) and high-frequency (HF, 0.15-0.50  
184 Hz) bands. The frequency bands were normalized ( $LFn=LF/(LF+HF)$  and  $HFN=HF/(HF+LF)$ ). HF reflects  
185 modulation of vagal activity by respiration while LF represents vagal and sympathetic activity and  
186 LF/HF is an index of sympatho-vagal balance (28).

187

#### 188 **Blood pressure**

189 Nocturnal BP was obtained and analyzed every second from lights-OFF to lights-ON with the  
190 validated cuffless continuous BP monitor SOMNOtouch™ NIBP (SOMNOmedics, Randersacker,  
191 Germany) which derives systolic and diastolic BP levels from pulse transit time (29).

192

#### 193 **Autonomic arousals (AA)**

194 AA, defined as sudden increase in HR followed by a return to initial values, were detected using  
195 Somno-Art technology, based on an algorithm by Muzet et al. (30). The algorithm used 1Hz HR and  
196 1Hz wrist actimetry obtained from the SOMNOtouch™ device. AA were detected and quantified as  
197 changes in the steady state of average HR to higher or lower values and were often co-occurring with  
198 body movements. AA occurring during wakefulness were excluded.

199

200

#### 201 **Statistical analysis**

202 Statistical analyses were performed using the SAS statistical software package (SAS Institute Inc.,  
203 Cary, NC; version 9.4). Mixed model analyses of variance were carried out for each outcome variable  
204 separately and included the repeated within-subject factor “scenario” (baseline, 45-Motorway-IR30,  
205 45-Road-IR70, 45-Urban-street-IR80, 45-Railway-IR90, recovery) and the random factor “subject”  
206 with a variance component covariance structure. Contrasts were assessed with the LSMEAN

207 statement and p-values were based on Kenward-Roger's corrected degrees of freedom (31). Multiple  
208 post-hoc comparisons were corrected using the Tukey-Kramer method. Data were log-transformed  
209 when residuals were not normally distributed. Correlations were calculated with the Pearson or  
210 Spearman correlation coefficient, as appropriate. Correlation outliers were detected and removed  
211 according to the absolute deviation around the median (32). Data are presented as mean  $\pm$  standard  
212 error (SE) and statistical significance was set at  $p < 0.05$ . Although two men quit the study on the fifth  
213 day for personal reasons, their data were included in the analysis. For all women, except two, the  
214 entire lab protocol was conducted during the follicular phase; the two remaining women did not  
215 impact the statistical significances. Missing values, due to technical reasons are summarized in a  
216 supplementary table, as well as the exact number of individuals and samples for each variable (Table  
217 A).

218

## 219 RESULTS

220 Twenty-six young lean volunteers (12 women,  $24.6 \pm 0.69$  yrs, BMI:  $22.2 \pm 0.41$  kg/m<sup>2</sup>) participated in  
221 the study. Participants were good sleepers (baseline sleep efficiency=  $93.9 \pm 0.86$  %) and not noise  
222 sensitive (LEF-K= $11.0 \pm 0.79$ , NoiseQ= $1.29 \pm 0.08$ ).

223

### 224 1. Sleep and cardiovascular diseases markers during nocturnal noise exposure

225 Noise annoyance and sleep variables upon the different noise scenarios are illustrated in Figure 2.  
226 Participants were more annoyed by the transportation noise than by the quiet ambient baseline and  
227 recovery scenario. The quality of sleep was perceived as better during recovery compared to 45-  
228 Motorway-IR30 and 45-Road-IR70. No significant changes in objective sleep efficiency and the  
229 amount slow wave sleep could be observed between the different noise scenarios. Participants took  
230 longer to fall asleep during recovery compared to the other nights. The number of CA and AA were  
231 not different between the noise scenarios. However, the mean duration of AA was higher during 45-  
232 Railway-IR90 and recovery compared to baseline and cumulative duration of AA was higher during  
233 45-Motorway-IR30, 45-Urban-street-IR80 and recovery compared to baseline.

234

235 Nocturnal mean HR and systolic BP were not affected by the exposure to transportation noise  
236 scenarios (Table 2). Nevertheless, mean overnight diastolic BP was higher during baseline than during  
237 45-Motorway-IR30 ( $p=0.01$ ) and 45-Urban-street-IR80 ( $p=0.0004$ ). SDNN increased significantly  
238 during 45-Railway-IR90 compared to baseline ( $p=0.02$ ) but pN50 and RMSSD did not differ between  
239 the nights. Spectral analysis of the full-night HRV yielded no differences in LFn and HFn powers nor in

240 LF/HF ratio. No correlation between diastolic BP or mean SDNN and the above mentioned sleep  
241 variables were observed except for the relative change between baseline and 45-Railway-IR90 in  
242 mean SDNN and the number AA per hour TST ( $r_{\text{pearson}}=0.77$ ,  $p<0.01$ ). Creatinine normalized nocturnal  
243 urinary epinephrine ( $F_{5,74}=0.52$ ,  $p=0.76$ ) and norepinephrine ( $F_{5,77}=1.7$ ,  $p=0.14$ ) concentrations were  
244 not affected by the noise exposure (Table B).

245

## 246 **2. Cardiovascular diseases markers following nocturnal noise exposure**

247

248 Morning cytokines IL-6 ( $F_{2,44}=2.24$ ,  $p=0.12$ ), TNF $\alpha$  ( $F_{2,42}=1.33$ ,  $p=0.28$ ), CRP ( $F_{2,44}=0.86$ ,  $p=0.43$ ) and the  
249 adipokines adiponectin ( $F_{2,44}=1.77$ ,  $p=0.18$ ) and leptin ( $F_{2,42}=1.64$ ,  $p=0.21$ ) were not affected by  
250 nocturnal noise exposure (Table C).

251 Diurnal cortisol profiles are illustrated in Figure 3. The rate of decrease of the cortisol profile was not  
252 significantly altered by the preceding noise exposure ( $F_{4,95}=0.36$ ,  $p=0.84$ ). Cortisol awakening  
253 response tended to be marginally higher after sleeping with 45-Railway-IR90 compared to baseline  
254 ( $p=0.08$ ) and 45-Road-IR70 ( $p=0.09$ , Figure 3). Evening cortisol levels were higher after sleeping with  
255 45-Urban-street-IR80 compared to baseline ( $p=0.002$ , Figure 3). The percentage increase in evening  
256 cortisol between baseline and 45-Urban-street-IR80 was correlated with the percentage increase in  
257 cumulative duration of AA (Figure 4).

258

## 259 **DISCUSSION**

260 We aimed at determining the importance of sleep alterations as a potential mediating factor of  
261 nocturnal transportation noise related cardiovascular impairments. Additionally, we examined  
262 whether the IR is an acoustical marker for transportation noise effects on cardiovascular functions.

### 263 **Effect of nocturnal transportation noise on sleep and nocturnal cardiovascular markers**

264 In contrast to the subjective feeling of a better recovery night, sleep macrostructure and the amount  
265 of cortical arousals (CA) were not affected by noise exposure. CA are usually accompanied by  
266 autonomic arousals (AA) but the reverse is not true (33). AA are good candidates for promoting  
267 nocturnal transportation noise induced cardiovascular diseases (12, 34). While we did not find more  
268 AA compared to baseline, the mean duration was higher for 45-Railway-IR90 and total duration was  
269 higher during the noise nights 45-Motorway-IR30, 45-Urban-street-IR80 and recovery. Surprisingly,  
270 full-night spectral analysis of HRV reflected no changes in autonomic nervous activity, probably this  
271 analysis is less sensitive to detect subtle short-term changes. Catecholamines are also important

272 markers of sympathetic activity. The effect of nocturnal transportation noise on these hormones are  
273 mixed: one laboratory study found higher overnight urinary levels (35), while others did not (13, 36).  
274 Again, full-night values are possibly too rough to detect subtle acute variations. Global HRV obtained  
275 from SDNN increased during the exposure to 45-Railway-IR90 compared to the baseline. Low HRV  
276 has been associated with increased risk of a first cardiovascular event (37). However, increased  
277 variability also mirrors the increase in AA, as the relative change from baseline to 45-Railway-IR90 of  
278 SDNN was positively correlated with the number of AA. Nocturnal mean HR and BP were not  
279 significantly different during the exposure to various transportation noise scenarios, a result  
280 consistent with Schmidt et al. (9). Haralabidis (10) reported an increase in BP but it was minor with  
281 only +0.81 mmHg per 5dB increase in  $L_{Amax,indoor}$  road noise for systolic BP.

### 282 **Effect of nocturnal transportation noise exposure on diurnal cortisol levels**

283 Using 20 saliva samples per day, we were able to quantify the circadian baseline secretion profile  
284 with a peak level in the morning, followed by a decline over the day to reach minimum levels in the  
285 late evening (38). The rate of decrease of the cortisol profile was not changed after sleeping with  
286 transportation noise. In accordance with previous studies (11, 39), cortisol awakening response was  
287 not affected by nocturnal transportation noise exposure. Based on sleep deprivation studies, evening  
288 hours may be a more critical time window for noise induced hypothalamic–pituitary–adrenal axis  
289 dysregulation (40, 41). Lefèvre et al. (42) reported an increase in the field, and our laboratory study  
290 confirms this finding with increased evening cortisol after sleeping with 45-Urban-street-IR80  
291 compared to baseline. Moreover, this increase correlated with the increase in the cumulative  
292 duration of AA revealing the role of subcortical activation in the noise-stress response pathway of  
293 sleeping individuals.

### 294 **Limitations**

295 The laboratory study strictly controlled possible confounders such as sleep duration, caloric intake,  
296 light exposure and physical activity. Even though participants had an adaptation night in the  
297 laboratory prior to the study, the unusual environment while wearing various devices could have led  
298 to the so-called “first-“ or “last night effect”. This could explain the lack of changes in sleep variables,  
299 longer sleep latency during recovery and higher diastolic BP during baseline compared to the other  
300 nights. Moreover, participants arrived to the lab on the day of the baseline night without controlling  
301 daytime transportation noise exposure which may also impact the variables explored here. Taking  
302 into consideration the effect observed in our study, we would recommend future studies to add a  
303 supplemental wash-out night before the baseline night. We studied a low-risk population (non-noise  
304 sensitive healthy good sleepers) which is not representative of the overall population. Finally, the

305 level of  $L_{Aeq,indoor}=45\text{dB}$  corresponding to  $L_{Aeq,outdoor}=60\text{dB}$  for a tilted window (43) may not have been  
306 high enough to elicit strong acute health effects.

### 307 **Summary and conclusion**

308 To the best of our knowledge, this is the first study integrating polysomnographically assessed sleep  
309 variables, autonomic arousals (AA), stress hormones, hemodynamic, HRV and inflammatory markers  
310 under controlled laboratory conditions. The exposure to nocturnal transportation noise, which was  
311 perceived as more annoying than the quiet ambient baseline and recovery nights, had no effect on  
312 sleep macrostructure, nocturnal mean HR, BP and catecholamine levels and did not lead to  
313 inflammation in young healthy adults. Nevertheless, the cumulative duration of AA increased during  
314 the highly intermittent road noise scenario and was correlated with the increase in next evening  
315 cortisol level. This result confirms previous studies that indicated that a low  $L_{Aeq} (\leq 45\text{dB})$  nocturnal  
316 noise might affect the cardiovascular function by a subcortical activation (12, 34). Thus,  
317 cardiovascular outcomes are sensitive markers for the very early negative impact of nocturnal  
318 transportation noise before cortical sleep alterations may occur.

319

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326

### 327 **Author contributions**

328 L.T., F.R., K.S., R.L., R.P., J.M.W., M.F., D.V., M.B., N.P.-H., M.R., C.C. conceived the study design; L.T.,  
329 F.R., C.G. collected the data; R.P. created and analyzed the acoustical stimuli; L.T., F.R., J.K., R.L., K.S.,  
330 C.C. analyzed the data; L.T., F.R., J.K., N.W., K.S., R.L., R.P., J.M.W., M.F., H.H., I.C.E., D.V., C.G., M.B.,  
331 N.P.-H., M.R., C.C. prepared the manuscript and approved the final submitted version.

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458 **Tables:**

Scenario	Source	$L_{Aeq,1h}$ [dB]	$L_{AFmax}$ [dB]	IR
30-Ambient-IR30	ambient	30	39	0.3
45-Motorway-IR30	road	45	53	0.3
45-Road-IR70	road	45	60	0.7
45-Urban-street-IR80	road	45	62	0.8
45-Railway-IR90	rail	45	62	0.9

459 **Table 1.** Acoustical characteristics of the noise scenarios. 30-Ambient-IR30 represents the quiet ambient  
 460 scenario of the baseline and recovery nights. The four transportation noise scenarios were randomly  
 461 introduced during the noise nights.  $L_{Aeq,1h}$ : equivalent continuous sound level,  $L_{AFmax}$ : maximum sound level, IR:  
 462 intermittency ratio (22).

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	Baseline	45-Motorway-IR30	45-Road-IR70	45-Urban-street-IR80	45-Railway-IR90	Recovery	Main effect P-value
<b>Hemodynamic variables</b>							
HR (bpm)	56.24 ± 1.34	55.00 ± 1.19	54.79 ± 1.24	54.77 ± 1.37	55.87 ± 1.41	55.61 ± 1.39	0.24
Systolic BP (mmHg)	115 ± 2.54	110 ± 2.39	111 ± 2.23	109 ± 2.37	109 ± 2.43	107 ± 3.79	0.16
Diastolic BP (mmHg)	72 ± 1.41	66 ± 1.76 *	69 ± 1.54	65 ± 1.69 *	69 ± 1.28	68 ± 1.61	0.001
<b>Time domain analysis</b>							
pNN50 (%)	47 ± 3	47 ± 3	46 ± 3	48 ± 3	48 ± 3	46 ± 3	0.43
SDNN (ms)	97.4 ± 4.20	99.8 ± 3.99	98.6 ± 4.43	103 ± 4.88	104 ± 5.35 *	97.4 ± 4.49	0.01
RMSSD (ms)	79.7 ± 5.00	79.5 ± 5.03	78.1 ± 4.85	82.0 ± 5.34	86.0 ± 6.55	77.8 ± 5.71	0.12
<b>Spectral analysis</b>							
LFn (ms <sup>2</sup> )	0.55 ± 0.020	0.57 ± 0.023	0.57 ± 0.023	0.57 ± 0.022	0.57 ± 0.023	0.56 ± 0.026	0.61
HF <sub>n</sub> (ms <sup>2</sup> )	0.45 ± 0.020	0.43 ± 0.023	0.43 ± 0.023	0.43 ± 0.022	0.43 ± 0.02	0.44 ± 0.026	0.55
LF/HF (ms <sup>2</sup> )	1.79 ± 0.19	2.22 ± 0.35	2.08 ± 0.26	2.07 ± 0.30	2.11 ± 0.32	2.02 ± 0.28	0.35

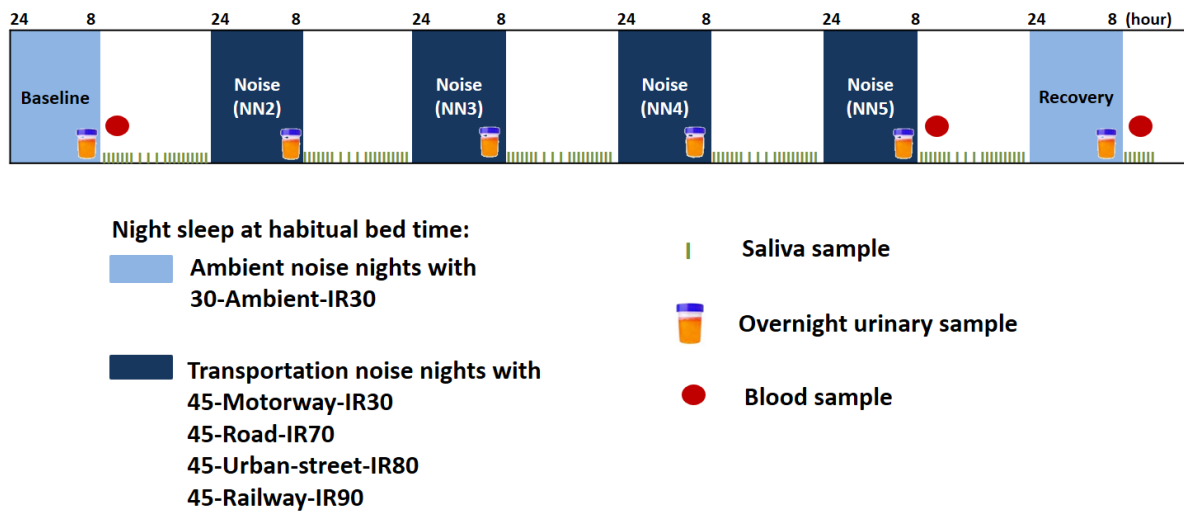
464 **Table 2.** Overnight hemodynamic and heart rate variability variables. Baseline and recovery were nights with a  
 465 quiet ambient scenario exposure, while night 45-Motorway-IR30, 45-Road-IR70, 45-Urban-street-IR80 and 45-  
 466 Railway-IR90 were transportation noise exposed nights. Mean ± SE. P-value corresponds to the main effect,  
 467 while asterisks \*(p<0.05) represent significance of post-hoc analyses in comparison to the baseline night. HR:  
 468 heart rate, BP: blood pressure, pNN50: percentage of N-N interval differences greater than 50 ms, SDNN:  
 469 standard deviation of successive N-N intervals, RMSSD: root mean square of successive N-N intervals, LFn:  
 470 normalized low frequency, HF<sub>n</sub>: normalized high frequency.

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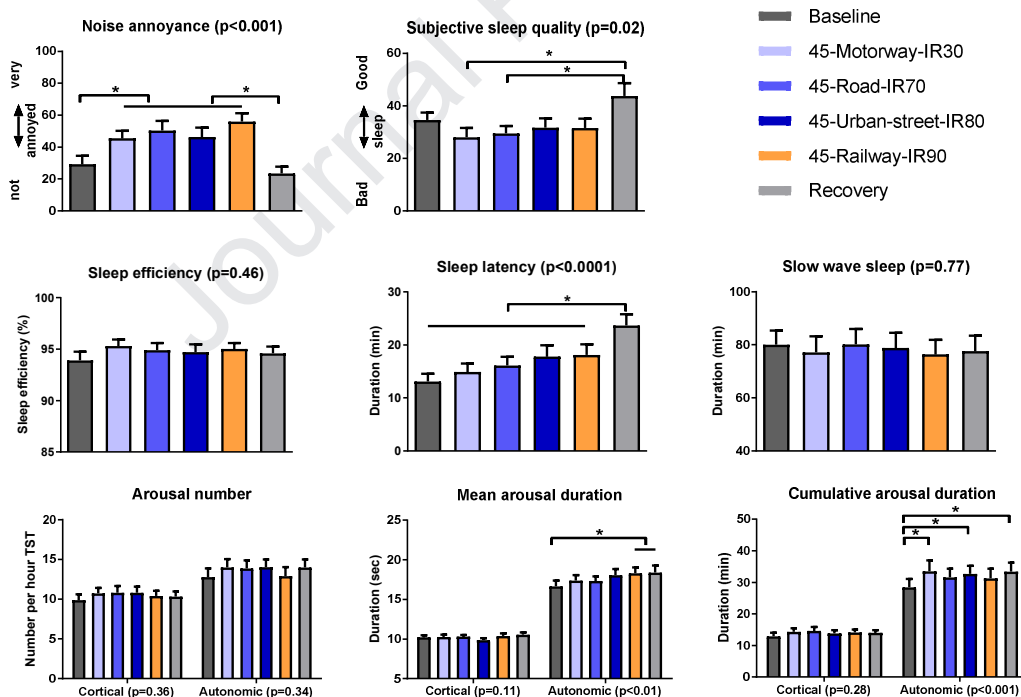
473 **Figures:**

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476 **Figure 1.** Schematic illustration of the study protocol. Time in bed was scheduled according to each  
 477 participant's habits (e.g. 24-8h). The order of exposure to the four different transportation noise scenarios was  
 478 randomized between participants. Noise scenario= « $L_{Aeq,1h}$ -Noise source-IR (intermittency ratio)».

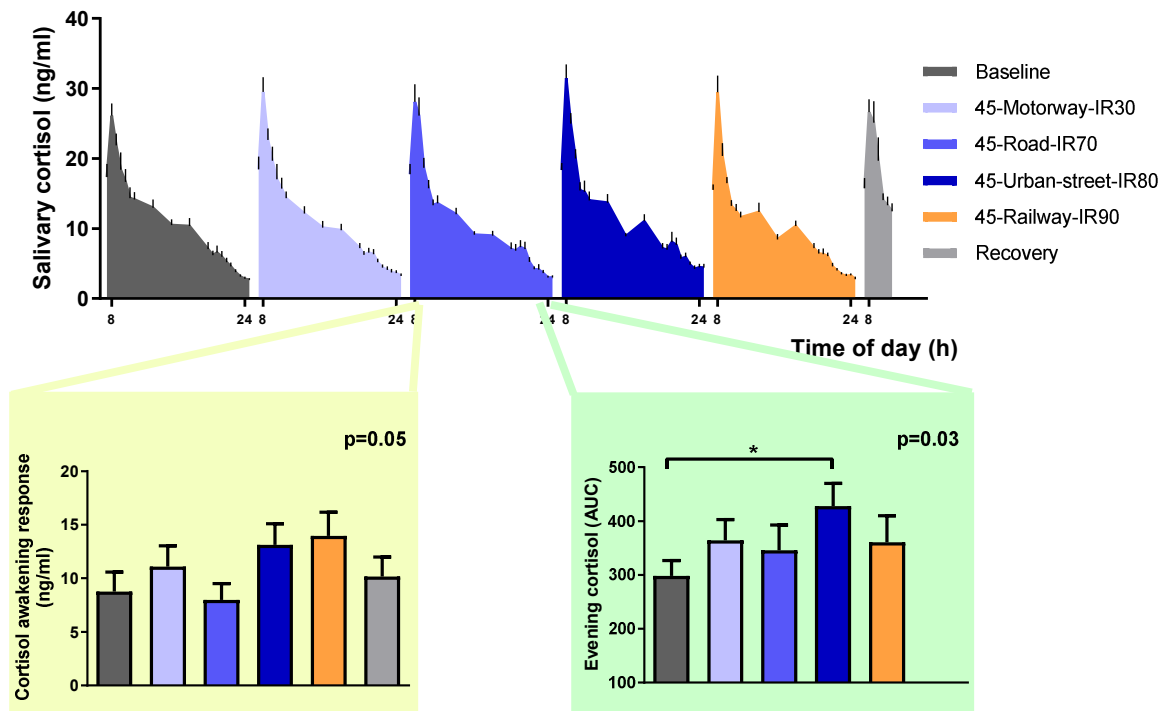


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480 **Figure 2.** Noise annoyance, subjective sleep quality and objective sleep variables for the different noise  
 481 scenarios. Baseline and recovery were nights with a quiet ambient scenario exposure, while night 45-  
 482 Motorway-IR30, 45-Road-IR70, 45-Urban-street-IR80 and 45-Railway-IR90 were transportation noise exposed  
 483 nights. TST: total sleep time. P-values indicate the noise effect, and asterisks significances at p<0.05.

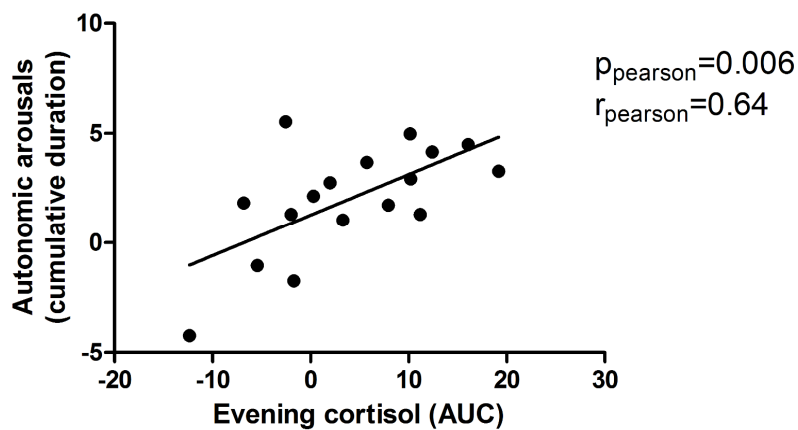
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487 **Figure 3.** Upper panel: Diurnal salivary cortisol profiles. Lower panel: Cortisol awakening responses and evening  
 488 cortisol levels after sleeping with different noise scenarios. Baseline and recovery after sleeping with the quiet  
 489 ambient scenario; 45-Motorway-IR30, 45-Road-IR70, 45-Urban-street-IR80 and 45-Railway-IR90 after sleeping  
 490 with the corresponding noise scenario. AUC: Area under the curve. Mean  $\pm$  SE.



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492 **Figure 4.** Relative change in cumulative duration of autonomic arousals (AA) during sleep and next-day evening  
 493 cortisol between baseline and 45-Urban-street-IR80 noise scenario.

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**Highlights:**

- Nocturnal transportation noise does not affect sleep macrostructure of healthy subjects
- Blood pressure, catecholamines and cytokines are not impacted by noise exposure
- Sleeping with highly intermittent road noise increases evening cortisol levels
- The increase in cortisol is related to longer autonomic arousals during sleep

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**Declaration of interests**

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

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: