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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 ± 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, TNF α , 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 ± 0.69 yrs, BMI: 22.2 ± 0.41 kg/m²) participated in
221 the study. Participants were good sleepers (baseline sleep efficiency= 93.9 ± 0.86 %) and not noise
222 sensitive (LEF-K= 11.0 ± 0.79 , NoiseQ= 1.29 ± 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 α ($F_{2,42}=1.33$, $p=0.28$), 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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336 REFERENCES

- 337 1. Kempen EV, Casas M, Pershagen G, Foraster M. WHO Environmental Noise
338 Guidelines for the European Region: A Systematic Review on Environmental Noise and
339 Cardiovascular and Metabolic Effects: A Summary. *International journal of environmental
340 research and public health.* 2018;15(2).
- 341 2. Stansfeld SA. Noise Effects on Health in the Context of Air Pollution Exposure.
342 *International journal of environmental research and public health.* 2015;12(10):12735-60.
- 343 3. Munzel T, Sorensen M, Gori T, Schmidt FP, Rao X, Brook FR, et al. Environmental
344 stressors and cardio-metabolic disease: part II-mechanistic insights. *European heart journal.*
345 2017;38(8):557-64.
- 346 4. Aich P, Potter AA, Griebel PJ. Modern approaches to understanding stress and
347 disease susceptibility: A review with special emphasis on respiratory disease. *Int J Gen Med.*
348 2009;2:19-32.
- 349 5. Munzel T, Schmidt FP, Steven S, Herzog J, Daiber A, Sorensen M. Environmental
350 Noise and the Cardiovascular System. *Journal of the American College of Cardiology.*
351 2018;71(6):688-97.
- 352 6. Heritier H, Vienneau D, Foraster M, Eze IC, Schaffner E, Thiesse L, et al. Diurnal
353 variability of transportation noise exposure and cardiovascular mortality: A nationwide
354 cohort study from Switzerland. *Int J Hyg Environ Health.* 2018;221(3):556-63.
- 355 7. Jarup L, Babisch W, Houthuijs D, Pershagen G, Katsouyanni K, Cadum E, et al.
356 Hypertension and exposure to noise near airports: the HYENA study. *Environ Health
357 Perspect.* 2008;116(3):329-33.
- 358 8. Cappuccio FP, Miller MA. Sleep and Cardio-Metabolic Disease. *Current cardiology
359 reports.* 2017;19(11):110.
- 360 9. Schmidt FP, Basner M, Kroger G, Weck S, Schnorbus B, Muttray A, et al. Effect of
361 nighttime aircraft noise exposure on endothelial function and stress hormone release in
362 healthy adults. *European heart journal.* 2013;34(45):3508-14a.
- 363 10. Haralabidis AS, Dimakopoulou K, Vigna-Taglianti F, Giampaolo M, Borgini A, Dudley
364 ML, et al. Acute effects of night-time noise exposure on blood pressure in populations living
365 near airports. *European heart journal.* 2008;29(5):658-64.
- 366 11. Griefahn B, Robens S. Experimental studies on the effects of nocturnal noise on
367 cortisol awakening response. *Noise & health.* 2010;12(47):129-36.
- 368 12. Basner M, Muller U, Elmenhorst EM. Single and combined effects of air, road, and
369 rail traffic noise on sleep and recuperation. *Sleep.* 2011;34(1):11-23.
- 370 13. Carter NL, Hunyor SN, Crawford G, Kelly D, Smith AJ. Environmental noise and
371 sleep--a study of arousals, cardiac arrhythmia and urinary catecholamines. *Sleep.*
372 1994;17(4):298-307.
- 373 14. Foraster M, Eze IC, Schaffner E, Vienneau D, Héritier H, Endes S, et al. Exposure to
374 Road, Railway, and Aircraft Noise and Arterial Stiffness in the SAPALDIA Study: Annual
375 Average Noise Levels and Temporal Noise Characteristics. *Environ Health Perspect.*
376 2017;125(9):097004.
- 377 15. Thiesse L, Rudzik F, Spiegel K, Leproult R, Pieren R, Wunderli JM, et al. Adverse
378 impact of nocturnal transportation noise on glucose regulation in healthy young adults:
379 Effect of different noise scenarios. *Environment International.* 2018.
- 380 16. Heritier H, Vienneau D, Foraster M, Eze IC, Schaffner E, Thiesse L, et al.
381 Transportation noise exposure and cardiovascular mortality: a nationwide cohort study from
382 Switzerland. *European journal of epidemiology.* 2017;32(4):307-15.
- 383 17. Buysse DJ, Reynolds CF, 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep
384 Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.*
385 1989;28(2):193-213.
- 386 18. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness
387 scale. *Sleep.* 1991;14(6):540-5.
- 388 19. Zimmer K, Ellermeier W. Ein Kurzfragebogen zur Erfassung der
389 Lärmempfindlichkeit. . *Umweltpsychologie* 2(2), 54-63. 1998.

- 390 20. Schutte M, Marks A, Wenning E, Griefahn B. The development of the noise sensitivity
391 questionnaire. *Noise & health*. 2007;9(34):15-24.
- 392 21. Rudzik F, Thiesse L, Pieren R, Wunderli JM, Brink M, Foraster M, et al. Sleep spindle
393 characteristics and arousability from nighttime transportation noise exposure in healthy
394 young and older individuals. *Sleep*. 2018;41(7):zsy077-zsy.
- 395 22. Wunderli JM, Pieren R, Habermacher M, Vienneau D, Cajochen C, Probst-Hensch N,
396 et al. Intermittency ratio: A metric reflecting short-term temporal variations of
397 transportation noise exposure. *J Expo Sci Environ Epidemiol*. 2015:1-11.
- 398 23. Parrott AC, Hindmarch I. Factor analysis of a sleep evaluation questionnaire.
399 *Psychological medicine*. 1978;8(2):325-9.
- 400 24. Berry RB, Brooks R, Gamaldo CE, Harding SM, Lloyd RM, Marcus CL, et al. The
401 AASM manual for the Scoring of Sleep and Associated Events v2.3. . Darien, IL: American
402 Academy of Sleep Medicine. 2016.
- 403 25. Pruessner JC, Wolf OT, Hellhammer DH, Buske-Kirschbaum A, Auer K, Jobst S. Free
404 cortisol levels after awakening: a reliable biological marker for the assessment of
405 adrenocortical activity. *Life Sci*. 1997;61.
- 406 26. Van Cauter E. Method for characterization of 24-h temporal variation of blood
407 constituents. *The American journal of physiology*. 1979;237:E255-E64.
- 408 27. HRV. Heart rate variability: standards of measurement, physiological interpretation
409 and clinical use. Task Force of the European Society of Cardiology and the North American
410 Society of Pacing and Electrophysiology. *Circulation*. 1996;93(5):1043-65.
- 411 28. Malliani A, Pagani M, Montano N, Mela GS. Sympathovagal balance: a reappraisal.
412 *Circulation*. 1998;98(23):2640-3.
- 413 29. Bilo G, Zorzi C, Ochoa Munera JE, Torlasco C, Giuli V, Parati G. Validation of the
414 Somnotouch-NIBP noninvasive continuous blood pressure monitor according to the
415 European Society of Hypertension International Protocol revision 2010. *Blood pressure
416 monitoring*. 2015;20(5):291-4.
- 417 30. Muzet A, Werner S, Fuchs G, Roth T, Saoud J, Viola A, et al. Assessing sleep
418 architecture and continuity measures through the analysis of heart rate and wrist movement
419 recordings in healthy subjects: comparison with results based on polysomnography. *Sleep
420 Medicine*. 2016;21:47-56.
- 421 31. Kenward MG, Roger JH. Small sample inference for fixed effects from restricted
422 maximum likelihood. *Biometrics*. 1997;53(3):983-97.
- 423 32. Leys C, Ley C, Klein O, Bernard P, Licata L. Detecting outliers: Do not use standard
424 deviation around the mean, use absolute deviation around the median. *Journal of
425 Experimental Social Psychology*. 2013;49(4):764-6.
- 426 33. Sforza E, Jouny C, Ibanez V. Cardiac activation during arousal in humans: further
427 evidence for hierarchy in the arousal response. *Clinical neurophysiology : official journal of
428 the International Federation of Clinical Neurophysiology*. 2000;111(9):1611-9.
- 429 34. Griefahn B, Brode P, Marks A, Basner M. Autonomic arousals related to traffic noise
430 during sleep. *Sleep*. 2008;31(4):569-77.
- 431 35. Maschke C, Breinl S, Grimm R, Ising H. The influence of nocturnal aircraft noise on
432 sleep and on catecholamine secretion. *Schriftenreihe des Vereins für Wasser-, Boden- und
433 Lufthygiene*. 1993;88:395-407.
- 434 36. Maaß H, Basner M. Effects of nocturnal aircraft noise (Vol. 3): Stress hormones. FB
435 2004-09/E. Cologne: Deutsches Zentrum für Luft- und Raumfahrt. 2006.
- 436 37. Hillebrand S, Gast KB, de Mutsert R, Swenne CA, Jukema JW, Middeldorp S, et al.
437 Heart rate variability and first cardiovascular event in populations without known
438 cardiovascular disease: meta-analysis and dose-response meta-regression. *EP Europace*.
439 2013;15(5):742-9.
- 440 38. Horrocks PM, Jones AF, Ratcliffe WA, Holder G, White A, Holder R, et al. Patterns of
441 ACTH and cortisol pulsatility over twenty-four hours in normal males and females. *Clinical
442 endocrinology*. 1990;32(1):127-34.
- 443 39. Wayne KP, Clow A, Edwards S, Hucklebridge F, Rylander R. Effects of nighttime low
444 frequency noise on the cortisol response to awakening and subjective sleep quality. *Life Sci*.
445 2003;72(8):863-75.

- 446 40. Leproult R, Copinschi G, Buxton O, Van Cauter E. Sleep loss results in an elevation of
447 cortisol levels the next evening. *Sleep*. 1997;20(10):865-70.
- 448 41. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine
449 function. *Lancet*. 1999;354(9188):1435-9.
- 450 42. Lefèvre M, Carlier MC, Champelovier P, Lambert J, Laumon B, Evrard AS. Effects of
451 aircraft noise exposure on saliva cortisol near airports in France. *Occupational and*
452 *environmental medicine*. 2017;74(8):612-8.
- 453 43. Locher B, Piquerez A, Habermacher M, Ragetti M, Roosli M, Brink M, et al.
454 Differences between Outdoor and Indoor Sound Levels for Open, Tilted, and Closed
455 Windows. *International journal of environmental research and public health*. 2018;15(1).

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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).

463

	Baseline	45-Motorway- IR30	45-Road- IR70	45-Urban- street-IR80	45-Railway- IR90	Recovery	Main effect P- value
Hemodynamic variables							
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
Time domain analysis							
pNNS50 (%)	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
Spectral analysis							
LFn (ms ²)	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 _n (ms ²)	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 ²)	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

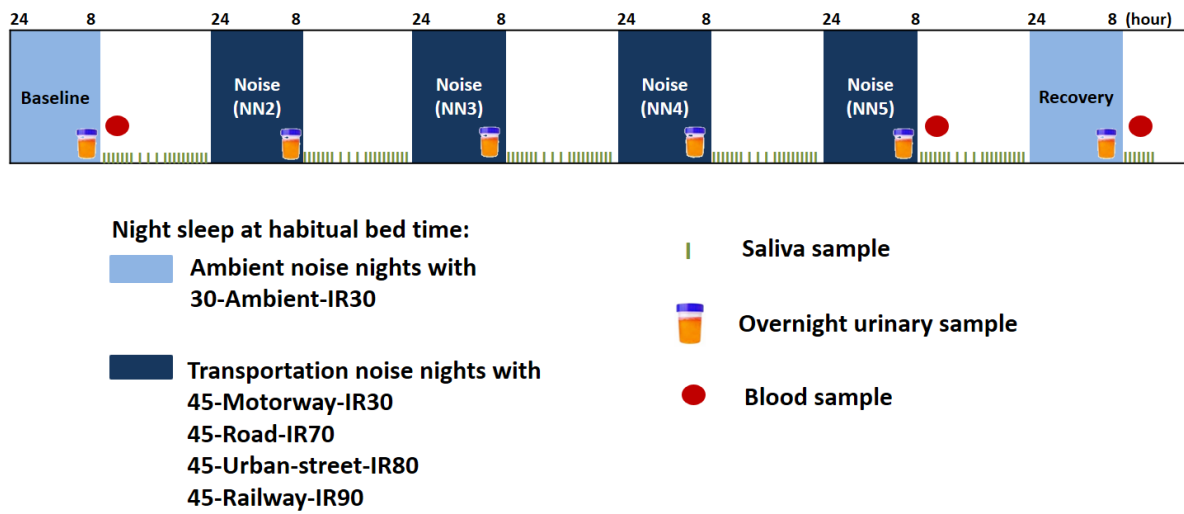
464 **Table 2.** Overnight hemodynamic and heart rate variability variables. Baseline and recovery were nights with a
 465 quiet ambient scenario exposure, while night 45-Motorway-IR30, 45-Road-IR70, 45-Urban-street-IR80 and 45-
 466 Railway-IR90 were transportation noise exposed nights. Mean ± SE. P-value 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, pNNS50: 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_n: normalized high frequency.

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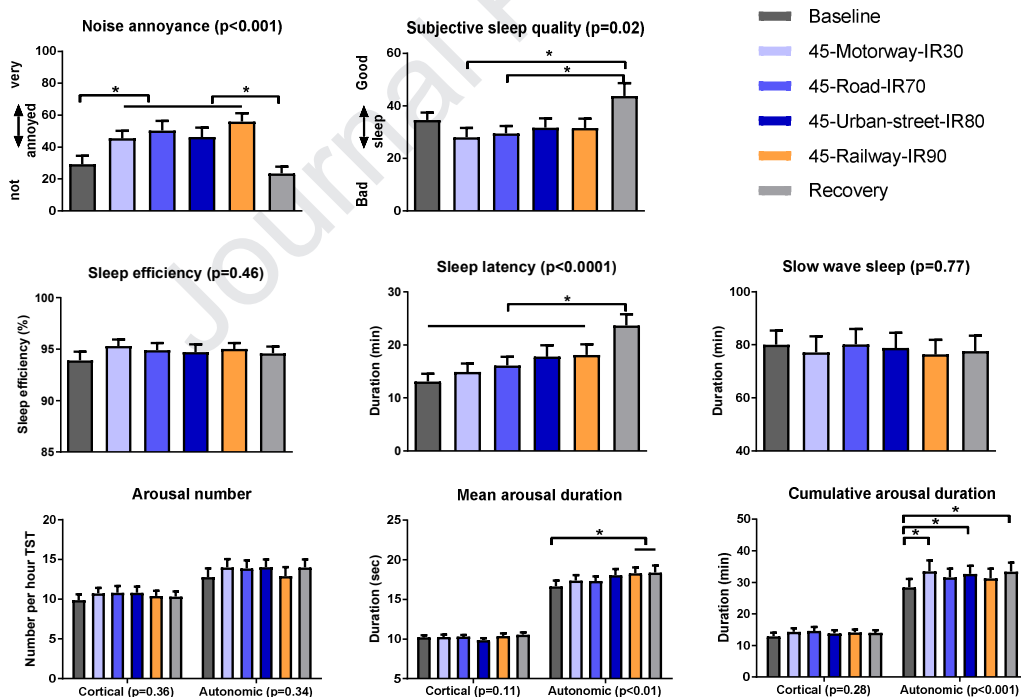
473 **Figures:**

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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)».

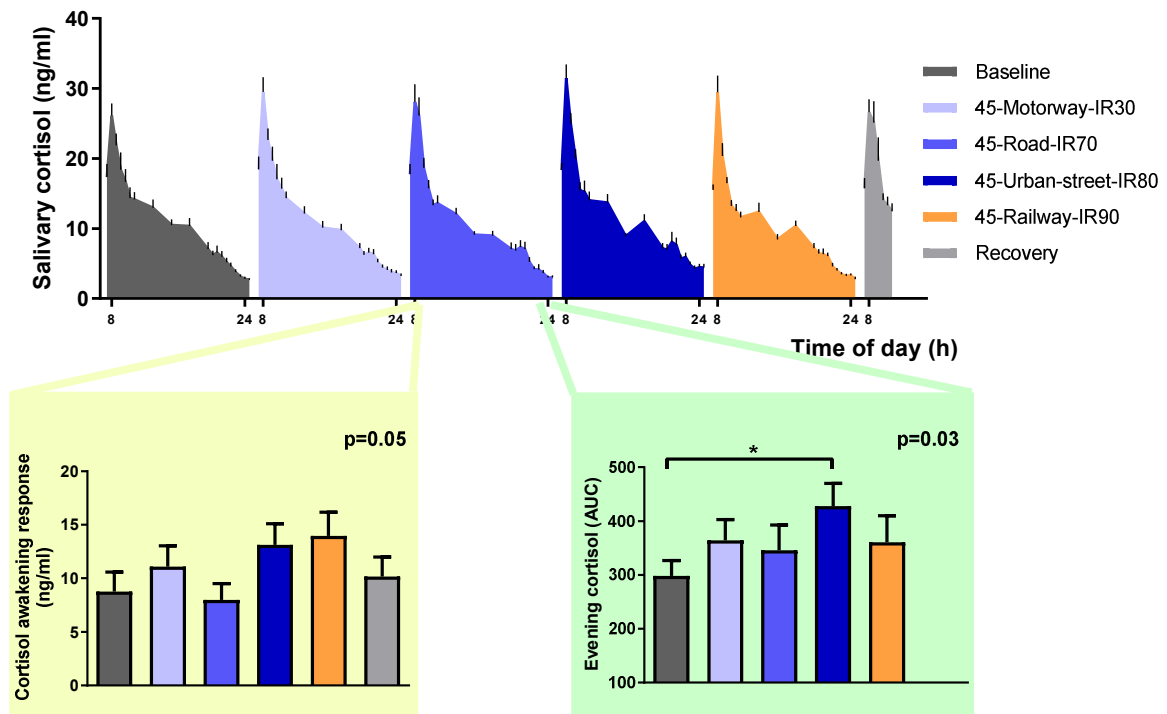


479

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.

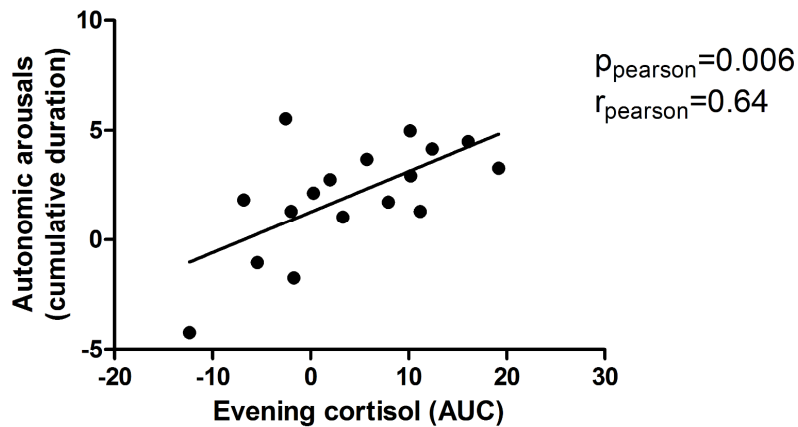
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487 **Figure 3.** Upper panel: Diurnal salivary cortisol profiles. Lower panel: Cortisol awakening responses and evening
 488 cortisol levels after sleeping with different noise scenarios. Baseline and recovery after sleeping with the quiet
 489 ambient 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: