

## **Short and long term effects of transportation noise exposure (SiRENE): an interdisciplinary approach**

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### **ABSTRACT**

This symposium presents results of the Swiss SiRENE study on acute, short- and long-term effects of transportation noise exposure on annoyance, sleep disturbances and cardiometabolic risks. SiRENE aims at identifying those noise exposure patterns that most strongly affect individuals and thus may ultimately result in long-term health consequences. The study includes a representative population survey on noise annoyance and sleep disturbance, an experimental study in the sleep laboratory applying contrived noise exposure scenarios, and the analysis of the SAPALDIA Biobank and Swiss National Cohort (SNC) data where cardiometabolic morbidity and cardiovascular mortality risks due to noise exposure as well as disease pathways were addressed. Further, a nationwide assessment of road, railway and aircraft noise exposure was conducted to estimate noise levels and the degree of noise intermittence for the whole Swiss population. Key findings of all aspects are presented as an example for how mutual combination of human experimental and observational epidemiological research contributes to a better understanding of the role of disturbed sleep, diurnal variation of noise and extent of intermittence for acute, short- and long-term noise effects on cardiometabolic outcomes.

### **INTRODUCTION**

Humans react to environmental noise not only during daytime, but also while asleep. Laboratory and field studies have consistently demonstrated that traffic noise induces acute and short-term sleep disturbances [1, 2]. Acute physiological responses to noise events during the night include conscious and unconscious awakenings, shifts to lighter sleep stages,

cortical and cardiovascular arousals (increases of heart rate and blood pressure), and body movements. Short-term or so called secondary effects of a night disturbed by noise may include impaired mood, increased subjective and objective daytime sleepiness, and impaired cognitive performance [3, 4].

Regarding long-term somatic health effects, epidemiological studies have mainly focused on cardiovascular outcomes [5]. Other health endpoints such as metabolic factors [6, 7], cognition [8, 9], behavior in children [10, 11] or depression [12, 13] were only marginally addressed so far. Recent evidence indicates that nocturnal noise exposure may be more relevant for the genesis of long-term health outcomes than daytime noise exposure, probably due to repeated autonomic arousals (e.g. heart rate increases) during sleep that have been shown to habituate to a much lesser degree than cortical arousals [1, 14]. In epidemiological studies on long term effects, environmental noise assessment is usually based on average source-specific sound pressure levels such as  $L_{Aeq,24h}$ ,  $L_{day}$ ,  $L_{night}$ ,  $L_{dn}$ , or  $L_{den}$ . There is, however, a broad consensus among noise effect researchers that such measures do not optimally predict a range of more specific effects of noise, in particular – sleep disturbances [15]. It has been repeatedly shown that annoyance and sleep effects depend not only on average levels, but also strongly on the time of day (i.e. night noise) [16, 17], the distribution of maximum sound pressure levels [1, 15], and the slope of rise of noise events [2, 18]. Because many effects (e.g. awakening reactions or cardiovascular arousals) can be better explained by characteristics of individual noise events, we developed a metric (Intermittency Ratio; IR [19]) that reflects the "eventfulness" of a noise exposure situation. The intermittency ratio was used as an additional exposure metric alongside established measures such as the  $L_{eq}$ .

## OBJECTIVES

In the SiRENE study, we aimed to address the following research questions:

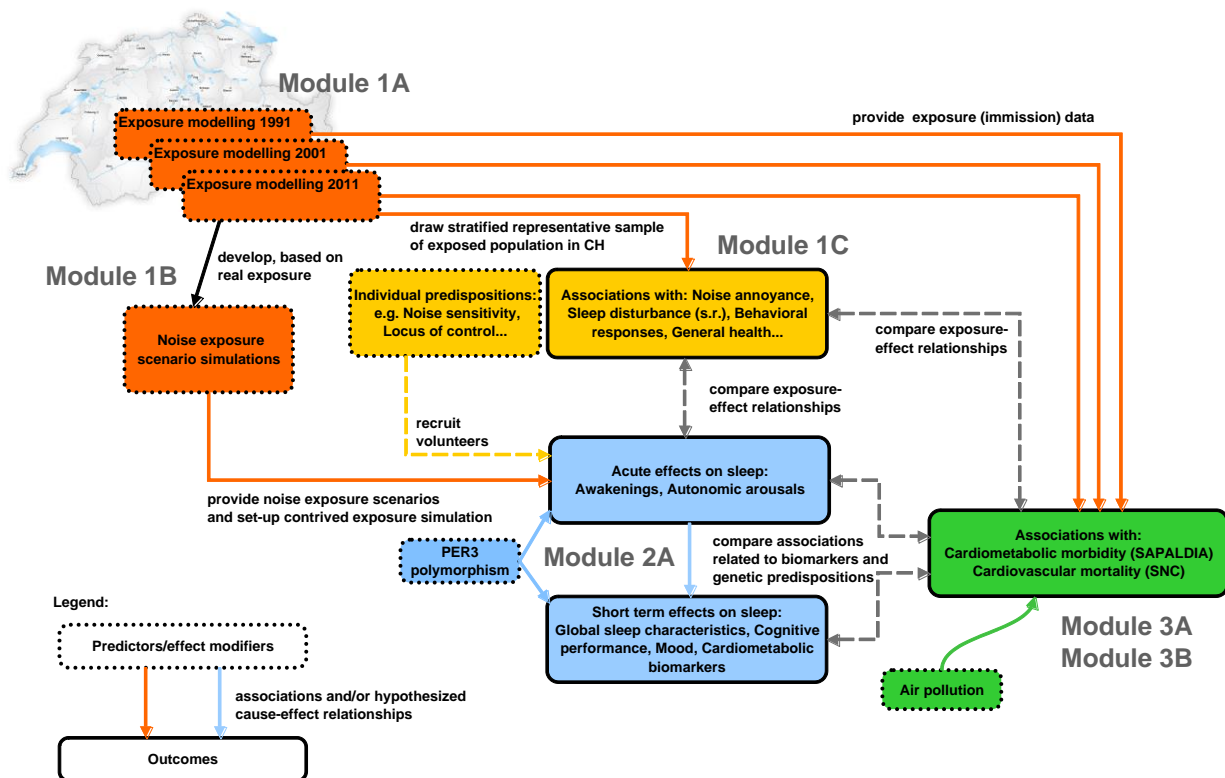
- What is the association between transportation noise exposure from road traffic, railways and aircraft with annoyance, sleep disturbances, cardiometabolic risk factors and cardiovascular mortality?
- To what degree do different exposure characteristics (e.g. type of traffic source, average level, degree of intermittence, diurnal exposure variation) account for the exposure-effect associations regarding annoyance, sleep disturbances and daytime cognitive performance, cardiometabolic risk factors, and cardiovascular mortality?
- What are the relevant personal characteristics that modify individual vulnerability to acute, short- and long-term effects of noise exposure?
- Which genetic variations and underlying pathophysiological pathways could play a role for noised-induced sleep disturbances and cardiometabolic effects?

## METHODS

### General approach

This interdisciplinary project consisted of 3 sub-projects and 6 associated modules, spanning the disciplines acoustics, human ecology and psychology, sleep research, and epidemiology. Sub-project 1 (*"Exposure, annoyance and coping responses"*) provided noise exposure data for the entire project (Module 1A) and carried out a nation-wide survey on self-reported noise annoyance, sleep disturbance, and other health-related quality of life factors (Module 1C). Furthermore, in Sub-project 1 scenarios of contrived noise exposure for playback in the sleep laboratory experiments of Sub-project 2 were developed (Module 1B). Sub-project 2 (*"Acute and short-term effects of night-time transportation noise exposure on sleep"*) investigated

acute and short-term effects of different transportation noise exposure conditions on sleep architecture, daytime cognitive performance and cardiometabolic phenotypes in the sleep laboratory (Module 2). Sub-project 3 (“*Long term effects of transportation noise exposure on cardiometabolic outcomes in the general population*”) investigated chronic effects of transportation noise exposure on cardiometabolic morbidity and mortality in two population-based cohorts, the SAPADIA biobank (Module 3A) with information on lifestyle and associated blood and DNA bank for the interrogation of mediating molecular pathways, and the Swiss National Cohort (Module 3B). The individual modules were organized such that they interacted with each other in an interdisciplinary manner. Figure 1 provides a structural overview and identifies the dependencies and relationships of individual modules in the project.



**Figure 1:** Overall project framework of SiRENE (for details refer to the text)

## Exposure assessment

A nation-wide exposure modelling was performed for road, rail, and air traffic for the years 2011, 2001 and with some restrictions also for the year 1991, the start year of the SAPADIA cohort study [20]. Briefly, the aircraft noise calculations included a military airfield and the three international civil airports. Noise levels were calculated with the FLULA2 model and a combination of radar data (Zurich Airport), traffic statistics (Federal Office of Civil Aviation), and acoustic footprints (Basel and Geneva airports) and idealized flight paths and number and time of flights for the military airfield (Payerne). Railway emission levels were derived using sonRAIL and the sound propagation was derived using the Swiss railway noise model SEMIBEL. Geometry of the railway tracks, location of switch points, noise barriers, train types, driving speed, and traffic statistics were considered in the calculation. Road traffic noise levels were calculated using sonROAD as emission model and StL-86 as propagation model, with input data from 3-D geometry, including bridges, noise barriers, road slopes, type and width, speed limits, traffic statistics, and noise barriers location and height. In addition to model Leq-based quantities a new metric, called *intermittency ratio (IR)*, was developed that accounts for the number of intermittent noise events and their level of emergence within the exposure

situation [19]. "Intermittent sound" is, according to ISO 1996-1 [21] "sound that is present at the observer only during certain time periods that occur at regular or irregular time intervals...". The exposure modelling was performed in an hourly resolution for 54 Mio façade points of 1.8 Mio residential buildings and more than 6 Mio dwelling units. In addition, address data and population figures from official registers were integrated. Building polygons were thereby linked to the "Register of houses and dwellings" (GWR), maintained by the Swiss Federal Statistical Office (BFS) who also hold census records with many attributes of the legal residents in these dwelling units.

## **Population survey**

Module 1C involved a representative, nation-wide mail survey which centered around annoyance, self-reported sleep disturbances, and coping responses due to transportation noise, complemented the efforts in Module 2 (effects on sleep) and the Modules 3A and 3B (long-term health effects), and harmonized questions between the modules as far as possible. The main goal of this module was to formalize exposure-annoyance functions for the three sources of transportation noise and to investigate the role of annoyance, coping responses, perceived control, and individual differences in noise sensitivity which are potential intermediates of noise effects on cardiometabolic health.

The factorial design employed for the sampling of dwelling units accounted for three sources (road, rail, air), two time periods ( $L_{Aeq,16h,Day}$  and  $L_{Aeq,08h,Night}$ ), three categories of intermittency (0-33%, 33-66%, 66-100%), and ten  $L_{Aeq,16h,Day}$  resp.  $L_{Aeq,08h,Night}$  exposure categories (2.5 dB steps, from the lowest (<45 dB(A)) to the highest (>65 dB(A)) category). This results in  $3 \times 2 \times 3 \times 10$  (=180) factor levels (cells). For each cell, we randomly selected 100 dwelling units and corresponding individual (postal) addresses based on a joint recordset of building and census data provided by the Swiss Federal Statistical Office. The employed stratification and wide range of exposure levels provides optimal exposure contrast and equally sized cells that are necessary to derive statistically sound exposure-effect relationships. Sample size calculations for the survey were carried out previously. Expecting a response rate of at least 25%, we posted 4x4500 questionnaires in 4 seasonal waves (total N=18000). A total of 5592 paper and pencil as well as online questionnaires of all 4 waves were received, which translated to an overall return rate of 31%.

## **Sleep laboratory experiments**

Module 2 assessed acute and short-term effects of night-time transportation noise on sleep under controlled conditions in a six day and night laboratory study. Four main research questions were addressed: the short-term effects of night-time noise on glucose metabolism, the moderating effects of sleep spindle rhythms on arousability from sleep and the moderating effect of the clock gene variant PER3 on noise disturbed sleep as well as the effects of night-time noise on daytime cognitive functioning.

Five different noise scenarios were applied (pre-recorded and provided by Sub-project 1). The four noise scenarios differed with respect to noise source (railway noise and different road traffic situations) and short-term exposure variation over time (IR low, medium or high) [33]. All had a constant hourly  $L_{Aeq}$  of 45 dB at the sleeper's ear. Noise scenarios A, B and C included road traffic noise with low, medium and high intermittence each and noise scenario D included railway noise (high intermittence). One scenario was used during both the baseline and recovery night and comprised ambient sound with a constant hourly  $L_{Aeq}$  of 30 dB at the ear of the sleeper. The sequence of the noise scenarios was randomized and incompletely balanced over participants.

A total of 44 men and women participated in the study. The sample consisted of two age groups: 26 participants with a mean age of 24.5 y (range 19-33 y, 12 women, 14 PER3<sup>4/4</sup>, 12 PER3<sup>5/5</sup>) and 18 participants with a mean age of 61.6 y (range 52-70 y, 9 women). All participants were healthy by medical history, physical examination and one night of polysomnographic screening.

Polysomnography was recorded continuously during the nights. Sleep stages and EEG arousals were scored manually by four experienced raters according to standard criteria. The carbohydrate metabolism was assessed by oral glucose tolerance tests (OGTT) conducted on the mornings after the baseline night, the last noise night and the recovery night. Cognitive performance on different domains (memory, working memory (n-back), and sustained attention (PVT)) was assessed at regular intervals four times during wakefulness.

## **Epidemiological studies**

Data from the two large ongoing epidemiological studies in Switzerland were used: SAPALDIA (Swiss study on Air Pollution And Lung Disease in Adults) biobank and SNC (Swiss National Cohort). SAPALDIA contributes data on important preclinical outcomes and on molecular and non-molecular effect modifiers. The SNC provides cause of mortality data for the whole Swiss population.

The SAPALDIA Cohort & Biobank is a large chronic disease cohort recruited in a population-representative manner from 8 different rural and urban communities across Switzerland in 1991 [22]. Eligible participants were aged 18 to 61 years who a) were listed in the local population registries, b) had lived in the community for at least 3 years, and c) spoke and understood German, French or Italian. The baseline examination of 9,651 subjects included a detailed computer-based interview and refined lung function and allergy testing. In the first follow-up with 8047 participants in 2002, a DNA and blood bank was established and the collection of cardiovascular data (24-hr ECG; blood pressure measurement) was introduced. The second follow-up was conducted in 2012 with close to 6,000 participants living all over Switzerland by then. Blood and DNA sampling was repeated. Cardiovascular and respiratory assessment was broadened to additionally include measurement of carotid intima media thickness and pulse wave; post-bronchodilation spirometry was added to the protocol. Assessment of BMI at follow-up 1 and follow-up 2 was repeated and broadened to include waist-hip ratio measurement, bioelectrical impedance analysis (BIA) and assessment of body shape. Questionnaire information was increasingly broadened to obtain relevant information on lifestyle risk factors for common non-communicable diseases. The 2012 survey included a food frequency questionnaire and the long IPAQ for physical activity assessment. SAPALDIA includes exact geo-coded addresses of all participants throughout the 25 year of follow-up.

The SNC is a national longitudinal research platform funded by the Swiss National Science Foundation. It is based on probabilistic linkage of census with mortality records (see also <http://www.swissnationalcohort.ch/>) [23] Participation in the census was mandatory and enumeration is near-complete. The SNC spans the period 1990-2008 and includes 6.4 million residents from the 1990 census, 7.2 million residents from the 2000 census, 108 million person-years of follow-up and 1.0 million linked death records. The SNC data include exact geo-coded addresses of all participants, whether persons lived on the ground floor or above, data on the type of the building (e.g. detached house, apartment house), and age of the building or time period of the last renovation as well as date of birth, sex, civil status, nationality, educational level, occupation, language region and neighborhood socio-economic status [24].

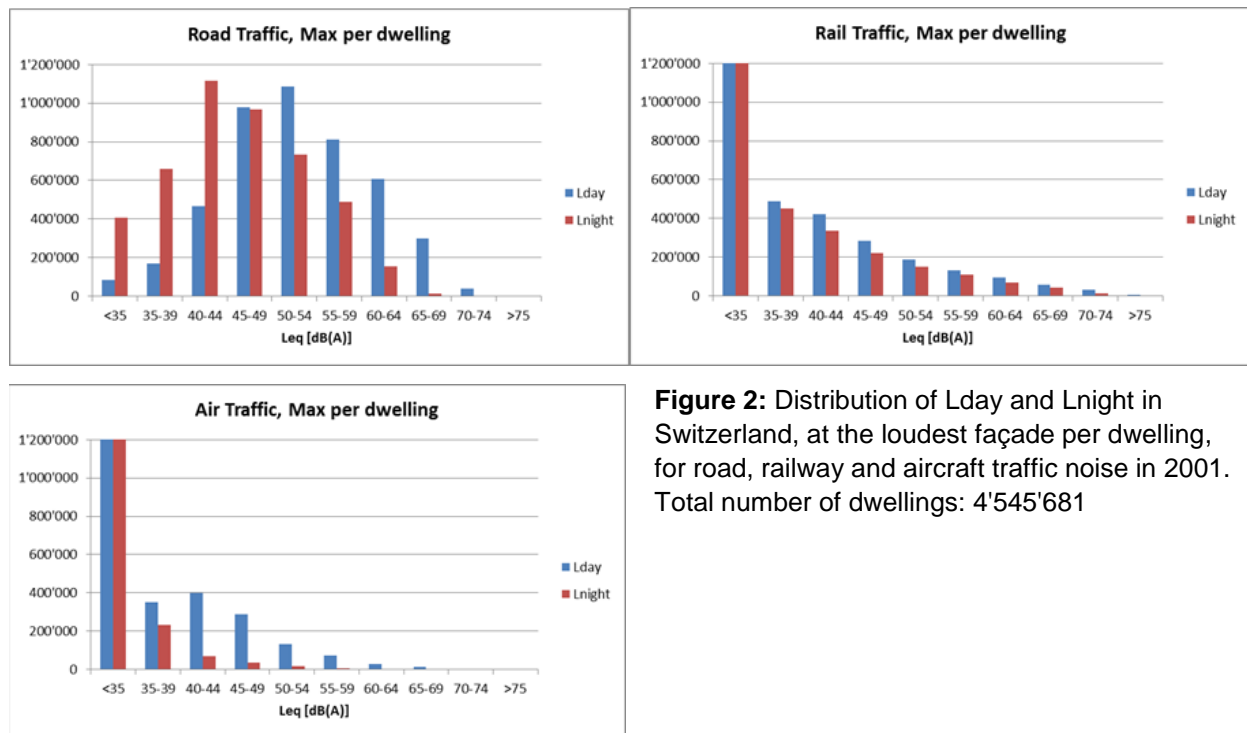
For the purpose of the SiRENE study, the address history of both the SAPALDIA participants and the SNC cases were linked to the noise exposure database established in beforehand covering each dwelling in Switzerland.

## RESULTS

In the following, a brief overview about the main results of the study is given. For details refer to the articles on the SIRENE study that have been published so far [5, 19, 25-30].

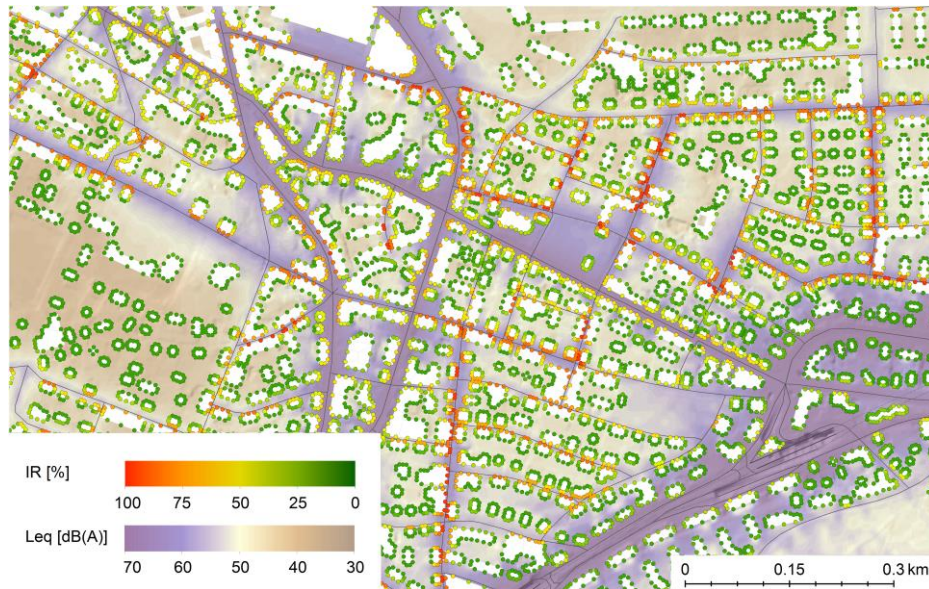
### Road, rail, and aircraft traffic noise exposure

Figure 2 shows the distribution of the average daytime and night time noise exposure for the loudest façade in Switzerland for the year 2001 for the three traffic sources. Exposure status in 2001 was used in the longitudinal epidemiological analyses.



**Figure 2:** Distribution of L<sub>day</sub> and L<sub>night</sub> in Switzerland, at the loudest façade per dwelling, for road, railway and aircraft traffic noise in 2001. Total number of dwellings: 4'545'681

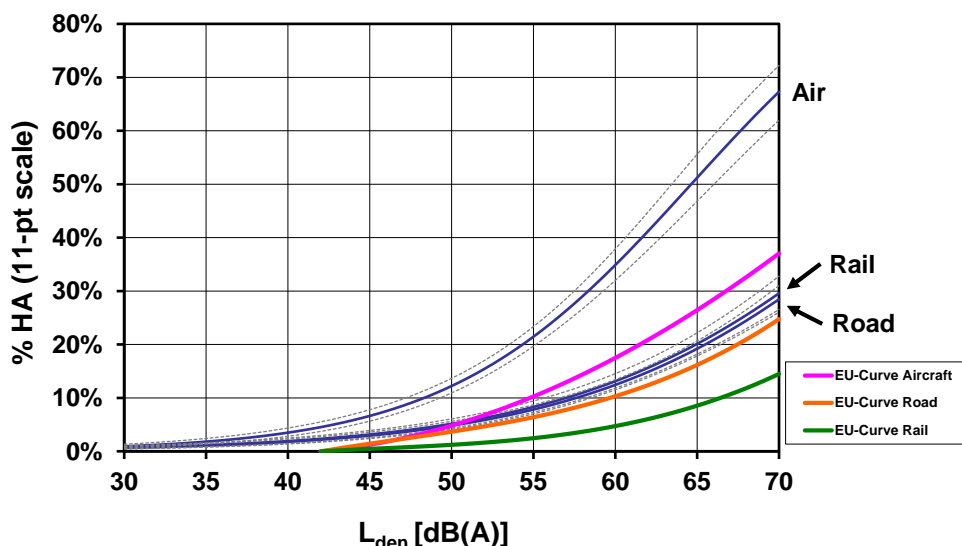
Beyond normal average exposure metrics, the IR, as described in Wunderli et al. [19], was calculated for each dwelling unit. An example how IR corresponds with average road traffic noise is given in Figure 3. At major roads, Leq is high but IR is low since the high amount of traffic creates a rather continuous noise exposure without any distinct events. At smaller city streets, IR tends to be higher, especially on the front side of buildings.



**Figure 3:** Intermittency ratio (IR) and road traffic noise (Leq, day) in an area around Zürich.

### Noise annoyance of the population

In the population survey the relationships between average exposure level, intermittency of noise, and the probability for being highly annoyed (HA) and being highly sleep disturbed (HSD) were investigated. A primary goal of the survey was to derive the exposure-%HA functions for the three transportation noise sources and compare them with commonly used curves for noise impact assessment. Figure 4 depicts the bivariate exposure-response relationship for %HA due to road, rail, and aircraft noise in the survey sample, including – for comparison – the so called "EU curves" [31].



**Figure 4:** Exposure-response curves for %HA for road, rail, and aircraft noise, incl. 95% confidence intervals. For comparison, the "EU-curves" are drawn also. Bivariate logistic regression model (Road N=5364; Rail N=4188; Air N=3189)

Figure 4 reveals for a given exposure level higher proportion of HA compared to the "EU curves", whose empirical groundwork is now 20 or more years old. The shift is particularly

pronounced for aircraft noise. The trend over the last decades of increasing aircraft noise annoyance at a given exposure level truly seems to be a persistent phenomenon which was recently also demonstrated in the NORAH-Study in the vicinity of several airports in Germany [32]. Interestingly, road and railway noise exposure display almost identical exposure-response curves. In addition to average  $L_{eq}$ , also IR affects %HA. For railway and aircraft noise, higher IR leads to slightly higher values of %HA and %HSD. This trend is reversed with road traffic noise, where low levels of IR elicit more %HA responses and more %HSD responses up to about 60 dB(A)  $L_{Night}$ .

Epidemiological research demonstrates that noise annoyance is a critical mediator for noise induced health effects. For instance, in the Qualifex cohort of 1'375 adults, the link between road traffic noise exposure and self-reported quality of life was strongly mediated by annoyance and sleep disturbance [27]. In the SAPALDIA cohort, transportation noise annoyance in the year 2002 predicted decrease in physical activity 10 years later [25].

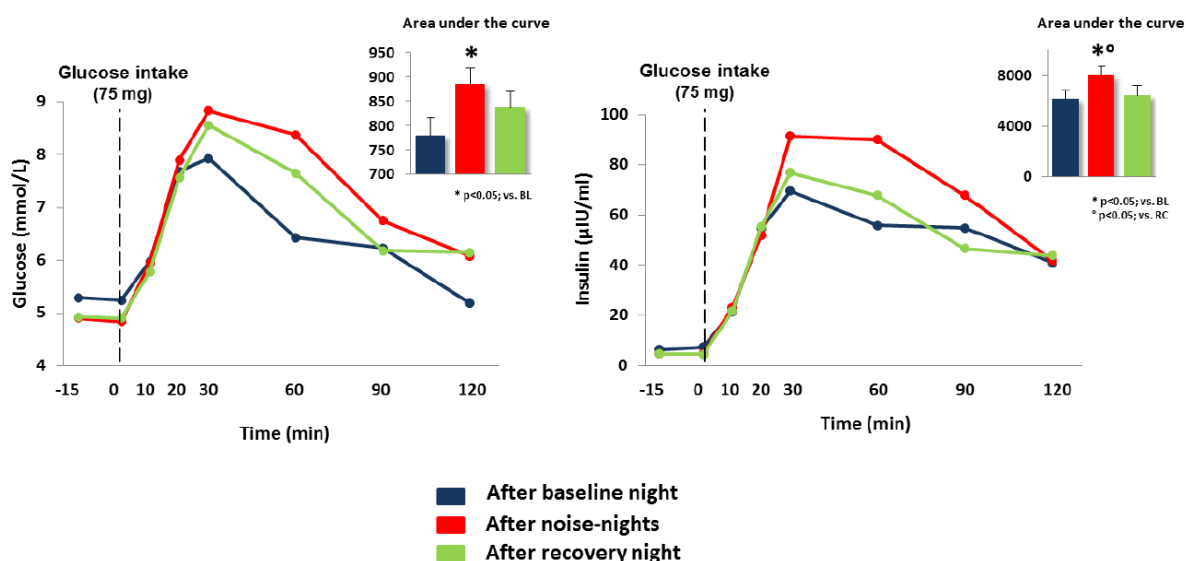
### **Short-term effects of noise on sleep**

The analyses of the vast amount of data gathered in the sleep laboratory are still on-going. Electroencephalographically (EEG) quantified sleep variables such as total sleep time, sleep efficiency, amounts of non-rapid eye movement (NREM) and REM sleep averaged per night, did not significantly differ between the noise exposure nights and the baseline night (BL) without noise exposure. Percentages of total sleep time, of Stage 1, 2 and SWS and intrasleep wake differed significantly between age groups so that a factor age was included in the analyses. Noise affected latency to sleep Stage 2 (SL2) irrespective of the age group ( $F(5,183) = 6.5, p < .001$ ). Post-hoc analyses revealed that latency to SL2 was prolonged in noise exposure night B as compared to the quiet BL night (17.48 min vs 13.25 min). Sleep continuity was affected by noise as measured by the number of sleep stage changes per hour ( $F(5,183) = 2.97, p = .013$ ). The number of sleep stage changes per hour was significantly higher in noise nights with medium and high road traffic IR as compared to the quiet BL night in the older age group (29.86/30.45 vs 26.69 per hour). Thus, it was rather the temporal dynamics of sleep variables within the noise exposure nights which were affected by noise than the absolute amount of a particular sleep stage averaged over night.

Further analyses of the microstructure including spectral analysis and noise-event related methods will hopefully reveal mechanisms on the noise impact on sleep and its negative repercussion on subjective sleep quality and daytime performance. First analyses on subjective sleep quality and daytime performance show that study participants perceived a worsening of sleep quality when rated immediately after waking up from the noise exposure nights, which varied according to the noise scenario ( $F(5, 171) = 3.47, p = .005$ ) such that post-hoc analyses revealed a significant difference for the noise nights with medium and high road traffic IR as compared to the BL night.

The analysis of the glucose and insulin levels revealed significant changes after four nights of nocturnal transportation noise showing an impaired glucose tolerance in young participants (Figure 5). Interestingly, a stronger effect was seen after nights with high IR. After a high IR night, one recovery night was not enough to come back to baseline glucose levels. These are first indications that the short-term effect of highly intermittent night noise is more deleterious for glucose metabolism than low intermittency noise.





**Figure 5:** Glucose and Insulin responses to the oral glucose tolerance tests the baseline, noise nights, and recovery night

### Long-term health effects

The findings from the sleep laboratory are in line with epidemiological results on long term effects. In the SAPALDIA cohort, incident diabetes between 2002 and 2011 was associated with road traffic and aircraft noise levels (RR per IQR: 1.35; 95% CI: 1.02-1.78 and 1.86; 95% CI: 0.96-3.59), independent of railway noise and air pollution [29]. Stronger effects of road traffic noise were seen among participants reporting poor sleep quality or sleeping with open windows. The interplay of sleep and glucose metabolism is further supported by the observation that road traffic noise led to a greater change in glycosylated hemoglobin (HbA1c) among diabetic participants with high genetic risk for melatonin dysregulation (a marker for circadian rhythm) and for participants with self-reported sleep problems [33].

In terms of cardiovascular risk of noise, cross-sectional associations between railway noise and arterial stiffness were observed in the SAPALDIA cohort using data from the second follow-up [34]. This association was greater with high night-time IR and also for participants reporting high daytime sleepiness scores. Associations between road noise and arterial stiffness were suggestive in urban areas. Associations were also observed between night-time noise events, mostly correlated to road noise levels ( $r=0.67$ ) and arterial stiffness. Arterial stiffness is a potential relevant pathway towards cardiovascular disease. And indeed cardiovascular mortality in the SNC was clearly associated with transportation noise [26]. The most consistent associations were seen for myocardial infarction: adjusted hazard ratios (HR) (95% CI) per 10 dB increase of exposure were 1.038 (1.019-1.058), 1.018 (1.004-1.031), and 1.026 (1.004-1.048) respectively for Lden(Road), Lden(Rail), and Lden(Air). In addition, total IR at night played a role and a bell shaped association was found with elevated HRs in the 3rd and 4th quintiles. This suggests that either continuous noise or highly intermittent noise with long quiet periods between noise events is less problematic than mid-range intermittency. In further analyses it was revealed that the diurnal pattern of noise exposure is also relevant for cardiovascular mortality, which itself shows a strong diurnal pattern [35]. For acute cardiovascular diseases, nocturnal noise exposure tended to be more relevant than daytime exposure, whereas it was the opposite for chronic conditions such as heart failure. This suggests that for acute diseases, sleep is an important mediator for long term health

consequences of transportation noise, whereas for chronic conditions, noise induced prolonged activation of the hypothalamus-pituitary-adrenal (HPA) axis may be more relevant.

## DISCUSSION

It is well established that transportation noise affects health in a complex manner including psychological and physiological pathways. Thus, towards causal understanding of transportation noise effects, only interdisciplinary studies will help to elucidate this complex interplay between physical noise exposure, noise annoyance including coping behaviour and lifestyle factors, individual noise sensitivity and short and long-term health outcomes. The overall aim of SiRENE was to shed light on the mechanisms that lead to noise related health impediments. Although analyses and interpretation of the results of the SiRENE study are not yet finalized, a few achievements are highlighted in the following:

1. The role of noise characteristics: At the beginning of the study, we intensively discussed which characteristics of noise could be most detrimental for health and how these can be operationalized in an objective manner suitable for noise modelling, and experimental and epidemiological research. This debate resulted in a novel metric for noise characteristics: the intermittency ratio IR [36]. Subsequently, we could apply the same exposure measures, including IR, in all aspects of the study, which allowed direct comparison of the results.
2. We could demonstrate that IR is relevant for noise effects in addition to Leq in all parts of the study (population survey, sleep experiments and epidemiological analyses). However, the pattern was complex and IR did not affect all outcomes in the same direction. Low levels of IR characterized by absence of quiet intervals seems to be most critical for %HA and %HSD (at least for road traffic), where high levels of IR were most critical for acute sleep effects. For cardiovascular mortality, a medium level of IR was most detrimental. Possibly, in the everyday environment, high levels of IR are likely to go along with longer periods of quietness between events which may be beneficial for health in the long run.
3. Role of annoyance for health effects: Respondents to the population survey clearly were annoyed by transportation noise, especially by aircraft noise. Annoyance can be seen as both a health effect in itself, but may also act as an intermediate between noise exposure and long term health effects. However, effect modification by annoyance or noise sensitivity was not seen for the observed noise effects on diabetes or arterial stiffness.
4. Associations between incident diabetes and long term exposure to transportation noise are in line with the results from the experimental sleep study indicating short term effects of noise on glucose and insulin levels. This consistency supports thus a causal link between noise exposure and metabolic diseases.
5. Although the exact sleep mechanisms remain little understood, the effect modification by self-reported sleep indicators observed in SAPALDIA suggests a potential role of sleep on the impact of noise on cardiovascular endpoints and diabetes. More importantly, circadian rhythm disruption may play a role in diabetic patients as observed with the melatonin related genetic risk score. The modification of these gene variants in the acute noise effect scenario in the sleep lab is currently under investigation.
6. By modelling all three transportation sources for different time windows during day and night, we were able to estimate source specific exposure-response functions for each traffic source independent from each other and to evaluate the relevance of the diurnal

pattern of noise exposure for health effects. By expressing noise characteristics with the additional variable IR, exposure-response functions may be even extrapolated to other non-transportation related sources of low or high intermittency.

The SiRENE project is not finished yet and various analyses are still on-going. This will hopefully further stimulate the exchange between all project partners. SiRENE will hopefully further contribute to the understanding of noise-induced health risks. We believe that the present (published) and yet to produce future results will be highly relevant for regulating environmental noise in an efficient manner.



**Figure 6:** The SiRENE team's interdisciplinary exchange stimulated by the quiet Swiss mountains...

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