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Short-term effects of nocturnal transportation noise on glucose metabolism

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ABSTRACT

Traffic noise is a growing cause for sleep disturbances and has been associated with a higher risk of type 2 diabetes. However, the relationship between traffic noise, sleep disturbances and cardio-metabolic diseases remains to be investigated.

Nine lean young volunteers (BMI: 18.5-25; age: 19-32 y) participated in a six-day laboratory study starting with a noise-free baseline night (BL) followed by four nights with night-time noise scenarios (railway or road traffic noise with an hourly Leq of 45 dB(A) at the ear of the sleeper, NN2-NN5), and ending with a final noise-free recovery night (RC). Carbohydrate metabolism was evaluated during an oral glucose tolerance test scheduled on BL, NN5 and RC.

Post-charge glucose and insulin levels increased after four nights of nocturnal traffic noise compared to the baseline night ($p=0.022$ and $p=0.002$, respectively), while sleep efficiency (SE) and slow wave sleep (SWS) did not significantly differ between the six nights.

Four nights of nocturnal traffic noise decreased glucose tolerance in lean young volunteers - an effect, which is most likely not related to changes in the macrostructure of sleep. These results could elucidate the first step initiating the development of metabolic syndromes as seen in traffic dense regions.

Keywords: nocturnal traffic noise, sleep, glucose metabolism
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1. INTRODUCTION

There is epidemiological evidence that people living in traffic dense regions are more at risk of developing cardiometabolic diseases such as type 2 diabetes or obesity (1). Besides traditional risk factors such as the lack of physical activity or unhealthy food which are more prominent in these urbanized regions, traffic noise *per se* also has deleterious effects on health (2). Thus, noise acts as a stressor and activates stress responses (3, 4), which on a chronic state, inhibits insulin secretion and reduces insulin sensitivity (5) leading at long-term to diabetes state. It may also be that some of these effects are mediated by the deleterious effects of noise on sleep quality (6, 7), since disturbed sleep *per se* impairs glucose metabolism (8, 9, 10), and can lead to diabetes in the long-run (11). Under laboratory settings, Spiegel and colleagues shortened sleep down to 4 hours and compared it to a night of 12 hours of sleep, glucose tolerance was considerably impaired (8). However, besides sleep duration, sleep quality and especially the amount of slow-wave sleep (i.e. deep sleep) seems also primordial for glucose homeostasis (9, 10). The aim of our study is to investigate the mechanism underlying the association between traffic noise, sleep disturbances, stress response and glucose metabolism impairment.

2. MATERIAL AND METHODS

2.1 Subjects

Nine healthy young men were included in the study (age (mean±SEM): 26.5±1.34). Participants were lean (BMI: 21.8±0.62) and their average weight did not change in the course of the study week. Exclusion criteria were smoking or any other drug consume, chronic or acute illness, medication treatment, hearing problems, shift work or travel in another time zone. Prior to the study begin, participants underwent a screening night in the sleep laboratory to exclude any sleep disorders. Participants should not have given blood three months before the study start and a blood screening to insure the possibility of taking blood during the study (standard blood screening: blood count, fasting glucose and cholesterol levels) has been carried out for each participant.

2.2 Procedure

During the week before they reported to the chronobiology laboratory, participants wore an actigraphic device (actiwatch L, Cambridge Neurotechnologies, Cambridge, UK) and were asked to sleep eight hours per night according to their habitual sleep time in order to maintain a regular sleep-wake rhythm. The laboratory session started with a noise-free baseline night (BL) followed with four continuous different night-time noise scenarios (NN2-NN5) and ended with a noise-free recovery night (RC). Noise scenarios differed in term of noise source (railway or road traffic noise) and in term of short-term temporal variations exposure (intermittency ratio low, medium or high). The hourly Leq was 45 dB(A) at the ear of the sleeper corresponding to an outdoor level of approx. 60 dB for a tilted window.

Participants had to stay inside the laboratory during the entire week under controlled luminosity (light in room: 500lux) and environmental temperature (22°C) levels. Caloric intake was controlled based on their estimated energy calculated by the Mifflin equation with an activity factor of 1.3 (12). Meals were served depending on the participants' bedtimes (breakfast 35 min, lunch 5 hours and dinner 11.5 hours after wake up time), and no snacks were allowed. The energy balance of the diets was 35% lipids, 50 % carbohydrates and 15 % protein.

Sleep was continuously recorded via standard polysomnographic methods (F3, FZ, F4, C3, CZ, C4, P3, PZ, P4, O1, OZ and O2 electroencephalographic derivations, two electrooculographic, two electromyographic and two electrocardiographic derivations (Vitaport-3 digital recorder; TEMEC Instruments BV, Kerkrade, The Netherlands)). Sleep was scored according to the 2012 AASM roles by 4 different scorers (scorer agreement >85%). Sleep efficiency was calculated as the percent of sleep time including stages N1, N2, N3 and REM sleep between lights off and lights on.

Carbohydrate metabolism was assessed during a 120-min oral glucose tolerance test (OGTT) realized one hour after wake-up time in the morning of BL, NN5 and RC. Each test started with two fasting time points (t-15 and t0) then participants had to drink 75gr of diluted glucose and blood samplings were realized each 10 to 30 min during two hours (time points: t10, t20, t30, t60, t90 and t120). In total 360ml blood was taken per participant (120ml per OGTT). Blood was distributed in Na-fluorid tubes for glucose and in serum tubes for insulin measurement. Plasma for glucose assessment was obtained by immediate centrifugation while serum was obtained after 30 min clotting at room temperature. Tubes were centrifuged at 4°C for 10 min at 3500rpm. All samples were then stored at -80°C until analysis. Plasma glucose was analyzed via the hexokinase method (Glucose GOD-PAP test; Roche) and serum insulin was measured with an ELISA test (80-INSHU-E01.1; ALPCO). Insulin sensitivity was estimated via the QUICKI and the MATSUDA indexes. QUICKI: 1/(log(fasting glucose)+log(fasting insulin)) , MATSUDA: 10000/squareroot((fasting glucose*fasting insulin)*(mean(postcharge glucose)*mean(postcharge insulin))). Glucose unit: mg/dl, insulin unit: mU/L.

2.3 Statistics

For all analyses, the statistical package SAS was used (SAS Institute Inc., Cary, NC; version 9.4). Statistical analyses were carried out for each variable (fasting glucose, fasting insulin, post-charge glucose and post-charge insulin, sleep efficiency and slow wave sleep amount) separately with the mixed-model analysis of variance for repeated measures (PROC MIXED), with within factors ‘‘protocol” (baseline [BL], last noise night [NN5] and recovery [RC]) and corrected with the post-hoc analysis Tukey-Kramer for multiple comparison.

Fasting glucose and insulin were calculated by the mean of the blood sampling t-15 and t0. Post-charge glucose and insulin were calculated by the area under the curve (AUC) from t0 to t120.

Fasting hormones results as well as QUICKI index are here shown for n=9 subjects, while because of missing points post-charge results and MATSUDA index had to be calculated for n=8.

The level for establishing significant differences was taken at *, $p<0.05$; **, $p<0.001$.

3. RESULTS

3.1 Glucose metabolism

3.1.1 Fasting levels:

Fasting glucose significantly decreased after 4 nights of traffic noise compared to the baseline ($F_{2,16}=6.24$, $p=0.01$). After one recovery night fasting glucose levels did not significantly change compared to the noise night.

Fasting Insulin did not change after 4 nights of traffic noise compared to the baseline. Levels stayed also at the same level after the recovery night.

3.1.2 Post-charge levels:

Post-charge glucose levels significantly increased after four nights of nocturnal traffic noise compared to baseline ($F_{2,14}=3.36$, $p=0.022$). Although, AUC glucose decreased after one noise-free recovery night, it did not reach significance ($F_{2,14}=3.36$, NN5-RC: $p=0.31$).

Post-charge insulin levels significantly increased after four nights of nocturnal traffic noise compared to the baseline night ($F_{2,14}=6.98$, $p=0.002$) and returned to baseline levels ($F_{2,14}=6.98$, NN5-RC: $p=0.041$) after one noise-free recovery night.

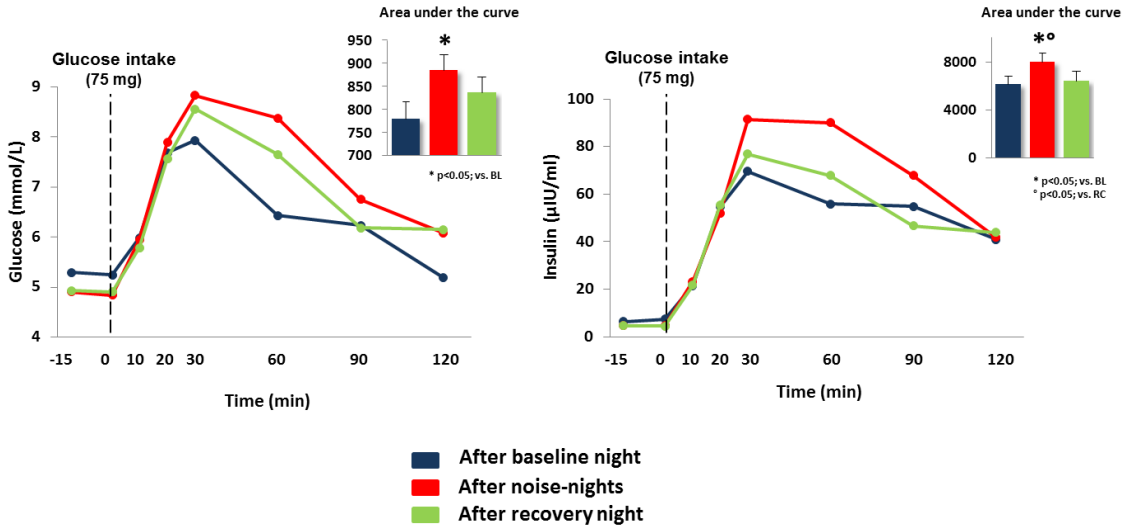

Figure 1 - Glucose (left) and insulin (right) responses to an oral glucose tolerance test. (mean with standard error)

Insulin sensitivity, estimated via the QUICKI and MATSUDA equations, did not yield any significance.

3.2 Sleep Characteristics

Mean sleep efficiency (SE) was at least 90% and slow wave sleep (SWS) at least 14% and did not significantly differ between BL, NN5 and RC (see Table 1 for details).

Table 1- Sleep parameters for the different night scenarios

Night	TST (min)	SE (%)	WASO (min)	SL2 (min)	RL (min)	S1 (%)	S2 (%)	S3 (%)	S4 (%)	SWS (%)	NREM (%)	REM (%)
BL	437 (±18)	91 (±4)	37 (±18)	14 (±3)	71 (±6)	14 (±2)	52(±2)	7 (±1)	7 (±2)	14 (±3)	80 (±1)	20 (±1)
NN5	453 (±5)	94 (±1)	16 (±5)	21 (±3)	57 (±5)	14 (±2)	50 (±2)	8 (±1)	7 (±2)	15 (±2)	79 (±2)	21 (±2)
RC	451 (±7)	94 (±2)	18 (±8)	23 (±3)	54 (±3)	15 (±1)	46 (±2)	7 (±1)	8 (±2)	15 (±2)	76 (±1)	24 (±1)

Values in Mean±SEM. S1 to S4: Sleep stages 1 to 4; TST: Total sleep time (S1+S2+S3+S4+REM); SE: Sleep efficiency ((TST/480)*100); WASO: Wake after sleep onset; SL2: Sleep latency to S2; RL: SL to REM.

4. DISCUSSION AND CONCLUSION

We have preliminary evidence that under laboratory conditions, four nights of nocturnal traffic noise decreased glucose tolerance in lean young volunteers. This is an important finding as impaired glucose tolerance is the first step in the development of type 2 diabetes. After one recovery night, post-charge insulin levels decreased significantly compared to the noise night, a result that suggests that one noise-free night was sufficient to come back to baseline levels. In contrast, glucose levels also decreased after one noise-free but the difference to baseline did not reach significance. Thus, glucose probably needs more than one night to come back to baseline levels.

Insulin sensitivity, calculated with the QUICKI and MATSUDA indexes did not change significantly after the noise night. This is certainly due to the fact that fasting glucose decreased after the noise nights, the reason for this is not clear now and will need further analysis.

One of our preliminary hypotheses was that glucose metabolism could be impaired via changes in sleep duration or sleep quality. However, and to our surprise, overall sleep efficiency and the amount of slow wave sleep, a marker of sleep quality, were not affected by the four transportation noise scenarios. We are currently analyzing sleep microstructure by looking at arousals (see Rudzik *et al*. in this issue) and sleep spindle activity throughout the night, a brain wave activity, which has been shown to have a noise-protective function (13). Additionally, we will look at stress markers such as nighttime catecholamine secretion, which could also be an important candidate in the pathway affecting glucose tolerance.

The strength of your study is that participants had to stay the entire time in the laboratory under controlled conditions. Thus, we can affirm that the observed changes in glucose tolerance were not due to changes in caloric intake throughout the week. However, one could argue that these particular laboratory conditions are not “natural”, since participants were less able to be physically active what in turn could influence the results. Nevertheless, the significant decrease in post-charge insulin levels seen after one noise-free recovery night permits us to assume that noise per se and not the “unnatural” laboratory conditions elicited the observed changes in insulin. To strengthen our argumentation, we are currently realizing a control group of 6 young participants, staying one week in the sleep laboratory without any noise to exclude potential effects of the laboratory conditions on our results.

These preliminary findings are very intriguing, as they may indicate the first step in the development of metabolic syndromes in traffic dense regions and thus relates to long-term effects of noise on type 2 diabetes reported in epidemiological studies.

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