The impact of railway vibration and noise on sleep

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“Science is the first expression of punk, because it doesn't advance without challenging authority. It doesn't make progress without tearing down what was there before and building upon the structure.” Greg Graffin

The impact of railway vibration and noise on sleep

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Abstract

Sleep is a vital component of good health, and sleep loss is associated with impaired cognition, decreased psychomotor performance, cardiovascular disease, adverse effects on endocrine and metabolic function, negative mood, impaired memory, and more. A growing burden of freight transportation on global railway networks will likely lead to an increase in nocturnal vibration and noise at nearby dwellings. However, there is currently limited knowledge on how railway freight vibration and noise may disrupt sleep.

Over a series of laboratory studies in young healthy adults, the effect of vibration and noise from railway freight was investigated. Objective sleep was recorded with polysomnography, cardiac activity was recorded with electrocardiography and subjective sleep quality and disturbance was recorded with questionnaires. Increased cardiac activation occurred at vibration amplitudes only slightly above wakeful perceptual detection thresholds. Arousals, awakenings and alterations of sleep structure began to manifest at only slightly higher vibration amplitudes. With increasing vibration amplitude, heart rate and the probability of event-related cortical response increased in a dose-dependent manner, with accompanying adverse effects on perceived sleep quality and sleep disturbance. Perceived disturbance was more pronounced among noise-sensitive individuals, although no significant physiologic differences were found relative to non-sensitive counterparts. Rather than affecting overall sleep architecture, vibration and noise interfered with the normal rhythms of sleep, although the impact of this on long-term physical and mental health is currently unclear. Cardiac response persisted with increasing number of events, indicating an absence of habituation. Vibration and noise were additive regarding their effect on cortical arousal and sleep stage change, demonstrating that both exposures differentially contribute to sleep fragmentation. From a public health perspective, interventions to protect the sleep of populations near railway lines should therefore consider both exposure types.

Keywords: railway vibration, noise, sleep disturbance, polysomnography, cardiovascular disease **ISBN (e-pub):** 978-91-629-0257-5

Sammanfattning på svenska

Godstrafiken på järnvägsnätet kommer sannolikt att öka i framtiden, dels på grund av minskad lastbilstrafik av miljöskäl, och dels på grund av en allmänt ökad efterfrågan på godstransporter. Detta leder till en ökad risk för exponering av buller och vibrationer för bostäder nära järnvägen. För de boende kan detta påverka sömnen negativt, och sömn är en viktig del i en god hälsa. Samband har påvisats mellan sömnbrist och försämrad kognition, minne, psykomotorisk prestanda, sinnesstämning, samt på längre sikt påverkan på hjärta kärl, endokrina och metabola system. Kunskapen om hur vibrationer och buller från godståg kan störa sömnen är dock begränsad.

I experimentella försök undersöktes hur vibrationer och buller från godståg påverkade sömnen hos unga friska forskningspersoner. Deras sömn registrerades objektivt med polysomnografi, hjärtaktivitet registrerades med elektrokardiografi och sömnkvalitet och sömnstörning registrerades med frågeformulär. Ökad hjärtfrekvens noterades vid vibrationsamplituder strax över detektionsgränsen för perception i vaket tillstånd. Ökad mikrouppvaknanden (”arousals”), uppvaknanden och förändring av sömnstadier uppkom vid ytterligare något högre vibrationsamplituder. Med en förhöjd vibrationsamplitud vid godstågspassager följde en ökning i hjärtfrekvens och ökad sannolikhet av kortikal respons. Även negativ upplevelse av egen sömnkvalitet och sömnstörningar rapporterades. Personer som klassats som bullerkänsliga rapporterade mer störning, dock kunde inga signifikanta fysiologiska skillnader identifieras mellan känsliga och icke-känsliga personer.

Sömnstrukturen över hela natten påverkades inte signifikant av buller och vibrationer, däremot påverkades den normala cykliska sömnrytmen. Hur sådana förändringar påverkar mental och fysisk hälsa på sikt är oklar. Ett ökat antal exponeringar under natten ledde fortsatt till förändringar av hjärtfrekvens viket kan indikera att ingen tillvänjning av exponeringen skedde. Effekterna av vibrationer och buller på kortikal respons och sömnstadieförändringar var additiva vilket visar att båda exponeringarna bidrar på olika sätt till sömnfragmentering. Ur ett folkhälsoperspektiv bör därför insatser för att skydda sömnen hos befolkningar nära järnvägslinjer omfatta båda exponeringarna.

List of papers

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Smith, M. G., Croy, I., Ögren, M. and Persson Waye, K.

On the influence of freight trains on humans: A laboratory investigation of the impact of nocturnal low frequency vibration and noise on sleep and heart rate

PLOS ONE 2013; 8(2): e55829.

II. Smith, M. G., Croy, I., Hammar, O. and Persson Waye, K.

Vibration from freight trains fragments sleep: A polysomnographic study

Scientific Reports 2016; 6: e24717

III. Smith, M. G., Croy, I., Ögren, M., Hammar, O., Lindberg, E. and Persson Waye, K.

Physiological effects of railway vibration and noise on sleep

Journal of the Acoustical Society of America 2017; 141(5): 3262–3269

IV. Smith, M. G., Ögren, M., Hussain-Alkhateeb, L., Lindberg, E. and Persson Waye, K.

Physiological reaction thresholds to vibration during sleep

Manuscript

Content

Abbreviations

AASM	American Academy of Sleep Medicine
ARAS	Ascending reticular activating system
BPM	Beats per minute
CPAP	Continuous positive airway pressure
CVD	Cardiovascular disease
dB	Decibel
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyogram
EOG	Electrooculogram
HR	Heart rate
HRA	Heart rate amplitude
MC	Meissner corpuscle
MSLT	Multiple sleep latency test
NREM	Non rapid eye movement
OSA	Obstructive sleep apnoea
PC	Pacinian corpuscle
PSG	Polysomnography
PVT	Psychomotor vigilance test
R&K	Rechtschaffen and Kales

RA-LTMR	Rapidly adapting low threshold mechanoreceptor
REM	Rapid eye movement
RMS	Root mean square
RLS	Restless legs syndrome
SE	Sleep efficiency
SOL	Sleep onset latency
SPT	Sleep period time
SSC	Sleep stage change
SWS	Slow wave sleep
TIB	Time in bed
TST	Total sleep time
WASO	Wakefulness after sleep onset
WBV	Whole body vibration
WHO	World Health Organization

1. Introduction

Humans spend approximately one third of their lives asleep, which is time not spent ensuring their physiological needs are met, including gathering food and water, procreating, or seeking shelter from the elements. Furthermore, sleep is not unique to humans, but has been demonstrated to exist in one form or another throughout the animal kingdom, at least in organisms in which it has been studied [1]. The question of "why do we sleep?" has not been satisfactorily answered, but it is universally accepted to be important. As stated by the noted sleep researcher Allan Rechtschaffen,

> *"If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process has ever made"* [2].

One of the hallmarks of sleep that distinguishes it from coma is its reversibility. Sleep can be reversed by both endogenous and environmental factors, and noise and vibration are two contemporary environmental factors that are becoming increasingly pervasive.

Noise may promote or impair sleep. Many readers are likely familiar with the phenomenon of passengers in cars or trains falling asleep during the journey, despite noise and vibration levels that they would consider unacceptable in their bedroom. This phenomenon has been informally named "carcolepsy", and the presence of noise of generally constant level and frequency may "mask" other auditory signals, which might otherwise disturb sleep. Similarly, broadband noise with equal acoustic energy across all frequencies, termed "white" noise, may actually serve as a sleep aid, rather than an impediment. White noise promotes sleep onset in neonates [3], and improves sleep time, depth and continuity in intensive care units, presumably by partially masking the disturbing background sound in these environments [4, 5].

On the other hand, it is likely that many, if not all, readers have first-hand experience of sound actually disturbing sleep. Whether it be a motorcycle speeding by, the snoring of a partner, music from the late-night party of a neighbour or the cries of an infant, noise from a multitude of sources has the potential to intrude into our sleep. There are very good evolutionary reasons why changes in the environment may serve as progenitors of wakefulness. For instance, a distressed child may require the attention of a parent, and indeed the emotional relevance of a sound affects brain activation during sleep [6].

As with noise, vibration also may foster or impede sleep. For instance, shaking a sleeping individual can be highly effective in arousing them to wakefulness. Conversely, a link between whole body vibration and decreased wakefulness, as measured by decreasing alpha and increasing theta activity in the electroencephalogram (EEG), was reported in 1985 [7]. This experimental study involved 48 seated subjects exposed to either sinusoidal or broadband (2-20 Hz) vibration over a period of 105 minutes, with periods of non-exposure and exposure alternating in 15 minute increments. The EEG power spectral densities were averaged over each of these 15 minute intervals, thus nothing can be said of the temporal progression of changes in EEG frequency following vibration onset or cessation.

It is likely that a change in the background environment, rather than the noise or vibration *per se*, may illicit a response, such as awakening. Therefore the sleeping passenger may wake up when the car reaches its destination and the engine is switched off; the *absence* of noise and vibration reflects a striking change in the environment. At home, in an otherwise quiet bedroom, it is instead the introduction of a stimulus intruding from the background that potentially leads to sleep disturbance.

There is an extensive body of previous research into the effects of environmental noise, particularly from traffic, on sleep. However, the effects of environmental vibration on sleep are almost totally absent from the scientific literature. This thesis aims to provide a step towards elucidating the effects of vibration on objective and subjective sleep.

1.1. Background

Global railway networks are one of the primary means of transporting freight. For instance, in the United States almost 40% of freight transport is by rail [8], and over the past decades there has generally been an increase in the transport of commodities by railway (Figure 1). Furthermore, future increases are forecast, particularly in Europe. In a 2001 European Commission (EC) white paper, railway stakeholders agreed to achieve an increase from 8% to 15% in the market share of goods traffic transported by rail in the European Union [9]. Ten years later, another EC white paper further highlighted the need to increase goods transport by rail, stating that

"30% of road freight over 300 km should shift to other modes such as rail or waterborne transport by 2030, and more than 50% by 2050" [10].

Although it remains to be seen whether these goals will be accomplished, some areas of Europe have seen an increase in railway freight, although the trend can differ substantially between countries [11]. To facilitate an increased burden on the railway networks, at least in the absence of new infrastructure, more trains, more cargo per train, or a combination of both is required. The maximum length of freight trains, and therefore the freight they can haul, is regulated, for instance limited to 750 m in several European nations, including Sweden [12]. An increase in the total number of freight trains is therefore to be expected. However, the majority of railway networks are not used exclusively for freight. Passenger trains operate primarily during the daytime, with the result that for the railway networks to accommodate a significant increase in the number of freight trains, an increase in night-time freight traffic is anticipated. The night represents a particularly sensitive time of day regarding the possible effects of disturbance, and it is therefore important to understand how individuals react when subjected to the increased exposures associated with railway traffic.

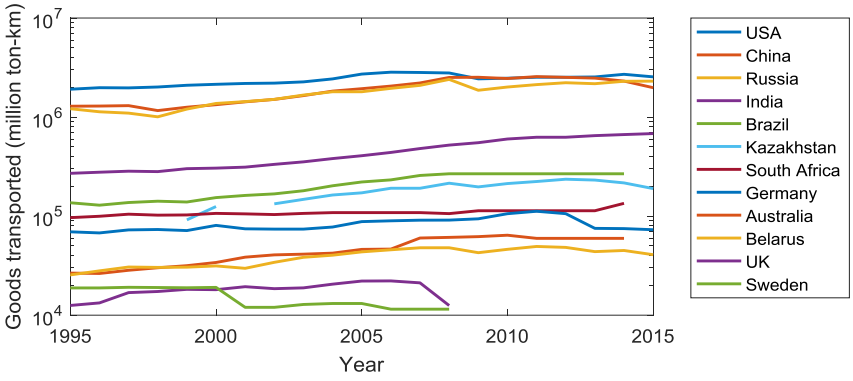

Figure 1 Freight transported by railway in selected nations. Data from the World Bank World Development Indicators collection [13].

1.2. Exposure

Moving freight trains, as with other traffic modes, generate sound, which is audible in the vicinity of the railway line. Additionally they may generate vibrations, which is palpable, that along with sound may propagate away from the

track (Figure 2). If the railway is located in a populated area, individuals may therefore be exposed to unwanted vibration and sound.

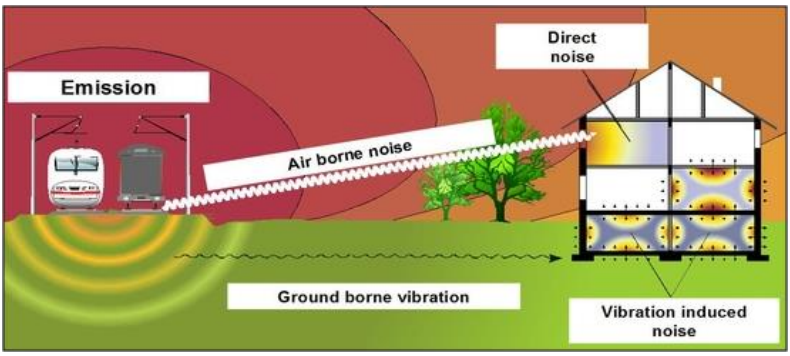

Figure 2 Vibration and noise exposure from railways. Reproduced from RIVAS project website [14].

1.2.1. Vibration and sound: A brief primer

The following sections present a brief overview of the physical quantification and measurement of vibration and sound.

1.2.1.1. Vibration

Vibration can be defined most simply as 'oscillatory motion'. This is motion that

> *"is not constant but alternately greater and less than some average value."* [15]

The rate of change of the motion is defined as its frequency f and is measured in cycles per second, termed Hertz (Hz). Vibration magnitude can be expressed in three principal ways; displacement $|x|$ measured in metres m, velocity $|v|$ measured in metres per second ms^{-1}, and acceleration $|a|$ measured in metres per second squared ms^{-2} or occasionally G (i.e. expressed as a ratio to acceleration from Earth's gravity, which is approximately 9.81 ms^{-2}). All three are interrelated, whereby instantaneous velocity is the rate of change of displacement, and instantaneous acceleration is the rate of change of velocity. For sinusoidal vibration, the interrelationships of these descriptors are given by formulae (1)-(3);

$$|x| = \frac{v}{2\pi f} = \frac{a}{(2\pi f)^2} \tag{1}$$

$$|v| = 2\pi f x = \frac{a}{2\pi f} \tag{2}$$

$$|a| = (2\pi f)^2 x = 2\pi f v \tag{3}$$

Furthermore, each of these descriptors may be expressed as a maximum, an average or a cumulative value. The maximum may be the peak vibration or the difference between the peak vibration in one direction and the opposite direction, i.e. the peak to peak vibration. Measurements of the maximum value of a vibration signal are typically exponentially averaged using a time constant, termed the "time weighting". This exponential averaging attaches greater importance to the most recent measurements. Time weightings of fast (0.125 s) and slow (1 s) are commonly used.

The descriptor of an average vibration most frequently used is the root mean square (RMS), which is the square root of the arithmetic mean of the squared values of vibration. For sinusoidal motion, the RMS is the peak vibration divided by √2. The more general form for calculating the RMS of an acceleration signal $a(t)$ measured over period T is given by (4). Additionally, the RMS of a vibration velocity is proportional to the kinetic energy transferred by the vibration.

$$a_{RMS} = \left[\frac{1}{T}\int_0^T a^2(t)\,dt\right]^{\frac{1}{2}} \tag{4}$$

Vibration is sometimes reported in decibels, which is a logarithmic value of the ratio of the vibration amplitude to a reference value. However, this reference value can vary between investigators. For example, 10^{-5} ms^{-2} has been used in Japan [16], but 10^{-6} ms^{-2} is recommended in ISO 1683 [17].

In summary, the quantification of vibration is often complex. It is a frequency-dependent motion which can be described in terms of the peak, average or dose of a displacement, velocity or acceleration. It may be reported in either SI or imperial units, either as absolute values or relative to some other value (i.e. *G*), which then itself may or may not be reported as a logarithmic ratio to a non-universal reference value. When considering human response, there is no general agreement on which vibration descriptor is most appropriate, with a resulting lack of coherence in reporting in the literature and across national standards. It is

however possible to calculate any desired metric if a full time-history of a vibration signal is available. In this thesis, vibration will primarily be reported according to the Swedish standard SIS 460 48 61 [18], as a maximum velocity expressed in millimetres per second (mms^{-1} or mm/s) with slow (1 s) time weighting, and alternative descriptors will be presented concurrently where appropriate.

1.2.1.2. Sound

Fundamentally, sound represents a special case of vibration, where the fluctuations in a medium are received by the ear and perceived as sound by the brain. Unwanted, unpleasant or disturbing sound is generally termed "noise", and this definition of noise will be used throughout this thesis, unless otherwise noted (e.g. signal noise when measuring activity in the central nervous system).

A sound wave is a fluctuation in pressure. When considering human response, the level of noise is frequently described as a sound pressure level L_p, which is a logarithmic value of the ratio of the sound pressure p to the reference value p_0 defined as the threshold of human hearing (20 µPa). Sound pressure level is calculated according to (5) and is measured in decibels (dB).

$$L_p = 20\log_{10}\left({}^{p}/_{p_0}\right) \tag{5}$$

Sound may vary in level, in frequency and over time, so a number of additional parameters are frequently used to quantify noise. The equivalent continuous sound pressure level L_{Eq} is an average of the total sound energy measured over a defined time period T. It is calculated according to (6), where $L_p(t)$ is the time varying sound pressure level at time t.

$$L_{Eq} = 10\log_{10}\left[\frac{1}{T}\int_0^T 10^{L_p(t)/10}dt\right] \tag{6}$$

The maximum sound pressure level L_{max} over a measurement period is often of interest. Analogously to the time weighting for vibration measurements, L_{max} involves exponentially averaging the square of the sound using a predefined time constant. These two main time weightings are fast (averaged over 0.125 s, denoted F in indicator subscript) and slow (every 1 s, denoted S). The difference between L_{max} measurements with fast or slow time weightings can reasonably be expected to be around 5 dB [19].

The human ear can detect sound from approximately 20 Hz-20 kHz, although it can detect lower frequencies if the sound is of sufficient level [20]. However, it is not equally sensitive to all frequencies, being less sensitive to very low and very high frequencies. When considering human response, sound levels are often weighted in the frequency domain to account for this uneven response. The A-weighting filter was designed to approximate human hearing at relatively low sound pressure levels (around 40 dB), and is the weighting most commonly used in environmental acoustics. If a sound pressure level has been A-weighted, it is noted in the descriptor subscript along with the time T for an equivalent level, or the time weighting for maximum levels. For instance, the A-weighted equivalent sound pressure over 8 hours would be denoted $L_{\mathrm{AEq,8h}}$ and the maximum A-weighted sound pressure level measured with a fast time weighting would be denoted $L_{\mathrm{AF,max}}$.

1.2.2. Vibration from railway freight transportation

The interaction between the train wheels and the rail of the track is frequently irregular, including irregularities in track evenness such as variations in level and track defects, irregularities in track support stiffness, and wheel irregularities such as non-roundness and flats [21]. These irregular interactions give rise to vibration. Freight trains generally have much higher axle loads than other forms or railway transportation, such as passenger or automotive trains, and thus the generated vibrations can be of greater magnitude. Furthermore, vibration from freight trains tends to have a dominant spectral peak in the 5-10 Hz region, and it is low frequency vibrations such as these that attenuate least with distance [22].

An overall characterisation of vibration generation, propagation and reception was provided by Madshus et al. [22]. The region where vibration is generated is composed of the train, track, embankment, foundation and the nearby soil, and each of these contributes to the spectral characteristics of the vibration signal. From this region, vibration may propagate outwards from the railway. The propagation in this zone is determined primarily by the dynamic properties of the soil, and the softer the ground, the more dominant the low frequency peak becomes. Furthermore, the ground properties are not determined solely by their constituent materials (e.g. silt, clay, sand, granite, sandstone) but also environmental factors including water content and temperature [23]. Following propagation, a reception region is the zone where humans are exposed to the vibration, which will generally be indoors for assessing the effects of vibration on human response in exposed populations. The reception region therefore includes the soil interacting with the building foundation, the foundation itself, and the building

structure. Vibration is not uniform throughout a building, and due to cantilever "swaying" motion, horizontal vibration in particular actually increases monotonically with floor height [24]. Furthermore, vibration can vary significantly within a single room. Analogously to a plucked string, the floor can oscillate more freely perpendicular to its length (i.e. vertically) at its mid-span, rather than at the edges where it is fixed to the adjoining walls. Consequently, vertical vibrations will often dominate in the centre of a floor, and horizontal vibration may dominate towards the edges. In addition to position within a room, the path between the floor and the receiver should also be considered. Soft versus hard propagation paths, for instance carpet versus laminate flooring or sitting on a wooden chair versus sitting on a soft sofa, have different dynamic properties influencing the vibration at the receiver. In an example of lying in bed, the mass of the individual may cause more or less compression of the mattress springs, in turn affecting the directionally dependent transmissibility.

Predicting the vibration from railway traffic that an individual may be exposed to is therefore not a simple process, involving frequency-, environmentally-, structurally- and individually-moderated factors. Should vibration reach an individual, it may or may not be perceived, and may or may not induce a response, as described in the following sections.

1.2.3. Somatosensory sensory system

The body senses motion in a distinct number of ways, but the primary manner in which whole body vibration from railways is sensed is through mechanoreceptors in the somatosensory system. The class of mechanosensors primarily responsible for the sensing of vibration are the rapidly adapting low threshold mechanoreceptors (RA-LTMRs) [25]. These are divided into two further subclasses, RAI- and RAII-LTMRs. In humans, RAI-LTMRs are termed Meissner corpuscles (MCs), are located in the dermal papillae of glabrous skin (see Figure 3), respond optimally to skin movement, and are responsible for sensing very low frequency vibration (1-10 Hz). Pacinian corpuscles (PCs) are RAII-LTMRs located in the deep dermis of glabrous skin (Figure 3), and respond optimally to vibration. Although PCs are more sensitive to higher frequency vibration than MCs, being most sensitive around 80-300 Hz, they also respond at lower frequencies [26].

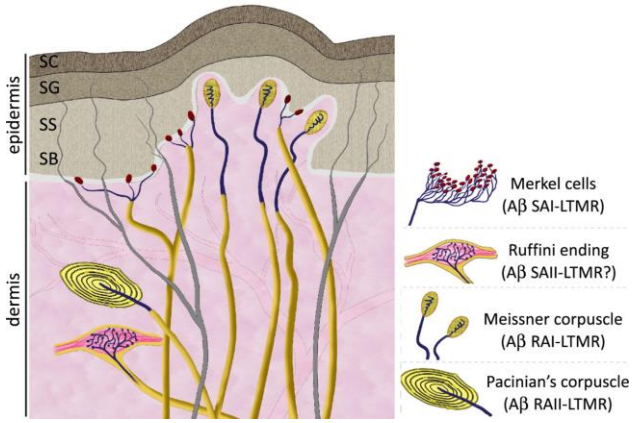

Figure 3 Mechanoreceptors in glabrous skin. SC, stratum corneum; SG, stratum granulosum; SS, stratum spinosum; SB, stratum basalis. Adapted from [25] with permission.

In the central nervous system, the RA-LTMRs project to the brainstem dorsal column nucleus via the dorsal columns (Figure 4) [25]. Second-order neurons ascend through the medial lemniscus pathway to the ventral posterior nuclear complex of the thalamus. From the thalamus, third-order neurons project to the somatosensory cortex, where much of the integration and processing of the vibration begins.

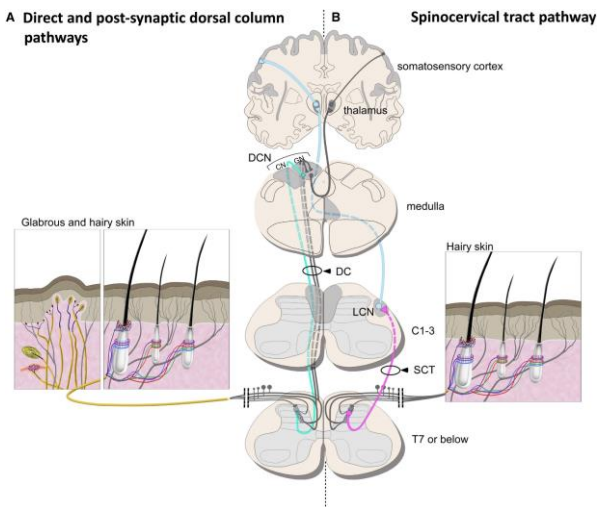

Figure 4 Somatosensory circuits in the central nervous system. Vibration is sensed by receptors in glabrous skin, and projected along the direct and post-synaptic dorsal column pathways. DC, dorsal columns; DCN, dorsal column nuclei; CN, cuneate nucleus, GN, gracile nucleus. Reproduced from [25] with permission.

1.2.4. Vibration perception thresholds

In humans, the conscious detection of vibration depends upon the excitation direction and frequency [27], signal duration [28, 29], posture [30] and age [29]. Vibration detection thresholds are lower when recumbent than in other postures [30], with sensitivity to vertical (i.e. perpendicular to the plane in which the floor lies) vibration highest around 4-10 Hz and horizontal vibration around 2-5 Hz [15]. Furthermore, the biomechanical behaviour of the human body can influence the perception of whole body vibration (WBV). Different body sections have different resonant frequencies, and thus there can be different vibration amplitudes at different body positions [31].

Frequency-dependent perception thresholds for vibration have been measured by a number of researchers, but the paradigms employed in such measurements are not representative of how vibration is experienced in real-world environments. For instance, some of the more recent thresholds for recumbent positions were measured with individuals lying on a hard vibrating plate [16]. A material more easily deformed by the force of the body upon it, such as a mattress, would result in a more uniform distribution of contact between the individual and the surface of the vibrating body, but would likely undergo localised deformation influencing the consequent vibration amplitudes in these regions. Furthermore, perception thresholds provide information only on whether an individual can or cannot perceive the presence of vibration typically sinusoidal in character; they are less useful regarding response to vibration signals with more complex spectra, or the subjective experience of the vibration.

Despite the shortcomings of vibration perception thresholds, they have been used to design filters to weight a vibration signal such that it approximates human perception (Figure 5) [32, 33]. These weighting filters include W_d and W_k weighting, designed to filter a whole body vibration signal in the horizontal and vertical directions respectively [32]. A further weighting, termed W_m weighting, was also introduced for assessing the comfort and annoyance in buildings, and is independent of posture and direction [33].

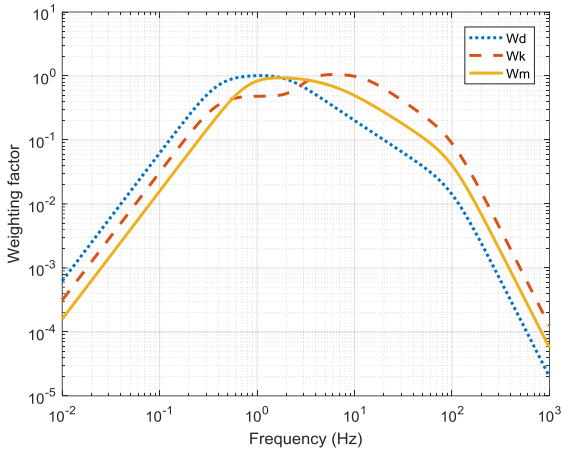

Figure 5 Vibration weighting filters Wd, Wk and Wm.

1.2.5. Auditory sensory system

Humans sense sound via the auditory sensory system, an overview of which is presented in Figure 6.

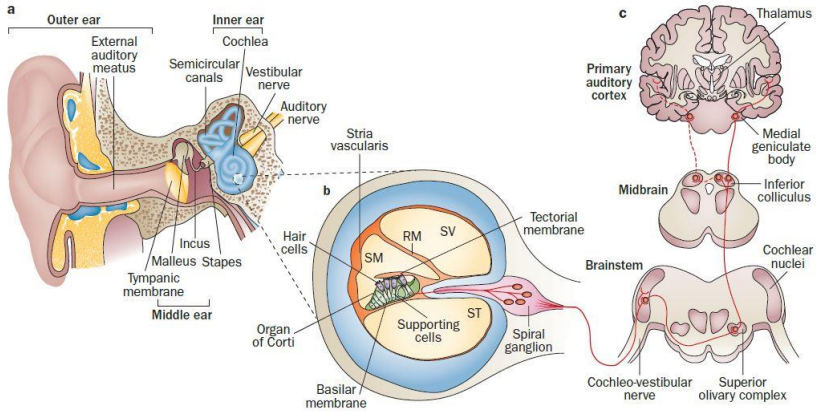

Figure 6 The human auditory system. A. cross-section of the ear. B. Cross-section of the cochlear. C. Ascending central auditory pathways. Reproduced from [34] with permission.

In the outer ear, airborne sound is collected and transmitted along the ear canal to the tympanic membrane (eardrum). This sound, being changes in pressure, causes movement of the tympanic membrane, which is in turn connected to three

bones (ossicles) in the middle ear. The ossciles (malleus, incus and stapes) transfer the motion to the cochlear in the inner ear. Motion of the perilymph and endolymph fluids inside the cochlea is transmitted to the basilar membrane, upon which sits the organ of Corti. The organ of Corti is responsible for converting the sound from a mechanical to an electrical signal. From the cochlea, the first-order auditory nerve projects to the cochlear nuclei in the brainstem. The majority of second-order projections ascend to the contralateral superior olivary complex (SOC). From the SOC, projections ascend through the lateral lemniscus pathway to the inferior colliculus (IC) in the midbrain. From the IC, the projections continue to the medial geniculate body (MGB), where all fibres of the ascending auditory pathway will synapse. Located in the thalamus, the MGB is the final subcortical relay before the signal is projected to the auditory cortex, where much of the processing of auditory information occurs [35].

1.2.6. Perception and response following multisensory exposure

Signals from the somatosensory and auditory systems, along with other inputs including visual, olfactory and gustatory, interact at higher brain levels, forming a coherent and multisensory perception of the environment [36]. Because of these neural cross-modal interactions, the perception of one stimulus can be enhanced (or suppressed under certain conditions) by the presence of a second modality [37]. Stochastic resonance is the phenomenon whereby the addition of random noise (signal noise, rather than unwanted sound) to a signal of subthreshold level may increase the level of the signal above threshold, leading to a response [38]. For instance, the presence of sound has been found to lower the detection threshold for localised vibration delivered to the finger, with an increasing sound level lowering the threshold in a dose-dependent manner [39]. Animal studies have demonstrated that low-level tactile and auditory stimulation have a synergistic effect on neuronal response, but that at higher sound levels the effect became additive rather than multiplicative [40].

Railways, particularly those carrying freight, represent a source of both vibration and noise. A cross-sectional field study found that for the same noise levels, annoyance by railway noise is higher in areas with strong railway vibration than in areas with no vibration [41]. The same study showed that for the same vibration exposure, annoyance by railway vibration was higher in areas with higher noise levels (56-65 dB $L_{AEq,24h}$) than in areas with lower noise levels (51-55 dB $L_{AEq,24h}$). This finding supported earlier work, demonstrating that annoyance in areas with vibration corresponded to an increase in noise level of around 10 dB $L_{A,max}$ in areas with noise alone [42, 43]. It is however unclear whether such

studies truly reflect cross-modal psychological effects, whether the presence of vibration leads to secondary noise exposure such as rattle that in turn elicits higher annoyance, or whether respondents are accurately able to disentangle their degree of response attributable to the separate noise and vibration sources.

The interactions of railway noise and vibration on human physiological response are furthermore less well understood. Cross-modal effects of vibration and noise from railway freight have not previously been investigated, and represent a knowledge gap worthy of attention if the physiological response of exposed individuals is to be understood.

1.3. Sleep

Sleep is ubiquitous throughout the animal kingdom, although a single "core function" remains elusive [1]. Some of the proposed functions of sleep include immune functions [44], reduced whole-body and brain-specific energy consumption [45], macromolecular biosynthesis [46], clearance of β-amyloid that accumulates during wakefulness [47], reducing cellular stress (unfolded protein response) [48], restoration of cognitive performance degradation [49], memory consolidation [50, 51] and synaptic homeostasis [52, 53]. Whatever the function or functions of sleep, it is vital for health, and in the most extreme cases, prolonged sleep deprivation leads to death in flies and mammals [54, 55].

1.3.1. Sleep physiology

In broad terms, sleep can be classified into two states: non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep. NREM sleep is further divided into three stages, which are – in order of increasing depth – N1, N2 and N3 [56]. Stage N3 is also known as slow wave sleep (SWS) due to its characteristically low frequency, high amplitude EEG. Following sleep onset in healthy individuals, sleep progresses quickly from N1 through to N2, followed by N3 and then REM. This "sleep cycle" progresses over approximately 90 minutes, before repeating over the course of the total sleep period. Early in the sleep period, SWS dominates the cycle, with an increasing proportion of N2 and REM sleep and a corresponding reduction of SWS as time asleep progresses (see Figure 7).

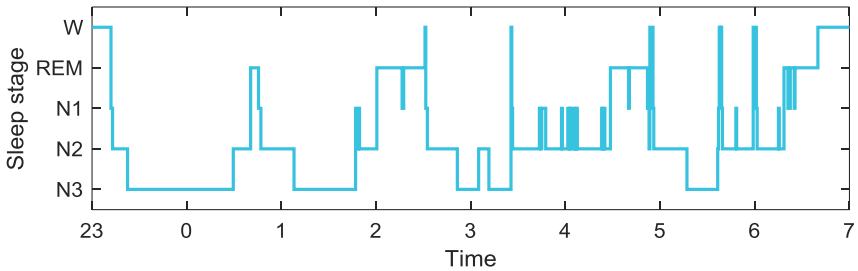

Figure 7 Hypnogram illustrating typical sleep rhythm across the night.

1.3.2. Measurement of sleep

A number of techniques exist for measuring different components of sleep. The major methods are outlined in the following section.

1.3.2.1. Physiologic measurement of sleep

Polysomnography (PSG) involves recording the surface EEG, bilateral electrooculogram (EOG) and submental electromyogram (EMG) [56]. The recorded data are analysed in 30 s epochs to determine sleep stage, based on EEG frequency and amplitude, the presence or absence of specific EEG features (K-complexes and spindles), eye movements and muscle tone. EEG arousals, which are frequently considered as indicators of sleep fragmentation [57, 58], are characterised by abrupt shifts in the EEG frequency of >16 Hz, lasting ≥3 s and preceded by ≥10 s of stable sleep. During REM sleep, there must also be a concomitant increase in submental EMG of ≥1 s in order for an arousal to be scored. Although polysomnography is frequently seen as the "gold standard" of sleep research (e.g. [59, 60]), an ideal measurement method would not interfere with sleep, but the PSG apparatus requires at least one night of habituation before sleep data can be considered as normal [61]. Furthermore, manual sleep scoring is required, and results can vary between [62, 63] and within [64] scorers. Under the sleep scoring criteria of Rechtschaffen and Kales (R&K) [65], SWS with moderate or high amplitude was scored as Stage 3 or Stage 4 respectively, but these two stages were combined together as Stage N3 by the American Academy of Sleep Medicine (AASM) in 2007 [56]. Although the AASM scoring criteria improved inter-rater reliability, they are not universally accepted without criticism, particularly regarding some of the rules for EEG placement and arousal scoring, and the lumping together of stages 3 and 4 in N3 [66]. Re-

garding this final point, some authors eschew the AASM scoring guidelines and continue to report sleep scored according to the R&K criteria.

Actigraphy is a measurement method where movement is recorded and used to extrapolate sleep information. Compared to PSG it is inexpensive and straightforward to setup, so can easily be applied to larger populations and in settings where the presence of a trained individual for PSG electrode application is troublesome. Actigraphy is furthermore non-invasive, so can be used on populations who may be sensitive to electrodes, for instance insomniacs and children. Total sleep time (TST), sleep efficiency and wakefulness determined with actigraphy correlates reasonably well with corresponding PSG measures [59], but sleep microstructure may be disturbed even while preserving TST, making actigraphy unreliable for detecting subtle sleep disturbances [67]. The use of proprietary hardware and sleep-scoring algorithms by different actigraph manufacturers further complicates comparisons not only between PSG and actigraph data, but also between different actigraphy studies.

Cardiac activity is frequently recorded concurrently with EEG, using electrocardiography (ECG). Increased heart rate is a commonly used indicator of autonomic activation, and such activations as seen in the ECG data are frequently accompanied by EEG arousal [68]. However, autonomic arousal may occur at the sub-cortical brain stem level [69], and consequently ECG modifications may occur without apparent EEG arousal [70, 71]. Thus ECG in parallel with EEG provides a sensitive measure of vegetative arousal during sleep. Event-related cardiac alterations following noise and vibration exposure are of particular interest, given that repeated induced autonomic activations have been proposed as a risk factor for developing cardiovascular disease [72].

1.3.2.2. Measuring perception and effects of sleep disturbance

Somnolence is one of the hallmarks of sleep disruption or restriction. Daytime sleepiness can be measured objectively, for instance with the Multiple Sleep Latency Test (MSLT) which is a measure of the ability or tendency to fall asleep [73]. Wakefulness, being distinct from but perhaps related to sleepiness, can be measured objectively using the Maintenance of Wakefulness Test, where the sleep latency of an individual instructed to remain awake during quiet restfulness is measured [74]. Both procedures are time-intensive throughout the day, precluding participants from engaging in normal daytime activity. The MSLT furthermore requires participants to attempt to nap. This may lead to reduced sleep pressure, which may cause difficulties attaining sleep the following evening.

Introspective sleepiness is measured with the application of questionnaires. A number of instruments measure habitual sleepiness and sleep quality, for instance the Epworth Sleepiness Scale [75], Pittsburgh Sleep Quality Index [76] and Karolinska Sleep Questionnaire [77]. These are retrospective self-assessments over an extended time, and are hence unsuitable for detecting short-term effects on sleep, for example following a single night of railway traffic exposure. Instantaneous measures such as the Karolinska Sleepiness Scale [78] and the Stanford Sleepiness Scale [79] are useful for detecting momentary sleepiness, but it is unclear whether they are suitable for detecting sleepiness following nocturnal noise exposure [80]. In laboratories, numerical scales with fixed endpoints and semantic scales have proved capable of detecting the effects of single nights of noise on morning tiredness, as well as other measures of sleep including perceived sleep quality and perceived sleep depth [81, 82], although data regarding their suitability for field studies are mixed [83, 84].

According to the World Health Organization (WHO), self-reported sleep disturbance is the largest contributor to the estimated disease burden of environmental noise [85]. There is currently no standardised question for assessing exposure-induced sleep disturbance. However, there are standardised questions for noise-induced annoyance [86], which form a useful basis for constructing questionnaire items to assess the perceived impact of a specific exposure on sleep. These questions should have high specificity to the exposure of interest. However, individuals spend the majority of the night in an unconscious state, and cannot therefore critically appraise the disturbing effects of exposure on sleep during these periods [85]. As such, there can be a lack of coherence between objective and subjective measures of sleep. For example, subjective sleep quality of a specific sleep episode (as opposed to habitual sleep) has been positively related to PSG measures of sleep efficiency SWS and N2, and negatively related to N1 [87-89]. However, it has also been found that time in various sleep stages had *no* relation with sleep quality, and time in N2 has been *negatively* associated with habitual sleep quality [87, 90]. Nevertheless, questionnaires can provide a useful indicator of the subjective experience of sleep.

1.3.3. Individual moderators

Sleep can vary greatly between individuals. The following sections summarise some of the most important sleep-moderating factors to consider.

1.3.3.1. Age

Sleep architecture changes with age, including a reduction in slow wave and REM sleep and corresponding increase in lighter sleep stages, reduction in total sleep time and sleep efficiency, and increased wakefulness and sleep fragmentation among older individuals than in their younger counterparts [91-95]. Furthermore, the prevalence of sleep-related disorders including insomnia, restless legs syndrome (RLS) and obstructive sleep apnoea (OSA) increases with age [96-98]. The worsening of objective sleep may be partially offset by older individuals downwardly adjusting their criteria for good subjective sleep, and so may perceive their sleep as good whereas younger individuals would perceive the same objective sleep as poor [99].

1.3.3.2. Sex

Lighter sleep has been found in men than in women [100], and healthy women have been seen to have a higher percentage of SWS, longer sleep time and indicate less objective sleep disturbance than men [101]. Despite better objective sleep in women, they frequently report greater sleep disturbance [102], and are at increased risk for developing sleep disorders including insomnia [103] and RLS [104]. Age may differentially affect how women and men rate their sleep. Peri- and post-menopausal women are more likely to be dissatisfied with their sleep than premenopausal women [105], although evidence from PSG studies provides only mixed support for prominent effects of menopause [101, 105-107].

1.3.3.3. Sensitivity

Noise sensitivity was defined by Job as

> *"the internal states (be they physiological, psychological [including attitudinal], or related to life style or activities conducted) of any individual which increase their degree of reactivity to noise in general"* [108].

Noise sensitivity has been estimated to have a prevalence of 22-50% [109, 110]. Aside from moderating annoyance to traffic noise [109], noise sensitivity can modify the subjective evaluation of sleep quality and sleep disturbance, with sensitive individuals generally reporting worse subjective sleep and higher noise-induced sleep disturbance than non-sensitive persons [111-113].

Cardiovascular activation to noise during wakefulness has been found to be higher among noise-sensitive individuals, but the moderating effects of sensitivity disappeared during sleep [114]. The sleep-disrupting effects of noise vary between individuals, [115, 116], and it is unclear whether noise sensitivity is at least partially responsible.

1.3.3.4. Chronotype

Chronotype, i.e. an individual's morning or evening preference, describes the preferred timing of sleep and wake times, has a genetic basis [117], is age- and sex-dependent, and furthermore may relate to the photoperiod at birth [118]. Variations in the dynamics of slow wave activity during NREM sleep have been observed between morning and evening types, with the authors suggesting this may indicate underlying chronotype-dependent differences in the glutamatergic and GABAergic neurotransmitter systems [119].

1.3.3.5. Summary

Because sleep is highly dependent upon a number of inter-individual moderators, it is vital when performing any form of research on sleep to account for these factors if any valid conclusions are to be drawn. The studies presented in this thesis were therefore designed to account for several of the major factors, including sex, age, and noise sensitivity.

1.3.4. Effects of disturbed sleep

A wide spectrum of social, clinical, endogenous, environmental and behavioural factors may result in the disturbance of sleep. Sleep disturbance itself can be classified into three broad states: total sleep deprivation, chronic sleep deprivation, and sleep fragmentation. These three classifications and their associated health consequences are discussed in the following paragraphs.

1.3.4.1. Acute total sleep deprivation

Total sleep deprivation refers to depriving an individual of at least one full night of sleep. As early as the late 19th century, it was shown that prolonged total sleep loss in animals could lead to death [120]. The impact of experimentally induced sleep loss in humans varies between individuals, being dependent upon a multitude of circadian, sleep, arousal, individual and experimental factors [121]. These factors include the quality of the previous sleep period, time awake, circadian time, physical activity, light, noise, temperature, posture, motivation, drug intake, age, sensitivity, personality, and experimental test duration, complexity, difficulty, timing, and objectivity or subjectivity.

Despite the wide disparity of determinants influencing the effect of sleep loss, many studies in humans have shown consistent findings. Sleep loss can lead to both objective, as measured by the MSLT, and subjective sleepiness [121-125], decrease in alpha activity [126], impaired cognition and performance [125, 127, 128], negative changes in mood [128], impaired short term memory [129] and impaired hippocampal function [130].

1.3.4.2. Chronic sleep deprivation

Chronic sleep deprivation refers to partial sleep restriction over an extended period. The immediate effects of partial sleep restriction include objective and subjective daytime sleepiness, and the effects increase with the accumulation of sleep loss. For instance, the decreasing sleep latency measured with the MSLT found across 7 days of partial sleep restriction indicates an increasing sleep propensity [122]. Insomnia is defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as

> *"A predominant complaint of dissatisfaction with sleep quantity or quality, associated with one (or more) of the following symptoms:*
>
> 1. *Difficulty initiating sleep.*
> 2. *Difficulty maintaining sleep, characterised by frequent awakenings or problems returning to sleep after awakenings.*
> 3. *Early-morning awakenings with inability to return to sleep"* [131].

Furthermore, in order to make a diagnosis of insomnia, DSM-5 notes that

"the sleep disturbance causes clinically significant distress, or impairment in social, occupational, educational, academic, behavioural or other areas of functioning; occurs at least three nights per week; is present for at least three months; occurs despite adequate opportunity for sleep."

Insomnia is associated with reduced perceived sleep quality, dissatisfaction with sleep duration and, over time, an increased incidence of mental disorders [96]. Reduced sleep time leads to a decrease in performance measured using the psychomotor vigilance test (PVT, [132]), and the duration of vigilance lapses increasing monotonically with sleep debt [133].

Chronic sleep deprivation is associated with, in addition to deleterious behavioural and cognitive effects, negative health outcomes. Habitual short sleep time (<6 h/night) is associated with increased risk for obesity, among both adults and children [134]. The pathways responsible for this link between short sleep and obesity, and furthermore with an increased risk for developing diabetes, have been proposed to be alterations in glucose metabolism, increased appetite and reduced energy expenditure arising from sleep loss [135].

Cardiovascular morbidity has been linked with short sleep time [136]. Furthermore, short sleep duration has been associated with hypertension [137] and cardiovascular disease [138, 139]. In addition to the adverse effects of chronic short sleep, sleep duration follows a U-shaped association with the risk for mortality, with individuals who sleep less than 6 hours or more than 8 hours per night having an increased risk for all-cause mortality compared to persons who sleep 7-8 hours per night [140-143]. Short sleep duration correlates with higher BMI, smoking, hypertension, and poor general health, and there are plausible explanatory mechanisms [144]. However, the pathways between mortality and long sleep are currently not well understood.

1.3.4.3. Sleep fragmentation

Whereas sleep deprivation refers to either acute or chronic reductions in the total sleep time, sleep fragmentation arises from the repeated disturbance of sleep during the night, rather than simply a shortening of sleep. One classical indicator of sleep fragmentation is abrupt shifts in the EEG frequency, termed an EEG arousal [58].

Obstructive sleep apnoea is a condition characterised by occlusion of the airway during sleep, causing oxygen desaturation, disrupted sleep architecture and arousal from sleep [145]. Sleep fragmentation during OSA, as indicated by prominent EEG arousals, is thought to be the underlying cause of many of the associated adverse effects [146], which includes excessive daytime sleepiness [75]. In addition to consequent subjective tiredness, this sleepiness may contribute to work-related and motor vehicle accidents [147]. OSA, via intermittent hypoxia and autonomic arousal [148], may lead to cardiovascular outcomes including hypertension [149], myocardial infarction [150], coronary heart disease [151] and stroke [152]. OSA is also associated with diminished psychomotor function [153] and problems with concentration [154], both outcomes typical consequences of sleep fragmentation.

Sufferers of RLS frequently report increased fatigue and somnolence, symptoms linked with the severe sleep disruption that accompanies the condition [155].

1.3.4.4. Summary

Chronic sleep deprivation is associated with a number of adverse health consequences, including impaired cognition, increased risk for obesity and diabetes, cardiovascular disease and all-cause mortality. Sleep fragmentation may have deleterious effects on restoration comparable to chronic deprivation, for instance manifest as daytime somnolence, even without reducing sleep time. The disturbance of sleep by external factors may therefore have negative health consequences.

1.3.5. Arousal from sleep

Most wake-regulating stimuli are integrated in the ascending reticular activating system (ARAS) [156]. The ARAS originates mainly in the reticular formation of the brainstem, and via separate pathways can directly or indirectly activate the thalamus and cortex [157, 158]. High activity in the ARAS forms a wake promoting system, whereas low activity in the ARAS is a requirement for NREM sleep [157]. The ARAS and the ventrolateral preoptic nucleus regulate wakefulness and sleep respectively, normally under the influence of homeostatic and circadian processes [159]. The auditory and somatosensory systems involve projections to the reticular formation [160], and hence external stimuli are capable via ARAS activation of overriding the homeostatic and circadian regulation of

sleep, leading to arousal or awakening. Nocturnal vibration and noise exposure therefore may lead to sleep disruption.

A noise effects reaction scheme was proposed by Babisch [161, 162]. Noise exposure during sleep can directly affect neuroendocrine homeostasis; sympathetic arousal and release of corticosteroids, which involve subcortical brain regions including the hypothalamus. The hypothalamus, which forms part of the ARAS [163], projects to the endocrine, limbic and autonomic nervous systems. The stress responses can lead to physiologic changes in blood pressure, cardiac output, blood lipids, blood glucose, blood viscosity and blood clotting factors. These physiologic outputs are established risk factors for manifest cardiovascular disease (CVD), including hypertension, atherosclerosis, ischaemic heart disease, and stroke [164], and indeed cardiovascular disease has repeatedly been associated with night-time noise exposure from traffic [164-166]. Given that the somatosensory system has inputs to the ARAS, it is biologically plausible that vibration, as with noise, may contribute to physiologic stress reactions during sleep.

1.4. Vibration, noise and sleep

A graphical overview of noise- and vibration-induced sleep disturbance is presented in Figure 8. The impact of noise on sleep has been extensively studied (see section 1.4.1), but the effect of environmental vibration on sleep is comparatively neglected. Due to the paucity of data on vibration-induced sleep disturbance, the following section will additionally describe noise-induced sleep disturbance as a proxy for the possible biological effects of nocturnal vibration.

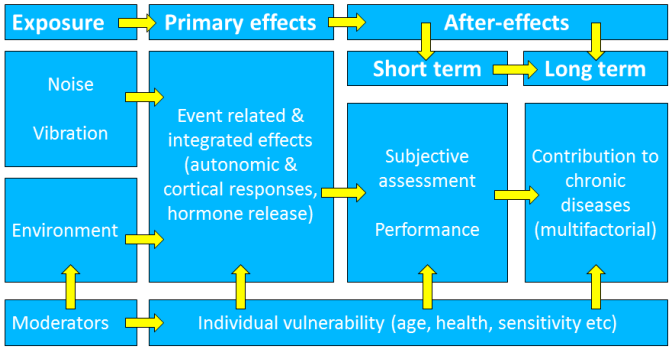

Figure 8 Hypothesis for vibration- and noise-induce–d sleep disturbance. Adapted from [167]

1.4.1. Traffic noise and sleep disturbance

The following sections present a summary of existing research into the effects of traffic noise on sleep.

1.4.1.1. Primary effects

Night-time traffic noise can adversely affect sleep structure, both in terms of the overall sleep architecture and autonomic and cortical arousal immediately following exposure. An early study found that aircraft and truck traffic noise led to increased event-related arousal, defined as increased alpha (8-12 Hz) activity in the EEG, and sleep stage changes in subjects with cardiac arrhythmia [168]. Road, rail and aircraft noise can lead to autonomic arousal, reflected by elevated heart rate [72]. These elevations in heart rate may be accompanied with increased probability of event-related EEG arousal and awakening, with the response increasing as a function of $L_{AS,max}$ [169]. Furthermore, autonomic and cortical response may be greater following road and rail traffic than road traffic of the same noise level [169], and railway noise may be more likely to induce event-related transitions to wake or N1 sleep than aircraft noise [83]. The greater response for train noise could be due to shorter rise time, higher frequency content above 4 kHz and possibly shorter duration [83, 169, 170]. However, there is also evidence in the opposite direction, whereby arousal and awakening probabilities were greater following train noise with longer rise times and durations [171]. Physiological response to noise appears dependent upon the acoustical characteristics, but it is unclear exactly which acoustic factors aside from noise level are most relevant.

Induced physiologic response occurs only when the exposure level exceeds a certain threshold, for instance 33 dB $L_{AS,max}$ for the probability of awakening or transitioning to stage N1 following an aircraft noise event [172]. Motility reactions, which increase with night-time railway noise [170], begin at a maximum aircraft noise level of 32 dB $L_{AS,max}$ [173]. Behavioural awakening following night-time aircraft noise begins at 42 dB $L_{AS,max}$. [174].

Night-time traffic noise can negatively impact on sleep macrostructure. At levels ≥39 dB $L_{AEq,8h}$, it has been experimentally observed that road, rail and air traffic noise can have adverse effects on SWS latency, wakefulness after sleep onset (WASO), sleep efficiency (SE) and percent of sleep period time in wakefulness and N1 sleep [81]. Time in SWS and REM both decreased linearly with increasing $L_{AEq,8h}$, with corresponding decreases of subjective sleep quality and increas-

ing fatigue and reaction time. Furthermore, railway noise had more deleterious effects on SWS latency, time in SWS, and wakefulness, N1 sleep and SWS during the first sleep cycle. The adverse effects of railway noise are supported by other laboratory data showing that nights with railway noise can lead to reductions in SE, SWS, subjective sleep quality and mood compared to quiet control nights, along with increased N1 sleep and tiredness [175]. In nights with ≥40 dB L_{AEq} there was an increase in time awake and reduction in REM compared to 32 dB L_{AEq} nights, with a further increase to 44 dB L_{AEq} causing a reduction in SWS. Furthermore, noise from railway but not road traffic may have negative effects on WASO and time in REM in the field [176]. Reduced SWS, with a corresponding increase in N1 and awakenings, has also been found following aircraft noise exposure in the laboratory, with sleep fragmentation increasing with the number and maximum noise levels of events [177].

1.4.1.2. Short-term after-effects

There is a large body of evidence supporting the adverse effect of traffic noise on perceived sleep disturbance. The prevalence of insomnia has been found to be higher in areas with high volumes of night-time road traffic than in low traffic areas [178]. Accordingly, self-reported insomnia symptoms, namely *difficulties falling asleep*, *awakenings during the night*, and *waking too early* were recently positively associated with increased road noise of 5 dB $L_{AEq,23\text{-}07}$ [179]. Self-reported disturbance by road traffic noise can be partly mitigated by reducing the noise exposure via access to a quiet side of the building and closing windows [180], supporting a direct causal link between exposure and disturbance. A meta-analysis of 28 datasets found that self-reported sleep disturbance increased in a dose-dependent manner with increasing outdoor levels of road, rail and aircraft noise [181]. Air traffic led to the highest disturbance, followed by road and then rail, with disturbance following a U-shaped dependence on age, with noise being most disturbing to those in middle age. A later field study however found greater sleep disturbance for railway noise than for road traffic [182].

Sleep has been rated as subjectively worse in the laboratory following nights with air and rail noise compared to road noise nights [169]. In the field, perceived sleep disturbance can increase with maximum levels of airborne railway noise and noise structurally reradiated from railway tunnels [113, 183], and sleep medication use has been related to daytime railway noise levels [170]. Disturbance to railway noise may furthermore be influence by train pass-by frequency [113]. There is therefore evidence that noise from railways can lead to subjective

sleep disturbance, but it is unclear how this disturbance relates to other traffic modes.

There is mixed evidence for the effect of nocturnal traffic noise on cognitive performance. For instance, reaction time and fatigue have been demonstrated to increase as a function of night-time noise level [81, 184], and has been linked with reduced time in SWS [81]. Contrastingly, a field study on railway noise found no link between noise levels and reaction time in the PVT [83].

1.4.1.3. Long-term after-effects

Traffic noise exposure has been associated with CVD [164, 185]. In particular, night-time traffic noise may be more relevant for the development of CVD than daytime noise, at least for aircraft traffic [165]. Emerging data have linked the intermittency of traffic events intruding from the background level during the night with CVD [186]. There are fewer studies of the long-term effects of railway noise exposure than for other traffic modes, and the particular importance of nocturnal railway noise is even less well understood. There are however some epidemiological findings of positive associations between night-time railway noise levels and heart failure and hypertensive heart disease [187], as well as with systolic and diastolic blood pressure [188], although research is often lacking.

1.4.2. Freight trains

Freight trains during the night may be of more relevance than other train types. A field study found the probability of freight noise eliciting event-related transitions to wake or N1 sleep increased with $L_{AS,max}$, and furthermore these reactions were more probable than for passenger train noise above approximately 50 dB $L_{AS,max}$ [83]. Self-reported awakening in the field has been related to the number of freight trains during the night, but not to the number of passenger trains [189]. Laboratory studies have found that noise from freight trains lead to a higher awakening probability and greater cardiac arousal than passenger or automotive trains, with the authors speculating this was a consequence of their longer duration [171, 190]. No effects were seen on overall sleep macrostructure in the presence of nocturnal noise. Nocturnal exposure to freight train noise (n=30) led to increased alpha, beta and delta activity in the waking EEG and decreased reaction time (PVT) among persons who lived near railway lines than

residents of quiet areas [191], indicating that railway exposure leads to persistent sleepiness and impaired cognition in the long term.

There is therefore some evidence that the particular case of night-time railway freight noise may have a greater impact on sleep than other train types. Furthermore, field studies on the effects of night-time railway freight have only examined the influence of noise. It is plausible that these freight passages additionally involved vibration. If environmental vibration negatively impacts sleep, this could partly explain the consistently deleterious effects of freight relative to other train types.

1.4.3. Vibration and sleep

Vibration from road, rail, and tramways may negatively affect subjectively assessed sleep disturbance, early awakenings, waking during the night, and difficulties falling asleep [192-194]. However, research into the acute effects of vibration on objective sleep is largely lacking.

Subjective effects on sleep following night-time vibration were examined within the TVANE project. In an experimental study, when increasing vertical vibration velocities from 0.4 to 1.4 mms^{-1} while maintaining the noise level, a reduction in the self-reported outcomes of sleep quality, movements, morning tiredness, daytime tiredness and evening tiredness was found [195-197]. Furthermore, in nights with 1.4 mms^{-1} vibration, participants reported being more annoyed by vibration, vibration causing difficulties falling asleep, vibration causing awakenings and vibration causing worse sleep quality. Interestingly, also in the 1.4 mms^{-1} vibration night relative to the 0.4 mms^{-1} night, participants felt that noise caused difficulties falling asleep and that noise caused awakenings, even though the noise exposure was identical in both nights. This could indicate cross-modal influences of the separate exposures, where the increased vibration exposure enhanced the subjective response to noise. It could alternatively suggest that participants were not able to accurately evaluate which exposure led to their increased disturbance, or simply that they confused both exposures with one another.

The physiological effects of vibration on sleep are even less well examined than self-reported outcomes. In an early small-scale laboratory study, Arnberg et al. found that simulated vibration from heavy road traffic elicited changes in sleep structure and a decrease in REM sleep [198]. Body movements and short changes in EEG activity felt to indicate arousal (the study predates current EEG arous-

al scoring rules [56, 58]) occurred more frequently during vibration than during noise, and furthermore more frequently during combined exposure. However, vibration-only led to an increased likelihood of sleep stage changes than when presented alongside noise. As the brain continues to process auditory information during sleep [6], it is possible that without the noise providing a cue regarding the exposure source, the vibration was perceived as more threatening, with the body preparing to react accordingly. Enhanced arousal during sleep following combined exposure was partly supported by a later finding using auditory stimulation and vibration applied to the arm [199].

In summary, there is to our knowledge no previous research into the physiological effects of railway vibration on sleep, and only limited evidence for self-reported outcomes, which may be confounded by concurrent noise exposure. When two or more exposures are present, as can be the case with freight trains, it can be difficult to disentangle their differential effects.

1.5. Summary

Sleep is a vital component of human health and wellbeing. The sleeping brain attends to and may subsequently respond to arousing stimuli, leading to sleep disturbance, in terms of both changes of sleep structure and the reduction of total sleep time. Night-time railway noise can lead to autonomic and cortical arousal, with corresponding negative effects on sleep macrostructure. Freight trains in particular may have a greater impact than other train types, and can furthermore give rise to vibration. It is there important to understand the impact that vibration will have among exposed populations.

Physiological effects of railway vibration have not previously been investigated, and there is only limited work examining vibration and subjective sleep outcomes. Furthermore, previous work may be confounded by concurrent noise exposure. It is not well understood how railway noise and vibration interact regarding physiologic and self-reported response.

A growing burden of goods transportation on global railway networks will likely lead to an increase in nocturnal vibration and noise at nearby dwellings. The impact these exposures will have on the sleep of exposed populations reflects a nascent public health concern. The effects of railway freight vibration and noise on sleep physiology will therefore be the focus of this thesis.

2. Aims

The overall purpose of this thesis is to examine how nocturnal whole body vibration at levels corresponding to those occurring in residences alongside freight railway lines impact on human sleep. This will be addressed by the research questions.

- What are the acute effects of nocturnal railway vibration on sleep, and how are these effects related to vibration exposure?
- What are the differential and interacting effects of railway freight noise and vibration with regards to sleep?
- How are any associations between sleep and railway vibration modified by noise sensitivity?
- At what amplitude of vibration do acute physiological effects on sleep begin to manifest?

3. Participants and Methods

One of the advantages of measuring sleep in the laboratory, rather than in the field, is the precise regulation of noise and vibration exposure afforded by the controlled setting. We therefore performed a series of laboratory studies to determine the impact of railway freight vibration on sleep.

3.1. Sound environment laboratory

3.1.1. Laboratory setting

Three rooms in the sound environment laboratory were equipped with a bed, cabinet, desk, chairs and lamps to simulate a typical bedroom (Figure 9A). Each room was constructed as a separate module, and rested upon concrete slabs, which in turn rested upon isolating rubber blocks. The ventilation system was designed with a damped fan assembly in a separate area of the building and a series of silencers, with resultant operational background noise levels of ≤13 dB L_{AEq}. Hence, the rooms were well isolated from external noise and vibration, allowing accurate control of the experimental exposures.

The laboratory also included a private living space for the study participants, including a living area with sofa and television, fully equipped kitchen, dining area with table and chairs, three lavatories and a shower (Figure 9C and D). Participants had a private entrance to this simulated apartment, and each had an individual access card and key, the latter also allowing them to lock their respective bedrooms.

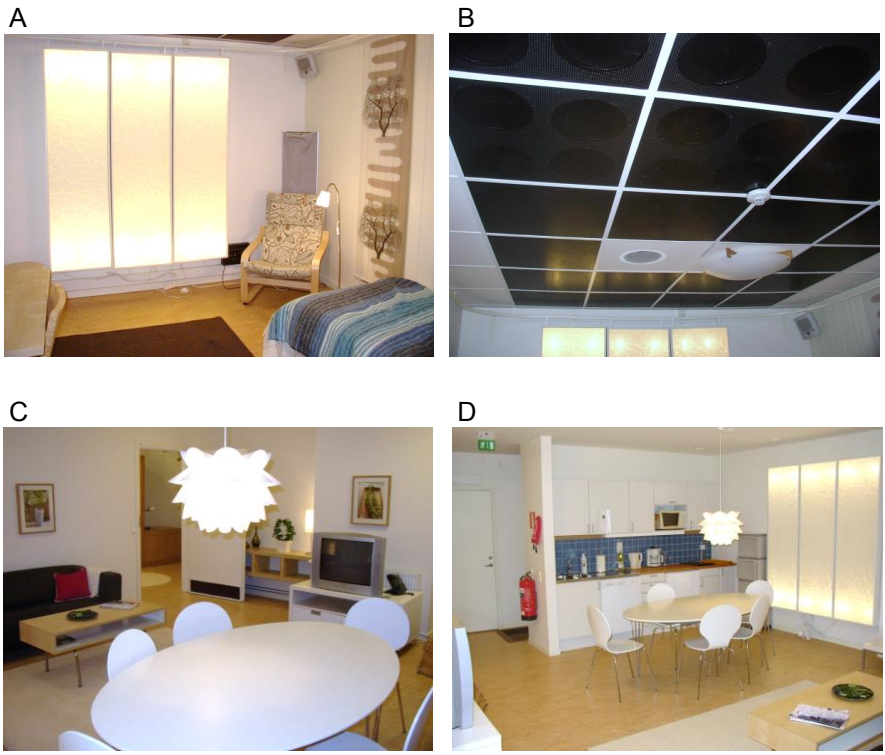

Figure 9 Sound environment laboratory. **A:** Bedrooms, with speaker cabinet for high frequencies visible in the corner. **B:** Bedroom ceiling with concealed speakers. **C:** Living and dining area. **D:** Dining and kitchen area.

3.1.2. Exposure reproduction

Eighty-eight 25 cm loudspeakers were mounted within the ceiling of each bedroom (Figure 9B), and were used to reproduce audio at frequencies below 125 Hz. Loudspeaker cabinets mounted in two of the upper corners were used to reproduce frequencies above 125 Hz.

Electrodynamic transducers were mounted to the underside of the bed frames, perpendicular to the head-foot axis. These were driven by 1000W power amplifiers, and were used to vibrate the bed frame horizontally, i.e. along the same head-foot axis in which the transducer was mounted. A preliminary investigation indicated that vertical vibration, when measured on the frame and beneath the lower back of a supine individual, was attenuated by around 80% (Figure 10). Horizontal vibration on the other hand was less attenuated, and even amplified,

with the result that WBV for the same driving vibration amplitude would be higher in the horizontal direction. The preliminary work also revealed that horizontal vibration was subjectively perceived as more annoying for the same amplitude [200]. It was therefore concluded that horizontal vibration was of greater relevance for potential response during sleep.

Each bed rested upon foam to decouple the bed from the floor, thus avoiding transfer of vibration to the floor. The vibration-inducing shakers were mounted within custom enclosures to minimise audible operational noise at the pillow position. Furthermore, the headboards of the beds were removed to avoid re-radiation of vibration as auditory noise close to the participant's head.

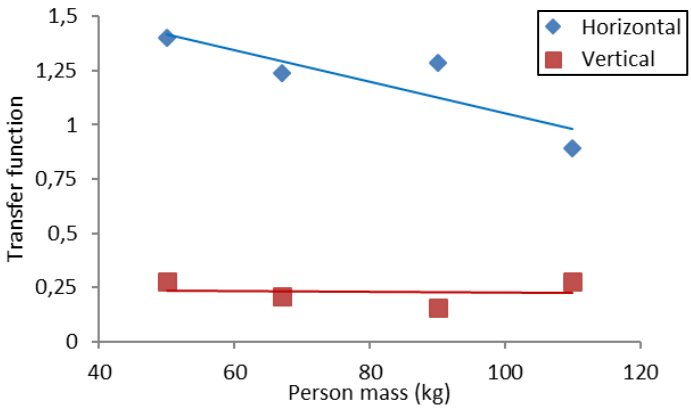

Figure 10 Transfer function (TF) between 10 Hz vibration measured on the bed frame and vibration measured between the mattress and the lower back of recumbent persons of different masses. Transfer functions are calculated by averaging measurements at between 4-88 mms^{-2}. TF<1: Vibration attenuation. TF>1: Vibration amplification.

3.2. Participants

3.2.1. Recruitment and participation

Recruitment was predominantly performed via public advertisements placed around various campuses of the two major universities in Gothenburg. All applicants completed a screening questionnaire to assess their suitability, with the following exclusion criteria: self-reported sleep problems; medication that might affect sleep as determined via FASS [201]; tobacco use; caffeine dependence; or a BMI outside of the normal range (<18.5 or >25) [202].

The screening questionnaire included a single item to assess noise sensitivity. This was a semantic scale with the following possible responses; Not at all sensitive, Not particularly sensitive, Quite sensitive, Very sensitive, Extremely sensitive. Individuals rating themselves as Quite, Very or Extremely sensitive were classified as noise sensitive. Individuals giving ratings of Not at all sensitive or Not particularly sensitive were classified as non-noise sensitive. Noise sensitivity has previously been shown to moderate psychological response to noise, including sleep disturbance, with sensitive individuals reporting a higher response than their non-sensitive counterparts for the same exposure [113, 182]. It was therefore hypothesised that if this heightened subjective reactivity correlated with a greater objective reactivity, then any physiological response observed in a non-sensitive population would be at least as strong, if not greater, in a sensitive population. Sleep study 4A (Table 1), as a pilot study, therefore had the participation criterion that accepted applicants must be non-sensitive to noise, with the reasoning being that such a group represented a "best case" population; any effects observed therein could reasonably be expected to occur to at least the same degree in a sensitive group, whereas the reverse was not necessarily true.

Noise sensitivity was additionally recorded on the first study evening using the same measure as during screening. The distribution of the differences in sensitivity scores obtained at both times is presented in Figure 11. A positive difference indicates that participants rated themselves more highly noise sensitive on the screening questionnaire. With the exception of Study 2, the majority of individuals rated themselves equally on both questionnaires.

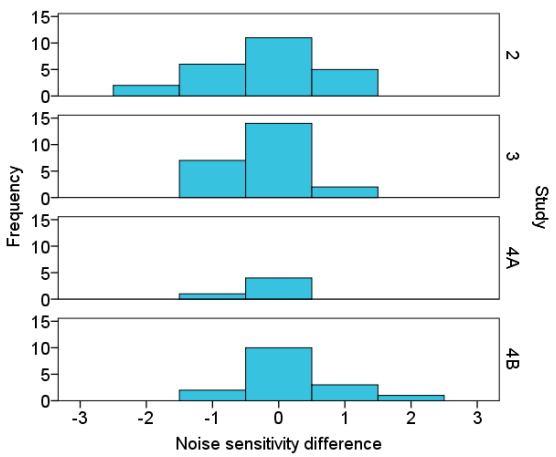

Figure 11 Difference in noise sensitivity score between the screening and first evening questionnaires

The hearing of all participants was assessed for each ear using pure tone audiometry to a screening level of 20 dB HL at frequencies of 0.25, 0.5, 1, 2, 4 and 8 kHz.

During the study period, participants were prohibited from consuming alcohol. They were also prohibited from consuming caffeine after 15:00. Each evening they were required to arrive at the laboratory by 20:00 to allow sufficient time for PSG setup and to provide a three-hour period of relaxation prior to bedtime.

The volunteers were informed the purpose of the study was to investigate the effect of railway vibration on sleep. They were informed that the first evening would serve as a habituation period and would be free from vibration and noise. They were further informed that the subsequent nights may or may not involve noise and/or vibration exposure, but were kept blind to the particular exposures of any given night.

3.2.2. Demographics

Across the five studies performed in *Papers I-IV*, 80 volunteers participated (Table 1). The distribution of men and women was approximately equal, and the participants were on average in their early twenties, as expected given advertising was primarily at universities.

Table 1 Overview of all participants across *Papers I-IV*.

Sleep study	Paper	Nights	Participants	Women	Mean age ±SD (years)	Noise sensitive (%)
1	I	6	12	5 (42%)	22.3±2.5	3 (25%)
2	II	6	24	13 (54%)	22.9±2.8	10 (42%)
3	III	6	23	13 (57%)	23.7±3.1	8 (35%)
4A	IV	5	5	2 (40%)	22.2±3.4	0 (0%)
4B	IV	5	16	8 (50%)	22.0±2.7	7 (44%)
		Total	**80**	**41 (51%)**	**22.9±2.8**	**28 (35%)**

There was an unequal distribution of sensitive and non-sensitive participants between the different studies. In *Paper 1*, noise sensitivity was not part of the selection criteria, and the proportion of persons rating themselves as noise-sensitive accordingly agrees with a previously reported prevalence of 22% [109].

In sleep studies 2, 3 and 4B, it was endeavoured to recruit an even distribution of sensitive and non-sensitive participants, but in practice, many of the applicants rating themselves as sensitive often failed to meet a number of other suitability criteria. A pragmatic approach was adopted, with preference given to applicants fulfilling all of the selection criteria regardless of sensitivity, while aiming to recruit the necessary number of noise sensitive persons to achieve a 50% distribution, but not at the expense of lost study weeks. Consequently, the 35-44% distribution of sensitive participants in studies 2, 3 and 4B was lower than desired.

3.2.3. First evening questionnaires

Data were collected on the first study evening regarding occupation, residence, noise environment of home bedroom, rating of sleep quality at home, vibration tolerance (not at all tolerant, not particularly tolerant, quite tolerant, very tolerant, extremely tolerant), noise sensitivity, and disturbance at home by road noise, railway noise, tram noise, road vibration, railway vibration, tram vibration, neighbours, refrigerators or fans in the home, and any other sources.

3.3. Experimental protocol

Participants slept for 5 or 6 nights, depending upon the study (Table 1). Lights out was at 23:00, and an automated alarm call was played into the bedrooms at 07:00 the following morning. Participants were allowed to sleep only during this 8-hour period, including the prohibition of daytime napping.

All sleep trials were longitudinal with a repeated-measures cross-over design. No train noise or vibration was introduced in the first or second study nights. The first night served as an adaptation period to the laboratory setting and PSG apparatus [61]. The second night served to measure an individual's normal baseline sleep. Nights 3-6 served as periods for experimental intervention, and railway noise, vibration or a combination of both was introduced at 20, 36 or 52 times during the night (see 3.4 for more details). The order of experimental nights was counterbalanced within each study (see Table 2).

Table 2 Arrangement of study nights in *Papers I-III*. Nights A-D indicate exposure nights, comprising of noise, vibration and variable numbers of trains.

Week	Study night					
	1	2	3	4	5	6
1	Habituation	Control	A	B	C	D
2	Habituation	Control	B	C	D	A
3	Habituation	Control	C	D	A	B
4	Habituation	Control	D	A	B	C

3.4. Exposures

3.4.1. Vibration

Based on analysis of vibration time histories and frequency information of measured freight train pass-bys in northern Europe [203, 204] and data from 15 measurement sites in Sweden [205], a vibration signal deemed representative of a typical freight passage was synthesised. The resulting signal *c(t)* was an amplitude-modulated 10 Hz sinusoid, described by (7). Amplitude *A* was adjusted to give the desired experimental amplitudes in each study, presented in Table 3. The synthesised vibration signal with a maximum velocity of 0.4 mms^{-1} is visualised in Figure 12, with a measured freight train vibration signal presented for comparison.

$$c(t) = \mathrm{A}[\sin(2\pi 1.72t) + \sin(2\pi 1.443t + 0.1) + \sin(2\pi 0.551t + 0.2) + 2\sin(2\pi 0.168t + 0.3)] \quad (7)$$

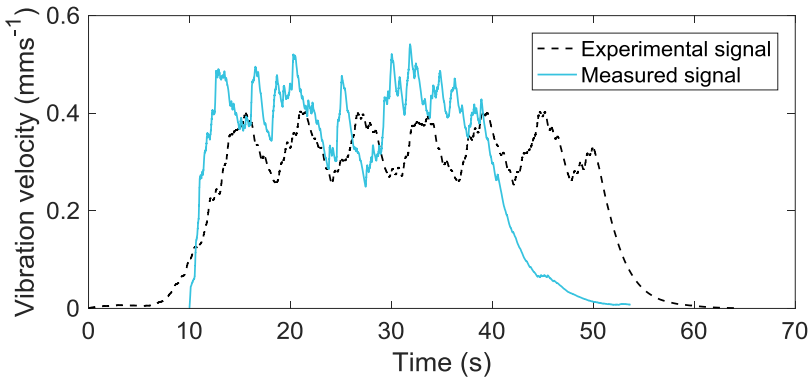

Figure 12 Time history of experimental and measured vibration signals. The presented experimental signal has a maximum frequency weighted acceleration of 0.4 mms^{-1}.

The vibration exposures used across all studies are presented in Figure 13 along with perception thresholds measured by a number of authors [16, 28, 206]. The experimental vibration in studies 1-3 was the same amplitude in a single night, and varied in amplitude across nights. In studies 4A and 4B, there were 3 different amplitudes within each night, and the presentation order was counterbalanced across nights.

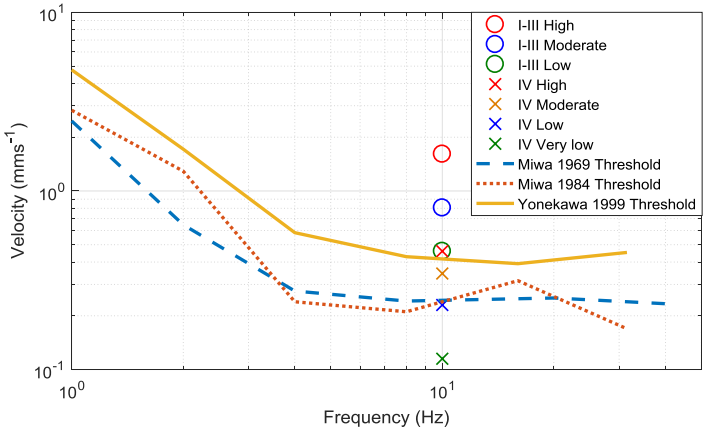

Figure 13 Unweighted vibration exposures used across *Papers I-IV*, compared against horizontal vibration perception thresholds in the recumbent position, as measured by Miwa et al. 1969 [206], Miwa et al. 1984 [28] and Yonekawa et al. 1999 [16].

Table 3 Vibration and noise exposures across all papers.

Sleep study	Experimental night	Number of trains (n)	Max. W_d acceleration (ms^{-2})	Max. velocity (mms^{-1})	$a_{d,rms,8h}$ (ms^{-2})	$L_{AEq,8h}$ (dB)	$L_{AF,max}$ (dB)	Comments
1, 3	N36	36	-	-	-	31.3	49.8	
4A	VAp36, VBp36, VCp36	36	0.0015, 0.0029, 0.0043	0.1, 0.2, 0.3	0.0005	25.4	30	Multiple amplitude trains per night (12 per velocity)
4B	VA36, VB36, VC36	36	0.0029, 0.0043, 0.0058	0.2, 0.3, 0.4	0.0007	25.4	30	"
1	NVl36	36	0.0058	0.4	0.0007	31.3	49.8	Single amplitude night
2	NVm20	20	0.0102	0.7	0.0010	29.3	49.8	"
1, 2	NVm36	36	0.0102	0.7	0.0014	31.3	49.8	"
2	NVh20	20	0.0204	1.4	0.0019	29.3	49.8	"
3	Vh36	36	0.0204	1.4	0.0027	-	-	"
1, 2, 3	NVh36	36	0.0204	1.4	0.0027	31.3	49.8	"
3	NVh52	52	0.0204	1.4	0.0033	31.5	49.8	"

3.4.2. Noise

Artificial ventilation noise was introduced into the bedrooms at all times at a level of 25 dB L_{AEq}.

The train noise exposures used were free-field recordings of freight train passages. Five recordings with similar rise times (7.9-9.8s) but different duration (11.5-56.9 s) and temporal characteristics were filtered according to ISO 717-1 to represent the frequency-dependent attenuation of a closed window [207]. The equivalent and maximum noise levels at the pillow for each train are given in Table 4. All five trains were used with the same noise levels across *Papers I-III*. Only two of the trains were used in *Paper IV*, and at lower levels than *Papers I-III*. The lower levels in *Paper IV* were chosen to lie below the response threshold to noise [158].

Table 4 Acoustic characteristics of the individual trains across each paper. $L_{AEq,pb}$ Equivalent A-weighted noise level for the train pass-by.

Train	Duration (s)	Paper	$L_{AEq,pb}$ (dB)	$L_{AF,max}$ (dB)
1	11.5	I-III	44.0	48.4
2	46.2	I-III	42.7	47.2
		IV	24.7	30.0
3	23.7	I-III	44.5	49.8
		IV	24.7	30.0
4	29.2	I-III	45.6	49.8
5	56.9	I-III	42.4	47.2

3.5. Sleep measurement

The following section describes the application of PSG and questionnaires for the objective and subjective measurement of sleep. Despite the shortcomings of PSG, it is currently accepted as the best available technique for the physiologic measurement of sleep, particularly when subtle changes are anticipated, as would be expected close to threshold (*Paper IV*). PSG does not however capture the perception of sleep or the subjective after-effects of impaired sleep, and so questionnaires were administered in tandem with PSG.

3.5.1. Polysomnography

Sleep was recorded with polysomnography, with measurements performed according to AASM recommendations [56].

Prior to electrode attachment, skin at the measurement sites was cleaned with a mild abrasive skin preparation gel. Gold cup 10 mm electrodes filled with conductive electrode cream were affixed to the EEG, EOG and EMG measurement sites recommended by the AASM [56]. Electrodes within hairy regions (i.e. the scalp, and beard if present) were furthermore fixed in place with additional electrode cream and a 25×25 mm^2 gauze pad placed on the non-contact side of the electrode. Electrodes on non-hairy locations with fixed in place with surgical tape.

Electrodes were placed according to the international 10-20 system [208] in positions C_Z, O_1, O_2, C_3, C_4, F_3, F_4, M_1, M_2 and Fp_Z to record the EEG. Two electrodes were placed in positions E_1 and E_2, 1 cm below the left outer canthus and 1 cm above the right outer canthus respectively, to measure the EOG. The EMG reference electrode was placed 1cm above the mandible midline, and two electrodes were placed 2 cm below the inferior edge of the mandible and 2 cm right and left of the midline respectively to record the EMG.

The electrical impedance at all measurement sites was checked to ensure a low impedance ($\leq$5kΩ), indicating a good connection between the electrode and skin. Voltage and frequency of each channel was checked to ensure correct function of the apparatus. If data acquisition appeared faulty or suboptimal, as indicated by high impedance or unexpectedly high or low signal amplitudes and frequencies (including no signal), the electrode or electrodes in question were removed, the contact sites cleaned again with the skin preparation gel, and the electrodes reattached with new electrode cream. If the signal from an electrode was intermittent or totally absent, the electrode was replaced.

ECG was recorded with a single modified Lead II with torso electrode placement [56]. The electrodes were single-use adhesive pads filled with a conductive electrolyte gel and a silver/silver chloride conductor. The positive electrode was placed on the left sixth intercostal space and the negative electrode was placed below the right clavicle in the midclavicular line.

Finger pulse plethysmography and peripheral oxygen saturation were recorded with an optical pulse oximeter.

Leg movements and respiratory effort were recorded in Studies 1 and 2, but data were not analysed. Surface electrodes were placed on the anterior tibialis muscle of each leg to record leg movements. Abdominal and thoracic respiratory effort was recorded with separate piezoelectric effort belts.

Data were recorded offline onto ambulatory PSG devices (SOMNOscreen plus, SOMNOmedics, Germany). The sampling and filter frequencies used are given in Table 5. Recorded data were uploaded daily to an external storage device, and visually inspected to identify any problems with the recording, for instance electrode detachment, signal intermittency or equipment failure. Any problems were then rectified before the next recording. The device clock time was synchronised to the master clock used to signal the timing of the experimental exposures.

Table 5 PSG electrode sampling and filter frequencies

	Sample rate (Hz)	Low frequency filter (Hz)	High frequency filter (Hz)
EEG	256	0.3	35
EOG	256	0.3	35
EMG	256	10	-
ECG	256	-	-

3.5.2. PSG analysis

To minimise inter-scorer variability [62, 63], the same single trained sleep technologist throughout all studies manually scored sleep. Furthermore, the technologist was kept blind to the study design. Sleep was scored in 30 s epochs from EEG derivations O_1-M_2, C_3-M_2, F_3-M_2, O_2-M_1, C_4-M_1 and F_4-M_1, EOG and EMG. Abrupt shifts in the EEG frequency of more than 16 Hz and lasting at least 3 s following 10 s of stable sleep were classified as EEG arousals, in accordance with current guidance [58]. During REM sleep, an accompanying increase in submental EMG of ≥1 s was required in order for an arousal to be scored. EEG arousals occupying more than half of an epoch, i.e. >15 s, were classified as awakenings. An example output of the PSG data is given in Figure 14.

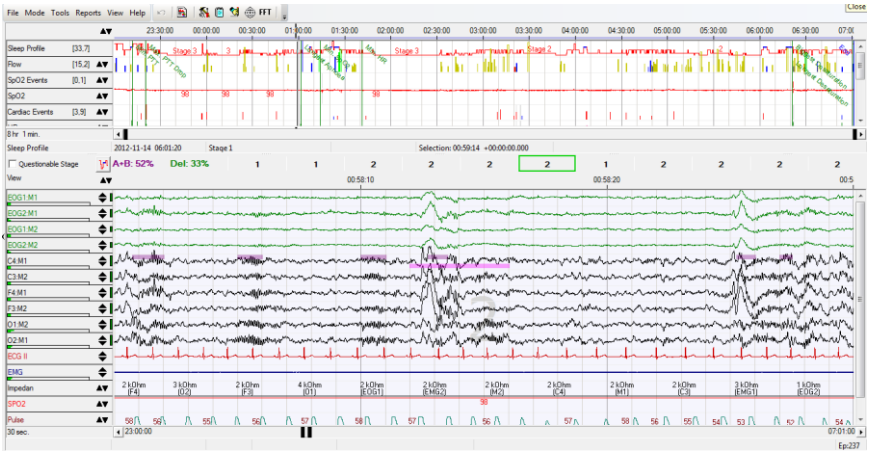

Figure 14 Example output of PSG data. Sleep spindles and k-complexes, both indicators of stage N2 sleep, are visible in the EEG.

3.5.3. Questionnaires

Questionnaires were completed every night shortly prior to lights out, and within 15 minutes of waking up in the morning. There were additional questionnaires completed once, on the first evening of each study period, regarding general participant information and sensitivity. All questionnaires were in Swedish, but are described here translated into English.

The questionnaires were developed based on extensive previous research carried out within the research group over the last few decades, including recent work investigating the influence of the sound environment in intensive care units [82]. Questions on sleep disturbance by vibration and noise were based on standardised questions used in assessing noise annoyance [86]. Questions on perceived sleep and recuperation were based on numerical and semantic scales that have previously proved sensitive to the disturbing effects of nocturnal noise [81, 82]. A number of the questions were later validated against PSG parameters [84]. Sleep quality correlated positively with REM latency and sleep period time (SPT), and negatively with sleep onset latency (SOL) and WASO. Difficulty sleeping correlated positively with SOL, WASO, and time in N1, and negatively with SPT and time in SWS. A number of correlations were found between other questions and PSG data but are not reported here.

As part of the European CargoVibes project, cross-sectional field studies into the effects of vibration from railway freight were conducted by research groups in

Poland (Instytut Kolejnictwa) and The Netherlands (Netherlands Organisation for Applied Scientific Research) [209]. The questionnaires used in the experimental sleep studies and the field studies were designed concurrently such that a number of the questions were directly comparable, allowing for comparison between data from both settings.

3.5.3.1. Evening questionnaires

The evening questionnaires included the same measures of mood and Stress-Energy as the morning questionnaires. They furthermore included the five items in Table 6 as indicators of daytime function.

Table 6 Evening questionnaire items.

How have you felt today?	Response choices (same for all questions)
Alert and strong Full of energy Exhausted Tired/sleepy Glad	All day Most of the day A large part of the day Some of the day A small part of the day Not at all

3.5.3.2. Morning questionnaires

The morning questionnaire items are given in Table 7. In addition, two measures of mood, "pleasantness" and "social orientation", were constructed from responses to 4-point assessments (Definitely, Somewhat, Not, Definitely not) of 23 different words describing emotional state [210]. The words were as follows: sullen, generous, pleased, optimistic, helpful, pessimistic, unreasonable, uneasy, accommodating, unhappy, glad, in good humour, friendly, cooperative, cross, worried, dejected, irritated, good natured, resigned, harmonious, angry, unconcerned.

A measure of "Stress-Energy" was constructed from responses to 6-point assessments (Not at all, Hardly at all, Somewhat, Quite, Very, Extremely) of twelve words describing emotional state [211]. The words were as follows: relaxed, active, tense, dull, stressed, energetic, ineffective, at ease, sharp, under pressure, passive, calm.

Table 7 Morning questionnaire items

Short name	Full question	Response, or scale endpoints
Sleep qual num	How would you rate your sleep quality during the night?	0-10 (Very poor - Very good)
Sleep qual sem	How would you rate your sleep quality during the night?	5-point semantic (Very poor, Poor, Not particularly good, Good, Very good)
Tired-Rested	How are you feeling right now?	0-10 (Very rested - Very tired)
Tense-Relaxed	How are you feeling right now?	0-10 (Very relaxed - Very tense)
Irritated-Happy	How are you feeling right now?	0-10 (Very irritated - Very glad)
Est. SL	How long did it take you to fall asleep last night?	____ minutes
Perceived awakenings	How many times do you estimate that you woke up during the night before the morning alarm?	Woke ____ times
Hard to sleep after awakenings?	Did you have difficulty falling back to sleep after an awakening?	Did not wake/No/Yes
Easy-Difficult to sleep	How was your experience of the night and your sleep?	0-10 (Easy to sleep - Difficult to sleep)
Slept better-Worse than usual	How was your experience of the night and your sleep?	0-10 (Better sleep than usual - Worse sleep than usual)
Deep-Light sleep	How was your experience of the night and your sleep?	0-10 (Slept deeply - Slept lightly)

Table 7 continued Morning questionnaire items

Short name	Full question	Response, or scale endpoints
Never woke-woke a lot	How was your experience of the night and your sleep?	0-10 (Never woke - Woke often)
Vib dist	How disturbed was your sleep by vibration from trains during the night?	0-10 (Not at all - Extremely)
Vib poor sleep	Do you think that vibration during the night disturbed your sleep so that you slept poorly?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Vib wakes	Do you think that vibration during the night disturbed your sleep so that you were awoken?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Vib difficulty	Do you think that vibration during the night disturbed your sleep so that you had difficulty falling asleep?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Vib tiredness	Do you think that vibration during the night disturbed your sleep so that you were tired in the morning?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Noise dist	How disturbed was your sleep by vibration from trains during the night?	0-10 (Not at all - Extremely)
Noise poor sleep	Do you think that noise during the night disturbed your sleep so that you slept poorly?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Noise wakes	Do you think that noise during the night disturbed your sleep so that you were awoken?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Noise difficulty	Do you think that noise during the night disturbed your sleep so that you had difficulty falling asleep?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)
Noise tiredness	Do you think that noise during the night disturbed your sleep so that you were tired in the morning?	5-point semantic (Not at all, Slightly, Moderately, Very, Extremely)

3.6. Analysis

3.6.1. Sleep macrostructure

Variables describing overall sleep macrostructure are presented in Table 8.

3.6.2. Event-related cortical response

To determine the likelihood of an exposure eliciting a physiological response, a screening window of 60 s length, beginning at the start of each discrete event (train noise, vibration, or both) was analysed. A detailed description of the calculation of event-related probabilities for EEG arousals, awakenings and sleep stage changes (SSCs) is given in *Paper II* Supplementary Methods. The probability of these reactions occurring as part of the normal sleep rhythm, i.e. spontaneously, was determined by analysing the control night at time points corresponding to vibration or noise in the exposure nights. No effect of the number of these "phantom" trains (20, 36 or 52) on spontaneous probability was found.

Only SSCs to a "lighter" sleep stage were considered. REM sleep was defined as the lightest sleep stage due to it's similarity to wakefulness in the EEG [212], and thus occupied a position on the sleep depth scale between N1 and Wake.

Table 8 Sleep macrostructure variables calculated from PSG data

Variable	Short name	Units	Definition
Time In Bed	TIB	min	Time between lights out and alarm call
Total Sleep Time	TST	min	Total time in non-wake stage during TIB
Sleep Period Time	SPT	min	Time between first non-wake epoch and final awakening
Sleep Efficiency	SE	%	(TST/TIB)×100
Sleep Onset Latency	SOL	min	Time between lights out and first non-wake epoch
Wakefulness After Sleep Onset	WASO	min	Total time in wake stage between SOL and final awakening
REM latency	RL	min	Time between SOL and first REM epoch
SWS latency	SWSL	min	Time between SOL and first N3 epoch
First awakening	Aw_{first}	min	Time between SOL and first W epoch
N1 minutes	N1	min	Total number of minutes in stage N1 during TIB
N2 minutes	N2	min	Total number of minutes in stage N2 during TIB
N3 minutes	N3	min	Total number of minutes in stage N3 during TIB
REM minutes	REM	min	Total number of minutes in stage REM during TIB
Percentage of sleep time in N1	N1%	%	(N1/TST)×100
Percentage of sleep time in N2	N2%	%	(N2/TST)×100
Percentage of sleep time in N3	N3%	%	(N3/TST)×100
Percentage of sleep time in REM	REM%	%	(REM/TST)×100
Maximum continuous SWS	SWS_{max}	min	Maximum time spent in N3 with no changes to any other sleep stage
Maximum continuous REM	REM_{max}	min	Maximum time spent in REM with no changes to any other sleep stage
Sleep stage changes	SSCs	n	Total number of changes to light sleep during TIB
Arousals	Ar	n	Total number of EEG arousals during TIB
Awakenings	Aw	n	Total number of EEG awakenings during TIB
Sleep stage change frequency	SSC/h	n/hour	(SSCs/TST)×60
Arousal frequency	Ar/h	n/hour	(Arousals/TST)×60
Awakening frequency	Aw/h	n/hour	(Awakenings/TST)×60

3.6.3. Heart rate change

Event-related autonomic activation was analysed by investigating changes of heart rate (HR) in the ECG. HR response during a 60 s window following the start of exposure was compared to a mean baseline value during the 10 s prior to exposure onset. HR response to noise differs between waking and sleeping states, following a monophasic pattern with higher HR elevation during wake [72], a finding corroborated in *Paper III*. HR response during sleep without accompanying awakening was therefore the main outcome considered.

In *Paper I*, the overall event-related change in HR was determined by analysing the integral of the second-by-second average HR response. Effects of HR are not reported in for the study in *Paper II*, but are presented elsewhere [213]. Here, the same approach of analysing the integral of the average HR was adopted. In *Paper III*, heart rate amplitude (HRA) was calculated according to Tassi et al. [190, 214]. HRA is the difference between the highest and lowest HR in the screening window. In *Paper IV*, the maximum transient elevation of HR relative to baseline was calculated according to Griefahn et al. [72].

3.6.4. Statistics

It was hypothesised that a worsening of self-reported sleep, adverse effects on sleep macrostructure, increased cortical reaction probability and increased autonomic response would follow increasing vibration in a dose-dependent manner. Thus exposure, either exposure night or vibration amplitude, was included in all models as the primary predictor outcome. Post-hoc comparisons between exposure conditions thus revealed the relationships between vibration and noise exposure conditions, and were suitably adjusted to account for multiple hypothesis testing. A significance level of $\alpha=0.05$ was used for minimising the rate of type I error.

Questionnaire data were analysed in repeated measurement ANOVA (IBM SPSS versions 18 and 22). Experiment night (excluding the habituation) and sex were included as predictor variables. Noise sensitivity was furthermore included in the model in *Papers II-IV*. If statistically significant main effects of study night were found, post-hoc testing was performed to identify between-night differences. Additional analysis of noise sensitivity was performed within this thesis, with data pooled data from multiple papers. For each response item, data from all exposure nights were averaged as a single variable describing the effect of exposure. The resulting exposure variable was compared with control nights in a

mixed model. Exposure (control vs. pooled exposure) and noise sensitivity (binary) were included as fixed effects with participant included as random effects.

Sleep macrostructure (*Papers II-IV*) was analysed in repeated measurement ANOVA or linear mixed models, with experiment night, sex and noise sensitivity included as the predictor variables (*Paper II* & *III*: SAS 9.4; *Paper IV*: IBM SPSS version 22).

Event-related cortical response was analysed in generalised linear mixed models (*Papers II* & *III*, SAS 9.4) or mixed effect logistic regression (*Paper IV*, STATA 14.1). The exposure (vibration and noise) was the same within exposure nights for *Papers I-III*, but varied within nights in *Paper IV*. Therefore experiment night was included as the predictor variable in *Papers I-III*, but was included as a random effect in *Paper IV* with vibration amplitude as a fixed effect. In *Papers II* & *III*, sex and sensitivity were additionally included as predictor variables. Odds ratios for the effect of vibration amplitude were calculated in *Paper IV*, adjusted for sleep stage at event onset. Since event-related outcomes are dichotomous (response observed or no response observed) a binary distribution was assumed.

Heart rate response was analysed in a repeated measurement ANOVA (*Paper I*, SPSS 18) or mixed model with random intercept (*Paper III*: SPSS 22; *Paper IV*: SAS 9.4). Experiment night was included as the predictor in *Papers I* & *III*, and vibration amplitude was included as a fixed effect in *Paper IV*. Several models were tested in *Paper III* using Akaike's information criterion [215].

In all analyses, data and residuals were visually inspected to ensure compliance with the model assumptions, and were transformed if appropriate.

3.6.5. Ethical considerations

The studies followed the Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects and were approved by the local ethics committee at the University of Gothenburg (920-11). Prior to acceptance onto the study, all volunteers were given a tour of the laboratory, shown the PSG apparatus, and informed of how their sleep would be measured. They were financially compensated for participating and provided informed written consent prior to the commencement of the study. They were free to discontinue their participation at any time, and without providing a reason.

4. Results and Discussion

The main results of the four papers presented in this thesis can be summarised as follow: The amplitude of heart rate change and the probability of event-related cortical activation and sleep stage change increased with increasing vibration amplitude. The threshold above which these event-related responses occurred was around 0.3-0.4 mms^{-1}. Vibration and noise contributed separately to the outcomes. In nights with high vibration amplitudes and 36 trains, statistically significant negative effects on objective sleep macrostructure were observed in *Paper II* but not in *Paper III*. Effects of exposure were observed for perceived sleep disturbance across all studies. These outcomes will be discussed in further detail in the following chapter, along with some additional analyses.

4.1. Event-related cortical response (Papers II-IV)

The following section discusses acute cortical response, as measured in the EEG, to discrete vibration and noise events.

4.1.1. Response threshold

Event-related cortical reaction probabilities following low amplitude vibration velocities were calculated in *Paper IV*, accounting for sleep stage at event onset (Figure 15 and Table 9) [216]. The influence of sleep stage is discussed in section 4.1.4. At vibration amplitudes of 0.2 mms^{-1}, which is close to the perception threshold for vibration at the experimental frequency (see Figure 13), no increase in probabilities for arousals, awakenings or SSCs relative to the spontaneous baseline was seen, although there was an effect of borderline significance for SSCs (OR=1.50). Vibration of 0.2 mms^{-1} does not seem to be of sufficient amplitude to induce a cortical response. At 0.3 mms^{-1}, significant event-related changes of sleep stage (OR=1.59) were observed, and there was an effect of borderline significance for arousals (OR=1.51). At higher vibration velocities of 0.4 mms^{-1}, the OR for SSCs increased from 1.59 to 1.88, and there was some evidence of awakenings beginning to manifest (OR=1.73). The OR for arousals was lower than following 0.3 mms^{-1} vibration, and no longer significantly different from the spontaneous baseline, yet the overall probability for either an arous-

al or awakening was greater than at baseline (OR=1.55), indicating that awakenings occurred instead of arousals.

Biological response at and around thresholds is expected to be small. For instance, the awakening threshold for aircraft noise is around 33 dB, but only around 0.2% of individuals awake at this level [172]. Given the modest sample size in *Paper IV* (n=16), it is not surprising to find effects of borderline significance, and these non-significant results should perhaps not be ignored outright. Taken together, the data show that the thresholds for SSCs, arousals and awakenings lie somewhere around or slightly above 0.2, 0.3 and 0.4 mms^{-1} respectively.

Table 9 Results of mixed-effect logistic regression for effects of vibration and sleep stage on cortical response probability. OR, Odds ratio; CI, Confidence interval. Reference categories as follows: † 0.0 mms^{-1}; ‡ Stage N1. Statistically significant (p<0.05) effects are highlighted with bold typeface. Borderline significance (p=0.05-0.1) effects are highlighted with italic typeface.

Event-related reaction	Vibration amplitude				Sleep stage			
	Amplitude (mms^{-1})†	**OR**	**95% CI**	**p-value**	**Sleep stage‡**	**OR**	**95% CI**	**p-value**
SSC	*0.2*	*1.50*	*0.99-2.23*	*0.055*	*N2*	*0.67*	*0.45-1.01*	*0.054*
	0.3	**1.59**	**1.06-2.39**	**0.027**	**N3**	**0.48**	**0.31-0.75**	**0.001**
	0.4	**1.88**	**1.26-2.82**	**0.002**				
Arousal	0.2	1.13	0.76-1.68	0.53	**N2**	**0.57**	**0.38-0.85**	**0.007**
	0.3	*1.51*	*1.04-2.20*	*0.06*	**N3**	**0.27**	**0.17-0.45**	**<0.001**
	0.4	1.37	0.94-2.01	0.11	**REM**	**0.55**	**0.35-0.89**	**0.012**
Awakening	0.2	0.95	0.50-1.83	0.886	N2	0.78	0.39-1.55	0.476
	0.3	0.82	0.42-1.61	0.571	*N3*	*0.47*	*0.21-1.04*	*0.064*
	0.4	*1.73*	*0.97-3.10*	*0.063*	REM	0.67	0.31-1.46	0.316
Combined EEG reaction	0.2	1.1	0.78-1.56	0.593	**N2**	**0.58**	**0.40-0.45**	**0.005**
	0.3	*1.35*	*0.96-1.89*	*0.082*	**N3**	**0.29**	**0.18-0.45**	**<0.001**
	0.4	**1.55**	**1.11-2.17**	**0.009**	**REM**	**0.55**	**0.36-0.83**	**0.005**

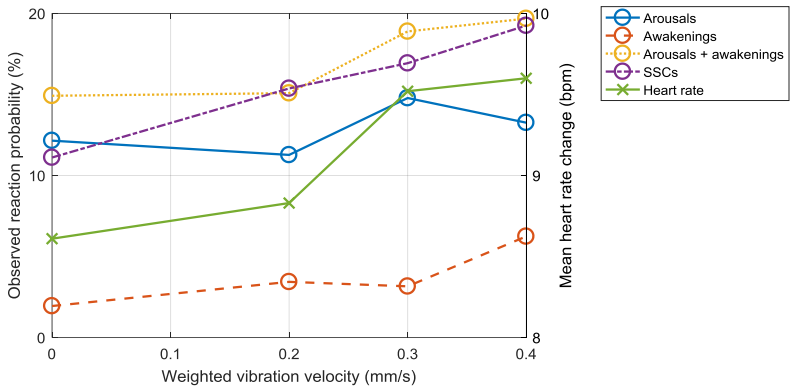

Figure 15 Probability of observing arousals, awakenings, combined EEG reactions, and SSCs (left axis), and mean change of heart rate (right axis), at baseline (0 mms^{-1}) and low velocity vibration exposure. Reproduced from *Paper IV* [216].

4.1.2. Response at vibration velocities above threshold

At vibration amplitudes above the response thresholds, event-related cortical reaction probabilities increased in a dose-dependent manner as anticipated, presented in Figure 16 from *Paper II* [217]. The combined arousal or awakening probability in excess of spontaneously occurring reactions was approximately 20% following trains at 0.7 mms^{-1} (nights NVm20 and NVm36), and around 16% for the SSC probability. The reaction probabilities for SSCs and combined EEG response both increased, to around 32% and 35% respectively, at 1.4 mms^{-1} (nights NVh20 and NVh36). However, the exposures leading to these reaction probabilities included train noise in addition to the vibration, at a noise level of 49.8 dB $L_{AF,max}$. According to the WHO, cortical response to noise during sleep begins at 35 dB $L_{AS,max}$ [158], which is lower than the noise level used in *Papers II* and *III*. The difference in maximum noise levels between measurements with slow (1 s) or fast (0.125 s) integration constants is around 5 dB [19], meaning that the noise levels in the experimental studies were around 10 dB above the response threshold. As with railway vibration, railway noise of sufficient level can induce event-related arousals and awakenings [169], so it is likely that the additional response probabilities in Figure 16 are at least partly a result of the sleeping body reacting to the noise, rather than only to vibration.

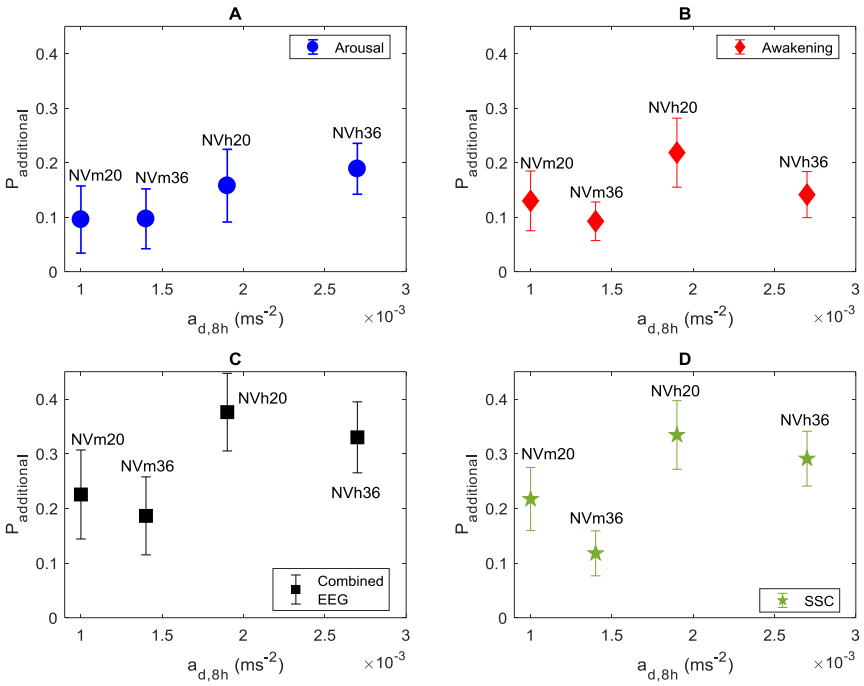

Figure 16 Additional probabilities and 95% confidence intervals of arousals (A), awakenings (B), combined EEG response (C) and sleep stage changes (D) with increasing 8-hour weighted RMS acceleration. Reproduced from *Paper II* [217].

4.1.3. Interactions between vibration and noise

There is overlap in low-level cortical regions responsible for processing of auditory and somatosensory input [218, 219], and at low stimulus levels neuronal activity is greater following combined noise and tactile exposure than the sum of the separate unimodal responses [40, 220]. Hence, at low vibration levels, for instance around detection thresholds, the presence of noise can enhance the perception of vibration [39, 221]. At higher stimulation levels however, neuronal activation during wake in monkeys has been seen to be a direct summation of the responses to the separate modalities [40]. Similarly, it was found in *Paper III* that the effects of simultaneous vibration and noise on arousal and SSC probability were additive, as presented in Figure 17 [222]. This suggests that at vibration and noise levels occurring near railway lines, both exposures are evaluated separately by the sleeping brain, rather than the vibration stimulus enhancing response to noise [199].

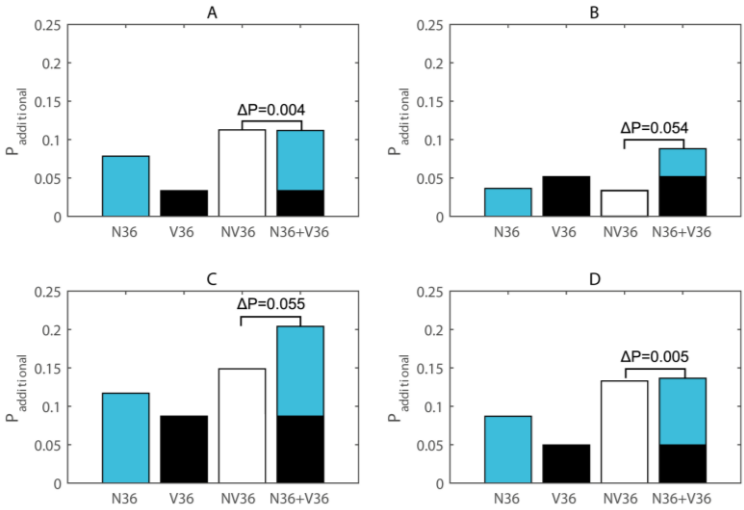

Figure 17 Contributions of noise and vibration exposure to event-related arousal (A), awakening (B), combined EEG (C) and sleep stage change (D) probabilities. Reproduced from *Paper III* with permission [222].

Vibration and noise did not have additive contributions to awakenings. However, awakenings were slightly more probable following vibration-only than following noise-only or noise and vibration together (increase in $P_{additional}$ from slightly below 4% to 5.6%). Without the noise signal identifying the source as a train, the sleeping brain may be less well able to characterise the vibration exposure. An unfamiliar exposure may be evaluated as potentially threatening, with the sleeping brain preparing to react by waking up.

In the opposite direction to awakenings, arousals were less likely (albeit statistically non-significant) following vibration only than noise-only or noise and vibration together. Arousals may serve to adapt sleep to meet the demands of external influences [223]. A decreased arousal probability could therefore suggest that the brain is less able to integrate vibration exposure while maintaining sleep, and instead prepares for awakening, as discussed earlier. Even if sleep continuity is preserved, vibration affects the overall impact of exposure on sleep fragmentation, as evidenced by the additive effect on arousals and SSCs.

4.1.4. Effect of prior sleep stage

It was the aim of *Papers II* and *III* to provide reaction probabilities reflective of what may occur at a population level in the field, and the study designs accordingly had a distribution of events simulating typical scenarios. The probabilities presented in Figure 16 and Figure 17 were calculated from all events within nights, and thus represent an overall response likelihood, independent of within-night factors including time of night, elapsed sleep time and sleep stage at event onset. These studies had more events during the early and late parts of the night, with events during these periods more likely to occur during SWS or REM/N1 sleep respectively. Rather than adjusting for these factors on the level of individual events, they were instead accounted for in the overall study design.

It was found in *Paper IV* that event-related arousal, awakening, combined EEG response and SSCs were all least probable during N3 sleep, although the effect for awakenings was of borderline significance (Table 9). Arousal threshold is greatest during deep sleep [224], and correspondingly the awakening probability following noise exposure has previously been demonstrated to be highest in stage N1 and lowest in stage N3 [169]. It is likely that vibration-induced awakenings follow a similar dependence on sleep depth as arousals, indicated by the OR of 0.47 and also by the significant effect of N3 on arousals and SSCs. The marginal significance of N3 on awakenings found here is likely due to lack of sufficient statistical power rather than indicative of an independence of sleep depth.

The event-related arousal and awakening probability was broadly similar in REM and N2 sleep. However, previous research has found that awakening and arousal probabilities following noise exposure were lower in REM than stage 2 [169, 171]. REM sleep can be divided into two further substates; phasic REM, characterised by bursts of rapid eye movements, and tonic REM, where no rapid eye movements occur. Higher thresholds for behavioural arousal, event-related brain potentials and activation of the auditory cortex following acoustic stimulation have been found during phasic REM sleep, whereas the threshold for behavioural arousal during tonic REM is similar to during stage N2 [225-227]. Therefore it is possible that much of the REM sleep during exposure in *Paper IV* was tonic REM, whereas a lower arousal probability as observed in [169, 171], would be expected during phasic REM.

4.1.5. Clinical implications/relevance

The likelihood of event-related arousals, awakenings and sleep stage changes increased following vibration exposure, but there was generally no concurrent increase in the total number of these reactions across the night (see section 4.3). Rather than inducing reactions additional to those that would have occurred spontaneously, the event-related responses generally replaced those that would have occurred spontaneously outside of the 60 s analysis windows, a phenomenon observed previously for railway noise [169]. EEG arousals are a normal component of sleep [228], although their precise function is unclear. It has been argued that they serve to maintain the reversibility of sleep and adapt sleep to meet the demands of internal and external influences [223]. Are these forced reactions therefore important when considering possible adverse effects of vibration on sleep, especially if they would have occurred at other times anyway?

Much of the evidence for the adverse effect of arousals comes from clinical populations, often patients with OSA. EEG arousal occurs more frequently than usual among OSA sufferers, with the fragmentation of sleep leading to after-effects including sleepiness [146]. Treatment of moderate-to-severe OSA with continuous positive airway pressure (CPAP) may reduce daytime sleepiness, anxiety, and depression, and improve physical and mental quality of life [229]. However, the risk of death from cardiovascular causes, myocardial infarction, stroke, or hospitalisation for heart failure, unstable angina or transient heart attack among patients treated with CPAP and usual care did not differ compared to patients that received usual care only. If one assumes that the reduced sleepiness observed in [229] is a result of reduced sleep fragmentation (which is not necessarily true), it could be inferred that sleep fragmentation does not affect long-term cardiovascular health. Night-time noise has been repeatedly associated with incident CVD [164, 166], yet EEG-based indicators of sleep fragmentation are perhaps unsuitable for predicting long-term cardiovascular effects. Autonomic activation however, which often accompanies EEG arousal, may be more suitable.

On the other hand, it is also possible that sleep functions may be disrupted by forced cortical arousal. It is sometimes assumed that sleep must be uninterrupted for a minimum duration in order to be beneficial, and that the disturbance of this minimum period, even by a short arousal, precludes restoration prior to the disturbance [230]. This idea is supported by the finding that sleep fragmentation, even while preserving overall sleep macrostructure, can lead to increased daytime sleepiness (assessed by MSLT) and impaired awakening mood [231, 232]. Similar findings for sleepiness following this “invisible” sleep fragmentation

have been seen in mice, which furthermore implicated an important mechanistic role of tumour necrosis factor-alpha (TNF-α), a proinflammatory cykotine involved in sleep-wake regulation [233]. Arousals have been associated with increased levels of blood lipids, which could be risk factor for metabolic disorders [234]. Disruption of slow wave activity can lead to increased levels of β-amyloid, which is a risk factor for developing Alzheimer's disease [47, 235]. A reduced percentage of sleep in REM and increased REM latency have been associated with increasing incidence of dementia [236]. At present it is not clear how vibration- and noise-induced changes of sleep microstructure may impact upon many of the processes occurring during sleep. Future work could elucidate a causal relationship between the interruption of sleep rhythmicity and adverse health outcomes. If the redistribution of cortical arousal is deleterious, the event-related response in the present data implicates vibration from railways as potentially harmful for long-term health.

4.2. Heart rate (Papers I, III & IV)

In addition to analysis of heart rate in *Papers I*, *III* and *IV*, heart rate was analysed in the study presented in *Paper II*, the results of which are presented elsewhere by Croy et al. [213]. The main outcomes of this latter paper will however be presented in the following section.

4.2.1. Exposure-response relationship

The mean change of heart rate following low amplitude vibration velocities were calculated in *Paper IV* (Figure 15) [216]. Relative to spontaneous fluctuations in HR determined from the control nights, event-related maximum change in HR was found to be significantly greater during 0.3 mms^{-1} ($p=0.0157$) and 0.4 mms^{-1} ($p=0.0097$) train passages. No effect was observed during 0.1 or 0.2 mms^{-1} events, indicating that the autonomic response threshold to vibration lies somewhere around or slightly below 0.3 mms^{-1}.

With increasing vibration amplitude above the response threshold, greater changes in HR were observed (Figure 18 and Figure 19), and furthermore in *Paper I* the latency of the HR response was found to decrease (Figure 18) [237]. Whereas the effects of exposure amplitude have been seen for traffic noise previously, both for the degree of HR increase and latency [72, 169, 190], this is the first time they have been demonstrated for vibration.

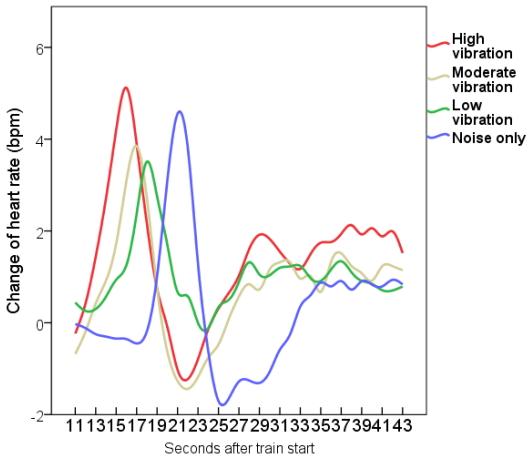

Figure 18 Changes in heart rate response and latency averaged across all individuals for the four exposure conditions in *Paper I*. Adapted from *Paper I* [237].

Heart rate increase was observed following vibration exposure even in the absence of noise (*Paper III*). Although not statistically significant, heart rate amplitude was slightly higher following combined vibration and noise than either vibration- or noise-only. This suggests that both exposures contribute to response.

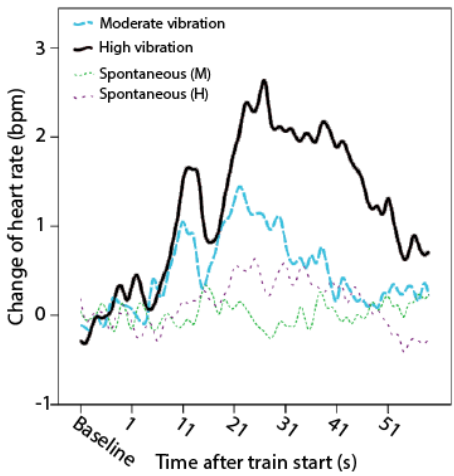

Figure 19 Average temporal change of heart rate following moderate and high vibration exposure relative to baseline. Also shown are spontaneous changes in heart rate during quiet periods in the moderate (M) and high (H) exposure nights. Adapted from Croy et al. [213].

4.2.2. Characteristics of response

Paper I reported an average event-related change in HR across all participants, with the result reproduced in Figure 18. This approach revealed a biphasic nature of the cardiac response; an initial increase was followed by a deceleration to below the baseline with the HR then stabilising at a rate slightly above the rate prior to event onset. The initial increase likely indicates a reduction in parasympathetic activity, which may or may not be accompanied with increased sympathetic tone [238-240]. The subsequent deceleration has been suggested to result from increased vagal tone and sympathetic inhibition [72]. This biphasic pattern has previously been shown to occur during sleep following traffic noise exposure [72], but this was the first time it was found following vibration.

In both papers, following an initial biphasic response the heart rate returned to a value slightly above baseline, about 2 bpm following 1.4 mms^{-1} vibration and 1 bpm following 0.7 mms^{-1} vibration. However, the maximum HR acceleration during the initial response differed substantially between papers, being around 3-3.5 bpm higher in *Paper I*. Additionally, contrary to the finding of *Paper I*, no effect of vibration amplitude was found for HR response latency in Croy et al. [213]. The discrepancies between the papers for the degree of HR acceleration and latency may be a consequence of how the data were averaged. The average response curves in Figure 18 and Figure 19 are not normalised to the point of maximum HR acceleration. Since there are inter- and intra-individual temporal variations in the HR maxima, these overall response curves effectively smooth out the absolute maxima and minima for individual events, as well as averaging out any differences in response latency. With a greater number of participants, as is the case in Croy et al. relative to *Paper I*, a larger degree of smoothing would be expected. In Croy et al. for example, high vibration elicited HR response of *at least* 3 bpm for 74-79% of the trains, yet a naïve interpretation of the averaged response (Figure 19) could be that the maximum HR change was only around 2.5 bpm, between 20-30 seconds after event onset.

Autonomic response has been considered only in the absence of awakenings. When awakenings accompany event-related cardiac arousals, a greater increase of heart rate than during sleep would be anticipated, as was supported in by the finding in *Paper III* ($F(1,4096)=368$, $p<0.001$). Additionally, a monophasic rather than biphasic response would be expected following concurrent awakening [72]. Taken together with the averaging of response discussed earlier, the heart rate response data presented in all papers therefore is an underestimation of autonomic response following vibration exposure.

4.2.3. Clinical implications

Cardiac arousals are induced by brainstem activation [241], and as such can occur without concomitant cortical arousal [69]. This supports the present data, where the threshold for autonomic arousal was lower than for cortical arousal, demonstrating a hierarchical relationship.

A study of 140 subjects across four European cities reported a link between night-time road and aircraft noise and acute effects of increased heart rate and blood pressure [242]. Field studies have reported associations between nocturnal noise (mainly from aircraft) and cardiovascular diseases including hypertension, arrhythmia, stroke, and coronary heart disease [165, 242-244]. Activation of the sympathetic nervous system and related blood pressure increase by OSA-associated cardiovascular arousal is thought to cause endothelial dysfunction [148]. Furthermore, nocturnal noise has been found to impair endothelial function [245], demonstrating one plausible mechanism linking noise exposure and cardiovascular disease [164], although other pathways may also be responsible, including changes in blood pressure, cardiac output, blood lipids, blood glucose, blood viscosity and blood clotting factors [161, 162].

Previous laboratory studies have found that cardiac response to noise does not habituate across nights [169, 239]. Furthermore, autonomic response to night-time railway noise has been found among long-term residents in the vicinity of railway lines [214]. However, the cardiac response was lower than in non-exposed residents, indicating that while some degree of autonomic habituation may occur, it is not total. This absence of complete adaptation highlights the potential importance of noise-induced autonomic arousal for the risk of CVD [72, 246]. Vibration exposure, which we found lead to increased heart rate in a dose-dependent manner, could also represent a risk factor for the genesis of CVD, and should be considered alongside noise exposure in areas with vibration.

4.3. Sleep macrostructure (Papers II-IV)

Macrostructure variables for which significant main effects were found are summarised in Table 10. Across all studies, only limited effects of railway vibration were seen on overall sleep architecture. Despite noise and vibration leading directly to event-related EEG response (see section 4.1), no overall differences in the total number of reactions between exposure conditions were found, with the single exception of SSCs in *Paper II*. In general, vibration-induced changes of

sleep replaced reactions that would have occurred spontaneously during the normal sleep rhythm, as has been found previously for railway noise [169].

Table 10 Sleep macrostructure variables for which statistically significant main effects were found.

Paper	Variable	Main effect predictor	Between-group effects
II	SSCs (n)	Night ($p<0.05$)	5.2 more SSCs in NVh36 than control
II	First awakening	Night ($p<0.05$)	25.3 minutes earlier awaking in NVh36 than control
II	Max continuous N3	Night ($p<0.05$)	5.6 minutes shorter continuous time in N3 in NVh36 than control
II	WASO	Night ($p<0.05$)	7.2 minutes more WASO in NVh36 than NVh20
II	Arousals (n)	Sex ($p=0.025$)	Mean 13.5 more arousals per night for men than women
IV	N2 (minutes)	Night ($p<0.05$)	No significant differences between nights after correction for multiple testing
IV	N1 (minutes)	Sex ($p=0.017$)	Mean 13.5 minutes longer in N1 per night for men than women

In *Paper II*, a single event in the NVh36 night had a probability of around 30% of evoking a SSC (Figure 16), and was significantly higher than in the control. Furthermore, the total number of SSCs in the NVh36 night (n=38.3) was significantly greater than in the control night (n=33.1). However, rather than the total number of SSCs being 30% higher than in the control (a theoretical increase of 9.9), the mean increased by instead by 5.2, suggesting that the event-related reactions occurred at least partly instead of spontaneous SSCs.

No statistically significant differences between nights for time spent in different sleep stages were found in any of the studies. Vibration and noise led to event-related awakenings, arousals and SSCs, but without greatly affecting overall sleep macrostructure. The distribution of sleep stages across all participants in the NVh36 nights from *Paper II* (Figure 20) shows a frequent cessation of N3 sleep following exposure, particularly between 00:00-04:00, and a corresponding increase in other sleep stages such as N1 (i.e. a SSC). In the periods between exposures, the often expeditious increase in the proportion of participants in N3 sleep demonstrates a compensatory effect, whereby the suppressed SWS is recovered. This finding is not unexpected, since SWS is not only prioritised by the sleeping body after sleep deprivation [247], but is recovered within the same sleep session following earlier SWS disturbance, if there is sufficient time asleep to do so [248, 249]. However, the rhythmic nature of sleep might nevertheless be

impacted by the exposures, with possible negative consequences for restoration as discussed earlier (see section 4.1.5).

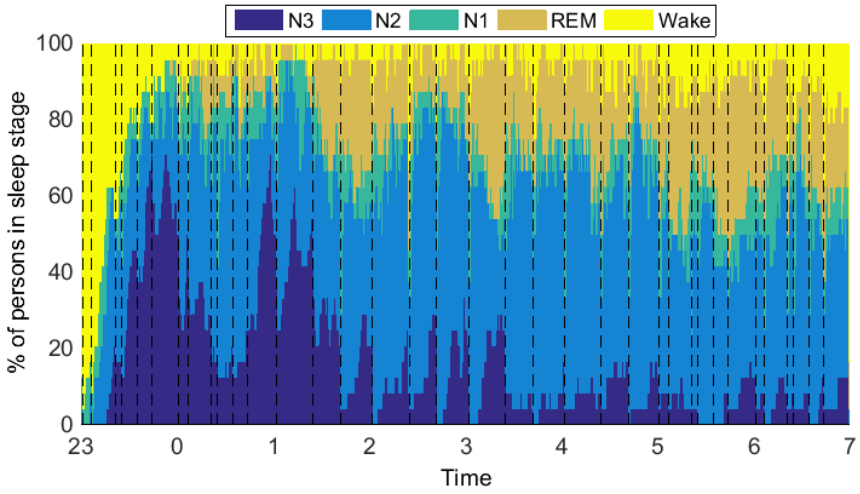

Figure 20 Distribution of sleep stages across all participants in NVh36 night in *Paper II*. Dashed lines indicate onset of vibration and noise events.

4.4. Self-reported sleep (Papers I-IV)

Morning and evening questionnaire data were recorded for the study in *Paper III*, but were not presented in the paper itself, and so are summarised here. Disturbance by vibration was higher in all nights with vibration (Vh36, NVh36 and NVh52) relative to N36 ($p<0.001$). Vibration disturbance did not differ between nights with vibration. Disturbance by noise was higher in all nights with train noise (N36, NVh36 and NVh52) relative to Vh36 ($p<0.001$). Noise disturbance did not differ between nights with train noise. No effects of noise sensitivity or sex were found for sleep disturbance. No main effects of exposure were observed for any of the other variables. These findings have been incorporated into the following discussion on the effects of vibration and noise exposure on the self-reported outcomes.

4.4.1. Sleep disturbance by vibration

Data from *Papers I-III* for sleep disturbance by vibration were combined to form common dose-response relationships. Three measures of sleep disturbance were calculated, based on the proportion of subjects reporting being at least slightly

disturbed (rating of ≥3 on the 11-point numerical scale), disturbed (rating of ≥5) or highly disturbed (rating of ≥8). The resulting probabilities of an individual reporting the different degrees of disturbance are presented in Figure 21. Reported disturbance is indicated by the position of the bubbles, and the sample size at a given vibration amplitude is indicated by the area of the bubble. The dose-response curves were weighted according to the sample size at each vibration exposure. Because exposure was included in the model as a logarithmic value, the vibration amplitude was set to a non-zero value of 10^{-4} mms^{-2} in the control and noise-only nights. The prediction of the model between this value and the first true vibration at 0.4 mms^{-1} should therefore be treated with caution.

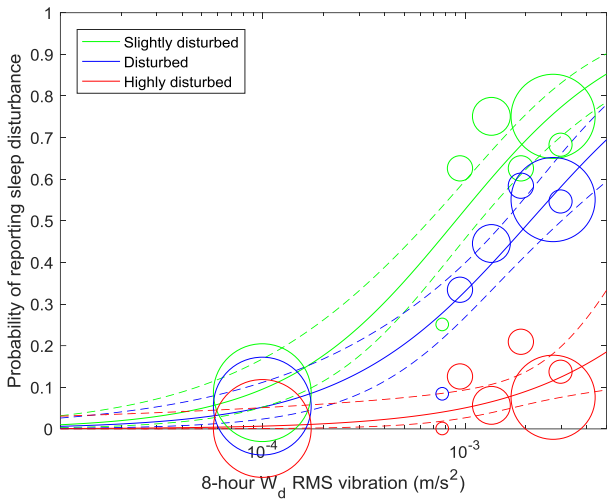

Figure 21 Probability of reporting sleep being slightly disturbed, disturbed or highly disturbed by vibration. The experimentally observed disturbance probabilities are indicated by the bubbles, with the size of the sampled population indicated by the bubble area. 95% confidence intervals are indicated by dashed lines.

Sleep disturbance by vibration increased in a dose-dependent manner, with 10-20% of individuals being highly sleep disturbed in nights with trains of 1.4 mms^{-1} ($a_{d,RMS}$=1.9–3.3×10^{-3} ms^{-2}), and around 75% of participants reporting at least some degree of disturbance. It has previously been seen that self-reported sleep disturbance by railway noise follows a similar dose-dependent relationship [181]. Vibration-dependent annoyance from railways has been reported by a number of authors [42, 43, 192, 250-252], and furthermore has been seen to be greater during the night than during the day [253]. It is plausible that sleep disturbance would feed in to annoyance, and indeed general disturbance and interference with intended activities are covered within the concept of noise

annoyance [254], but care should be taken when drawing comparisons between the fundamentally different response measures of annoyance and sleep disturbance.

4.4.2. Effects of vibration on perceived sleep

Vibration negatively affected self-reported sleep in *Paper I*, with sleep quality decreasing and vibration-induced poor sleep, difficulty falling asleep and tiredness in the morning all increasing as a function of vibration amplitude. Furthermore, no negative subjective effects were seen for noise, showing that participants were able to discern the source of their disturbance and that presence of vibration did not enhance the effect of noise on self-reported sleep outcomes.

Questionnaire data from *Papers I-III* for Control, N36, NVl36, NVm36 and NVh36 nights were combined to further investigate a possible influence of vibration amplitude on self-reported sleep [255]. A significant effect of exposure (univariate ANOVA, participants as random effects) was found for numerical sleep quality ($p=0.021$, Figure 22). Uncorrected post-hoc tests showed that sleep quality was significantly lower in NVh36 compared to the control ($p=0.026$), N36 ($p=0.031$) and NVl36 ($p=0.048$).

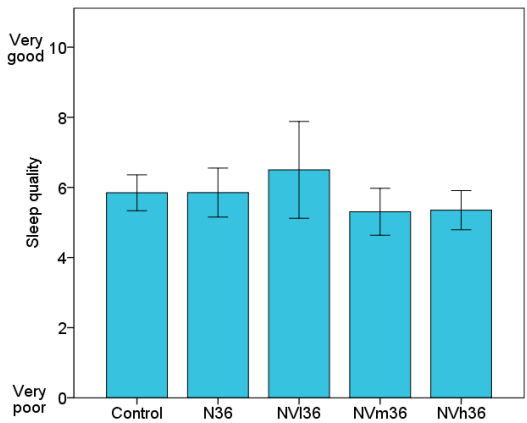

Figure 22 Mean sleep quality in 36 train exposure nights across *Papers I-III*. Error bars indicate 95% confidence intervals.

PSG data are not available from *Paper I*, although it was found in the later studies that sleep quality correlated positively with SPT and negatively with SOL and WASO [84]. This suggests that the subjective assessment of sleep quality is

related to the timing of sleep, supporting associations found by other authors linking sleep quality and TST, SE, SOL and wakefulness during the SPT [87, 99, 256]. Vibration velocities of 1.4 mms^{-1} could therefore have modest, non-statistically significant effects on physiological sleep time, leading individuals to perceive their sleep quality as lower, even without any effects on time in the various sleep stages. Given that by definition a conscious appraisal of one's own sleep cannot be made, it is unsurprising that time awake could be of particular importance for self-reported measures. Furthermore, any vibration and noise events occurring during extended wakeful periods are likely to be perceived as disturbing.

4.5. The influence of event-related disturbance on sleep macrostructure and questionnaire data

EEG arousals are frequently thought to fragment sleep [57, 58]. An increase in arousals during sleep is associated with increased sleepiness during the following period awake, even without affecting global sleep macrostructure [232]. In fact, the effects of sleep fragmentation can have adverse effects comparable to total sleep deprivation, including impaired psychomotor performance [230] and negative mood [257]. It has been suggested that in order for sleep to be restorative, it must persist for at least 10 minutes without arousal, although this 10 minute requirement is not universally accepted [230]. Studies into the sleep fragmenting effect of EEG arousals typically induce arousals at a much higher rate than would be expected in the current studies (frequently one arousal per 1-10 minutes), and furthermore overall sleep architecture is often not preserved [69, 230, 232]. Since the current studies had an average of 13.7 minutes of recovery time between events, and sleep macrostructure was generally unaffected, the sleep-fragmenting effects of the event-related cortical reactions may have been minor. This would explain the dearth of short-term after effects, as measured via the questionnaires. However, the very fact that sleep serves not one but many functions makes it problematic to ascertain the detrimental impact of induced arousals and SSCs on long-term health and wellbeing.

The absence of effects of vibration on morning questionnaire data despite significant event-related sleep disturbance is not necessarily in disagreement with existing literature. Noise from nocturnal road traffic has been correlated with actigraphy sleep efficiency, but with no statistically significant associations with self-reported restfulness of sleep or wellbeing in the morning [258]. A field study of 33 individuals found that increasing railway noise levels had a higher

probability of eliciting event-related transitions to wake or N1 sleep, but no relationships were seen between the railway noise and subjective sleep quantity, quality, or depth [83], much like in the present data.

With a higher number of event-related cortical reactions, effects on sleep macrostructure may follow, as was seen in *Paper II* compared to *Paper III* (see section 4.7.1). In some areas of Europe, there may be up to 150 freight trains during the night [83]. A greater number of event-related cortical and autonomic reactions would be anticipated in such situations than observed in nights with 20, 36 or 52 trains, with sleep fragmentation having accordingly larger effects on sleep architecture and perceived disturbance.

No effects were found in any of the evening questionnaires, suggesting that the event-related cortical and autonomic arousal and perceived sleep disturbance did not negatively affect daytime functioning. It is possible that the evening questionnaire was insensitive to small adverse impacts on restorative properties of sleep, or that the participants were unable to retrospectively assess their daytime feelings adequately. Alternatively, the objective effects of vibration and noise on sleep may have been insufficient to impair the restorative function of sleep for wellbeing, which is supported by the lack of observed effects on the self-reported data following nights with the highest vibration exposures.

4.6. Number of events (Papers II & III)

Across all studies, only modest effects were found for the number of events during the night.

When the number of moderate vibration trains was increased from 20 to 36, there was no difference in overall sleep architecture, but the total number of event-related awakenings was almost doubled in the NVm36 night. There was a corresponding increase in perceived sleep disturbance by both vibration and noise, presumably since participants recalled at least some of these additional awakenings and ascribed the exposure as the source of their disturbance. However, in nights with high vibration, no effects were found for any of the self-reported or event-related (cortical or autonomic) outcomes when comparing nights with 20, 36 and 52 trains. Between these high vibration nights, only one effect was seen on sleep macrostructure, with WASO 7.2 minutes longer in the 36 than the 20 train night (Table 10). Furthermore, relative to the control night, the first awakening occurred earlier, the maximum continuous time in N3 sleep was shorter and the total number of SSCs was greater in the NVh36 night in *Pa-*

per II. Taken together, these data suggest that both the passage frequency and vibration amplitude of discrete events contribute to global sleep outcomes, but only to a point. If sleep is disturbed, there are likely carry-over effects during the subsequent sleep time within the same night, including periods of compensatory SWS [248, 249]. Additional events during these periods would be less likely to overcome the body's homeostatic sleep need.

Following moderate vibration trains, SSC probability was lower in nights with 36 events than in nights with 20. With higher numbers of events, there were also slight but non-significant reductions in awakening probability in *Paper II*, and HRA and arousal probability in *Paper III*. There is evidence that the body habituates to repeated train noise exposure within nights, with the likelihood of event-related response decreasing with a higher number of events [169], but the present data are less conclusive for vibration exposure. The sleeping brain may perceive vibration as a more noxious stimulus than noise, precluding habituation.

4.7. Individual moderators

4.7.1. Inter-individual differences

In addition to the control night, *Papers II* and *III* both involved an experimental night with 36 trains of high vibration amplitudes with accompanying noise. The respective event-related arousal, awakening and SSC probabilities are presented in Figure 23. Comparison of the changes in sleep microstructure in the control nights between the two trials suggests that both study groups were broadly similar regarding their spontaneous change in sleep architecture, as would be expected for participants of similar demographics. However, in the NVh36 night, the likelihood for cortical reaction following exposure was lower in *Paper III* than in *Paper II*. These data are supported by findings in sleep macrostructure, where negative effects relative to the control night were observed in NVh36 on SSCs, first awakenings and SWS continuity in *Paper II* but not *Paper III* (Table 10). This shows that either the participants in *Paper II* were more reactive to exposure than the *Paper III* group, or to phrase it differently that the participants in *Paper III* were more resistant to exposure.

The ability to maintain stable sleep in the presence of noise has been shown to differ between individuals [115], and inter-individual differences have been demonstrated to explain around 40-45% and 50-55% of the variance in cortical awakening and arousal probability respectively following traffic noise [116].

With the limited group sizes of 24 and 23, it is therefore unsurprising to find differences between the studies, even in a homogeneous sample. Without further data it cannot be concluded whether the reaction probabilities following exposure observed in *Paper II* or *III* are truly representative of young, healthy individuals with good sleep. The external validity of the results should therefore be treated with caution, even when considering the effects amongst a group of similar demographics to those in the sleep studies. However, given the repeated measure design of both studies, the internal validity of the results is not expected to be influenced by a possible sampling bias.

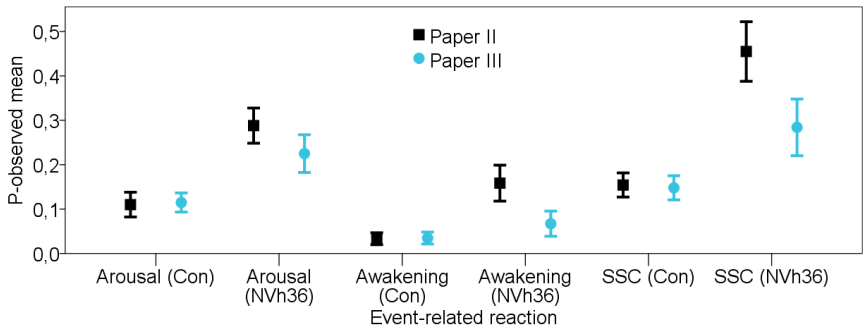

Figure 23 Comparison of event-related arousal, awakening and SSC probabilities in control nights (Con) and high vibration, 36 train nights (NVh36) in *Papers II* and *III*.

4.7.2. Noise sensitivity

All self-reported data from *Papers I-III* were combined. Outcomes where a significant main effect of noise sensitivity were found are presented in Table 11. Relative to non-sensitive counterparts, the noise sensitive group reported reduced overall sleep quality ($p=0.008$), longer sleep latency ($p=0.026$), more awakenings ($p<0.001$), greater difficulty sleeping ($p=0.048$), sleeping worse than usual ($p=0.001$), and waking more often ($p=0.048$). The sensitive group also reported reduced nocturnal restoration, reflected by rating themselves as more tired ($p<0.001$), more tense ($p=0.005$), more irritated ($p=0.011$), and impaired mood reflected by lower scores for pleasantness ($p=0.001$) and social orientation ($p<0.001$). No interaction between exposure and sensitivity was found for any of these outcomes, suggesting that vibration and noise exposure had a similar effect on both sensitivity groups, but that the sensitive group had worse self-reported sleep even in the absence of exposure. Previous work has found that noise-sensitive individuals report a greater reduction in sleep quality following nights with traffic noise exposure than non-sensitive persons [112], an effect not ob-

served presently. Volunteers were only accepted into the studies if they had good normal sleep. This sensitive sample may then represent a somewhat resilient subgroup of the wider noise sensitive population, which would go some way towards explaining the similarity that exposure had on both sensitivity groups in terms of subjective parameters including sleep quality.

Table 11 Mean and standard deviation (SD) of self-reported sleep outcomes in control and pooled exposure nights, stratified by noise sensitivity.

Variable	Non-sensitive (n=38)		Sensitive (n=21)	
	Control	Exposure	Control	Exposure
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Sleep quality (0-10)	6.1±2.0	6.0±2.1	5.3±1.8	5.0±2.2
Disturbance from vibration (0-10)	0.4±1.2	3.1±2.5	0.7±1.6	4.8±3.0
Disturbance from noise (0-10)	0.5±1.5	3.5±2.6	0.7±1.8	5.3±2.8
Time to fall asleep (min)	25.5±17.1	27.9±16.2	31.3±21.4	36.3±24.4
Estimated awakenings (n)	2.5±1.8	2.8±1.8	4.1±3.6	4.2±2.7
Easy/difficult to sleep (0-10)	4.2±2.6	4.3±2.5	4.6±2.8	5.2±2.6
Slept better/worse (0-10)	5.9±1.9	5.6±2.0	6.5±1.9	6.6±2.0
Woke never/often (0-10)	4.9±2.5	5.3±2.1	6.3±2.1	6.0±2.3
Rested/tired (0-10)	4.2±2.1	4.1±2.1	4.8±1.9	6.2±2.3
At ease/tense (0-10)	3.4±1.7	3.6±1.7	3.3±1.5	4.5±1.9
Glad/irritated (0-10)	3.2±1.6	3.6±2.2	3.8±2.1	4.4±1.9
Pleasantness (1=min, 4=max)	3.2±0.4	3.2±0.5	3.0±0.4	2.9±0.5
Social orientation (1=min, 4=max)	3.2±0.4	3.2±0.5	3.1±0.4	2.9±0.5

The differences in self-reported sleep were not supported by any variations in physiologic sleep macrostructure between the sensitivity groups. Furthermore, no effects of noise sensitivity on event-related arousals, awakenings or SSCs were found, even when increasing statistical power by combining all data from the NVh36 nights in *Paper II* and *III* (Figure 24). Öhrström et al. found in a laboratory study that heart rate increase and body movements among noise sensitive individuals was significantly higher following noise exposure compared to non-sensitive individuals [259]. However, the heart rate was only 0.7 bpm higher for the noise sensitive persons, and other studies examining the nocturnal effect of noise have not found differences in physiologic response between sensitivity groups [111, 112, 114, 260]. This suggests that noise sensitivity as it is currently understood is not an important modifier of physiological measures of sleep.

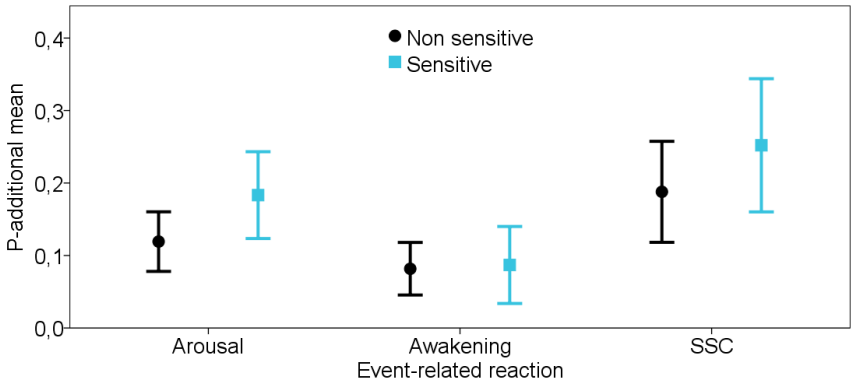

Figure 24 Comparison of event-related arousal, awakening and SSC additional probabilities for non-sensitive and sensitive groups in NVh36 nights.

Overall sleep disturbance by vibration ($p<0.001$) and noise ($p<0.001$) was higher among noise sensitive persons than non-sensitive individuals. Furthermore, interactions between exposure and sensitivity (vibration disturbance $p=0.061$, noise disturbance $p=0.038$) indicate differential effects of exposure on the two groups, with sensitive individuals reacting more strongly to exposure. This indicates that exposure during periods of nocturnal wakefulness was more negatively perceived by sensitive individuals. This is in line with sleep disturbance and annoyance studies whereby sensitive persons report higher sleep disturbance or annoyance for a given noise exposure [109, 113, 182]

Heart rate response following noise exposure during wake has previously been found to be greater in noise sensitive than in non-sensitive individuals, although no differences between sensitivity groups were found during sleep [114, 261]. In agreement with this finding, we observed no statistically significant influence of sensitivity for any of the measures of heart rate response, either in *Papers I-IV* or elsewhere [213].

Interestingly, the combined EEG reaction probability following vibration and/or noise exposure was higher for sensitive individuals around full moon than at other lunar phases [262]. This finding is difficult to interpret, particularly in the absence of any other physiologic differences between sensitivity groups. Furthermore, noise sensitivity has been proposed to have a genetic basis [263]. Characteristics of EEG activity during sleep and the detrimental impacts of sleep deprivation are regulated genetically [264, 265]. The observed differential effects in the EEG between sensitivity groups may therefore arise from underlying

genetic factors, but at the present the evidence is weak and so warrants future investigation.

"Noise sensitivity" has been found in a field study to be a better predictor of self-reported sleep disturbance by vibration than "vibration tolerance" [266]. Many people are frequently exposed to noise of one form or another, and so may have a reasonable awareness of how they react to such exposures. Vibration tolerance or sensitivity on the other hand are rather more abstract concepts, particularly when considering whole body vibration. Fewer people are exposed to environmental vibration than noise, so may have difficulty in conceptualising how they may respond. Accordingly, the association between noise sensitivity and vibration tolerance was weak across data from all papers (Spearman's ρ=-0.201, p=0.074). The predictive capacity of noise sensitivity for response to vibration can be explained by considering that noise sensitivity overlaps with other forms of environmental intolerance [267]. It is therefore perhaps an indicator of overall general sensitivity, not only noise-specific sensitivity.

4.7.3. Sex

Across all studies only a limited number of effects of sex were seen. Men had a greater number of EEG arousals than women in *Paper II* (59.9 vs 46.4), and also had longer in N1 than women in *Paper IV* (13.5 minutes longer averaged across all nights). No statistically significant effects of sex were found for any other outcomes across all papers, including event-related cortical or autonomic response, sleep macrostructure with the two exceptions noted earlier, or any of self-reported outcomes analysed. Previous work has reported that sleep among women may be objectively better than among men, even though it may be rated as subjectively worse [100-102]. The absence of statistical differences in the current work suggests that any sex-related differences in young healthy adults are limited. It is possible that the sample size was insufficient to reveal any effects of sex, but no statistically significant effects were seen when further combining event-related EEG data from NVh36 in *Papers II* and *III*, although there was a borderline effect for awakening probability (ANOVA p=0.06, Figure 25).

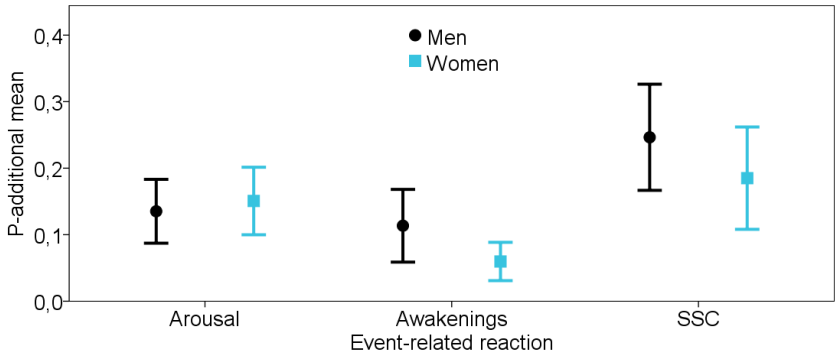

Figure 25 Comparison of event-related arousal, awakening and SSC additional probabilities for men and women in NVh36 nights.

It is possible that the lack of differences was due to menstrual-related sleep factors. EEG power density in the 14.25-15 Hz frequency band, the upper frequency range of sleep spindles, may vary over the menstrual cycle [268]. Spindles have been proposed to indicate thalamocortical gating of external stimuli [115, 269]. High spindle density has been demonstrated to be protective against auditory stimulation during sleep [115], and high sigma (12.5-15 Hz) spectral power across the full night and spindle density in the first sleep cycle might protect against the development of insomnia symptoms [270]. If women happened to participate around their mid-follicular phase, spindle spectral power could be lower than at other phases [268], which may reduce their ability to maintain stable sleep. This would go some way to explaining why sleep was not objectively better amongst women in *Papers II-III*.

4.7.4. Chronotype

Chronotype was not measured, but poor agreement between the habitual sleep and wake times of the participants and the sleep and wake times in the laboratory (23:00 and 07:00 respectively) was an exclusion criterion. These habitual sleep times could indicate that the recruited participants were either morning types or neither evening nor morning types, but likely not evening types [271, 272]. No differences in sleep macrostructure or subjective sleep quality would be expected between morning and evening types if they followed their regular sleep routines, but for evening types the earlier-than-usual timings in the current studies would likely have resulted in increased SOL and reduced TST and SE [273]. However, there is evidence that sleep pressure dissipates more rapidly during sleep among

morning types than evening types [119, 273]. This would have the net effect of evening types spending a greater proportion of their early sleep in protective sleep, by which point morning types would have been asleep for several hours and spending more time in the more reactive sleep stages. Following vibration and noise exposure, event-related arousal probabilities measured in the field would therefore perhaps differ between chronotypes as a function of time of night, which should be considered when undertaking such studies.

4.8. Validation

Some PSG outcomes agree between laboratory and field settings, but differences have been seen for TST, SE, REM and N1 [274, 275], although these studies are notable for the absence of a habituation period. A first-night effect, where sleep is generally worse than in subsequent nights, has been seen in laboratory work [276], but an early study found that a single night of habituation is sufficient for EEG studies [61]. In the following sections, sleep data from *Papers I-IV* will be compared against normative values to investigate the validity of the results of the present laboratory studies.

4.8.1. Baseline sleep architecture

The mean time spent in each sleep stage in the control night for each study is compared with age-related expected norms in Table 12. Across *Papers II-IV* there was an expectedly good agreement in the time spent in the relative sleep stages, indicating good internal validity.

The study participants spent more time in SWS than in laboratory and field studies, as well as compared to values obtained across several nights in a meta-analysis for a nominal 25 year old [91]. Furthermore, WASO was similar to the meta-analysis [91] and lower than other laboratory and field studies. The differences to [95, 169, 277] could be due to age-related factors, but data from [228] were obtained from a similarly aged group as in the present studies, although there was no acclimatisation period in [228]. Taken together these data suggest that the participants in *Papers II-IV* were good sleepers and that they were well habituated to the experimental setup.

Table 12 Comparison of mean sleep stage distribution (minutes) of control nights in the present work with age-dependent norms.

Reference	Age (years)	n	N1	N2	SWS*	REM	WASO
Paper II	19-28	24	42.6	212.0	90.0	88.0	21.0
Paper III	19-30	23	39.3	217.7	89.6	93.5	19.9
Paper IV (study 4B)	19-27	16	39.2	214.4	96.7	82.1	20.1
Bonnet & Arand [228] ♪	21-30	13	40.1	240.8	58.0	85.0	-
Basner et al. 2008 [277] ♪	22-62	10	10.7	231.7	63.4	102.3	45.6
Basner et al. 2011 [169] ♪	18-71	72	21.5	243.7	64.7	96.5	38.7
Ohayon et al. [91] †	25	3,577	31	223	80	99	18
Sahlin et al. [95] ‡	20-44	152	27	251	45	86	45

*Depending on scoring criteria used, can be stage N3 (AASM [56]), or stages S3+S4 (R&K [65])
♪ Laboratory study
†Meta-analysis, values taken from age-related trend for age=25 years
‡Field study, women only

The similar or high values for time in N1 relative to other studies might arise from methodological differences in PSG analysis. Only one study explicitly determined SOL using the same definition as *Papers II-IV*, i.e. the latency to the first occurrence of N1 sleep [169]. In this paper, the termination of an awakening was defined as the first occurrence of a sleep stage other than W or N1. The exclusion of N1 during bouts of wakefulness would therefore reduce the apparent total time in this stage across the night. One study defined SOL as the first occurrence of N2 [277], meaning that if only sleep after SOL was considered in the calculation of time in various sleep stages, any N1 prior to SOL would not be included. This could explain the low value of N1 in that study. SOL was not defined in [95, 228], so it is unclear whether time in N1 reported in these studies is an underestimation.

4.8.2. Spontaneous cortical response

The likelihood of EEG arousals, awakenings or SSCs occurring spontaneously within a 60 s screening window are presented in Table 13, along with data from other laboratory studies. These arousal and awakening probabilities are slightly lower than have been observed among 21-30 year olds in previous work, where a mean of 83 arousals and 23 awakenings over an average sleep time of 446

minutes, corresponding to spontaneous probabilities in a 60 s period of 18.6% and 5.2% respectively, were found [228]. Other authors have also found higher spontaneous arousal and awakening probabilities than in our studies, although a wider age range was examined [169, 277]. This suggests a number of possibilities; first, that the subjects in our work were well habituated to the experimental setting, or at least more so than the study sample in [228]; second, that our subjects were resilient sleepers, as was endeavoured during recruitment; or third a combination of both.

Table 13 Spontaneous cortical reaction probabilities

Reference	Age (years)	Arousal prob. (%)	Awakening prob. (%)	Combined EEG prob. (%)	SSC prob. (%)
Paper II	Mean 22.9 Range 19-28	10.7	3.1	14.1	14.9
Paper III	Mean 23.7 Range 19-30	11.2	3.2	14.4	14.9
Paper IV	Mean 22.0 Range 19-27	12.2	1.9	14.9	11.1
Basner et al. 2008 [277]	Mean 35.3 Range 22-62	24.3	6.6*	30.8*	13.6†
Basner et al. 2011 [169]	Mean 40 Range 18-71	24.2	5.3	29.5	-
Bonnet & Arand [228]	Range 21-30	18.6	5.2	23.8	-

*Includes motility reactions >15s

†Includes changes to wake; S4 to S3 possible; REM sleep was classified as same depth as SWS.

4.8.3. Comparison with field studies

Concurrently with the sleep studies presented in *Papers I-III*, field studies into the effects of railway vibration were performed in Poland and The Netherlands by partners with the EU-funded CargoVibes project [209]. The dose-response relationships for the likelihood of an individual reporting sleep disturbance by vibration in the field were calculated according to Miedema and Oudshoorn [278], assuming a cut-off for disturbance of 50 on a 100-point scale. The resulting relationships are presented in Figure 26, along with the dose-response curve from the laboratory studies ("Disturbed" from Figure 21) for comparison [279]. There was no statistically significant difference between the laboratory and the combined field settings (ordinal logistic regression OR=1.37, p=0.464), suggesting a good ecological validity for the laboratory studies, at least regarding subjective outcomes. This agrees with previous work where following a single

habituation night, no differences between field and laboratory settings were seen when assessing sleep using wrist actigraphy and self-reported sleep [280, 281].

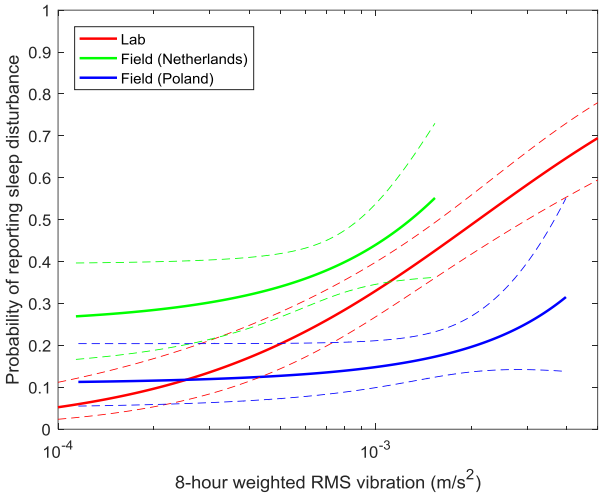

Figure 26 Self -reported sleep disturbance as a function of 8-hour night-time vibration, measured in the laboratory (*Papers I-III*) and two field locations. Dashed lines indicate 95% confidence intervals. Presented at ICBEN 2017 [279].

4.9. Relevance for the field

It was recently estimated that approximately 54,100 people in Sweden are exposed in their homes to vibrations of 0.4 mms^{-1} from railway traffic [282]. Based on the present data, acute cortical effects on sleep begin to manifest around this velocity, and alterations of heart rate were observed at somewhat lower velocities. Substantial numbers of residents living close to freight lines are then likely exposed to vibrations which may illicit physiological response. Although the long-term impact of acute cortical response is unclear, autonomic response has a biologically plausible link with CVD [161]. Noise abatement measures can be taken to address excessive noise, but we observed that physiological response to vibration occurred even in the absence of noise. Furthermore, self-reported sleep disturbance could conceivably contribute to the burden of disease from vibration in terms of healthy life years lost [85]. Railway vibration is therefore of concern within a public health perspective for the wellbeing of exposed populations.

4.10. Limitations and methodological considerations

4.10.1. Study protocol

The control night was always the second night of the study. One night could be sufficient for habituation to the PSG apparatus [61], but it cannot be excluded that there were carry-over effects following disrupted sleep in the preceding habituation night. Compensatory sleep in the control night, for instance increased SWS if it was adversely affected during habituation [283, 284], could potentially lead to lower spontaneous reaction probabilities and an exaggeration of effect sizes during exposure nights relative to the control. Without baseline sleep data from time points other than the second night to serve as validation, it also cannot be totally excluded that participants had not fully acclimatised to the study environment. In conditions with low exposure (*Paper IV*), the ordering of nights had no effect on any outcomes, providing some support to the notion that participants were habituated. In future studies, randomisation of the position of the control night and the inclusion of additional baseline nights are nevertheless recommended.

4.10.2. Event-related analysis window

The optimal window length should be that which maximises the likelihood for an event to exploit its potential for a reaction [285]. Across all studies it was found to be 60 s, indicating good internal validity. Furthermore, this window length is the shortest possible that is of sufficient duration to contain the very longest events within it, whilst still being a multiple of the smallest unit of time required in the analysis (i.e. SSCs measured with an epoch length of 30 s). This length also matches that used by other authors when considering cortical and autonomic response to railway noise during sleep [72, 169, 214, 277], although a longer window length of 90 s has also been used [83, 172].

4.10.3. Vibration exposure

In all studies, the bed frame was excited longitudinally only, whereas in a real setting, vibration would be present in varying degrees of amplitude in all three directions. This decision was made based on a pilot study, which found that hor-

izontal vibration was, in addition to being less attenuated by the mattress, perceived as subjectively more disturbing than vertical vibration [203]. It cannot be excluded that the addition of vertical and lateral vibration would contribute further to the likelihood and magnitude of physiological reactions, thus the results presented here may underestimate the response in the field.

The true WBV experienced by an individual in the studies may have slight variations to the values given in Table 3. The dominant vibration was in the same direction as the horizontal excitation, but because of the bed's dynamic material properties there was vibration at frequencies other than the 10 Hz excitation signal, and also in the vertical direction. Furthermore, different masses on the topside of the mattress result in different degrees of deformation and compression of the mattress materials and springs. This has the consequence that the transmissibility of vibration between the bed frame and the body may be increased, resulting in an amplification of vibration relative to the frame, or decreased, resulting in an attenuation of vibration. This effect depends on both vibration direction and the loading mass on the system, i.e. the weight of the study subjects (Figure 10). The participants across all studies had a mass of 48-90 kg, thus variations in the true WBV amplitude are likely.

As discussed in the introduction, the prediction of vibration from railways in the field is not straightforward. The particular amplitude and frequency content of a vibration exposure in the field is highly variable between individuals, which is also an issue for noise but even more problematic for vibration. Analysis of indoor measurements of freight pass-bys indicated that horizontal vibration in most dominant around 6-8 Hz and vertical vibration is most dominant between 8-10 Hz [203]. It would therefore have been desirable for the vibration signals to have had a dominant component slightly below the 10 Hz frequency used. However, due to limitations of the equipment and unwanted distortion products below this frequency, it was necessary to use signals with a 10 Hz main component. Furthermore, human perception of vibration is most sensitive around 5-10 Hz. If reactions would indeed be stronger at lower frequencies, then it is conceivable that the results might slightly underestimate the effects of vibration exposure in the field.

4.10.4. Body position

Although all participants were lying down when asleep, a variety of possible postures may still be adopted: supine, prone or laterally on either side. Perception thresholds have not been found to differ among these varying positions [16,

286]. Therefore, while perception and physiologic response are not analogous, we tentatively assume that an individual's response would be independent of their sleep position. However, there is some evidence that sleeping in a supine position leads to increased EEG arousal length during apnoeic events among suffers of OSA [287], and the assumption may be incorrect.

Should a part of the body make contact with the bad frame during vibration excitation, this localised area would likely be subject to a higher amplitude vibration than the rest of the body. Any bridging of the vibration-attenuating mattress system would be associated in an increase in the localised, but not necessarily whole-body, vibration. No data are available regarding bodily contact with the bed frame, so it is not possible to determine whether any corresponding localised higher amplitude vibration contributed to higher degrees of response. Video recordings synchronised with exposures would have enabled control of such possible effect moderation, but was not implemented for reasons of integrity.

4.10.5. Homogeneity of study population

Only young volunteers participated, limiting the conclusions that should be drawn regarding potential effects of vibration on a more general population. With increasing age, the proportion of SWS and REM decreases, with corresponding increases in N1 [91, 95]. Cortical response to vibration and noise is most likely during N1 and least likely during SWS, so it follows that an older population would have a higher number of event-related reactions over the course of the night, with reaction probabilities accordingly higher.

All participants rated their normal sleep as good. They may represent a robust sleep subgroup, who react less strongly to vibration and noise than poor sleepers. In the field, the prevalence of sleep problems and disorders may be around 27% [288], and it is plausible that event-related response would have a greater effect on these individuals with pre-existing sleep issues.

4.10.6. Sex issues

Menstrual phase was not assessed, limiting the possibilities to investigate any sex-dependent factors. Sleep disturbance among women may depend on menstrual phase, [289, 290], oral contraceptive use [291], pregnancy [292], and menopause [105]. Vibration exposure in the field could therefore have differential effects among women compared to those observed in the present studies.

5. Conclusion

Vibration at amplitudes corresponding to those occurring in dwellings close to freight railway lines contributes to acute event-related physiological effects during sleep. Vibration-induced autonomic and cortical arousal and self-reported sleep disturbance increased in a dose-dependent manner with vibration amplitude.

Vibration had very limited effects on global sleep architecture, but event-related responses occurred at the expense of spontaneous reactions. The impact of this redistribution of sleep rhythmicity on health and wellbeing is currently unclear.

Vibration or noise exposure led to fragmented sleep. Vibration and noise were additive regarding their effect on event-related arousal and sleep stage change, demonstrating that both exposures differentially contribute to sleep fragmentation.

Noise sensitivity negatively affected the perceived impact of vibration on sleep. There were no corresponding differences in physiologic sleep between sensitive and non-sensitive individuals, providing support for the idea that noise sensitivity is an indicator of a more general psychological environmental sensitivity.

Event-related elevations of heart rate were evident at vibration amplitudes only slightly above perceptual detection thresholds. Event-related sleep stage changes, arousals and awakenings began to manifest at only slightly higher vibration amplitudes. This indicates that if vibration can be sensed during sleep, it can contribute to autonomic and cortical arousal.

6. Future Perspective

It is currently often assumed that acute effects on sleep, including awakenings, arousals and cardiac activations, lead to adverse health outcomes. However, the causal link between noise- or vibration-induced cortical response, sleep fragmentation and negative health outcomes is unclear. Furthermore, physiological habituation may reduce the biological relevance of an exposure for the development of adverse health outcomes. There is some evidence that cortical response to noise habituates over time, but the same may not be true of vibration. Prospective epidemiological studies could provide insight into whether short-term responses to nocturnal noise and vibration translate in the long-term to the genesis of disease, although the methodological expense of such studies will likely prove prohibitive. Animal models could provide a potential alternative, as the lifetime exposure and response can be tracked.

The present work involved only young healthy participants with good normal sleep. Individuals who do not regularly sleep well may be more susceptible to vibration-induced sleep disturbance. This includes pregnant woman, people in poor health, and the elderly. Children sleep for longer than adults, and their sleep is believed to be important for development, which could be sensitive to disruption. Shift workers sleep during the daytime when exposure may be higher, and their circadian rhythms are already under stress. The effects of vibration and noise on these vulnerable groups could be more deleterious than in the current work, and is worth future investigation.

The current standard method of scoring sleep may be insensitive to small but clinically relevant changes in sleep structure. For instance, slow wave activity can be present in sleep other than SWS, yet reduced slow wave activity in these non-SWS stages following vibration or noise exposure would not necessarily be reflected by a change in the sleep scored as N3. Power spectral analysis incorporated into future studies would allow for a more sensitive measure of effects of exposure-induced changes to global sleep structure. Similarly, heart rate variability can provide a more detailed picture of response in the autonomic nervous system than analysing heart rate alone.

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