Physiological recovery from night-call duty - a field study of physicians

Malmberg, Birgitta

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LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Physiological recovery from night-call duty – a field study of physicians

FACULTY OF MEDICINE
Lund University

Birgitta Malmberg

Occupational and Environmental Medicine

Department of Laboratory Medicine

Lund University

SE-221 85 Lund

Sweden

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In the beginning there was rhythm…

Contents

List of papers

This thesis is based on three papers, which are included in the end and referred to in the text according to their Roman numerals:

I. Malmberg B, Persson R, Jönsson BAG, Erfurth E-M, Flisberg P, Ranklev E, Ørbaek P. Physiological restitution after night-call duty in anaesthesiologists: impact on metabolic factors. Acta Anaesthesiol Scand 2007;51:823-830.

II. Malmberg B, Persson R, Flisberg P, Ørbaek P. Heart rate variability changes in physicians working on night call. Int Arch Occup Health 2011;84:293-301.

III. Malmberg B, Kecklund G, Karlson B, Persson R, Flisberg P, Ørbaek P. Sleep and recovery in physicians on night call: a longitudinal field study. BMC Health Services Research 2010;10:239.

Abbreviations

ANEST	Anaesthesiologists
ANS	Autonomic Nervous System
AW	Actiwatch
BIC	Bayesian Information Criterion
BMI	Body Mass Index
CHD	Coronary Heart Disease
CNS	Central Nervous System
CRP	C-Reactive Protein
CV	Coefficient of Variation
ECG	Electrocardiography
EEG	Electroencephalography
EOG	Electrooculography
ENT	Ear, Nose and Throat
FFT	Fast Fourier Transformation
GH	Growth Hormone
GHQ	General Health Questionnaire
HDL	High Density Lipoprotein
HF	High Frequency
HFnu	High Frequency normalized units
HPA axis	Hypothalamic-Pituitary-Adrenocortical axis
HRV	Heart Rate Variability
IGF-1	Insulin-like Growth Factor 1
IHD	Ischemic Heart Disease
KSD	Karolinska Sleep Diary
KSQ	Karolinska Sleep Questionnaire
KSS	Karolinska Sleepiness Scale

LC-MS-MS	Liquid chromatography-electrospray tandem mass spectrometry
LDL	Low Density Lipoprotein
LF	Low Frequency
PENT	Paediatricians and ENT surgeons
PSG	Polysomnography
QUICKI	Quantitative insulin sensitivity check index
REM	Rapid Eye Movements
SA	Sinoatrial node
SCL-35	Symptom Check List
SCN	Suprachiasmatic nuclei
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
SWS	Slow Wave Sleep
T3	Triiodo-thyronine
T4	Thyroxin
TG	Triglycerides
TP	Total Power
TSH	Thyroid Stimulating Hormone
VLF	Very Low Frequency
WTD	Working Time Directive

Background

To provide 24-hour health care, physicians have to work on recurrent night-call duty. This is in conflict with the biological diurnal rhythms designed for daytime activity.

Requirements for work on call have changed over the past few decades, with a tendency towards more intense night-call duty, often resembling a full night shift, but with a successive shortening of shift lengths in return. Indeed, physician’s work on night-call duty has several similarities with classical rotating shift work, although direct comparisons are not possible, because of the different character of night-call, with its extended night shifts and pronounced irregularity of schedules.

The impetus behind the present study was a request from a group of anaesthesiologists for an evaluation of their 16 hour night-call duty, carried out from a physiological perspective. They had experienced an increasing load owing to their work on night call during recent years and worried about potential health consequences. Their concerns were reinforced by the presentation of an epidemiological study (Svärdsudd et al. 2002), which indicated a higher mortality rate among Swedish anaesthesiologists compared with other physicians and which discussed occupational stress as one of the possible explanations. However, the methodology and interpretation of this study were criticized (Hagmar 2003; Katz 2004), and researchers in the other Nordic countries failed to confirm the results (Aasland 2002; Juel et al. 2002; Ohtonen and Alahuhta 2002). In addition, the material was too small to show any cause-specific mortality rates. Still, their study contributed to a general concern about physicians’ working conditions, especially among anaesthesiologists.

Indeed, studies of physicians have shown that night-call duty entailing high demands, long working hours and disrupted sleep may cause a strain on the individual leading to impaired performance and discomfort (Denisco et al. 1987; Lockley et al. 2004; Arnedt et al. 2005), while less is known about the physiological effects of working on night call. It has been well documented that night shifts of 24 hours or longer are, in most cases, detrimental to both performance and subjective health (Howard et al. 2003; Landrigan et al. 2004; Lockley et al. 2004; Arnedt et al. 2005). However, specific studies focusing on shorter night-duty schedules are scarce, and there is considerable controversy regarding the optimal length of a night-call shift. Therefore, it is important to study these aspects in current night-call schedules to obtain empirical evidence on which to base sound shift scheduling (Lockley et al. 2006; Landrigan et al. 2007).

Not only the length of the night-call shift, but also its intensity and associated mental demands may be assumed to affect recovery patterns. Anaesthesiologists are reported to have a higher mental workload during night duty compared with many other physician groups working on call (Larsson et al. 2003; Nyssen et al. 2003; Lindfors et al. 2006; Lindfors et al. 2007). Indeed, during recent years, occupational stress and reduced well-being in anaesthesiologists have also been frequently addressed in the scientific literature (Coomber et al; Cooper et al. 1999; Bartel et al. 2004; Lindfors et al. 2006). For the anaesthesiologists on call, the cognitive and emotional load of constantly handling patients with life-threatening conditions, which requires fast and accurate action, may have a greater impact on their sleep and recovery compared with other specialists.

As stated earlier, studies of the physiological effects of physicians' night-call duty are scarce. However, one might assume effects similar to those reported in studies of shift work. There are many reports on classic rotating shift work that show negative effects on subjective health, well-being, and sleep, also implying an increased risk of ischemic heart disease (IHD) and metabolic syndrome. For a clinical diagnosis of metabolic syndrome, at least three of the following criteria have to be met: (i) abdominal obesity; (ii) elevated triglycerides; (iii) decreased high density lipoprotein-cholesterol (HDL-cholesterol); (iv) high blood pressure; (v) increased fasting glucose (Wolk and Somers 2007). The exact mechanism for the negative impact of shift work on health is unknown. However, disruption of circadian rhythms of metabolic, nutritional and cardiac function as well as sleep disturbance are plausible causative factors (Härmä 2006).

Naturally a certain amount of mental and physiological activation is expected to accompany night-call duty, but the crucial issue, from a health perspective, is to what degree such activation is sustained post-call. In the present thesis, the concept of recovery is equivalent to the psychophysiological unwinding following work efforts while on night-call duty. Based on results from previous research, incomplete recovery is considered to be one crucial link between acute physiological stress reactions, shift work and chronic health effects (Geurts and Sonnentag 2006).

As a consequence of the anaesthesiologists' request, a comprehensive field study of physiological restitution after nigh call duty was initiated. Anaesthesiologists as well as physicians from other specialities were asked to participate. The main issue was to clarify whether there was an adverse influence of customary night-duty schedules that would compromise adequate post-call recovery. If physicians on night call have recurrent periods of deficient physiologic recovery, this might be a potential health risk in a longer perspective. The biological clock, which generates diurnal variations in physiological activity, has a major impact on recovery patterns after night-call duty. This is described below to provide a background for the subsequent presentation of specific physiological systems, that may potentially be affected by night-call duty.

Diurnal rhythms

In the majority of physiological systems in the body there are rhythmic variations in function. These are generated by the circadian clock system, which has a periodicity of approximately 24 hours (Czeisler and Gooley 2007). In mammals, the central circadian pacemaker is located in the suprachiasmatic nuclei (SCN) of the hypothalamus. The “circadian clock” refers to the Latin word “circa Diem”, which means “approximately one day”. This autonomic, self-sustainable mechanism is driven by a genetically operated timekeeping system that has a period of about 24.2 hours. The clock ensures that all physiological processes are correctly adjusted to the time of day and coordinated with each other (Czeisler and Gooley 2007; Chung et al. 2011). It is essential for survival that the clock is exactly synchronized to a 24-hour periodicity. This is provided by different internal and external stimuli, called “zeitgebers”, of which information about light from the retina is the most important, but food intake and social activities also have an impact. The resulting 24-hour rhythm is called the “diurnal rhythm”.

In humans, the rhythmic changes are designed for daytime activity and the sleep hormone melatonin therefore reach its highest levels during the night time, whereas the opposite is true of the adrenal hormone cortisol and body temperature. When travelling across time zones, a full adjustment for all physiological systems takes about 4-5 days after a flight westward from Scandinavia to New York (6 hours delay in time). However, during a journey eastward, the adjustment is slower.

The situation is quite different during shift work, where there is usually only a limited adjustment of the diurnal rhythms, or none at all. Light as well as social activities keep the shift worker from changing rhythms even after several night shifts in a row. The only work setting for which complete physiological adaptation to night-work has been identified is duty on oil platforms in Norway, where the workers were isolated from natural light and the outer world while on duty (Bjorvatn et al. 1998). Thus, the majority of shift workers are in conflict with the circadian rhythms and have to perform even when their biological clock is set for sleep and low metabolism and then try to recover sleep during the day when their clock is set for activity. Additionally, some physiological parameters are more influenced by the sleep-wake cycle than the diurnal rhythm, which makes the situation even more complex. Naturally, these circumstances may lead to several problems for shift and night workers, and these will be addressed in the following sections.

Sleep

Sleep is indispensable for health and survival and physiologically it is characterized by anabolism and restitution. During sleep, heart- and respiratory rate are lowered and blood pressure and body temperature are reduced. There is also increased secretion of growth hormone (GH) and testosterone, and lowered levels of cortisol and thyroid stimulating hormone (TSH). The general sleep duration is partly dependent on inherent factors. A dual control of sleep and wakefulness is accomplished through an interaction between two systems. The first is a homeostatic process, which is a function of sleep and the urge to sleep builds up during wakefulness. The second is the circadian drive to wakefulness, which is independent of sleep and varies rhythmically during the day and night. Under normal conditions these systems help to optimize sleep and wake periods for the individual, but during work in shifts the interplay may be less fruitful (Van Dongen et al. 2003; Olson et al. 2009).

Electroencephalography (EEG) is the classic method of measuring sleep, through registration of brain activity with scalp electrodes. It is used together with electrooculography (EOG) for describing eye movements, and electromyography (EMG) for describing muscle tension. These three measures constitute "polysomnography" (PSG), which is used to classify sleep into stages 1-4 and rapid eye movements (REM) (Rechtschaffen and Kales 1968). During stage 1, there is a transition from being awake to sleeping. Stage 2 represents basic sleep. During stage 3-4, there are large waves in the EEG. These are characteristic of deep sleep or "slow wave sleep" (SWS). Sleep is an active process during which cortical neurons more or less synchronize their rest and activity periods, especially during stage 3-4 (Saper et al. 2001). REM sleep is similar to stage 1 sleep, except for the rapid eye movements and loss of muscle tone. During this stage dreams occur, and it also seems to be important for memory consolidation. However, stage 3-4 is considered to be the most important for recuperation in general.

The sleep stages repeat themselves in cycles during the night, and a period of deep sleep (stage 3-4) is always followed by a period of rapid eye movements characterizing REM sleep. However, the use of PSG is rather time-consuming and difficult to apply in a field study where the research subjects perform clinical work with patients. There is an alternative method called actigraphy, which is suitable for field studies. The actigraph is a small wrist-worn device that detects motion of the wrist. Actigraphic data have shown to be a good proxy for sleep duration measured by EEG. This method is frequently used both in clinical and occupational field studies (Sadeh and Acebo 2002; Morgenthaler et al. 2007). Sleep may also be assessed with subjective ratings. Of course, the results of these questionnaires depend on a good compliance and the occurrence of method bias is always a potential problem in behavioral research (Podsakoff et al. 2003). However, results of daily subjective scores of sleepiness, fatigue and recovery in the Karolinska sleepiness Scale (KSS) and Karolinska Sleep diary (KSD) have shown good correlation with objective EEG sleep measures and may thereby provide relevant information about sleep quality (Åkerstedt and Gillberg 1990b; Åkerstedt et al. 1994a; Åkerstedt et al. 1994b; Kecklund and Åkerstedt 1997).

For most people, 7-8 hours of sleep is sufficient for restitution. The working population generally has a shorter sleep duration during the working week and a longer sleep duration during weekends. According to recent reviews, sleep duration and mortality seem to be related to each other in a U-shaped fashion. From the lowest risk at 7-8 hours of sleep, there is an increasing risk both with shorter and longer sleep duration. The exact mechanisms may be complex and have not been fully elucidated (Grandner and Patel 2009; Cappuccio et al. 2010b). However, there are clearly individual differences, both in the amount of sleep needed to maintain alertness and in sensitivity to sleep loss (Balkin et al. 2008). Stress is considered to be a main cause of sleep disturbances (Åkerstedt 2006). The physiological systems of sleep function well in most cases, but it is physiological arousal due to stress, that prevents sleep. Indeed, anticipated stress and strain the following day, which are manifested by rumination and cognitive arousal, are considered an important cause of insomnia. Physiological activation at bedtime disrupts sleep. However, high stress indicated by high workload during the day may not necessarily be negative for sleep. It has been suggested that a high workload increases the need for sleep, which may cause shorter sleep latency and a more consolidated sleep (Åkerstedt 2006; Bonnet and Arand 2010).

There is evidence for detrimental metabolic effects caused by sleep reduction, above all an increased risk for a metabolic syndrome, and specifically for diabetes and obesity (Knutson et al. 2007). In a recent review and meta-analysis of the relation between disrupted sleep and diabetes, it was demonstrated that both quantity and quality of sleep can predict the risk for type 2 diabetes (Cappuccio et al. 2010a). Reduced sleep also implies an increased risk for cardiovascular disease (Åkerstedt 2006; Chandola et al. 2010) and has an adverse impact on the immune system (Vgontzas et al. 2005).

The effects of shift work on sleep are well known today and sleep disturbances are common (Sallinen an Kecklund 2010, Åkerstedt 2003). Shift workers usually have a day-sleep period of 2-4 hours directly after a full night shift, and the following night's sleep may be extended by 1-2 hours (Lowden 1998). Naturally, impaired or shortened sleep has detrimental effects on cognitive function and alertness, which implies increased risks for occupational accidents during night shifts in industry and transport (Philip and Åkerstedt 2006; Sallinen and Kecklund 2010). Impairment of neurobehavioral functions after acute and severe sleep loss is well known and uncontroversial. However, also partial sleep reduction affects both subjective well-being and cognitive performance, which has been demonstrated in a clinical experiment in which night sleep was restricted to 6 hours for a period of two weeks (Van Dongen et al. 2003). Fortunately, during sleep recovery following substantial sleep loss, there is more “efficient” sleep characterized by a temporary increase in deep sleep, which is why there is no need for full compensation in time. It is well known that both a daytime nap and/or recovery sleep the following night after a substantial sleep loss have beneficial effects on sleepiness and performance (Vgontzas et al. 2007; Faraut et al. 2011). Positive effects on alertness and performance have been observed after a normal night’s sleep, after night sleep restriction and following prolonged night-shift work (Gillberg et al. 1996; Dhand and Sohal 2006). Additionally, the timing and duration of the nap may influence the benefits of the nap (Milner and Cote 2009).

Shift work and disease

Shift work in a broad sense includes all working schedules that imply work outside conventional daytime (Bøggild and Knutsson 1999). However, concerning potential health effects, one usually refers to research on rotating shift work with night shifts or permanent night shifts. There are well-known short-term adverse effects of shift work, such as lowered performance, accentuated fatigue, sleep disorders and occupational accidents. Additionally, in the long-term perspective, there are increased risks of gastrointestinal (Knutsson and Boggild 2010) and cardiovascular disease (Knutsson et al. 1986; Knutsson 2003; Härmä 2006). It has been shown that there is an increased risk by 30-40% for coronary heart disease (CHD) based on several well-designed studies of shift workers, even when traditional risk factors are controlled for, although there is still limited evidence for causality according to recent reviews (Frost et al. 2009; Puttonen et al. 2010). Shift work is also associated with an increased risk for metabolic syndrome and type 2 diabetes (Karlsson et al. 2001; Karlsson et al. 2003; Pietroiusti et al. 2010; Puttonen et al. 2010). Night-shift work implies an increased risk for breast cancer, but it seems that an exposure of at least 20 years is needed to be at risk. Still, there is limited evidence for a causal association (Kolstad 2008).

Stress physiology and allostatic load

The present thesis mainly focus on the stress response in the sense of different aspects of physiologic stress recovery after demanding work in shifts and at odd hours, which is why the general physiological systems of stress are described below.

There are two major physiological systems involved in the stress response. The first is the hypothalamic-pituitary-adrenocortical (HPA) axis and its end effector cortisol, which is released from the adrenal gland. The second is the autonomic nervous system (ANS) and its end effectors nor-epinephrine and epinephrine. The ANS consists of two branches: the sympathetic branch, which is the most active during acute stress and stimulates energy expenditure, and the parasympathetic branch, which dominates during rest and stimulates anabolism. These systems are fundamental to survival, and they communicate with each other for optimal adaptation to day/night activity and stress. However, dysregulation in either of the systems can elicit serious adverse effects (Nader et al. 2010). Indeed, the prime actors in the acute stress response are the HPA axis and the ANS, but it also involves several other metabolic factors, the cardiovascular system and the immune system.

The acute stress response

When a person is confronted with a stressor, the ANS reacts immediately through suppression of the parasympathetic branch, followed by activation of the sympathetic branch, which elicits the release of epinephrine in the blood. After a few minutes, the HPA-axis is also activated and the adrenal gland release cortisol to mobilize energy supplies to sustain the stress response, which implies increased levels of glucose and free fatty acids.

Allostasis

The concept “allostasis” was introduced by Sterling and Eyer to describe the physiological reactions to stress by maintaining homeostasis through change (Sterling and Eyer 1988). Regulation of these reactions ensues that the individual is well adapted to the environment through changes in the physiological systems of stress, which tolerate considerable variation, in contrast to the homeostatic systems (e.g. temperature control and oxygen saturation), which tolerate very small changes (Chrousos and Gold 1992). McEwen introduced the term “allostatic load” to describe “the wear and tear” on the body caused by these reactions (McEwen 1998). Allostasis is essential to homeostasis, which in turn is necessary for survival. Nevertheless, when the allostatic systems are too frequently activated, fail to shut off after stressful events or do not respond adequately, the result is an allostatic load, which may be harmful in the long run.

Physiological aspects of stress, sleep reduction and shift work

Metabolic balance

Cortisol

Cortisol is a steroid hormone that functions as the end effector of the HPA axis. It influences the function of nearly all organs and is essential to homeostasis of the CNS, the cardiovascular system, intermediary metabolism and the immune system. Cortisol is a prime actor in the metabolic balance through energy mobilization that involves stimulation of gluconeogenesis and release of free fatty acids. The fact that it is easy to measure using saliva samples makes it ideal for repeated measures in field studies.

Cortisol levels fluctuate according to a 24-hour circadian rhythm. The nadir (lowest point) usually occurs shortly after midnight, and is followed by a steady rise during the night, reaching its peak in the morning hours, to fall again during the day. Strenuous physical activity and food intake cause a temporary increase in cortisol levels (Garde et al. 2009). Sleep onset is associated with inhibition of cortisol secretion, while morning awakening further increases the already high morning cortisol levels (Broussard and Brady 2010). One important measure is the normal decline over the day, which mirrors the capacity for unwinding in the evening. Chronically stressed individuals have shown a blunting of the evening decrease in cortisol. Persistent stimulation of the HPA axis will shift the intermediary metabolism towards catabolism and fat accumulation. Elevated glucocorticoids stimulate gluconeogenesis, glycogenolysis, lipolysis and degradation of proteins to amino acids, which may in due time lead to obesity, insulin resistance, diabetes and dyslipidemia (high triglycerides and low HDL-cholesterol) (Nader et al. 2010). These effects can also be observed in patients with Cushing's syndrome. Moreover, subjective reports of short sleep duration are reported to be associated with increased evening cortisol levels (Broussard and Brady 2010).

Another frequently used measure is the so-called "awakening response" (Pruessner et al. 1997), which is the fast increase in cortisol during 30 min after awakening in the morning. This measure has been closely related to stress and psychosocial health in several studies (Clow 2004). Cortisol measures have shown positive correlations in studies of sleep reduction (Geurts and Sonnentag 2006), as well as in studies of self-reported work stress (Kudielka et al. 2007). However in many cases the findings have been rather complex and sometimes contradictory, which is why the usability of cortisol measures in occupational settings has been questioned during recent years. Different methodologies as well as the influence of confounders and effect modifiers may have an impact (Hansen et al. 2008). However, rather heavy stress exposure is probably needed to evoke measurable effects. Such exposure is easily achieved during experimental conditions, for example using the Trier Social Stress Test (Kudielka et al. 2004; Jönsson et al. 2010). In contrast, during field studies in regular workplaces these stress levels may not be easily evoked (Hjortskov et al. 2004a).

Glucose, blood lipids and insulin sensitivity

The previously mentioned increased risk for diabetes in shift workers is in accordance with the hyperglycaemia and insulin resistance after sleep reduction found by Spiegel et al. in their classic experimental study on healthy young males (Spiegel et al. 1999). Dyslipidemia, too, with a raised level of triglycerides (TG) and lowered HDL-cholesterol, has been observed in several studies of shift workers (Karlsson et al. 2001; Karlsson et al. 2003; Sookoian et al. 2007; Puttonen et al. 2010). This was also the case in a study of nurses with high stress levels (von Thiele et al. 2006). Reduced sleep seems not only to be associated with diabetes, but also with obesity. Recent studies indicate that the adipocyte in fat tissue is a direct target for sleep disruptions. The exact mechanisms have not been established, but a coordinated activation of the sympathetic nervous system and the HPA axis combined with a dysregulation on the cellular level is plausible (Broussard and Brady 2010). Thus, sleep appears to play a critical role in the modulation of energy metabolism in peripheral tissues.

Testosterone

Testosterone is an anabolic hormone for both sexes. During sleep there is a substantial increase in the secretion of testosterone. Plasma levels of testosterone have been shown to decrease in response to insufficient sleep and shift work (Axelsson et al. 2003; Axelsson et al. 2005). In a study of construction workers with an extended work week (12 hours/7 days), there was a significant decrease in testosterone between workday 5 and 7 (Persson et al. 2006). Additionally, data from a longitudinal study of working men showed increased levels of testosterone when strain due to work diminished (Theorell et al. 1990).

Growth hormone (GH)

GH is the prime anabolic hormone and is essential for promoting somatic growth. In adults it also has a homeostatic role (Gan and Quinton 2010). Indeed, GH has been shown to decrease in response to insufficient sleep (Weibel et al. 1997), but the pulsatile excretion, with the highest levels during deep sleep, makes it impossible to use in a field study, where only a few samples are taken. However, many of the physiological effects of GH are mediated through insulin-like growth factor 1 (IGF-1), which is easier to monitor and is secreted by the liver. The mean

GH level is highly correlated with serum IGF-1 concentration, which therefore may be used as a marker of GH activity.

Thyroid stimulating hormone (TSH)

TSH is an important catalyst for all metabolic processes in the body. It is secreted from the pineal gland, regulated by the hypothalamus and stimulates the release of thyroxin (T4) and triiodo-thyronine (T3) from the thyroid gland. Circulating T4 and T3 exert a negative feedback on the activity on this pathway. Sleep inhibits overnight TSH secretion. Acute sleep deprivation causes an increased plasma level of TSH, T3 and T4. In contrast, an extended sleep debt seems to decrease TSH levels (Goichot et al. 1998; Spiegel et al. 1999; Kessler et al. 2010). In an experimental study of a 3-hour sleep reduction over a period of two weeks, there was a significant, but modest, decline in TSH and free T4, mainly in the female participants (Kessler et al. 2010).

Heart rate variability

For several hundred years, clinicians have perceived the importance of heart rhythms in health and disease, but it was not until 1963, that the clinical value of studying subtle variations in heart rate (heart rate variability, HRV) became obvious. At that time, Hon and Lee could demonstrate that foetal distress was preceded by changes in HRV, which were not detectable in the heart rate itself (Hon and Lee 1963). An important application in adult medicine became apparent during the mid 1980s, when HRV was shown to be a strong and independent predictor of post-infarction mortality (Bigger et al. 1993). Later, with the advent of modern digital processing of 24–hour multi-channel electrocardiography (ECG), the full potential of HRV has become clear both to clinicians and to researchers.

Heart rate is controlled by the cardiac sinoatrial (SA) node. This rate is then modulated by the sympathetic and parasympathetic division of the ANS. These modulations result in the small variations in heart rate that constitute the HRV.

It is generally accepted that the parasympathetic modulations of heart rate are mainly due to respiratory sinus arrhythmia, which implies that the heart rate accelerates during inspiration and slows down during expiration. These modulations have a faster course than the alterations mediated by sympathetic activity. Because these two systems operate at different frequencies their actions can be identified by different frequency spectra. These spectra can be studied using spectral analysis. When analysing HRV data in the so-called frequency domain, the periodic, interpretable components of the ECG signal can be distinguished and quantified.

The fine-tuned balance between the sympathetic and parasympathetic impact on the heart is essential for survival (TaskForce 1996; Pumprla et al. 2002; Kara et al.

2003). A generally high level of HRV is advantageous from a health perspective, and especially a large fraction of high frequency (HF) power, which is related to parasympathetic action. The sympathetic activation during acute stress is related to low frequency (LF) power, but this measure also comprises some parasympathetic modulations. Therefore, the most clear-cut effect of acute stress on HRV is usually a lowered impact of HF power. Additionally, deficient recovery (inability to unwind) at the end of the day may be detected as a slower return to parasympathetic domination of HRV after work (Hanson et al. 2001).

Indeed, HRV offers a powerful tool to study psychological and physiological processes through ANS fluctuations. However, there are several methodological caveats. For instance, abundant artefacts, abnormal beats and strenuous physical activity may seriously disturb analysis and interpretation of the ECG-curve (TaskForce 1996; Berntson et al. 1997). It has to be mentioned that both mental and physical stress affect the autonomic balance, moving it towards sympathetic dominance. Moreover, diurnal variations in HRV with a higher impact of sympathetic tone during daytime and a nocturnal peak of parasympathetic tone have to be accounted for (Bonnemeier et al. 2003). Apart from large inter-individual differences in HRV, there also seems to be an impact of age and gender. Total HRV is suggested to have a slow linear decline with age and females are reported to have a higher HF, but the difference seem to even out after the middle age (Kuo et al. 1999; Britton and Hemingway 2004). Unfortunately there is no general agreement on normative data for short-term HRV. A recent review including 44 studies revealed conflicting results, probably owing to several methodological factors (Nunan et al. 2010).

Psychological stress experiments (Delaney and Brodie 2000; Schnall 2000; Hall et al. 2004; Hjortskov et al. 2004b) and field studies measuring perception of work stressors (Clays et al. 2011) and job strain at work (Collins et al. 2005) have shown a decreased parasympathetic influence on HRV. Studies of classical rotating shift work and of physicians on night call revealed findings of changed autonomic balance using HRV analyses (Adams et al. 1998; van Amelsvoort et al. 2001). Lowered HRV has been related to ischemic heart disease (IHD) and is known to be a strong and independent predictor of mortality after myocardial infarction (Bigger et al. 1993). There also seems to be a growing body of evidence specifically for the role of decreased vagal function in cardiovascular disease and mortality (Thayer and Lane 2007). Therefore, cardiac autonomic dysfunction has been proposed as a potential link between stress and heart disease (Eller et al. 2006; Frost et al. 2009; Puttonen et al. 2010).

Recovery from night-call duty - incentives for the thesis

Recovery is suggested to be the vital link between acute physiological stress reactions and long-term health effects (Geurts and Sonnentag 2006). Recovery after work (external recovery) is especially important, when there is limited opportunities for recovery at work (internal recovery), which is the case during night-call duty. Insufficient sleep is clearly related to recovery, and may be the most important pathway from long work hours and work stress to chronic disease (Åkerstedt 2006; Härmä 2006). Night call implies long stressful work hours with high demands, reduced sleep and an activity period that is in conflict with our natural diurnal rhythms. This may lead to a sustained activation with an incomplete recovery and potentially, long-term health effects according to the “allostatic load theory” (McEwen 1998).

The main theme for the present thesis was to disclose whether the participants had levels of physiological activation post night-call comparable to ordinary daytime work, and in some cases also compared to a weekend day off duty. Equally important was to ascertain whether there were divergent recovery patterns between specialities. Still, there is no firm knowledge about which levels of physiological changes that are sufficiently large to constitute a raised risk for long-term health effects. Therefore the general dynamics in physiological changes during and after work on night call were in focus, rather than the detection of specific levels of changes. By monitoring several physiological systems with repeated measures on daytime work, night-call duty and during recovery post-call, in combination with subjective rating and questionnaires, the intention was to get a comprehensive picture of the questions at issue. The measures used in the present studies were chosen to reflect potential physiological effects of insufficient sleep, shift work and stress.

Concerning the metabolic factors, it was generally expected to find levels in the direction of a metabolic syndrome post-call, if the recovery was not sufficient. More specifically for the HPA axis, deficient unwinding in the evening, measured by cortisol after a post-call recovery period, would be considered insufficient. Further, a generally more catabolic state post-call with raised blood glucose, lowered insulin levels, and dyslipidemia post-call would signal deficient recovery as well as lowered testosterone and a reduced impact of GH as signs of deficient anabolism. However, for TSH, the direction of change was difficult to anticipate. Both a significantly raised or lowered level would be considered deficient. The lowest level of parasympathetic influence measured by HRV was expected during night-call duty, because of the stressful work on call. In contrast, a lowered relative parasympathetic tone on post night-call duty would be considered deficient recovery. It was predicted that sleep duration and quality of sleep would be negatively affected in all physicians during night call and that there would be a few hours of extra sleep post-call for a sufficient recovery. A majority of the participants had 1-2 days off duty after their night on-call, why it was a main interest to investigate if this period of time was sufficient for recovery. According to the literature, the time needed for full recovery after night shift is most often reported to be 1-3 days, depending on the work type and schedule (Totterdell et al. 1995; Åkerstedt et al. 2000). Thus, in the present study, the main question was whether full recovery would be completed within 1-3 days post-call.

Concerning differences between specialist groups, it was expected that the anaesthesiologists would generally show less sufficient recovery post-call compared with other physician specialists who had the same length and frequency of night-call duties each month, but who had less focus on life-threatening conditions when on night call. The participating clinics agreed that if the results of these studies indicated insufficient recovery, the work schedules would be adjusted.

Aims

General aim

The general aim was to determine whether working schedules with 16-hour night-call duty were compatible with sufficient physiological recovery within 1-3 days post-call.

Specific aims

The specific aims were to investigate:

- Whether there was a blunting of the normal evening decrease in cortisol post-call, which is characteristic of deficient unwinding.
- Whether there was a more catabolic state post-call, with raised blood glucose and TG, and lowered levels of insulin and HDL-cholesterol.
- Whether testosterone and the impact of GH were reduced post-call as signs of deficient anabolism.
- Whether TSH and/or T4 levels were changed post-call, indicating effects on the metabolic rate.
- Whether there were signs of an autonomic imbalance post-call owing to a lowered parasympathetic impact on HRV.
- Whether there was deficient sleep recovery post-call.
- Whether there were divergent patterns of physiological recovery post-call between anaesthesiologists and other physician specialists handling less life-threatening conditions when on call.

Methods

Participants and working conditions

Participants

Two groups of physicians were enrolled. The first group consisted of anaesthesiologists (ANEST; n=19). The second group consisted of paediatricians and ear, nose, and throat (ENT) surgeons (PENT; n=18). These two groups had different work characteristics when on call (see below). Originally, only paediatricians were planned to constitute the control group; during recruiting, however, fewer physicians were available in clinical work than expected, thus we chose to augment the control group by including ENT surgeons. The physicians in both groups worked at Lund University Hospital in Sweden and had recurrent night-call duties. All physicians holding the above-mentioned positions were asked to participate. The participation rate was 19/24 (79%) in the ANEST group and 18/25 (72%) in the PENT group. The most common reason for external drop-outs was that the subject did not participate in night-call duty during the study period. Internal drop-outs were mainly due to technical errors or failure to find a suitable monitoring period in the subject's schedule. For further details, see **Paper I-III.**

Descriptive data from a baseline inventory showed that both participating physician groups reported equally good mental health and did not differ from a corresponding socioeconomic group in the general local population in terms of their results on the *General Health Questionnaire (GHQ)* and *Symptom Check List (SCL-35)*, which are further described under the subheading Measures. None of the participants reported diabetes, cardiovascular disease, insomnia or neurological disease. However, one participant had sleep apnoea syndrome. None of the participants reported medication that could affect the monitored measures. In addition, the family situation was almost identical in the two groups of physicians, and alcohol consumption was low to moderate. A health check using blood screening for thyroid and liver function, serum insulin, plasma glucose, blood lipids, plasma haemoglobin, leukocytes and C-reactive protein (CRP) was performed. Except for two cases of mild hypothyroidism, all tests were normal. In Table 1 the number of participants in each study and the basic descriptive data are presented. For more detailed descriptions, see each paper separately.

Table 1. Descriptive data for participants in Paper I-III

	Paper I *		Paper II		Paper III	
	ANEST	PENT	ANEST	PENT	ANEST	PENT
Subjects invited	24	25	24	25	24	25
Subjects participating	19	18	19	17	19	17
Subjects analysed	18	17	19	16	15	17
Age	42	39	42	40	43	37
[median (range)]	(32-55)	(26-45)	(32-55)	(26-45)	(37-55)	(26-45)
Women (%)	7 (39)	10 (59)	7 (37)	8 (50)	6 (40)	8 (47)
Smokers (%)	1 (5)	0	1 (5)	0	0	0

* Data for Paper I refer to participants in blood sampling. For cortisol saliva sampling, 18 subjects participated and 17 were analysed in the ANEST group and in the PENT group the corresponding figures were 15 and 14 respectively.

Working conditions

The two groups, ANEST and PENT, were chosen as participants because the general characteristics of their working conditions, when on night call, implied a clear between-group exposure difference with regard to activity levels and mental demands. All participants had strictly hospital-bound work on call. During night-call duty, the ANEST group took care of patients' vital functions in major traumas, cardiac arrest, and acute operations. They were also in charge of post-operative ward and the intensive care unit, handling patients with vital organ failure. All participating physicians could expect to have a high workload on call, but the ANEST group also had to focus generally on life-threatening conditions. Furthermore, they differed from the PENT group in that they provided service to the whole hospital and facilitated the work of several other physicians caring for severely ill patients (Larsson et al. 2003). In contrast, the PENT group worked on the emergency ward taking care of acute cases in their speciality, but they did not have the kind of service and facilitation duties required of the ANEST group.

The specific information on working conditions was collected through interviews with the specialists and by scrutinizing all working schedules. For all physicians, ordinary daytime work was performed from 08:00 to 16:30. Night-call duty started at approximately 16:00 and lasted for about 16 hours (until around 08:00 the next day). All participants had on average three night-call duties per month and at least one day off after each night call, but work schedules differed somewhat between specialities. The ANEST group and paediatricians in the PENT group had separate night-call weeks approximately every fourth to sixth week, during which they worked 2-3 nights. Then they had 1-2 days off after the last call. Moreover, there was often one additional night-call separate from the night-call week in each cycle. If the physician had 3 night calls in one week, then he/she had the other days off duty. In contrast, if the physician only had 2 nights on call, it was usually combined with 1-2 days of ordinary daytime work in the same week. In the PENT group, the ENT surgeons had single nights on call every second or third week, and in contrast to the two other specialities, they generally had a normal working day directly before night call, but always 1-2 days off post-call. Breaks during on-call duty were allowed for meals, rest, or even sleep if there were no patients in need of attention; on-duty rooms were always available.

Measures

Baseline questionnaire

This inventory contained questions for descriptive data as gender, age, family situation, work position, experience of night-call duty, and personal health data. The participants filled in the baseline questionnaire at the start of studies and data were used as descriptive data. For details, see **Paper I-III**. In addition, the *General Health Questionnaire-12 (GHQ-12)* comprising 12 items to assess recent deterioration in mental health was also used (Goldberg and Williams 1988) as well as the *Symptom Checklist-35 (SCL-35)* as an inventory of current mental distress (Derogatis 1992). These two measures were included as descriptives, exclusively in the thesis. The baseline questionnaire also contained the *Karolinska Sleep Questionnaire (KSQ)*, which was used to assess participants' habitual quality of sleep (Akerstedt et al. 2002b) as background data for **Paper III**. This questionnaire comprises 15 items measured on a 5-point scale. Three indices were calculated from 12 of the 15 items: "disturbed sleep", "sleepiness index," and "awakening index," with 5 as the most favourable score.

Logbook

During the entire study period, the participants kept a separate logbook for daily notes on bedtime, rising time, and special circumstances or events of significance for monitoring results. The latter could be an emergency alarm during work on call, physical training, or removal of the monitoring devices while working in aseptic conditions or taking a shower. This information was mainly used when analysing the sleep data in **Paper III**, but was also used as background information in **Paper I and II**.

Daily subjective ratings

Subjective ratings were used in **Paper III** as measures of fatigue, sleepiness and recovery.

Karolinska Sleepiness Scale (KSS) was used to assess current sleepiness. This scale has been used in many studies and has been validated against EEG parameters (Akerstedt and Gillberg 1990b). It consists of a 9-point scale with the following verbal anchors: 1 = very alert, 3 = alert, 5 = neither alert nor sleepy, 7 = sleepy, but with no difficulty staying awake and 9 = very sleepy, fighting against sleep, requiring great effort to stay awake. The intermediate values were also used, but had no labels.

Mental fatigue was assessed on a scale similar to the KSS with the following verbal anchors: 1 = very alert, 3 = alert or energetic, 5 = neither fatigued nor alert, 7 = fatigued but not strained, and 9 = very fatigued, exhausted and incapable of any mental strain. The intermediate values were also used, but had no labels. The mental fatigue scale has demonstrated higher levels of fatigue during workdays compared to weekends, a time-of-day profile (peaking in the evening), and elevated levels of fatigue in association with early morning shifts (Söderstrom et al. 2001; Söderström et al. 2006).

Karolinska Sleep Diary (KSD) was used to assess daily variations in the subjective aspects of sleep and recovery as experienced in the morning (Åkerstedt et al. 1994b). This questionnaire has been validated against polysomnography and shows a good correlation with objective EEG sleep measures (e.g. amount of slow-wave sleep and sleep efficiency) (Åkerstedt et al. 1994a; Åkerstedt et al. 1994b; Kecklund and Åkerstedt 1997). The questionnaire consists of several items concerning the previous night's sleep and aspects of sleep recovery. All variables are scored from 1 to 5, where 5 is the most positive. A Sleep Quality Index (SQI) was constructed from the mean scores on the questions regarding "restless sleep", "ease of falling asleep," "sleep quality," and "sleep through the night." The SQI ranged from 1 (low quality) to 5 (high quality). The questions on "sufficient sleep," "ease of awakening," and "feeling well rested," reflecting aspects of sleep and recovery, were studied as single items. The single item "feeling well rested" has been reported to correlate to high work demands and to shift work with night shifts (Åkerstedt et al. 2002a).

The KSS and mental fatigue scores were completed at bedtime in the evening and KSD was completed in the morning soon after awakening. Sufficient recovery, in subjective terms, was defined in **Paper III** as the score on KSD for feeling well rested after a Saturday night's sleep.

Salivary cortisol

Salivary cortisol was sampled to study the effects on the HPA-axis of stress and potentially deficient recovery from night-call duty (**Paper I**). Repeated saliva samples were collected four times a day on each sampling day. All samples were collected in Sarstedt salivette® tubes (Sarstedt AG & Co., Nümbrecht, Germany) and analysed by use of liquid chromatography-electrospray tandem mass spectrometry (LC-MS-MS) (Jonsson et al. 2003). Sampling times were: (i) on awakening, (ii) +30 min, (iii) + 8h, and (iv) at approximately 21 h. Besides mean cortisol levels, the outcome variables included maximum morning levels (the highest value of sample 1 or 2), awakening response (the percentage increase between sample 1 and 2), and the decline over the day (the difference between the morning maximum sample and the sample obtained at 21:00).

Blood samples

To study potential metabolic changes during night call and recovery in **Paper I**, analyses were made for levels of glucose, TSH, T4, testosterone, HDL-cholesterol, low-density lipoprotein (LDL)-cholesterol and TG in plasma and insulin in serum. For detection of insulin resistance, the quantitative insulin sensitivity check index (QUICKI) was calculated from values of fasting insulin and glucose (Katz et al. 2000). IGF-1 was also measured in plasma. This measure was used as a marker of GH activity, because GH itself was difficult to use in a field study due to its pulsatile excretion. The blood samples were analysed consecutively at the clinical chemistry laboratories at the university hospitals in Lund and Malmö. All analyses except for IGF-1 [coefficient of variation (CV) = 16%] were accredited with a precision (CV) $\leq$ 10% for the hormone analyses and $\leq$ 6% for the remaining analyses.

Heart Rate Variability

ECG data were used in **Paper II** as markers of activity and balance in the ANS input to the heart. ECG monitoring and calculation of primary and secondary HRV variables were carried out in a standardized manner (TaskForce 1996) using a digital, portable monitoring unit for 2-channel Holter ECG (DXP 1000; Braemar systems, Chicago, IL, USA) and Aspect software (Danica Biomedical AB, Borlänge, Sweden) (Nygårds and Hulting 1979). After computerized primary analysis, all ECG files were edited manually for detection of artefacts and categorization of non-sinus beats by a trained biomedical analyst. HRV power spectra were calculated using fast Fourier transformation (FFT) and expressed as power spectral density in ms^2. The primarily computed variables were: high frequency (HF) (0.15–0.4 Hz), low frequency (LF) (0.04–0.15 Hz), very low frequency (VLF) (< 0.04 Hz) and total power (TP), i.e., the sum of all frequency components.

HF mirrors the parasympathetic modulation of HR, while LF mirrors the sympathetic modulation, and some parasympathetic modulations (TaskForce 1996). Total power has no specific physiological correlate, but mirrors total variability. Very low frequency (VLF) is suggested to reflect slow thermoregulation in the body. According to recommendations (TaskForce 1996) VLF was subtracted from the TP in the indices below. In addition, two HRV indices were calculated as follows: HF in normalized units (%), calculated as HFnu (%) = (HF/(TP-VLF)) x 100 and reflecting relative parasympathetic influences, and LF/HF, often referred to as "sympathovagal balance", with values fairly reciprocal to HFnu. Mean HR was also calculated.

In the present study, the specific time period, the so-called "strategic time window" (TaskForce 1996; Schnall 2000) for frequency domain analysis was chosen to reflect the degree of "unwinding" at the end of the day, but was not to interfere with sleeping time. *Analyses were therefore performed during one hour in the evening (21:00–22:00) for each monitoring period.*

Actigraphy

For sleep monitoring in **Paper III**, a wrist-worn accelerometer, actigraph, was used (Actiwatch (AW), Cambridge Neurotechnology Ltd, UK) (Sadeh and Acebo 2002). This device measures wrist activity, which is a good proxy for EEG-registered sleep (Lockley et al. 1999; Reid and Dawson 1999). According to recent reviews, actigraphy has also been shown to provide acceptably accurate sleep estimates in studies of jet lag and shift-work sleep disorders (Morgenthaler et al. 2007).

For each participant the watch was calibrated and set to personal computer (PC) time. An epoch length of 0.5 minutes and a medium sensitivity were chosen. The watch had to be removed when taking a shower, during strenuous physical training and during work in aseptic conditions. This was noted in the logbook as were bedtime and rising time. To define the start and endpoints for night sleep, we used the AW sleep-wake registrations as primary information. However, notes in logbooks about sleep times, special circumstances and AW removal periods were also used as complimentary data to define the most accurate start and end points for sleep analysis. The Actiwatch Sleep Analysis Program (version 5.48) was used for data scoring and calculations of total sleep time and sleep efficiency (% of time in bed actually spent sleeping).

Table 2. Overview of measures in Paper I-III

	Baseline question-naire	Logbook	Subjective ratings	Actigraphy	Blood samples	Salivary cortisol	HRV
Paper I	X	X			X	X	
Paper II	X	X					X
Paper III	X	X	X	X			

Study design and procedures

General description

All three studies were performed simultaneously (during a period of approximately three months from the end of February to May in 2002) and on the same groups of physicians. They were all field studies of authentic work and spare time and had a repeated measures design. Comparisons within subjects and between groups through measures of different physiologic systems as well as subjective ratings were used to reflect the strain during and recovery after work on night call. Fig 1 (Study design) provides an overview of the design and methods used for repeated measures in **Paper I-III.**

The starting-point for all three studies was that the participants filled in the baseline questionnaire. During the next step, an individual schedule was made, where the ECG-monitoring, blood and saliva samples were coordinated with a specific night–duty period for each participant. The monitoring days were distributed rather evenly during the whole study period. Only in a few occasions there were more than one physician monitored simultaneously during night-call duty.

At the individual start of AW monitoring and daily subjective ratings/logbook, the AW and the participant's private watch were set at PC time. Specific instructions for the monitoring period were also given by the research leader (specialist physician). During the whole individual study period (10-22 days), the participants made daily subjective ratings (KSS, KSD, mental fatigue), filled in the logbook and wore the AW.

Requirements for several sub-studies and the specific personal night-call schedules dictated the total length of the monitoring period for each participant. It should be pointed out that strategic time windows for analysis of sleep using AW and HRV using ECG were chosen at the beginning of the study. If the participant had several night calls in the same week, the last one was chosen for monitoring, to ensure that there was no additional night-call during the recovery period. Each ECG monitoring was started by the research leader or specially trained medical staff. The blood samples were taken at the hospital laboratory, and the saliva samples were collected by the participants themselves according to specific instructions.

To compensate for the possible effect of habituation to the sampling procedures, the days used for analyses were selected in a counter-balanced design. Accordingly, the first occasion of sampling/analysis was equally distributed between ordinary work days, days related to night-call duty and in **Paper III** also Saturdays. The specific time points for data collection and analysis varied somewhat across studies and are described in flowcharts for **Paper I-III** (Figure 2-4).

Specific procedures of Paper I-III

Paper I:

Blood samples were collected fasting in the morning on an ordinary workday, and after one and three days post-call. Salivary cortisol was collected on an ordinary workday, during the day preceding night call and after three days post-call. For the ANEST group, cortisol samples were also collected on a separate day off duty.

Paper II:

Holter electrocardiography (ECG) was carried out on three occasions: (i) from one ordinary workday to the next (16:00–16:00); (ii) during night-call duty (16:00–08:00); and (iii) continuously during the following post-call period (08:00–08:00). Then HRV analyses were performed in time windows based on ECG data collected on a night after daytime work, during night call and the first post-call night. The analyses were performed for means of six consecutive 10-minute periods during one hour in the evening (21:00–22:00).

Paper III:

For practical reasons, sleep monitoring using AW was performed during the whole study period for each participant. The AW data were analysed on a night after daytime work, during night call, on the first and second nights post-call, and on a Saturday night. A separate analysis of daytime naps was also performed on the first post-call day using the same method as described for night sleep. KSS, KSD and mental fatigue were analysed in the mornings and evenings concomitant with all the AW-analyses of sleep, except for naps.

Statistics

In all three papers, the statistical computations were made using the Statistical Package for the Social Sciences (SPSS) 15.0 (version 12.0 in **Paper I**) and P-values <0.05 were considered statistically significant. A repeated measures model was specified using the linear mixed models module of SPSS. This method made it possible to compensate for missing data and to adjust for covariates. The choice of model was governed by Schwarz's Bayesian Information Criterion (BIC) and the covariance structures that showed the best fit for each measure. Categorical predictors were sampling day and group, and dependent variables were all blood and cortisol data, as well as HRV measures, sleep measures using actigraphy and subjective ratings in KSS, KSD, and mental fatigue. The repeated cortisol sampling during each monitoring day also included time of day as a categorical predictor, when appropriate. The selection of covariates included age, gender, weight and body mass index (BMI), with some variation across studies.

Cortisol data in **Paper I** and HRV data in **Paper II** had a positively skewed distribution and were therefore logarithmically transformed (log 10) before being subject to analysis. However, for the cortisol indices, a restriction of ± 3 SD was applied, as it was observed that exclusion of a few extreme outliers generated a normal distribution. In **Paper III** a univariate analysis using the General Linear Module was applied to test for KSQ group differences and comparisons of day sleep and no day sleep post-call (cross sectional data). Also in **Paper III**, the use of parametric methods on ordinal data or data with skewed distributions implied a risk for biased results. Therefore, the outcomes of AW, KSS and KSD measures were also checked using nonparametric methods (which do not rely on assumptions). However, these analyses gave largely the same results as the mixed models. In **Paper II** there were several missing files. To examine whether the results were dependent on subjects with incomplete sets of data, a complementary analysis exclusively on the subjects with complete data sets (n=27) was made. This analysis generated similar results with only minor changes in estimates and p values.

Power- analysis was made by the G-power software (Faul et al. 2007). In **Paper I-III** the study design with repeated measures showed to be sufficiently powerful to find effects of approximately 0.5 SD with a power of 0.8. This was valid for interaction between day and group as well as for main effect of day for a total sample size of 30-35 participants including two groups and comparisons between 3-5 days. Power was also checked to be sufficient for the number of participants that remained after internal drop-outs and exclusions. However, the power analyses were not fully presented in each of **Papers I-III**.

Results

Metabolic factors

Saliva cortisol

Repeated sampling of cortisol during the day enabled us to study the separate values as well as the morning rise and the decline in the afternoon (**Paper I**). Except for a few extreme outliers, the diurnal curves were normal. As expected, the cortisol levels differed between sampling times during the day ($p<0.001$), with the highest levels in the morning. In contrast, there was no difference between days or groups in the general comparisons. Still, exclusively in the PENT group, the morning maximum cortisol level turned out to be 48% higher in the morning before night call duty compared with ordinary day-time work ($p<0.001$). In this context, it should be pointed out that the ENT surgeons who comprised about half of the subjects in the PENT group in most cases had to work during the day preceding night-call duty, which was not the case in the ANEST group (**Table 4, Paper I**).

In the monitoring schedules for the ANEST group, it was possible to fit in an additional sampling on a separate day off duty (≥4 days after the latest night call). Therefore we could make further comparisons between days exclusively in this group. The morning maximum level of cortisol turned out to be 35% lower on this day off duty compared with both daytime work ($p=0.005$) and three days post night-call ($p=0.001$).

Blood samples

There were no significant differences between groups or days for glucose, the QUICKI test (insulin sensitivity), HDL, LDL, TG, testosterone or IGF-1. Only for thyroid function there was a significant effect. In both the PENT and ANEST group, the TSH level was distinctly lowered one day post night-call (26-28 % less, $p<0.001$) compared with ordinary daytime work (**Table 2-3, Paper I**). However, the physician groups had different patterns during the late recovery phase: After three days post night-call, the TSH level for the PENT group had returned to the baseline level, but was not fully recovered in the ANEST group. The T4 level was 3% lower after three days post-call compared with the other days, $p=0.033$.

Heart Rate Variability

The ANS impact on the heart was studied by analysing HRV in **Paper II**.

In the whole group of physicians, the relative parasympathetic impact on the heart, measured by HFnu at 21-22 h was lower on night-call duty and night after daytime work compared with the night post-call ($p<0.001$ and $p= 0.002$). This means that one day of rest after night-call duty resulted in a more favourable autonomic balance than directly after daytime work and night call. Surprisingly there was no statistically significant difference between post-daytime work and night call for HFnu (**Table 3, Paper II**).

The lack of difference between days for HF (representing the purely quantitative marker of parasympathetic tone) was at first puzzling. However, there turned out to be an interaction between day and group for HF. A post-hoc evaluation showed that the two physician groups had roughly the opposite patterns of change between days, which explained the results (**Table 4, Paper II**). The most important result was that ANEST had a quantitatively lower parasympathetic impact on the night after daytime work and on night call compared with PENT, but the levels were not different between groups on post-call. Somewhat unexpectedly, the ANEST group turned out to have generally lower levels of both the absolute (HF) and relative (HFnu) parasympathetic tone and also total variability (TP), compared with the PENT group ($p<0.05$).

All the results of day and group comparisons for LF/HF were, as expected, reciprocal to those for HFnu, which is why they are not discussed further. To assure that data from the two physicians groups were comparable regarding heart rate (HR), it was also checked that the HR was fairly stable both between groups and days. An additional analysis was also carried out with HR as a covariate, and this did not turn out to affect the results at all.

Sleep and subjective ratings of fatigue and recovery

In Study III, the specific night sleep analyses (AW data) were used together with their concomitant subjective ratings of KSS, KSD and mental fatigue in mornings/evenings for evaluation of recovery from night call duty. Note that for formal reasons, the daytime nap on the first post-call day was presented separately from the sleep during the first post-call night, but they both contributed to the total recovery sleep during the first 24 hours post night-call (**Table 2, Paper III**).

The total night sleep differed significantly between days ($p<0.001$) (**Table 3, Paper III**). As expected, the shortest sleep was on night call, amounting only to a few hours. A somewhat longer sleep was recorded during the night after daytime work, but still unexpectedly short in comparison with both the two nights post-call and Saturday night. There was also a significant difference between the sleep efficiency on adjacent days, but the effects were rather small and therefore of limited importance (**Table 2-3, Paper III**). In the ANEST group, all participants but one took a substantial daytime nap during the first post-call day, but only 50% in the PENT group, which is why statistical comparisons were not meaningful. A common feature was that all participants who had slept less than 3 hours during night-call duty took a daytime nap. There was a clear-cut difference between days for the KSD score of feeling well rested (p=0.013). The lowest score, which, as expected, was in the morning after the first post-call night, reached on the second post-call night levels equal to that of the morning after Saturday night (i.e., Sunday morning), indicating the same level of recovery two days post night-call as on a Sunday morning. Similar patterns were seen in the reports of mental fatigue. There were no group differences or interactions between group and day for any of the AW measures or subjective ratings. One exception was that those who took a nap on the first post-call day had a shorter sleep on the following (first post-call) night (p=0.04). However, the difference disappeared when the day-sleep duration was accounted for.

It has to be mentioned that the AW analyses only measure sleep and non-sleep and do not contribute detailed information about sleep quality, such as sleep stages. However, notes in the participants' logbooks gave us the strong impression that the ANEST group had more frequent involuntary awakenings for patient consultations during the later part of the night call (after bedtime from about 02:00 onwards), and four of the anaesthesiologists did not get any sleep at all during the night on call.

Brief summary of the results

The results demonstrate significant changes in responses from some of the physiological systems in relation to work on night call and during recovery. However the majority of metabolic factors seemed to be unaffected.

There was a considerable dip in TSH one day post-call in both physician groups, with complete recovery 3 days post-call only for the PENT group, while the ANEST group had limited recovery.

Unexpectedly, the findings from salivary cortisol were rather limited, and there was no effect detected during the recovery period.

Measures of autonomic balance using HRV indicated a more favourable state on the first post-call night compared with the night after daytime work and during night call for the whole group of physicians, however the ANEST group generally had lower levels of HRV.

Obviously recovery sleep was obtained during the post-call period, and according to subjective ratings, the participants reported being well rested after two nights post-call.

Sleep during night call was strongly reduced. In addition, the mean sleep length after ordinary daytime work was surprisingly short. This should be taken into consideration when discussing recovery from work in a long-term perspective.

The participating physician groups turned out to have rather similar recovery patterns, but there was still a divergence between groups on some points.

General discussion

Night-call duty entails long and stressful working hours with high demands, reduced sleep and an activity period in conflict with the natural diurnal rhythms. Indeed, physicians' work on night-call duty may affect their wellbeing, performance and health, and adverse effects have been reported in several studies since the 1970s (Orton and Gruzelier 1989) and during recent years, especially among anaesthesiologists (Larsson et al. 2003).

The appropriate length of night calls has been a matter of discussion, with reference to occupational health aspects, performance and the risk for attention failures, especially among physician residents. Some clarifying studies have been presented by Landrigan (Landrigan et al. 2004) and Lockley (Lockley et al. 2004), who found that a reduction of residents' work shifts from 24 hours to 16 hours reduced their attention failures, increased their sleep and improved their quality of life. Recent reviews also confirm these results (Levine et al. 2010).

The working time directive (WTD) for the European countries set some rules and limits for long work hours, and night work, but a number of exceptions for night-call duty still make it possible to apply working-schedules that are not compatible with human physiology. Still, we do not know what the biological limits are for sustainable work on night call. In the present studies (**Paper I-III**) physiological recovery from a 16-hour night-call schedule was studied using repeated blood and saliva samples for analysis of metabolic factors, and repeated monitoring of HRV and sleep.

Metabolic factors

The lack of effects on cortisol post call may have several explanations (**Paper I**). There might have been a transient effect in the early recovery phase, which was not monitored, but the most important clinical question is whether there was a more long-standing effect during recovery. There was a higher maximum morning cortisol level in the morning preceding night-call duty for the PENT group. This may be due to the fact that the ENT surgeons, who comprised about half of the subjects in the PENT group, in most cases had to work during the day preceding night-call duty and therefore had a higher activation of the HPA axis in the morning. Another explanation could be that there was a larger share of residents with possibly higher expectations of strain in the PENT group, compared with the ANEST group. The lowered activation of the cortisol system on a day off duty for the ANEST group was expected and has been demonstrated in earlier studies (Schlotz et al. 2004). These two findings are of limited interest for the evaluation of recovery, but clearly demonstrate reactivity in the HPA-axis.

There are several potential methodological problems when concerns cortisol monitoring in field studies (Hansen et al. 2008). It is well known that lack of compliance to sampling times, especially at awakening may affect the results. However, in **Paper I**, there were exact notes on the awakenings time and it was also adjusted for in analyses. Strenous physical exercise may raise the cortisol values by 80% during one hour (Garde et al. 2009). However, during the days of cortisol sampling in **Paper I**, the participants did not report any physical exercise. During recent years it has been reported that probably a rather heavy stress exposure in occupational settings is needed to evoke measurable effects in cortisol (Hjortskov et al. 2004a). The most probable explanation, for the lack of effects on cortisol, is therefore that the actual work on night call did not result in any serious long-standing disturbances in the HPA-axis.

The lowered TSH-levels in the early recovery phase post call might be due to an influence of stress or sleep reduction on the hypothalamic level (Goichot et al. 1998; Scanlon 2001) (**Paper I**). However, the lack of a substantial reciprocal change in T4 may speak against a clinically significant effect on metabolic rate. The ANEST group had a limited reversibility of TSH levels 3 days post call compared with the PENT group. This might be due to a more extended effect of night-call duty for the ANEST group. Still, there are a limited number of scientific reports on stress and hyperthyroidism and only one study of subclinical hypothyroidism in shift workers, suggesting a possible association between stress/shift work and thyroid disease, but no firm causality has been shown (Magrini et al. 2006). In the present study, an effect of multiple inference cannot be completely ruled out. However, the TSH findings were plausible from a biological point of view, they were highly significant ($p<0.001$) and they were detected in two different monitoring days.

For all the other metabolic measures there was no significant divergence between groups during recovery. Thus, there was no indication of a general metabolic change post call of clinical significance or difference between groups in that respect. Because of the limited study size, these findings have to be interpreted with caution.

Heart Rate Variability

The findings in **Paper II** indicate that one day of rest after night-call duty was sufficient to obtain a more favourable autonomic balance in terms of HFnu compared with both daytime work and night-call duty, which is interpreted as sufficient recovery post-call.

Indeed, there are no occupational HRV studies that are fully comparable to **Paper II**, but the findings of lowered HFnu during night-call are supported by the results of Adams et al. (Adams et al. 1998), who monitored emergency physicians on call. However, in that study, there was no ECG- monitoring post-call. In another study of surgeons during a 24-hour shift there were increased levels of both HF and LF, but no significant change in sympathovagal balance. These somewhat unexpected results may be explained by the fact that HRV monitoring was restricted to 10-min resting periods, during which probably the physicians could relax (Langelotz et al. 2008). Rauchenzauner et al. monitored physicians from several different specialities during 24 hours on call and during 24 hours with 8 hours ordinary daytime work and 16 hours of leisure time (Rauchenzauner et al. 2009). During night call the level of low-frequency normalized units (LFnu) increased, but the reciprocal measure HFnu did not change, which is somewhat confusing. The absence of any adjustments for sleep and wake periods during the monitoring period may have had a substancial impact on the results.

The lowered parasympathetic impact on HRV during night-call duty and after daytime work for the ANEST group compared with the PENT group in **Paper II** may indicate a higher physiological stress level in the ANEST group, potentially related to work. Influence of physical activity (Elliot et al. 2011), which changes the autonomic balance towards sympathetic dominance cannot be ruled out. Very detailed objective information on real-time work tasks may further explain these findings, but there may also be some group differential characteristics causing the different HRV patterns. For future research there is also a need for some improvement and standardization of methods for ambulatory HRV monitoring in occupational settings.

Sleep

Sleep is considered to be the most important mechanism for both mental and physiological recovery. Therefore the sleep patterns of physicians are crucial to their recovery process. The limited sleep duration when on night call (**Paper III**) was expected and defines a substantial sleep loss to be recovered post call. Fortunately, there is no need to recover the total hours of sleep loss. Experimental studies have shown that recovery sleep after moderate sleep deprivation (~24 hours time awake) contains a higher amount of slow-wave sleep (Webb and Agnew 1971). Therefore even a severe sleep debt might be overcome by a modest recovery sleep (Horne 2010).

According to the actigraphic measures, the majority of physicians were not totally sleep-deprived after night call. The extra hours of sleep the physicians had during two nights post call and, for the majority, the nap on the first post-call day were therefore considered to be sufficient for recovery. This was also confirmed by the reports on fatigue and feeling well rested on the third post-call morning. Thus, the short-term sleep recovery from night call seems to be sufficient. However, one concern is the seemingly short sleep of about six hours after ordinary daytime work. This may give rise to a general sleep deficit, which potentially affects long-term recovery. Naturally the need for sleep and vulnerability to sleep loss differs between individuals. It is not plausible that the whole study group consisted of habitual “short sleepers”, because in the baseline questionnaire the mean sleep requirement for feeling well rested was reported by the participants to be 7.5 hours (**Paper III**).

The results of **Paper III** may be compared with the findings of Åkerstedt et al., who monitored EEG in six physicians on night-call duty (Åkerstedt et al. 1990a). Compared with the physicians in **Paper III**, they had approximately one hour longer sleep duration when on night call, after daytime work, during daytime nap post-call and recovery sleep on post-call night. The different methods used for sleep monitoring render these studies not fully comparable, and differences in work setting and speciality probably have an impact as well. In addition, successively shorter sleep seems to be a general trend in modern society.

In a study of ships’ engineers, the effects of on-call duty were monitored using EEG. During on-call nights, when they slept on board, they had shorter sleep with reduced slow wave sleep and REM sleep. Effects on sleep quality could be observed even before there were any alarms, which was probably related to increased apprehension (Torsvall and Åkerstedt 1988). This study clearly showed that on-call conditions disturb not only the actual sleep time, but also the quality of sleep. One could speculate as to whether the circumstances for physicians’ sleep on night call might be approximately the same. Therefore it would be interesting to replicate **Paper III** using ambulatory EEG monitoring, which would give more exact information both on sleep duration and on sleep quality.

There is a more recent study by Gander et al., who investigated sleep loss and performance among anaesthesiologists using Actiwatch monitoring (Gander et al. 2008). However, they used the “assumed sleep” function in the Actiwatch program module, which means, that all potential awakenings during sleep were not accounted for. Therefore the measure of sleep duration may be unreliable and the total sleep time overestimated. Unfortunately it is not possible to compare their results with the findings in **Paper III**. Gander et al found that among physicians working on 12 consecutive days with alternating day/night shifts and days off duty, sleep loss was associated with a progressive decline in performance tests. However, there was no presentation of actual sleep duration for each condition.

Methodological considerations

One limitation in the present three studies is the limited sample size. However, for practical reasons it is difficult to carry out observational studies of this kind, using comprehensive monitoring for each individual in a large group. The sample size was also limited by the number of physicians that were available at the participating clinics.

In addition, we did not have any precise measure of individual workload, but chose the physician speciality, which implied different tasks and responsibilities during work on call as the exposure assessment. The total monitoring period was rather long and it was not realistic to require detailed reports on workload. Because the participants were blind to some of the analysis windows, we could not ask for information specifically during these time windows. Naturally a real-time assessment of objective workload and specific work tasks, conducted by a passive observer would have been of interest

A major strength of **Paper I-III** is the repeated measures design, which allowed us to follow the dynamics of the recovery patterns using measures on several days for each participant. Also monitoring of various physiological systems in combination with both global and real-time self-reports is an advantage. Strategic analysis windows for HRV and a good participant compliance to the study protocol further contributed to the study strength. The strict design involving comparisons between specific days in the night-call schedules meant that only a limited number of days monitored by actigraphy could be used. According to the participants' logbooks, the days used for analyses were fully representative of the entire period of AW registration, which is why the results of sleep analysis do not seem to rely on any "extreme" days.

It has to be mentioned that the present studies (**Paper I-III**) were deliberately performed on a group of physicians who generally had a moderate to long experience of working on night call. This means, however, that a group with less experience would likely not have given the same results. It is well known that experienced physicians are often more confident of their ability to handle emergency situations. This may have an impact on, for example, cortisol secretion with attenuated reactions in critical care nurses and physicians with long professional experience (>8 years) (Fischer et al. 2000) and possibly on other stress-reactive systems as well. However, knowledge of this issue is limited. It cannot be ruled out that there is a selection bias in the choice of speciality, and especially to a position at a university hospital, but this is so far merely speculative.

Naturally, individual factors as resilience to night work, work organization and other factors at work and home possibly had a modifying effect. However, this was not investigated in the present studies and would have required a different study design. Generally there were none or very limited effects by age and gender, but adjustments were made, when needed.

Recovery

There are of course many different measures of recovery. Up to now most studies on physicians' recovery from night-call duty have focused on subjective wellbeing and performance. In the present thesis the short-term physiological aspects were chosen a priori because they were the most neglected in the research and may be of importance for evaluation of potential long-term health risks of night-call work. The total results of **Paper I-III** indicate that there was a full recovery from night-call within two days. This is consistent with reports in the baseline questionnaire referred to in **Paper III**, where a majority of the participants stated a need of two nights' sleep to get sufficient recovery from night-call duty. It is also in accordance with earlier experience from shift work with moderate disturbance of circadian rhythms (Åkerstedt et al. 2000) and recent findings in a postal questionnaire which was sent to young physicians, who had several on-call nights in the same week (Tucker et al. 2010). However, there are no similar studies on physiological recovery to compare with.

The results of the present thesis can be regarded as one piece of the jigsaw puzzle of understanding the biological limits of night-call duty. When we have solid knowledge of the possibilities and limitations for biologically sound shift scheduling, important prerequisites will be in place for a positive development towards risk reduction, both concerning employee health and well-being and concerning patient safety. In a recent review on shift work, sleep and shift schedules, Sallinen and Kecklund called attention to the need for controlled intervention studies on different shift schedules (Sallinen and Kecklund 2010). This would almost certainly be applicable to further studies on physicians' recovery from work on night call.

Conclusions

The normal evening cortisol decline was not altered on post-call, why there is no support for a deficient unwinding. Additionally, there were no changes in blood glucose, insulin, TG or HDL cholesterol tending towards catabolism. Nor were there signs of deficient anabolism in the form of decreased testosterone or lowered impact of GH. Thus, there was no indication of a general metabolic change post-call.

There were lowered TSH levels in the early recovery phase post-call, but the lack of any substantial change in T4-levels gives no support for any clinical effects on metabolic rate.

The relative parasympathetic impact on HRV was not lowered on post-call, which implies that there was no indication of an autonomic imbalance related to recovery from night-call duty.

Short-term recovery sleep post-call was considered sufficient, but the rather limited night sleep following ordinary daytime work may have an adverse effect on long-term recovery.

Differences in recovery patterns between physician specialities were less than expected.

The lowered parasympathetic impact on HRV for the ANEST group compared with the PENT group of both night-call duty and after ordinary daytime work may indicate a higher physiological stress level for the ANEST group, but there was no divergence between groups concerning post-call recovery.

Considering the total results of **Paper I-III**, the 16-hour night-call schedules examined seem to be compatible with a sufficient physiological short-term recovery within two days after night-call duty. Indeed, the limited night sleep after ordinary daytime work was somewhat unexpected, and may constitute a long-term health concern.

These results may not be generalized to other work settings or groups of less experienced physicians. The limited study size implies that the findings have to be interpreted with caution.

Sleeping patterns in relation to physicians' working time should be further studied, with the purpose of optimizing working schedules to achieve sustainable work on night-call duty.

Practical implications

After the monitoring for **Paper I-III** was completed, the Department of Anaesthesiology made a small adjustment to alleviate the situation for resident physicians, by removing the separate day duties that occurred during some of their night-call weeks. This decision was most likely influenced by an increased awareness of the need to schedule in a way compatible with adequate recovery.

Basic knowledge of work-time issues, sleep recovery and strategies for a sustainable working life are of the utmost importance to young physicians. Therefore, some of these aspects and experiences from the studies are now included in training in occupational medicine for medical students.

In addition to providing up-to-date knowledge on shift work and recovery, the experiences and results from **Paper I-III** could be used in designing a small pamphlet containing practical advice for physicians involved in night-call work.

The results of the three studies and the profound knowledge gathered during the project will be of great value when giving advice to the occupational health services, or directly to the hospital clinics when they are having trouble with existing schedules or planning for new ones. Individual employees may also have problems related to night-call work that require special attention. Not only physicians, but also nurses and other staff working in shifts and at odd hours even outside the health-care sector may benefit from the present results as well.

Issues for future research

Physicians' night sleep and sleeping habits in relation to night-call duty should be further investigated. It would be of great interest to monitor the effects of different types of schedules on recovery sleep, wellbeing and performance. This would preferably be accomplished through an intervention study using a longitudinal approach and applying a crossover design. Night-call schedules of different duration and type could thereby be evaluated.

To further elucidate the quality and quantity of sleep both during on and off night-call duty, monitoring using EEG or preferably using a full PSG with equipment suitable to field studies might be an option. Indeed, a detailed picture of the different sleep stages during sleep on call, during recovery period and after ordinary daytime work would give further insights into the recovery patterns in physicians. Monitoring HRV during the night-time in combination with EEG would enable us to evaluate possible changes in autonomic balance in relation to sleep stages and thereby further evaluate the quality of recovery time. A combination of AW and EEG–monitoring would give opportunities to validate the use of AW, specifically for night-call studies. This might facilitate the monitoring of sleep in longitudinal studies of physician's working time, where EEG is not suitable.

Another approach would be to scrutinize the "healthy worker". This would involve a qualitative study of fruitful individual strategies for coping with night-call duties during a whole working life and for handling sleep deficit in a constructive manner. In this way, strategies that promote healthy on-call work could be extracted and validated using physiological measures and questionnaires. A specific study with a recovery-time perspective on the use of short and long naps before and/or after night-call duty, using advanced sleep physiological measurements and performance tests, would improve our knowledge of how to plan for sustainable night-call work.

All the above studies could result in increased knowledge and practical examples of how to find optimal working schedules that are compatible with good health and a long working life. Sound working schedules for physicians on night-call duty may also prevent attention failures related to sleepiness and fatigue.

In a recent review it was concluded that elimination of resident work shifts exceeding 16 hours was associated with improved patient safety and physicians' quality of life (Levine et al. 2010). Still, there is a need for implementation of evidence-based work-hour limits for physicians' night-call duty.

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Populärvetenskaplig sammanfattning

Läkares nattjour innebär långa arbetspass, höga krav, stress och sömnbrist. I dagens läge liknar nattjouren ofta ett nattskift med begränsade möjligheter till vila under arbetspasset. Skiftarbete med nattskift har i många undersökningar visats ge ökad risk för bland annat hjärtinfarkt och diabetes, samt även ha en negativ inverkan på välbefinnande och sömn. Samtliga dessa effekter anses bero på en störning av sömn och dygnsrytm, men sannolikt är orsakerna mer komplexa. Det har diskuterats om nattjoursarbete skulle kunna innebära liknande risker. Eftersom läkares jourpass är betydligt längre och dessutom mer oregelbundna än vid sedvanligt skiftarbete är det problematiskt att göra direkta jämförelser. Långa nattjourspass ger ofta en akut ökad trötthet som påverkar subjektivt välbefinnande och arbetsprestation. Dock är fysiologiska effekter och tänkbara långsiktiga hälsoeffekter av nattjoursarbete ytterst ringa studerat.

Det kan förväntas att ett nattjourspass innebär en påtaglig belastning både mentalt och fysiologiskt. Det viktiga ur hälsosynpunkt är dock att man får en adekvat återhämtning efter jouren. Det är nämligen vanligtvis inte belastningen i sig utan upprepade episoder med bristande återhämtning som i ett långsiktigt perspektiv kan leda till sjukdom. Många läkare upplever nattjourtjänstgöringen som en mycket belastande del av arbetet. I jämförelse med det stora antal studier som finns av skiftarbete inom industrin är den speciella typ av skiftarbete som läkares nattjour innebär till stora delar ännu outforskad. Initiativet till de studier som avhandlingen bygger på kom från en grupp av anestesiläkare som var oroliga över potentiella hälsoeffekter av en tilltagande jourbörda.

En omfattande fältundersökning av läkare med 16-timmars nattjour genomfördes år 2002 på Universitetssjukhuset i Lund. Deltagarna bestod av en grupp med 19 anestesiläkare och en grupp med 18 barnläkare och öron-näsa-hals-läkare. Läkarna var i genomsnitt 40 år och de flesta hade mångårig erfarenhet av nattjour. Anestesiläkare har rapporterats ha en hög belastning under nattjour. Det ständiga handhavandet av patienter med livshotande tillstånd skulle kunna tänkas medföra ett större behov av återhämtning efter nattjour än inom många andra specialiteter. Den huvudsakliga frågeställningen var om aktuella nattjourscheman gav utrymme för en adekvat återhämtning inom 1-3 dagar efter nattjour och om det fanns någon skillnad i återhämtningsmönster mellan de två studerade läkargrupperna.

I studien undersöktes ett flertal fysiologiska system, som är kända för att påverkas av stress, nattarbete och sömnbrist. Upprepade mätningar vid dagarbete, nattjour och återhämtningsperioden efter nattjour gjordes enligt följande: blodprov för analys av metabola faktorer såsom blodsocker, blodfetter och sköldkörtelhormon; salivprov för fastställande av kortisolhalt; indirekt mätning av sömnlängd via detektion av handledsrörelser (aktigrafi); elektrokardiografi (EKG) för analys av hjärtfrekvensvariationer (Heart Rate Variability, HRV). Förutom denna provtagning fick deltagarna dagligen fylla i ett flertal frågeformulär med skattning av trötthet, sömnighet och upplevd återhämtning.

De kemiska analyserna och de fysiologiska registreringarna indikerade att läkarna återhämtat sig till fullo två dagar efter nattjour. Det framkom inga omfattande skillnader mellan de två läkargrupperna avseende återhämtningsmönster. Vad gäller variationer i hjärtfrekvens hade anestesiläkarna tecken på en högre fysiologisk stressnivå, men ingen av läkargrupperna visade en bristande återhämtning efter nattjour. Sömnen under nattjour var endast cirka tre timmar i genomsnitt, vilket dock var förväntat. Återhämtningen av sömn efter nattjour, både i form av extra tupplur på dagtid efter jourpasset och nattsömn efter jour, bedömdes som tillräcklig. Dock visade det sig att läkarnas nattsömn endast var ca sex timmar efter en vanlig arbetsdag, vilket var överraskande.

De 16-timmars scheman för nattjour som undersöktes verkade visserligen vara förenliga med en tillräcklig kortsiktig fysiologisk återhämtning inom 2 dygn, men den begränsade nattsömnen efter vanligt dagarbete skulle kunna ge en långsiktig påverkan på hälsan. Det bör påpekas att nattjoursarbetets struktur och innehåll kan ha avsevärda variationer beroende på specialitet. Detta innebär att de aktuella resultaten inte automatiskt kan generaliseras till nattjoursjourarbete i allmänhet. Man kan dessutom inte utesluta att läkare med kort erfarenhet av nattjour hade uppvisat ett annat återhämtningsmönster. Den observerade tiden för återhämtning stämmer väl med den erfarenhet som finns från undersökningar av skiftarbetare, men någon motsvarande studie av läkares återhämtning efter nattjour finns inte att jämföra med.

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References

Aasland OG (2002). Mortality of anesthesiologists, pediatricians, and other specialists in Norway. *Acta Anaesthesiol Scand* 46(10): 1200-1202.

Adams SL, Roxe DM, Weiss J et al. (1998). Ambulatory blood pressure and Holter monitoring of emergency physicians before, during, and after a night shift. *Acad Emerg Med* 5(9): 871-877.

Åkerstedt T (2003). Shift work and disturbed sleep/wakefulness. *Occup Med (Lond)* 53(2): 89-94.

Åkerstedt T (2006). Psychosocial stress and impaired sleep. *Scand J Work Environ Health* 32(6): 493-501.

Åkerstedt T, Arnetz B and Anderzen I (1990a). Physicians during and following night call duty - 41 hour ambulatory recording of sleep. *Electroencephalogr Clin Neurophysiol* 76(2): 193-196.

Åkerstedt T and Gillberg M (1990b). Subjective and objective sleepiness in the active individual. *Int J Neurosci* 52(1-2): 29-37.

Åkerstedt T, Hume K, Minors D et al. (1994a). The meaning of good sleep: a longitudinal study of polysomnography and subjective sleep quality. *J Sleep Res* 3(3): 152-158.

Åkerstedt T, Hume K, Minors D et al. (1994b). The subjective meaning of good sleep, an intraindividual approach using the Karolinska Sleep Diary. *Percept Mot Skills* 79:287-296.

Åkerstedt T, Kecklund G, Gillberg M et al. (2000). Sleepiness and days of recovery. Transportation Research Part F: Traffic *Psychology and Behaviour* 3(4): 251-261.

Åkerstedt T, Knutsson A, Westerholm P et al. (2002a). Sleep disturbances, work stress and work hours. A cross-sectional study *J Psychosom Res* 53(3): 741-748.

Åkerstedt T, Knutsson A, Westerholm P et al. (2002b). Work organisation and unintentional sleep: results from the WOLF study. *Occup Environ Med* 59(9): 595-600.

Arnedt J, Owens J, Crouch M et al. (2005). Neurobehavioral performance of residents after heavy night call vs after alcohol ingestion. *Jama* 294(9): 1025-1033.

Axelsson J, Åkerstedt T, Kecklund G et al. (2003). Hormonal changes in satisfied and dissatisfied shift workers across a shift cycle. *J Appl Physiol* 95(5): 2099-2105.

Axelsson J, Ingre M, Åkerstedt T et al. (2005). Effects of acutely displaced sleep on testosterone. *J Clin Endocrinol Metab* 90(8): 4530-4535.

Balkin TJ, Rupp T, Picchioni D et al. (2008). Sleep Loss and Sleepiness. *Chest* 134(3): 653-660.

Bartel P, Offermeier W, Smith F et al. (2004). Attention and working memory in resident anaesthetists after night duty: group and individual effects. *Occup Environ Med* 61(2): 167-170.

Berntson GG, Bigger JT, Jr., Eckberg DL et al. (1997). Heart rate variability: origins, methods, and interpretive caveats. *Psychophysiology* 34(6): 623-648.

Bigger J, Fleiss J, Rolnitzky L et al. (1993). The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. *Circulation* 88(3): 927-934.

Bjorvatn B, Kecklund G and Akerstedt T (1998). Rapid adaptation to night work at an oil platform, but slow readaptation after returning home. *J Occup Environ Med* 40(7): 601-608.

Bøggild H and Knutsson A (1999). Shift work, risk factors and cardiovascular disease. *Scand J Work Environ Health* 25(2): 85-99.

Bonnemeier H, Richardt G, Potratz J et al. (2003). Circadian profile of cardiac autonomic nervous modulation in healthy subjects: differing effects of aging and gender on heart rate variability. *J Cardiovasc Electrophysiol* 14(8): 791-799.

Bonnet MH and Arand DL (2010). Hyperarousal and insomnia: State of the science. *Sleep Medicine Reviews* 14(1): 9-15.

Britton A and Hemingway H (2004). Heart rate variability in healthy populations: correlates and consequences. *Dynamic electrocardiography*. M. Malik and A. Camm. New York, Blackwell Publishing Futura: 90-111.

Broussard J and Brady MJ (2010). The impact of sleep disturbances on adipocyte function and lipid metabolism. *Best Practice & Research Clinical Endocrinology & Metabolism* 24(5): 763-773.

Cappuccio FP, D'Elia L, Strazzullo P et al. (2010a). Quantity and Quality of Sleep and Incidence of Type 2 Diabetes. *Diabetes Care* 33(2): 414-420.

Cappuccio FP, D'Elia L, Strazzullo P et al. (2010b). Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. *Sleep* 33(5): 585-592.

Chandola T, Ferrie JE, Perski A et al. (2010). The effect of short sleep duration on coronary heart disease risk is greatest among those with sleep disturbance: a prospective study from the Whitehall II cohort. *Sleep* 33(6): 739-744.

Chrousos GP and Gold PW (1992). The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. *Jama* 267(9): 1244-1252.

Chung S, Son GH and Kim K (2011). Circadian rhythm of adrenal glucocorticoid: Its regulation and clinical implications. *Biochimica et Biophysica Acta* 1812(5): 581-591.

Clays E, De Bacquer D, Crasset V et al. (2011). The perception of work stressors is related to reduced parasympathetic activity. *International Archives of Occupational and Environmental Health* 84(2): 185-191.

Clow AT, L. Evans, P. Hucklebridge, F. (2004). The awakening Cortisol Response: Methodological Issues and Significance. *Stress* 7(1): 29-37.

Collins SM, Karasek RA and Costas K (2005). Job strain and autonomic indices of cardiovascular disease risk. *Am J Ind Med* 48(3): 182-193.

Coomber S, Todd C, Park G et al. (2002). Stress in UK intensive care unit doctors. *Br J Anesth* 89(6): 873-881.

Cooper C, Clarke S and Rowbottom A (1999). Occupational stress, job satisfaction and well-being in anaesthetists. *Stress Medicine* 15(2): 115-126.

Czeisler CA and Gooley JJ (2007). Sleep and circadian rhythms in humans. *Cold Spring Harb Symp Quant Biol* 72: 579-597.

Delaney JP and Brodie DA (2000). Effects of short-term psychological stress on the time and frequency domains of heart-rate variability. *Percept Mot Skills* 91(2): 515-524.

Denisco R, Drummond J and Gravenstein J (1987). The effect of fatigue on the performance of a simulated anesthetic monitoring task. *J Clin Monit* 3(1): 22-24.

Derogatis L (1992). *SCL-90 -R. Administration, scoring and procedures. Manual-II*. Towson, MD, Clinical Psychometric Research.

Dhand R and Sohal H (2006). Good sleep, bad sleep! The role of daytime naps in healthy adults. *Curr Opin Pulm Med* 12(6): 379-382.

Eller NH, Malmberg B and Bruhn P (2006). Heart rate variability and intima media thickness. *Int J Behav Med* 13(3): 201-213.

Elliot AJ, Payen V, Brisswalter J et al. (2011). A subtle threat cue, heart rate variability, and cognitive performance. *Psychophysiology*: 2011 DOI: 10.1111/j.1469-8986.2011.01216.x.

Faraut B, Boudjeltia KZ, Dyzma M et al. (2011). Benefits of napping and an extended duration of recovery sleep on alertness and immune cells after acute sleep restriction. *Brain, Behavior, and Immunity* 25(1): 16-24.

Faul F, Erdenfelder E, Lang A-G et al. (2007). "G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods* 39:175-191.

Fischer JE, Calame A, Dettling AC et al. (2000). Experience and endocrine stress responses in neonatal and pediatric critical care nurses and physicians. *Crit Care Med* 28(9): 3281-3288.

Frost P, Kolstad HA and Bonde JP (2009). Shift work and the risk of ischemic heart disease - a systematic review of the epidemiologic evidence. *Scand J Work Environ Health* 35(3): 163-179.

Gan E-H and Quinton R (2010). Physiological Significance of the Rhythmic Secretion of Hypothalamic and Pituitary Hormones. *Progress in Brain Research*. M. Luciano, Elsevier. Volume 181: 111-126.

Gander P, Millar M, Webster C et al. (2008). Sleep loss and performance of anaesthesia trainees and specialists. *Chronobiol Int* 25(6): 1077-1091.

Garde AH, Persson R, Hansen AM et al. (2009). Effects of lifestyle factors on concentrations of salivary cortisol in healthy individuals. *Scand J Clin Lab Invest* 69(2): 242-250.

Geurts SA and Sonnentag S (2006). Recovery as an explanatory mechanism in the relation between acute stress reactions and chronic health impairment. *Scand J Work Environ Health* 32(6): 482-492.

Gillberg M, Kecklund G, Axelsson J et al. (1996). The effects of a short daytime nap after restricted night sleep. *Sleep* 19(7): 570-575.

Goichot B, Weibel L, Chapotot F et al. (1998). Effect of the shift of the sleep-wake cycle on three robust endocrine markers of the circadian clock. *Am J Physiol* 275:243-248.

Goldberg D and Williams PA (1988). *User's guide to the general health questionnaire*. Oxford, NFER-Nelson.

Grandner MA and Patel NP (2009). From sleep duration to mortality: implications of meta-analysis and future directions. *Journal of Sleep Research* 18(2): 145-147.

Hagmar L (2003). Is the life expectancy of anesthesiologists decreased? *Scand J Work Environ Health* 29(2): 83-84.

Hall M, Vasko R, Buysse D et al. (2004). Acute stress affects heart rate variability during sleep. *Psychosom Med* 66(1): 56-62.

Hansen ÅM, Garde AH and Persson R (2008). Sources of biological and methodological variation in salivary cortisol and their impact on measurement among healthy adults: A review. *Scandinavian Journal of Clinical & Laboratory Investigation* 68(6): 448-458.

Hanson EK, Godaert GL, Maas CJ et al. (2001). Vagal cardiac control throughout the day: the relative importance of effort-reward imbalance and within-day measurements of mood, demand and satisfaction. *Biol Psychol* 56(1): 23-44.

Härmä M (2006). Workhours in relation to work stress, recovery and health. *Scand J Work Environ Health* 32(6): 502-514.

Hjortskov N, Garde AH, Ørbaek P et al. (2004a). Evaluation of salivary cortisol as a biomarker of self-reported mental stress in field studies. *Stress and Health* 20(2): 91-98.

Hjortskov N, Rissen D, Blangsted AK et al. (2004b). The effect of mental stress on heart rate variability and blood pressure during computer work. *Eur J Appl Physiol* 92:84-89

Hon EH and Lee ST (1963). Electronic Evaluation of the Fetal Heart Rate. Viii. Patterns Preceding Fetal Death, Further Observations. *Am J Obstet Gynecol* 87: 814-826.

Horne J (2010). Sleepiness as a need for sleep: When is enough, enough ? *Neuroscience and Biobehavioral Reviews* 34(1): 108-118.

Howard S, Gaba D, Smith B et al. (2003). Simulation study of rested versus sleep-deprived anesthesiologists. *Anesthesiology* 98(6): 1345-1355.

Jönsson BA, Malmberg B, Amilon A et al. (2003). Determination of cortisol in human saliva using liquid chromatography-electrospray tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci* 784(1): 63-68.

Juel K, Husum B, Viby-Mogensen J et al. (2002). Mortality among anesthesiologists in Denmark, 1973-95. *Acta Anaesthesiol Scand* 46(10): 1203-1205.

Jönsson P, Wallergård M, Österberg K et al. (2010). Cardiovascular and cortisol reactivity and habituation to a virtual reality version of the Trier Social Stress Test: A pilot study. *Psychoneuroendocrinology* 35(9): 1397-1403.

Kara T, Nykodym J and Somers VK (2003). Heart rate variability: back to the beginning. *J Cardiovasc Electrophysiol* 14(8): 800-802.

Karlsson B, Knutsson A and Lindahl B (2001). Is there an association between shift work and having a metabolic syndrome? Results from a population based study of 27,485 people. *Occup Environ Med* 58(11): 747-752.

Karlsson BH, Knutsson AK, Lindahl BO et al. (2003). Metabolic disturbances in male workers with rotating three-shift work. Results of the WOLF study. *Int Arch Occup Environ Health* 76(6): 424-430.

Katz A, Nambi SS, Mather K et al. (2000). Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab* 85(7): 2402-2410.

Katz JD (2004). Do Anesthesiologists Die at a Younger Age Than Other Physicians? Age-Adjusted Death Rates. *Anesth Analg* 98(4): 1111-1113.

Kecklund G and Åkerstedt T (1997). Objective components of individual differences in subjective sleep quality. *Journal of Sleep Research* 6(4): 217-220.

Kessler L, Nedeltcheva A, Imperial J et al. (2010). Changes in serum TSH and free T4 during human sleep restriction. *Sleep* 33(8): 1115-1118.

Knutson KL, Spiegel K, Penev P et al. (2007). The metabolic consequences of sleep deprivation. *Sleep Medicine Reviews* 11(3): 163-178.

Knutsson A (2003). Health disorders of shift workers. *Occup Med (Lond)* 53(2): 103-108.

Knutsson A, Åkerstedt T, Jonsson BG et al. (1986). Increased risk of ischaemic heart disease in shift workers. *Lancet* 2(8498): 89-92.

Knutsson A and Bøggild H (2010). Gastrointestinal disorders among shift workers. *Scand J Work Environ Health* 36(2): 85-95.

Kolstad HA (2008). Nightshift work and risk of breast cancer and other cancers--a critical review of the epidemiologic evidence. *Scand J Work Environ Health* 34(1): 5-22.

Kudielka BM, Buchtal J, Uhde A et al. (2007). Circadian cortisol profiles and psychological self-reports in shift workers with and without recent change in the shift rotation system. *Biological Psychology* 74(1): 92-103.

Kudielka BM, Schommer NC, Hellhammer DH et al. (2004). Acute HPA axis responses, heart rate, and mood changes to psychosocial stress (TSST) in humans at different times of day. *Psychoneuroendocrinology* 29(8): 983-992.

Kuo TB, Lin T, Yang CC et al. (1999). Effect of aging on gender differences in neural control of heart rate. *Am J Physiol* 277: 2233-2239.

Landrigan C, Czeisler C, Barger L et al. (2007). Effective implementation of work-hour limits and systemic improvements. *Jt Comm J Qual Patient Saf* 33(11Suppl): 19 - 29.

Landrigan C, Rothschild J, Cronin J et al. (2004). Effect of reducing interns' work hours on serious medical errors in intensive care units. *N Engl J Med* 351(18): 1838-1848.

Langelotz C, Scharfenberg M, Haase O et al. (2008). Stress and Heart Rate Variability in Surgeons During a 24-Hour Shift. *Arch Surg* 143(8): 751-755.

Larsson J, Holmstrom I and Rosenqvist U (2003). Professional artist, good Samaritan, servant and co-ordinator: four ways of understanding the anaesthetist's work. *Acta Anaesthesiol Scand* 47(7): 787-793.

Levine AC, Adusumilli J and Landrigan CP (2010). Effects of reducing or eliminating resident work shifts over 16 hours: a systematic review. *Sleep* 33(8): 1043-1053.

Lindfors P, Meretoja O, Toyry S et al. (2007). Job satisfaction, work ability and life satisfaction among Finnish anaesthesiologists. *Acta Anaesthesiol Scand* 51(7): 815-822.

Lindfors P, Nurmi K, Meretoja O et al. (2006). On-call stress among Finnish anaesthetists. *Anaesthesia* 61(9): 856 - 866.

Lockley S, Cronin J, Evans E et al. (2004). Effect of reducing interns' weekly work hours on sleep and attentional failures. *N Engl J Med* 351(18): 1829-1837.

Lockley S, Landrigan C, Barger L et al. (2006). When policy meets physiology: the challenge of reducing resident work hours. *Clin Orthop Relat Res* 449: 116-127.

Lockley SW, Skene DJ and Arendt J (1999). Comparison between subjective and actigraphic measurement of sleep and sleep rhythms. *J Sleep Res* 8(3): 175-183.

Lowden A, Kecklund G, Axelsson J et al. (1998). Change from an 8-hour shift to a 12-hour shift, attitudes, sleep, sleepiness and performance. *Scand J Work Environ Health* 24 (Suppl 3): 69-75.

Magrini A, Pietroiusti A, Coppeta L et al. (2006). Shift work and autoimmune thyroid disorders. *Int J Immunopathol Pharmacol* 19(4 Suppl): 31-36.

McEwen BS (1998). Protective and damaging effects of stress mediators. *N Engl J Med* 338(3): 171-179.

Milner CE and Cote KA (2009). Benefits of napping in healthy adults: impact of nap length, time of day, age, and experience with napping. *Journal of Sleep Research* 18(2): 272-281.

Morgenthaler T, Alessi C, Friedman L et al. (2007). Practice parameters for the use of actigraphy in the assessment of sleep and sleep disorders: an update for 2007. *Sleep* 30(4): 519-529.

Nader N, Chrousos GP and Kino T (2010). Interactions of the circadian CLOCK system and the HPA axis. *Trends in Endocrinology & Metabolism* 21(5): 277-286.

Nunan D, Sandercock GR and Brodie DA (2010). A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing Clin Electrophysiol* 33(11): 1407-1417.

Nygårds M-E and Hulting J (1979). An automated system for ECG monitoring. *Computers and Biomedical Research* 12(2): 181-202.

Nyssen A, Hansez I, Baele P et al. (2003). Occupational stress and burnout in anaesthesia. *Br J Anaesth* 90(3): 333-337.

Ohtonen P and Alahuhta S (2002). Mortality among Finnish anesthesiologists from 1984-2000. *Acta Anaesthesiol Scand* 46(10): 1196-1199.

Olson EJ, Drage LA and Auger RR (2009). Sleep deprivation, physician performance, and patient safety. *Chest* 136(5): 1389-1396.

Orton DI and Gruzelier JH (1989). Adverse changes in mood and cognitive performance of house officers after night duty. *BMJ* 298(6665): 21-23.

Persson R, Ørbaek P, Kecklund G et al. (2006). Impact of an 84-hour workweek on biomarkers for stress, metabolic processes and diurnal rhythm. *Scand J Work Environ Health* 32(5): 349-358.

Philip P and Åkerstedt T (2006). Transport and industrial safety, how are they affected by sleepiness and sleep restriction? *Sleep Medicine Reviews* 10(5): 347-356.

Pietroiusti A, Neri A, Somma G et al. (2010). Incidence of metabolic syndrome among night-shift healthcare workers. *Occup Environ Med* 67(1): 54-57.

Podsakoff PM, MacKenzie SB, Lee JY et al. (2003). Common method biases in behavioral research: a critical review of the literature and recommended remedies. *J Appl Psychol* 88(5): 879-903.

Pruessner JC, Wolf OT, Hellhammer DH et al. (1997). Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity. *Life Sci* 61(26): 2539-2549.

Pumprla J, Howorka K, Groves D et al. (2002). Functional assessment of heart rate variability: physiological basis and practical applications. *International Journal of Cardiology* 84(1): 1-14.

Puttonen S, Harma M and Hublin C (2010). Shift work and cardiovascular disease - pathways from circadian stress to morbidity. *Scand J Work Environ Health* 36(2): 96-108.

Rauchenzauner M, Ernst F, Hintringer F et al. (2009). Arrhythmias and increased neuro-endocrine stress response during physicians' night shifts: a randomized cross-over trial. *European Heart Journal* 30(21): 2606-2613.

Rechtschaffen A and Kales A (1968). *A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects*. Bethesda, US Department of Health, Education and Welfare, Public Health Service.

Reid K and Dawson D (1999). Correlation between wrist activity monitor and electrophysiological measures of sleep in a simulated shiftwork environment for younger and older subjects. *Sleep* 22(3): 378-385.

Sadeh A and Acebo C (2002). The role of actigraphy in sleep medicine. *Sleep Med Rev* 6(2): 113-124.

Sallinen M and Kecklund G (2010). Shift work, sleep, and sleepiness - differences between shift schedules and systems. *Scand J Work Environ Health* 36(2): 121-33.

Saper CB, Chou TC and Scammell TE (2001). The sleep switch: hypothalamic control of sleep and wakefulness. *Trends in Neurosciences* 24(12): 726-731.

Scanlon M (2001). Thyroid-releasing hormone and thyroid-stimulating hormone. *Endocrinology*. L. DeGroot. Philadelphia, Saunders. 2: 1279-1289.

Schlotz W, Hellhammer J, Schulz P et al. (2004). Perceived work overload and chronic worrying predict weekend-weekday differences in the cortisol awakening response. *Psychosom Med* 66(2): 207-214.

Schnall PB, K. Landsbergis, P. Baker, D., Ed. (2000). *Occupational Medicine*: The Workplace and Cardiovascular Disease. State of the Art Reviews. Philadelphia, Hanley and Belfus, INC.

Söderström M, Ekstedt M and Åkerstedt T (2006). Weekday and weekend patterns of diurnal cortisol, activation and fatigue among people scoring high for burnout. *Scand J Work Environ Health* (suppl 2): 35-40.

Söderström M, Ingre M, Kecklund G et al. (2001). *Train drivers workload - effects on sleep, fatigue and performance* (internal report in Swedish). Stockholm, Institute for Psychosocial Medicine, IPM, Stockholm, Sweden: 1-47.

Sookoian S, Gemma C, Fernandez Gianotti T et al. (2007). Effects of rotating shift work on biomarkers of metabolic syndrome and inflammation. *J Intern Med* 261(3): 285-292.

Spiegel K, Leproult R and Van Cauter E (1999). Impact of sleep debt on metabolic and endocrine function. *Lancet* 354: 1435-1439.

Sterling P and Eyer J (1988). Allostasis: a new paradigm to explain arousal pathology. *Handbook of life stress, cognition and health*. S. Fisher and J. Reason. New York, John Wiley: 629-649.

Svärdsudd K, Wedel H and Gordh T, Jr. (2002). Mortality rates among Swedish physicians: a population-based nationwide study with special reference to anesthesiologists. *Acta Anaesthesiol Scand* 46(10): 1187-95.

TaskForce (1996). Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology:Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. *Task Force of. Eur Heart J* 17(3): 354-381.

Thayer JF and Lane RD (2007). The role of vagal function in the risk for cardiovascular disease and mortality. *Biological Psychology* 74(2): 224-242.

Theorell T, Karasek RA and Eneroth P (1990). Job strain variations in relation to plasma testosterone fluctuations in working men--a longitudinal study. *J Intern Med* 227(1): 31-36.

Torsvall L and Åkerstedt T (1988). Disturbed sleep while being on-call: an EEG study of ships' engineers. *Sleep* 11(1): 35-38.

Totterdell P, Spelten E, Smith L et al. (1995). Recovery from work shifts: how long does it take? *J Appl Psychol* 80(1): 43-57.

Tucker P, Brown M, Dahlgren A et al. (2010). The impact of junior doctors' worktime arrangements on their fatigue and well-being. *Scand J Work Environ Health* 36(6): 458-465.

van Amelsvoort LG, Schouten EG, Maan AC et al. (2001). Changes in frequency of premature complexes and heart rate variability related to shift work. *Occup Environ Med* 58(10): 678-681.

Van Dongen HP, Maislin G, Mullington JM et al. (2003). The cumulative cost of additional wakefulness: dose-response effects on neurobehavioral functions and sleep physiology from chronic sleep restriction and total sleep deprivation. *Sleep* 26(2): 117-126.

Webb W and Agnew H (1971). Stage 4 sleep: influence of time course variables. *Science* 174(16): 1354 - 1356.

Weibel L, Follenius M, Spiegel K et al. (1997). Growth hormone secretion in night workers. *Chronobiol Int* 14(1): 49-60.

Vgontzas AN, Bixler EO and Chrousos GP (2005). Sleep apnea is a manifestation of the metabolic syndrome. *Sleep Medicine Reviews* 9(3): 211-224.

Vgontzas AN, Pejovic S, Zoumakis E et al. (2007). Daytime napping after a night of sleep loss decreases sleepiness, improves performance, and causes beneficial changes in cortisol and interleukin-6 secretion. *Am J Physiol Endocrinol Metab* 292(1): 253-261.

Wolk R and Somers VK (2007). Sleep Apnoea & Hypertension: Physiological bases for a causal relation: Sleep and the metabolic syndrome. *Exp Physiol* 92(1): 67-78.

von Thiele U, Lindfors P and Lundberg U (2006). Self-rated recovery from work stress and allostatic load in women. *Journal of Psychosomatic Research* 61(2): 237-242.

Figure 1 – 4

Figure 1:

Study design

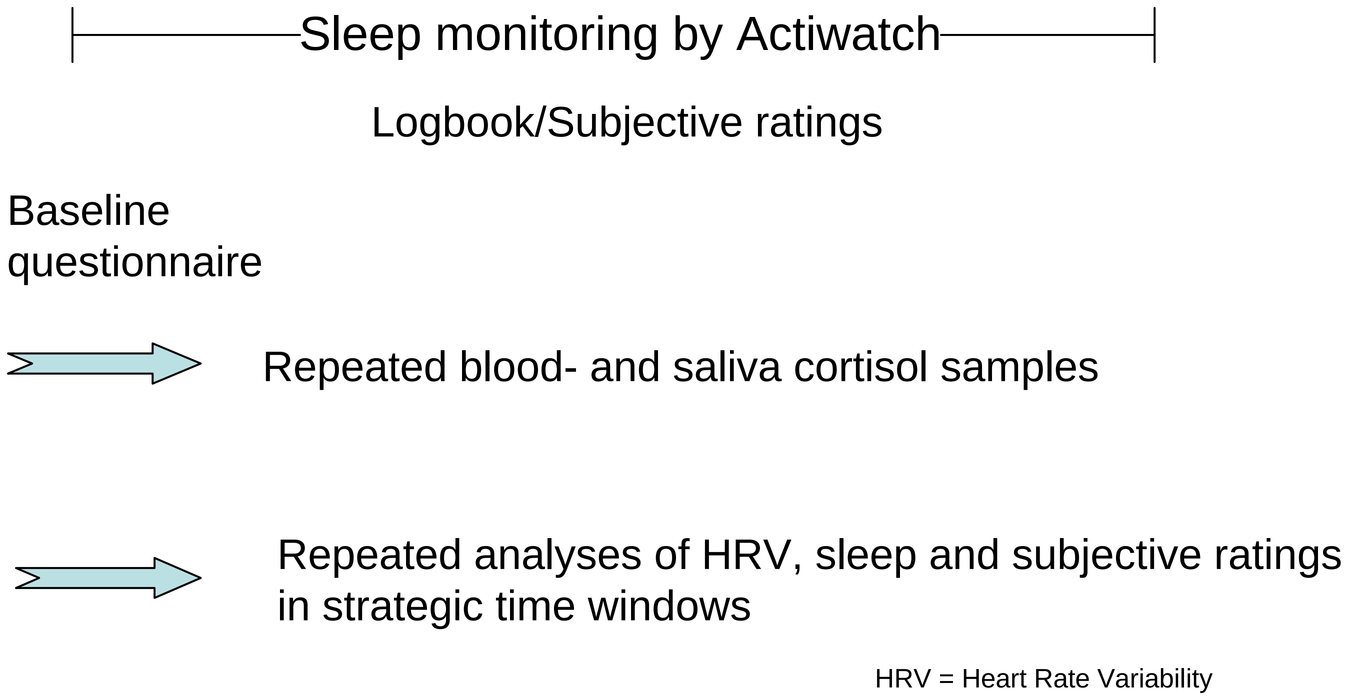


Figure 2:

Flowchart Paper I

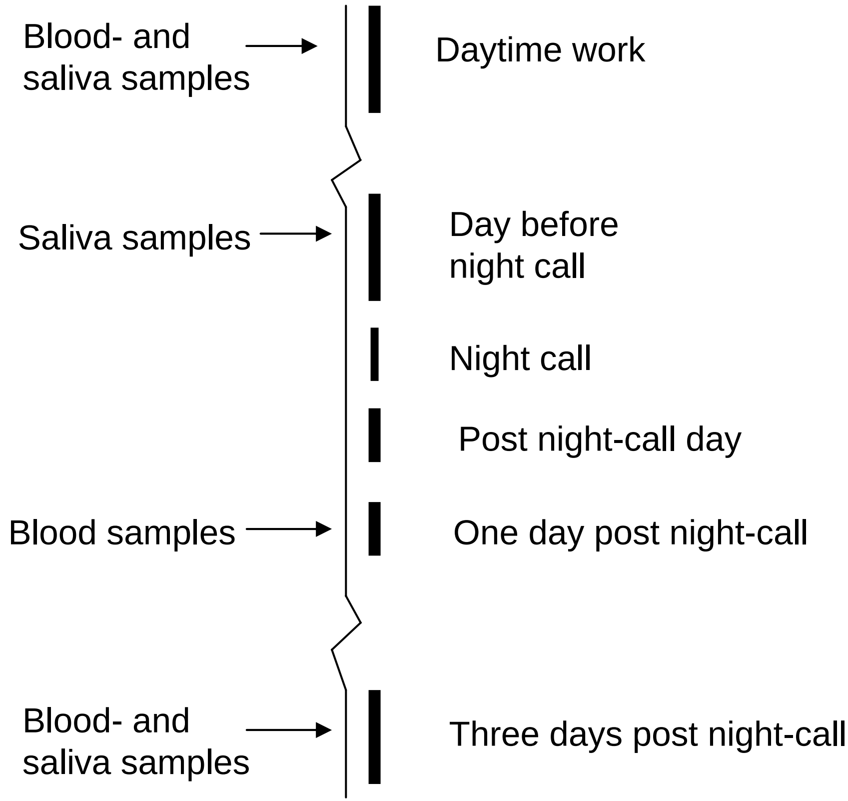


Figure 3:

Flowchart Paper II

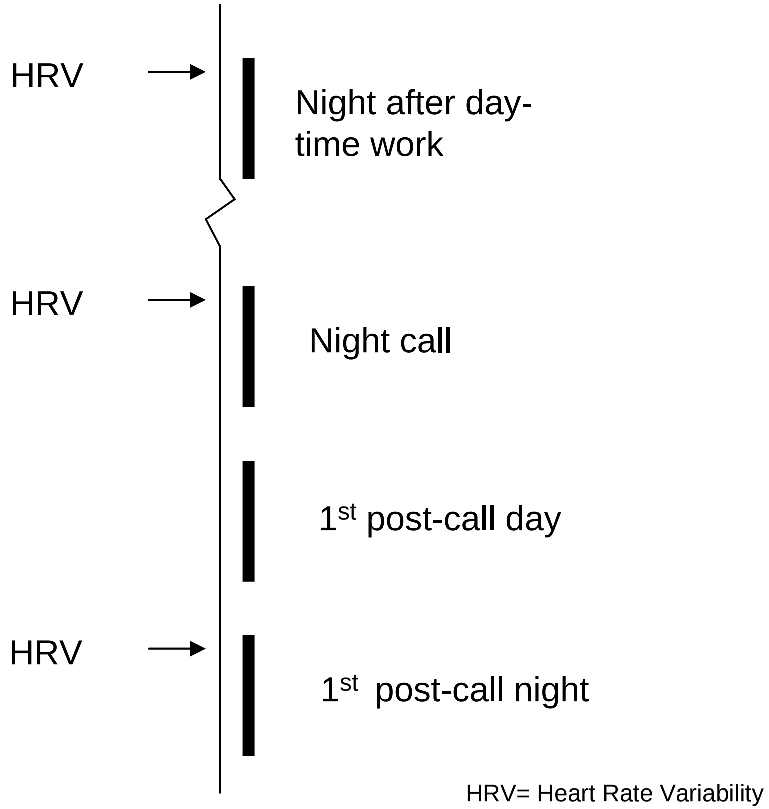
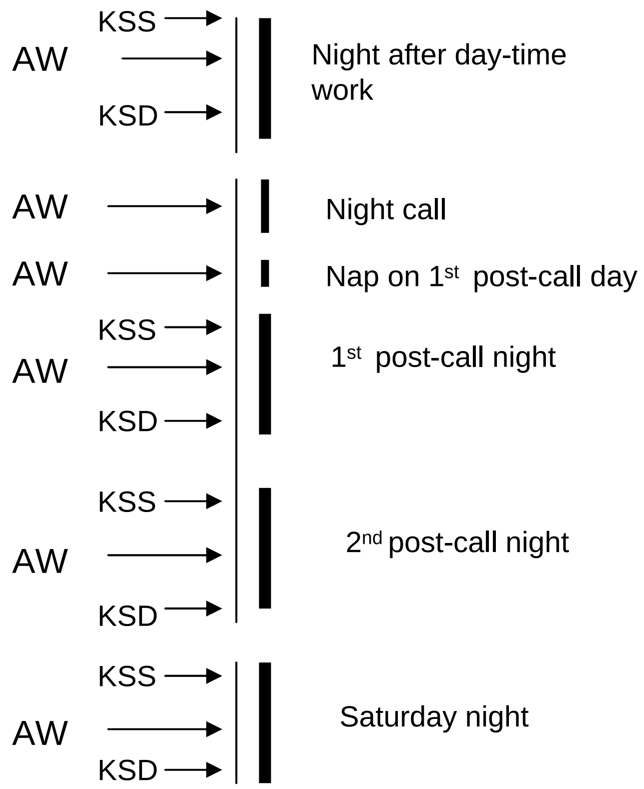


Figure 4:

Flowchart Paper III



AW = Actiwatch (black lines indicate sleep analysis period)

KSS = Karolinska Sleepiness Scale

KSD = Karolinska Sleep Diary

Study I

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Physiological restitution after night-call duty in anaesthesiologists: impact on metabolic factors

B. Malmberg[1], R. Persson[2], B. A. G. Jönsson[1], E.-M. Erfurth[3], P. Flisberg[4], E. Ranklev[4] and P. Ørbaek[2]
[1]*Department of Occupational and Environmental Medicine, Lund University Hospital, Lund, Sweden,* [2]*National Research Center for the Working Environment, Copenhagen, Denmark and Departments of* [3]*Endocrinology and Diabetes and* [4]*Anaesthesiology and Intensive care, Lund University Hospital, Lund, Sweden*

Background: Several studies have shown impaired mental well-being and performance in physicians work on call, but knowledge of the physiological effects is scarce. The aims of the present study were to investigate if there was a metabolic stress response in the restitutional phase after night-call duty, indicating potential negative health effects, and determine whether there were differences between physician specialities.
Methods: Anaesthesiologists ($n = 19$) were compared with paediatricians/ear, nose and throat (ENT) surgeons ($n = 18$). On an ordinary workday, 1 and 3 days after work on night call, blood samples were taken for analysis of glucose, thyroid-stimulating hormone (TSH), free thyroxine, testosterone, insulin growth factor-1 (IGF-1), high- and low-density lipoprotein cholesterol (HDL and LDL), triglycerids (TG) and insulin. Saliva cortisol was sampled on an ordinary working day, a day including 16-h night call, the third day following, and for anaesthesiologists also on a day off work.
Results: TSH differed significantly between days in both groups, with a 26% lower level 1 day after on-call duty ($P < 0.001$). A 48% cortisol rise in the morning preceding night duty was found for paediatricians/ENT surgeons ($P < 0.01$).
Conclusion: The significant dip in TSH level 24 h after night-call duty indicates a metabolic effect of working on night call and should be studied further. However, the levels were within the normal range and the overall results do not imply any serious metabolic changes and only minor differences were seen between specialist groups.

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Key words: Cortisol; TSH; shift work; diurnal; stress; physician.

For a physician, night-call duty is often synonymous with long working hours, reduced sleep and stress. Questionnaire and experimental studies have shown that mental well-being and performance is impaired during work on call for long time periods, but knowledge of physiological effects is scarce (1–3). It has been argued that the work situation of anaesthesiologists, in particular, is characterized by frequent stressful situations and a need for sustained vigilance. Indeed, an epidemiological study showed a higher mortality rate among anaesthesiologists compared with other physicians; and occupational stress was discussed as one of the possible explanations (4). Methodology and interpretation of this study has been criticized (5, 6) and other researchers have failed to confirm these results (7–9). Nevertheless there has been a great concern among Swedish physicians, and especially anaesthesiologists, about potential adverse effects of work on night call.

Stress, sleep deficit and desynchronization of circadian rhythms are important for neurohormonal regulation (10). For example, acute sleep deprivation causes an increased plasma level of thyroid-stimulating hormone (TSH), while extended sleep debt or displaced sleep (e.g. daytime sleep) seems to decrease the TSH (11, 12). Additionally, plasma levels of testosterone and growth hormones are known to decrease in response to insufficient sleep (13–15). Experimental research has shown that sleep debt negatively influences the carbohydrate metabolism and endocrine function, leading to impaired glucose tolerance and increased serum cortisol levels in the afternoon (11). As regards exposure to psychosocial stress, the hypothalamic–pituitary–adrenal (HPA) axis and subsequent cortisol secretion have been found to respond in acute social stress situations, in both experimental and real-life settings (16). Cortisol shows a marked circadian rhythm with low levels during the first part of the night, rising values in the early morning and a peak at awakening and decreasing values over the rest of the day, except for stress surges that superimposes on the circadian rhythm (17). As a well-established marker of catabolism, cortisol stimulates gluconeogenesis, dyslipidemia and insulin resistance (18). There are strong indications that frequent activation of the HPA axis could lead to a metabolic syndrome (19–21).

Physicians' work on night call has many similarities with classic shift work, and one would expect these groups to share increased risks of metabolic syndrome and cardiovascular disease (22). However, in contrast to classic rotating shift work, physicians' night call schedules are more irregular, with longer working hours (16 h or more), and cannot be directly compared with shift work. Specific studies of night-call duty are therefore needed.

The aims of the present study were to investigate if there was a metabolic stress response in the restitutional phase after physicians' night-call duty, and if there were differences between anaesthesiologists and other specialists.

Methods

Participants

Blood and saliva samples were used to compare anaesthesiologists with paediatricians and ear, nose and throat (ENT) surgeons. Participants were employed at a university hospital and worked regularly on call during the study period. All such physicians were asked to participate. The total participation rate for blood samples was 19/24 (79%) in anaesthesiologists and 18/25 (72%) in paediatricians and ENT surgeons. The corresponding rates for saliva were 18/24 and 15/25, respectively. Demographic data were collected using a questionnaire (Table 1). The whole group of physicians had a low-to-moderate alcohol consumption, normal liver function and blood lipids. Two subjects with hypothyreosis were excluded from statistical analyses, because endocrine disease might distort the results; the others had no diseases or medication influencing the physiological variables studied. The family situation was almost identical in the two groups of physicians as well as the reported degree of negative impact of family matters on work, sleep insufficiency in general, and need for recovery after night duty. All participants gave written informed consent, and the study was approved by the Ethics committee at Lund University (LU 732–01).

Working conditions

During night-call duty, the anaesthesiologists took care of the patient's vital functions in major traumas, cardiac arrest and acute operations. They were also in charge of the post-operative ward and intensive care unit (ICU), handling patients with vital organ failure. The paediatricians and ENT surgeons worked at the emergency ward taking care of acute cases in their speciality, but did not have the type of work tasks as

Table 1

Demographic data for participating physicians.

	Anaesthesiologists (n = 19)	Paediatricians and ENT surgeons (n = 18)
Age [median (range)]	42 (32–55)	39 (26–45)
Years' experience of night call [median (range)]	9 (4–27)	10 (0–19)
Women (%)	37	59
Smokers (%)	5	0
Position		
Consultants (%)	32	12
Registrars (%)	42	29
Residents (%)	26	59
Social status		
Single	0	7
Living with other adult, but no children (%)	26	20
Living with other adult and children (%)	68	73
Living with children, but without other adult (%)	5	0
Work/home interface		
Worries for family matters influence focus on work (%)	33	40
Regular work on overtime (once a week or more) (%)	50	40
Sleep		
Reports of insufficient sleep (%)	78	72
1–2 nights sleep required for recovery from night-call duty (%)	95	87

mentioned above for the anaesthesiologists. It could be added that the participating paediatricians were not dealing with child surgery or neonatal patients. All participating physicians could naturally have a high work load on call, but the anaesthesiologists had a general focus on life-threatening conditions. Furthermore, they differed from the other two specialities by giving service to the whole hospital and facilitate the work of several other physicians in the care of severely ill patients (23), which generally may provide an extra stress exposure. These circumstances gave a clear exposure contrast and were the reasons for choosing the actual specialist groups.

Night-call duty started at approximately 16.00 hours and lasted for about 16 h. All participants worked at the hospital during the whole night duty, and had at least one day off after night call. However, working schedules differed somewhat between specialities. Anaesthesiologists and paediatricians had separate night call weeks every fourth to sixth week, during which they worked 2–3 nights. The ENT surgeons had single nights on call every second or third week, and in contrast to the two other specialties, they generally had a normal working day before night call. Every day during the study, simple diaries were filled in by the participants. The majority of participants made a complete recording on the night on call. They revealed that the median time for going to bed was 01.25 hours (range 22.30 to 05.00 hours) for paediatricians/ENT surgeons (n = 14) and 02.55 hours (range 23.20 to 05.50 hours) for anaesthesiologists (n = 14) on the monitored night on call. They slept until approximately 07.00 hours. During time in bed, they generally had one call (often including active work with patients) which resulted in just a few hours of undisturbed sleep, and for some, no sleep at all. Four of the anaesthesiologists got one or two alarm calls (caridac arrest or trauma) after bed time, but there were none of such for the paediatricians/ENT surgeons.

Biological sampling

Blood

On three occasions (an ordinary workday, plus 1 and 3 days after night-call duty), repeated specimens were taken, fasting in the morning, of glucose, TSH, free thyroxine (fT4), testosterone, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL) and triglycerids (TG) in plasma and insulin in serum. For detection of insulin resistance, the QUICKI index was calculated from values of fasting insulin and glucose, which is considered to give the same information as a glucose clamp test, which is golden standard, but not suitable for field studies (24). Because the secretion of growth hormone (GH) is highly pulsatile, and therefore less suited to single sample measurements, insulin growth factor-1 (IGF-1) was selected as a marker for GH. This hormone was also measured in plasma. The samples were analysed consecutively at the clinical chemistry laboratories at the University Hospitals of Lund and Malmö. All analyses except for IGF-1 [coefficient of variation (CV) = 16%] were accredited with a precision (CV) = 10% for the hormone analyses and = 6% for the remaining analyses.

Saliva

Saliva samples for analysis of cortisol were taken on an ordinary working day, a day including 16 h of night-call duty, the third day after working on night call, and for anaesthesiologists, also on a separate day off work. Sampling times were: (i) on awakening, (ii) + 30 min, (iii) + 8 h, and (iv) at approximately 21.00 hours. All samples were collected in Sarstedt salivette® tubes (Sarstedt AG & Co., Nümbrecht, Germany) and analysed using liquid chromatography-electrospray tandem mass spectrometry (LC-MS-MS) (25). This method is very accurate concerning spiked cortisol samples, but produces lower values than radioimmunoassay (RIA) methods. The CVs were 7% in-run at 0.7 μg/l, and 11% between-run at 2.5 μg/l. The detection limit of quantification was 0.5 μg/l. Besides mean cortisol levels, the outcome variables included maximum morning levels (the highest value of sample 1 or 2), awakening response (the percentage increase between sample 1 and 2), and the decline over the day (the difference between the morning maximum sample and the sample obtained at 21.00 hours).

Study design and procedures

In this observational field study, each participant followed an individually designed schedule for sampling corresponding with their work on night call. To compensate for the possible effect of habituation to the sampling procedures, the cortisol and blood samples were collected in a counter-balanced design. Accordingly, the first occasion of sampling was equally distributed between ordinary work days and days related to night-call duty.

Statistics

The statistical computations were made using SPSS 12.0 (SPSS Inc., Chicago, IL). A repeated measures model was specified. Categorical predictors were sampling day and group, and dependent variables were all blood and cortisol data. As a result of repeated cortisol sampling each monitoring day, analyses of cortisol data also included time of day as a categorical predictor, when appropriate. For each analysis, the selection of covariates was governed by biological considerations, and included irrespective of the level of statistical significance. P-values < 0.05 were considered to be statistically significant.

Blood samples

All data were normally distributed and were therefore described as means and standard deviations (SD). Blood sample estimates and corresponding P-values were adjusted for age, gender and weight. A compound symmetry covariance structure provided the best fit and was applied in all cases. Interactions between day and group were statistically significant only for TSH and therefore retained in the model exclusively for this variable.

Saliva samples

As a result of a positively skewed distribution, crude data were described as medians and percentiles and then logarithmically transformed (log10) before analysis. However, for the cortisol indices a restriction of ± 3SD (standard deviations) was applied as it was observed that exclusion of a few extreme outliers generated a normal distribution. However, analyses without this restriction gave the same results. Estimates of cortisol saliva and corresponding P-values were adjusted for age, gender and sampling time, with the exception of the cortisol indices, where only the awakening sample time was used for time adjustment. Interactions between day, group and time of day were studied. A first order autoregressive covariance structure was applied because it provided the best fit.

Results

Blood

Descriptive statistics for biomarkers assessed in blood are presented in Table 2. The main effect of sampling day on TSH was significant ($P < 0.001$) whereas the effect of group was not ($P = 0.349$). A statistically significant interaction effect was observed between group and sampling day for TSH plasma levels ($P = 0.025$), which means that the two physician groups had somewhat different patterns of change over the sampling days. Post hoc

Table 2

Crude means and standard deviations (SD) for metabolic variables.

	Anaesthesiologists ($n = 18$)						Paediatricians and ENT surgeons ($n = 17$)					
	Day work		1 day after night work		3 days after night work		Day work		1 day after night work		3 days after night work	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Glucose (mmol/l)	5.2	(0.5)	5.2	(0.4)	5.2	(0.4)	4.8	(0.3)	4.9	(0.4)	5.0	(0.4)
Insulin (mIE/l)	4.5	(2.4)	5.0	(2.2)	5.1	(2.8)	3.6	(1.3)	4.0	(1.5)	3.5	(1.1)
QUICKI	0.4	(0.04)	0.4	(0.3)	0.4	(0.02)	0.4	(0.03)	0.4	(0.04)	0.4	(0.02)
TSH (mU/l)	1.9	(0.6)	1.5	(0.5)	1.6	(0.6)	1.9	(0.9)	1.4	(0.6)	2.0	(0.8)
fT4 (pmol/l)	16.2	(1.7)	16.2	(1.5)	15.9	(1.6)	16.1	(2.4)	16.1	(2.3)	15.5	(2.5)
HDL (mmol/l)	1.5	(0.5)	0.9	(0.4)	1.4	(1.5)	0.8	(0.2)	0.7	(0.2)	0.8	(0.2)
LDL(mmol/l)	3.0	(0.4)	1.6	(0.4)	1.5	(0.3)	1.6	(0.3)	1.5	(0.4)	1.5	(0.4)
TG (mmol/l)	0.9	(0.6)	3.2	(0.7)	3.2	(0.8)	3.0	(0.9)	2.8	(0.8)	2.7	(0.6)
IGF-1 (µg/l)	191	(43)	179	(46)	187	(50)	184	(40)	186	(64)	175	(56)
Testosterone (nmol/l)												
Women	1.2	(0.6)	0.9	(0.2)	1.1	(0.4)	1.7	(0.7)	2.1	(0.9)	1.8	(0.9)
Men	15	(3.9)	14.0	(3.7)	16	(4.5)	17	(4.6)	17	(5.0)	17	(2.6)
Testosterone/SHBG (nmol/l)												
Women	0.03	(0.03)	0.02	(0.01)	0.03	(0.02)	0.02	(0.02)	0.03	(0.02)	0.02	(0.01)
Men	0.4	(0.1)	0.4	(0.1)	0.4	(0.2)	0.5	(0.1)	0.5	(0.2)	0.5	(0.2)

QUICKI, measurement of glucose intolerance; TSH, thyroid-stimulating hormone; fT4, free thyroxine; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglycerides; IGF-1, insuline growth factor-1; SHBG, steroid hormone binding globuline.

Table 3

Post hoc evaluation of the interaction between day and group on TSH levels (mU/l).

	Anesthesiologists ($n = 18$)		Paediatricians and ENT surgeons ($n = 17$)		P-value (between groups)
	Mean	95% CI	Mean	95% CI	
Day work	1.83	1.51; 2.14	1.92	1.56; 2.29	0.693
1 day after night work	1.37	1.04; 1.70	1.43	1.06; 1.79	0.83
3 days after night work	1.52	1.19; 1.86	2.03	1.67; 2.40	0.054
	P-value		P-value		
Day work vs. 1 day after night work	<0.001	–	<0.001	–	–
Day work vs. 3 days after night work	0.015	–	0.411	–	–
1 day after night work vs. 3 days after night work	0.230	–	<0.001	–	–

CI, confidence interval; TSH, thyroid-stimulating hormone. Results are adjusted for age, gender and weight.

evaluation showed that both the anaesthesiologists and paediatricians/ENT surgeons secreted less TSH 1 day after night-call duty compared with an ordinary workday (28% and 26% less, respectively). In contrast to the anaesthesiologists, the plasma levels of paediatricians/ENT surgeons returned to baseline levels when measured 3 days after night-call duty (Table 3).

Regarding fT4, there was a statistically significant main effect of sampling day ($P = 0.033$), but no effect of group and no interaction. Pairwise post hoc testing showed a reduction of 3% in fT4 on the third day after night call, compared with fT4 plasma levels on the ordinary workday and 1 day after night-call duty ($P = 0.028$ and $P = 0.018$, respectively).

Because of the marked differences in testosterone plasma levels between men and women, these were analysed separately for each gender. There were no significant differences in testosterone levels between physician groups or days (Table 2). Adjustment for steroid hormone-binding globulin levels did not change the results.

Table 4

Crude medians and percentiles for salivary cortisol measures in anaesthesiologists ($n = 17$) and paediatricians and ENT surgeons ($n = 14$).

	Day work			Night work on call			3 days after night work on call			Day off work		
	Median	10th perc.	90th perc.	Median	10th perc.	90th perc.	Median	10th perc.	90th perc.	Median	10th perc.	90th perc.
Anaesthesiologist												
Separate cortisol samples (μg/l)												
Awakening	2.8	1.3	5.5	2.4	1.5	6.0	3.3	1.0	6.0	2.3	0.8	4.1
+ 30 min	3.4	1.7	6.9	2.9	1.6	6.9	4.4	2.2	5.6	2.7	1.0	4.8
+ 8 h	0.7	0.2	3.0	0.8	0.2	1.9	0.6	0.1	15	0.7	0.2	8.2
At 21.00 hours	0.2	0.04	0.8	0.2	0.05	1.0	0.1	0.03	150	0.1	0.02	36
Cortisol index												
Max. morning level (μg/l)	4.4	2.0	6.9	3.0	1.7	7.2	4.7	2.5	6.3	3.2	1.7	5.2
Awakening response (%)	41	−41	200	17	−40	65	35	−5.6	379	30	−58	372
Decline over the day (μg/l)	−3.9	−6.6	−1.8	−2.9	−6.7	−1.6	−4.4	−5.5	144	−2.2	−5.2	33
Paediatricians and ENT surgeons												
Separate cortisol samples (μg/L)												
Awakening	2.9	1.1	23	3.7	1.4	8.3	2.2	0.4	4.7	–	–	–
+ 30 min	4.1	1.8	5.8	3.2	0.5	8.7	3.8	2.3	9.3	–	–	–
+ 8 h	0.8	0.02	2.8	1.0	0.4	3.6	1.0	0.1	2.9	–	–	–
At 21.00 hours	0.3	0.01	1.3	0.6	0.07	1.3	0.3	0.02	44	–	–	–
Cortisol index												
Max. morning level (μg/l)	4.3	2.8	23	5.2	1.4	8.8	4.0	2.4	9.2	–	–	–
Awakening response (%)	32	–88	312	–16	–82	269	121	–27	673	–	–	–
Decline over the day (μg/l)	–3.7	–22	–2.6	–5.6	–8.7	–2.2	–2.8	–9.2	37	–	–	–

Saliva

As expected, the cortisol levels differed significantly between the various sampling times of the day ($P < 0.001$). Descriptive data are presented in Table 4. There was a significant interaction between sampling day and group for morning maximum cortisol level ($P = 0.047$). Post hoc analysis of the interaction revealed that paediatricians/ENT surgeons had a higher maximum cortisol level on the morning preceding night-call duty than on the morning of an ordinary workday [mean difference: + 1.91 μg/l (95% CI: 0.49–3.32), $P < 0.009$], corresponding to a difference of 48%. Additional sampling for the anesthesiologists on a day off work (at least 4 days from work on call) made it possible to make further comparisons within this group, and showed a 35% lower morning maximum level on the day off compared with both day work ($P = 0.005$) and the third day after work on call ($P = 0.001$).

Discussion

There are several studies on physicians' well-being and performance in relation to night-call duty, but knowledge of the physiological effects is scarce. In contrast to our expectations, the metabolic response to night-call duty was modest. Only TSH and fT4 plasma levels were affected by night-call duty, whereas plasma levels of glucose, insulin, HDL, LDL, TG, IGF-1, testosterone and cortisol were fairly unaffected. However, night-call duty seemed to affect TSH levels among anaesthesiologists more than among paediatricians and ENT surgeons. While both groups initially showed suppressed TSH levels in response to night-call duty, it was only among the group of paediatricians/ENT surgeons that TSH returned to levels similar to the ordinary workday when measured 3 days after night-call duty. Although all values were within the reference limits of the laboratory, these differences might be of biological importance. To our knowledge, such an effect has not been reported before, and should be further studied. Paediatricians/ENT surgeons also showed a higher maximum morning cortisol level on the morning preceding night-call duty indicating a stronger activation of the HPA axis on this day. This pattern was not observed among the anaesthesiologists. But as the participants showed normal diurnal variations of cortisol, with low values in the evening, the observed difference is not likely to be of any great practical significance.

Despite the considerable effort required from the study subjects, the participation rate was satisfactory. A lower participation among the paediatricians and ENT surgeons in saliva sampling was explained by unforeseen family matters and schedule changes on short notice, but probably did not affect the results. In view of the few differences, one might consider whether the paediatricians/ENT surgeons had a work situation equally demanding to that of the anaesthesiologists. This cannot be excluded. However, the purpose was not to find specialities with the largest possible discrepancies in work load, but rather to answer the question whether the physiological effects of the total work situation for the anaesthesiologist was different from that of other specialists. Accordingly, the clearly defined differences in work tasks and areas of responsibilities during night-call duty associated with the position as anaesthesiologist or paediatrician/ENT surgeon seem not to be reflected in physiological reactions.

The comprehensive monitoring could have been a stress exposure in itself; however, the use of a counter-balanced design made this problem redundant. The monitoring schedule for cortisol was not fully congruent with that for TSH. Instead of sampling 1 day after night-call duty, samples were taken during the day, when night-call duty commenced, in order to capture a possible stress effect of expectation. Our saliva cortisol analyses were precise and sensitive; however, not fully compatible with results obtained using RIA methods, as a result of cross-reactivity with other substances in the RIA. There is a lack of sensitivity in the immunological methods for measuring urinary cortisol and not applying chromatographic separation (26) and interlaboratory comparisons for determination of saliva cortisol point in the same direction (25, 27). Cortisol values beneath the formal detection level for the method were included in the statistical analyses, but exclusion of these values did not change the main results.

The most insensitive statistical test performed in the study was an independent samples *t*-test between two means for 15–19 persons. On these premises, the power was 0.8 for detecting a difference of about 1 standard deviation (SD), which was considered to be biologically significant. The repeated measurements tests yielded an even higher power. Thus, the prerequisites for finding clinically meaningful differences were fulfilled.

The TSH findings indicate a metabolic change caused by working on night call. This effect is probably a result of a stress-induced inhibition on the hypothalamic level. In both animal and human experimental studies, acute stress has been shown to cause a decline in TSH plasma levels, without any parallel drops in fT4 (28). The TSH decline may therefore represent a direct stress effect or mediated by recovery sleep after sleep debt (12). Such sleep includes a larger fraction of deep sleep, which is known to inhibit the TSH secretion to some extent; this effect might also be mediated by a phase shift in the diurnal rhythm. In comparison to cortisol, TSH is more easily affected in this respect (12, 29). The fT4 changes were so small that they were considered to be irrelevant from a biological perspective. The results were not explained by different sampling times and we do not believe that they were an effect of multiple inference.

In contrast to our expectations, there was no clear-cut effect on cortisol in the restitutional phase. However, the cortisol rise for paediatricians/ENT surgeons in the morning preceding night call may indicate a higher physiological stress level. The anaesthesiologists' lower morning maximum level on the day off, is in concordance with earlier studies (30, 31).

During recent years there have been several reports on alterations in the diurnal circadian cortisol secretion of shift workers (17, 32); however, these studies are dealing with classic rotating shift work and are not fully comparable to night-call duty.

The limited reactivity in the HPA axis of the present physicians related to work on call, and the stability in most other metabolic factors, may be explained by a 'healthy worker selection', meaning that those who could not stand the workload had left. Furthermore, the majority of participants had a considerable experience of working on call, and were probably confident of being able to handle emergency situations. Human experimental studies have shown that an individual's expectation of coping with a stressful work situation has a great impact on cortisol secretion (33). In addition, experienced intensive care nurses and physicians had lower cortisol levels and reactivity than their less-experienced colleagues (34). Accordingly, the larger share of residents in relation to fully licensed specialists in the group of paediatricians/ENT surgeons might explain the higher morning maximum cortisol before work on call. It has been argued that data on links between cortisol levels and mental stress under working-life conditions are inconsistent. It might be that greater stress than is normally encountered in the work place, even that found in demanding night-call work, is needed to evoke and sustain a measurable HPA activation (35).

The present findings do not imply any serious health effects concerning metabolic changes and only minor differences between specialist groups by work on call. However, the physiological data reflect only a short-term perspective.

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References

1. Denisco RA, Drummond JN, Gravenstein JS. The effect of fatigue on the performance of a simulated anesthetic monitoring task. *J Clin Monit* 1987; **3**: 22–4.
2. Åkerstedt T. *Arbetstider, Hälsa och Säkerhet [working time, health and security]. Report No: 299*. Solna: Institute of psychosocial medicine. Karolinska Institute, 2001.
3. Arnedt JT, Owens J, Crouch M, Stahl J, Carskadon MA. Neurobehavioral performance of residents after heavy night call vs after alcohol ingestion. *JAMA* 2005; **294**: 1025–33.
4. Svärdsudd K, Wedel H, Gordh T Jr. Mortality rates among Swedish physicians: a population-based nationwide study with special reference to anesthesiologists. *Acta Anaesthesiol Scand*, 2002; **46**: 1187–95.
5. Hagmar L. Is the life expectancy of anesthesiologists decreased? *Scand J Work Environ Health* 2003; **29**: 83–4.
6. Katz JD. Do anesthesiologists die at a younger age than other physicians? Age-adjusted death rates. *Anesth Analg* 2004; **98**: 1111–3.
7. Aasland OG. Mortality of anesthesiologists, pediatricians, and other specialists in Norway. *Acta Anaesthesiol Scand* 2002; **46**: 1200–2.
8. Juel K, Husum B, Viby-Mogensen J, Viskum S. Mortality among anesthesiologists in Denmark, 1973–95. *Acta Anaesthesiol Scand* 2002; **46**: 1203–5.
9. Ohtonen P, Alahuhta S. Mortality among Finnish anesthesiologists from 1984–2000. *Acta Anaesthesiol Scand* 2002; **46**: 1196–9.
10. Elenkov IJ, Wilder RL, Chrousos GP, Vizi ES. The sympathetic nerve–an integrative interface between two supersystems: the brain and the immune system. *Pharmacol Rev* 2000; **52**: 595–638.
11. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. *Lancet* 1999; **354**: 1435–9.
12. Goichot B, Weibel L, Chapotot F, Gronfier C, Piquard F, Brandenberger G. Effect of the shift of the sleep-wake cycle on three robust endocrine markers of the circadian clock. *Am J Physiol* 1998; **275**(2 Part 1): E243–8.
13. Axelsson J, Ingre M, Åkerstedt T, Holmback U. Effects of acutely displaced sleep on testosterone. *J Clin Endocrinol Metab* 2005; **90**: 4530–5.
14. Axelsson J, Åkerstedt T, Kecklund G, Lindqvist A, Attefors R. Hormonal changes in satisfied and dissatisfied shift workers across a shift cycle. *J Appl Physiol* 2003; **95**: 2099–105.
15. Weibel L, Follenius M, Spiegel K, Gronfier C, Brandenberger G. Growth hormone secretion in night workers. *Chronobiol Int* 1997; **14**: 49–60.
16. Kudielka BM, Kirschbaum C. Sex differences in HPA axis responses to stress: a review. *Biol Psychol* 2005; **69**: 113–32.

17. Kudielka BM, Buchtal J, Uhde A, Wust S. Circadian cortisol profiles and psychological self-reports in shift workers with and without recent change in the shift rotation system. *Biol Psychol* 2007; **74**: 92–103.
18. Munck A. Gucocorticoid action: physiology. In: De Groot LJ, Jameson JL, Burger HG et al. *Endocrinology* 4th edn. Philadelphia: WB Saunders Co., 2001: 1632–46.
19. Chrousos GP, Gold PW. A healthy body in a healthy mind–-and vice versa–the damaging power of 'uncontrollable' stress. *J Clin Endocrinol Metab* 1998; **83**: 1842–5.
20. Rosmond R, Dallman MF, Björntorp P. Stress-related cortisol secretion in men: relationships with abdominal obesity and endocrine, metabolic and hemodynamic abnormalities. *J Clin Endocrinol Metab* 1998; **83**: 1853–9.
21. Rosmond R. Stress induced disturbances of the HPA axis: a pathway to Type 2 diabetes? *Med Sci Monit* 2003; **9**: RA35–9.
22. Knutsson A. Health disorders of shift workers. *Occup Med (Lond)* 2003; **53**: 103–8.
23. Larsson J, Holmstrom I, Rosenqvist U. Professional artist, good Samaritan, servant and co-ordinator: four ways of understanding the anaesthetist's work. *Acta Anaesthesiol Scand* 2003; **47**: 787–93.
24. Katz A, Nambi SS, Mather K et al. Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab* 2000; **85**: 2402–10.
25. Jönsson BAG, Malmberg B, Amilon A, Garde AH, Orbaek P. Determination of cortisol in human saliva using liquid chromatography-electrospray tandem mass spectrometry. *J Chromatogr B Analyt Technol Biomed Life Sci* 2003; **784**: 63–8.
26. Murphy BEP. Lack of specificity of urinary free cortisol determinations: why does it continue? *J Clin Endocrinol Metab* 1999; **84**: 2258–9.
27. Garde AH, Hansen AM, Nikolajsen TB. An inter-laboratory comparison for determination of cortisol in saliva. *Accred Qual Assur* 2003; **8**: 16–20.
28. Scanlon M. Thyroid-releasing hormone and thyroid-stimulating hormone. In: DeGroot L, ed. *Endocrinology*, 4th edn. Philadelphia: Saunders, 2001: 1279–89.
29. Tsigos C, Chrousos GP. Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress. *J Psychosom Res* 2002; **53**: 865–71.
30. Schlotz W, Hellhammer J, Schulz P, Stone AA. Perceived work overload and chronic worrying predict weekend-weekday differences in the cortisol awakening response. *Psychosom Med* 2004; **66**: 207–14.
31. Kunz-Ebrecht SR, Kirschbaum C, Marmot M, Steptoe A. Differences in cortisol awakening response on work days and weekends in women and men from the Whitehall II cohort. *Psychoneuroendocrinology* 2004; **29**: 516–28.
32. Karlson B, Eek F, Hansen AM et al. Diurnal cortisol pattern of shift workers on a workday and a day off. *Scand J Work Environ Health* 2006; Suppl. 2: 27–34.
33. Gaab J, Rohleder N, Nater UM, Ehlert U. Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal. *Psychoneuroendocrinology* 2005; **30**: 599–610.
34. Fischer JE, Calame A, Dettling AC, Zeier H, Fanconi S. Experience and endocrine stress responses in neonatal and pediatric critical care nurses and physicians. *Crit Care Med* 2000; **28**: 3281–8.
35. Hjortskov N, Garde AH, Örbaek P, Hansen AM. Evaluation of salivary cortisol as a biomarker of self-reported mental stress in field studies. *Stress and Health* 2004; **20**: 91–8.

Address:
Birgitta Malmberg
Department of Occupational and Environmental Medicine
Lund University Hospital
SE-221 85 Lund
Sweden
e-mail: birgitta.malmberg@med.lu.se

Study II

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ORIGINAL ARTICLE

Heart rate variability changes in physicians working on night call

Birgitta Malmberg · Roger Persson · Per Flisberg · Palle Ørbaek

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Abstract

Purpose Adverse effects by night-call duty have become an important occupational health issue. The aim of this study was to investigate whether the heart rate variability (HRV) differed during recovery from day work and night-call duty between distinct physician specialities.

Methods We studied the impact of a 16-h night-call duty on autonomic balance, measured by HRV, among two physician groups differing with respect to having to deal with life-threatening conditions while on call. Nineteen anaesthesiologists (ANEST) and 16 paediatricians and ear, nose and throat surgeons (PENT) were monitored by ambulatory digital Holter electrocardiogram (ECG). Heart rate variability was analysed between 21:00 and 22:00 after an ordinary workday, on night call and in the evening post-call. Absolute and normalized high-frequency power (HF, HFnu) were the main outcome variables, expressing parasympathetic influence on the heart.

Results ANEST had lower HF power than PENT while on night call and post-daytime work ($p < 0.05$), but not at post-night call. In the whole group of physicians, HFnu was lower on call and post-daytime work compared with post-night-call duty ($p < 0.05$).

Conclusions The physiological recovery after night duty seemed sufficient in terms of HRV patterns for HFnu, reflecting autonomic balance and did not differ between specialities. However, the less dynamic HRV after daytime work and during night-call duty in the ANEST group may indicate a higher physiological stress level. These results may contribute to the improvement of night-call schedules within the health care sector.

Keywords Shift work · Occupation · Cardiovascular · Stress · Biomarker · Anaesthesiologist

B. Malmberg (✉)
Division of Occupational and Environmental Medicine, Department of Laboratory Medicine, Lund University, 221 85 Lund, Sweden
e-mail: birgitta.malmberg@med.lu.se

R. Persson · P. Ørbaek
National Research Centre for the Working Environment, Copenhagen, Denmark

P. Flisberg
Department of Anaesthesiology and Intensive Care Medicine, Lund University, Lund, Sweden

Introduction

To provide 24-h health care, physicians have to work in shifts and on odd hours. There are many reports on classic rotating shift work and stress, showing negative effects on subjective health, well-being and sleep, and also implying increased risk of ischaemic heart disease and metabolic syndrome (Knutsson 2003). The irregular character and extended night shifts (16 h or more) makes it difficult to compare night call with classic rotating shift work. Indeed, studies of physicians have shown that night-call duty with high demands, long working hours and disrupted sleep may cause a strain on the individual leading to impaired performance and discomfort (Denisco et al. 1987; Lockley et al. 2004; Arnedt et al. 2005), while less is known about the physiological effects of working on call. Although a high degree of mental and physiological activation is expected to follow on-call duty, the crucial issue, from a health perspective, is to what degree such activation is sustained post-call. Hence, is it possible to recover the next day after working on call? The lack of scientific evaluation of restitution from on-call duty became obvious when the work situation of anaesthesiologists was subject to public debate in Sweden, some years ago (Svardsudd et al. 2002; Hagmar 2003). Indeed, correlations between high on-call workload and subjective symptoms have been reported for anaesthesiologists (Lindfors et al. 2006).

The incentive for this study was a request from a group of anaesthesiologists at a university hospital, for an evaluation of their work on night call, from a physiological perspective. Therefore, a comprehensive controlled longitudinal field study of physiological restitution after night-call duty was launched. It consisted of several sub-studies, each focusing on different aspects and potential physiologic effects of the physician's work-time schedules. We have previously reported that the impact of night-call duty on metabolic processes was limited (Malmberg et al. 2007), and effects on sleep were considerable (Malmberg et al. 2010). This study presents the results of heart rate variability (HRV) monitoring focusing on changes in activation of the autonomic nervous system (ANS). Frequency domain analysis of HRV was chosen as a sensitive non-invasive method for monitoring the dynamics of the ANS. By measuring HRV in the so-called frequency domain, it is possible to distinguish periodic, interpretable, components of the signal. These rhythms mirror the autonomic balance or, more precisely, periodic fluctuations in the absolute and relative impact of sympathetic and parasympathetic tone in the ANS, which seem crucial for survival and good health (TaskForce 1996; Pumprla et al. 2002; Kara et al. 2003). It is generally accepted that the parasympathetic modulations of HR are mainly due to respiratory sinus arrhythmia. These modulations have a faster course than the alterations mediated by sympathetic activity. Because they operate at different frequencies, the actions can be identified by different frequency spectra. Inability to unwind and recover is reflected on a low parasympathetic influence on HRV (Hanson et al. 2001). A high level of HRV is advantageous from a health perspective, and especially a high level of high-frequency (HF) power is energy-saving for the heart because of rapid regulation of activity. Psychological stress experiments (Delaney and Brodie 2000; Schnall et al. 2000; Hall et al. 2004; Hjortskov et al. 2004) and field studies measuring perception of work stressors (Clays et al. 2010) and job strain at work (Collins et al. 2005) have shown a decreased parasympathetic influence on HRV. Furthermore, low HRV levels have shown to be predictive of post-infarction mortality (Bigger et al. 1993) and have also been associated with work stress in cross-sectional studies (Vrijkotte et al. 2000).

The main objective of this study was to investigate whether the ANS regulation of the heart, measured by HRV, differed between two distinct groups of physicians in their recovery-patterns from day work and night-call duty. We compared one group consisting of paediatricians and ear, nose and throat surgeons (PENT), with a group of anaesthesiologists (ANEST) on night call. The latter group had, by means of their work characteristics, to deal with severe and immediately life-threatening conditions, the reason why it was hypothesized that the parasympathetic impact on HRV in the ANEST group would be lower, especially during night-call duty, compared with the PENT group. Additionally, we looked for general effects of physicians' night-call duty on autonomic balance. It was hypothesized that night-call work would imply a lowered relative parasympathetic tone on the heart, as measured by HRV, in comparison with post-daytime work and post-night call, and that there would also be lower levels during the first evening post-night call compared with post-daytime work, which in that case would be considered as an insufficient physiological recovery.

Methods

Participants

We studied two groups of physicians: anaesthesiologists, ANEST ($n = 19$) and paediatricians/ear, nose and throat surgeons, PENT ($n = 17$). These groups had distinctly different work characteristics when on call. Originally, only paediatricians were planned to constitute the control group. However, during recruiting there turned out to be fewer available in clinical work than expected, why we chose to include also ENT surgeons. All physicians worked at the same university hospital and performed on-call duty, which involved working recurrent night shifts. The participation rate was 19/24 (79%) in the ANEST group and 17/25 (68%) in the PENT group. Demographic data were collected using a questionnaire (Table 1). In both groups, 75% of the subjects had a minimum of 3 years' experience form night-call duty within the specialty. The family situation was almost identical in the two physician groups, as was the reported degree of sleep insufficiency (Karolinska Sleep Questionnaire, QSK (Akerstedt et al. 2002)) and negative impact of family matters on work (Family–Work Conflict Scale (Netemeyer et al. 1996)). The groups were homogenous, with low to moderate alcohol consumption, normal liver function, serum insulin, plasma glucose, and blood lipids (Malmberg et al. 2007) and also absence of cardiovascular or neurological disease. However, there were two subjects with sub-clinical hypothyroidism and one with sleep apnoea syndrome, who was well-functioning with CPAP treatment. All participants gave written informed consent, and the study was approved by the Ethics Committee at Lund University (LU 732-01).

Table 1 Demographic data for participating anaesthesiologists (ANEST) and paediatricians (PENT)

	ANEST (n = 19)	PENT (n = 16[a])
Age[b] (median (interquartile range))	42 (38–49)	38 (30–43)
BMI in kg/m^2 (mean (SD))	24 (2.6)	22 (1.9)
Years of experience of night-call duty[c] (median (interquartile range))	9 (8–17)	12 (3–18)
Years of experience of night-call duty within speciality[d] (median (interquartile range))	7 (3–14)	9 (3–13)
Women (%)	7 (37)	8 (50))
Smokers (%)	1 (5)	0
Position		
Consultants (%)	6 (32)	2 (14)
Registrars (%)	8 (42)	4 (29)
Residents (%)	5 (26)	8 (57)
Social status		
Single	0	1 (7)
Living with other adult, but no children (%)	5 (26)	2 (14)
Living with other adult and children (%)	13 (68)	11 (79)
Living with children, but without other adult (%)	1 (5)	0
Work/home interface		
Worries for family matters influence focus on work (%)	6 (32)	5 (36)
Regular overtime work (once a week or more) (%)	10 (53)	6 (43)
Sleep		
Reports of insufficient sleep (%)	15 (79)	10 (71)

[a] For two participants, only data on age and BMI were available

[b] Total range for ANEST (32–55) and for PENT (26–45)

[c] Total range for ANEST (4–27) and for PENT (0–19)

[d] Total range for ANEST (1–23) and for PENT (0–17)

Working conditions

Both groups had hospital-bound work on call, but with less focus on life-threatening conditions for the PENT group. During night-call duty, the ANEST group took care of the patients' vital functions in major traumas, cardiac arrest and acute operations. They were also in charge of the post-operative ward and intensive care unit, handling patients with vital organ failure. All participating physicians could expect to have a high workload on call, but the anaesthesiologists also had generally to focus on life-threatening conditions. Furthermore, they differed from the other two specialties by giving service to the whole hospital and facilitating the work of several other clinics in the care of severely ill patients (Larsson et al. 2003). In contrast, the PENT group worked at the emergency ward taking care of acute cases in their specialty, but they did not have the kind of service and facilitation tasks required of the ANEST group. These circumstances showed a clear between-group exposure contrast in activity levels and mental demands and were the reasons for choosing the present specialist groups. For all physicians, ordinary daytime work was performed from 08:00 to 16:30. Night-call duty started at approximately 16:00 and lasted for about 16 h (until around 08:00 the next day). All participants had on average three night-call duties per month and at least 1 day off after each night call, but work schedules differed somewhat between specialties. The ANEST group and paediatricians in the PENT group had separate night-call weeks every fourth to sixth week, during which they worked two to three nights. In the PENT group, the ENT surgeons had single nights on call every second or third week, and in contrast to the two other specialties, they generally had a normal working day directly before night call. On-duty rooms were available for rest or sleep if there were no patients in need of attention.

Heart rate variability

Monitoring and calculation of primary and secondary HRV variables were done in a standardized manner (TaskForce 1996) by the use of a digital, portable monitoring unit for Holter ECG (DXP 1000; Braemar systems, Chicago, IL, USA) and Aspect software (Danica Biomedical AB, Borlänge, Sweden) (Nygards and Hulting 1979). The sampling frequency was 125 Hz, and a mathematical algorithm was used to specify the fiducial point, which defined the ECG signal for contraction of the heart ventricles (the so-called QRS complex). After computerized primary analysis, all ECG files were edited manually for detection of artefacts and categorization of non-sinus beats by a trained biomedical analyst. Heart rate variability power spectra were calculated with fast Fourier transformation (FFT), and expressed as power spectral density in ms^2. The primarily computed variables were as follows: high-frequency (HF) (0.15–0.4 Hz), low-frequency (LF) (0.04–0.15 Hz), very low frequency (VLF) (<0.04 Hz) power and total power (TP), i.e., the sum of all frequency components. High-frequency power mirrors the parasympathetic modulation of HR, while LF power mirrors the sympathetic modulation, and some parasympathetic modulations (TaskForce 1996). Very low frequency is not well characterized, but is suggested to reflect slow thermoregulation in the body. According to recommendations (TaskForce 1996), VLF was subtracted from the TP in the indices below. Total power has no specific physiological correlate, but mirrors total variability. In addition, two HRV indices were calculated as follows: HF power in normalized units (%), calculated as HFnu (%) = (HF/(TP − VLF)) × 100 and reflecting relative parasympathetic influences, and LF/HF power, often referred to as "sympathovagal balance", with values fairly reciprocal to HFnu. Mean HR was also calculated.

Collection and analysis of heart rate variability data

All participants followed an individually designed schedule for sampling, corresponding to their work on night call. Holter electrocardiography (ECG) was made on three occasions: (1) from one ordinary workday to the next (16:00–16:00); (2) during night-call duty (16:00–08:00); and (3) continuously during the following post-call period (08:00–08:00). To compensate for any effect of habituation on the sampling procedures, ECGs were performed in a counterbalanced design. Accordingly, the first occasion for sampling was equally distributed between an ordinary workday and night-call duty. In this study, the specific time period, the so-called strategic time windows (TaskForce 1996; Schnall et al. 2000) for frequency domain analysis was chosen to reflect the degree of "unwinding" at the end of the day, but was not to interfere with sleeping time. Analyses were performed for means of six consecutive 10-min periods during 1 h in the evening (21:00–22:00) and compared between monitoring days. The participants were blind to the fact that this time window would be analysed, so we could not require detailed information of their activities during this hour. However, they kept a log book during the whole monitoring period where they were instructed to report potentially strenuous activities, e.g., if they had to respond to an emergency alarm while on call or had been exercising off duty. Except for one occasion, none of these activities were reported during the specific 1-h time windows where HRV was analysed. According to reports in the log book at bedtime, the outcome expectancy for the next day was fairly positive and similar for both physician groups irrespective of nights before ordinary day work or night duty.

During quality assurance, one participant in the PENT group had to be completely excluded because of too many non-sinus beats, which reduced the PENT group to $n = 16$.

Three of the 1-h ECG recordings had to be cancelled, because it was impossible to find a suitable period in the working schedule. In addition, seven recordings had to be excluded because of frequent non-sinus beats (>35 beats/hour) or abundant disturbances (25–50% of the registration). This resulted in a total of 10 (10%) missing files equally distributed between the physicians groups in the final analyses. In the remaining ECG files, there was a maximum of 4% of disturbances in a 1-h registration and the high quality enabled us to use 95–100% of each ECG recording in analyses.

Statistics

The statistical computations were done using SPSS 15.0 (SPSS, Inc., Chicago, IL, USA). p values <0.05 were considered statistically significant. Due to a positively skewed distribution, frequency domain crude data were described as medians and percentiles. Accordingly, frequency domain data were logarithmically transformed (log10) before being subjected to analysis and then converted back to their original scale units before presentation in tables. A repeated measures model was specified using the linear mixed models module of SPSS. Categorical predictors were ECG-recording day (three levels: (1) post-daytime work; (2) night call; and (3) post night-call) and specialist group (ANEST versus PENT). All HRV variables were dependent variables. To detect differential patterns of reactions between the two groups, the statistical modelling also included two-way interaction between ECG-recording day and group. The selections of covariates were governed by biological considerations and were included irrespective of statistical significance. Accordingly, all HRV estimates were adjusted for age, gender and body mass index (BMI) (weight (kg)/(length (m^2)). A first-order autoregressive covariance structure (AR1) was applied, because it provided the best fit. For post hoc testing of interaction effect between group and day, a new four-group variable was created, as follows: ANEST post-daytime work, ANEST night call, ANEST post night-call, PENT post-daytime work, PENT night call, and PENT post night-call. The study design that entailed repeated measurements on each individual was estimated with the G-Power software to be sufficiently powerful to find effects of about 0.5 SD of differences between means with a power of about 0.8 (Faul et al. 2007).

Results

Heart rate variability

Crude data for HRV are presented in Table 2. There were main effects of group for HF, HFnu and TP. In detail, HF

Table 2 Crude median (Mdn) and percentiles (10–90) for heart rate variability (HRV) frequency domain measures between 21:00 and 22:00 h

	ANEST ($n = 19$)		PENT ($n = 16$)	
	Mdn	10–90	Mdn	10–90
Post-daytime work	($n = 17$)		($n = 13$)	
HF power (ms^2)	174	48–578	286	83–1,388
HFnu (%)	15.8	8.5–28.3	18.0	10.9–38.5
LF/HF power	5.3	2.5–10.8	4.6	1.6–8.2
LF power (ms^2)	1,080	276–2,262	1,361	426–3,602
VLF power (ms^2)	1,293	429–3,264	2,392	759–7,528
TP (ms^2)	2,682	880–5,772	4,031	1,440–14,158
Night call	($n = 18$)		($n = 14$)	
HF power (ms^2)	222	69–524	352	69–1,280
HFnu (%)	12.9	7.4–26.6	17.5	10.3–30.2
LF/HF power	6.7	2.8–12.5	4.7	2.3–8.7
LF power (ms^2)	1,532	398–2,833	1,464	444–4,813
VLF power (ms^2)	1,414	484–3,619	1,976	493–5,842
TP (ms^2)	3,042	1,052–5,914	4,062	1,039–12,776
Post-night call	($n = 17$)		($n = 16$)	
HF power (ms^2)	261	91–812	350	87–1130
HFnu (%)	21.8	10.5–49.0	20.9	13.6–49.6
LF/HF power	3.6	1.0–8.5	3.8	1.0–6.4
LF power (ms^2)	992	272–2,568	1,066	243–3,461
VLF power (ms^2)	1,232	414–3,424	1,854	368–5,529
TP (ms^2)	2,956	1,014–6,467	3,032	1,087–10,417

ANEST anaesthesiologists; *PENT* paediatricians and ENT surgeons; *HF* high-frequency power; *HFnu* high-frequency power in normalized units (HF/(TP − VLF)) × 100; *LF* low frequency; *VLF* very low frequency; *TP* total power

power was lower for ANEST (mean = 185 ms^2, 95% CI = 134–255) compared with PENT (mean = 358 ms^2, 95% CI = 251–509) ($p = 0.01$). ANEST had also lower HFnu values (mean = 16.7, 95% CI = 16.0–20.3) compared with PENT (HFnu: mean = 21.2, 95% CI = 14.6–18.3) ($p = 0.02$). TP was lower for ANEST (mean = 2,393 ms^2, 95% CI = 1,941–2,951) compared with PENT (mean = 3,715 ms^2, 95% CI = 2,944–4,677) ($p = 0.01$).

There were significant main effects of day in HFnu, but not in HF power (Table 3). The whole group of physicians had lower HFnu on post-daytime work, as well as on night call compared with post-night call ($p = 0.002$ and $p < 0.001$, respectively). No significant difference was found between post-daytime work and night call ($p = 0.13$). The day and group differences for LF/HF power were as expected reciprocal to the patterns for HFnu, which is why they are not reported in detail. Furthermore, there was an interaction between day and group exclusively for HF power. A separate post hoc evaluation showed that ANEST had lower values on post-daytime work and while on night call compared with PENT. No group difference was found post-call. However, the changes in HF between days were divergent for the two groups (Table 4).

Hypothyroidism and sleep apnoea may affect the autonomic regulation of the heart (Inukai et al. 1998; Cacciatori et al. 2000; Aydin et al. 2004). However, results remained the same after exclusion of data from the three diagnosed participants, which is why they were included in the final analyses.

The use of linear mixed models analyses made it possible to use all data, despite the fact that some participants had missing files. However, to examine whether the results were dependent on subjects with incomplete sets of data, a separate analysis on subjects with complete data sets ($n = 27$) was made. These analyses generated the similar results with only minor changes in estimates and p values.

Heart rate

Mean HR was fairly stable between groups and days. For ANEST, the mean (SD) for HR was 74 (11) bpm for post-daytime work, 76 (13) bpm while on night call and 72 (7) bpm post-call. The corresponding values for PENT were 72 (13), 78 (13) and 74 (13). There was no group difference (data not shown in tables).

Discussion

We investigated possible adverse changes in autonomic balance, by means of HRV, in ANEST and PENT working on night call. The two groups of physicians, who were

Table 3 Comparison, between days, in heart rate variability (HRV), expressed as means of six 10-min periods between 21:00 and 22:00 for all participating physicians ($n = 35$), adjusted for age, gender and body mass index (BMI)

HRV estimates	Post-daytime work		Night call		Post-night call		Type III *F* test
	Mean	95% CI	Mean	95% CI	Mean	95% CI	*p* value
HF power (ms^2)	279	216–360	243	190–309	251	196–321	0.332
HFnu (%)	18.0	16.0–20.3	16.4	14.6–18.3	22.8	20.4–25.5	<0.001
LF/HF power	4.3	3.7–5.1	4.9	4.2–5.7	3.1	2.7–3.7	<0.001
LF power (ms^2)	1,156	931–1,432	1,178	964–1,442	813	662–998	<0.001
VLF power (ms^2)	1,694	1,383–2,075	1,507	1,247–1,820	1,259	1,042–1,524	0.072
TP (ms^2)	3,342	2,767–4,036	3,140	2,630–3,741	2,529	2,113–3,020	0.024

HF high-frequency power; *HFnu* high-frequency power in normalized units (HF/(TP − VLF)) × 100; *LF* low frequency; *VLF* very low frequency; *TP* total power

Table 4 Post hoc evaluation of the interaction between day and group on high-frequency (HF) power, in ms^2

Between-group effect	ANEST ($n = 19$)		PENT ($n = 16$)		ANEST versus PENT
	Mean	95% CI	Mean	95% CI	*p* value
Post-daytime work	166	116–238	468	312–703	0.001
Night call	162	115–230	361	245–533	0.006
Post-night call	233	163–333	270	183–340	0.601

Within-group effect	ANEST ($n = 19$)	PENT ($n = 16$)
	p value	*p* value
Post-daytime work versus night call	0.864	0.072
Post-daytime work versus post-night call	0.038	0.003
Night call versus post-night call	0.003	0.037

Linear mixed models were used for post hoc analyses of between- and within-group differences

ANEST anaesthesiologists; *PENT* paediatricians and ENT surgeons

selected to have contrasting work situations with respect to cognitive and emotional activation, showed some general differences. The ANEST group had lower levels of absolute and relative parasympathetic tone (HF power and HFnu), indicating partial support for the expected differences between the groups. Indeed, for this group, HF power was lower in the evening after daytime work and when on night call, but not in the evening post-night call, when compared with the PENT group. The changes in HF between days for ANEST were roughly in accordance with the HFnu changes. In contrast, the unexpected lowered HF-level for PENT post-call was difficult to interpret, particularly when it was not accompanied by significant HFnu changes in the same direction. Analyses on the entire group of physicians showed the normalized parasympathetic tone (HFnu) to be lower post-daytime work and when on night call compared with post-call. The lack of difference, contrary to the hypothesized gradient, between post-daytime work and night call suggests that the physiological impact on these two recordings was comparable and that the physiologically most favourable state, with the highest levels of relative parasympathetic tone, was reached post-call. Accordingly, 1-day rest after night call seemed to be sufficient to obtain a more favourable autonomic balance compared with what was observed during the short recovery after an ordinary workday. It should also be noted that HRV is only one of several potential markers of recovery and not necessarily converging with other physiological and psychological measures. Because standardized procedures for measurement and large reference materials for field-monitored HRV in healthy, ambulant adults are still lacking, detailed comparisons with other studies are difficult to make. Still, total HRV in both physician groups in this study was of the same magnitude as when recorded in supine, healthy persons (TaskForce 1996). Therefore, it may be noted that the general HRV levels observed among participants do not in the short term indicate any raised risk for cardiovascular disease. Whether the observed differences are of long-term relevance is not known.

It has earlier been shown that HRV is a sensitive measure of physiologic stress reactions caused by mentally demanding tasks (Kristiansen et al. 2009). According to a recent review, psychological workload and shift work has been identified as having associations with low HF power in occupational studies (Togo and Takahashi 2009). This is in accordance with our findings for the ANEST group. There are limited numbers of occupational HRV studies from the health care sector. However, nurses working on rotating three-shift system had a higher LF/HF ratio and lower HF during rest in the evening compared with nurses not working night shift (Ishii et al. 2005). Both findings suggested that shift work caused a sympatho-dominant state due to a depressed vagal tone. In a study of ambulance personnel working on 24-h shifts, Aasa and co-workers found a modest lowering of HF on a work shift compared to the following day off exclusively for the group with many health complaints (Aasa et al. 2006). Furthermore, in another study, ambulance men showed a similar pattern with disturbed circadian pattern of HFnu and LF/HF ratio when on call (Mitani et al. 2006). However, the specific study design focusing on diurnal changes limits the possibility to compare with other studies. The closest comparison to this study is the small but well-designed study of emergency physicians by Adams et al. (1998), where a significant increase in sympathetic versus parasympathetic tone was found during night-call duty compared with pre-work and post-call. These results are roughly in accordance with our study on physicians on call concerning the observed decrease in HFnu on night call compared with work on call and post-call. However, in the study by Adams and co-workers, there was no ordinary day work to compare with. Langelotz and co-workers found increased HRV levels in relation to on-call work and no change in LF to HF ratio. However, these unexpected results may be explained by the fact that the ECG monitoring was restricted to standardized 10-min resting periods (Langelotz et al. 2008). In a study of 24 h ECG monitoring on young physicians, an increased level of low-frequency normalized units (LFnu) during night call compared with a control night was shown (Rauchenzauner et al. 2009). These findings do not fully correspond to our results for HFnu, but may be due to different specialist groups and settings for the on-call work. The lack of adjustments for sleep and wake during monitoring in the Rauchenzauner study may also have an impact.

It is well known that physical activity and HR is of importance for instant HRV and that there is an inverse association between HR and HF power, which is somewhat weaker for HFnu (Kuch et al. 2001; Sacha and Pluta 2005). One could therefore suspect that differences in physical activity could account for the observed group and day differences. However, in view of the relatively stable mean HRs across groups and days, and because there were no signs of strenuous physical activity in the analysis windows of the ECG, we consider differences in physical activity to be of limited importance for the observed differences. As regards other potential sources of confounding, such as gender, age, BMI and respiration patterns (Schnall et al. 2000; Kuch et al. 2001), these were all adjusted for, except for breathing. However, considering the small variations in HR and the lack of apparent physical exertion, we do not believe that difference in breathing by physical causes would be the main explanation for day or group divergences. Physical fitness is reported to lower HR, and generally raise HRV, especially the parasympathetic influence, but not necessarily HFnu (Melo et al. 2005). In view of the fairly constant HRs and of adjustments made for BMI in the analyses, a potential divergence of fitness between physician groups would hardly explain the results of the study.

Studies of the general population have shown a decline of HRV with age, but at different rates for the parasympathetic and sympathetic components. It is also reported that women have lower LF and higher HF than men (Britton and Hemingway 2004). In this study, influence of gender was modest and of age very small. However, it was still adjusted for in the statistical analyses. A problem when monitoring HRV is the selection of time windows for analysis. Because of the diurnal variations in HRV, we found it necessary to select and compare the same time window across the three monitoring days. The time, 21:00–22:00, was a priori strategically chosen, as it was likely to reflect unwinding in the evening, but not likely to interfere with bedtime and sleep. On the other hand, this meant that focus was put on comparing night-call duty, with short-term recovery after an ordinary working day, and the longer and planned rest period following night-call duty. Observably, there is no golden standard for which HRV measures to choose when studying occupational stress at the workplace. The use of the relative influence of parasympathetic tone on HRV (HFnu) as a potential biomarker of mental activation is not unequivocal. In clinical field studies, the body position cannot be controlled for, and therefore changes in HF may depend at least partially on changes in total HRV (TP). Indeed, the absolute level of HF power is the best correlate for the specific parasympathetic tone, but it is not recommended to interpret it alone. Therefore, it is also important to look at normalized values, which makes HF power originating from different total power in HRV more comparable. The HFnu also more specifically represent the final outcome of SNS and PNS interaction. On the other hand, this index requires calculations involving LF and TP, which are physiologically somewhat less well characterized compared to HF. Therefore, we chose to present both HF power and HFnu.

There were several study strengths. HRV monitoring was performed during authentic work- and leisure time, with no interference from the researchers. Furthermore, day comparisons were made for identical time windows by a repeated measures design, to rule out effects by diurnal changes and inter-individual variability. Despite a few occasional test-specific drop-outs, the repeated measurements on each individual also gave sufficient power to find fairly small effects of about 0.5 SD of differences between means.

In conclusion, the physiological recovery after night duty seemed sufficient in terms of HRV patterns for HFnu, reflecting autonomic balance and did not differ between specialities. However, the less dynamic HRV after daytime work and during night-call duty in the ANEST group may indicate a higher physiological stress level. These results may contribute to the improvement of night-call schedules within the health care sector.

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References

Aasa U, Kalezic N, Lyskov E et al (2006) Stress monitoring of ambulance personnel during work and leisure time. Int Arch Occup Environ Health 80:51–59

Adams SL, Roxe DM, Weiss J et al (1998) Ambulatory blood pressure and Holter monitoring of emergency physicians before, during, and after a night shift. Acad Emerg Med 5:871–877

Akerstedt T, Knutsson A, Westerholm P et al (2002) Work organisation and unintentional sleep: results from the WOLF study. Occup Environ Med 59:595–600

Arnedt JT, Owens J, Crouch M et al (2005) Neurobehavioral performance of residents after heavy night call vs after alcohol ingestion. Jama 294:1025–1033

Aydin M, Altin R, Ozeren A et al (2004) Cardiac autonomic activity in obstructive sleep apnea: time-dependent and spectral analysis of heart rate variability using 24-hour Holter electrocardiograms. Tex Heart Inst J 31:132–136

Bigger J, Fleiss J, Rolnitzky L et al (1993) The ability of several short-term measures of RR variability to predict mortality after myocardial infarction. Circulation 88:927–934

Britton A, Hemingway H (2004) Heart rate variability in healthy populations: correlates and consequences. In: Malik M, Camm AJ (eds) Dynamic electrocardiography. Blackwell Publishing Futura, New York, pp 90–111

Cacciatori V, Gemma ML, Bellavere F et al (2000) Power spectral analysis of heart rate in hypothyroidism. Eur J Endocrinol 143:327–333

Clays E, De Bacquer D, Crasset V et al (2010) The perception of work stressors is related to reduced parasympathetic activity. Int Arch Occup Environ Health. doi:10.1007/s00420-010-0537-z

Collins SM, Karasek RA, Costas K (2005) Job strain and autonomic indices of cardiovascular disease risk. Am J Ind Med 48:182–193

Delaney JP, Brodie DA (2000) Effects of short-term psychological stress on the time and frequency domains of heart-rate variability. Percept Mot Skills 91:515–524

Denisco RA, Drummond JN, Gravenstein JS (1987) The effect of fatigue on the performance of a simulated anesthetic monitoring task. J Clin Monit 3:22–24

Faul F, Erdenfelder E, Lang A-G et al (2007) G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 39:175–191

Hagmar L (2003) Is the life expectancy of anesthesiologists decreased? Scand J Work Environ Health 29:83–84

Hall M, Vasko R, Buysse D et al (2004) Acute stress affects heart rate variability during sleep. Psychosom Med 66:56–62

Hanson EK, Godaert GL, Maas CJ et al (2001) Vagal cardiac control throughout the day: the relative importance of effort-reward imbalance and within-day measurements of mood, demand and satisfaction. Biol Psychol 56:23–44

Hjortskov N, Rissen D, Blangsted AK et al (2004) The effect of mental stress on heart rate variability and blood pressure during computer work. Eur J Appl Physiol 92:84–89

Inukai T, Takanashi K, Kobayashi H et al (1998) Power spectral analysis of variations in heart rate in patients with hyperthyroidism or hypothyroidism. Horm Metab Res 30:531–535

Ishii N, Dakeishi M, Sasaki M et al (2005) Cardiac autonomic imbalance in female nurses with shift work. Auton Neurosci 122:94–99

Kara T, Nykodym J, Somers VK (2003) Heart rate variability: back to the beginning. J Cardiovasc Electrophysiol 14:800–802

Knutsson A (2003) Health disorders of shift workers. Occup Med Lond 53:103–108

Kristiansen J, Mathiesen L, Nielsen P et al (2009) Stress reactions to cognitively demanding tasks and open-plan office noise. Int Arch Occup Environ Health 82:631–641

Kuch B, Hense HW, Sinnreich R et al (2001) Determinants of short-period heart rate variability in the general population. Cardiology 95:131–138

Langelotz C, Scharfenberg M, Haase O et al (2008) Stress and heart rate variability in surgeons during a 24-hour shift. Arch Surg 143:751–755

Larsson J, Holmstrom I, Rosenqvist U (2003) Professional artist, good Samaritan, servant and co-ordinator: four ways of understanding the anaesthetist's work. Acta Anaesthesiol Scand 47(7):787–793

Lindfors PM, Nurmi KE, Meretoja OA et al (2006) On-call stress among finnish anaesthetists. Anaesthesia 61(9):856–866

Lockley SW, Cronin JW, Evans EE et al (2004) Effect of reducing interns' weekly work hours on sleep and attentional failures. N Engl J Med 351:1829–1837

Malmberg B, Persson R, Jonsson BA et al (2007) Physiological restitution after night-call duty in anaesthesiologists: impact on metabolic factors. Acta Anaesthesiol Scand 51:823–830

Malmberg B, Kecklund G, Karlson B et al (2010) Sleep and recovery in physicians on night call: al longitudinal field study. BMC Health Serv Res 10:239

Melo RC, Santos MD, Silva E et al (2005) Effects of age and physical activity on the autonomic control of heart rate in healthy men. Braz J Med Biol Res 38:1331–1338

Mitani S, Fujita M, Shirakawa T (2006) Circadian variation of cardiac autonomic nervous profile is affected in Japanese ambulance men with a working system of 24-h shifts. Int Arch Occup Environ Health 79:27–32

Netemeyer R, Boles J, McMurrian R et al (1996) Development and validation of work-family conflict and family-work conflict scales. J Appl Psychol 81:400–410

Nygards M-E, Hulting J (1979) An automated system for ECG monitoring. Comput Biomed Res 12:181–202

Pumprla J, Howorka K, Groves D et al (2002) Functional assessment of heart rate variability: physiological basis and practical applications. Int J Cardiol 84:1–14

Rauchenzauner M, Ernst F, Hintringer F et al (2009) Arrhytmias and increased neuro-endocrine stress response during physicians' night shifts: a randomized cross-over trial. Eur Heart J 30:2606–2613

Sacha J, Pluta W (2005) Different methods of heart rate variability analysis reveal different correlations of heart rate variability spectrum with average heart rate. J Electrocardiol 38:47–53

Schnall PB, Bekic K, Landsbergis P, Baker D (eds) (2000) Occupational medicine: the workplace and cardiovascular disease. State of the art reviews. Hanley and Belfus, INC, Philadelphia

Svardsudd K, Wedel H, Gordh T Jr (2002) Mortality rates among Swedish physicians: a population-based nationwide study with special reference to anesthesiologists. Acta Anaesthesiol Scand 46:1187–1195

Task Force (1996) Task force of the European society of cardiology and the North American Society of pacing and electrophysiology: heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force Eur Heart J 17:354–381

Togo F, Takahashi M (2009) Heart rate variability in occupational health. A Systematic Review. Ind Health 47:589–602

Vrijkotte TG, van Doornen LJ, de Geus EJ (2000) Effects of work stress on ambulatory blood pressure, heart rate, and heart rate variability. Hypertension 35:880–886

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Sleep and recovery in physicians on night call: a longitudinal field study

Birgitta Malmberg[1*], Göran Kecklund[2], Björn Karlson[1], Roger Persson[3], Per Flisberg[4], Palle Ørbaek[3]

Abstract

Background: It is well known that physicians' night-call duty may cause impaired performance and adverse effects on subjective health, but there is limited knowledge about effects on sleep duration and recovery time. In recent years occupational stress and impaired well-being among anaesthesiologists have been frequently reported for in the scientific literature. Given their main focus on handling patients with life-threatening conditions, when on call, one might expect sleep and recovery to be negatively affected by work, especially in this specialist group. The aim of the present study was to examine whether a 16-hour night-call schedule allowed for sufficient recovery in anaesthesiologists compared with other physician specialists handling less life-threatening conditions, when on call.

Methods: Sleep, monitored by actigraphy and Karolinska Sleep Diary/Sleepiness Scale on one night after daytime work, one night call, the following first and second nights post-call, and a Saturday night, was compared between 15 anaesthesiologists and 17 paediatricians and ear, nose, and throat surgeons.

Results: Recovery patterns over the days after night call did not differ between groups, but between days. Mean night sleep for all physicians was 3 hours when on call, 7 h both nights post-call and Saturday, and 6 h after daytime work ($p < 0.001$). Scores for mental fatigue and feeling well rested were poorer post-call, but returned to Sunday morning levels after two nights' sleep.

Conclusions: Despite considerable sleep loss during work on night call, and unexpectedly short sleep after ordinary day work, the physicians' self-reports indicate full recovery after two nights' sleep. We conclude that these 16-hour night duties were compatible with a short-term recovery in both physician groups, but the limited sleep duration in general still implies a long-term health concern. These results may contribute to the establishment of safe working hours for night-call duty in physicians and other health-care workers.

Background

Studies of physicians have shown that night-call duty with long work hours, restricted sleep, stress, time pressure, and high demands may cause impaired performance and adverse effects on subjective health [1-4]. Working schedules involving long working hours also seem to have a negative influence on caregivers' decision-making capabilities, which may have a profound impact on patients' safety [5,6]. Although sleep is crucial to recovery and survival, there is limited knowledge about the effects of night-call duty on sleep duration, sleep quality, and recovery time. One might assume effects similar to those from classic rotating shift work, but the irregular character of night-call schedules and the longer shifts make comparison difficult. In a study from 1990, Åkerstedt and co-workers monitored six physicians on night call using ambulatory EEG, which revealed a considerable sleep deficit with only 3 hours of night sleep [7]. However, the requirements for on-call work have changed over the past few decades, with a tendency for more intense night-call work, often resembling a full night shift, but with a successive shortening of shift lengths in return. These changes have made the effects on sleep difficult to anticipate. It has been well documented that night shifts of 24 hours or longer are, in most cases, detrimental to both subjective health and performance [1,3,5,8]. However, studies focusing on shorter night schedules are scarce and there is considerable controversy regarding the optimal length of a night-call shift. Therefore, it is important to study these

* Correspondence: birgitta.malmberg@med.lu.se
[1]Occupational and Environmental Medicine, Dept of Laboratory Medicine, Lund University, Lund, Sweden
Full list of author information is available at the end of the article

aspects of sleep and performance in current night-call schedules to obtain empirical evidence on which to base sound shift scheduling [9,10]. Not only the length of the night-call shift, but also its intensity and mentally demanding character, may be assumed to affect sleep and recovery. Given the characteristics of their work, anaesthesiologists are reported to have a higher mental workload during night duty compared with many other physician groups working on call [11-14]. Indeed, during recent years, occupational stress and impaired well-being in anaesthesiologists have been frequently addressed in the scientific literature [13,15,16]. For the anaesthesiologist on call, the cognitive and emotional load of constantly handling patients with life-threatening conditions, which requires fast and accurate action, may have a greater impact on their sleep and recovery compared with other specialists.

A controlled longitudinal field study was performed at a university hospital. The present study was part of a large field study of physiological restitution after night-call duty, involving several sub-studies, each focusing on different aspects and potential negative health effects of the anaesthesiologists' work schedules: the impact on metabolic factors has been published earlier [17]. The participating clinics agreed that if the results indicated insufficient recovery, the work schedules would be adjusted. Hence, it was expected a priori that sleep duration and quality of sleep would be negatively affected in physicians on night call, especially for anaesthesiologists. The primary aim of this study was therefore to evaluate whether a 16-hour night-call schedule allowed for sufficient recovery in anaesthesiologists compared with other physician specialists handling less life-threatening conditions when on call.

Methods

Participants

We enrolled two groups of physicians. The first group consisted of anaesthesiologists (ANEST; n = 19). The second group consisted of paediatricians and ear, nose, and throat (ENT) surgeons (PENT; n = 17). The two groups had different work characteristics when on call (see below). Originally, only paediatricians were planned to constitute the control group; during recruiting, however, fewer physicians were available in clinical work than expected, thus we chose to augment the control group by including ENT surgeons. The physicians in both groups worked at the same university hospital and had on-call duties that involved working recurrent night shifts. All physicians holding the above-mentioned positions were asked to participate. The participation rate was 19/24 (79%) in the ANEST group and 17/25 (68%) in the PENT group. Self-report data missing for one anaesthesiologist and technical errors in three of the sleep registrations in this group forced us to discard data for four participants, hence the final ANEST sample consisted of 15 anaesthesiologists. Demographic data collected in the baseline questionnaire are presented in Table 1. Data from a baseline inventory showed that the family situations were almost identical in the two groups of physicians and that there were no cases of cardiovascular disease, diabetes, insomnia, or sleep apnoea syndrome. From data obtained in a previously published sub-study we also knew that they shared a low to moderate alcohol consumption, normal liver function, serum insulin, plasma glucose, and blood lipids [17]. Baseline data revealed no between-group differences concerning subjective reports on sleep sufficiency and recovery from work. In the pooled group of physicians, 17% reported the time generally needed for sufficient recovery from night call to be one night's sleep, 73% reported a need for two nights' sleep, and 10%, reported needing three nights' sleep or more. Morning diurnal type was reported by 37% and evening type by 63% [18]. The reported mean need of sleep for feeling well rested in the morning was 7:28 hours (SD = 44 min).

Ethics

All participants gave their written informed consent and the study was approved by the Ethics Committee at Lund University (LU 732-01).

Table 1 Demographic data for participating anaesthesiologists (ANEST) and paediatricians and ENT surgeons (PENT)

	ANEST (n = 15)	PENT (n = 17)[a]
Median age (range)	43 (37-55)	37 (26-45)
Mean BMI in kg/m^2 (SD)	24 (2.9)	22 (1.9)
Median years' experience of night call (range)	10 (4-27)	11 (0-19)
Women (%)	6 (40)	8 (47)
Smokers (%)	0	0
Position:		
Consultants (%)	6 (40)	2 (13)
Registrars (%)	6 (40)	4 (27)
Residents (%)	3 (20)	9 (60)
Social status		
Single (%)	0	1(7)
Living with other adult, but no children (%)	3 (20)	3 (20)
Living with other adult and children (%)	12 (80)	11 (73)
Living with children, but without other adult (%)	0	0
Work/home interface		
Worries about family matters influence focus on work (%)	5 (33)	5 (33)
Regular overtime (≥ once a week) (%)	7 (47)	6 (40)

[a] For two participants only data on age, gender, and BMI were available.

Working conditions

The reason for choosing the two groups ANEST and PENT as participants was motivated by that the characteristics of their working conditions, at the time of data sampling, implied a clear between-group exposure contrast in activity levels and mental demands. All participants had strictly hospital-bound work on call, but with less focus on life-threatening conditions for the PENT group. During night-call duty, the ANEST group took care of patients' vital functions in major traumas, cardiac arrest, and acute operations. They were also in charge of post-operative ward and the intensive care unit, handling patients with vital organ failure. All participating physicians could expect to have a high workload on call, but the ANEST group also had to focus generally on life-threatening conditions. Furthermore, they differed from the PENT group in that they provided service to the whole hospital and facilitated the work of several other physicians caring for severely ill patients [11]. In contrast, the PENT group worked at the emergency ward taking care of acute cases in their speciality, but they did not have the kind of service and facilitation duties required of the ANEST group. The specific information on working conditions was collected through interviews with the specialists and by scrutinizing all working schedules. For all physicians, ordinary daytime work was performed from 08:00 to 16:30. Night-call duty started at approximately 16:00 and lasted for about 16 hours (until around 08:00 the next day). All participants had on average three night-call duties per month and at least one day off after each night call, but work schedules differed somewhat between specialities. The ANEST group and paediatricians in the PENT group had separate night-call weeks every fourth to sixth week, during which they worked two to three nights. In the PENT group the ENT surgeons had single nights on call every second or third week, and in contrast to the two other specialities, they generally had a normal working day directly before night call. There were no scheduled breaks during on-call duty, but breaks were allowed for meals, rest, or even sleep if there were no patients in need of attention; on-duty rooms were always available.

Rating scales and activity measures

Karolinska Sleep Questionnaire (KSQ) was used to assess participants' habitual quality of sleep [19]. This questionnaire comprises 15 items measured on a 5-point scale, including difficulties falling asleep, disturbed sleep, too little sleep (< 6 h), repeated awakenings, premature awakening, exhaustion at awakening, not well rested on awakening, difficulties awakening, sleepiness during the day, nodding off at work, nodding off during leisure time, sleep quality, sufficient sleep, nightmares, and heavy snoring. The scores/response alternatives are: 1 = always/every day, 2 = mostly/several days a week, 3 = sometimes/several times a month, 4 = seldom/a few times a year, 5 = never. Three indices were calculated from 12 of the 15 items: "disturbed sleep", "sleepiness index," and "awakening index," with 5 as the most positive score. Three participants had missing data for KSQ.

Karolinska Sleepiness Scale (KSS) was used to assess current sleepiness and was completed at bedtime. This scale has been used in many studies and has been validated against EEG parameters [20]. This is a 9-point scale with the following verbal anchors: 1 = very alert, 3 = alert, 5 = neither alert nor sleepy, 7 = sleepy, but with no difficulty staying awake and 9 = very sleepy, fighting against sleep, requiring great effort to stay awake. The intermediate values are also used, but they have no labels.

Mental fatigue was assessed on a scale similar to the KSS with the following verbal anchors: 1 = very alert, 3 = alert or energetic, 5 = neither fatigued nor alert, 7 = fatigued but not strained, and 9 = very fatigued, exhausted, and incapable of any mental strain. The intermediate values were also used, but they had no labels. In a previous study, individuals with a high "burnout" score also scored high on the mental fatigue scale [21]. In addition, the mental fatigue scale has demonstrated higher levels of fatigue during workdays compared to weekends, a time-of-day profile (peaking in the evening), and elevated levels of fatigue in association with early morning shifts [21,22].

Karolinska Sleep Diary (KSD) was used to assess daily variations in the subjective aspects of sleep and recovery as experienced in the morning [23]. This questionnaire has been validated against polysomnography and shows good correlation with objective EEG sleep measures (e.g. amount of slow-wave sleep and sleep efficiency) [23-25]. The questionnaire consists of several items concerning the previous night's sleep and aspects of sleep recovery. All variables are scored from 1 to 5, where 5 is the most positive. A Sleep Quality Index (SQI) was constructed from the mean scores on the questions regarding "restless sleep", "ease of falling asleep," "sleep quality," and "sleep through the night." The SQI ranged from 1 (low quality) to 5 (high quality). The questions on "sufficient sleep," "ease of awakening," and "feeling well rested," reflecting aspects of sleep and recovery, were studied as single items. Sufficient recovery, in subjective terms, was defined as the score on KSD for feeling well rested after a Saturday night's sleep.

Actigraphy was used to record sleeping and waking activity (Actiwatch, Cambridge Neurotechnology Ltd, UK) [26]. The Actiwatch device is a wrist-worn accelerometer that measures wrist activity, which has proved to be a good proxy for EEG-registered sleep. The output sleep scores have a high correspondence with polysomnographically recorded sleep and are also validated for documenting longitudinal changes in sleep patterns [27,28]. The watch was calibrated and set to personal computer (PC) time and an epoch length of 0.5 minutes was chosen. A medium sensitivity was applied. The participants wore the Actiwatch (AW) on the non-dominant wrist during the whole study period, except when taking a shower, during strenuous physical training, and when they had to work in aseptic conditions. In addition, the participants kept a separate *log-book* for daily notes on bedtime, rising time, and special circumstances or events of significance for AW monitoring. The latter could be an emergency alarm, physical training, or removal of the AW. Participants were also instructed to press the event-button at bedtime and upon rising. Start and end times for night sleep were determined manually, with sleep onset defined as the first period of 5 minutes or more of immobility according to actigraphic recording in the evening and sleep end as the stable return of measurable actigraphic activity for at least 10 minutes in the morning. Although the AW sleep-wake registrations were used as primary information, the notes in the log books concerning special circumstances at bedtime upon rising and at AW removal were used as complementary information to define the most accurate start and end points for sleep analysis. All periods accepted as sleep were also checked against the sleep logs. In the majority of participants the correspondence between sleep log data and AW data was excellent. The Actiwatch Sleep Analysis program (version 5.48) was used for data scoring. Periods of waking and sleeping between sleep start and sleep end were scored automatically by the Actiwatch algorithm, which was also used to calculate total sleep time and sleep efficiency (% of time during the period from sleep start to sleep end spent actually sleeping). Bedtime and rising time were missing from some participants' log books, which is why the customary way of calculating sleep efficiency (which includes sleep latency) could not be used. Instead it was measured from sleep start to sleep end as recorded by the AW. A separate analysis of day-time naps was performed on the first post-call day using the same methodology as for the night sleep analyses.

Study design and procedures

The study was designed to answer questions about sleep and recovery in relation to night-call duty. At the beginning of the study, participants completed a baseline inventory containing the KSQ and other health- and background data in order to characterize the participants. Next, the monitoring period for studying the effects of daytime work, night call, and post night-call on the various measures was chosen to fit each individual's work schedule. Participants were then continuously monitored for 10 to 22 days, during both work and leisure time, depending on their individual schedule. Requirements for several substudies and the specific personal night-call schedules directed the total length of monitoring period for each participant.

The KSS and mental fatigue-scores were completed at bedtime in the evening and the KSD was completed in the morning soon after awakening. Because bedtimes and rising times were quite different when participants were on night call, and this could lead to both compliance problems and difficulties in interpretation, participants were instructed to refrain from completing the KSS and KSD when they were on night call.

Analyses of total sleep duration and sleep efficiency were performed, and comparisons were made between one night after daytime work, one night call, the following first and second nights post-call, and Saturday night for every participant (see Figure 1). These nights were determined a priori. However, for practical reasons the participants wore AW during the whole study period. For those who had more than one night-call duty in the same week during the monitoring period, the last one of these was chosen for analysis. To compensate for the possible effect of habituation to the sampling procedures, the days used for the analyses were selected in a counter-balanced design. Accordingly, the first occasion of sampling was equally distributed between ordinary work days, days related to night-call duty, and Saturdays. A control was added to ensure that the ordinary workdays and Saturdays included in the statistical

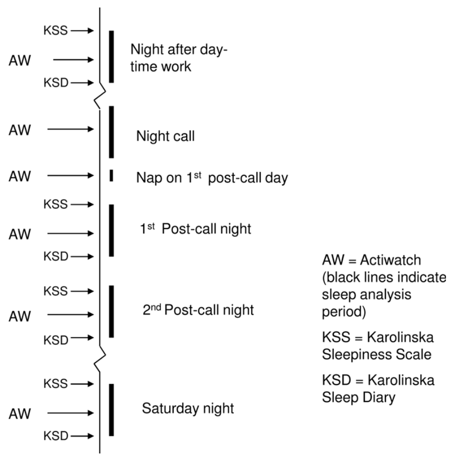

Figure 1 Flowchart for sampling of data.

analysis were always at least three days from a night call. The repeated measures made it possible for participants to serve as their own controls in the comparisons between days.

Statistics

The statistical computations were made using SPSS 15.0 (SPSS Inc, Chicago, IL). P-values below 0.05 were considered statistically significant. For the comparison across days a repeated measures model was specified, using the linear mixed models module of SPSS. The AW sleep variables were normally distributed in the majority of subgroups. KSD data were ordinal scale data, but the scores still showed a fairly normal distribution. The independent variables were *Day* (5 levels: [i] night after day-time work; [ii] night call; [iii] 1st post-call night; [iv] 2nd post-call night and [v] Saturday and *Specialist Group* (2 levels: ANEST vs. PENT), which was treated as a between-group factor. The dependent variables were the AW, KSS, and KSD variables. Gender and age were entered as covariates. Only age yielded a substantial impact ($p < 0.2$) and only on the AW measures. For this reason age was included as a covariate when analysing the AW measures [29,30].

The statistical modelling included the two-way interaction between Day and Group. However, the interaction term was not significant for any of the dependent variables (p = 0.1-0.8). The choice of model was governed by Schwarz's Bayesian Criterion (BIC) and a first order autoregressive (heterogeneous) covariance structure (ARH1) was applied, which showed the best fit. Residual analysis showed no outliers or marked deviations from normality assumptions. A univariate analysis using the General Linear Model module was used for testing group differences in the cross-sectional KSQ data and in comparisons between day sleep and no day sleep post-call. Because of the risk of obtaining biased results when applying parametric methods to ordinal data, or to data with skewed distributions, the outcome of AW, KSS, and KSD measures were also checked using nonparametric methods, which do not rely on assumptions. Specifically, Friedman's two-way analysis of variance test for overall testing of several related samples, Wilcoxon's Matched Pairs Signed Rank Test, as well as the Sign Test in comparisons of two related samples, and Mann-Whitney U test for two unrelated samples were used. However, the non-parametric analyses gave largely the same results as the mixed models analyses. Because the non-parametric analyses in the SPSS software do not allow for covariate inclusion, or the modelling of correlation between repeated measures, the parametric method was the preferred method in the end.

Results

Actigraphy

No interactions were found between Group and Day. For total sleep time and sleep efficiency there were main effects of Day ($p < 0.001$ and $p = 0.045$ respectively, Tables 2 and 3). Difference in total sleep time between nights ranged from 35-233 minutes, but the sleep efficiency differed by only 2-5%. The shortest sleep was recorded on night call, and a short sleep was also recorded on the night after daytime work when compared with both the two nights post-call and the Saturday night. Four participants in the ANEST group did not sleep at all during the night call. As might be expected, the sleep efficiency for all the other participants was somewhat lower on night call than on either the first or second post-call nights, but not different from the night after daytime work or Saturday night. As part of the recovery after night call, some participants (14/15 for ANEST, 8/17 for PENT) took a daytime nap (mean 2:30 hours, SD 1:27 hours) after their night call. An additional analysis of the effect of this on the following night's sleep showed, as expected, that those who took a nap had a shorter sleep the following night ($p = 0.04$). The difference disappeared when daytime sleep duration was included as a covariate ($p = 0.88$). Note that the daytime nap was presented separately from the sleep during first post-call night, but they both represent recovery sleep after night call.

Log-book

The participant's notes showed that 50% in the ANEST group got one or two emergency alarms (cardiac arrest, major trauma or likewise) during the night call, but there were none for the PENT group. The ANEST group reported more frequent involuntary awakenings for patient consultations after bedtime (usually 02:00 h or later). In addition, four participants in the ANEST group did not get the opportunity to sleep at all during night call. In the ANEST group 93% reported a nap on the first post-call day and in the PENT group 47%, which is in accordance with the sleep data in table 2. Only one of the ENT surgeons reported an acute operation during night-call.

Rating scales

There was no interaction between Group and Day in the self-reported KSS and KSD measures. The KSS sleepiness score at bedtime did not differ between days; however mental fatigue was significantly higher on the first post-call evening compared with the other days (1.0-1.3 difference in scores). The KSD scores indicated a feeling of being less well rested on the morning after the first post-call night, compared with the mornings after the

Table 2 Crude data of sleep monitored by Actiwatch in anaesthesiologists (ANEST) and paediatricians and ENT-surgeons (PENT)

	ANEST (n = 15)		PENT (n = 17)	
	Mean	**SD**	**Mean**	**SD**
Day-time work				
Sleep start	23:19	01:11	23:48	00:57
Sleep end	06:02	00:24	06:38	00:35
Total sleep time (hours and minutes)	06:01	1:04	06:06	0:46
Sleep efficiency (%)	90	5	89	6
Night call				
Sleep start	02:53	01:26	03:15	01:44
Sleep end	06:44	00:54	07:39	00:40
Total sleep time (hours and minutes)	02:22	01:48	03:42	01:36
Sleep efficiency (%)	89	10	85	8
1st post-call night				
Sleep start	23:35	01:12	23:29	01:35
Sleep end	06:35	00:38	07:52	01:28
Total sleep time (hours and minutes)	06:15	01:01	07:37	01:50
Sleep efficiency (%)	90	4	91	4
2nd post-call night				
Sleep start	00:10	01:27	00:18	01:25
Sleep end	07:06	01:09	07:56	01:09
Total sleep time (hours and minutes)	06:16	01:19	06:55	01:08
Sleep efficiency (%)	91	3	91	4
Saturday (off duty)				
Sleep start	23:42	00:44	00:53	01:18
Sleep end	07:28	01:00	08:35	01:25
Total sleep time (hours and minutes)	06:48	00:46	06.56	00:54
Sleep efficiency (%)	88	5	90	4
	ANEST (n = 14)		**PENT (n = 8)**	
	Mean	**SD**	**Mean**	**SD**
Day-time nap post-call				
Sleep start	11:53	01:52	13:51	03:35
Sleep end	14:47	02:24	15:54	03:29
Total sleep time (hours and minutes)	2:52	01:27	01:50	01:17
Sleep efficiency (%)	91	4	91	4

second post-call and Saturday nights (0.6-0.9 difference in scores), but not different from the morning after ordinary daytime work. There was no difference between the mornings after the second post-call night and Saturday night. No effect of Group was found for any of the KSS or KSD variables (Table 3). In the KSQ sleep indices there was no difference in habitual sleep between physician groups ($p > 0.5$). The respective scores (mean [SD]) for the ANEST and PENT groups were 3.6 (1.0) and 3.8 (0.5) for disturbed sleep, 3.7 (0.8) and 3.6 (0.7) for the sleepiness index, and 3.0 (0.9) and 3.0 (0.8) for the awakening index.

Discussion

The present study aimed to examine whether a 16-hour night-call schedule negatively affected recovery in the ANEST group compared with the PENT group. The results showed that, in terms of subjective scores, the main sleep restitution was completed for both physician groups in the first 24 hours after night call. However a full recovery required an additional 24 hours. This was indicated when the scores for being "well rested" had reached the same levels as after a Saturday night's sleep. Previous studies of shift work have shown that recovery sleep after a night shift is normally extended by only one or two hours [31]. Experimental studies of moderate sleep deprivation (≈24 hours time awake) have consistently shown that recovery sleep contains a higher amount of slow-wave sleep (SWS), whereas the increase in sleep duration is limited [32]. The temporary increase in SWS is regarded as the core component of recovery during sleep [33]. Accordingly, as long as sleep

Table 3 Comparison between days for all participant's Actiwatch night sleep measures (n = 32), KSS[2] (n = 29) and KSD[3], (n = 32) ratings

	Night after day-time work		Night call		1st post-call night		2nd post-call night		Saturday night		Type III F-test
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	P-value
AW sleep measures											
Total sleep time (min)	364[a]	344-383	186	148-224	419[b]	385-452	399[b]	373-425	412[b]	393-431	< 0.001
Sleep efficiency[1] (%)	90	88-92	86[c]	83-90	90	89-92	91	90-92	89[d]	88-91	0.045
KSS measures[2]											
Sleepiness (mean)	5.6	4.9-6.2	—		6.1	5.4-6.8	5.5	4.8-6.3	5.1	4.2-6.0	0.206
Mental fatigue	6.1	5.6-6.6	—		7.1[e]	6.5-7.7	6.1	5.4-6.9	5.8	5.0-6.7	0.004
KSD measures[3]											
SQI[4]	4.2	3.9-4.4	—		4.3	4.1-4.5	4.3	4.0-4.5	4.2	3.9-4.4	0.673
Sufficient sleep	3.0	2.7-3.4	—		2.9	2.5-3.3	3.1	2.7-3.6	3.6	3.2-4.0	0.052
Ease awakening	2.6[f]	2.2-3.0	—		2.8[f]	2.5-3.2	3.0	2.6-3.4	3.4	3.0-3.8	0.042
Well rested	2.6[f]	2.2-3.0	—		2.4[g]	2.0-2.8	3.0	2.6-3.4	3.3	2.9-3.7	0.013

(Estimated means are presented).

Note: 1. Sleep efficiency = the relative sleep time between sleep start and sleep end in %, (with awakenings during the night accounted for).

2. KSS (Karolinska sleepiness scale)-ratings are 1-10 (low-high). 3. KSD (Karolinska sleepiness diary)-ratings are scored 1-5, where 5 is the most positive. 4. SQI = (Sleep quality index) 1-5 (low quality-high quality), is the mean of 4 variables in the KSD.

[a] Higher than night call, but lower than 1st and 2nd post-call nights and Saturday night (P's < 0.05). [b] Higher than night after day-time work and night call (P's < 0.05). [c] Lower than 1st and 2nd post-call nights. [d] Lower than 2nd post-call night (P's <0.05). [e] Higher than daytime work, 2nd post-call night, and Saturday. (P' < 0.01). [f] Lower than Saturday night (P's < 0.05). [g] Lower than Saturday night and 2nd post-call night (P's < 0.05).

deprivation is not too severe, the temporary increase in SWS may be sufficient for biological restoration. Thus the few extra hours of sleep after night duty observed in the present study are probably compatible with sufficient sleep recovery. According to recent comprehensive reviews, even a severe sleep debt might be overcome by a modest recovery sleep [34]. However, the fact that the total sleep during not only the first post-call night, but also the second post-call night, was longer than sleep after normal daytime work could indicate that there was still some sleep deficit left to recover on the second night post-call. There were no significant group differences in either subjective reports of sleep and recovery from night call or objective sleep measures. This could be interpreted to mean that work on call is equally demanding for all the participating physician groups. However, there could be selection bias in physicians' choice of speciality, such that, as a group, those who choose anaesthesiology may be more resilient following on-call work and sleep loss. This is of course merely speculative and so far not confirmed in the scientific literature. Indeed there is reported to be a genetic polymorphism concerning resistance to prolonged wakefulness in the healthy population. However physicians do not seem to be overrepresented in the resistant group [35]. Indeed, even in a group of jet fighter pilots there was a systematic inter-individual difference in performance after sleep loss [36]. It may even be the case that work characteristics/demands are not the major determinants of changes in sleep and recovery in the studied physician groups.

As expected, the general subjective sleep quality according to KSQ was good and corresponded to a level usually found in a healthy population [37]. The differences in subjective sleep quality measured using KSD were relatively small, albeit significant for some of the variables. Thus, ratings of feeling refreshed from sleep (well rested) at awakening after the first night of sleep after night call and on mornings after daytime work were similar. However, two days after night call the scores were similar to Sunday morning (i.e. morning after Saturday, in the tables), which is interpreted as a reasonable level of full recovery from night call. The between-day differences in morning scores on KSD variables seemed to correspond to the patterns of mental fatigue in KSS in the preceding evenings, both indicating that two nights' sleep was needed for full recovery after night call. The KSS sleepiness scores followed the same pattern, but there was no statistical difference between days. The present findings are in accordance with previous shift work studies, where recovery from a night shift with moderate disturbance of circadian rhythms requires two nights' sleep [38]. This also corresponds closely to the subjective reports from the participants concerning estimated time needed for recuperation after night call in general.

The fact that the physicians did not report any problems with insomnia or sleepiness speaks against the present working schedules causing any severe adverse effects on sleep in general. However, the previous polysomnographic study of physicians on call showed a preserved amount of deep sleep during call, but a large loss of REM (rapid eye movement) sleep [7]. This is also a well-known pattern from experimental studies of shift work [39]. Even though the SWS was probably sufficiently recovered, some adverse effects of insufficient REM sleep in the present participants cannot be ruled out. Nevertheless, the unexpected finding of short sleep after their ordinary work days is more troubling. Hence, even though sleep quality and sleep efficiency were sufficient in the whole group of physicians, they may still have a general sleep deficiency, which may constitute a health risk in a long-term perspective. There are strong indications of an elevated risk of diabetes and myocardial infarction in short sleepers (5-6 hours) [40,41]. Too short or too long sleep has also been associated with higher mortality, and according to recent studies, 7 to 8 hours of night sleep seems to be optimal for long-term survival [42]. In fact, an epidemiological study of Swedish anaesthesiologists indicated higher mortality compared with other specialists, but this was not confirmed by other Scandinavian studies [43,44]. However, the sleep duration of only 6 hours after daytime work found in the present study seems to represent a chronic sleep deficit of 1.5 hours in view of subjective reports of a mean need for 7.5 hours of sleep, and may therefore constitute a health risk. Despite different methods of attaining sleep measures, it is interesting to compare the total sleep times based on AW in the present study with the sleep times measured using EEG in the study by Åkerstedt et al [7]. In that study, which had a design similar to the present study, physicians monitored by ambulant EEG had roughly the same sleep duration on call as our participants, but about 1 hour longer sleep on post-call recovery and after ordinary daytime work, and a somewhat shorter daytime nap post-call. In a study of internal medicine residents there was no difference in sleep duration by actigraphy on postcall nights compared with non-call nights [45]. However, in this study the length and starting point of the night shift and other characteristics of the night-call were not clearly accounted for. This made it difficult to compare with the results in our present study. Different length of the night call, absence of naps and of experienced specialist physicians in the Saxena study might explain the divergent results concerning recovery.

A major strength of the present study is the use of multiple kinds of measures and types of data, such as global and real-time self-report measures, as well as objective sleep registrations. Another strength is the repeated measures over several days using the subjects as their own controls. This design made it possible to follow the dynamics of the recovery pattern. As verified by the participants' logbooks concerning special circumstances during the AW-registration, the specific days that were analysed seemed fully representative of the whole period of days monitored. For this reason we do not believe that any "extreme" days can explain the results.

One limitation, common in observational studies taking the present approach, is the limited sample size, because for practical reasons it is difficult to carry out this type of study with a larger group. Moreover, we did not have any precise measure of individual workload or of leisure activities that might influence sleep duration and quality during the days analysed. Because of the long period of data collection it was not realistic to demand an extremely detailed information each day and night. However, there were strong indications in the personal log-books of a heavier work load for ANEST compared with PENT during night call duty. In general there were no group differences with respect to overtime work, family situation, or worries over family matters, and there were no reports of any extraordinary loads or adverse events for the participants during the monitored period. Concerning sports activities during leisure time, the reports did not differ between groups.

Conclusions

Despite considerable sleep loss during work on night call, the physicians' self-reports indicate that they recovered after two nights' sleep. We conclude that these 16-hour night duties were compatible with sufficient short-term recovery in both physician groups, but the limited sleep duration in general still implies a long-term health concern. These results may contribute to the establishment of safe working hours for night-call duty in physicians and other health-care workers.

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Author details

[1]Occupational and Environmental Medicine, Dept of Laboratory Medicine, Lund University, Lund, Sweden. [2]Stress Research Institute, University of Stockholm, Stockholm, Sweden. [3]National Research Centre for the Working Environment, Copenhagen, Denmark. [4]Department of Anaesthesiology and Intensive care, Skåne University Hospital, Lund, Sweden.

Authors' contributions

BM performed the data collection and statistical analyses, wrote the manuscript and made substantial contributions to the design of the study.

GK contributed to the design of the study and interpretation of data, and commented on the manuscript. BK contributed to the interpretation of data, statistical analyses and commented on the manuscript. RP contributed to the conception and design of the study, and commented on the manuscript. PF contributed to the conception of the study and commented on the manuscript. PØ conceived of the study, supervised the design and commented on the manuscript. All authors have read and approved the final manuscript.

Competing interests
The authors declare that they have no competing interests.

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References
1. Arnedt JT, Owens J, Crouch M, Stahl J, Carskadon MA: **Neurobehavioral performance of residents after heavy night call vs after alcohol ingestion.** *Jama* 2005, **294(9)**:1025-1033.
2. Denisco RA, Drummond JN, Gravenstein JS: **The effect of fatigue on the performance of a simulated anesthetic monitoring task.** *J Clin Monit* 1987, **3(1)**:22-24.
3. Lockley SW, Cronin JW, Evans EE, Cade BE, Lee CJ, Landrigan CP, Rothschild JM, Katz JT, Lilly CM, Stone PH, *et al*: **Effect of reducing interns' weekly work hours on sleep and attentional failures.** *N Engl J Med* 2004, **351(18)**:1829-1837.
4. Harrison Y, Horne JA: **The impact of sleep deprivation on decision making: A review.** *Journal of experimental psychology Applied* 2000, **6(3)**:236-249.
5. Landrigan CP, Rothschild JM, Cronin JW, Kaushal R, Burdick E, Katz JT, Lilly CM, Stone PH, Lockley SW, Bates DW, *et al*: **Effect of reducing interns' work hours on serious medical errors in intensive care units.** *N Engl J Med* 2004, **351(18)**:1838-1848.
6. Lockley SW, Barger LK, Ayas NT, Rothschild JM, Czeisler CA, Landrigan CP: **Effects of health care provider work hours and sleep deprivation on safety and performance.** *Jt Comm J Qual Patient Saf* 2007, **33(11 Suppl)**:7-18.
7. Akerstedt T, Arnetz BB, Anderzen I: **Physicians during and following night call duty–41 hour ambulatory recording of sleep.** *Electroencephalogr Clin Neurophysiol* 1990, **76(2)**:193-196.
8. Howard SK, Gaba DM, Smith BE, Weinger MB, Herndon C, Keshavacharya S, Rosekind MR: **Simulation study of rested versus sleep-deprived anesthesiologists.** *Anesthesiology* 2003, **98(6)**:1345-1355, discussion 1345A.
9. Landrigan CP, Czeisler CA, Barger LK, Ayas NT, Rothschild JM, Lockley SW: **Effective implementation of work-hour limits and systemic improvements.** *Jt Comm J Qual Patient Saf* 2007, **33(11Suppl)**:19-29.
10. Lockley SW, Landrigan CP, Barger LK, Czeisler CA: **When policy meets physiology: the challenge of reducing resident work hours.** *Clin Orthop Relat Res* 2006, **449**:116-127.
11. Larsson J, Holmstrom I, Rosenqvist U: **Professional artist, good Samaritan, servant and co-ordinator: four ways of understanding the anaesthetist's work.** *Acta Anaesthesiol Scand* 2003, **47(7)**:787-793.
12. Lindfors PM, Meretoja OA, Toyry SM, Luukkonen RA, Elovainio MJ, Leino TJ: **Job satisfaction, work ability and life satisfaction among Finnish anaesthesiologists.** *Acta Anaesthesiol Scand* 2007, **51(7)**:815-822.
13. Lindfors PM, Nurmi KE, Meretoja OA, Luukkonen RA, Viljanen AM, Leino TJ, Harma MI: **On-call stress among Finnish anaesthetists.** *Anaesthesia* 2006, **61(9)**:856-866.
14. Nyssen AS, Hansez I, Baele P, Lamy M, De Keyser V: **Occupational stress and burnout in anaesthesia.** *Br J Anaesth* 2003, **90(3)**:333-337.
15. Cooper CL, Clarke S, Rowbottom AM: **Occupational stress, job satisfaction and well-being in anaesthetists.** *Stress Medicine* 1999, **15(2)**:115-126.
16. Bartel P, Offermeier W, Smith F, Becker P: **Attention and working memory in resident anaesthetists after night duty: group and individual effects.** *Occup Environ Med* 2004, **61(2)**:167-170.
17. Malmberg B, Persson R, Jonsson BA, Erfurth EM, Flisberg P, Ranklev E, Orbaek P: **Physiological restitution after night-call duty in anaesthesiologists: impact on metabolic factors.** *Acta Anaesthesiol Scand* 2007, **51(7)**:823-830.
18. Torsvall L, Akerstedt T: **A diurnal type scale. Construction, consistency and validation in shift work.** *Sand J Work Environ Health* 1980, **6(4)**:283-290.
19. Akerstedt T, Knutsson A, Westerholm P, Theorell T, Alfredsson L, Kecklund G: **Work organisation and unintentional sleep: results from the WOLF study.** *Occup Environ Med* 2002, **59(9)**:595-600.
20. Akerstedt T, Gillberg M: **Subjective and objective sleepiness in the active individual.** *Int J Neurosci* 1990, **52(1-2)**:29-37.
21. Soderstrom M, Ekstedt M, Akerstedt T: **Weekday and weekend patterns of diurnal cortisol, activation and fatigue among people scoring high for burnout.** *Scand J Work Environ Health* 2006, , **suppl 2:** 35-40.
22. Soderstrom M, Ingre M, Kecklund G, Akerstedt T, Kecklund L: **Train drivers workload - effects on sleep, fatigue and performance (internal report in Swedish).** Stockholm: Institute for Psychosocial Medicine, IPM, Stockholm, Sweden 2001, 1-47.
23. Akerstedt T, Hume K, Minors D, Waterhouse J: **The subjective meaning of good sleep, an intraindividual approach using the Karolinska Sleep Diary.** *Percept Mot Skills* 1994, **79(1 Pt 1)**:287-296.
24. Akerstedt T, Hume K, Minors D, Waterhouse J: **The meaning of good sleep: a longitudinal study of polysomnography and subjective sleep quality.** *J Sleep Res* 1994, **3(3)**:152-158.
25. Kecklund G, Akerstedt T: **Objective components of individual differences in subjective sleep quality.** *Journal of Sleep Research* 1997, **6(4)**:217-220.
26. Sadeh A, Acebo C: **The role of actigraphy in sleep medicine.** *Sleep Med Rev* 2002, **6(2)**:113-124.
27. Lockley SW, Skene DJ, Arendt J: **Comparison between subjective and actigraphic measurement of sleep and sleep rhythms.** *J Sleep Res* 1999, **8(3)**:175-183.
28. Reid K, Dawson D: **Correlation between wrist activity monitor and electrophysiological measures of sleep in a simulated shiftwork environment for younger and older subjects.** *Sleep* 1999, **22(3)**:378-385.
29. Maldonado G, Greenland S: **Simulation study of confounder-selection strategies.** *Am J Epidemiol* 1993, **138(11)**:923-936.
30. Mickey RM, Greenland S: **The impact of confounder selection criteria on effect estimation.** *Am J Epidemiol* 1989, **129(1)**:125-137.
31. Lowden A, Kecklund G, Axelsson J, Akerstedt T: **Change from an 8-hour shift to a 12-hour shift, attitudes, sleep, sleepiness and performance.** *Scand J Work Environ Health* 1998, **24(Suppl 3)**:69-75.
32. Webb W, Agnew HJ: **Stage 4 sleep: influence of time course variables.** *Science* 1971, **174(16)**:1354-1356.
33. Walsh JK, Snyder E, Hall J, Randazzo AC, Griffin K, Groeger J, Eisenstein R, Feren SD, Dickey P, Schweitzer PK: **Slow wave sleep enhancement with gaboxadol reduces daytime sleepiness during sleep restriction.** *Sleep* 2008, **31(5)**:659-672.
34. Horne J: **Sleepiness as a need for sleep: When is enough, enough ?** *Neuroscience and Biobehavioral Reviews* 2010, **34(1)**:108-118.
35. Czeisler CA: **Medical and genetic differences in the adverse impact of sleep loss on performance: ethical considerations for the medical profession.** *Trans Am Clin Climatol Assoc* 2009, **120**:249-285.
36. Van Dongen HPA: **Shift work and inter-individual differences in sleep and sleepiness.** *Chronobiology International* 2006, **23(6)**:1139-1147.
37. Akerstedt T, Ingre M, Broman J-E, Kecklund G: **Disturbed Sleep in Shift Workers, Day Workers, and Insomniacs.** *Chronobiology International* 2008, **25(2)**:333-348.
38. Akerstedt T, Kecklund G, Gillberg M, Lowden A, Axelsson J: **Sleepiness and days of recovery.** *Transportation Research Part F: Traffic Psychology and Behaviour* 2000, **3(4)**:251-261.
39. Akerstedt T, Gillberg M: **A dose-response study of sleep loss and spontaneous sleep termination.** *Psychophysiology* 1986, **23(3)**:293-297.
40. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, Rundle AG, Zammit GK, Malaspina D: **Sleep duration as a risk factor for diabetes incidence in a large U.S. sample.** *Sleep* 2007, **30(12)**:1667-1673.
41. Liu Y, Tanaka H: **Overtime work, insufficient sleep, and risk of non-fatal acute myocardial infarction in Japanese men.** *Occup Environ Med* 2002, **59(7)**:447-451.
42. Hublin C, Partinen M, Koskenvuo M, Kaprio J: **Sleep and mortality: a population-based 22-year follow-up study.** *Sleep* 2007, **30(10)**:1245-1253.
43. Hagmar L: **Is the life expectancy of anesthesiologists decreased?** *Scand J Work Environ Health* 2003, **29(2)**:83-84.

44. Svardsudd K, Wedel H, Gordh T Jr: **Mortality rates among Swedish physicians: a population-based nationwide study with special reference to anesthesiologists.** *Acta Anaesthesiol Scand* 2002, **46(10)**:1187-1195.
45. Saxena AD, George CF: **Sleep and motor performance in on-call internal medicine residents.** *Sleep* 2005, **28(11)**:1386-1391.

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