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**Daytime stress, shoulder/neck pain, and the
relation to nocturnal heart rate variability**

Acknowledgements

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Abstract

Stress and musculoskeletal pain (MSP) may affect the regulation of the autonomic nervous system. Earlier studies have revealed that subjects with MSP show reduced heart rate variability (HRV) during sleep indicating an increased sympathetic drive at rest. However, it is unclear whether daytime exposures, such as work stress, stress in leisure, and daytime MSP, affect nocturnal HRV. The aim of this study was therefore to investigate the possible association between daytime stress, shoulder/neck pain (SNP), and nocturnal HRV.

Twenty-five female subjects working in health care service participated in the study. Subjective scores of stress and pain were obtained on an hourly basis throughout the workday and subsequent evening. An index for long-term pain was also calculated. Electrocardiography (ECG) was monitored at the end of the workday and until 1 hour after awakening the morning after. Both time and frequency HRV parameters were extracted for further analyses.

High stress in leisure time was associated with higher nocturnal HRV ($p < .05$). In contrast, long-term pain tended to be associated with reduced HRV. Pain or stress during the workday had no effect on nocturnal HRV. The differences between groups were all found for the time domain variable pNN50. No difference was present for the frequency domain parameter.

The results of this study both agree with, and are in contrast to earlier studies of MSP and the association with nocturnal HRV. The contrasting results make it difficult to draw a conclusive remark and further studies are needed to elucidate the association between stress, shoulder/neck pain, and nocturnal HRV.

Introduction

Musculoskeletal pain (MSP) is one of the most frequent reasons for absence from work, use of health care service, and social security benefit (Ihlebaek et al., 2010). The prevalence of MSP in the Western world is high amounting to about 35% in the general adult population (Bergman, 2007). The cost associated with musculoskeletal disorders in the Nordic countries has been estimated to 0.5-2% of the gross national product (Larsson et al., 2007). In Norway MSP is the dominant cause of sick leave, rehabilitation, and disability pension, i.e. MSP contributed to 33.7% of the total sick leave in 4th quarter in 2010 (NAV). MSP is most frequent in neck/shoulders and low back and affects more women than men (Larsson et al., 2007). MSP comprises a wide spectrum of symptoms and diagnosis. Fibromyalgia (FM), repetitive strain injury, chronic fatigue syndrome (CFS) and chronic widespread pain are some of the diagnosis that includes MSP. Some occupations, such as health care are associated with a particular high prevalence of MSP (Ando et al., 2000).

Heavy physical work has long been accepted to represent a critical risk factor for musculoskeletal pain (Punnett and Wegman, 2004). However, in recent years several studies have revealed high prevalence of musculoskeletal pain among workers with low physical workload (Vasseljen and Westgaard, 1995; Sjøgaard et al., 2000; Holte and Westgaard, 2002). Thus, risk factors other than physical workload *per se* seem to play a critical role in the development of MSP. In particular, workers with low physical work demands but high perceived psychological and psychosocial stress commonly report musculoskeletal pain (Hansson et al., 2000). One possible mechanism is that elevated stress induces sustained low-level muscle activation (Larsman et al., 2007). It is hypothesized that this may lead to an overexertion of low-threshold motor units that eventually lead to muscle pain. However, empirical findings do not reveal a causal relation between stress, low-level muscle activity, and pain (Mork and Westgaard, 2006). Thus, other factors than sustained muscle activity seem to play an important role in the development of MSP.

Stress is defined as a state of disharmony or threatened homeostasis and its origin can be physical, psychological or biological. Stress in general is accepted to represent a risk factor for MSP (Westgaard, 1999). A study on rats has revealed some interesting results that may explain the mechanisms associated between stress and development of pain. During a laboratory test the rats were exposed to sound stress when kept in a sound-insulated box. During the protocol of 30 min a 5 or 10 sec tone was presented every minute. A paw pressure

test to quantify nociceptive threshold was used. The suggested pathway was that repeated sound stress would increase the level of plasma epinephrine and that sustained level of plasma epinephrine enhances the bradykinin hyperalgesia. By removing the adrenal medulla before exposure to sound stress a prevention of the stress-induced enhancement of epinephrine hyperalgesia was demonstrated. Rats that did not undertake adrenal medullectomy demonstrated that sound stress enhanced bradykinin mechanical hyperalgesia, which is known to sensitize nociceptors causing pain (Khasar et al., 2005). The study was followed up as they performed adrenal medullectomy 14 days after last exposure to sound stress to see if this could reverse the stress-induced enhancement of epinephrine hyperalgesia after it has been established. Nociceptive testing was performed further 14 days after the surgery. They found that hyperalgesia was still enhanced 28 days after sound stress exposure. This demonstrates that epinephrine may play a major role in maintaining the stress-induced enhancement of hyperalgesia (Khasar et al., 2009).

The unclear mechanisms that underlie development of MSP have given rise to the hypothesis that an imbalance in the autonomic nervous system (ANS) may play a causal role (Cohen et al., 2000). This imbalance is expressed by an increased sympathetic activity which normally reflects the body's fight or flight response. This fight or flight response corresponds to specific situations, e.g., in exercise, threatening, and stressful situations. Sustained physical stress can elicit homeostatic imbalance in the muscles resulting in accumulation of metabolites which stimulates nociceptors. Nociceptors are free nerve endings located in the skin, muscles and internal organs. A stimulation of nociceptors evokes the sensation of pain. Recurrent stimulation of nociceptors does not create an adaptation to the stimuli but a phenomenon called sensitization. A sensitization lowers the nociceptor threshold and increases the firing frequency to the same stimuli. This will be accompanied with an increased sensation of pain (Visser & van Dieen, 2006). An imbalance in the ANS has also been showed in human. An early study of Bengtsson & Bengtsson (1988) showed marked improvement of regional pain and tenderness as a response to a controlled therapeutic trial of stellate ganglion blockade in patients with FM whereas subjects with a sham injection in the neck area showed no effect.

A widely accepted and valid method that reflects the autonomic effect on the homeostasis is the HRV. This method is based on the fact that heart rate varies constantly from beat to beat. These oscillations reflect the modulation of ANS activity which affects the heart rate through sympathetic and parasympathetic input. HRV can be studied in the frequency domain. The frequency normally divides into low-frequency (LF) and high-

frequency (HF) band. The pioneering work by Akselrod and co-workers (1981) analysed the power spectrum of heart rate fluctuations (on a beat to beat basis) in adult conscious dogs. In their experiment they selectively blocked the parasympathetic transmission, sympathetic β -adrenergic receptors and the renin-angiotensin system respectively. They showed that sympathetic activity made contribution at the LF band and parasympathetic activity at HF band while the Renin-angiotensin system activity was associated with a spectral peak located at 0.04 Hz. The LF/HF-ratio is therefore regarded to reflect a sympathetic activity. HRV can also be studied in time domain and higher time domain variability means more parasympathetic influx on the sinus node of the heart. Thus, low HRV reflects a state of sympathetic ANS predominance (Martinez-Lavine, 2007).

Several groups of patients suffering from MSP have shown a reduced HRV (Boneva et al., 2007; Burton et al., 2010; Martinez-Lavine, 2007; Cohen et al., 2000; Clauw and Williams, 2002). Higher mean HR with reduced HRV during sleep was observed and higher level of plasma norepinephrine and lower aldosterone suggested a state of sympathetic ANS predominance among patients with CFS (Boneva et al., 2007). Patients with FM recorded among other things significantly higher levels of pain, fatigue, depression, anxiety, and stress scores than healthy women. HR was significantly higher and HRV significantly lower in FM patients compared with controls. The FM patient's higher LF component and lower HF component than controls indicate low cardiac parasympathetic tone and elevated sympathetic activity during rest than healthy controls (Cohen et al., 2000).

The effect of daytime stress on autonomic regulation during sleep in healthy subjects has been studied by Hall and co-workers (2004). Participants randomly assigned to stress condition or control group were recorded during sleep in order to identify effect on sleep HRV. The stress group performed a standard speech task immediately before sleep to evoke acute stress. ECG was recorded during sleep and the LF/HF-ratio (0.04-0.15 Hz / 0.15-0.4 Hz) was used to reflect sympathovagal influence whereas the power in the HF domain (0.15-0.4 Hz) was used to reflect parasympathetic influence. Sleep stages were divided in non-rapid eye movement sleep (NREM) and rapid eye movement sleep (REM) based on polysomnography. HRV between the groups was significantly different during both NREM and REM sleep. The stress group elicited decreased levels of parasympathetic influence and increased levels of sympathovagal influence during NREM sleep, whereas the control group showed increased parasympathetic influence. Thus, the study suggests that lower HRV during sleep was associated with acute stress.

A population of specific interest due to the association between pain, stress, and HRV are health care workers. In recent years their work conditions has been changed toward a less physical demanding challenge due to more advanced lifting equipment and other facilities (Arbeidstilsynet, 2008). Li and co-workers (2004) showed in an inventory study that injury rates became reduced after introduction of mechanical patient lifts. Despite this fact health care workers still suffers from MSP and most frequently in the shoulder and neck region. However, in the same period their job demands have been characterized by strict focus on improving the efficiency, i.e., a minimum amount of time is restricted to each patient. Thus, health care workers seem to be exposed to more psychological and psychosocial stress at work than before and therefore a stress reaction similar to the study from Hall and co-workers (2004) can be hypothesized. Furthermore, resting strategies reflected through stress during leisure might give a broader insight in the effect on nocturnal autonomic regulation.

The aim of this study was therefore to investigate whether daytime stress and MSP with emphasis on SNP, is associated with altered nocturnal autonomic regulation, assuming that stress- and pain-afflicted subjects will reveal lower HRV as a reflection of nocturnal sympathetic dominance.

Methods and materials

Subjects

The study sample consisted of 25 females recruited from four units of home health care in Trondheim, Norway. Subjects were employed as nurse (n=11), auxiliary nurse (n=8), or welfare worker (n=6). Subject characteristics are presented in table 1. Workers with heart disease, chronic diseases or on medication affecting outcome variables of the study were excluded, as were pregnant women. Included in the study were only registered nurses or other health care workers with corresponding responsibility working normal day shift on two subsequent weekdays.

The Regional committee for Medical Research Ethics approved the study protocol and the study was carried out according to the declaration of Helsinki. All participants received oral and written information before they signed a written consent to participate in the study. The study was a cross-sectional field study.

Table 1. Characteristics of the study sample (n=25)

	Mean (SD)	Range
Age, years	35.2 (10.8)	21 - 58
Height, cm	167.6 (5.0)	155 - 175
Weight, kg	67.2 (7.9)	55 - 80
BMI, kg/m ²	23.9 (2.7)	19.6 - 29.4
Sleep quality, (VAS)	42.0 (19.8)	1 - 72
Years at present work	8.7 (6.9)	0.5 - 27
Work hours per week	34.7 (3.2)	28 - 38

Abbreviations: SD, standard deviation; BMI, body mass index.

Work description

All participants were working in the first line service performing medication administering as well as assistance with feeding, washing, housework, shopping, and toilet visits. Some of their clients were functionally disabled and therefore required substantial physical support. Lifting equipment and adjustable beds eased their work to some extent. An apportioned amount of time was set to each patient based on their individual health care demands.

Questionnaire

Self-constructed questionnaires were presented to the subjects. Once every hour throughout the long-term field recordings, the workers scored the level of SNP, work stress, and physical fatigue. Physical fatigue was scored on Borgs scale (Borg, 1970) whereas the other variables were scored on a 10cm visual analogue scale (VAS) with end points very little and very much. If the subject reported SNP, the subject was asked to indicate whether pain was perceived on left, right, or both sides. Intensity and frequency of SNP last 6 months was used to calculate an index of long-lasting SNP. The participants received information regarding the questionnaires at the start of the workday and before leisure-time. The information focused among other things on the difference between stress, physical fatigue, and tension.

Procedure

This study was part of a larger project that included full 24 hr ECG recording from 07:00 a.m to 07:00 a.m, i.e., including leisure time, and sleep. However, this study emphasised to investigate the effect of daytime stress exposures and pain on autonomic regulation during sleep. Subjects were instructed to maintain normal daily activities except heavy physical exercise and showering.

Physiological recordings

ECG was recorded by Medilog AR4 (Cardiff, UK), a 3-channel 7 lead monitor with a capacity of 72 hours recording. After cleansing of the recording area on the participants chest with alcohol the seven electrodes were placed at the xiphoid process (of the sternum), left and right medium clavicle, the 5th and 7th left rib, and 5th and 7th right rib, respectively, with a minimum distance of 5mm to avoid artefacts. The device detects the R-wave of the ECG and records the time in milliseconds with a resolution of 1024 Hz.

HRV analysis

Lab Chart AD Instruments, UK was used to process and analyze recorded ECG data. The ECG- recordings were on an off- line mode and analyse settings were set after the recording. Every half an hour of the recording a 5 min segment was extracted for manually inspection and corrected for disturbances. Based on the detection of the QRS complex, the normal-to-normal (NN) beat intervals were calculated. Each detected NN interval was checked for artefacts (i.e. non-sinus beats and muscle artefacts), and ectopic heart beats. NN intervals resulting from artefacts were omitted from further analyses. Inadequate recordings of ECG during sleep were detected in one subject and another subject only slept for 2.5 hours which is considered to be insufficient for analysis. Thus, the study sample consisted of 25 subjects.

The HRV was analysed in both the time and the frequency domain. Time domain analysis included the percentage of beats with a variance in NN interval above 50ms (pNN50). A low level of pNN50 indicates a sympathetic drive to the heart whereas high level of pNN50 indicates parasympathetic drive.

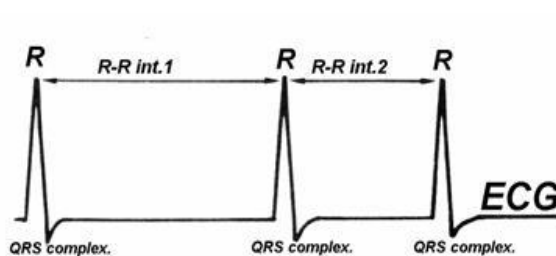


Figure1 showing RR-intervals with varying time intervals between several successive beats. Normal RR-intervals are expressed as NN.

Frequency domain analysis were divided in HF power (0.15-0.4Hz) which quantifies HF variability of the heart rate related to parasympathetic nervous system (PNS) drive and LF power (0.04-0.15Hz) which quantifies LF variability of the heart rate mainly related to sympathetic nervous system (SNS) drive. The LF/HF-ratio is thought to represent the balance between PNS and SNS drive to the heart and a ratio above 1 reflects SNS predominance.

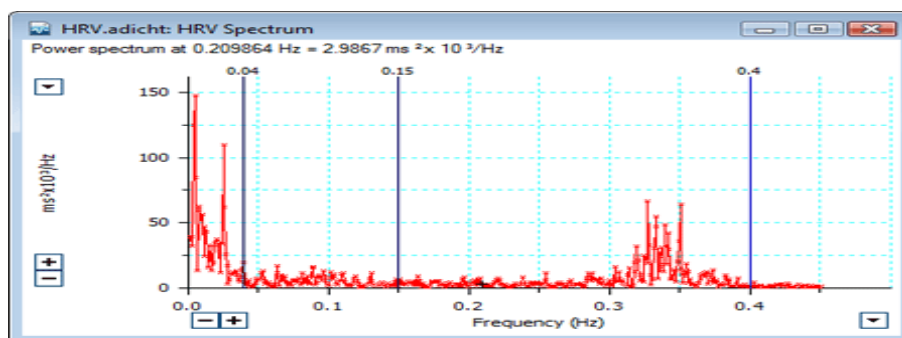


Figure 2 showing a typical power spectral density. Low frequency at 0.04-0.15 Hz and high frequency at 0.15-0.4 Hz.

Group classification

Based on subjective reports of perceived pain and stress the subjects were grouped by median split of the subjective scores i.e., dividing the study sample into high and low responders (table 2). Groups were divided by median split on the mean level or max level based on the VAS scores. To ensure that several aspects of pain and stress were studied multiple group comparisons were investigated. Stress/and pain indicators were divided in mean and max level in work and leisure, respectively. There was no significant difference in heart rate between groups (i.e., by the median split; table 2) during any of the recorded 5-min segments ($p > 0.05$ for all segments). Neither was there any difference for BMI, age, and sleep quality ($p > .05$ for all comparisons).

Table 2. Group classification by median split

	Cut-off value
Stress (VAS, 0-100)	
Mean work	31.6
Max work	50.0
Mean leisure	8.0
Max leisure	27.0
Short-term pain (VAS, 0-100)	
Mean work	15.6
Mean leisure	4.1
Long-term pain index (0-6)	2

Long term effect of neck/shoulder pain was based on the long-term pain index. The index is based on the recordings of two aspects of pain; intensity and frequency last 6 months. A summary of the five point scale of intensity and three point scale of frequency gives a combined symptom score with a maximum score of 6 (Westgaard and Jansen, 1992).

Statistical analysis

The software package SPSS 18 for Windows was used for all statistical analysis.

Mixed design ANOVA for repeated measure was used to determine effect of independent variables (stress and pain) on HRV during 5 min sleep segments. HRV variables were tested for normality using Kolmogorov-Smirnov test. All variables showed normal distribution and all statistical analyses were performed with parametric tests. If the assumption of sphericity was violated the degrees of freedom were corrected using Greenhouse-Geisser estimate of sphericity. Group comparisons were evaluated by Student's *t*-test. A value of $p < .05$ was used to define statistical significance.

Results

Stress

Figure 3 shows nocturnal HRV divided by max stress in work (A and B), and leisure (C and D) among high and low responders. There was no difference in nocturnal HRV between high and low stress responders during work (Figure 3A and B). In contrast, there was a significant effect of time ($p = .015$), and a main group effect on pNN50, ($F [1, 23] = 9.54, p = .005$) for the high stress responders during leisure. However, there was no interaction in the model ($p = .288$). Group comparisons for individual 5 min segments revealed that the high stress responders during leisure showed higher pNN50, except for the first 5-min segment of sleep (Figure 3C). Similarly, the group classification based on mean stress in leisure showed a clear tendency indicating higher levels of pNN50 among high stress responders (data not shown in figure). There was a significant effect of time ($p = .013$), and main group effect of stress on pNN50, ($F [1, 23] = 5.1, p = .034$), but no significant interaction in the model ($p = .144$). No significant differences were found between any other group comparisons on stress in leisure time ($p > .05$). Max and mean stress in leisure time was not associated with any group differences for the LF/HF-ratio.

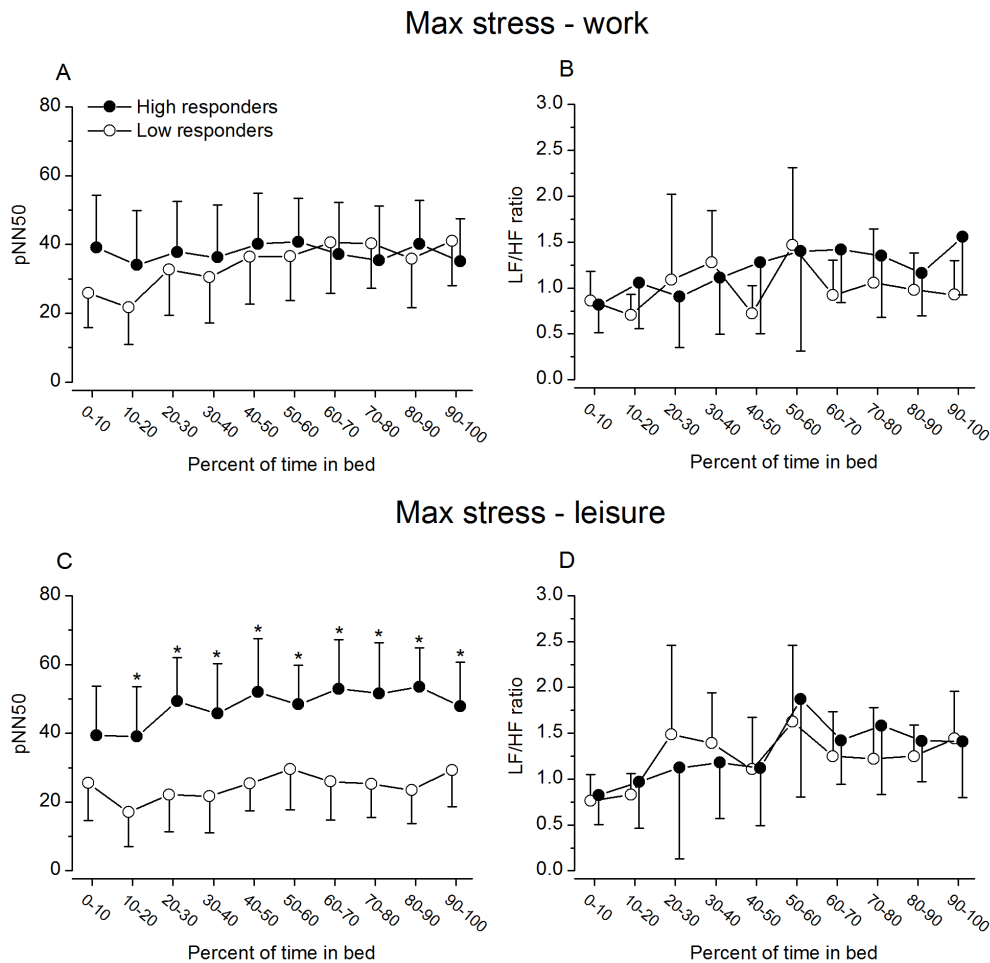


Figure 3. Group mean HRV with 95% CI for all segments during sleep. HRV associated with max stress at work is shown for pNN50 (A) and LF/HF (B). HRV associated with max stress in leisure is shown for pNN50 (C), and LF/HF (D). The x-axis represents the relative time expressed as percent of total time in bed.

* = significant difference

Pain

Figure 4 shows nocturnal HRV divided by mean short-term SNP at work and leisure, and long-term SNP. Short-term mean pain based on VAS at work showed no significant effect on pNN50 (Figure 4A). One segment differed significantly for LF/HF-ratio, $p = .02$ (Figure 4B). For pain in leisure time one segment of sleep in pNN50 (Figure 4C), and two segments of sleep in LF/HF-ratio showed a significant difference between groups. Otherwise there were no significant differences. There was a significant effect of time ($p = .009$), but no significant main group effect of long-term pain ($F [1, 23] = 3.34, p = .081$) and there was no interaction in the model ($p = .233$). When splitting groups by long-term SNP, (Figure 4E and F) there was a significant difference between the groups for three sleep segments (10-40%) for pNN50. The rest of the sleep segments were not significant but showed a tendency indicating that pain

afflicted subjects had lower levels of pNN50 than the pain-free group (Figure 4E). Long-term pain showed no significant differences between groups for the LF/HF-ratio (Figure 4F).

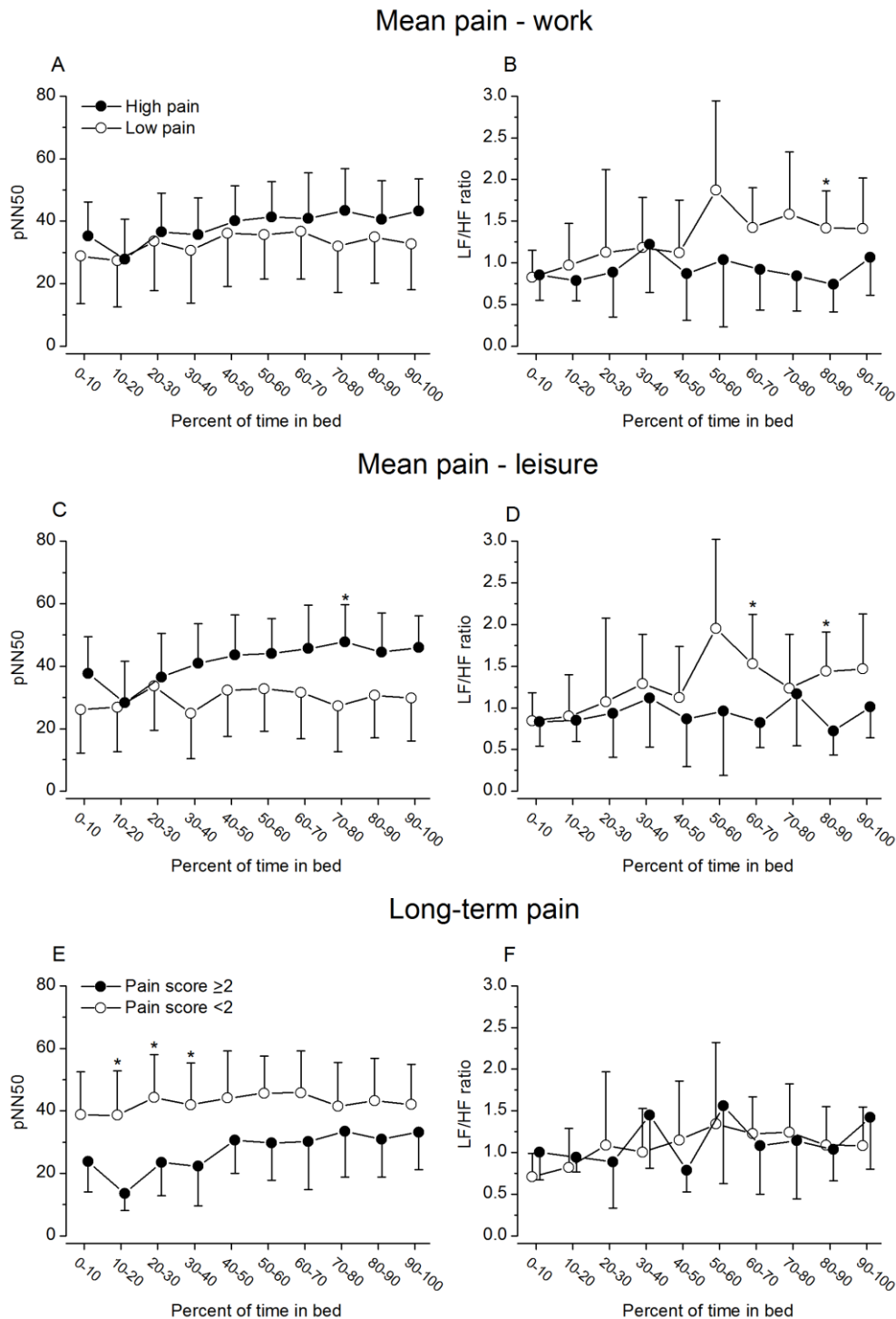


Figure 4. Group mean HRV with 95% CI for all segments during sleep. HRV associated with short-term pain at work is shown for pNN50 (A) and LF/HF (B). HRV associated with short-term pain in leisure is shown in pNN50 (C) and LF/HF (D). HRV associated with long-term pain is shown in pNN50 (E) and LF/HF (F). The x-axis represents the relative time expressed as percent of total time in bed.

* = significant difference.

Discussion

The aim of the present study was to investigate whether stress and SNP during daytime affect nocturnal HRV among female health care workers. Throughout the work day and leisure time the workers reported perceived level of stress and SNP. They also reported long-term SNP last 6 months. Nocturnal HRV was measured and the outcome variables were pNN50 and the LF/HF-ratio. It was hypothesised that subjects reporting high levels of stress and SNP would show decreased nocturnal HRV. The main finding of this study was that subjects perceiving high level of stress or pain at work were not associated with lower HRV. However subjects reporting high level of stress during leisure were found to have higher HRV indicating predominant vagal tone during sleep. In contrast to this, subjects reporting long-term pain showed a decrease in HRV indicating a predominant sympathetic tone during sleep. Thus, the study shows contradictory results with regard to the association between stress, SNP, and nocturnal HRV. In the following the main results of the study will be discussed in relation to findings in previous studies.

Daytime stress and shoulder/neck pain, and nocturnal HRV

Stress and SNP during work did not induce significant differences between groups on nocturnal HRV in this study. However, measurement of nocturnal HRV revealed that high stress responders in leisure time had higher scores of pNN50 than low responders. Thus, the result does not support the hypothesis that high stress at work induces an elevated nocturnal sympathetic tone. This study is in line with previous studies. Kageyama and co-workers (1998) studied 223 male white-collar workers. They found that self-reported work stress disrupted sleep quality, but was not associated with low HRV. Kang and co-workers (2004) studied 169 male workers employed in a shipbuilding industry. They found evidence for decreased standard deviation of NN intervals (SDNN) but no significant association between stress at work and increased LF/HF-ratio. The results obtained from these studies were based on short-term recordings of HRV (2 and 5 min) and only men were included. Furthermore, the HRV were recorded during daytime, leaving it difficult to compare with this study.

Other studies have reported no association between stress and HRV based on 24hr HRV recordings. Riese and co-workers (2004) studied the effect of job strain on HRV as a predictor of cardiovascular disease (CVD) among 159 female nurses. They found that job strain was not associated with differences in physiological recovery during sleep after work

or leisure indicating no effect on HRV. These results are confirmed by a study of 135 men and women occupied as shift workers and daytime workers. They found decreased HRV during sleep in shift workers but not for other workplace stressors (van Amelsvoort et al., 2000). Although these studies were based on recordings of nocturnal HRV, different measurements of work stress make it difficult to compare with this study. In contrast to these studies, work stress has been associated with lower HRV in other studies (e.g., Chandola et al. 2008). Daytime recording of HRV and its association with stress has shown predominance of sympathetic tone. Sloan and co-workers (1994) studied 33 healthy subjects with no history of disorders on the possible association between psychological stressors during everyday life and changes in cardiac autonomic activity. Psychological stress increased the LF/HF- ratio significantly indicating a sympathetic dominance during stressful periods of the day. However, the subjects were not measured during work which can affect the association. Daily worry and stressors has been shown to be related to low HRV during waking and sleep. A study from Brosschot and co-workers (2007) on 52 healthy subjects, mainly women, was conducted in the Netherlands. Their findings indicate that stress and worry were prolonged into sleep and were associated with higher heart rate and low HRV. However, their study did not measure stress during the workday and other HRV variables than in the current study was used. Studies on both men and women with larger sample sizes than the present study suggests a less favourable cardiovascular autonomic regulation reflected through sympathetic dominance (Collins et al., 2005; Vrijkotte et al., 2000). A study on 653 male workers also found that work stress was associated with an autonomic imbalance and decreased parasympathetic tone. Similar to the present study pNN50 and LF/HF- ratio were assessed. However, their study sample only consisted of men reporting high work stress (Clays et al., 2011). A recent study by Reyes del Paso and co-workers (2011) showed that both acute stress and pain were associated with reduced HRV. They also showed increased LF/HF ratio among FM patients in contrast to our study. However, their study used experimentally evoked pain (i.e., cold pain) in contrast to this study which emphasised real life conditions.

In summary, the results from this study cannot support the assumption of elevated sympathetic activity among subjects reporting daytime pain or stress like most of the abovementioned studies, but are more in line with Riese and co-workers (2004) who showed that job strain among female nurses was not associated with decreased HRV. However, one has to be cautious to draw conclusive remarks of this assumption due to methodological differences between the studies.

The findings in the present study of predominant nocturnal parasympathetic tone among high stress responders in leisure have not been showed in other studies. Hynenen and co-workers (2011) found no significant difference between low stress and high stress subjects for stress hormone secretion and HRV during sleep. An orthostatic test after awakening did however show that stress was associated with lower HRV. In contrast to this study, with emphasis on short-term stress, the participants in the study of Hynenen and co-workers (2011) were divided into two groups based on self-reported perceived stress in real life conditions the last month.

In this study, perceived stress during work did not affect nocturnal HRV whereas stress during leisure time did. One might therefore assume that perceived stress upon bedtime will affect nocturnal HRV different from stress perceived at work. However, Hall and co-workers (2004) found opposite results than in the present study. They found that stress evoked prior to sleep was associated with low nocturnal HRV, with decreased level of parasympathetic modulation. Despite using an experimental design this study must be considered comparable and therefore negates the findings in this study.

Athletes can experience an overtraining syndrome which is thought to produce an imbalance in the ANS. A greater parasympathetic activity at both rest and during exercise has been reported and is thought to be more common in endurance sports (Hoffman, 2002). This is supported by Hedelin and co-workers (2000) that reported increased HRV in a young endurance athlete with a suggestive overtraining syndrome. However, a comparison between our study and studies on athletes might be considered vague and should not be extensively emphasised.

The parasympathetic nocturnal predominance found in this study may indicate an altered regulation of the ANS. Symptoms of autonomic dysfunction among subjects with stress or pain has been studied with emphasis on other variables than HRV. Activation of the hypothalamic-pituitary-adrenal (HPA) axis stimulates the release of cortisol, an anti-inflammatory hormone which normally is highest in the morning and may reduce pain. Perceived stress is normally associated with elevated levels of cortisol the first hour after awakening. However, teachers reporting burnout showed a lower overall cortisol secretion. The authors suggest that an adaptation to stressors causes a shift in cortisol secretion (Pruessner et al., 1999). Stress related illnesses as FM have also been associated with decreased secretion of cortisol (Sarzi-Puttini, 2006; Riva et al., 2010) whereas others have found higher cortisol values among FM patients than among healthy controls (Catley et al., 2000). The inconsistent findings are suggested to be associated with different number of

years with the symptoms of FM. It is hypothesised that chronic stress might lead to a hyperactive HPA axis in the initial phase. Maintenance or development of stress will cause exhaustion and the individual are no longer in able to cope with stressors and the system turns into a state of hypoactivity (Riva et al., 2010) which can be compared to the findings in this study. It is, however, difficult to compare the studies because of methodological differences.

If the persons with parasympathetic predominance during sleep shown in this study suffer from long-term pain or stress, they should be present in the long-term pain group. However, only 3 of 12 subjects were present in the pain afflicted group and we therefore reject this assumption. Alternatively, the increased HRV among high stress responders may be explained by their good health. Being at good health might be associated with good resting strategies leaving the subjects able to expose themselves to stressful situations. Furthermore, one might speculate that these subjects even seek out stressful situations because of their certainty to cope with stressful situations. This might be associated with a study on parachuters that showed no difference on nocturnal HRV between the night before the jump and the control night (Hynenen et al. 2009). In summary, this study is to the best of my knowledge, the first study to show an association between daytime stress and nocturnal parasympathetic predominance.

Long-term pain and nocturnal HRV

The present study partly supports the hypothesis that subjects with long-term pain show reduced HRV during sleep. A tendency of the relation was clear and three segments of nocturnal HRV were significantly different between the groups. The results from this study showed similar decrease in nocturnal HRV as reported in previous studies (Cohen et al., 2000; Boneva et al., 2007). Martinez-Lavin and co-workers (1998) conducted a 24hr recording of HRV. They reported increased sympathetic modulation of the sinus node during sleep among 30 patients with FM compared to controls. Similar finding has also been reported by others, i.e., a study on 15 women with FM and 15 controls underwent multiple sleep latency test including 24 hours recording of HRV. Despite failure to show differences in standard polysomnographic measures they found changes in HRV consistent with decreased parasympathetic activity and relatively high sympathetic activity during both daytime and night-time hours (Chervin et al., 2009). Both long-/and short-term recordings was associated with lower HRV in the time domain in a study of Raj and co-workers (2000). Similar to this study only women were measured. However, the FM group were older than controls, which

can further enhance the differences, leaving it less comparable to the present study. Sympathetic hyperactivity among men with FM has also been reported, although this was a short-term recording (Cohen, 2001). Decreased HRV in CFS patients has been reported, but unlike the present study also heart rate was significantly higher than among controls (Boneva et al., 2007; Burton et al., 2010).

Studies supporting lack of association between pain and reduced HRV are sparse. Sympathetic hyperactivity in women, but not in men with FM during 24hr HRV recording has been reported in a case-control study (Stein et al., 2004). Another study of women with FM confirmed this association. Despite sleep disturbance they could not find evidence for autonomic dysregulation during sleep as measured by HRV (McMillan et al., 2004). A study by Sjørs and co-workers (2009) investigated whether 18 women with chronic trapezius myalgia showed higher muscle activity and more increased sympathetic tone in low-force, stressful work conditions than 30 pain-free controls. They found that the cases had increased muscle activity during rest but not an increased sympathetic activity. Thus, they could not support the hypothesis that trapezius myalgia was associated with elevated sympathetic activity. However, their study measured other variables on autonomic regulations than HRV.

In summary, even though the difference between groups are not significant in all segments of sleep, the results from this study show a tendency of altered autonomic regulation indicating an association between long-term SNP and nocturnal sympathetic predominance.

Methodological considerations

The major strength of this study is the long-term ambulatory ECG recording in a real life condition. On the other hand, this study is a cross-sectional study and it is not possible to make inference about causality. It should be noted that the sample size was rather small in the present study, and lower than other comparable studies (Riese et al., 2004; Martinez-Lavin et al., 1998; van Amelsvoort et al., 2000). Large effects would therefore be needed to detect differences between groups. The subjects reported their level of pain and stress through self-reported VAS. No characteristics of the subjects' personality are known. Modulation of stress and pain may depend upon factors like anxiety, expectations, or level of neuroticism (Fields, 2004).

The recordings of HRV in this study showed significant results only in the time domain. Time domain will in this case reflect parasympathetic activity more accurate than frequency domain. Several studies have showed that low frequency band includes both

sympathetic and parasympathetic drive while only parasympathetic activity contributes to the high frequency band (Saul et al., 1990; Stein et al., 1994; Toscani et al., 1996; Lombardi et al., 1996). A parasympathetic tone will in such cases affect both the high and low frequencies leaving the fraction less sensible for parasympathetic activity. Collins (2001) stated that there is a variance in HRV measures. When HRV is used as a measure of work stress, the time of day, gender, age and training status significantly impact HRV. Furthermore, time domain methods are considered ideal for analysis of long-term recordings (Malik et al., 1996). The different HRV parameters that have been used in the studies discussed in this report are not necessarily comparable to those used in this study. For instance, the time domain HRV-parameter SDNN correlates to both LF and HF power of HRV while pNN50 correlates with HF power (Malik et al., 1996).

This study did not measure EEG during sleep. A recording of the sleep stages (i.e. NREM and REM sleep) could give broader insight in autonomic regulation and probably reveal more nuanced differences between subjects (Hall et al., 2004; Busek et al. 2005).

The findings in this study regarding long-term pain have been compared to studies on subjects with chronic MSP. Comparing healthy subjects with patients with FM or CFS might seem inappropriate. However, a study of Westgaard and Jansen (1992) showed that healthy workers reporting intensity and frequency of pain last 6 months similar to the cut-off value in this study had a substantial risk in developing MSP and seek medical consultations. Comparison between the subjects in this study and studies on patients with FM or CFS must therefore be considered relevant.

Organizational restructuring affected workers in two of the four units in this study. By introduction of a new programme they intended to improve routines and internal structures. Despite no threat of job loss this could affect the participants regarding strain and stress due to the reorganization. The programme will be introduced at the other two units during 2011. However, workers from affected units were not dominant in any groups that were analysed in this study. Finally, this study does not allow drawing firm conclusions concerning the relevance in other occupations. However, this occupational field study measure real life situations under normal working conditions and might therefore be comparable to other similar occupations.

Conclusion

This study investigated the association between daytime stress, SNP and the effect on autonomic regulation during sleep. The hypothesis was that stress- and pain-afflicted workers would show altered autonomic regulation during sleep indicated by lower HRV. Workers reporting high level of stress in leisure time showed higher HRV than low responders. This controversial result indicates nocturnal parasympathetic dominance rather than sympathetic. In contrast, the results also demonstrate that workers reporting long-term SNP show a tendency of sympathetic predominance during sleep. These conflicting findings warrant further investigation to elucidate the association between SNP, stress, and autonomic regulation.

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