Stress and relaxation during sleep and awake time, and their associations with free salivary cortisol after awakening.

Rusko H[1], Rönkä T[1], Uusitalo A[1,2], Kinnunen U[1,3,4], Mauno S[1,3], Feldt T[1,3], Kinnunen M-L[1,3], Martinmäki K[1], Hirvonen A[5], Hyttinen S[5], Lindholm H[5].

1 Department of Biology of Physical Activity, University of Jyväskylä, Jyväskylä, Finland
2 Helsinki University Central Hospital, HUSLAB Meilahti/Division of Clinical Physiology and Nuclear Medicine, Helsinki, Finland
3 Department of Psychology, University of Jyväskylä, Jyväskylä, Finland
4 Department of Psychology, University of Tampere, Tampere, Finland
5 Finnish Institute of Occupational Health, Helsinki, Finland

heikki.rusko@sport.jyu.fi

Abstract
We investigated whether stress and relaxation states can be determined from heart rate (HR) and heart rate variability (HRV) indices. Ambulatory heartbeat intervals were recorded during sleep and working day from 17 hospital employees, and analysed for stress and relaxation times using the Firstbeat PRO Wellness Analysis Software®. Significant differences were observed between sleep and awake time: stress dominated awake hours and relaxation dominated sleep. Significant correlations were found between cortisol after awakening and indicators of stress and relaxation during sleep. These results suggest that stress and relaxation states can be determined from HR and HRV indices.

Key terms: Heart rate variability, work stress, recovery, sleep time

Introduction
Heart rate variability (HRV) has been shown to be a strong and independent predictor of mortality after acute myocardial infarction and it has also been used as a non-invasive tool for predicting cardiovascular morbidity and mortality in healthy subjects (1, 2). HRV analysis has also been proposed as a suitable non-invasive method to study the effects of work-related stresses on cardiovascular autonomic regulation during work and sleep (3, 4, 5). Employees exposed to high job strain or work stress have indicated a shift in autonomic cardiac balance towards sympathetic dominance during both working hours and sleep (3, 4). It has been suggested that work-stress may have more pronounced effects on vagal tone during recovery and restoration after work than during the actual work time because low vagal tone during sleep was more predictive for mild hypertension than the values during work (4).
Numerous previous studies have shown that HR is lower during the night than during the daytime period and heart rate variability during daytime indicates relative sympathetic dominance, while the night is characterized by parasympathetic, or vagal dominance (e.g. 3, 4, 5, 6, 7, 8). As far as we know, no studies using a more general scoring describing stress and relaxation state based on both HR and HRV during work, leisure time and sleep have been published. Recently, new promising software has been introduced for the analysis of stress and relaxation states of autonomic nervous system (ANS) based HR and HRV indices (9).
The golden standard for evaluating work stress has been urinary and blood cortisol. Recently, early morning salivary cortisol levels and responses have also been shown to be reliable biological markers for the individual's adrenocortical activity, and acute and chronic stress, when measured repeatedly with strict reference to the time of awakening (10, 11).

Objectives
We investigated whether stress and relaxation states can be determined from heart rate (HR) and heart rate variability (HRV) indices using the Firstbeat PRO Wellness Analysis Software®. More specifically the research problems were as follows: 1) are there differences in stress and relaxation times between sleep and awake time in healthy hospital workers, and 2) are there differences between workers in stress and relaxation times during sleep and awake time and are these differences related to salivary cortisol variables after awakening.

Methods
This study is part of the "Heart Rate and Work Stress" research project at the University of Jyväskylä. The subjects of the present study were 17 employees (16 nurses, one physician) from the Central Hospital of Central Finland. In the present study 24-h ambulatory R-to-R interval (RRI) data and awakening salivary cortisol data were collected at the end of the working week. Five subjects from the original sample of 22 were rejected due to diseases influencing RRI-data or error percentage of RRI recordings. Average age of the employees was 42 years ranging from 24 to 57 years.
Variables describing stress and relaxation during sleep and awake time were determined from 24-h ambulatory RRI data based on Heart Rate (HR) and Heart Rate Variability (HRV) indices using Firstbeat PRO Wellness Analysis Software® (WAS) version 1.4.1 (9). The analysis of stress and relaxation is based on the detection of sympathovagal reactivity that exceeds momentary metabolic requirements for the autonomic nervous system. The program calculates HRV indices second-by-second using the short-time Fourier Transform method (STFT), and HR- and HRV-derived variables that describe respiration rate and oxygen consumption (VO2) using neural network modeling of data (12, 13, 14, 15). The program also calculates second-by-second indices of stress and relaxation, reflecting activity of the sympathetic (absolute stress vector, ASV) and parasympathetic (absolute relaxation vector, ARV) nervous system. ASV is calculated from HR, high frequency power (HFP), low frequency power (LFP) and HRV-derived respiratory variables. ASV is high when heart rate is elevated, HRV is reduced and respiration rate is low relative to HR and HRV. ARV is calculated from HR and HFP and it is high when HR is close to the basic resting level and HRV is great and regular (9, 13). From the above variables the program draws conclusions on the duration of different physiological states of the body during night sleep and working day by segmenting the data into stationary segments. The data segments, including movement, physical activity at different intensities and recovery from physical activity, are detected using HR, HRV-derived respiration rate, estimated VO2 and movement-related ANS responses. For non-exercise data segments, the time when the body is in a stress state (*Stress time*), relaxation state (*Relaxation time*) or an unrecognized state is determined. The stress state is defined as an increased activation in the body, induced by external and internal stress factors (stressors), during which sympathetic nervous system activity is dominating and parasympathetic (vagal) activation is decreased. This definition does not take into account the nature of the stress response, that is, whether it is positive or negative. The relaxation state is defined as a decreased activation in the body during relaxation, rest and/or peaceful working, related to the lack of external and internal stress factors when parasympathetic activation is dominating. In the present study, stress and relaxation times were calculated separately for the sleep time and for the awake hours including work and leisure time.
Awakening cortisol level (AC_0) and 30-min cortisol awakening response (CAR_{30} = difference between AC_{30} and AC_0) were analyzed from saliva samples taken immediately after and 30-min after awakening according to Pruessner et al. (10). Free salivary cortisol was analyzed using chemiluminescence detection (IBL Hamburg: Cortisol Saliva LIA RE62011).

Results

Significant differences were found in all variables between sleep and awake time, Table 1.

Table 1. Mean, standard deviation (SD) and range of total time, stress time and percentage, relaxation time and percentage, and average heart rate during awake hours and sleep (n=17).

	Awake Mean ± SD (range)	**Sleep** Mean ± SD (range)	**P**
Total time	1013 ± 39 (925 - 1070)	438 ± 51 (343 – 522)	<0.001
Stress time, min	580 ± 230 (56 - 884)	125 ± 101 (0 – 317)	<0.001
Stress %	57 ± 22 (5 – 87)	28 ± 22 (0 – 71)	=0.017
Relaxation time, min	41 ± 61 (0 – 231)	262 ± 110 (97 – 410)	<0.001
Relaxation %	4 ± 6 (0 – 21)	60 ± 24 (21 – 93)	<0.001
Average Heart rate	83 ± 8 (73 – 105)	61 ± 5 (53 – 73)	<0.001

AC_0 averaged 13.6±2.0 and CAR_{30} 10.5±2.7 (mean±SE). Total awake or sleep time did not correlate with either AC_0 or CAR_{30}. Significant correlations were observed only between awakening cortisol variables and indicators of stress and relaxation during sleep. AC_0 correlated with average heart rate during sleep (r = 0.74, p<0.001) and tended to correlate with stress percentage during sleep (r = 0.42, p = 0.097). CAR_{30} correlated with relaxation (r = 0.50, p = 0.043) and stress percentages during sleep (r = -0.49, p = 0.046) and tended to correlate with relaxation time (r = 0.42, p = 0.090), stress time (r = -0.46, p = 0.065) and average heart rate (r = -0.44, p = 0.081) during sleep.

Discussion and Conclusions

Significant differences in stress and relaxation variables between sleep and awake time were observed so that stress dominated awake hours and relaxation dominated sleep. These results agree with previous studies that HR is lower during the night than during daytime, and that HRV during daytime indicates relative sympathetic dominance while the night is characterized by parasympathetic dominance (e.g. 3, 4, 5, 6, 7, 8). Interestingly, the variation in stress and relaxation times between subjects was wide during both awake hours and sleep. Similarly to previous studies (e.g. 10, 16) sleeping time did not correlate with awakening cortisol variables. Instead, significant and close to significant correlations were found between awakening cortisol variables and variables of stress and relaxation during sleep. These correlations suggest that the present HR and HRV based detection method seems to give similar information as awakening cortisol variables. Taking into consideration that some of the correlations were not significant they were logical in a sense that those employees who had long relaxation time and short stress time during night had low AC_0 and high CAR_{30}. This finding on healthy hospital workers is contrary to the recent results on subjects including insomnia patients that subjective sleep disturbances are correlated with decreased awakening cortisol but that correlation was due mainly to the significantly decreased AC_0 in the insomnia patients (16).

In conclusion, the present findings show that it is possible to determine stress and relaxation states based on HR and HRV analysed from ambulatory RRI recordings using WAS.

Stress dominated awake hours and relaxation dominated sleep as could be expected according to the previous studies. Wide variation between subjects was observed in stress and relaxation times during both awake hours and sleep. The correlations between cortisol variables after awakening and indicators of stress and relaxation during sleep suggest that ANS function based recovery during sleep may influence cortisol awakening response. Finally, the results suggest that stress and relaxation states based on HR and HRV can be used for investigating the effects of work stress during both awake time and sleep.

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3. Contact information:

Heikki Rusko, Ph.D., Professor
Department of Biology of Physical Activity, University of Jyväskylä
Jyväskylä, Finland
Email: heikki.rusko@sport.jyu.fi
Phone: +358142603112; +358142603172
Mobile phone: +358400641596
Fax: +358142602011
Postal Address: P.O.Box 35 (LL), 40014 University of Jyväskylä, Finland
Street Address: Rautpohjankatu 8, 40700 Jyväskylä, Finland