

## No stress after 24-hour on-call shifts?

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**Abstract:** No stress after 24-hour on-call shifts? : Birgit HARBECK, *et al.* Department of Medicine I, University of Luebeck, Germany—**Objectives:**

Irregular sleep patterns can adversely affect physiological functions and have been associated with increased physiological and psychological stress. Nocturnal work of physicians during 24-hour on-call shifts (OCS) disrupts the sleep/wake cycle. Chronic exposure to distress has been shown to affect cardiovascular homeostasis and to impair performance in neurocognitive and simulated clinical tasks. **Methods:** In a prospective cohort study, biochemical and physiological stress parameters were assessed in 11 female and 9 male physicians (median age: 32 years, range 26–42 years) before a normal working day and after a 24-hour OCS in internal medicine. In addition, various tests of attentional performance (TAP) were conducted.

**Results:** The levels of thyroid stimulating hormone (TSH) were significantly higher after a 24-hour OCS, while there were no significant changes in cortisol, epinephrine, and norepinephrine levels. Heart rate variability and skin resistance increased following an OCS, although the differences were not statistically significant. Intrinsic alertness was comparable, while phasic alertness was significantly improved following a 24-hour OCS. Focused attention tended to be better following a night shift. There was no correlation with age or medical working experience; however, men experienced more stress than women. **Conclusions:** Following a 24-hour OCS, (i) TSH may be an early and sensitive biochemical predictor of stress; (ii) other classical biochemical stress parameters do not depict the psychological stress perceived by physicians; (iii) there may be a mismatch between experienced and objective stress levels; (iv) neurocognitive functions are not impaired, while performance may even be improved; and (v) men might be more sensitive to distress.

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Occupational stress may lead to hormonal changes and may impair mental and physical performance. This appears particularly important for 24 hour-on-call shifts (OCSs) in hospitals. Extended on-duty shifts result in acute and chronic sleep loss and circadian disruption<sup>1</sup>. Sleep deprivation with disturbed sleep patterns exerts negative effects on physiological functions and is associated with increased physiological and psychological distress<sup>2</sup>. Following night shift work during OCS the sleep/wake cycle is disturbed, which causes desynchronization of the natural biological rhythms<sup>3</sup> and may impact clinical performance<sup>4</sup>. Furthermore, it has been shown that experience of distress leads to elevated blood pressure, decreased heart rate variability, and endothelial dysfunction, thereby increasing the risk of cardiovascular disease<sup>5,6</sup>.

Various biochemical and in particular endocrine parameters have been identified as responsive to stress. Increased physical or psychological demands lead to enhanced synthesis of growth hormone-releasing hormone (GHRH) and corticotropin-releasing-hormone (CRH) within the hypothalamus, which is followed by the secretion of growth hormone (GH) and adrenocorticotropic (ACTH) from the anterior pituitary. ACTH stimulates the secretion of corticosteroids in the adrenal glands. However, it has been shown that early morning cortisol levels are significantly attenuated following a 24-hour OCS<sup>7,8</sup>. In addition, stressors lead to increased activity of the sympathetic nervous system (SNS) and the adrenal medulla, resulting in increased discharge of epinephrine and norepinephrine. Ernst *et al.*<sup>8</sup> demonstrated that urinary noradrenaline excretion was greater during an OCS when compared with a normal working day. Several complex interactions determine the physiologic responses.

Catecholamine biosynthesis in the adrenal medulla is regulated by glucocorticoids, whereas catecholamines, cytokines (TNF $\alpha$ , interleukin-1, and interleukin-6), and various peptides stimulate the secretion of CRH.

Acute and chronic stress may also induce an increase in interleukin-6<sup>9</sup>), which is mainly secreted by lymphoid and endothelial cells as well as by fibroblasts. In addition, increased stress results in an increased release of glucagon from pancreatic  $\alpha$ -cells. Cortisol secretion stimulated by increased activity of the sympathetic nervous system leads to high levels of glucose as well as changes in lipid metabolism. Besides, acute and chronic stress can foster the release of thyroid stimulating hormone (TSH)<sup>10</sup>. Thus, changes in the endocrine system may reflect stress on various levels.

A variety of physiological variables have been identified as affected following stress; endothelial dysfunction was found after night shift work and resulted in increased risk of cardiovascular disease. Flow-mediated dilation, as a measurement for brachial artery endothelial function, decreased in physicians after a 24-hour shift and in those who reported fewer sleeping hours during the shift<sup>11,12</sup>). In addition, coronary microcirculation has been shown to be impaired after night shift work<sup>6</sup>). Diastolic blood pressure was significantly elevated throughout a 24 hours period and during a night shift<sup>13</sup>), and heart rate variability (HRV) showed a significant increase in sympathetic tone before work and during work compared with after work<sup>8,14</sup>). During periods of high stress, as indexed by high cortisol levels, Looser *et al.*<sup>15</sup>) found significant associations between high cortisol levels and HRV. Surprisingly, during low stress periods, these associations were not significant. Moreover, heart rate abnormalities more often occurred following a 24-hour shift<sup>16</sup>).

Previous studies point at a possible impact of night shifts and related stress on neurocognitive performance in physicians<sup>17,18</sup>). However, it remains unclear if changes in physicians' schedules affect the well-being of health-care workers and patients' outcomes. There are different methods available to determine various aspects of stress. Ernst *et al.*<sup>8</sup>) used a multi-disciplinary approach to assess the effect of stress in 30 physicians of different specialties and found changes in both the sympathetic-adrenomedullary system and the hypothalamic-pituitary-adrenocortical axis. In the present study, we expanded this approach by combining assessment of biochemical, physiological, and neurocognitive parameters in internal medicine physicians. We intended to examine the impact of a 24-hour OCS in this population on biochemical and physiological stress parameters and neurocognitive performance.

## Materials and Methods

### Participants

Twenty physicians working in a department of internal medicine were recruited in this study. The study was designed as a prospective crossover trial with each physician completing a 24-hour OCS and a 24-h control period including a regular 8-h non-OCS. Biochemical, physiological, and neurocognitive stress parameters were assessed in 11 female and 9 male physicians (median age: 32 years, range 26–42 years) at 08.00 a.m. prior to a normal working day and 2–4 weeks later directly following a 24-hour OCS in internal medicine at 08.00 a.m. The design allowed for comparison of the differences in stress levels prior to a normal working day and following a 24-hour OCS. Circadian rhythm-dependent effects were minimized by testing participants at similar time points in the morning.

Medical working experience differed from low (1–2 years, n=5) to medium (3–4 years, n=7) and high (more than 4 years, n=8). The age distribution was as follows: 25–29 years, 4 physicians; 30–34 years, 11 physicians; 35 to 39 years, 3 physicians; 40 to 45 years, 2 physicians. Following the 24-hour OCS, physicians were asked to assess the experienced stress level (1=low stress level; 2=medium; 3=high) with respect to activity and events during their shift. While cardiopulmonary resuscitation and other potentially life-threatening situations were considered to be stressful events, routine work without much time for recreation usually reflected medium stress experience, and uneventful nights with many rest periods were designated as relatively unstressful.

In order to identify potentially confounding sleep parameters, all participants were asked to complete a sleep questionnaire with questions regarding sleep disorders, intake of stimulants, sleep behavior prior to the tests, and normal sleep performance.

### Laboratory methods

Biochemical stress parameters included cortisol, epinephrine, norepinephrine, interleukin-6, growth hormone, glucose, glucagon, insulin, triglyceride, cholesterol, uric acid, urea, and TSH. In addition, LH, FSH, estradiol, and testosterone were assessed. Blood samples were transferred on ice immediately and centrifuged at 2,500x g at 4°C for 10 minutes, and the supernatants were stored at –20°C until analysis. Cortisol and growth hormone were analyzed by chemiluminescence immunoassay. Epinephrine and norepinephrine in plasma were analyzed using high-performance liquid chromatography. Testosterone, estradiol, TSH, insulin, interleukin-6, LH, and FSH were measured by chemiluminescence immunoassay.

Cholesterol, triglyceride, urea, uric acid, and glucose were assessed using photometric measurement. Glucose was analyzed by radioimmunoassay.

#### *Physiological parameters*

Pulse, blood pressure, electrocardiogram, heart rate variability, and skin resistance were assessed as follows:

##### 1) Heart rate variability (HRV)

The evaluation of HRV was performed in a quiet and temperature-controlled room according to the guidelines of the Task Force for Pacing and Electrophysiology<sup>19</sup>. A continuous 10-minute ECG was recorded by using an applanation tonometer interface with HRV software (CardioScan 4.0, MTM, Huenfelden, Germany). Heart rate variability was recorded as beat-to-beat intervals. Variation in the beat-to-beat interval is a physiological phenomenon resulting mainly from inputs of the sympathetic and parasympathetic nervous system (SNS and PSNS, respectively) and humoral factors. Decreased PSNS activity or increased SNS activity will result in reduced HRV. HRV analysis was done using frequency domain methods.

The high-frequency and low-frequency components of HRV (measured in absolute units; i.e., ms<sup>2</sup>) were obtained. Low frequency (LF) was defined as 0.04–0.15 Hz, and high frequency (HF) was defined as 0.15–0.40 Hz<sup>19</sup>. HF activity is associated with PSNS activity. LF activity reflects a mixture of both the SNS and PSNS. Frequency domain variables including the HF and LF powers and LF:HF ratio were derived from spectral analysis of successive R-R intervals. Total power (TP) of HRV was also calculated for use in regression analysis as a global marker of cardiac autonomic function.

##### 2) Skin resistance

Skin resistance was determined by a device producing weak constant current between the middle phalanges of digit II and digit IV of the nondominant hand. The mean resistance (in kilo-ohms) of five measures within a time interval of one minute was recorded at the beginning of the procedure and at the end.

#### *Neurocognitive parameters*

In addition, neurocognitive performance was tested by using various tests of attentional performance (German version of a computerized attentional test: Go/No Go, vigilance, alertness<sup>20</sup>) and divided attention (d2 letter cancellation test<sup>21</sup>). Intrinsic alertness represents the internal control of wakefulness and arousal in the absence of a preceding warning stimulus; phasic alertness describes the ability to increase response readiness subsequent to external cueing<sup>22</sup>. Both aspects of attention intensity are important abili-

ties required for patient care in internal medicine. The d2 letter cancellation test is a timed-based test of divided attention measuring processing speed, rule compliance, and quality of performance<sup>23</sup>. Visual attention and task switching were assessed by the Trail Making Test (TMT A and B<sup>24</sup>). Memory functions were tested by Digit Span (short-term memory<sup>25</sup>), Digit Symbol Substitution Test (DSST, memory and speed of processing<sup>25</sup>), and the Wechsler Memory Scale<sup>25</sup>.

#### *Ethics statement*

The study protocol was approved by the Ethics Committee of the Christian-Albrechts-University of Kiel, Germany. All participants provided written informed consent.

#### *Statistical analysis*

Results obtained on the two occasions were compared using a paired Student's *t*-test in case of normally distributed data. In all other cases, results were compared using the nonparametric Wilcoxon signed-ranks test. A *p*-value of less than 0.05 was considered significant. Sample size calculation (<http://biomath.info/power/>) was performed for two-group tests with an  $\alpha=0.05$  and a statistical power of 80% assuming stress prevalence of maximum 25% in the controls and 75% following a 24-h OCS, respectively, resulting in a minimum number of 18 subjects in each group.

## **Results**

#### *Experienced stress and sleep performance*

Physicians were asked to assess the experienced stress levels after a 24-h OCS. Experienced stress levels during the OCS differed from low ( $n=8$ ) to medium ( $n=8$ ) and high ( $n=4$ ) and did not correlate with age or working experience (see Appendix Table 1), although male physicians were more likely to experience medium or high stress levels when compared with their female colleagues (78% vs. 45%, see Appendix Table 1).

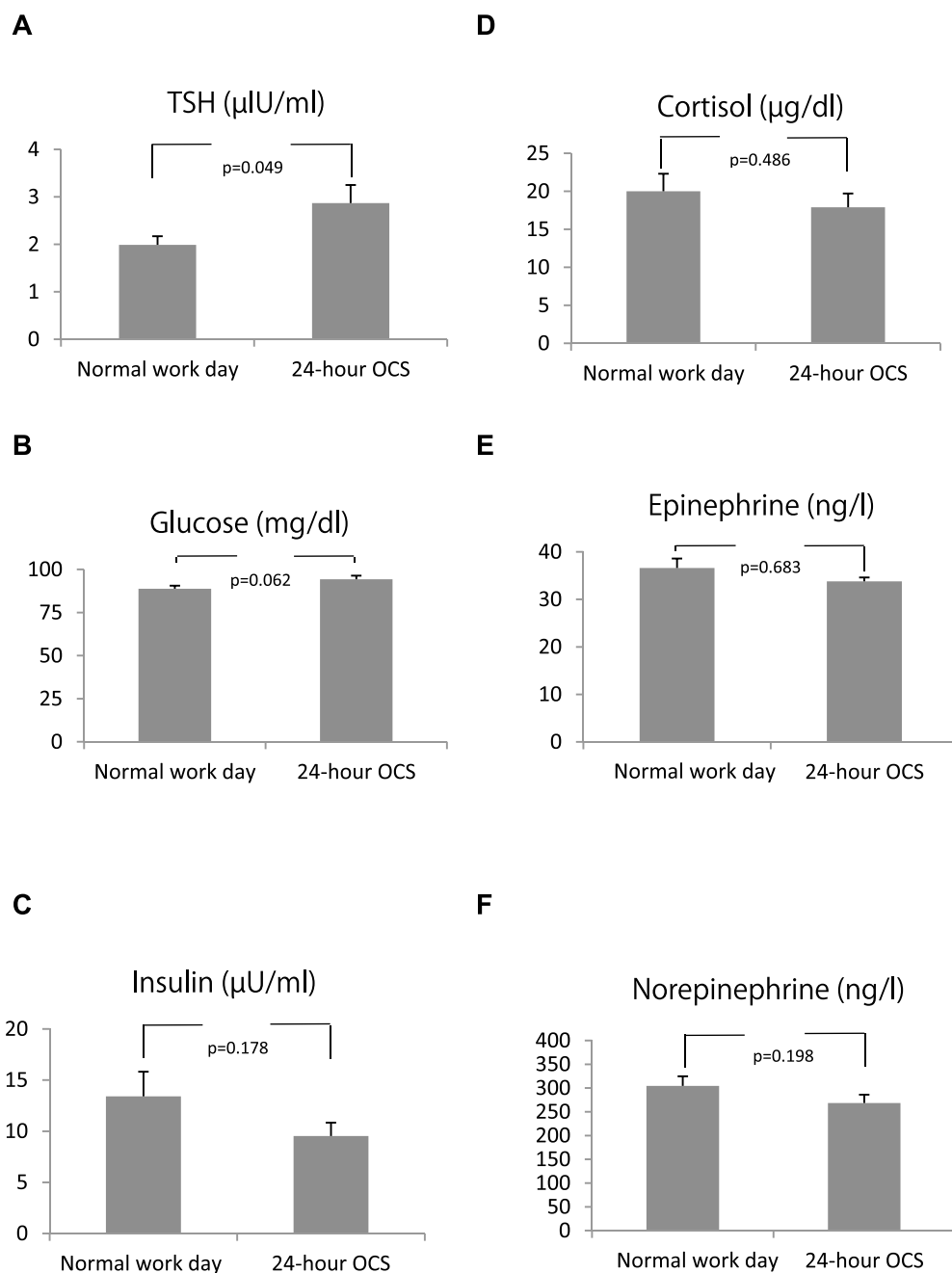
None of the study participants had a known sleep disorder, and 6–8 hours of sleep was normal during the week, with more individuals having >8 hours of sleep during normal weekends (see Appendix Table 2A). Stimulants such as coffee or tea were used by all individuals, and in both groups during the 24-h OCS, most of the physicians had limited sleep time and significantly increased disturbances (see Appendix Table 2B).

#### *Biochemical parameters*

Interestingly, there were no significant changes in biochemical parameters except for TSH. TSH

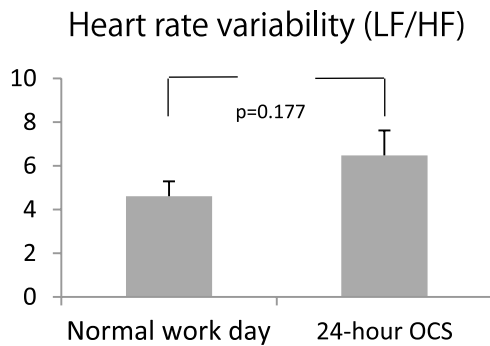
levels were significantly higher after the 24-hour OCS ( $p=0.049$ , Fig. 1A). However, there was a tendency for higher glucose levels after shift work ( $p=0.062$ ), whereas insulin levels seemed to be lower after the OCS, although the difference was not statistically significant (Fig. 1B–C). In particular, there were no significant differences in cortisol,

epinephrine, and norepinephrine levels after the OCS (Fig. 1D–F) and no significant increase in interleukin-6, growth hormone, glucagon, triglyceride, cholesterol, uric acid, and urea as well (see Appendix Table 3). OCS had no apparent influence on secretion of gonadotropins, estrogen, and testosterone when the levels were compared between before a normal

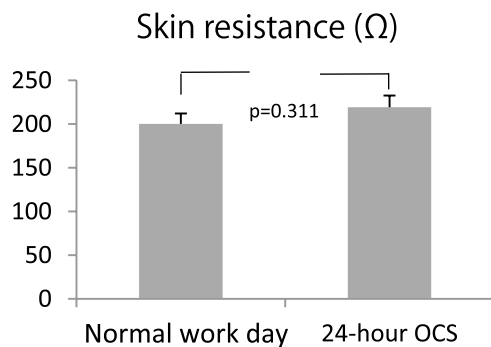


**Fig. 1.** Biochemical parameters assessed prior to a normal working day and following a 24-hour on-call shift, showing significantly increased levels of thyroid stimulating hormone (TSH; A). Glucose levels tended to be higher (B) with an antidromic development for insulin (C). Classical biochemical stress parameters like cortisol, epinephrine, and norepinephrine did not change (D–F).

A



B



**Fig. 2.** Physiological parameters assessed prior to a normal working day and following a 24-hour on-call shift. Heart rate variability (A) and skin resistance (B) did not show significant differences.

working day and after the 24-h OCS. Of note, these results did not show any correlation with age, medical working experience, or experienced stress levels during the OCS.

#### Physiological parameters

Heart rate variability (Fig. 2A) and skin resistance (Fig. 2B) increased following the OCS, although the differences were not statistically significant. Cardiac arrhythmias were seen in one physician after the OCS who presented with intermittent left bundle branch block. There were no significant differences in pulse and blood pressure (see Appendix Table 4).

#### Neurocognitive parameters

With respect to neurocognitive performance, intrinsic alertness was comparable on both occasions, while phasic alertness was significantly improved following the 24-hour OCS ( $p=0.022$ , Table 1). In addition, vigilance was similar before the work schedule and after the 24-hour OCS, while focused attention (d2 test) tended to be better following a night shift ( $p=0.066$ , Table 1). Otherwise, there were no significant differences regarding neurocognitive variables (Table 1).

Of note, these results did not show any correlation with age, medical working experience, or experienced stress levels during the OCS.

#### Discussion

Stress is an important physiological reaction to a challenge that disrupts homeostasis, with the body responding by stimulating the nervous, endocrine, and immune systems. The combination of reactions to stress is known as the “fight-or-flight response”, having evolved as a survival mechanism that enables people to react quickly to life-threatening situations. However, repeated stress responses may have a negative impact on physical and mental health. It has been shown that prolonged stress contributes to a variety of diseases, e.g., obesity and diabetes type 2 as well as hypertension<sup>26</sup>), and may impair neurocognitive performance.

Long-term effects of extended shifts on health in physicians are largely unknown. Several studies showed an increased risk for development of a burn-out syndrome<sup>27</sup>), which is mainly caused by chronic stress<sup>28</sup>). In a Chinese study, 60.6% of 457 physicians from 21 hospitals in Shanghai suffered from a mild degree of burnout, with 5.9% experiencing a severe degree of burnout<sup>29</sup>). Other studies showed that shift workers are at an increased risk of cardiovascular disease, breast cancer<sup>30,31</sup>) and metabolic disturbances, e.g., obesity and type 2 diabetes<sup>32</sup>). Thus, this non-physiological response may endanger the health and life of physicians as well as those of their patients<sup>33</sup>) and might result in significant socioeconomic costs. In the present study, we used a multidisciplinary approach and uncovered some unexpected results regarding biochemical, physiological, and neurocognitive parameters following an OCS in physicians.

The endocrine and metabolic response to stress is generally related to the intensity of the stimulus and mainly depends on an individual’s perception of potentially stressful situations. In our study, participants felt stressed ( $n=12$ ), although we could hardly find any objective proof for physical stress, and there was no correlation to experienced stress levels during the 24-hour OCS. Of interest, TSH was the only parameter showing significant changes. Hormonal rhythms are influenced by circadian and sleep/wake-dependent processes, and TSH secretion is regulated by the timing of sleep and the human circadian pacemaker. In the human system, serum TSH levels exhibit diurnal variation, with rising levels in the evening prior to bedtime and a maximum peak occurring around midnight. TSH levels decrease during sleep to approximately 50% by 08.00 to 09.30 a.m., as sleep has an inhibitory effect on TSH secretion<sup>34</sup>).

**Table 1.** Results of neurocognitive tests at 8 a.m. SD: standard deviation

	Prior to a normal work day		Following a 24-hour OCS		<i>p</i> -value
	Mean	SD	Mean	SD	
Alertness					
Intrinsic alertness (%)	57.1	24.6	62.7	± 22.6	0.469
Phasic alertness (%)	24.8	15.6	38.3	± 21.5	0.033
Go/No go test (%)	59.5	26.6	58.5	± 24.4	0.909
Vigilance (%)	45.6	6.1	45.7	± 5.3	0.949
Digit span (n)	12.5	1.8	12.6	± 2.4	0.829
DSST (n)	53.5	8.8	55.4	± 10.5	0.549
D2 test (errors/hits [%])	5.45	5.1	2.92	± 2.90	0.066
TMT A (s)	21.6	± 6.2	19.9	± 4.2	0.329
TMT B (s)	41.7	± 11.0	39.2	± 9.2	0.453
Wechsler Memory Scale					
W1	5.2	± 1.1	5.2	± 1.7	1.000
W2	6.6	± 1.4	6.5	± 2.0	0.928
W3	7.7	± 1.5	7.8	± 1.8	0.856

In addition, TSH increases in response to stressful events. Therefore, the present data confirm disruption in the rhythm of TSH secretion by 24-hour OCSs even after a single night. This might result from altered sympathetic and parasympathetic activity that affects the endocrine response via activation of the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system.

Of interest, glucose levels tended to be elevated following the 24-hour OCS, while insulin showed the opposite trend. This may be due to the fact that participants were not restricted with regard to eating during the OCS, with glucose levels possibly reflecting food intake during the night. The significance of the observed decrease in mean insulin levels, however, remains unclear. Very surprisingly, cortisol and catecholamines, classical stress markers, and interleukin-6, glucagon, triglyceride, cholesterol, uric acid, and urea did not show significant changes. These findings are in contrast to a report by Ernst *et al.*, who found urinary noradrenaline excretion to be higher during an OCS when compared with during a normal working day. Moreover, serum cortisol was lower in the morning after an OCS compared with the morning before an OCS<sup>8</sup>). However, in our study, catecholamines were assessed before or after work but not during the OCS, potentially reflecting normalization in endocrine stress markers that rapidly adapt to increasing demands. This applies in particular to plasma catecholamines due to their short half-life of a few minutes, with plasma metanephrines and normetanephrines being potentially better markers.

Heart rate variability showed a tendency to increase

after the OCS. Although not statistically significant, the results may reflect the physiological response to acute stress, since HRV is an index of the beat-to-beat changes in heart rate and is mediated by the parasympathetic and sympathetic nerves, demonstrating the capacity for parasympathetic inhibition of autonomic arousal. Increased HRV reflects a healthy autonomic nervous system being able to respond to changing environmental circumstances. Decreased HRV is a marker of autonomic inflexibility, which may favor negative effects on human health<sup>35</sup>). Two frequency domain measures were quantified: high frequency, a measure of parasympathetic activity, and the LF/HF ratio, a measure of sympathovagal balance. Similarly, Ernst *et al.* found HRV to be significantly higher during an OCS compared with during a normal working day<sup>8</sup>). The fact that our results did not reach statistical significance may also reflect rapid adaptation and normalization after an OCS.

In contrast, skin resistance increased after the OCS, suggesting the presence of even less stress, as skin resistance increases with advancing relaxation. A relaxed state or higher parasympathetic nervous system activity is usually associated with drier skin and higher electrical skin resistance, whereas stress is often associated with skin sweating, which lowers skin electrical resistance. This result may point to an ability of physicians to adapt rapidly to various stressors. On the other hand, complete exhaustion after a 24-hour OCS may also lead to a state of mental and physical relaxation resulting in decreased skin resistance.

Recently, much attention has been paid to neuro-

cognitive performance depending on work shifts; for example, Lockley *et al.* demonstrated that reducing extended work shifts in an intensive care unit significantly decreased attentional failures during night work hours<sup>17)</sup>. Of note, interns made 35.9 percent more serious medical errors during 24-hour OCSs in comparison with an intervention schedule that eliminated extended work shifts<sup>36)</sup>. Moreover, the risk of motor vehicle crashes increased after an extended work shift<sup>37)</sup>. However, Yaghoubian *et al.*<sup>38)</sup> found similar favorable outcomes in trauma surgery performed at night by residents who had worked longer than 16 hours compared with those performed during the day. Similarly, in our study, neurocognitive parameters showed a significant better response subsequent to external cueing and a tendency to score better in the divided attention test after the 24-hour OCS. In fact, physicians may have become accustomed and adapted to extraordinary work loads and passed through a learning process with improved attentional performance during the 24-hour OCS. Our findings are contrary to results of Rauchenzauner *et al.*<sup>13)</sup> and Looser *et al.*<sup>15)</sup>, who demonstrated higher psychological stress in physicians after a 24-hour OCS. Similarly, Ernst *et al.*<sup>8)</sup> showed significantly impaired concentration-endurance performance after an OCS. Comparison of physicians working a series of 5 night shifts with those working day shifts showed a substantial decline in cognitive performance after night shifts<sup>18)</sup>. Similarly, it has been shown that short-term memory appears to decline after both day and overnight shifts<sup>39)</sup>. Our data though may rather demonstrate the difference in conditions before and after a stressful working day.

Differences in performance are of clinical and judicial significance if patient safety incidents are affected by shift work, cognitive failure, and job stress, as demonstrated by Park and Kim<sup>33)</sup>. A detailed investigation of a working schedule including sleep fragmentation and extended work hours demonstrated that concentration-endurance performance was significantly reduced after a 24-hour OCS<sup>8)</sup>. However, it remains unclear if changing the work schedules of physicians has a positive effect on clinical performance and patient outcome. In a recent study, Kerlin *et al.* surprisingly demonstrated that nighttime in-hospital intensivist staffing did not improve patient outcomes. Compared with nighttime telephone availability of the daytime intensivist, there was no evidence that this staffing model had a significant effect on length of stay in the ICU or hospital, ICU or in-hospital mortality, readmission to the ICU, or the probability of discharge to home<sup>40)</sup>. Our findings support the idea that a 24-hour OCS may not have the widely suspected impact when compared with the work and

stress load of physicians on normal work days or in prior work, respectively.

A potential limitation of the present study is the relatively small sample size. This is in part due to the complex approach and departmental structure, which did not allow recruiting of more participants during the study period. In addition, stress levels did not differ as much as expected for the underlying sample size calculations.

Despite the small sample size of our study, we assume that the effect of a long OCS may not be as predicted and may even improve psychophysiological parameters, with enhanced attention and memory functions. The positive effects may be the result of long-term gating of attentional properties.

## Conclusions

In conclusion, we showed that there may be a mismatch between experienced and objective stress levels in physicians following a 24-hour OCS when compared with before work. Of note, TSH may be the earliest and most sensitive parameter indicating even mild stress, whereas other biochemical stress parameters are less influenced by an OCS; and male physicians experience more stress than their female colleagues. Moreover, neurocognitive functions in physicians are not impaired, while performance may even be improved. This may result from long-term gating of attentional properties. Overall, it is conceivable that physicians have the ability to adapt to the workload and stressful events during a 24-hour OCS. Since these data are in contrast to data from previous reports, further studies are needed to study the sequelae of OCS-related stress in physicians and effects on patient care in greater detail.

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**Appendix Table 1.** Experienced stress following a 24-hour OCS

Experienced stress	Working experience			Sex		Age (years)			
	Low (n=5)	Medium (n=7)	High (n=8)	Female (n=11)	Male (n=9)	25–29 (n=4)	30–34 (n=11)	35–39 (n=3)	40–45 (n=2)
Low (n=8)	2	2	4	6	2	2	5	0	1
Medium (n=8)	1	4	3	3	5	1	5	2	0
High (n=4)	2	1	1	2	2	1	1	1	1

**Appendix Table 2.** General sleep characteristic of participants (A) and during the study (B), n=17; 3 participants did not answer the sleep questionnaire

A			
Known sleep disorders			0
Drinking tea and/or coffee			17
Usual sleeping time (hours)		On normal work days	On weekends
	<4	0	0
	4–6	4	2
	6–8	13	8
	>8	0	7
B			
Parameters		Prior to a normal work day	Following a 24-hour-OCS
Sleep disturbances (number)	0	14	2
	1	2	6
	2	1	8
	3	0	1
	4	0	0
	>4	0	0
Sleep during prior night (hours)	<2	0	1
	2–4	1	8
	4–6	2	6
	>6	14	2

**Appendix Table 3.** Biochemical parameters (mean  $\pm$  SD)

Laboratory data	Prior to a normal work day	Following a 24-hour OCS	<i>p</i> -value
Urea (mg/dl)	30.2 $\pm$ 7.5	32.7 $\pm$ 6.7	0.286
Uric acid (mg/dl)	4.6 $\pm$ 1.1	4.5 $\pm$ 1.0	0.712
Glucose (mg/dl)	88.8 $\pm$ 8.0	94.3 $\pm$ 9.4	0.062
Triglycerides (mg/dl)	109.2 $\pm$ 57.4	99.4 $\pm$ 87.7	0.686
Cholesterin (mg/dl)	183.7 $\pm$ 28.1	176.3 $\pm$ 29.1	0.433
TSH ( $\mu$ IU/l)	2.0 $\pm$ 0.8	2.9 $\pm$ 1.7	0.049
Insulin ( $\mu$ U/ml)	13.4 $\pm$ 10.8	9.5 $\pm$ 5.8	0.178
Cortisol ( $\mu$ g/dl)	20.0 $\pm$ 10.4	17.9 $\pm$ 8.2	0.486
LH (IU/l)	6.6 $\pm$ 8.9	4.9 $\pm$ 3.8	0.463
FSH (IU/l)	4.4 $\pm$ 3.4	4.6 $\pm$ 2.2	0.798
Estradiol (pg/ml)	77.1 $\pm$ 86.4	144.8 $\pm$ 164.0	0.281
Testosterone (ng/ml)	5.8 $\pm$ 1.6	5.2 $\pm$ 1.5	0.447
GH (ng/ml)	1.78 $\pm$ 2.19	1.59 $\pm$ 1.94	0.788
IL-6 (pg/ml)	2.2 $\pm$ 0.5	2.1 $\pm$ 0.3	0.627
Glucagon (pg/ml)	50.2 $\pm$ 17.5	43.6 $\pm$ 13.8	0.255
Norepinephrine (ng/l)	304.6 $\pm$ 90.6	268.5 $\pm$ 78.6	0.198
Epinephrine (ng/l)	36.6 $\pm$ 24.0	33.8 $\pm$ 17.4	0.683

**Appendix Table 4.** Physiological parameters

Physiological parameters	Prior to a normal work day	Following a 24-hour OCS	<i>p</i> -value
Heart rate variability	4.61	6.48	0.177
Skin resistance	200.3	219.2	0.311
Heart beats (bpm)	75.2	74.2	0.782
Systolic blood pressure (mmHg)	120.5	116.5	0.349