Original Article

Euromediterranean Biomedical Journal
for young doctors
(formerly: Capsula Eburnea)

EFFECTS OF SHIFT WORK ON CARDIOVASCULAR ACTIVITY, SERUM CORTISOL AND WHITE BLOOD CELL COUNT IN A GROUP OF ITALIAN FISHERMEN

Emanuele Cannizzaro[1],Carla Cannizzaro [1],Daniela Martorana [2], Salvatore Moscadini [2], Daniele Lo Coco [3]

SUMMARY

We analyzed the effects of working activity and working shifts on the circadian rhythmicity and circadian phase relations of serum cortisol level, white blood cell count, resting heart rate and systolic/diastolic blood pressure in a group of Italian fishermen.

We observed a shift-induced displacement of cortisol secretion and a change in leukocyte count. Moreover, systolic/diastolic blood pressure and resting heart rate were markedly influenced by the night shift, whereas no appreciable changes were observed after the morning and afternoon shifts, compared to pre-working values. These data suggest that the human circadian system is greatly influenced by shift work, and that serum cortisol level, leukocyte count, systolic and diastolic blood pressure as well as resting heart rate are sensitive indicators of the biological responses to a stress workload in shift workers, especially after a night shift.

Introduction

The human circadian system regulates rhythmicity in the human body and establishes normal sleep and wake phases. Since the circadian system is the foundation of the sleep-wake cycle, disorders or abnormalities in the circadian system are often connected with disorders and abnormalities in sleep and compromised health status (1). As a result, sleep dysfunctions are among the most prevalent mental illnesses, and are core symptoms of several neurologic diseases and other mental disorders (2-10). Chronic exposure to life stressors, including work-related stress, and alterations in the neuroendocrine stress system are among the most important causes of disrupted sleep (11), and are well known causes of many behavioral and biochemical changes (12-18).

Many of these changes have been analyzed after long and short periods of working time. It was observed that shift work produces modifications in the circadian rhythms, and that longer working periods are associated with more evident variations of the circadian system. Few studies, however, have investigated the effects on the circadian rhythmicity of multiple physiological variables induced by work shifts, particularly by the night shift. Moreover, although the sympathetic and parasympathetic systems are also modulated by the biological clock to produce an autonomic balance, it is unclear whether shift work is

Address of the authors

[1]Dipartimento per la Promozione della Salute "G. D'Alessandro", University of Palermo, Italy
[2]Dipartimento di Ortopedia e Traumatologia, University of Palermo, Italy
[3]U.O. Neurologia, Dipartimento di Neuroscienze, Ospedale Civico - ARNAS, Palermo, Italy

***Send correspondence to**: Dr. Emanuele Cannizzaro, emanuele.cannizzaro@unipa.it*

***Received**: September 10th, 2012 — **Revised**: October 14th, 2012 — **Accepted**: October 21th, 2012*

associated with changes in the functional activity of the autonomic system.
Therefore, in this study, we selected a group of shift workers, specifically fishermen, whose employment periodically takes place during the night. We then examined the consequences of working activity and the effects of working shifts on the circadian rhythmicity and circadian phase relations of the most important biological variables, specifically regulated by the human circadian system: blood cortisol level, leukocyte count, resting heart rate, and systolic/diastolic blood pressure.

Material and Methods
We included in this study 40 male workers (mean age: 35 ± 10 years; average employee seniority: 10 ± 7 years), submitted to periodic health surveillance by a qualified medical doctor for more than five years. The working schedule was set on three shifts per day (first shift: from 6:30 a.m. to 2:30 p.m.; second shift: from 2:30 p.m. to 10:30 p.m.; third shift: from 10:30 p.m. to 6:30 a.m.). During their working activity, fishermen have to lower fishing equipment in the sea, and, after few hours, pull them back on board, using motorized winches. All recruited subjects had no history of biochemical or behavioral changes.
Preliminarily, we collected information about their social and economic status and about the level of work satisfaction, through a standardized questionnaire. The analysis of the obtained data shows that the workers included in the study belong to a low/middle socioeconomic class. Most of the workers reached the middle school diploma, and they felt motivated in their work, that requires a fair decision-making autonomy.
Biological measurements and samplings were carried out during April and May 2011, at the end of each work shift and after a 15-minute rest period in the infirmary. All biochemical parameters (except serum cortisol level) were measured from serum within 3 hours from blood withdrawal with an automatic analyzer. The serum used for the evaluation of cortisol level was frozen at -80 °C. The cortisol test was carried out with the Baxter Stratus method and a Dasit analyzer.
All data were statistically analyzed using the Student t test for paired data.

Results
Serum proteins, fat panel, liver and kidney function, and hematocrit, measured before the three working shifts, were within normal values in all subjects (data not shown).
Results of the analysis of serum cortisol level and leukocyte count are summarized in **Table 1**. As expected, when we examined the samples obtained at the beginning of each working shift, cortisol level showed different values during the day, with higher values in the morning and lower values in the evening, confirming its characteristic circadian pattern. However, when we examined the samples obtained at the end of working shifts, we observed a trend in cortisol levels toward increased values after the third shift ($p=0.08$), and significantly reduced levels at the end of the second shift ($p<0.05$).
White blood cell count was within normal values in all the workers at the beginning of each working shift, and at the end of the first and second shifts. However, there was

	Pre-shift			Post-shift		
	06.30	14.30	22.30	06.30	14.30	22.30
Cortisol (ng/ml)	**14.5 ± 1.5**	**8.4 ± 1.1**	**6.4 ± 0.8**	**16.7 ± 1.4**	**9.7 ± 1.0**	**4.3 ± 0.6**
Leuko-cytes (x 10^3/µl)	**6.4 ± 1.1**	**7.0 ± 1.1**	**6.6 ± 1.0**	**8.3 ± 1.0**	**6.5 ± 0.9**	**7.0 ± 1.0**

Table 1: Average values of serum cortisol level and leukocyte count at the beginning and end of all shifts.

a trend toward increased values at the end of the third shift (p=0.09).
Results of the systolic/diastolic blood pressure and resting heart rate measurements are cumulatively shown in **Figure 1**. All values recorded before the beginning of each shift were within physiological limits. Also, no significant variations were recorded at the end of the first and second shift compared to pre-working values.

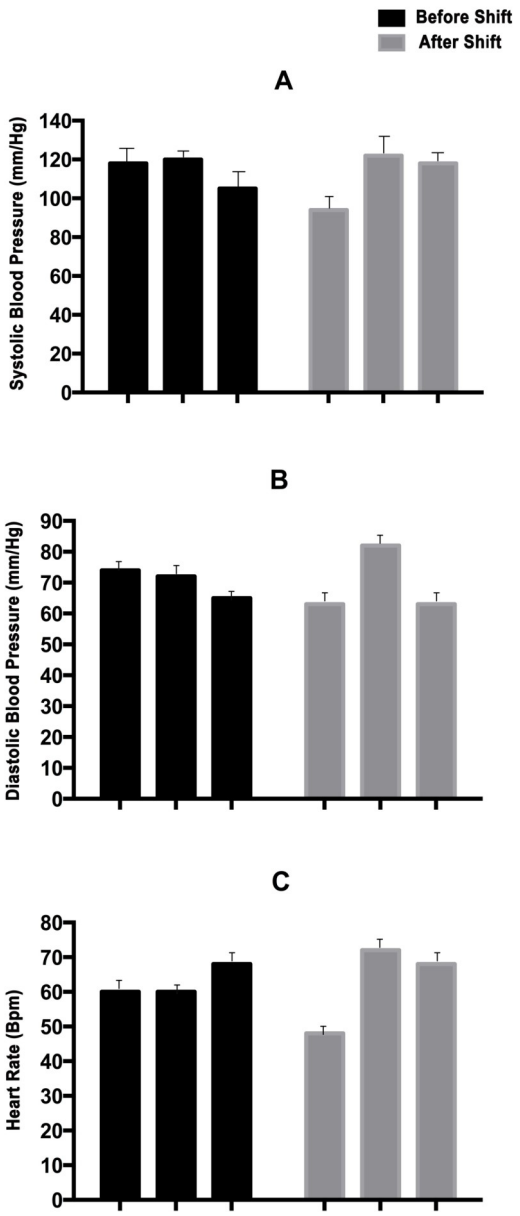

Figure 1: Average values of the systolic/diastolic blood pressure and resting heart rate measurements at the beginning and end of all shifts.

However, at the end of the third shift, both blood pressure and resting heart rate measurements were significantly reduced (mean decrease in diastolic blood pressure: 15%; means decrease in systolic blood pressure: 22%; mean decrease in resting heart rate:16%; p<0.05).

Discussion

In this study, we evaluated the acute effects of three different shifts on the circadian rhythm of serum cortisol levels, leukocyte count, systolic/diastolic blood pressure and resting heart rate in a group of fishermen.
It is known that under physiological conditions, cortisol is secreted according to the circadian rhythm, characterized by greater secretion during the night (that reaches its maximum in the early morning hours) and by a progressive decrease in the following hours (achieving a minimum at the end of the evening). The results of our study show that the circadian pulsatility of cortisol secretion is not affected per se by shift work, confirming previous studies suggesting that the endogenous physiological cortisol feedback system is not influenced by working conditions that alter the sleep-wake cycle of the subject.
However, our data also show that serum cortisol level might be modified at the end of most shifts. In particular, at the end of the night shift, cortisol expression showed a trend toward increased values, suggesting that even one night shift might change the circadian rhythm of serum cortisol. Moreover, cortisol levels were significantly reduced at the end of the afternoon shift, suggesting a role for both physical and psychological load in shift work.
The available data are not sufficient to fully explain the changes observed, and future studies in larger populations of subjects are warranted. However, our results are in accordance with a previous study, in which it was found that high levels of stress and anxiety can disrupt the normal pattern of plasma cortisol levels in healthy subjects (19). Job strain is also a variable that might induce circadian rhythm disturbance and influence serum cortisol levels. A relevant role could have also been played by sleep deprivation and work-induced sleep schedule changes because of the night shift. Indeed, previous studies have shown that in subjects who regularly work in shifts, as in the case of hospital nurses,

cortisol secretion depends on both its baseline serum level and on the timing of sleep (20). However, cortisol suppression does not seem to be a specific feature linked to the afternoon shift, since our previous studies have shown similar results in subjects who were involved in working activities during the whole day (21).

In regard to the leukocyte count, our data show a trend toward increased values at the end of the night shift, even if it did not reach statistical significance, probably because of the large variation of values between single subjects. This finding further confirms that night sleep deprivation is a relevant variable in the short- and long-term adjustment of circadian rhythms, and is in agreement with previous studies reporting an increase in the number of leukocytes in health care workers at the end of the night shift (22). On the contrary, no significant changes were observed in white blood cell count at the end of the less fatiguing morning and afternoon shifts.

Finally, we report a significant decrease in systolic/diastolic blood pressure and resting heart rate after the night shift. These results suggest that the alteration of the sleep-wake rhythm, induced by stressful working conditions, such as that of the fishermen studied, have a great influence on the nightly physiological predominance of vagal tone on cardiovascular function.

In conclusion, although the relatively low number of subjects included in the study may limit the generalization of the results, we demonstrated that serum cortisol level, leukocyte count, systolic and diastolic blood pressure, and resting heart rate are sensitive indicators of biological responses to a stress workload in shift workers, especially after a night shift, when there is a displacement of cortisol secretion and a modification in leukocyte count, accompanied by a significant reduction in cardiovascular parameters.

References

1. Richardson GS. The human circadian system in normal and disordered sleep. J Clin Psychiatry 2005; 66(Suppl 9):3-9.
2. Hermann DM, Bassetti CL. Sleep-related breathing and sleep-wake disturbances in ischemic stroke. Neurology 2009; 73:1313-1322.
3. Caminero A, Bartolomé M. Sleep disturbances in multiple sclerosis. J Neurol Sci 2011; 309:86-91.
4. Cupidi C, Realmuto S, Lo Coco G, Cinturino A, Talamanca S, Arnao V, Perini V, D'Amelio M, Savettieri G, Lo Coco D. Sleep quality in caregivers of patients with Alzheimer's disease and Parkinson's disease and its relationship to quality of life. Int Psychogeriatr 2012; 24:1827-1835.
5. Lo Coco D, La Bella V. Fatigue, sleep, and nocturnal complaints in patients with amyotrophic lateral sclerosis. Eur J Neurol 2012; 19:760-763.
6. Lo Coco D, Mattaliano P, Spataro R, Mattaliano A, La Bella V. Sleep-wake disturbances in patients with amyotrophic lateral sclerosis. J Neurol Neurosurg Psychiatry 2011; 82:839-842.
7. Lo Coco D, Cannizzaro E, Lopez G. Restless legs syndrome in a patient with multifocal motor neuropathy. Neurol Sci 2009; 30:401-403.
8. Lo Coco D, Cupidi C, Mattaliano A, Baiamonte V, Realmuto S, Cannizzaro E. REM sleep behavior disorder in a patient with frontotemporal dementia. Neurol Sci 2012; 33:371-373.
9. Lo Coco D, Cannizzaro E, Spataro R, Taiello AC, La Bella V. Sleep–wake problems in patients with amyotrophic lateral sclerosis: implications for patient management. Neurodegen Dis Manage 2012; 2:315-324.
10. Ford D, Kamerow D. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? J Am Med Assoc 1989; 262:1479–1485.
11. Meerlo P, Sgoifo A, Suchecki D. Restricted and disrupted sleep: effects on autonomic function, neuroendocrine stress systems and stress responsivity. Sleep Med Rev 2008; 12:197-210.
12. Cannizzaro C, Plescia F, Gagliano M, Cannizzaro G, Mantia G, La Barbera M, Provenzano G, Cannizzaro E. Perinatal exposure to 5-methoxytryptamine, behavioural-stress reactivity and functional response of 5-HT1A receptors in the adolescent rat. Behav Brain Res 2008; 186:98-106.
13. Cannizzaro C, Plescia F, Gagliano M, Cannizzaro G, Provenzano G, Mantia G, Cannizzaro E. Effects of pre- and postnatal exposure to 5-methoxytryptamine and early handling on an object-place association learning task in adolescent rat offspring. Neurosci Res 2007; 59:74-80.

14. Cannizzaro C, Plescia F, Martire M, Gagliano M, Cannizzaro G, Mantia G, Cannizzaro E. Single, intense prenatal stress decreases emotionality and enhances learning performance in the adolescent rat offspring: interaction with a brief, daily maternal separation. Behav Brain Res 2006; 169:128-136.
15. Cannizzaro E, Martire M, Gagliano M, Plescia F, La Barbera M, Mantia G, Mineo A, Cannizzaro G, Cannizzaro C. Reversal of prenatal diazepam-induced deficit in a spatial-object learning task by brief, periodic maternal separation in adult rats. Behav Brain Res 2005; 161:320-330.
16. Cannizzaro C, Martire M, Steardo L, Cannizzaro E, Gagliano M, Mineo A, Provenzano G. Prenatal exposure to diazepam and alprazolam, but not to zolpidem, affects behavioural stress reactivity in handling-naïve and handling-habituated adult male rat progeny. Brain Res 2002; 953:170-180.
17. Cannizzaro C, Martire M, Cannizzaro E, Monastero R, Gagliano M, Mineo A, Provenzano G. Effects of 8-OH-DPAT on open field performance of young and aged rats prenatally exposed to diazepam: a tool to reveal 5-HT1A receptor function. Eur Neuropsychopharmacol 2003; 13:209-217.
18. Cannizzaro C, Martire M, Cannizzaro E, Provenzano G, Gagliano M, Carollo A, Mineo A, Steardo L. Long-lasting handling affects behavioural reactivity in adult rats of both sexes prenatally exposed to diazepam. Brain Res 2001; 904:225-233.
19 Chatterton Jr R, , Doole, SL. Reversal of diurnal cortisol rhythm and suppression of plasma testosterone in obstetric residents on call. J Soc Gyn Invest 1999; 6:50-54.
20 Fujiwara S, Shinkai S, Kurokawa Y, Watanabe T. The acute effects of experimental short-term evening and night shifts on human circadian rhythm: The oral temperature, heart rate, serum cortisol and urinary catecholamines levels. Int Arch Occup Envirom 1992; 63:409-418.
21 Allegri F, Passarello B, Orru G, Coppola A, Antona A, Cannizzaro M, Gagliano M. Effetti del lavoro prolungato sui pescatori "d'altura": influenza sulla cortisolemia, prolattinemia e catecolamine urinary. Acta Med Med 1997; 13S:317
22. Folkard S, Monk TH, Lobban MC. Short and long term adjustment of circadian rhythms in "permanent" night nurses. Ergonomics 1978; 21:785-799.