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DEPRESSION AND CIRCADIAN TYPOLOGY

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SUMMARY

Background: *The relationship between circadian disruptions and depressive disorders is a topic of great interest in contemporary psychiatry. Circadian rhythms include all physiological processes displaying a period around 24 hours. Sleep/wake cycles, body temperature, hormone secretion and other functions are subjected to person's individual circadian rhythm. Circadian typology includes three chronotypes: morning, neither and evening. The aim of this study was to examine the chronobiological aspects of depression.*

Methods: *This cross-sectional study aimed to determine circadian rhythmic expression in 60 patients suffering from depression. The patients were in remission and were treated as outpatients at the Department of Psychiatry of the University Hospital Center Zagreb. The data were compared to a control group consisting of 40 medical workers employed at the University Hospital Centre Zagreb. A self-report measure of circadian typology was utilized - the Morningness-Eveningness Questionnaire.*

Results: *According to our findings, among depressed patients 35% were morning, 58.3% neither and 6.7% evening types. In the control group 46% were morning, 48% neither and 6.0% evening types. Depressed patients reported stronger morning fatigue. Further, they tended to go to sleep earlier and felt more tired earlier in the evening, and they were less prone to choosing morning periods for completing complex cognitive tasks.*

Conclusion: *This study supports the association between depression and some alterations in circadian rhythms of behavior and sleep. Depression may be considered as the consequence or trigger of circadian disturbances. However, both depression and circadian rhythm disturbances may have a common aetiology: a decreased cellular resilience associated with lower resistance to stressful events.*

Key words: *depression - circadian rhythm - circadian typology – morning - evening*

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INTRODUCTION

The relationship between circadian disruptions and depressive disorders is a topic of great interest in contemporary psychiatry. Large evidence for an involvement of the circadian clock dysfunction in depressive disorder has emerged (Racagni et al. 2009). Circadian rhythms include all physiological processes displaying a period around 24 hours. Sleep/wake cycles, body temperature, hormone secretion and other functions are subjected to person's individual circadian rhythm (Takahashi et al. 2008). The main pacemaker is located in the suprachiasmatic nuclei (SCN). Circadian desynchronization is probably triggered by an intrinsic disorganization of the SCN (de Bodinat et al. 2010, Milan 2006, Boivin 2000). Melatonin is synthesized in the pineal gland the second main synchronizer of circadian rhythms. The secretion is regulated by the environmental light/dark cycle via suprachiasmatic nucleus. Melatonin levels rise before bed time, stay high during nocturnal sleep period, decrease quickly around wake time, and is almost undetectable during daytime, as light inhibits melatonin secretion (Lewy et al. 1980, Zeitzer et al. 2000). Other zeitgebers are food intake, work activity or social cues. Synchrony between the mind-body rhythms is of the great importance for the health and normal functioning. Sleep restores body and mind. It is a basic human need. Impaired wakefulness and fatigue not only negatively affect quality of life, for example in several inflammatory and malignant diseases; they are also a direct serious risk factor for impaired social functioning, accidents and injuries (Weschenfelder et al. 2012). Circadian rhythmic expression differs among individuals and may be classified with the concept of circadian typology (CT) which consisits of three chronotypes: morning, neither and evening type. It has also been reported that differences in CT are associated with differences in the regulation of sleep homeostasis. Major depression is frequently associated with alteration in circadian rhythms of behavior, sleep, core body temperature, cardiac rhythms, blood pressure, pulse, the secretion of melatonin, cortisol, growth hormone, thyrotropin and other hormones as well as inflammatory cytokines and neurotransmitters (de Bodinat et al. 2010**,** Weschenfelder et al. 2012). Mental disorders, particularly depression, are common in people with circadian rest-activity cycle disturbances and sleep-wake problems. The interest in the systematic study of the circadian typology (CT) is relatively recent and has developed rapidly in the two last decades. The aim of this study was to examine the chronobiological aspects of depression.

SUBJECTS AND METHODS

This cross-sectional study aimed to determine circadian rhythmic expression in 60 patients suffering from depression. The patients were in remission and were treated as outpatients at the Department of Psychiatry of

the University Hospital Center Zagreb. The data were compared to a control group consisting of 40 medical workers employed at the University Hospital Centre Zagreb. The study used a self-report measure of circadian typology - the Morningness-Eveningness Questionnaire (MEQ) (Horne & Östberg 1976). It consists of 21 items and its objective is to depict patients' sleeping habits as well as their mood and physical activities. The MEQ is the most widely used morningness measure.

RESULTS

According to our findings, among depressed patients 35% were morning, 58.3% neither and 6.7% evening types. In the control group 46% were morning, 48% neither and 6.0% evening types (Figure 1). Morning type subjects go to bed early and wake up early and achieve their peak mental and physical performance in the early part of the day. By contrast, evening type subjects go to bed and wake up late, and perform at their best toward the end of the day and evening hours. Depressed patients reported stronger morning fatigue (Table 1). Further, they tended to go to sleep earlier and felt more tired earlier in the evening (Table 2), and they were less prone to choosing morning periods for completing complex cognitive tasks (Table 3).

Table 1. Reported morning fatigue among depressed patients and healthy control

		Frequency	Percent
Depressed patients	tired	49	79.2
	alert	13	21
Healthy control	tired	15	30
	alert	35	70

Table 2. Time of reported evening fatigue among depressed patients and healthy control

	Time	Frequency	Percent
Depressed patients	2:00-3:00	2	3.2
	0:45-2:00	4	6.5
	22:15-0:45	24	38.7
	21:00-22:15	25	40.3
	20:00-21:00	7	11.3
Healthy control	0:45-2:00	6	12.0
	22:15-0:45	31	62.0
	21:00-22:15	9	18.0
	20:00-21:00	4	8.0

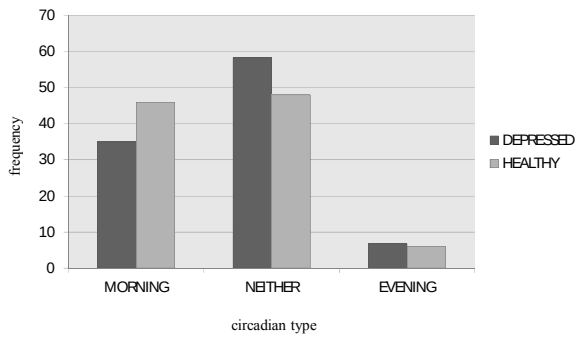

Figure 1. Circadian types in depressed patients and healthy control group

Table 3. Peak performance time

	Time	Frequency	Percent
Depressed patients	19:00-21:00	3	4.8
	15:00-17:00	9	14.5
	11:00-13:00	35	56.5
	8:00-10:00	15	24.2
Healthy control	19:00-21:00	3	6.0
	15:00-17:00	2	4.0
	11:00-13:00	19	38.0
	8:00-10:00	26	52.0

DISCUSSION

The morningness and eveningness dimension shares some behavioral components with mental disorders. The interaction between shift type and CT suggested the earlier types had better adaptation to day work but worst adaptation on night shift (Adan et al. 2012). Our data showed that among control group 46% were morning types and 30% of control group reported morning fatigue which may be associated with sleep disruption during shiftwork (Akerstedt 2003). Vela-Bueno et al. (2010) indicated then ″non-adapted″ workers were morning oriented, had rigid sleeping habits and were languid. The DTS (Torsvall & Akerstedt 1980) reported strong correlations between morningness and a number of sleep complaints. Depression may be viewed as the net result of disturbances of various interdependent neurobehavioral response systems, including affective (mood) dysregulation, impaired behavioral quieting, dimished behavioral facilitation increased stress responsiveness (Thase 1997) as well as instability of circadian synchronization. Sleep disturbances represent a common symptom that can be found in all stages of depression (Benca et al. 1992, Tsuno et al. 2005). It has been reported (Ilankovic at al. 1986) that the index of endogenous perturbation of sleep (IEP) is a significant marker of in patients with major depression. The IEP represents the ratio between REM1/NREM1. Subjects with depression show abnormal sleep architecture- especially during REM sleep periods (Steiger & Kimura 2010). Chronic sleep insufficiency is associated with decreased cognitive performance (Doghramji et al. 2010). The circadian rest-activity and sleep wake cycle disturbances are a risk factor for developing and recurrence of mental disorders and what is very important, the circadian rhythm disorders are associated with worse outcome (Jakovljević 2011). There is mounting evidence suggesting the evening type may be a risk factor linked to chronodisruption aspects and also with a number of psychiatric symptoms. Studies in healthy individuals using different measurement instruments have shown that the depressive symptoms that present higher discriminate coefficients among CT are those related to sadness, inner tension, sleep reduction and pessimism (Hidalgo et al. 2009). Circadian disruption is associated, and may in part be a consequence of the changes in behavior and sleep patterns that are seen in depression. It is well known that some diseases have predictable cyclic rhythms and the timing regimens of medication can improve outcome. Chronopharmacology

studies the interaction of biologic rhythms with medications involving both the drug effects as a function of biologic timing and the drug effects upon rhythm characteristics (Reinberg 1976). Agomelatine opens an innovative chronobiological approach to understanding and treating depression related to cell resilience and stress resistance model (Jakovljević 2011).

CONCLUSION

This study supports the association between depression and some alterations in circadian rhythms of behavior and sleep. An additional indication that circadian misalignment contributes to depressive symptoms is the finding that ET people are prone to depressive symptoms. Depression may be considered as the consequence or trigger of circadian disturbances. However, both depression and circadian rhythm disturbances may have a common aetiology: a decreased cellular resilience associated with lower resistance to stressful events. The evidence that chronodisruption can be linked to depression has opened a new approach for its treatment. Resynchronizing circadian rhythms and so normalizing biological alostasis seems to provide acute and sustain symptoms relief and prevent relapse over the long term.

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