The association of circadian typology with cognition and smoking status: a cross-sectional Egyptian study

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Introduction
Circadian rhythmic expression differs among individuals. These differences are often labeled as morningness–eveningness or chronotype. Three main phenotypic variants of human chronotype exist: morning type, neither type, and evening type. Nicotine is a psychoactive stimulant that is abundantly present in cigarettes. Few data are available about the possible associations between the stimulant effect of nicotine and the phase shift of circadian rhythm and chronotype of individuals abusing nicotine (smokers). Different brain pathways explain the associations between chronotypes and various addictive behaviors, although the impact of nicotine on cognition remains unclear. This study is based on the hypothesis that circadian typology is a risk factor for smoking and for higher levels of nicotine consumption, dependence, and associated cognitive changes in smokers.

Aim
This study aimed to estimate the possible associations between circadian typology and smoking. Measures quantifying nicotine dependence and smoking status were applied to the recruited sample. In addition, cognitive assessment of the sample was carried out.

Participants and methods
A representative sample of smokers (total $N=100$) of both sexes were randomly selected. All patients had been smoking for at least 5 years. An age-matched and sex-matched control group of healthy nonsmokers was also recruited. Each participant was subjected to a clinical psychiatric interview using the Arabic version of the Mini-International Neuropsychiatric Interview. The chronotype of the participants was evaluated using the Horne and Ostberg Morningness–Eveningness Questionnaire. Cognition was assessed with the Montreal Cognitive Assessment scale. Smoking status was assessed with the Fagerström Test for Nicotine Dependence, the self-administered Nicotine Dependence Syndrome Scale, and the Questionnaire of Smoking Urges.

Results
The majority of smokers were of neither typology, followed by moderately evening type. Smokers had statistically significant cognitive impairment in terms of visuospatial ability, verbal fluency, delayed recording, and total Montreal Cognitive Assessment score compared with nonsmokers. Sex affected chronotype, education, duration of smoking, and Fagerström level of dependence scale score. Higher level of nicotine dependence was associated with greater cognitive impairment in smokers.

Keywords:
chronotype, cognitive impairments, nicotine dependence, smoking

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Introduction

Circadian rhythmic expression differs among individuals and these differences are often labeled as morningness–eveningness (ME), diurnal preferences, circadian typology, or chronotype. Three main phenotypic variants of human chronotype exist: morning type (MT), neither type (NT), and evening type (ET) [1]. They are determined by a number of self-assessment questionnaires such as the Horne and Ostberg Morningness–Eveningness Questionnaire (MEQ) and its variants such as the Munich Chronotype Questionnaire [2]. About 40% of the adult population is classified into one of the two extreme groups, whereas 60% are NT [1].

ME or preference of sleep timing can be considered as a continuum between two ends: MTs (larks) and ETs (owls). This classification mainly depends upon sleep habits including bedtime, wake-up time, and favorite periods of diurnal activity, such as working hours or recreation habits [3]. Extreme MTs prefer to wake up very early, go to bed early, and achieve their peak mental and physical performance in the early part of the day. On the contrary, extreme ETs prefer to go to bed in the late

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hours of the night, wake up late, and perform their best toward the end of the day and during evening hours [4].

Other studies define chronotype as a phase angle of entrainment. This denotes chronotypical differences in the phase relationship between one's endogenous circadian rhythm (sleep–wake cycle) and external synchronizers (zeitgeber: time cues) [5]. For instance, light exposure in the evening causes circadian rhythms to shift later, whereas light exposure in the early morning causes circadian rhythms to shift earlier [6]. Therefore, another definition of chronotype denotes the 'phase shift' of circadian rhythmicity [e.g. the rhythm onset, peak, offset, and timing of their physiological circadian markers (core body temperature and melatonin) in relation to the external clock time]. When the circadian markers occur earlier than the expected clock time, it is known as a phase advance. If it occurs later than expected, it is known as a phase delay [7]. Chronotype is influenced by individual and environmental factors; it appears that an individual's chronotype is not uniform throughout life but changes remarkably. In general, younger individuals have a strong tendency toward eveningness, whereas aging is strongly associated with morningness [4]. Most children are morning oriented. This morning tendency gradually evolves into a strong shift toward eveningness during adolescence, which reaches a peak around age 20, then progressively moves towards morningness again with aging [8]. Therefore, eveningness may be considered as a biological marker for the end of adolescence [9]. These changes may be interpreted as being associated with pubertal development, and hence linked with the increase of sexual hormones, but it is also influenced by social and family factors, such as the school year or parental control on the individual's schedule and an increasing interest toward evening-related activities [10].

In addition, the possibility that sex influences chronotype has been approached in several studies. Many studies reported that eveningness is observed in a larger proportion of men compared with females [11]; these results tend to be found in large samples that have used the MEQ. It appears that the diurnal variations in women produce a phase advance with respect to men. Moreover, the intrinsic circadian period was significantly shorter in women than in men [12].

However, some studies have not found any sex differences [13], and others reported that the dynamics of the age-related transition from eveningness to morningness appear to be sex sensitive, and hence the phase delay of adolescents and the phase advance of the elderly are markedly more present in men than in women [14].

Nicotine is a psychoactive stimulant, and there may be some associations between this stimulant effect and the phase of circadian rhythms. Nicotine is a direct agonist of nicotinic acetylcholine receptors and activates mesolimbic dopaminergic pathways [15]. Melatonin levels are associated with chronotype variations. Dim light melatonin onset, but not sleep onset or melatonin offset times, has been shown to be related to chronotype [16]. In addition, in patients who have developed dependence disorder there may be a decrease in the genetic expression of most of the circadian genes (clock, per, cycle, and double-time) [17].

MT and ETs are different not only in their rhythmic expression but also in personality traits and habits. The pioneering study by Adan [18] found differences in the consumption of psychoactive substances (nicotine, alcohol, and caffeine) among circadian typologies, the ET individuals being those who showed more consumption of the three substances.

Different pathways can explain the association between ME or chronotypes, and addictive behaviors. The first assumes the role of the personality traits, such as novelty seeking [19], conscientiousness [20], and self-control [21]. The second theory assumes that the association happens through the links between ME and the physiological markers of endogenous circadian rhythmicity like melatonin rhythms and changes in core body temperature [22]. The third theory is related to the construct of social jetlag, which is the misalignment of social and biological time [23]. Social jetlag is suggested as a possible mediator [24] between diurnal preferences, drug use, and physical inactivity. Drug use might be a self-medication of the negative impact of social jetlag; on the other hand, drug use and physical inactivity can also increase social jetlag with the disturbance of circadian rhythmicity, quality of sleep, and distorted sleep–wake patterns [25].

Data regarding these associations are scarce in the Arab population. Thus, we aimed to describe the chronotypic variations of smokers and detect whether circadian typology is a risk factor for smoking by studying the associations concerning the circadian typology and measures of nicotine dependence and smoking status, together with cognitive assessment of a group of smokers.

Participants and methods

A representative sample of smokers (total $N = 100$) of both sexes (males: $N = 86$, females: $N = 14$), aged 20–50 years, were randomly selected (the first 100 patients came to the Addiction Unit's Outpatient Clinic for smoking cessation and agreed to participate in this study). All patients had been smoking for more than 5 years. Twelve participants had been smoking for a duration of 5–7 years, 44 participants for 7–10 years, and 44 for more than 10 years. A control group ($N = 100$) of age-matched and sex-matched healthy nonsmokers were recruited from attendants at the blood bank of Mansoura University Hospital for blood donation. Consent to participate in the study was taken from each participant. Participants were ensured confidentiality and privacy protection and that any collected information would remain anonymous. Each participant was subjected to a clinical psychiatric interview using the Arabic translated version of the Mini-International Neuropsychiatric Interview, version 5 [26], to exclude any other psychiatric disorders except nicotine dependence (ND).

The inclusion criteria were age 20–50 years, generally healthy status, and being a current cigarette smoker with a smoking duration of not less than 5 years. Exclusion criteria were being mentally retarded or diagnosis of other medical or psychiatric disorders.

Chronotype measurements

Participant's chronotype was assessed using the Horne and Ostberg MEQ [27], which is a self-evaluation instrument for identifying the individual circadian typology. The use of this instrument suggests the idea that the ME dimension could be considered a continuum between two extremes [28,29]. This scale has been translated into Arabic and validated for use by BaHammam *et al.* [30].

Cognitive assessment

Cognition was assessed by means of the Montreal Cognitive Assessment (MoCA) scale. The MoCA assesses several cognitive domains, including the short-term memory recall task (five points), which involves two learning trials of five nouns and delayed recall after ~5 min. Visuospatial abilities are assessed using a clock-drawing task (three points) and a three-dimensional cube copy (one point). Multiple aspects of executive functions are assessed using an alternation task adapted from the trail-making B task (one point), a phonemic fluency task (one point), and a two-item verbal abstraction task (two points). Attention, concentration, and working memory are evaluated using a sustained attention task (target detection using tapping; one point), a serial subtraction task (three points), and digits forward and backward (one point each). Language is assessed using a three-item confrontation naming task with low-familiarity animals (lion, camel, rhinoceros; three points), repetition of two syntactically complex sentences (two points), and the aforementioned fluency task. Finally, orientation to time and place is evaluated (six points) [31]. This scale has been translated into Arabic and validated for use by Rahman and El Gaafary [32].

Smoking status was assessed using the following:

(1) Fagerström Test for Nicotine Dependence (FTND) [32]: The FTND is a standard instrument for assessing the intensity and severity of the physical addiction on nicotine. This scale has been translated into Arabic and validated for use [33].
(2) The self-administered Nicotine Dependence Syndrome Scale (NDSS) [34]: This is a 19-item questionnaire designed to yield continuous measures of multiple theoretically derived dimensions of dependence. It yields scores for the following: (i) drive, which captures craving and withdrawal and compulsion to smoke; (ii) priority, the behavioral preference of smoking over other reinforces; (iii) tolerance, reduced sensitivity to smoking effects; (iv) continuity, the regularity of smoking; and (v) stereotypy, the rigidity of smoking patterns and tendency to smoke in the same way regardless of circumstances. It also yields a single summary score (NDSS-T) for dependence. The scale was previously translated into Arabic and validated [35].
(3) Questionnaire of Smoking Urges (QSU-brief) [36]: The brief version of QSU consists of 10 questions designed to measure the desire to smoke and anticipation of positive outcome (factor 1: positive reinforcement) as well as a strong urge to smoke and anticipation of relief of withdrawal (factor 2: negative reinforcement). The scale was previously translated into Arabic and validated for use in Arabic culture [37].

This study was approved by the Ethics Committee of Mansoura Faculty of Medicine and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Statistical analysis

Parametric data were summarized as mean ± SD. Nonparametric data were described as frequencies and percentages. χ^2-Test and *T*-test were used to measure associations among different nonparametric data and parametric data, respectively. The results were computed using SPSS (version 20) [38].

Results

There was no statistically significant difference between smokers and nonsmokers regarding age, sex, and education. Eighty-six percent of the participants were men. The majority of cases and controls ($n = 48$ and $n = 46$, respectively) fell into the age group of 20–30 years (Table 1). Among the 100 smokers included, 65% were NT, 16% were moderately ET, and 15% were moderately MT, whereas 6% were definitely ET. In the nonsmoker group also the majority of participants showed neither typology, followed by moderately morning typology. Chronotype variation between cases and controls is presented in Fig. 1. Questionnaires quantifying smoking status are presented in Table 2. It was observed that the mean ± SD score of FTND was 4.40 ± 2.06. The mean ± SD overall score for NDSS was −1.19 ± 0.57, whereas the mean ± SD score for smoking urge was 30.49 ± 8.78. The mean ± SD of the subscales of each questionnaire are further summarized in Table 2.

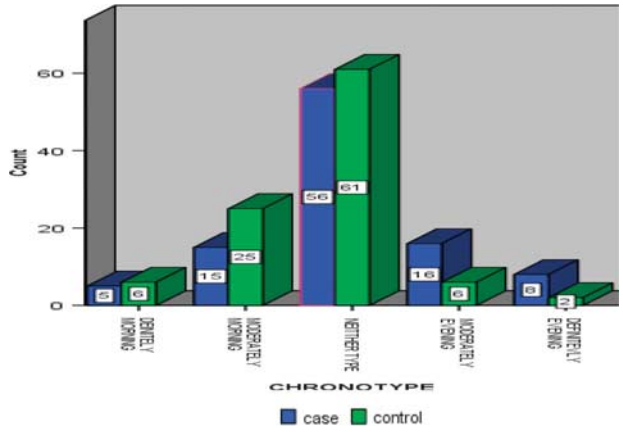
The variation of sample characteristics in relation to circadian typology is summarized in Table 3. We tried to determine which factor is strongly affected by chronotypes.

Table 1 Demographics and history data

	Cases (*N*)	Controls (*N*)	*d.f.*	*P*
Age (years)				
20–30	48	46	2	0.948
30–40	30	32		
40–50	22	22		
Sex				
Males	86	86	4	1.00
Females	14	14		
Education				
Illiterate	4	6	1	0.748
Educated	96	94		

It is clearly noted that chronotype is significantly affected by sex ($P = 0.00$), education ($P = 0.00$), duration of smoking ($P = 0.00$), and Fagerström level of dependence ($P = 0.00$), meaning that each of these factors might have a cause/effect relationship with chronotypology.

Figure 1



Circadian typology of smokers and nonsmokers.

Table 2 Means and standard deviations of questionnaires quantifying smoking status

Nicotine dependence measures	Mean ± SD
Fagerström Test for Nicotine Dependence (FTND)	4.40 ± 2.06
Very-low dependence	
Low dependence	
Medium dependence	
High dependence	
Very-high dependence	
Nicotine Dependence Syndrome Scale (NDSS)	
Overall score	−1.19 ± 0.57
Drive	−0.64 ± 0.84
Stereotype	−0.86 ± 0.47
Continuity	0.24 ± 0.93
Priority	−0.37 ± 0.32
Tolerance	−0.71 ± 0.61
Questionnaire of Smoking Urges (QSU-brief)	
Total score	30.49 ± 8.78
Factor 1 (intention/desire to smoke)	19.27 ± 5.03
Factor 2 (relief of negative affect and urgent desire to smoke)	11.22 ± 4.67

We compared smokers with nonsmokers with respect to the various subscales of MoCA. It was noted that smokers had statistically significant cognitive impairments in terms of visuospatial ability ($P = 0.038$), verbal fluency ($P = 0.00$), delayed recording ($P = 0.00$), and total MoCA score ($P = 0.00$) compared with nonsmokers. The number of participants in each cognitive group is summarized in Table 4. We then divided the smokers according to their MoCA scores into those with normal cognition and those with impaired cognition. Factors such as age and sex showed no effect on cognitive impairment ($P = 0.059$ and 0.21, respectively). In contrast, factors like duration of smoking and level of ND did affect the levels of cognitive impairment. The findings are shown in Table 5.

Discussion

In this study, chronotype was examined in a target group of smokers in relation to cognitive function and smoking status. The majority of the sample was a NT followed by definitely ET in comparison with the control group, which was mainly MT. This might be explained by the young age of the participants, as most of them fell in the age range of 20–30 years. It also indicates the strong association of the chronotype with addictive behaviors and degree of smoking problem. Not being a morning chronotype but being an ET makes the person have to deal with a discrepancy between their preferred time of day and the time of day that is expected by the society. Continuous trials to adapt to a social rhythm that is contrary to their biological rhythm might lead to frustration and inability to exert self-control. This behavior was highlighted by Milfont and Schwarzenthal [39]. Consequently, these people engage in more smoking and might resist quitting. Furthermore, applying the principles of chronotherapy might be beneficial for such a group of smokers. These data were similar to those of Urbán *et al.* [26], who performed a detailed analysis of 134 daily smokers and 366 nonsmokers. They found that smokers tend to be later chronotypes. Similarly, Prat and Adan [40,41] and Adan [40,41] reported a higher prevalence of consumption of addictive substances, both legal (nicotine) and illegal (cannabis and ecstasy), in ET

Table 3 Association of circadian typology with smoker's criteria

	Definitely morning	Moderately morning	Neither	Moderately evening	Definitely evening	*d.f.*	*P*
Sex							
Males	8	31	109	18	10	10	0.00
Females	3	9	12	4	0		
Education							
Illiterate	0	0	4	4	0	10	0.00
Educated	11	40	113	18	10		
Duration of smoking							
Nonsmoker	6	25	61	6	2	20	0.00
5–7 years	3	0	5	3	1		
>7–10 years	1	10	26	2	6		
>10 years	1	5	25	11	2		
Fagerström level of dependence							
Very low	3	7	21	2	2		
Low	1	8	28	5	4	8	0.00
Medium	1	0	7	9	2		

Summary of variations of chronotype according to sex, education, duration of smoking, and Fagerström Test for Nicotine Dependence.

Table 4 Cognitive performance of smokers and nonsmokers

	Cases	Controls	*d.f.*	*P*
Montreal Cognitive Assessment subscale				
Visuospatial ability				
1	1	0	4	**0.038**
2	2	0		
3	3	0		
4	36	25		
5	58	75		
Naming				
2	23	27	1	0.22
3	67	773		
Forward and backward digits				
0	1	0	2	0.09
1	35	23		
2	64	77		
Vigilance				
0	1	5	2	0.15
1	99	94		
2	0	1		
Serial sevens				
0	2	0	3	0.2
1	8	9		
2	47	37		
3	43	54		
Sentence perception				
0	7	2	2	0.19
1	56	55		
2	37	43		
Verbal fluency				
0	85	54	1	**0.00**
1	15	46		
Abstraction				
0	15	13	2	0.17
1	41	30		
2	44	57		
Delayed recording				
0	7	0	5	**0.00**
1	5	5		
2	28	12		
3	37	22		
4	18	36		
5	5	25		
Orientation				
4	2	0	2	0.25
5	36	31		
6	62	69		
Level of impairment				
Normal	29	67	2	**0.00**
Cognitively impaired	71	32		

Each subscale of the Montreal Cognitive Assessment and the total score are shown; differences between cases and controls are also recorded and whether these differences are statistically significant.

Table 5 Effect of age, sex, duration of smoking, and level of nicotine dependence on cognitive impairments

	MoCA groups [*n* (%)]		
Variables	Normal	Mild cognitive impairment	*P*
Age (years)			
20–30	19 (65.5)	28 (39.4)	0.059
30–40	6 (20.7)	28 (39.4)	
40–50	4 (13.8)	19 (26.8)	
Sex			
Males	23 (79.3)	63 (88.7)	0.21
Female	6 (20.7)	8 (11.3)	
Smoking duration (years)			
1–3	5 (17.2)	7 (9.9)	**0.001**
3–10	20 (69)	24 (33.8)	
>10	4 (13.8)	40 (56.3)	
Fagerström Test for Nicotine Dependence			
Very low	12 (41.4)	9 (12.7)	**0.002**
Low	8 (27.6)	10 (14.1)	
Moderate	6 (20.7)	29 (40.8)	
High	3 (10.3)	17 (23.9)	
Very high	0 (0)	6 (8.5)	

As noted the higher the level of dependence and the longer the duration of smoking the more cognitive impairment that is shown on MoCA scores.
MoCA, Montreal Cognitive Assessment.

compared with MT and NT participants. Furthermore, earlier studies, mostly with relatively small sample sizes, have demonstrated an association between diurnal type and smoking, such as among university students in Japan [42], 14-94-year-olds in Germany and Austria [23], Hungarian adolescents [25], as well as Finnish adolescents [6] and adults [43]. These are in line with recent study of Finnish twins aged 50 [44], which showed on the basis of a single question on diurnal type, the FTND, and *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) diagnosis of ND (51 APA 1994) that the ET was strongly associated with not only being a smoker but also with ND.

We found a positive relationship between chronotype and level of ND, which further elucidates what Adan [41] found in the early stage of their research. They found that ETs consumed more alcohol, nicotine, and caffeine (coffee and cola), whereas MTs consumed more caffeine from tea. The number of females in this study was quite small compared with the number of men, although sex differences in the association between diurnal type and smoking have been found in other studies so that risk of current smoking among ETs was higher among women compared with men [6].

The present study clearly demonstrates modest and domain-specific cognitive impairments in smokers, mainly visuospatial abilities, verbal fluency, delayed recording, and total MoCA score. There were no significant group differences in any other cognitive domain. Screening for cognitive defects in smokers is crucial as it may be an early sign of developing dementia. Smokers are at increased risk of cognitive impairments. Moderate to severe smokers are exposed to high concentrations of nicotine. Exposure to high nicotine levels is neurotoxic and harmful to brain cells. The link between cognitive impairment and later life dementia is well established. Smoking disturbs the balance between generation and reduction of oxidants and free radicals. The consequent overload of oxidants and free radical species triggers oxidative stress. Increased oxidative stress leads to formation of senile plaque and neurofibrillary tangles, signifying the occurrence of dementia [43]. Our results are in line with previous studies examining the same variables. Zhong *et al.* [44] found that smokers had significant decline in their cognitive performances when compared with nonsmokers. With the increase in the intensity of smoking, cognitive performances were also significantly reduced compared with that in never-smokers in a large population-based sample of adult, psychiatrically healthy participants. Consistent deficits were found in several tests contributing to the visual attention domain score. Mild smokers are

exposed to minimal doses of nicotine. Exposure to minimal doses of nicotine produces cognitive enhancement [45]. This effect results in addiction and they find it very difficult to kick the habit of smoking. Gradually their intensity of smoking increases.

Strengths and limitations

This study is the first of its kind in Egypt. We investigated the associations of circadian typology using a strong self-reported questionnaire. Another strength is the recruitment of a control group to compare with the group of smokers, which is a weak point in previous similar studies. Despite that, it has some limitations: the possible causality behind the observed association remains unknown as a cross-sectional survey does not provide adequate data to determine causality for the association between diurnal type and smoking. Follow-up data are needed to answer this question. We did not investigate associations with other addictive behaviors and we concentrated solely on smoking. Longitudinal studies are required to assess the changes and interdependencies in diurnal type, smoking habits, and ND. In addition, as in this study the information on diurnal type is derived from a self-report, there is a further need for studies that use a biologically based confirmatory measure of diurnal type (such as melatonin rhythm, core body temperature, or rest-activity cycle) for assessment. Gene determination, usage of more complex cognitive batteries, and structural brain imaging to confirm neurotoxicity correlated with cognitive impairment could be a future research goal.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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