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SLEEP BREATHING PHYSIOLOGY AND DISORDERS • REVIEW

The effect of intermittent fasting during Ramadan on sleep, sleepiness, cognitive function, and circadian rhythm

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Abstract
Purpose Studies have shown that experimental fasting can affect cognitive function, sleep, and wakefulness patterns. However, the effects of experimental fasting cannot be generalized to fasting during Ramadan due to its unique characteristics. Therefore, there has been increased interest in studying the effects of fasting during Ramadan on sleep patterns, daytime sleepiness, cognitive function, sleep architecture, and circadian rhythm.
Method In this review, we critically discuss the current research findings in those areas during the month of Ramadan.
Results Available data that controlled for sleep/wake schedule, sleep duration, light exposure, and energy expenditure do not support the notion that Ramadan intermittent fasting increases daytime sleepiness and alters cognitive function. Additionally, recent well-designed studies showed no effect of fasting on circadian rhythms. However, in non-constrained environments that do not control for lifestyle changes, studies have demonstrated sudden and significant delays in bedtime and wake time.
Conclusions Studies that controlled for environmental factors and sleep/wake schedule reported no significant disturbances in sleep architecture. Nevertheless, several studies have consistently reported that the main change in sleep architecture during fasting is a reduction in the proportion of REM sleep.

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Introduction

Like many religions and cultures that practice voluntary fasting, Muslims all over the world fast every year during the holy month of Ramadan. Fasting during Ramadan is the fourth pillar of Islam, and approximately 1.6 billion Muslims worldwide fast during Ramadan every year. During Ramadan fasting, Muslims are required to refrain from food or fluid intake between sunrise and sunset. This practice displaces energy intake and hydration to the hours of darkness and partially reverses the normal circadian pattern of eating and drinking.

Although previous studies have found that experimental fasting affects the sleep-wakefulness pattern in different species, the results of experimental fasting cannot be generalized to fasting during Ramadan because of its unique characteristics. Furthermore, fasting during Ramadan is intermittent, whereas each experimental fasting episode is usually more prolonged. Nevertheless, the long duration of this practice (1 month) may allow for adaptation to the new regimen compared with experimental fasting. Moreover, Ramadan follows the lunar system and therefore occurs during a different season every 9 years; this change can affect the duration of fasting hours, with longer durations of fasting in the summer than in the winter [1]. Additionally, several lifestyle changes that accompany Ramadan may have significant impacts on sleep, sleepiness, and circadian rhythms (Fig. 1). Consequently, these factors should be taken into consideration when interpreting the available published data.

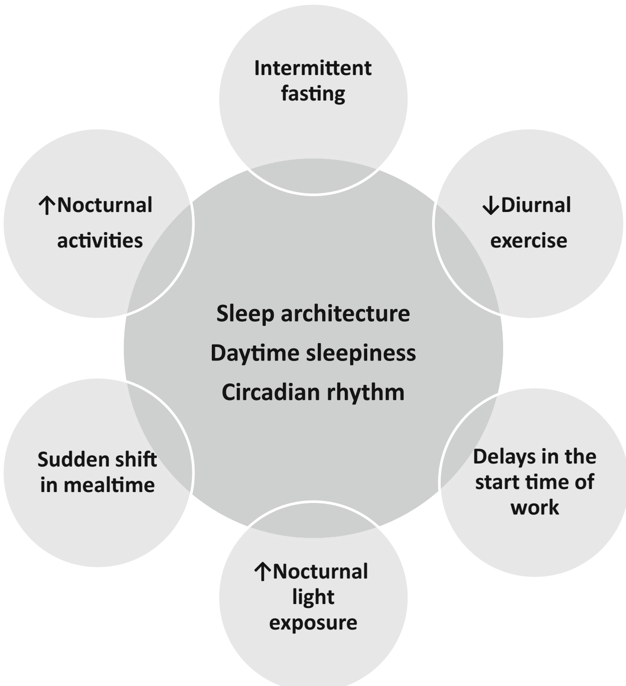

Fig. 1 Factors that may influence sleep, daytime sleepiness, and circadian rhythms during Ramadan fasting

Review method

The literature search began on the 1st of April 2016 with keyword searches of "sleep," "sleep pattern," " daytime sleepiness," "cognitive function," "polysomnography," "sleep architecture," "circadian rhythm," "intermittent fasting," and "Ramadan," using PubMed (20 results), Google Scholar (47 results), and Medline (61 results). The reference lists of identified articles were also searched for any additional sources. Publications were then filtered on the basis of whether or not they reported original findings, provided background information, or contained relevant theoretical speculation of the effect of intermittent fasting during Ramadan on the areas addressed in this review.

Sleep pattern

In some Islamic countries, the start of work is delayed and working hours are adjusted during Ramadan so they are shorter for individuals who fast. Studies conducted in three Islamic countries [2–6] consistently reported a significant sudden delay in bedtime and rise time. Interestingly, this delay in bedtime during Ramadan was observed even in non-Muslim residents of Saudi Arabia [4]. This observed delay in bedtime and rise time could be partially explained by the delay in the start of work during the month of Ramadan. However, other environmental factors, such as delayed work hours for stores, shopping malls, and restaurants and the broadcasting of interesting TV programs until late at night, could also play a role [1].

Conversely, there are conflicting results regarding sleep duration during Ramadan. In a study conducted in Morocco, nighttime sleep duration was significantly reduced during Ramadan [6]. A similar reduction in nighttime sleep duration was also reported in another study conducted in the United Arab Emirates, but this reduction was ameliorated by an increased duration of daytime naps [5]. Two other studies conducted in Saudi Arabia assessed sleep duration during Ramadan in medical students and employed healthy nonsmokers between the ages of 25 and 55 years and reported no significant changes in the duration of nighttime sleep during the first and third weeks of Ramadan compared with baseline values [2, 4]. However, another study used the SenseWear Pro Armband™ to objectively assess the duration and distribution of sleep in eight Muslim and eight non-Muslim volunteers during a baseline period (1 week before Ramadan) and the first and second weeks of Ramadan. In this study, a delay in bedtime and wake time and a significant reduction in total sleep time were observed for the Muslim volunteers compared with the non-Muslim participants [7].

The differences in these studies may reflect cultural and lifestyle changes in the different study countries or the use of different subjective assessment methods. In this context, it is important to consider both nighttime sleep duration and daytime naps when assessing sleep duration during Ramadan [1].

Daytime sleepiness

Several studies have assessed daytime sleepiness during Ramadan fasting both subjectively by using the Epworth Sleepiness Scale (ESS) [2–9] and objectively by using the Multiple Sleep Latency Test (MSLT) [3, 8, 9]. However, the results of these studies have been contradictory, which may be due to differences in methodology, the lack of objective assessment, or the lack of controlling for potential confounders that could potentially affect daytime alertness and cognitive function.

The results of the subjective studies using the ESS score have been conflicting and inconsistent. Some studies have reported a significant increase in daytime sleepiness [2, 6], whereas others have found no significant differences [3–5].

Three objective studies used the MSLT to evaluate sleepiness under controlled conditions [3, 8, 9]. In the first study, increased daytime sleepiness at the 10:00 and 12:00 naps was reported towards the end of Ramadan [9]. However, it is important to note that a portable polysomnography recording device was used in this study, which forced the operator to program the computer to end the test 20 min after the beginning of recording regardless of sleep onset.

To avoid this limitation, another study used a standard MSLT that was performed in the sleep laboratory [3]. In this study, there were no observed differences in sleep latency, sleep onset latency, and wake efficiency between the first and third weeks of Ramadan compared with the baseline measurements [3]. Moreover, spectral analysis of EEG activity during individuals' naps revealed no difference between baseline and Ramadan recordings [3]. The third study [8] was designed to objectively assess the effects of intermittent fasting during Ramadan on daytime sleepiness in eight healthy volunteers by using a fixed sleep-wake schedule, fixed caloric intake, and controlled light exposure and assessing the MSLT and ESS on four occasions. The subjects attended sleep lab for adaptation and were given wrist actigraphy before the start of the study to monitor their sleep at home. This was followed by assessment of daytime sleepiness using MSLT and ESS as follows: 3 weeks before Ramadan after 1 week of Islamic fasting (baseline fasting); 1 week before Ramadan (non-fasting baseline); 2 weeks after the start of Ramadan; and 2 weeks after the end of Ramadan (recovery). The authors reported no change in the ESS during the four study periods. In addition, the MSLT analysis also revealed no difference in sleep latency between the "non-fasting baseline," "baseline fasting," "Ramadan," and the "Recovery" time points.

Cognitive function

Cognitive function has also been reported to be affected by Ramadan fasting. For example, the percentage of medical students who reported falling asleep in class increased from 15% at baseline to 36% during the first week of Ramadan [2]. When a Visual Analog Scale was used to assess subjective alertness during Ramadan [10], a decrease in alertness was observed at 09:00 and 16:00, whereas increased alertness was observed at 23:00 [8, 10]. However, those studies did not control for sleep duration and sleep/wake pattern.

In a recent study that assessed cognitive function in trained cyclists from the Middle East using the Cambridge Neuropsychological Test Automated Battery (CANTAB), the Reaction Time Index (RTI), and the Rapid Visual Information Processing (RVP) test, Ramadan fasting did not negatively impact cognitive performance [11]. Another study [7] objectively assessed daytime sleepiness using the John Drowsiness Scale (JDS) [12] and mean reaction time (MRT) using a visual reaction time test in eight Muslim and eight non-Muslim volunteers during the week before Ramadan (baseline) and the first and second weeks of Ramadan. The study showed that the JDS values were normal at baseline in both Muslims and non-Muslims (non-fasting group) and no changes were observed during Ramadan, which indicates that fasting during Ramadan did not increase daytime sleepiness. In addition, there were no differences between the two groups by MRT [7]. The effects of intermittent fasting on drowsiness during and outside Ramadan were objectively assessed in a well-designed study that measured total blink duration (measured using infrared reflectance (IR) oculography) and MRT under controlled conditions with fixed light/dark exposure, caloric intake, sleep/wake schedule, and sleep duration. The results of this study showed that intermittent fasting had no impact on drowsiness or vigilance [13]. In another study, the effects of fasting on cognition were found to be heterogeneous and domain specific. Specifically, better performance was observed in the morning compared with in the late afternoon for functions requiring sustained rapid responses, whereas the accuracy of non-speed-dependent functions was more resilient [14]. The study also demonstrated that psychomotor function and vigilance were improved at 09:00 hours during fasting, whereas verbal learning and memory were poorer at 16:00 hours. Additionally, a time-of-day effect was present for psychomotor function, visual learning, verbal learning, and memory, with poorer performances observed at 16:00 hours. Moreover, there was no significant effect of fasting on visual learning or working memory [14]. However, a major limitation of this study was that sleep duration and quality were not objectively assessed during the study period.

In one experiment, individuals were subjected to a controlled experimental underfeeding for 1 week while objectively monitoring sleep duration and quality [15]. The results showed that daytime energy, concentration, and emotional balance were increased during fasting. Table 1 presents a summary of the studies that have assessed daytime sleepiness during Ramadan.

Because even minimal sleep restriction may affect daytime sleepiness and function, sleep deprivation or disruption cannot be ruled out as a possible cause for most of the findings listed above [16]. Therefore, it is important to use controlled conditions when assessing cognitive function during Ramadan.

The relationship between fasting and increased alertness and improved cognitive function is an interesting topic that deserves further research. Food restriction has been shown to increase wakefulness in different species [17]. In animal models, fasting has been shown to up-regulate orexin gene expression [17]. Orexin is a wake-promoting neurotransmitter secreted by the hypothalamus. In animal models, direct injection of orexin into the laterodorsal tegmental nucleus increased wake time and decreased REM sleep time [18]. However, these experiments included fasting that was usually more prolonged than diurnal intermittent fasting during Ramadan; therefore, these findings cannot be generalized to diurnal intermittent fasting. Moreover, it has been shown that intermittent fasting induces the expression of brain-derived neurotrophic factor (BDNF) in different regions of the brain [19]. BDNF can improve learning and memory and cognitive function and stimulate neurogenesis [19, 20].

Table 1 A summary of the studies that assessed daytime sleepiness and daytime cognitive function during Ramadan fasting

Author	Study population	Assessment tool	Findings	Study details
BaHammam et al. [2]	56 healthy medical students	Epworth Sleepiness Scale	Increase in daytime sleepiness	Subjective assessment; assessment was conducted in a non-constrained environment
Benchekroun et al. [6]	264 young subjects	Epworth Sleepiness Scale	Increase in daytime sleepiness	Subjective assessment; assessment was conducted in a non-constrained environment
BaHammam et al. [4]	101 healthy fasting and non-fasting subjects	Epworth Sleepiness Scale	No change in daytime sleepiness	Subjective assessment; assessment was conducted in a non-constrained environment
Margolis et al. [5]	109 healthy medical students	Epworth Sleepiness Scale	No change in daytime sleepiness	Subjective assessment; assessment was conducted in a non-constrained environment
Roky et al. [10]	10 healthy young subjects	Visual Analog Scale; movement reaction time (MRT); critical flicker fusion (CCF); at 6 different times of the day: 09:00, 11:00, 13:00, 16:00, 20:00, and 23:00 hours	Decreased daytime alertness; MRT increased at beginning of Ramadan; CCF did not change	Controlled for sleep/wake pattern; compared with baseline, volunteers slept 1 h less during Ramadan; controlled for meal composition and physical activity
BaHammam et al. [7]	16 fasting and non-fasting	Johns Drowsiness Scale to assess sleepiness; visual reaction time test; Epworth Sleepiness Scale	No decrease in alertness; no change in daytime sleepiness	Assessed sleep duration objectively using SenseWear Pro Armband™. There was a significant reduction in sleep duration during Ramadan in the fasting group; assessment was conducted in a non-constrained environment
BaHammam et al. [13]	8 healthy young male subjects	Johns Drowsiness Scale; infrared reflectance for blink total duration and a visual reaction time test	No decrease in alertness	Controlled for sleep/wake schedule, sleep duration, caloric intake, energy expenditure, and light exposure; actigraphy to assure adequate sleep duration in days prior to the study
Chamari et al. [11]	11 healthy trained cyclists	CANTAB, RTI, and RVP tests	No decrease in alertness; RTI was not affected by Ramadan intermittent fasting or time of day; overall, RVP accuracy increased in Ramadan and post-Ramadan compared with baseline; in the last week of Ramadan, accuracy was higher at the end of the day	Sleep duration was not assessed during the 24 h; tests were conducted at different times during and out of Ramadan
Roky et al. [9]	8 healthy young subjects	Portable MSLT; Visual Analog Scale	Increase in daytime sleepiness; subjective alertness decreased on day 11 at 12:00 of Ramadan but did not change on day 25; on MSLT, there was a decrease in sleep latency on days 11 and 25 of Ramadan	Portable device used—programmed to end test after 20 min of recording; sleep duration was significantly lower during Ramadan; meals during baseline and Ramadan were according to a fixed schedule and composition; did not rule out possible sleep deprivation in nights prior to study
BaHammam et al. [3]	8 healthy young subjects	Epworth Sleepiness Scale and standard MSLT	No change in daytime sleepiness	Did not rule out possible sleep deprivation in nights prior to study; MSLT was preceded by an overnight in lab PSG
BaHammam et al. [8]	8 healthy young subjects	Epworth Sleepiness Scale and standard MSLT; actigraphy to assess sleep duration in days prior to the study	No change in daytime sleepiness during Islamic intermittent fasting	Sleepiness was assessed while the volunteers were performing intermittent fasting during and outside Ramadan; controlled for sleep duration in nights prior

Table 1 (continued)

Author	Study population	Assessment tool	Findings	Study details
				to study and when at home by objective measurements (actigraphy)
Tian et al. [14]	18 male athletes	Computerized neuropsychological testing	Performance in functions requiring sustained rapid responses was better in the morning and declined in the late afternoon; performance in non-speed-dependent accuracy measures was more resilient	Standardized meals were provided; participants' lifestyle and training in between test sessions were not controlled for; sleep duration was significantly shorter during Ramadan; previous night's sleep and daytime naps, as well as the time of awakening, were not controlled for in this study; participants answered questionnaires regarding diet and sleep duration in the previous 24 h

CANTAB Cambridge Neuropsychological Test Automated Battery, *RTI* Reaction Time Index, *RVP* Rapid Visual Information Processing, *JDS* John Drowsiness Scale, *IR* infrared reflectance, *MSLT* multiple sleep latency test

Polysomnography and sleep architecture

Several studies have assessed sleep architecture during Ramadan using polysomnography; two used ambulatory unattended polysomnography at home [11, 21], whereas the other two used attended in-laboratory polysomnography [3, 8]. In the three studies that controlled for sleep/wake schedule, there were no significant differences between Ramadan and baseline levels of NREM sleep stages, arousal index, stage shifts, or cardiorespiratory parameters [3, 8, 21]. The fourth study was conducted among young athletes and showed no changes in sleep duration between baseline and Ramadan; however, there was a significant increase in the number of awakenings during Ramadan [11]. Nevertheless, in this study, the participants suddenly shifted their primary sleep time from night to daytime. Moreover, the study did not account for naps. This sudden shift in bedtime and sleep pattern might be responsible for the observed changes in sleep architecture in this study [22, 23].

In one study, to control for the lifestyle changes associated with Ramadan, sleep architecture was assessed at baseline (when the participants were fasting outside the month of Ramadan, Islamic intermittent fasting), during Ramadan, and after Ramadan while controlling for sleep/wake schedule, caloric intake, meal composition, light exposure, and circadian rhythm [8]. REM sleep was reduced while fasting during and outside Ramadan compared with baseline; however, the level of REM sleep returned to normal after the completion of fasting [8]. Similar findings of reduced REM sleep during Ramadan have been reported in three other studies [3, 11, 21]. These findings are in agreement with an animal study that assessed the effects of experimental fasting on sleep architecture [24]. The investigators reported an absence of REM sleep in piglets following 18 h of fasting, which was ameliorated after feeding [24]. Several theories have been proposed to explain the reduction in REM sleep during fasting. One possibility is that the reduction in REM sleep could be related to the nocturnal rise in cortisol and insulin [25, 26]. Some studies have shown that eating meals exclusively at night during Ramadan can increase nocturnal body temperatures [10, 21]. Given that REM sleep is inversely proportional to core body temperature, nocturnal increases in temperature could lead to decreases in REM sleep [27, 28]. Moreover, interrupting sleep for the predawn meal during the early morning hours, which is the period in which the largest portion of REM sleep usually occurs, is another possible mechanism for the reduction in REM sleep during Ramadan [3].

The available literature regarding sleep latency and total sleep time has reported conflicting results. One study reported no change in sleep latency in the first week of Ramadan and a drop in sleep latency during the third week of Ramadan, with no change in total sleep time [3]. Conversely, another study reported a significant increase in sleep latency and a significant reduction in total sleep time [21]. These discrepancies could be related to time differences between dinner and bedtime. In the study that showed an increase in sleep latency, the difference in time between dinner and bedtime was 1 h (dinner was served at 22:30, and polysomnography recording started at 23:30) [21], whereas there was a 3-h difference in the other study [1, 3]. In the study that assessed the effect of intermittent fasting on sleep architecture during Ramadan and outside the month of Ramadan month, there was no change in sleep latency during Ramadan [8]. The absence of changes in sleep architecture when controlling for sleep/wake schedule, prior sleep duration, caloric intake, energy expenditure, and light exposure suggests that intermittent fasting does not affect sleep architecture (apart from the reduction in REM sleep) [8]. However, in the free-living non-constrained environment that does not control for lifestyle changes associated with Ramadan, such as delayed bedtime, sleep architecture may become disturbed [11]. Table 2 presents a summary of the studies that have assessed sleep architecture during Ramadan.

Circadian rhythm

During Ramadan, fasting Muslims usually eat two to three meals after sunset: breakfast at sunset, dinner after night prayer (1–3 h after breakfast), and a predawn meal. Therefore, food and fluid intake are shifted to the hours of darkness, which partially reverses the normal circadian pattern of eating and drinking. Theoretically, these changes may affect the circadian rhythm and biological clock of fasting Muslims. Studies have shown that high fat and sugar intake can lead to changes in clock gene expression in the suprachiasmatic nucleus (SCN) and other peripheral brain nuclei (non-SCN brain nuclei) [29, 30]. Moreover, animal studies have shown that enforced meal times and temporal food restriction are potent synchronizers for secondary clocks in peripheral organs, such as those in certain brain regions and the suprachiasmatic clock, even when animals are exposed to a fixed light/dark cycle [31]. In addition, daily mealtime schedules can activate the expression of neural and circadian clock genes in many mammalian species, which is thought to be directed by a food-entrainable clock [31, 32].

Table 2 A summary of the studies that assessed polysomnography and sleep architecture during Ramadan fasting

Author	Study population	Sleep architecture assessment tool	Findings	Study details
Roky et al. [21]	8 young healthy adults	Ambulatory 8-channel unattended PSG	Significant increase in sleep latency and reduction in total sleep time; increase in stage N2 and reduction in slow wave sleep; reduced REM sleep	Unattended PSG; dinner was served at 22:30, and PSG recording started at 23:30; did not objectively account for the prior sleep/wake pattern before assessing sleep; did not monitor for daytime naps prior to overnight sleep study; meals in and outside Ramadan were according to fixed schedule and composition
BaHammam et al. [3]	8 young healthy adults	Full attended level-1 in--laboratory PSG	Significant drop in sleep latency at the end of Ramadan, with no change in total sleep time; reduced REM sleep at the end of Ramadan; no significant changes in NREM sleep	Controlled for sleep schedule, naps and caloric intake; did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory
BaHammam et al. [8]	8 young healthy adults	Full attended level-1 in--laboratory PSG	Reduced REM sleep during intermittent fasting (during and outside Ramadan); no significant changes in NREM sleep; no differences in sleep latency, arousal index, or sleep efficiency	Controlled for sleep schedule, naps, light exposure, caloric intake, and energy expenditure; assessed the effect of fasting during and outside Ramadan; controlled for sleep/wake and naps for 2 weeks before assessing sleep in the laboratory via actigraphy
Chamari et al. [11]	11 young healthy trained cyclists	Portable PSG	No change in sleep duration; significant increases in the number of awakenings and light sleep in Ramadan; progressive decrease in duration of deep and REM sleep stages that became significant 2 weeks post-Ramadan	Unattended PSG; did not control for sleep/wake pattern or sleep duration; during Ramadan, volunteers slept during daytime and at night pre- and post-Ramadan; during Ramadan, the volunteers slept in the morning after eating a main meal; naps were not controlled for; did not account for the prior sleep/wake pattern before assessing sleep; cyclists were in a training camp; the used portable device had relative weakness at the level of the number of awakenings; data regarding sleep duration were highly heterogeneous

Table 3 A summary of the studies that objectively assessed changes in the circadian pattern of body temperature and melatonin during Ramadan fasting

Author	Study population	Assessment tool	Findings	Study details
Circadian pattern of temperature				
Roky et al. [21]	6 healthy young adults	Rectal thermistor probe for at least 24 h	Delay in acrophase and bathyphase	The participants were of intermediate chronotype determined by the Morningness-Eveningness questionnaire; controlled for meal composition; dinner was served 1 h before bedtime during Ramadan and 3 h during baseline; no objective assessment of prior sleep pattern
Roky et al. [10]	10 healthy young adults	High-precision medical oral thermometer at 09:00, 11:00, 13:00, 16:00, 20:00, and 23:00	Reversal of circadian pattern of temperature	Subjects were intermediate chronotype as determined by the Morningness-Eveningness questionnaire; controlled for meal composition; sleep duration was 1 h shorter during Ramadan; no objective assessment of prior sleep pattern
BaHammam et al. [3]	8 healthy young adults	High-precision medical oral thermometer at 08:00, 16:00, and 00:00	No change	No objective assessment of prior sleep pattern; subjects stayed in the laboratory during monitoring
BaHammam et al. [33]	6 healthy young adults with delayed sleep phase disorder (DSPD)	SenseWear Pro Armband™ that measure proximal skin temperature during the last week of Shaban and the first 2 weeks of Ramadan	Further delay in temperature acrophase	Subjects were evening chronotypes; sleep patterns were monitored for 2 weeks prior to the study by use of sleep diaries (no objective assessment); sleep/wake schedule and sleep duration during the study were assessed objectively via Armband; participants lived in an unconstrained environment during the study
Circadian pattern of melatonin				
Bogdan et al. [36]	10 healthy male volunteers	Blood samples were obtained every 4 h, omitting the 02:00, before and on the 23rd day of Ramadan	A smaller delayed night peak and flatter slope of serum melatonin concentration in Ramadan	Volunteers slept 1 h less during Ramadan; melatonin concentrations were not measured late at night, which overlooked the possibility of a late peak in melatonin concentration; did not control for light exposure, sleep schedule or social habits that accompany Ramadan
BaHammam et al. [3]	8 healthy young adults	Saliva samples were collected at three time points over a 24-h period (08:00, 16:00, and 00:00) before and on the 7th and 21st days of Ramadan	A significant decrease in melatonin concentrations at 00:00 and 16:00 during Ramadan. Melatonin profiles continued to show the same trend during Ramadan but with a flatter slope	Controlled for sleep duration; did not control for light exposure or social habits that accompany Ramadan; melatonin concentrations were not measured late at night, which overlooked the possibility of a late peak in melatonin concentration
BaHammam et al. [37]	8 healthy young adults	Blood samples were collected at 22:00, 02:00, 04:00, 06:00, and 11:00 before Ramadan and while performing fasting outside Ramadan month and on the second week of Ramadan	Intermittent fasting during Ramadan has no significant effects on the circadian pattern of melatonin	Controlled for light exposure, sleep schedule, sleep duration, and meal composition; controlled for sleep duration and energy expenditure during the study period; assessed melatonin level when volunteers were fasting outside Ramadan month to control for lifestyle changes that accompany Ramadan.

Different physiological systems in the body exhibit circadian rhythms, including some hormones and core body temperature, which rises during the day and falls at night. The fall in core body temperature induces sleep, whereas the rise in temperature triggers wakefulness [2]. Studies that assess changes in body temperature have reported conflicting results (Table 3). Roky et al. continuously recorded body temperature for 24 h in six healthy subjects during Ramadan using a rectal thermistor probe and reported delays in both the occurrence of the acrophase and bathyphase of body temperature (i.e., the times at which the calculated maximum and minimum values, respectively, occur in the cycle) [21]. Another study by the same group reported that the body temperature circadian rhythm was reversed during Ramadan, with a remarkable decrease in oral temperature at 09:00, 11:00, 13:00, and 16:00 and a significant increase in temperature at 23:00 and 00:00 hours [10]. However, another study that measured oral temperature at 08:00, 16:00, and 00:00 using a high-precision medical thermometer during the first and third weeks of Ramadan and controlled for meal composition and sleep duration did not show changes in body temperature [3]. A fourth study assessed circadian changes in proximal skin temperature and energy expenditure before Ramadan and during the first and second weeks of Ramadan in an unconstrained environment using a portable armband physiological and activity sensor in six young adults with delayed sleep phase disorder, also known as evening chronotypes (i.e., during the non-Ramadan period, the volunteers typically slept during daytime and were awake and eating at night) [33]. During Ramadan, there was a further delay in the acrophase of skin temperature and energy expenditure, which indicates a shift in the circadian pattern. These results suggest that, in addition to a sudden shift in meal times, other factors may affect sleep patterns and circadian rhythms during Ramadan [33]. Table 3 presents a summary of the studies that have assessed circadian rhythm of body temperature during Ramadan.

Melatonin is another important marker for circadian rhythm disruption because it is highly reproducible and less prone to masking effects than other rhythm markers, such as core temperature and cortisol [10, 34, 35]. Therefore, changes in the circadian pattern of body temperature during Ramadan may also be associated with alterations in the circadian pattern of melatonin secretion. In one study [36], melatonin levels were assessed in blood samples obtained every 4 h (omitting the 02:00 time point to prevent causing sleep disturbances) before and on the 23rd day of Ramadan. The authors observed a smaller delayed night peak and flatter slope in serum melatonin concentrations during Ramadan [36]. In another study, the investigators collected saliva samples from eight healthy volunteers at three time points over a 24-h period (08:00, 16:00, and 00:00) 1 week before Ramadan and on the 7th and 21st days of Ramadan [3]. After controlling for sleep duration, the study reported a significant decrease in melatonin concentrations at 00:00 and 16:00 during Ramadan relative to baseline levels. However, similar trends in melatonin profiles were observed during Ramadan but with a flatter slope [3]. A major limitation in these two studies was that melatonin was not measured late at night, which overlooks the possibility of a late peak in melatonin concentrations. Moreover, neither study controlled for differences in light exposure, sleep schedule, or social habits that accompany Ramadan. To overcome the shortcomings of these studies, we assessed circadian patterns in melatonin during intermittent fasting outside the month of Ramadan and during the second week of Ramadan after controlling for light exposure, sleep schedule, sleep duration, and meal composition [37]. Serum melatonin was measured in eight healthy volunteers at five time points (22:00, 02:00, 04:00, 06:00, and 11:00) on three occasions: 4 weeks before Ramadan while performing Islamic fasting for 1 week; 1 week before Ramadan while living a routine life; and during the second week of Ramadan while fasting. After controlling for light exposure, sleep schedule, and sleep duration, a trough in melatonin levels was observed at 11:00 during all studied occasions, which indicates that intermittent fasting has no significant influence on the circadian pattern of melatonin. Therefore, the changes in melatonin levels reported in the previously published studies could reflect lifestyle changes in the participants during Ramadan.

Nevertheless, most studies consistently report a decrease in melatonin concentrations during fasting, even during short-term experimental fasting [3, 15, 38]. Although the exact mechanisms involved in the reduction in melatonin levels during fasting are unknown, several mechanisms have been proposed, including increases in nocturnal cortisol levels during Ramadan [39, 40] and decreases in melatonin synthesis due to decreased glucose supplies [41]. The latter hypothesis is supported by findings that show that melatonin levels are decreased secondary to mild hypoglycemia, and glucose supplementation during fasting ameliorates the decrease in melatonin levels [38]. Nevertheless, hypoglycemia is not believed to occur in healthy individuals during Ramadan fasting [42]. Another mechanism that could explain the reduction in melatonin levels during Ramadan fasting is a reduction in tryptophan, which is both an essential amino acid and a precursor of melatonin. However, this explanation is implausible because intermittent fasting is unlikely to cause a reduction in tryptophan and glucose supplementation restores normal melatonin levels during fasting [38].

Leptin and ghrelin are two hormones that are affected by feeding and fasting. Therefore, the sudden shift in mealtime during Ramadan may entrain the diurnal rhythm of both hormones. Two studies have used a cosinor analysis to assess the effect of Ramadan fasting on leptin and ghrelin. Bogdan et al. demonstrated a significant shift (approximately 5 h) in the peak and nadir serum leptin levels on the 23rd day of

Ramadan fasting [43]. However, no significant changes were observed in the amplitude or 24 h mean concentrations of leptin compared with the findings before Ramadan. Alzoghaibi et al. suggested that a nocturnal reduction in leptin likely reflects changes in meal times during fasting; however, in this study, no significant changes were observed in the circadian rhythm of leptin following the cosinor analysis [44]. One possible explanation for the differences between the two studies is that the second study controlled for behavioral customs (such as eating habits) and environmental conditions (such as light exposure), whereas the first study did not, which might have resulted in a shift delay in the circadian rhythm of the participants in the first study. To date, only one study has assessed circadian patterns during Ramadan using a cosinor analysis while controlling for eating habits and environmental conditions, and it reported no significant changes in the acrophase of the circadian rhythm of ghrelin [44].

The findings reported above suggest that there is a shift delay in the circadian clock during Ramadan. However, when eating habits and environmental conditions are controlled, intermittent fasting does not significantly influence the circadian rhythm.

Circadian rhythms can also be assessed by examining the chronotype of fasting individuals. One study assessed the chronotype in fasting and non-fasting individuals during Ramadan using an abridged version of the Horne and Ostberg questionnaire to establish three behavioral categories: morning type, neither type, and evening type [4, 45]. An increase in the evening-type circadian rhythm was observed among fasting individuals both at the beginning and the end of Ramadan compared with baseline. Similar changes in chronotype were also observed in non-fasting non-Muslim residents in Saudi Arabia during Ramadan, which suggests that factors other than fasting may affect the circadian rhythm during Ramadan [4]. This finding supports the notion that lifestyle changes that accompany Ramadan may affect circadian rhythm.

Summary

The effect of diurnal intermittent fasting during Ramadan on sleep patterns, daytime sleepiness, cognitive function, sleep architecture, and circadian rhythm is an interesting topic that provides a highly complex context for future research. Although some researchers believe that Ramadan intermittent fasting increases daytime sleepiness and alters daytime functioning, this notion is not supported by the available data. Earlier studies have shown that Ramadan fasting delays the circadian rhythm of core body temperature and hormonal secretion. However, those studies did not control for lifestyle changes that influence circadian rhythm. Recent studies that controlled for sleep/wake schedule, sleep duration, light exposure, and energy expenditure showed no effect of fasting on circadian rhythms. In non-constrained environments that do not control for lifestyle changes, studies have demonstrated sudden and significant delays in bedtime and wake time. Furthermore, one study reported an increase in the number of awakenings in participants who shifted their major sleep time during Ramadan from nighttime to daytime. These changes could be related to lifestyle changes that accompany Ramadan fasting rather than the act of fasting itself because studies that controlled for environmental factors and sleep/wake schedule reported no significant disturbances in sleep architecture. Several studies have consistently reported that the main change in sleep architecture during fasting is a reduction in the proportion of REM sleep.

Larger studies that control for different confounding factors, such as environmental and cultural factors, are needed to assess the impact of Ramadan fasting on sleep, sleepiness, and circadian rhythms. In addition, it is important to assess the impact of Ramadan fasting in different Islamic cultures using the same assessment methods.

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Compliance with ethical standards

Conflict of interest All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge, or beliefs) in the subject matter or materials discussed in this manuscript.

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