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### REVIEW

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## How does diurnal intermittent fasting impact sleep, daytime sleepiness, and markers of the biological clock? Current insights

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**Abstract:** Mealtimes and feeding schedules may interfere with the circadian system and impact sleep. The practice of intermittent fasting (IF) in its different formats is increasing worldwide. However, most studies addressing the effect of IF on circadian rhythms, daytime sleepiness, and sleep architecture have been conducted during diurnal IF for Ramadan. In this article, we analyze the effect of diurnal IF on the circadian clock, sleep, and daytime sleepiness. In free-living, unconstrained environments that do not control for lifestyle changes such as sleep/wake schedules, sleep duration, and light exposure, studies have demonstrated sudden and significant delays in bedtime and wake time during diurnal intermittent fasting for Ramadan. However, subsequent studies that accounted for lifestyle factors and sleep/wake patterns have reported no changes in markers of the biological clock, daytime sleepiness, or sleep parameters. Nevertheless, several researchers have demonstrated a reduction in the proportion of rapid eye movement stage sleep as the significant alteration in sleep architecture during fasting.

**Keywords:** mealtime, Ramadan, chronotype, sleep architecture, alertness, food, light, caloric restriction

### Introduction

Fasting, mealtime, and sleep may interact and impact the circadian rhythm of various body organs and cells when food is not consumed at a suitable time relative to the timing of the circadian clock of the body.<sup>1,2</sup> Intermittent fasting (IF), in which one voluntarily refrains from food intake for specific times, is an old tradition that is implemented in different practices by various societies around the world.<sup>3,4</sup> Several religions practice periods of fasting in their rituals, including Islam, Christianity, Judaism, Hinduism, and Buddhism.<sup>5</sup> Recently, IF practice has become popular, and there has been great attention to the physiological and metabolic consequences of IF among researchers.<sup>1</sup>

IF is different from caloric restriction (CR), in which caloric intake is lowered for long periods by 20%–40% but meal frequency is preserved.<sup>6</sup> Several types of IF have been described in the literature, including complete fasting every other day,<sup>7</sup> significant CR every other day,<sup>8</sup> eating only a small amount of calories (500–700) 2 consecutive days/week,<sup>9</sup> "time-restricted feeding," where food intake is restricted to a specified time daily,<sup>10</sup> fasting 1 or 2 days per week and allowing 5–6 days ad libitum ingestion of food, and the spiritual diurnal IF practiced during Ramadan, in which there is total abstinence from food and drink during daytime (dawn to dusk).<sup>11,12</sup>

Most of the previous studies on experimental IF have assessed its effect on metabolic and cardiovascular risks.<sup>1</sup> Most studies addressing the impact of IF on sleep and circadian rhythm have been conducted during diurnal IF for Ramadan. Therefore, in this article,

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we address the impact of diurnal IF on some markers of the circadian clock, sleep parameters, and daytime sleepiness.

### IF for Ramadan

Diurnal IF for Ramadan is distinct from other forms of experimentally studied fasting for several reasons; therefore, it needs to be treated as a separate entity. Ramadan fasting comprises diurnal IF from dawn to sunset, where participants refrain from eating and drinking during the specified period. Ramadan is a month of the Arabic (*Hijri*) year and hence follows the lunar system. This implies that Ramadan comes during a different season every 9 years, which could affect the duration of daytime and hence fasting duration, where daytime is longer during the summer than in the winter.<sup>13</sup>

Moreover, diurnal IF is practiced for the full month of Ramadan; this long duration may permit greater adjustment to the fasting protocol than that typically occurs in other forms of experimental IF. Furthermore, several studies have shown that Ramadan is accompanied by lifestyle changes that may influence sleep and circadian rhythms (Figure 1).

### **Review method**

The literature search started on the May 1, 2018, with the following keywords: "sleep," "sleep pattern," "daytime sleepiness," "polysomnography," "sleep architecture," "circadian rhythm," "intermittent fasting," and "Ramadan," using PubMed (80 results), Clarivate (94 results), and Google Scholar (105 results). In addition, the reference lists of the

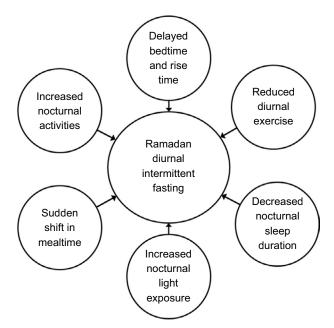


Figure I Lifestyle changes that accompany the month of Ramadan and that may affect sleep and circadian rhythms.

identified articles were also searched for further references. The following inclusion criteria for human studies were used: children, men, and women were accepted as participants, and both randomized controlled trials and nonrandomized trials were accepted.

# Impact of diurnal IF on the circadian rhythm

All cells of the human body have circadian clocks, which are generally classified into peripheral and central clocks based on their anatomical place. The central master clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus. On the other hand, the peripheral clocks are located in different organs and tissues.<sup>14</sup> Both central and peripheral clocks act to preserve the circadian rhythm of different tissue physiology via controlling "tissue-specific gene expression."<sup>14</sup>

With the aim of ensuring external synchrony between the body and the surrounding environment, besides internal synchrony and correct chronological alignment between the central and peripheral clocks, the timing of the body circadian system must be calibrated repeatedly.14 The main entrainment factor (or "Zeitgeber") for the SCN is light, while peripheral circadian clocks are affected by "neurohumoral modulation."15 Therefore, certain behaviors such as the timing of feeding and the timing of abstinence of food may affect the circadian rhythm.<sup>1,12,16</sup> Data that address the impact of IF on the circadian rhythm are limited, and most of those data address the impact of Ramadan diurnal IF on the circadian rhythm. However, current evidence shows that high caloric consumption can lead to alterations in "clock gene expression" in the SCN and other central nuclei.<sup>17,18</sup> In addition, animal studies have shown that temporal food restriction and enforced meal times are powerful synchronizers for body clocks in peripheral tissues, while maintaining a fixed light-dark cycle exposure.<sup>19</sup> Moreover, it has been shown that mealtime schedules can trigger the activation of neural circadian clock genes in several species, which is assumed to be controlled by a "food-entrainable clock."2,20

Almost all physiological systems in the body follow a circadian rhythm, which is reflected by measuring certain hormones and core body temperature.<sup>21</sup> During Ramadan diurnal IF, 2–3 meals are taken after sunset: breakfast (a light meal) is taken at sunset, dinner is taken following night prayer in some countries (~1–3 hour after sunset), and a "predawn meal" (Suhur), which means that food consumption, is moved to the hours of darkness. This food intake shift partly inverts the normal circadian pattern of food intake. In theory, this

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shift in mealtime may disrupt the circadian rhythm and biological clock of fasting participants.<sup>12</sup>

### Subjective assessment of chronotype

One study assessed chronotypes using an abridged version of the Horne and Ostberg questionnaire in fasting and nonfasting individuals during Ramadan diurnal IF in a "free-living environment" to define three behavioral groups: morning-type, evening-type, and neither-type.<sup>22,23</sup> Interestingly, the study reported an increase in the evening chronotype among the performers of fasting at both the beginning and the end of Ramadan month compared with baseline. Similarly, an increase in evening chronotype was also reported in nonfasting people during Ramadan, which advocates that lifestyle changes other than fasting may influence the circadian rhythm during Ramadan.<sup>23</sup> This result strengthens the hypothesis that lifestyle changes accompanying Ramadan may affect circadian rhythms.

## Effects of diurnal IF on body temperature

Core body temperature increases during the day and decreases at night. Sleep onset is accompanied by a decrease in core body temperature, whereas an increase in core body temperature initiates the wakefulness process.<sup>21</sup> Studies that assessed changes in core body temperature during Ramadan diurnal IF have reported conflicting results (Table 1). In general, studies that assessed the circadian rhythm during Ramadan diurnal intermittent fasting can be divided into two categories: category 1 encompasses studies that examined the changes in some markers of the circadian clock in an unconstrained "free-living environment" without controlling for confounders and lifestyle changes such as meal composition, caloric intake, total sleep time, energy expenditure, or light exposure,<sup>24–27</sup> and category 2 encompasses studies that controlled for the above confounders.<sup>28–30</sup>

Twenty-four-hour continuous monitoring of rectal temperature in six healthy volunteers during Ramadan revealed delays in both the "bathyphase" and the "acrophase" of body temperature (ie, the times at which the calculated minimum and maximum values of body temperature occur, respectively).<sup>25</sup> One more study reported that the circadian rhythm of body temperature was reversed during Ramadan diurnal IF, with significant decreases in oral temperature at the following times: 09:00, 11:00, 13:00, and 16:00, and considerable increases in temperature at 23:00 and 00:00 hours.<sup>26</sup> Conversely, a third paper that assessed the oral temperature of volunteers during the first and third weeks of Ramadan at 08:00, 16:00, and 00:00 using a "high-precision" thermometer while controlling for the composition of meals and sleep duration reported no changes in body temperature.<sup>30</sup> The above studies did not control for most of the lifestyle changes discussed earlier that may impact the circadian rhythm regardless of fasting. To assess the potential effects of lifestyle changes that accompany Ramadan, a well-designed study recruited young adults with "delayed sleep phase disorder" (evening chronotype) who used to sleep during the daytime and wake up and eat at night.<sup>24</sup> In an unconstrained, free-living environment, the investigators use a portable armband physiological and activity sensor to measure circadian alterations in proximal skin temperature and energy expenditure before Ramadan and during the first 2 weeks of Ramadan.<sup>24</sup> Interestingly, the study revealed a further delay in the "acrophase" of proximal skin temperature and energy expenditure denoting a shift in the circadian pattern. The findings of this study support the hypothesis that factors other than the sudden shift in mealtimes may influence sleep patterns and circadian rhythms during Ramadan.<sup>24</sup> Table 1 summarizes the studies that have examined the circadian rhythm of body temperature during diurnal IF for Ramadan.

# Effects of diurnal IF on melatonin and other hormones

Melatonin is a useful marker of circadian rhythm because it is highly precise and accurate.<sup>26,31,32</sup> Therefore, proper measurement of melatonin level is an excellent method to examine the impact of diurnal IF on the circadian rhythm. One study assessed the blood levels of melatonin every 4 hours (not including the 02:00 time point measurement to avoid sleep disruption) before and at the end of the third week of Ramadan.<sup>27</sup> The study revealed a reduced, delayed night peak and a flattened slope in serum melatonin concentrations during Ramadan.<sup>27</sup> Another study, which measured the salivary melatonin levels of eight healthy volunteers (who performed diurnal IF) over a 24 hours period (08:00, 16:00, and 00:00) at three time points -1 week before Ramadan and at the end of the first and third weeks of Ramadan - while controlling for total sleep time, revealed a statistically significant fall in melatonin concentrations at 00:00 and 16:00 during Ramadan compared to baseline levels.<sup>30</sup> Although the study reported comparable trends in melatonin circadian pattern during Ramadan and at baseline, the slope was flatter in the former case.<sup>30</sup> However, the above studies failed to measure melatonin late at night, neglecting the possibility of a latenight peak in melatonin concentrations.

None of the above studies accounted for potential confounders that may accompany Ramadan and affect the measured melatonin levels. In a subsequent study,

Study	Study population	Study design	Assessment tool	Study setting	Findings	Study details
Roky et al <sup>25</sup>	8 healthy young adults	Case crossover study	Rectal thermistor	Monitoring at home	Delay in acrophase and	The participants were of the
	(age: 20–28 years)	with repeated measures	probe for at least 24	Controlled for meal	bathyphase	intermediate chronotype as
	Location: Morocco		hours	composition and time, as		determined by the Morningness-
				well as bedtime and rising		Eveningness Questionnaire
				time		Dinner was served I hour before
						bedtime during Ramadan and 3
						hours before bedtime at baseline
						No objective assessment of prior
						sleep pattern
Roky et al <sup>26</sup>	10 healthy young adults	Case crossover study	High-precision medical	Monitoring at home	Reversal of circadian	Subjects were of the intermediate
	(age: 20–28 years)	with repeated measures	oral thermometer at	Controlled for meal	pattern of temperature	chronotype as determined by
	Location: Morocco		09:00, 11:00, 13:00,	composition and time, and		the Morningness-Eveningness
			16:00, 20:00, and 23:00	bed and rise time		Questionnaire
						Sleep duration was I hour
						shorter during Ramadan than at
						baseline
						No objective assessment of prior
						sleep pattern
BaHammam et al <sup>30</sup>	8 healthy young adults	Case crossover study	High-precision medical	Monitoring in the	No change	No objective assessment of prior
	(age: 31.8±2 years)	with repeated measures	oral thermometer at	laboratory		sleep pattern
	Location: Saudi Arabia		08:00, 16:00, and 00:00	Controlled for meal		Subjects stayed in the laboratory
				composition		during monitoring
BaHammam et al <sup>24</sup>	6 healthy young adults with	Case crossover study	SenseWear Pro	Free-living environment	Further delay in	Subjects belonged to the evening
	delayed sleep phase disorder	with repeated measures	Armband <sup>TM</sup> that		temperature acrophase	chronotype
	(age: 18-24 years)		measures proximal skin			Sleep patterns were monitored
	Location: Saudi Arabia		temperature during the			for 2 weeks prior to the study by
			last week of Shaban			using sleep diaries (no objective
			and the first 2 weeks of			assessment)
			Ramadan			Sleep/wake schedule and sleep
						duration during the study were
						assessed objectively via armband
						Participants lived in an
						unconstrained environment
						during the study

Table I A summary of the studies that objectively assessed changes in the circadian pattern of body temperature during diurnal intermittent fasting for Ramadan

we attempted to overcome those limitations by assessing circadian profiles of serum melatonin during diurnal IF outside Ramadan (to assess the impact of diurnal IF act in the absence of the lifestyle changes associated with Ramadan) and during the second week of Ramadan while controlling for light exposure, sleep pattern, total sleep time, and meal composition.<sup>28</sup> In eight healthy volunteers, serum melatonin was measured at five time points (22:00, 02:00, 04:00, 06:00, and 11:00) three times: 4 weeks before Ramadan where volunteers were asked to perform diurnal IF (fasting outside the month of Ramadan) for 1 week, 1 week before Ramadan during which volunteers were not fasting and living a routine life, and during the second week of Ramadan while performing diurnal IF. The trough in melatonin levels occurred 11:00 during the three studied periods, which shows that diurnal IF has no significant effect on the circadian rhythm of melatonin when other confounders are accounted for. In addition, a cosinor analysis of melatonin levels showed no significant changes in the "acrophase."28 Therefore, the previously reported changes in melatonin levels during Ramadan could be related to the lifestyle changes that accompany Ramadan. Nonetheless, more studies with larger sample sizes are required to evaluate the effects of diurnal IF on melatonin levels and circadian patterns. Table 2 summarizes the studies that have objectively addressed changes in the circadian pattern of melatonin during diurnal IF for Ramadan.<sup>27,28,30</sup>

Most studies assessing melatonin levels during diurnal IF have consistently reported a reduction in measured melatonin levels, even during short-term experimental fasting.<sup>30</sup> Several theories have been suggested to understand the decrease in melatonin levels during fasting. The nocturnal increase in cortisol levels during Ramadan is a possible mechanism.<sup>33,34</sup> In addition, it has been proposed that a decrease in the glucose supply during fasting may result in a decrease in melatonin synthesis,<sup>35</sup> as it has been shown in rats that mild hypoglycemia decreases melatonin levels, and administration of glucose improves the decrease in melatonin levels.<sup>36</sup> However, previous studies have shown that hypoglycemia does not happen in healthy individuals during diurnal IF.37 Reduction in tryptophan had been proposed as a possible mechanism of the reduction in melatonin levels during Ramadan diurnal IF, as tryptophan is essential for melatonin synthesis. Nevertheless, this proposed mechanism is improbable because short duration diurnal IF is not likely to cause a reduction in tryptophan.36

Both leptin and ghrelin hormones are influenced by fasting, mealtime, and sleep. Hence, the abrupt shift in mealtime during diurnal IF for Ramadan may entrain the circadian rhythms of both hormones.

Two previous studies have examined the impact of diurnal IF on the circadian patterns of leptin using a cosinor analysis. The first study was conducted on free-living participants and revealed a major shift (~5 hours) in the peak and nadir serum leptin concentrations in the third week of Ramadan.<sup>38</sup> However, the amplitude and 24 hours mean concentrations of leptin levels revealed no significant changes compared to the levels before Ramadan. Another study reported a significant decrease in plasma leptin concentration at 22:00; however, a cosinor analysis demonstrated no significant changes in the circadian rhythm of leptin.<sup>29</sup> The sudden change in mealtime during Ramadan may explain the nocturnal decrease in plasma leptin levels. The difference between the findings of the two studies could be explained by the fact that the second study controlled for lifestyle changes and environmental conditions, while the first study did not, which might have resulted in a delay in the circadian rhythm of leptin in the first study.

So far, only one study has evaluated circadian rhythm of ghrelin during Ramadan diurnal IF while controlling for eating habits and environmental conditions.<sup>29</sup> A cosinor analysis revealed no significant changes in the "acrophase" of the circadian rhythm of ghrelin.<sup>29</sup>

In summary, the above-reviewed studies suggest that during Ramadan diurnal IF, there is a delay in the circadian clock. However, when eating habits and environmental conditions are accounted for, diurnal IF does not significantly affect the circadian rhythm of body temperature and melatonin.

## **Effects of diurnal IF on sleep** Subjective assessment of sleep

When assessing the influences of diurnal IF during Ramadan on sleep, it is essential to consider the accompanying lifestyle changes during the holy month. For example, in some Muslim countries, the beginning of work is delayed and work duration is shortened during Ramadan. Some of the earlier studies that assessed sleep patterns during Ramadan used sleep diaries and self-reported data. Studies that assessed sleep/wake pattern in three Muslim countries revealed a significant sudden delay in bedtime and wake time during Ramadan in performers of diurnal IF.<sup>21,23,30,39,40</sup>

Interestingly, one study demonstrated bedtime delay during Ramadan even in nonfasting subjects.<sup>23</sup> This documented delay in bedtime and rise time reflects the delay in the start of work during Ramadan.

Study   Study population     Bogdan et al <sup>27</sup> 10 healthy male     volunteers   volunteers     (age: 32–40 years)   Location: France	ulation male veare)	Study design	Assessment tool	Study setting	Findings	Study details
	nale vears)					
volunteers (age: 32–40 Location: Fr	vearc)	Case	Blood samples	Free-living environment	A decreased and delayed	Volunteers slept I hour less
(age: 32–40 Location: Fr	vears)	crossover	were obtained	Controlled for meal	night peak and a flattened	during Ramadan than before
Location: Fr	la mal	study with	every 4 hours,	timing and composition	slope of serum melatonin	Ramadan
	rance	repeated	omitting the 02:00	Did not control for light	concentration in Ramadan	Melatonin concentrations
		measures	time point, before	exposure, sleep schedule,		were not measured late at
			and on the 23rd	or social habits that		night, which fails to address
			day of Ramadan	accompany Ramadan		the possibility of a late peak
						in melatonin concentration
BaHammam et al <sup>30</sup> 8 healthy young	gunc	Case	Saliva samples	In-laboratory monitoring	A significant decrease in	Melatonin concentrations
adults		crossover	were collected at	Controlled for meal	melatonin concentrations	were not measured late at
(age: 31.8±2 years)	2 years)	study with	three time points	timing and composition	at 00:00 and 16:00 during	night, which fails to address
Location: Saudi	iudi	repeated	over a 24-hour	Controlled for sleep	Ramadan	the possibility of a late peak
Arabia		measures	period (08:00,	duration	Melatonin profiles	in melatonin concentration
			16:00, and 00:00)	Did not control for light	continued to show	
			before and on the	exposure or social habits	the same trend during	
			7th and 21st days	that accompany Ramadan	Ramadan, but with a	
			of Ramadan		flatter slope	
Almeneessier et al <sup>28</sup> 8 healthy young	gunc	Case	Blood samples	In-laboratory monitoring	Intermittent fasting	Assessed melatonin level
adults		crossover	were collected	Controlled for light	during Ramadan has	when volunteers were
(age: 26.6±4.9	1.9	study with	at 22:00, 02:00,	exposure, sleep schedule,	no significant effect on	fasting outside Ramadan
years)		repeated	04:00, 06:00,	sleep duration, energy	the circadian pattern of	month to control for
Location: Saudi	iudi	measures	and 11:00 before	expenditure, and meal	melatonin	lifestyle changes that
Arabia			Ramadan and	composition		accompany Ramadan
			while performing			
			fasting outside			
			Ramadan month			
			and on the second			
			week of Ramadan			

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With regard to sleep duration, conflicting results were reported during Ramadan. Whereas some studies reported a reduction of sleep duration during Ramadan,<sup>39–41</sup> others reported no significant alterations in nighttime sleep duration during Ramadan.<sup>21,23</sup> Nevertheless, in a study that assessed sleep duration objectively using actigraphy in eight fasting (diurnal IF) and eight nonfasting volunteers in a free-living environment during Ramadan, bedtime and wake time were delayed in the fasting volunteers, and a significant reduction in total sleep time was observed in the fasting group.<sup>42</sup>

The discrepancies between the above studies may reflect cultural and lifestyle variations among countries or the use of different subjective assessment tools.<sup>12,13</sup>

# Objective assessment of sleep **Sleep architecture**

A few studies have objectively measured sleep parameters during the month of Ramadan among volunteers practicing diurnal IF using in-laboratory polysomnography and homebased ambulatory unattended polysomnography.<sup>25,30,43,44</sup> Table 3 summarizes the studies that have evaluated sleep architecture using polysomnography during Ramadan diurnal IF. In studies that controlled for sleep/wake pattern, diurnal IF had no effect on nonrapid eye movement sleep stages, stage shifts, arousal index, or measured cardiorespiratory parameters.<sup>25,30,44</sup> One study objectively assessed sleep among young athletes and revealed no changes in total sleep time during Ramadan diurnal IF; however, the study reported a significant increase in the number of awakenings.43 Nevertheless, a major limitation of the last study is the fact that the study athletes suddenly changed their primary sleep time from night to daytime, and the study did not account for naps. Therefore, the abrupt changes in bedtime and rise time may have accounted for the observed changes in sleep architecture.17,45

A recent study controlled for the lifestyle changes associated with Ramadan, such as sleep/wake pattern, caloric consumption, meal composition, and light exposure to eliminate variables other than meal timing that might affect sleep architecture; it objectively assessed sleep architecture at baseline, during diurnal IF outside Ramadan, during Ramadan, and during a nonfasting period after Ramadan.<sup>44</sup> Rapid eye movement (REM) sleep proportion decreased while fasting during and outside Ramadan compared with the baseline; however, the proportion of REM sleep reverted to normal during recovery (after Ramadan).<sup>44</sup> Three other studies reported a reduction in REM sleep during Ramadan.<sup>25,30,43</sup> In agreement with the above, studies that assessed the effect of experimental fasting on animals reported similar changes in sleep architecture.<sup>46</sup> REM sleep disappeared in piglets following 18 hours of fasting, which reverted to normal after feeding.<sup>46</sup>

Several hypotheses have been proposed to account for the decrease in REM sleep during fasting; however, the precise mechanisms are unknown.<sup>12</sup> In addition, the clinical consequences of reduced REM sleep during fasting are unknown. Proposed theories to understand the decrease in REM sleep during fasting include the documented nocturnal rise in cortisol and insulin,<sup>47,48</sup> and the possible increase in nocturnal body temperature as a result of eating exclusively at night during diurnal IF.<sup>25,26</sup> Increased nocturnal temperature could result in a reduction in REM sleep proportion.<sup>49,50</sup> Another proposed mechanism is the interruption of sleep in the early morning (predawn) for the predawn meal (Suhur), which is the period in which the major fraction of REM sleep usually occurs.<sup>30</sup>

### Sleep latency

With regard to sleep latency during Ramadan IF, studies have reported conflicting results. Roky et al showed a significant increase in sleep latency and a significant reduction in nocturnal sleep time.<sup>25</sup> However, in that study, dinner was served 30 minutes before going to bed; the short time between dinner and bedtime could have affected sleep latency. Later studies that provided dinner at an earlier time (3–3.5 hours before bedtime) and controlled daytime naps revealed no change in sleep latency.<sup>13,30,44</sup>

The above-reviewed studies suggest that when dinner is provided early and daytime naps are controlled for, diurnal IF does not have major influence in sleep architecture. The only change in sleep architecture consistently reported is the reduction in REM sleep.<sup>44</sup> However, in a free-living environment that does not control for confounders that usually accompany Ramadan such as mealtimes or the daytime naps, sleep latency and sleep architecture may be disturbed.<sup>43</sup>

### Daytime sleepiness

A discussion of the effect of diurnal IF on sleep would not be complete without reviewing the impact of daytime fasting on daytime sleepiness. Several studies have assessed the interaction between daytime sleepiness and diurnal IF during Ramadan both subjectively<sup>21,23,30,39,40,42,44,51</sup> and objectively.<sup>30,44,51</sup> However, these studies reported conflicting results, which may reflect the differences in the used assessment tools, the lack of objective assessment or the failure to control for potential confounders that could impact daytime

used for assessment       scuoy details         liatory B-channel       Unattended 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 overmight sleep study         Meals during and outside Ramadan       were according to a fixed schedule and coratory PSG         Composition       Controlled for sleep schedule, naps, and coratory PSG         Did not objectively account for the prior verse according to a fixed schedule and coratory PSG       Controlled for sleep schedule, naps, and caloric intake         Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory       Did not controlled for sleep schedule, naps, and caloric intake         Did not controlled for sleep schedule, naps, light oratory PSG       Did not controlled for sleep/wake pattern or sleep/wake pattern or sleep/wake pattern or befor sleep/wake and naps for 2 weeks before assessing sleep in the laboratory         Die PSG       Undattended for 1 do to controlled for 2 weeks before assessing sleep in the laboratory         Die PSG       Undattended for 1 do to controlled for 1 do to controlled for 1 do to account for the prior sleep/wake pattern before assessing sleep in the laboratory         Did not account for the prior sleep/wake       Did not account for the prior sleep/wake         Did not account for the prior sleep/wake       Did not account for the prior sleep/wake         Did not account for the pr	-					
Lunattended PSG     ended 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 during and outside Ramadan     mere according to a fixed schedule and composition   Composition     tended level I   Controlled for sleep schedule, naps, and caloric intake     Drid not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory   Meals and caloric intake     Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory   Meals and caloric intake     Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory   Meals and caloric intake     Did not controlled for sleep/wake and naps for the laboratory   Juntake, and energy     Did not controlled for sleep/wake and naps for the laboratory via actigraphy   Juntake and and conside Ramadan     Did not controlled for sleep/wake and naps for the portaked for   Juntateers slept furting daytime and at night before and after Ramadan     Did not controlled for sleep/wake and maps for the portaked for   During Ramadan, vounteers slept in the noriside Ramadan     Did not account for the prior sleep/wake   During Ramadan, vounteers slept in the prior garden and at night before and iter Ramadan     Did not account for the prior sleep/wake   During Ramadan     Did not c	Study	Study population	Study design	I est used for assessment	Study details	Findings
ended PSG   Dimer was served at 22:30, and PSG     recording started at 23:30   Did not objectively account for the prior sleep blid not monitor for daytime naps prior to overnight sleep study meals during and outside Ramadan were according to a fixed schedule and coractory PSG     tended level I   Composition     tended level I   Composition     tended level I   Composition     tended level I   Controlled for sleep schedule, naps, and coractory PSG     pid not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory     tended level I   Controlled for sleep schedule, naps, light coractory PSG     pid not objectively account for the prior sleep/wake pattern of avoing and outside Ramadan     tended level I   Controlled for sleep schedule, naps, light coractory PSG     pid not objectively account for the prior sleep/wake pattern or sleep duration     bie PSG   Unattended Fo.     bie PSG   Unattended Fo.     bie PSG   Did not corrorled for sleep/wake pattern or sleep during and ourside Ramadan     cortrolled for sleep/wake pattern or sleep during and ourside Ramadan     bie PSG   Did not corrorled for sleep/wake pattern or sleep during and ourside Ramadan     Did not corrorled for sleep/wake pattern or sleep during and ourside Ramadan   Did not corrorled for sleep/wake pattern or sleep during and ourside result     <	Roky et al <sup>25</sup>	8 young healthy adults	Case crossover study	Ambulatory 8-channel	Unattended PSG	Significant increase in sleep
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Did not objectively account for the prior sleep/wake pattern before assessing sleep Did not monitor for daytime naps prior to overnight sleep study       Maals during and outside Ramadan were according to a fixed schedule, naps, and composition       ttended level I     Controlled for sleep schedule, naps, and caloric intake       Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory       Ealoric intake     Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory       Ealoric intake     Controlled for sleep schedule, naps, light caloric intake       Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory       Etended level I     Controlled for sleep/wake pattern or sleep/wake pattern or sleep duration       Did not control for sleep/wake pattern or sleep duration     Did not control for sleep/wake pattern before and after Ramadan, volunteers slept during daytime and an night before and after Ramadan, the volunteers slept in the morning after eating a main meal Naps were not controlled for 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       Participants were outsed used in the study had relative weakenings     Did not account for the prior sleep/wake pattern before assessing sleep		Location: Morocco	-		recording started at 23.30	sleen time
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were according to a fixed schedule and composition     ttended level 1   Controlled for sleep schedule, naps, and caloric intake     oratory PSG   Did not objectively account for the prior sleep/wake pattern before assessing sleep in the laboratory     tended level 1   Controlled for sleep schedule, naps, light exposure, caloric intake, and energy exposure, caloric intake, and energy exposure, caloric intake, and energy expenditure     Assessed the effect of fasting during and outside Ramadan   Controlled for sleep/wake and naps for laboratory via actigraphy     ble PSG   Unattended PSG   Unattended PSG     Did not control of or sleep/wake and naps for advitine and at night before and after Ramadan   2 weeks before assessing sleep in the laboratory via actigraphy     Did not control of for sleep/wake and naps for ble PSG   Did not control for sleep/wake and naps for laboratory via actigraphy     Did not control of for sleep/wake and after Ramadan   During Ramadan, volunteers slept in the morning after eating daytime and at night before and after Ramadan     Did not account for the prior sleep/wake patter before assessing sleep in the patter before assessing sleep in the patter before assessing sleep in the patter before and atter or sleep/wake     Did not account for the prior sleep/wake patter before and atter or ble portable device used in the study had relative wealchess at the level of the number of awakenings					Meals during and outside Ramadan	
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Intermittent fasting, sleep, and circadian rhythm

alertness. Table 4 summarizes the studies that have assessed daytime sleepiness during diurnal IF in Ramadan.

### Subjective assessment

Studies that used the Epworth Sleepiness Scale (ESS) score to assess daytime sleepiness reported conflicting results. Some studies reported a significant increase in daytime sleepiness,<sup>21,40</sup> whereas other studies demonstrated no significant changes.<sup>23,30,39,52</sup>

### **Objective** assessment

In three studies, daytime sleepiness was measured objectively using the multiple sleep latency test (MSLT) under controlled conditions.<sup>30,44,51</sup> The first study demonstrated an increase in daytime sleepiness at the 10:00 and 12:00 naps in the last week of Ramadan.<sup>51</sup> However, the study used an unattended polysomnography recording device, which necessitated the end of the test 20 minutes after the beginning of recording regardless of sleep onset.

To avert the above shortcomings, a subsequent study used a standard attended MSLT.<sup>30</sup> This study measured sleep latency, sleep onset latency, or wake efficiency on the first and third weeks of Ramadan and reported no changes compared with baseline measurements.<sup>30</sup> Furthermore, spectral analysis of electroencephalography waves during each nap revealed no difference between Ramadan and baseline.<sup>30</sup> However, the previous studies did not control for the possibility of sleep deprivation on the nights prior to assessing sleep and daytime sleepiness. A recent study aimed to objectively assess the impact of diurnal IF during Ramadan on daytime sleepiness in eight healthy subjects while providing a fixed sleep-wake schedule, fixed caloric intake, controlled light exposure, and objective monitoring of sleep duration for several nights before the assessment of daytime sleepiness.44 The assessment was performed on four occasions using attended MSLT and the ESS. During the first visit (adaptation night), wrist actigraphy was provided before the start of the study to monitor sleep pattern while at home to ensure that they had a fixed sleep-wake pattern. In subsequent visits, daytime sleepiness was measured using MSLT and ESS in the following order: 21 days before Ramadan after 1 week of diurnal IF "baseline fasting," 7 days before Ramadan "nonfasting baseline," on the 24th day of Ramadan, and 14 days after Ramadan "recovery." The study revealed no changes in the ESS across the four study times. In addition, the MSLT measurements revealed no differences in sleep latency among the "nonfasting baseline," "baseline fasting," "Ramadan," and "recovery" time points.

Another study assessed the impact of diurnal IF during Ramadan on drowsiness under controlled conditions with a fixed light/dark exposure, caloric intake, sleep/wake schedule and sleep duration via measuring total blink duration (measured using infrared reflectance (IR) oculography) and the mean reaction time (MRT).<sup>61</sup> The results of this study showed that diurnal intermittent fasting had no impact on drowsiness or vigilance.<sup>61</sup>

CR has been reported to enhance alertness and to upregulate orexin gene expression in animal models.53,54 It has been proposed that mammals, when exposed to a negative energy balance, respond with enhanced alertness to improve their capability to find food.55,56 It has also been shown in animals that orexin (an excitatory neurotransmitter) neurons are important for this adaptive response during fasting.56,57 Moreover, orexin neurons interact closely with the "hypothalamic-pituitary-adrenal" (HPA) axis,58 and stimulation of the sympathetic and HPA tone secondary to fasting may further induce arousal through the orexin system.59 Therefore, a recent study assessed the effects of diurnal IF during the month of Ramadan on plasma orexin while controlling for lifestyle changes that may accompany Ramadan, like sleep duration, bedtime and wake time, energy expenditure, light exposure, and food, in eight healthy young men.<sup>60</sup> The results showed that plasma orexin levels increased during the fasting hours.

### Summary

The impact of diurnal IF on circadian rhythm, sleep, and daytime sleepiness is an exciting topic that deserves future research. Earlier studies have suggested that diurnal IF during Ramadan causes a delay in the circadian rhythm of core body temperature and hormonal secretion. However, more recent studies controlling for lifestyle changes that may influence circadian rhythm showed no effects of diurnal IF on the circadian rhythm.

In free-living, unconstrained environments that do not control for lifestyle changes, studies have revealed abrupt significant delays in bedtime and rise time. Nevertheless, studies that controlled for environmental conditions and sleep–wake pattern revealed no significant changes in sleep architecture, indicating that the earlier reported changes could be secondary to concomitant lifestyle changes rather than the fasting act per se. The only consistent change in all studies that assessed sleep architecture during diurnal IF is a decrease in the amount of REM sleep.

Although earlier subjective studies reported an increase in daytime sleepiness during diurnal IF, subsequent studies that controlled for confounding factors reported no changes.

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28 years)   study with repeated   MRT   MRT increased at the     -28 years)   measures   CFF   beginning of Ramadan     -28 years)   measures   CFF   beginning of Ramadan     : Morocco   All measurements taken at   CFF did not change     6 different times of the day:   09:00, 11:00, 13:00, 16:00,   20:00, and 23:00	Roky et al <sup>26</sup>	10 healthy young	Case crossover	Visual analog scale	Decreased daytime alertness	Controlled for sleep/wake
measures   CFF   beginning of Ramadan     All measurements taken at   CFF did not change     6 different times of the day:   09:00, 11:00, 13:00, 16:00,     20:00, and 23:00   20:00, and 23:00		subjects	study with repeated	MRT	MRT increased at the	pattern
All measurements taken at CFF did not change 6 different times of the day: 09:00, 11:00, 13:00, 16:00, 20:00, and 23:00		(age: 20–28 years)	measures	CFF	beginning of Ramadan	Volunteers slept I hour
		Location: Morocco		All measurements taken at	CFF did not change	less during Ramadan than
				6 different times of the day:		at baseline
				09:00, 11:00, 13:00, 16:00,		Controlled for meal
activity				20:00, and 23:00		composition and physical
						activity

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Table 4 (Continued)					
Study	Study population	Study design	Assessment tool	Findings	Study details
BaHammam et al <sup>42</sup>	l 6 fasting and nonfasting subjects 8 fasting (age: 36.25±4.46 years) 8 nonfasting (age: 34.75±3.33 years) Location: Saudi Arabia	Case-control with repeated measures	Johns Drowsiness Scale to assess sleepiness Visual reaction time test ESS	No decrease in alertness No change in daytime sleepiness	Assessed sleep duration objectively using the SenseWear Pro Armband <sup>TM</sup> . There was a significant reduction in sleep duration during Ramadan in the fasting group Assessment was conducted in an unconstrained environment
BaHammam et al <sup>61</sup>	8 healthy young male subjects (age: 25.3±2.9 years) Location: Saudi Arabia	Case crossover study with repeated measures	Johns Drowsiness Scale IR for total blink 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 <sup>43</sup>	I I young healthy trained cyclists (age: 21.6±4.8 years) Location: Qatar	Case crossover study with repeated measures	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 during and after Ramadan compared with baseline; in the last week of Ramadan, accuracy was highest at the end of the day	Sleep duration was not assessed during the 24 hours Tests were conducted at different times during and outside Ramadan
Roky et al <sup>s I</sup>	8 healthy young subjects (age: 20–28 years) Location: Morocco	Case crossover study with repeated measures	Portable MSLT Visual analog scale	Increase in daytime sleepiness Subjective alertness decreased at 12:00 on day I I of Ramadan but did not change on day 25 On the MSLT, sleep latency was decreased on day 11 and day 25 of Ramadan	Portable device used; programmed to end test after 20 minutes of recording Sleep duration was significantly lower during Ramadan than at baseline Meals during baseline and Ramadan followed a fixed schedule and composition Did not rule out possible sleep deprivation in nights prior to study
					(Continued)

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Junio	Study population	Study design	Assessment tool	Findings	Study details
BaHammam et al <sup>30</sup>	8 healthy young	Case crossover	ESS and standard MSLT	No change in daytime	Did not rule out possible
	subjects	study with repeated		sleepiness	sleep deprivation in nights
	(age: 31.8±2 years)	measures			prior to study
	Location: Saudi Arabia				MSLT was preceded by
					an overnight in bhomfory
RaHammam at a <sup>144</sup>	8 healthy vound		ESS and standard MSI T	No change in davtime	Slaaninges was assessed
	o reducty young				
	subjects	study with repeated	Actigraphy to assess sleep	sleepiness during Islamic	while the volunteers were
	(age: 26.6±4.9 years)	measures	duration in days prior to	intermittent fasting	performing intermittent
	Location: Saudi Arabia		the study		fasting during and outside
					Ramadan
					Controlled for sleep
					duration in nights prior to
					study and when at home
					by objective measurements
					(actigraphy)
Tian et al <sup>62</sup>	18 male athletes	Case crossover	Computerized	Performance in functions	Standardized meals were
	(age: 17–29 years)	study with repeated	neuropsychological testing	requiring sustained rapid	provided
	Location: Singapore	measures		responses was best in the	Participants' lifestyle
				morning and declined in the	and training in-between
				late afternoon	test sessions were not
				Performance in nonspeed-	controlled for
				dependent accuracy	Sleep duration was
				measures was more resilient	significantly shorter during
					Ramadan than at baseline
					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 hours

Larger studies that control for potential confounding factors, such as environmental and cultural conditions (the delay in the start of work and school, light exposure, exercise, and meal composition), are warranted to assess the impact of diurnal IF on circadian rhythms, sleep, and daytime sleepiness.

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### Disclosure

The authors report no conflicts of interest in this work.

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