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The Relationship Between Chrononutrition, Eating Behaviour, Obesity and Metabolic Health

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Abstract

There is evidence of the impact of chrononutrition on weight loss and metabolic control. However, the precise chrononutrition behaviours that promote these benefits are not fully described, and there are doubts if eating behaviour may be one of the factors affected by chrononutrition. The main aim was to evaluate the interactions between chrononutrition and eating behaviour, and their relationships with anthropometric and biochemical parameters among obese patients elected for bariatric surgery.

Eighty participants (76.3% females, mean age of 45 years, mean BMI of 41,6 kg/m^2) attending bariatric surgery consultations at Centro Hospitalar Universitário de São João were assessed regarding chrononutrition (Chrononutrition Profile – Questionnaire) and eating behaviour (Three-Factor Eating Questionnaire - R21 and General Eating Self-Efficacy Scale). Height, weight, waist circumference and biochemical values (total, HDL and LDL cholesterol, triglycerides and glycated haemoglobin) were collected.

Eating window midpoint was positively correlated with uncontrolled eating and negatively with eating self-efficacy. Sleep duration and midpoint at free days negatively correlated with self-efficacy, mainly due to later waking times, supporting that predominantly later energy consumption may negatively impact eating behaviour.

Keywords: Chrononutrition; eating behaviour; eating misalignment; eating window; Chrononutrition Profile – Questionnaire; Three-Factor Eating Questionnaire – R21; General Eating Self-Efficacy Scale

Resumo

Há evidência de impacto da crononutrição na perda de peso e controle metabólico, porém os fatores da crononutrição mais preponderantes para se obterem estes benefícios não estão totalmente descritos e existem dúvidas se o comportamento alimentar pode ser um dos fatores afetados pela crononutrição. O objetivo principal foi avaliar as interações entre crononutrição e comportamento alimentar e suas relações com parâmetros antropométricos e bioquímicos em obesos eleitos para cirurgia bariátrica.

Foram avaliados 80 participantes (76,3% do sexo feminino, idade média de 45 anos e IMC médio de 41,6 kg/m^2) que frequentavam consultas de cirurgia bariátrica no Centro Hospitalar Universitário de São João relativamente à crononutrição (*Chrononutrition Profile – Questionnaire*) e comportamento alimentar (Questionário de Três Fatores do Comportamento Alimentar – R21 e Escala de Auto-Eficácia Alimentar Global). Foram coletados altura, peso, perímetro da cintura e valores bioquímicos: (colesterol total, HDL e LDL, triglicerídeos e hemoglobina glicada).

O ponto médio da janela alimentar associou-se positivamente com o descontrolo alimentar e negativamente com a autoeficácia alimentar. A duração e ponto médio do sono nos dias livres correlacionaram-se negativamente com a autoeficácia alimentar, principalmente devido a horários de acordar mais tardios, suportando que o padrão de ingestão energética predominantemente tardio pode afetar negativamente o comportamento alimentar.

Palavras-Chave: Crononutrição; comportamento alimentar; janela alimentar; Chrononutrition Profile – Questionnaire; Questionário de Três Fatores do Comportamento Alimentar – R21; Escala de Auto-Eficácia Alimentar Global

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Abbreviations

BMI	Body Mass Index
GESES	General Eating Self-Efficacy Scale
GLP-1	Glucagon-like Peptide-1
HbA1c	Glycated Haemoglobin
HDL	High Density Lipoprotein
LDL	Low Density Lipoprotein
PYY	Peptide Tyrosine Tyrosine
T3	Triiodothyronine
T4	Thyroxine
TFEQ-R21	Three-Factor Eating Questionnaire-R21
WC	Waist Circumference

Introduction and Aims

In the past decades we witnessed a marked evolution on our knowledge on circadian cycle and how it affects several metabolic and physiologic processes besides the sleep/awake cycle[1]. In fact, some hormonal, metabolic and physiologic processes follow a rhythmical cycle lasting approximately 24 hours that are regulated by the circadian clock systems through transcription and translation negative feedback loops of core clock genes[2]. The circadian system is a highly specialized, hierarchical and coordinated network of biological pacemakers controlled by molecular clocks that can be divided in two layers: the "central" circadian clock, placed in the suprachiasmatic nuclei of the hypothalamus, which works as an orchestra conductor, receiving signals from the environment through an input pathway and which subsequently generates rhythm through output pathways to the second layer - the peripheral clocks - placed in several tissues and organs, like brain, liver, and skeletal muscle[2, 3], controlling several metabolic, physiological, and behavioural processes[1, 4, 5].

Although the circadian cycle has self-regulation mechanisms through feedback loops[2], environmental cues have an important impact on this system's synchronization. Light is pointed to be the main external cue to provide temporal information, but food composition and consumption timing are also factors that impact the synchronization of circadian rhythmicity[6]. Therefore, not only the circadian rhythm impacts the response to food consumption, through the circadian variations of metabolic processes that determine the appropriate moment, amount and source of energy consumption, but the food consumption also impacts the circadian rhythm, because it can disrupt the synchrony of this system[4, 7, 8]. Thus, it is possible to identify an

interdependence between food consumption and the circadian rhythm, and this relationship is the foundation of the chrononutrition concept[4, 5, 9].

This interrelationship between food consumption and circadian rhythm influences many genes involved in the control of glucose and lipid metabolism. For example, the expression of the glycogen synthase 2, the rate-limiting enzyme for glycogenesis, is controlled by core clock component CLOCK, which directly binds to its promoter and drives its rhythmic activity[10]. A similar process occurs with lipogenesis, with Rev-erba/b, the main repressor of the core clock component BMAL1, repressing lipogenic genes involved in the process of converting glucose to fatty acids and triglyceride storage during the active phase[11]. Given these recent developments on our knowledge about the interdependence between food consumption and the circadian rhythm, it was speculated that optimizing nutrition in terms of its circadian domain could be an additional tool to control metabolic disruptions and obesity. Although chrononutrition is a relatively recent concept on the literature, the effects of meal timing or distribution have been object of study for a long time. In fact, back in 2003, Yunsheng Ma and colleagues found an association between breakfast skipping and an increased prevalence of obesity (OR = 4.5, 95% CI: 1.57, 12.90)[12]. Through the years other associations between chrononutrition and health outcomes were found, namely for obesity[1, 6, 13, 14], metabolic syndrome[6, 15], type 2 diabetes[5, 14, 16] and dyslipidaemia[15, 17]; however, these associations were not consistent throughout all studies[18, 19].

In 2013, Jakubowicz and colleagues conducted a controlled randomized trial that compared the weight loss of 93 overweight and obese women with metabolic syndrome submitted to isoenergetic diets (1400 kcal), but with different energy

distribution (high energy intake during breakfast or high energy intake at dinner) for 12 weeks[20]. Interestingly, they found that the group consuming most of the energy at breakfast and lunch lost significantly more weight and waist circumference, and although fasting glucose, insulin and ghrelin were reduced in both groups, fasting glucose, insulin, and HOMA-IR decreased significantly to a greater extent in the group that consumed less energy at dinner. This group also presented decreased triglyceride levels and better results in oral glucose test.

These results suggest that chrononutrition may be a relevant complementary measure to the dietary treatment of obesity and metabolic syndrome. However, the main barrier was, and still is, to identify the behaviours most affecting weight loss and metabolic control. In a pursuit to find the most preponderant chrononutrition behaviours and preferences that contribute to weight gain and metabolic disturbance, and how they are connected to eating behaviour we conducted this study analysing the chrononutrition and eating behaviours on a group of overweight and obese patients elected to bariatric surgery. Our main aims are: 1) to understand how chrononutrition preferences, behaviours and misalignments interact with eating behaviour dimensions; 2) to investigate the relationships between these chrononutrition features and anthropometric and biochemical values; and 3) to prospect the relevance of chrononutrition as a relevant factor in the nutritional therapy of obesity and metabolic disturbances in bariatric surgery patients.

Methods

This study assessed a convenience sample patients attending bariatric surgery consultations at Centro Hospitalar Universitário de São João, E.P.E. All study procedures, methods and instruments were approved by the Comissão de Ética do Centro Hospitalar Universitário de São João (CHUSJ) / Faculdade de Medicina da Universidade do Porto (FMUP) and by the Encarregado de Proteção de Dados (EPD) responsible for the complying of the Regulamento Geral de Proteção de Dados (RGPD).

Sample and procedures

The following inclusion criteria were used to select the patients eligible for surgery: 1) age between 18 and 65 years; 2) body mass index (BMI) ≥ 40 kg/m^2 or BMI ≥ 35 kg/m2 with at least one of the following comorbidities: a) type 2 diabetes mellitus; b) dyslipidaemia; c) obstructive sleep apnea syndrome; d) obese hypoventilation syndrome; e) arterial hypertension (especially if difficult to control); f) osteoarticular degenerative pathology, with marked functional limitation; 3) failure of non-surgical measures to reduce weight for at least one year; 4) obesity that was not secondary to an classic endocrine diseases; 5) ability to understand the surgical procedure and to adhere to a long-term follow-up program; 6) absence of psychiatric disturbances; 7) absence of alcohol or drug addiction [21]. Additionally, patients who had been pregnant in last 2 years, who travelled across places with two different time zones, work in shifts, are illiterate, had abnormal thyroid, liver or kidney function, cardiovascular disease, cancer or any mental disturbance were excluded from the sample.

Weight, height and waist circumference were recorded during the first multidisciplinary consultation, before any nutritional intervention. Weight was measured using a InBody27 scale, height was measured using a Tanita WB-3000 scale and waist circumference was measured by the standards of The International Society for the Advancement of Kinanthropometry (ISAK). Haemoglobin A1c, triglycerides and total, HDL and LDL cholesterol values were retrieved from the patients clinical records. All biochemical values were collected within the six months before the first multidisciplinary consultation.

Instruments

The Chrononutrition Profile - Questionnaire[22] was used to assess chrononutrition. It is an 18-question questionnaire designed to measure general chrononutrition patterns on typical work/school and free days which allows to calculate chrononutrition preferences and behaviours, eating misalignments (*i.e.*, differences between chrononutrition preferences and behaviours) and circadian misalignments (differences between timing on work versus free days). This tool also allows to calculate, for both school/working and free days: morning latency (time between wake up time and first eating event), lunch latency (time between first eating event and lunch), afternoon latency (time between lunch and dinner, night latency (time last eating event and between sleep), sleep duration, sleep midpoint (halfway point between fall asleep time and wake up time) and eating window (time between first and last eating events of the day). In order to access circadian misalignment, the differences between working and free days for all these chrononutrition features were calculated. Finally, we calculated the misalignments for sleep duration, sleep midpoint,

eating window, eating midpoint, morning latency and evening latency, through the discrepancies between chrononutrition preferences and behaviours (*e.g.*, preferred sleep duration - actual sleep duration). Eating misalignment was defined based on a secondary analysis of the CP-Q [23], where eating alignment was considered as having an eating window within 60 min of one's preferred eating window.

Self-efficacy allows to evaluate the beliefs in the ability to organize and put into practice the action plans necessary to achieve a certain result and a feeling of control over behaviour and the environment. To measure eating self-efficacy we used the General Eating Self-Efficacy Scale (GESES)[24], validated to the Portuguese population. This scale presents five items evaluated on a Likert-type scale rated from 1 to 5, with 1 corresponding to "I do not agree" and 5 to "I strongly agree". The scoring of each item was between 0 and 4 points resulting in an overall score ranging from 0 to 20 points, where higher scores indicate higher eating self-efficacy.

To assess eating behaviour, a version of Three-Factor Eating Questionnaire-R21 (TFEQ-R21)[25] validated to the Portuguese population was applied. This instrument allows to assess three eating behaviour dimensions: cognitive restraint (6 items), emotional eating (6 items) and uncontrolled eating (9 items). It consists of 20 items in a four-point Likert scale and one on an eight-point numeric scale. Responses to each of the items are given a score between 1 and 4. Before calculating domain scores, items 1–16 were reverse coded, and item 21 was recoded as follows: 1–2 scores as 1; 3–4 as 2; 5–6 as 3; 7–8 as 4. Higher scores in each subscale correspond to higher levels in the respective dimension.

Statistical Analysis

Statistical analysis was performed on IBM SPSS version 29.0 for Windows. Descriptive statistics consisted on absolute (n) and relative (%) frequencies, means and standard deviations (SD), and medians and percentiles (P25; P75). Normality was assessed using Kolmogorov-Smirnov's test. Spearman's correlation coefficient (r_s) was used to measure the association between pairs of variables. The null hypothesis was rejected when $p < 0.05$.

Results

Sample characterization

The final sample consisted on 80 participants, 76.3% females (n = 61), with a mean age of 45 years (SD = 11), mean BMI of 41.6 kg/m^2 (SD = 4,3), mean waist circumference 120 cm (SD = 12) for women and 131 cm (SD = 12) for men and mean waist circumference:height ratio of 0.76 (SD = 0.08). Participants were recruited from bariatric surgery consultations of Centro Hospitalar Universitário de São João, E.P.E.

Regarding biochemical values, the sample presented median HbA1c of 5.5% (P25; P75 = 5.3; 6.0), mean total cholesterol of 190 mg/dL (SD = 35), mean LDL of 112 mg/dL (SD = 30), median triglycerides of 112 mg/dL (P25; P75 = 79.5; 162.5) and median HDL of 47 mg/dL (P25; P75 = 38; 50) for men and 50 mg/dL (P25; P75 = 46; 66) for women.

Regarding eating behaviour, participants had a median score of 35.2 (P25; P75 = 22.2; 59.3) for uncontrolled eating, 55.6 (P25; P75 = 44.4; 66.7) for cognitive restrain, 36.1 (P25; P75 = 16.7; 72.2) for emotional eating and 10.0 (P25; P75 = 7.0; 12.0) for eating self-efficacy.

Table 1 presents the characterization of the sample in terms of chrononutrition preferences, behaviours and misalignments.

Table 1 - Chrononutrition preferences, behaviours and misalignments

	Median (P25;P75)
Preferred sleep duration	10.0 (9.0; 11.0)
Preferred sleep midpoint	4.0 (3.5; 4.5)
Preferred morning latency	0.5 (0.5; 1)
Preferred night latency	2.0 (1.5; 3.0)
Preferred eating window	11.2 (10.0; 12.0)
Preferred eating window midpoint	15.2 (14.8; 16.0)
Sleep duration working days	8.0 (7.5; 8.9)
Sleep midpoint working days	3.4 (2.8; 4.0)
Morning latency working days	0.9 (0.5; 1.9)
Lunch latency working days	5.5 (4.5; 6)
Afternoon latency working days	7.8 (7.1; 8.4)
Night latency working days	2.5 (2.0; 3.0)
Sleep duration free days	9.0 (8.0; 10.0)
Sleep midpoint free days	4.0 (3.5; 5.0)
Morning latency free days	1.0 (0.5; 1.5)
Lunch latency free days	4.5 (3.5; 5.4)
Afternoon latency free days	7.5 (7.0; 8.0)
Night latency free days	2.5 (2.0; 3.5)
Difference sleep duration working – free days	-1.0 (-2.0; 0.0)
Difference night latency working – free days	0.0 (-0.5; 0.0)
Mean sleep duration	8.2 (7.7; 9.0)
Mean sleep midpoint	3.5 (3.0; 4.0)
Mena morning latency	1.0 (0.5; 1.8)
Mean night latency	2.5 (2.0; 3.0)
Mean eating window	11.9 (11.2; 13.0)
Mean eating window midpoint	14.8 (14.3; 15.4)

Chrononutrition and eating behaviour

Most of chrononutrition elements were not significantly associated with eating behaviour (Table 2). Nevertheless, we found a significant positive association between lunch latency at free days and GESES values (r_s = 0.410, p < 0.001). Then this correlation was calculated controlling for lunch time differences between working and free days (partial r_s = 0.388, p < 0.001), and we found that these two correlations were not significantly different from each other (p = 0.873). It was also noticed that higher GESES scores were associated with lower differences between lunch latencies on working and free days (r_s = -0.309, p = 0.005).

Lower differences between afternoon latencies on working and free days were also correlated with GESES (r_s = -0.272, p = 0.015). This correlation was calculated controlling for the average lunch time (partial r_s = -0.268, p = 0.017), and we found that these two correlations were not significantly different from each other (p = 0.976).

The mean weekly sleep duration was significantly correlated with GESES scores (r_s = -0.278, p = 0.013), although this correlation was significant at free days (r_s = -0.410, p < 0.001) but not at working days (r_s = -0.179, p = 0.113). The correlations between GESES scores and sleep duration controlling for the wake-up time for working and free days (partial r_s = -0.097, p = 0.397 and partial r_s = -0.150, p = 0.186, respectively) were not significant.

Table 2 - Associations between chrononutrition and eating behaviour

	TFEQ_UE	TFEQ_CR	TFEQ_EE	GESES
	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep duration working days	-0.058 (0.608)	0.016 (0.891)	-0.018 (0.871)	-0.179 (0.113)
Sleep midpoint working days	0.178 (0.114)	0.019 (0.869)	0.160 (0.157)	-0.117 (0.300)
Morning latency working days	-0.051 (0.652)	-0.047 (0.679)	-0.018 (0.873)	0.008 (0.946)
Lunch latency working days	-0.078 (0.490)	0.070 (0.536)	-0.090 (0.426)	0.212 (0.058)
Afternoon latency working days	0.185 (0.101)	-0.050 (0.658)	0.165 (0.143)	-0.200 (0.075)
Night latency working days	-0.087 (0.442)	-0.034 (0.763)	0.006 (0.958)	0.138 (0.221)
Sleep duration free days	0.154 (0.172)	-0.058 (0.612)	0.100 (0.376)	**-0.410 (<0.001)**
Sleep midpoint free days	0.16 (0.156)	-0.202 (0.073)	0.027 (0.811)	**-0.303 (0.006)**
Morning latency free days	0.004 (0.975)	-0.042 (0.714)	0.032 (0.78)	0.054 (0.636)
Lunch latency free days	-0.145 (0.201)	0.163 (0.149)	-0.053 (0.64)	**0.410 (<0.001)**
Afternoon latency free days	-0.129 (0.255)	-0.031 (0.783)	-0.025 (0.828)	0.013 (0.908)
Night latency free days	-0.129 (0.255)	-0.031 (0.783)	-0.025 (0.828)	0.013 (0.908)
Difference sleep duration working - free days	-0.187 (0.096)	0.101 (0.374)	-0.092 (0.415)	**0.303 (0.006)**
Difference sleep midpoint working - free days	-0.099 (0.381)	**0.263 (0.018)**	0.084 (0.456)	**0.341 (0.002)**
Difference morning latency working - free days	-0.040 (0.727)	-0.075 (0.511)	-0.06 (0.598)	-0.099 (0.384)
Difference lunch latency working - free days	0.121 (0.284)	-0.181 (0.109)	-0.02 (0.861)	**-0.309 (0.005)**
Difference afternoon latency working - free days	0.062 (0.585)	-0.103 (0.363)	0.108 (0.340)	**-0.272 (0.015)**
Difference night latency working - free days	0.038 (0.739)	0.107 (0.346)	0.019 (0.870)	0.186 (0.099)
Mean sleep duration	0.009 (0.936)	0.002 (0.986)	0.002 (0.989)	**-0.278 (0.013)**
Mean sleep midpoint	0.195 (0.083)	-0.06 (0.595)	0.131 (0.246)	-0.199 (0.078)
Mena morning latency	-0.061 (0.588)	-0.074 (0.517)	-0.052 (0.648)	0.045 (0.692)
Mean night latency	-0.108 (0.341)	-0.022 (0.848)	-0.016 (0.888)	0.126 (0.264)
Mean eating window	0.102 (0.367)	0.102 (0.37)	0.038 (0.737)	0.046 (0.683)
Mean eating window midpoint	**0.275 (0.014)**	-0.180 (0.11)	0.187 (0.098)	**-0.278 (0.012)**

GESES – General Eating Self-Efficacy Scale; TFEQ-UE – Uncontrolled eating; TFEQ-CR – Cognitive restrain; TFEQ-EE –emotional eating

The mean eating window midpoint had a positive correlation with uncontrolled eating (r_s = 0.275, p = 0.014) and a negative correlation with eating self-efficacy (r_s = -0.278, p = 0.012). There were also positive correlations between

uncontrolled eating and late-night snacking (r_s = 0.165, p = 0.018), and between uncontrolled eating and waking up to eat (r_s = 0.313, p = 0.005; Table 3).

Table 3 - Associations between eating behaviour and chrononutrition behaviours

	Consuming breakfast	Biggest meal	Late night snack	Wake up to eat
	r_s (p)	r_s (p)	r_s (p)	r_s (p)
TFEQ_UE	0.053 (0.643)	0.190 (0.092)	**0.265 (0.018)**	**0.313 (0.005)**
TFEQ_CR	0.123 (0.278)	-0.196 (0.081)	-0.090 (0.425)	-0.049 (0.667)
TFEQ_EE	0.071 (0.531)	0.187 (0.096)	0.182 (0.105)	0.118 (0.297)
GESES	-0.026 (0.817)	-0.131 (0.246)	-0.035 (0.758)	-0.144 (0.202)

GESES – General Eating Self-Efficacy Scale; TFEQ-UE – Uncontrolled eating; TFEQ-CR – Cognitive restrain; TFEQ-EE –emotional eating

There was no association between eating window or other eating misalignment variables (Table 4) and uncontrolled eating, cognitive restraint, emotional eating or eating self-efficacy.

Table 4 - Associations between eating behaviour and chrononutrition misalignments

	TFEQ_UE	TFEQ_CR	TFEQ_EE	GESES
	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep duration misalignment	0.087 (0.444)	-0.180 (0.111)	0.139 (0.218)	-0.15 (0.185)
Sleep midpoint misalignment	-0.097 (0.392)	-0.055 (0.625)	-0.088 (0.439)	-0.031 (0.787)
Morning latency misalignment	0.005 (0.966)	-0.003 (0.979)	-0.036 (0.749)	0.007 (0.95)
Evening latency misalignment	-0.072 (0.525)	0.022 (0.847)	-0.079 (0.487)	0.074 (0.514)
Eating window misalignment	0.033 (0.774)	0.059 (0.605)	-0.009 (0.94)	0.076 (0.503)
Eating midpoint misalignment	-0.067 (0.552)	0.001 (0.991)	-0.073 (0.519)	0.045 (0.694)

GESES – General Eating Self-Efficacy Scale; TFEQ-UE – Uncontrolled eating; TFEQ-CR – Cognitive restrain; TFEQ-EE –emotional eating

Chrononutrition and biochemical and anthropometric values

Tables 5 to 8 present the relationships between chrononutrition and biochemical values and anthropometric data. There was a negative correlation between morning latency and total cholesterol (r_s = -0.283, p = 0.011), but not with other lipid profile markers. It was also found a positive correlation between evening latency at free days and LDL cholesterol (r_s = 0.222, p = 0.048).

A positive relation between haemoglobin A1c and the difference between working and free days sleep midpoints was found (r_s = 0.268, p = 0.016). Then we calculated this correlation adjusted for waking time (partial r_s = 0.172, p = 0.130), but we found that these two correlations were not significantly different (p = 0.529). Haemoglobin A1c was also correlated with the difference between working and free days lunch latencies (r_s = -0.262, p = 0.019).

Table 5 - Associations between biochemical values and chrononutrition

	Total Cholesterol	HDL Cholesterol		LDL Cholesterol	Triglycerides	HbA1c
		Male	Female			
	r_s (p)	r_s (p)	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep duration working days	-0.027 (0.809)	-0.093 (0.704)	-0.012 (0.927)	-0.050 (0.66)	-0.043 (0.702)	0.029 (0.796)
Sleep midpoint working days	0.054 (0.634)	0.097 (0.692)	-0.131 (0.313)	0.014 (0.903)	0.042 (0.712)	0.015 (0.896)
Morning latency working days	-0.024 (0.829)	0.175 (0.474)	0.037 (0.779)	0.003 (0.980)	-0.071 (0.531)	0.099 (0.384)
Lunch latency working days	-0.033 (0.77)	0.148 (0.544)	0.071 (0.585)	-0.026 (0.820)	0.043 (0.704)	0.011 (0.926)
Afternoon latency working days	-0.064 (0.573)	-0.084 (0.734)	0.044 (0.738)	-0.07 (0.536)	-0.031 (0.788)	-0.088 (0.439)
Night latency working days	0.13 (0.251)	-0.148 (0.546)	-0.063 (0.632)	0.180 (0.110)	-0.076 (0.505)	0.074 (0.515)
Sleep duration free days	0.034 (0.762)	0.215 (0.377)	-0.031 (0.812)	-0.018 (0.876)	0.021 (0.856)	-0.118 (0.299)

	Total Cholesterol	HDL Cholesterol		LDL Cholesterol	Triglycerides	HbA1c
		Male	Female			
	r_s (p)	r_s (p)	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep midpoint free days	0.191 (0.089)	0.119 (0.627)	-0.041 (0.756)	0.17 (0.131)	0.111 (0.329)	-0.191 (0.089)
Morning latency free days	**-0.283 (0.011)**	0.032 (0.896)	-0.053 (0.683)	-0.217 (0.053)	-0.216 (0.054)	-0.043 (0.703)
Lunch latency free days	-0.107 (0.346)	-0.076 (0.756)	0.020 (0.881)	-0.079 (0.487)	-0.066 (0.563)	0.208 (0.064)
Afternoon latency free days	-0.057 (0.614)	-0.045 (0.854)	0.184 (0.155)	-0.111 (0.326)	0.034 (0.767)	-0.198 (0.079)
Night latency free days	0.173 (0.124)	-0.150 (0.541)	-0.075 (0.564)	**0.222 (0.048)**	0.020 (0.860)	0.007 (0.950)
Difference sleep duration working - free days	-0.042 (0.709)	-0.249 (0.305)	0.042 (0.750)	-0.011 (0.923)	-0.037 (0.746)	0.106 (0.348)
Difference sleep midpoint working - free days	-0.144 (0.203)	-0.022 (0.929)	-0.005 (0.972)	-0.143 (0.205)	-0.129 (0.255)	**0.268 (0.016)**
Difference morning latency working - free days	0.175 (0.119)	0.143 (0.558)	-0.024 (0.857)	0.203 (0.072)	0.037 (0.743)	0.121 (0.286)
Difference lunch latency working - free days	0.103 (0.365)	0.148 (0.546)	0.043 (0.741)	0.079 (0.483)	0.118 (0.297)	**-0.262 (0.019)**
Difference afternoon latency working - free days	-0.048 (0.671)	0.164 (0.503)	-0.205 (0.113)	0.005 (0.965)	-0.089 (0.435)	0.139 (0.220)
Difference night latency working - free days	-0.033 (0.773)	0.37 (0.119)	0.109 (0.404)	-0.068 (0.549)	-0.163 (0.148)	0.118 (0.297)
Mean sleep duration	0.006 (0.957)	0.019 (0.938)	-0.037 (0.778)	-0.041 (0.719)	0.000 (0.999)	-0.007 (0.949)
Mean sleep midpoint	0.092 (0.417)	0.081 (0.743)	-0.127 (0.328)	0.052 (0.644)	0.078 (0.489)	-0.047 (0.679)
Mena morning latency	-0.112 (0.321)	0.136 (0.579)	-0.060 (0.644)	-0.068 (0.549)	-0.111 (0.328)	0.074 (0.512)
Mean night latency	0.165 (0.145)	-0.147 (0.547)	-0.066 (0.616)	0.216 (0.054)	-0.035 (0.758)	0.057 (0.615)
Mean eating window	-0.061 (0.588)	-0.143 (0.558)	0.102 (0.435)	-0.106 (0.349)	0.111 (0.328)	-0.081 (0.473)
Mean eating window midpoint	-0.023 (0.841)	0.156 (0.524)	-0.079 (0.544)	-0.014 (0.900)	-0.019 (0.867)	-0.123 (0.276)

Table 6 - Associations between chrononutrition and anthropometric values

	BMI	Waist Circumference		Waist Circumference/Height
		Male	Female	
	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep duration working days	0.051 (0.653)	0.206 (0.397)	0.166 (0.201)	0.167 (0.138)
Sleep midpoint working days	0.087 (0.441)	0.118 (0.630)	-0.019 (0.883)	0.103 (0.364)
Morning latency working days	-0.053 (0.640)	-0.053 (0.831)	-0.022 (0.869)	-0.073 (0.517)
Lunch latency working days	-0.207 (0.066)	-0.33 (0.168)	-0.081 (0.534)	-0.215 (0.055)
Afternoon latency working days	0.069 (0.544)	0.089 (0.718)	0.019 (0.885)	-0.044 (0.700)
Night latency working days	0.047 (0.678)	0.048 (0.846)	-0.137 (0.292)	0.050 (0.659)
Sleep duration free days	0.061 (0.589)	-0.145 (0.554)	-0.063 (0.631)	-0.036 (0.748)
Sleep midpoint free days	0.029 (0.797)	0.004 (0.989)	-0.162 (0.212)	-0.047 (0.681)
Morning latency free days	0.063 (0.580)	0.168 (0.492)	-0.020 (0.877)	-0.002 (0.985)
Lunch latency free days	-0.133 (0.240)	-0.108 (0.660)	0.090 (0.492)	-0.018 (0.872)
Afternoon latency free days	-0.023 (0.837)	0.095 (0.700)	-0.043 (0.741)	-0.072 (0.524)
Night latency free days	0.071 (0.534)	0.048 (0.844)	-0.003 (0.980)	0.088 (0.440)
Difference sleep duration working - free days	-0.048 (0.673)	0.271 (0.261)	0.138 (0.289)	0.125 (0.269)
Difference sleep midpoint working - free days	0.019 (0.870)	0.182 (0.457)	0.161 (0.214)	0.161 (0.155)
Difference morning latency working - free days	-0.020 (0.860)	-0.225 (0.354)	0.042 (0.750)	-0.010 (0.930)
Difference lunch latency working - free days	0.007 (0.953)	-0.212 (0.383)	-0.196 (0.129)	-0.208 (0.064)
Difference afternoon latency working - free days	0.077 (0.498)	-0.092 (0.708)	0.038 (0.770)	0.014 (0.905)
Difference night latency working - free days	-0.027 (0.810)	-0.09 (0.713)	-0.079 (0.545)	0.014 (0.902)
Mean sleep duration	0.074 (0.512)	0.148 (0.547)	0.103 (0.431)	0.133 (0.238)
Mean sleep midpoint	0.087 (0.444)	0.055 (0.823)	-0.079 (0.543)	0.072 (0.525)
Mena morning latency	0.003 (0.981)	0,002 (0,993)	-0,004 (0,978)	-0.035 (0.759)
Mean night latency	0.047 (0.682)	0,04 (0,871)	-0,117 (0,368)	0.047 (0.681)
Mean eating window	-0.128 (0.256)	-0,093 (0,705)	-0,039 (0,763)	-0.153 (0.177)
Mean eating window midpoint	0.069 (0.545)	0.156 (0.523)	-0.044 (0.737)	-0.008 (0.947)

There was no association between eating window or any eating misalignment variables and biochemical or anthropometric values (Tables 7 and 8).

Table 7 - Associations between chrononutrition misalignments and biochemical values

	Total Cholesterol	HDL Cholesterol		LDL Cholesterol	Triglycerides	HbA1c
		Male	Female			
	r_s (p)	r_s (p)	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep duration misalignment	0.017 (0.884)	0.085 (0.730)	0.066 (0.613)	0.051 (0.654)	0.059 (0.605)	-0.164 (0.147)
Sleep midpoint misalignment	0.021 (0.855)	0.008 (0.974)	0.152 (0.242)	0.054 (0.634)	-0.139 (0.220)	0.056 (0.619)
Morning latency misalignment	0.040 (0.723)	0.323 (0.177)	-0.061 (0.640)	0.112 (0.324)	-0.064 (0.574)	-0.131 (0.246)
Evening latency misalignment	0.032 (0.779)	0.067 (0.785)	0.165 (0.204)	0.005 (0.965)	0.084 (0.459)	-0.047 (0.678)
Eating window misalignment	-0.001 (0.994)	-0.149 (0.543)	-0.063 (0.629)	-0.031 (0.788)	0.085 (0.453)	0.023 (0.841)
Eating midpoint misalignment	0.013 (0.911)	-0.037 (0.880)	-0.014 (0,916)	0.048 (0.673)	-0.041 (0.715)	-0.081 (0.477)

Table 8 - Associations between chrononutrition misalignments and anthropometric values

	BMI	Waist Circumference		Waist Circumference/Height
		Male	Female	
	r_s (p)	r_s (p)	r_s (p)	r_s (p)
Sleep duration misalignment	-0.058 (0.612)	0.160 (0.514)	0.083 (0.523)	-0.068 (0.548)
Sleep midpoint misalignment	0.146 (0.195)	-0.267 (0.269)	-0.035 (0.790)	0.125 (0.267)
Morning latency misalignment	-0.166 (0.141)	-0.331 (0.166)	-0.009 (0.946)	-0.158 (0.161)
Evening latency misalignment	-0.044 (0.698)	0.014 (0.955)	0.084 (0.518)	-0.06 (0.596)
Eating window misalignment	-0.071 (0.531)	0.187 (0.444)	-0.087 (0.506)	-0.054 (0.634)
Eating midpoint misalignment	-0.122 (0.281)	-0.431 (0.066)	-0.131 (0.316)	-0.165 (0.144)

Eating behaviour and biochemical and anthropometric values

Uncontrolled eating was positively associated with age (r_s = 0.-317, p = 0.004), BMI (r_s = 0.237, p = 0.034), and waist circumference, but only for men (r_s = 0.571, p = 0.011). Waist circumference was also related to emotional eating (r_s = 0.626, p = 0.004) only for men. In terms of the relationships between eating behaviour and biochemical and anthropometric values, uncontrolled eating presented a positive association with HbA1c (r_s = 0.-430, p < 0.001), and with HDL, but just for men (r_s = -0.566, p = 0.012). Higher eating self-efficacy was weakly correlated with higher HbA1c (r_s = 0.318, p = 0.004).

Table 9 - Associations between eating behaviour and biochemical and anthropometric values

		TFEQ_UE	TFEQ_CR	TFEQ_EE	GESES
		r_s (p)	r_s (p)	r_s (p)	r_s (p)
Age		-0.317 (0.004)	0.172 (0.127)	-0.219 (0.051)	0.207 (0.066)
Waist circumference	**Male**	**0.571 (0.011)**	-0.355 (0.136)	**0.626 (0.004)**	-0.007 (0.977)
	Female	0.019 (0.882)	0.051 (0.694)	0.010 (0.938)	-0.089 (0.494)
Waist circumference /height		0.122 (0.28)	-0.038 (0.740)	0.037 (0.747)	-0.066 (0.560)
IMC		**0.237 (0.034)**	-0.188 (0.096)	0.099 (0.380)	-0.126 (0.264)
Total Cholesterol		0.029 (0.801)	0.015 (0.893)	-0.031 (0.782)	0.06 (0.595)
HDL Cholesterol	**Male**	**-0.566 (0.012)**	0.244 (0.313)	-0.315 (0.188)	0.233 (0.337)
	Female	0.099 (0.450)	-0.110 (0.398)	0.058 (0.659)	-0.024 (0.855)
LDL Cholesterol		-0.051 (0.651)	0.002 (0.983)	-0.048 (0.674)	0.099 (0.383)
Triglycerides		0.044 (0.696)	0.168 (0.137)	-0.093 (0.414)	0.007 (0.950)
HbA1c		**-0.430 (<0.001)**	0.181 (0.108)	**-0.259 (0.020)**	**0.318 (0.004)**

GESES – General Eating Self-Efficacy Scale; TFEQ-UE – Uncontrolled eating; TFEQ-CR – Cognitive restrain; TFEQ-EE –emotional eating

Discussion and Conclusion

In this study we intended to understand how chrononutrition behaviours and preferences interact with eating behaviours of patients elected for bariatric surgery, and how it can be related with their anthropometric, lipid and glucose metabolism values, in order to assess if chrononutrition could be an additional contributor to the nutritional therapy of obesity and metabolic syndrome.

Surprisingly, and unlike most of literature[15, 26] we didn't find any significant relationships between skipping breakfast and BMI, waist circumference, waist circumference:height ratio, glucose metabolism or eating behaviour. Skipping breakfast was also not correlated with most of lipid profile markers, except for triglycerides, with which it presented a week negative correlation.

Some studies also found no relationship between breakfast skipping and fasting measures of glucose, insulin, T3 and T4, leptin, ghrelin, PYY, GLP-1 or adiponectin, and their authors suppose that poorer metabolic health in individuals that skip breakfast may be attributed to other factors, such as changes in appetite, food choice, activity and other behavioural differences[4]. In fact, our results also point in that direction because, despite we didn't find direct relationships between skipping breakfast and health status or eating behaviour, participants with longer sleep durations had less eating self-efficacy, especially at free days. When analysing closely this correlation we noticed that it could be explained by the wake-up time, especially at free days. So, we can assume that those who have later wake-up times at free-days have lower eating self-efficacy. We also found that later eating window midpoints where associated with higher uncontrolled eating and lower eating self-efficacy. Additionally, when analysing why shorter time between breakfast and lunch at

free days were related with less eating self-efficacy, we noticed that the most relevant factor for this relation was the wake-up time. So, like Ruddick-Collins *et al.*[4] suggested, we noticed that participants who wake up later and, consequently, delay energy consumption for later in the day, present lower eating self-efficacy. Plus, Bandin and colleagues reported that constantly having meals delayed could blunt the daily profile of free cortisol variation [27]. Cortisol has a high daily variation, with a peak in the morning, close to wake-up time, and lowering in the evening, close to bedtime, and these cortisol fluctuations contribute to the rhythmicity of the sleep/awake cycle, being that the reason why cortisol fluctuations are used to track circadian cycle[4]. A highly daily fluctuation of cortisol is a sign of a typical diurnal rhythm, as opposed to a lower variability or flattened cortisol rhythmicity that has been related to chronic emotional or physical stress, obesity and metabolic syndrome[27-30]. This blunted daily variability in cortisol may result in a reduction of the circadian signalling to peripheral clocks, because as cortisol's amplitude decreases, cells gradually fall out of synchrony, thus contributing to lower glucose tolerance and oxidation[4, 27]. If this misalignment is maintained for long periods, it may also increase plasma concentrations of pro- and anti-inflammatory proteins[31], contributing to the low-grade inflammation typically present in obesity and metabolic syndrome[32], which retroactively worsens glucose and lipid metabolisms, resulting in a snowball effect that can impair weight loss.

Even though most of the correlations we found are week, they are congruent with other studies that suggest that predominantly later energy intake is associated with worse health outcomes[4, 33-35] and problematic eating behaviours[4], and that eating window *per se* is not the most relevant factor to

optimize metabolic status or weight gain among obese patients. A study conducted by Mazri and colleagues with 299 overweight/obese non-shift workers put light on this topic. They divided the sample into metabolic healthy and unhealthy participants, and both groups showed similar energy and macronutrient intake and eating windows, but metabolic unhealthy participants consumed a lower proportion of energy during the early window (59.0 vs. 63.0%, p = 0.008) and more energy during the late window (37.0 vs. 41.0%, p = 0.008). Additionally, those in the lowest quartile of energy intake (less than 893 kcal) during the early window had a 4 times higher risk of being metabolic unhealthy compared to the those in the highest quartile, after controlling for age, sex, BMI, and total energy intake[33]. In line with these studies, we also found no associations between eating window and biochemical or anthropometric values or eating behaviour, but rather that timing of energy consumption is the most relevant factor in terms of eating behaviour optimisation. We suppose that positively reinforcing the brain reward circuits involved in the hedonic aspects related to food is the main explanation for the benefits of predominantly early energy intake. And although we didn't find associations between earlier energy consumption and improvements on glucose or lipid metabolism or obesity level, it's possible that this strategy improves weight loss efficiency among obese patients, as shown in controlled and randomized trials[20, 36].

We also found some interesting relationships between chrononutrition behaviours and lipid metabolism, namely a positive correlation between night latency and LDL cholesterol. This means thathigher latencies between last meal and sleep are associated with higher levels of LDL cholesterol, unlike our expectations. Our results were different from what *Moon et al.* describe on a

recent systematic review and meta-analysis, that showed no significant associations between LDL cholesterol and fasting duration[37]. We assume that the association found in our work may be related to a process observed in shift-workers that skip breakfast. In their case, skipping breakfast increases the fasting duration, with concomitant prolonged lipolysis activation and increased lipogenesis. This altered not only glucose and lipid metabolism but also gastrointestinal function, leading to reduced availability of nutrients to the brain and likely adverse behavioural outcomes[16]. Despite the differences between samples, these mechanisms could partially explain how longer fasting periods could lead to higher LDL values.

Another interesting finding was reported in the National Health and Nutrition Examination Survey, that analysed cross-sectional data of 15,939 American adults and children, representative of the United States of America population and collected in 2-year cycles. When analysing results for cardiovascular markers, HDL was found to decrease with increased fasting duration, while total and LDL cholesterol increased[17]. Moreover, the analysis of the glucose metabolism markers in that study showed that every one-hour increase in fasting duration was associated with a 7%increase in the odds of abnormal insulin[17], supporting the idea that long fasting periods could be unproductive in improving metabolic health.

Our results also revealed relationships between HbA1c and chrononutrition behaviours, namely a positive correlation with the difference sleep midpoint between working and free days. After controlling for sleeping time at free days, we found that those who sleep later at free days have higher HbA1c values. This correlation probably has a multifactorial explanation, but we assume that when

people go to sleep later at free days, they may also have higher energy intakes later in that day and, as our results show, this is associated with lower eating self-efficacy. Moreover, besides sleeping later, we also observed that people sleep more at free days, and the conjunction of these factors may delay the eating midpoint, which also correlates with lower eating self-efficacy. This eating pattern also contributes to blunting the cortisol rhythmicity (that we already discussed), and is related to lower glucose tolerance, although this late night eating could have a bigger negative impact on glucose metabolism, as a previous study showed when analysing the eating patterns of diabetic patients, concluding that skipping breakfast and late dinner both contribute do higher BMI but only late night eating was associated with poor glycaemic control[26]. Surprisingly, HbA1c was positively correlated with eating self-efficacy and negatively correlated with emotional eating, which seems paradoxical regarding the other results we obtained. Nevertheless, we noticed that night eating and waking up to eat during sleep were positively associated with uncontrolled eating.

As we also emphasis, this relation between HbA1c and chrononutrition is multifactorial, and even if these values are not directly correlated with eating behaviour as we expected, the big picture points to negative impact of later predominant energy consumption on glucose and lipid metabolism as well as on eating behaviour.

the main limitation of this study is the relatively small convenience sample and small proportion of males, which conditions the extrapolation of results. On the other hand, to our knowledge, this is the first study to collect and analyse the interactions between chrononutrition behaviours, preferences and circadian

misalignments with eating behaviour and anthropometric and biochemical values. This analysis contributes to a more extensive comprehension on how chrononutrition may impact the nutritional treatment of obesity and metabolic syndrome.

In summary, our results show that predominantly later energy intake is associated with lower eating self-efficacy and that this pattern of eating may have a negative impact on weight loss and metabolic control. Moreover, shorter eating windows were not related to better behavioural, anthropometric or biochemical values and could even negatively impact metabolic control.

Therefore, chrononutrition behaviours, especially a predominantly earlier energy intake, may be useful as an additional measure in the nutritional therapy of obesity and for optimising glucose and lipid metabolism.

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