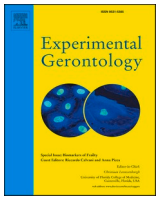
Experimental Gerontology 181 (2023) 112284

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero



Mediterranean diet and chronotype: Data from Italian adults and systematic review of observational studies

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ARTICLE INFO

Keywords:
Mediterranean diet
Diet quality
Chronotype
Morningness
Eveningness

ABSTRACT

Scientific evidence suggests a relation between dietary factors and sleep. Several studies show that higher adherence to the Mediterranean diet is associated with better sleep quality, but the relation with chronotype has been only recently explored. The aim of this study was to better understand the relation between chronotype and Mediterranean diet adherence. For this purpose, an analysis of 1936 adults (age 18–90 y) living in Italy was performed to investigate the association between chronotype (assessed with a short form of the morningness-eveningness questionnaire) and adherence to the Mediterranean diet (assessed through a 110-item food frequency questionnaire and the Medi-Lite literature-based Mediterranean adherence score). A multivariate logistic regression analysis was conducted to calculate odds ratios (OR) and 95 % confidence intervals (CIs) describing the association between chronotypes and high adherence to the Mediterranean diet (>14 points). Moreover, a systematic review of other observational studies published so far was performed. Individuals reporting having intermediate (n = 614) and evening (n = 173) chronotypes were less likely to have high adherence to the Mediterranean diet compared to morning chronotype (OR = 0.28, 95 % CI: 0.18, 0.42 and OR = 0.08, 95 % CI: 0.03, 0.27, respectively). When the analysis was conducted in subgroups of age, the results were similar in mid-age (>50 y) participants (for intermediate and evening chronotypes, OR = 0.21, 95 % CI: 0.10, 0.43 and OR = 0.92, 95 % CI: 0.01, 0.69, respectively) while the association with high adherence to the Mediterranean diet of evening compared to morning chronotype lost significance in older (>60 y) participants (for intermediate and evening chronotypes, OR = 0.27, 95 % CI: 0.09, 0.82 and OR = 0.22, 95 % CI: 0.02, 1.92, respectively). Out of 10 studies (date range of publication 2020–2022) included in the systematic review, there was a general consistence of findings showing higher adherence to the Mediterranean diet among morning chronotypes, although few studies reported null results. In conclusion, current evidence suggests that an intermediate and evening chronotype could be associated with lower adherence to a Mediterranean diet, but the association could be modified by other factors when considering older individuals.

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https://doi.org/10.1016/j.exger.2023.112284
Received 1 February 2023; Received in revised form 6 July 2023; Accepted 3 September 2023
Available online 8 September 2023

1. Introduction

The burden of reduced sleep quality is a leading risk factor for mental health globally, but also a condition occurring along brain disorders. Sleep quality is considered of paramount importance for a healthy living; besides its physiological role for the correct functioning of human brain and physical health, poor sleep quality has also been associated with increased risk of various cardio-metabolic conditions. Moreover, prolonged sleep disturbances are often associated with depressive disorders and might be prodromic to more invalidating conditions, such as age-related cognitive impairment. Nowadays, sleep quality may be affected by a variety of external stimuli, including altered light-dark cycle, excess stress exposure, scarce physical activity and prolonged mental fatigue, all leading to disruption of circadian rhythms (Schurhoff and Toborek, 2023). Such alteration of circadian rhythmicity may characterize the individual preferences for sleeping timing and activity, also referred to as chronotype (Horne and Ostberg, 1976). Specifically, inclination to perform activities in various timing of the day (with consequent opposite trends for sleeping) denotes morning, intermediate, and evening chronotypes (Horne and Ostberg, 1976). The identification of chronotype is of recent interest for the scientific community due to the retrieved association between certain chronotypes (i.e., evening chronotype) and negative health outcomes, including cardiometabolic disorders, certain cancers, and depression (Lotti et al., 2022b).

Overall, there is no univocal determinant of sleep quality and specific sleep features. However, an abnormal activation of the immune system and chronic inflammation seems to play a contributing role in neurodegeneration and consequent deterioration of brain health (Irwin, 2019). The increased production of proinflammatory cytokines and consequent microglia activation may be responsible for the variety of behavioral, neuroendocrine, and neurochemical alterations that are associated with a variety of psychiatric conditions, including potential alteration of sleep quality and circadian rhythms (Irwin and Vitiello, 2019). This may be promoted by external environmental factors (such as the aforementioned above) or in paraphysiological conditions, such as in older individuals, well described in the so-called phenomenon of inflammaging (Gordleeva et al., 2020). In this context, diet has been investigated for potentially influencing the risk of non-communicable diseases through its role in affecting low-grade subclinical inflammatory processes (Grosso et al., 2022b). While there is a general agreement of the effects of dietary risk factors on cardiometabolic disorders and certain cancers, emerging evidence suggest a potential role of diet on mental health (Godos et al., 2020), including sleep features (Godos et al., 2021). Among the most studied dietary patterns, the Mediterranean diet is by far the most investigated concerning the most common non-communicable diseases, while only recently it gathered interest for its possible relation with sleep features and chronotype. The aim of this study was to assess whether there were differences in adherence to the Mediterranean diet and sleep quality across chronotypes in a sample of southern Mediterranean mid-older adults and to systematically revise all the available evidence on the association between adherence to the Mediterranean diet and sleep features, including chronotype.

2. Methods

2.1. Cross-sectional study

2.1.1. Study sample

The sample included in this cross-sectional study is part of the Mediterranean Healthy Eating, Aging, and Lifestyles (MEAL) study, an observational investigation designed to examine the relation between dietary and lifestyle habits common to people in the Mediterranean area. The detailed study protocol, including the rationale, design, and methodologies, has been extensively discussed elsewhere (Grosso et al., 2017). A random sample of men and women (age 18+) registered in the medical records of residential general practitioners in the urban region of Catania, one of the major cities on the east coast of Sicily, southern Italy, constituted the cohort in the years 2014 to 2015. The sampling method involved stratifying the sample by age, sex, and municipality area, then randomly partitioning the sample into subgroups. General practitioners chosen at random served as the sampling units, and those who registered with them formed the final sample units. Pregnant women were not considered in this study. Participants randomly selected for recruitment were stratified by sex and 10-year age groups. The total sample size consisted of 2044 respondents (85 % response rate) out of the 2405 people originally addressed for this study. All the study procedures were carried out in accordance with the Declaration of Helsinki (1989) of the World Medical Association. The study protocol was approved by the Ethical Committee of Catania 2 (protocol code 802/23 December 2014) and participants supplied written informed consent.

2.1.2. Data collection

Data on demographic (i.e., age, sex, educational attainment, and occupation level) and lifestyle (i.e., physical activity, smoking, and drinking habits) aspects were acquired. Educational level was categorized as: (i) low (primary/secondary), (ii) medium (high school), and (iii) high (university). Occupational level was classified as: (i) unemployed, (ii) low (unskilled workers), (iii) medium (partially skilled workers), and (iv) high (skilled workers). Using the International Physical Activity Questionnaires (IPAQs) (Craig et al., 2003), which are a set of questionnaires (5 domains) on time spent being physically active in the previous 7 days, the level of physical activity was evaluated. The IPAQs allow classification of physical activity into three categories: (i) low, (ii) moderate, and (iii) high. Smoking status was divided into: (i) non-smoker, (ii) ex-smoker, and (iii) current smoker. Alcohol consumption was categorized as (i) none, (ii) moderate drinker (0.1–12 g/d) and (iii) regular drinker (>12 g/d).

2.1.3. Dietary assessment

Long and short food frequency questionnaires (FFQs), which were designed and previously standardized for the Sicilian population (Marventano et al., 2016; Buscemi et al., 2015), were used to collect dietary data. The FFQs included 110 food and beverage items representative of the diet during the preceding six months. Research participants were asked how frequently they had averagely consumed the meals and beverages listed in the FFQ, they were given nine options ranging from "never" to "4-5 times per day." Intake of seasonal food items pertained to consumption during the period in which the food was available and then adjusted by its proportional annual intake. A total of 1936 people were included in the analysis for the current study after the exclusion of 107 entries with inconsistent intakes (<1000 or >6000 kcal/d, checked case by case and verified due to missing food items or imprecise answers).

2.1.4. Adherence to the Mediterranean diet

Mediterranean diet adherence was assessed using the score developed by Sofi et al. (Marventano et al., 2018). In brief, three separate categories of intake for each food category were determined by weighing all the median (or mean) values for the sample size of each study population and then computing a mean value of all the weighted medians using a Medi-Lite scoring system defined according to existing literature. To determine that, two standard deviations were used. For Mediterranean food groups (fruit, vegetables, cereals, legumes and fish), two points were given to the highest category of consumption, one point for the middle category and zero points for the lowest category of intake. Conversely, for non-Mediterranean food groups (meat and meat-based products, dairy products), two points were given for the lowest category, one point for the middle category and zero points for the highest category of consumption. Furthermore, the amount of alcohol consumed has been categorized and evaluated based on alcohol units (one alcohol unit = 12 g of alcohol). The categories were established by giving two points to the middle category (1–2 alcohol units/d), one point to the

lowest category (>1 alcohol unit/d) and zero points to the highest category of consumption (>2 alcohol units/d). The nine food categories (including olive oil) considered in the final score, were evaluated from zero points (lowest adherence) to 18 points (highest adherence). Individuals were finally divided into quartiles and those in the highest quartile were considered to have high adherence to the Mediterranean diet (score > 14 points).

2.1.5. Chronotype

Chronotype was assessed through questions resembling the short version of the morningness eveningness questionnaire (MEQ) (Horne and Ostberg, 1976), consisting of a 6-item tool including questions 4, 7, 9, 15, 17, and 19 exploring preferences in timing during the day to perform activities, such as wake up, work, or hard physical tasks (Maukonen et al., 2017). The questions have been tested and reported to account for 83 % of the total variance of the original MEQ (Hätönen et al., 2008). The final score would range from 6 (extreme eveningness) to 27 (extreme morningness), with identification of morning (6–12 points), intermediate (13–18), and evening (19–27) chronotypes.

2.1.6. Statistical analysis

Categorical variables are described as frequencies of occurrence and percentages. Continuous variables are described as means and standard deviations. Differences between groups were estimated using the Chi-square test for categorical variables and the Kruskal–Wallis test for continuous variables, respectively. The association between high adherence to the Mediterranean diet and chronotype was assessed through performing a multivariate logistic regression analysis and calculating odds ratios (ORs) and 95 % confidence intervals (CIs) adjusted for potential confounding factors (including age, sex, educational and occupational status, smoking habits, and physical activity level). Values of $p < 0.05$ were deemed as statistically significant. All analyses were performed using the statistical package IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA).

2.2. Systematic review

2.2.1. Study selection

A systematic search on PubMed/EMBASE for all studies examining the relation between Mediterranean diet and chronotype was performed from their inception up to January 2023. The search strategy was based on the combination of the relevant keywords related to Mediterranean diet and chronotype. The following word combination was used: (chronotype OR morningness OR eveningness OR diurnal OR nocturnal) AND (Mediterranean OR Mediterranean diet OR a priori dietary pattern) without any restrictions. Reference lists of eligible studies were also screened for any additional studies not previously identified. The systematic search and study selection was performed by two independent authors. The design and reporting of this study will follow the Meta-analyses Of Observational Studies in Epidemiology (MOOSE) guidelines.

2.2.2. Inclusion/exclusion criteria

Studies were eligible if they met the following criteria: i) observational studies with a comparison group (cohort studies, cross-sectional studies, case-control studies), ii) adult population (≥18 years old), iii) reported on the relation between adherence to the Mediterranean diet and chronotype features. Studies reporting on: i) pregnant women, and ii) patients with end-stage degenerative diseases were excluded.

2.2.3. Data extraction and risk of bias

Data from all eligible studies were extracted using a standardized electronic form. The following information was extracted: first author name, publication year, study design and location, population age and gender, sample size, details on the assessment method and adherence to the Mediterranean diet, details of the assessment method, details on the assessment method of the outcome of interest, and main findings of the study. The risk of bias of each study was assessed according to the Newcastle-Ottawa Quality Assessment Scale, which consists of three constructs of quality, such as selection (4 points), comparability (2 points), and outcome (3 points), with a total score of 9 points (9 representing the highest quality). Studies scoring 7–9 points, 3–6 points, and 0–3 points were identified as low, moderate, and high risk of bias, respectively.

3. Results

3.1. Cross-sectional study

3.1.1. Study population

A total of 1149 individuals (59.3 %) resulted in having morning chronotype, 614 (31.7 %) had intermediate chronotype, and 173 (8.9 %) had evening chronotype. The distribution of the main background characteristics by chronotype is presented in Table 1. There were no substantial significant differences in background characteristics across chronotypes, with exception for sex (with higher proportion of women among morning and intermediate types; $p = 0.047$) and age (older mean age among morning type; $p = 0.005$).

3.1.2. Mediterranean diet and chronotype

The mean values of the score assessing the adherence to the Mediterranean diet by chronotypes are presented in Fig. 1. Individuals having morning chronotype had significantly higher adherence to the Mediterranean diet compared to intermediate and evening subjects (12.8 ± 2.0 vs. 11.3 ± 2.1 vs. 9.8 ± 3.1, respectively; $p < 0.001$). (See Fig. 1)

The analysis of the optimal responses (i.e., the choice that provided

Table 1
Demographic characteristics of the study participants according to chronotype ($n = 1936$).

	Morning type ($n = 1149$)	Intermediate type ($n = 614$)	Evening type ($n = 173$)	P-value
Age, mean (SD)	49.5 (17.6)	46.8 (17.6)	47.6 (17.5)	0.009
Sex, n (%)				0.047
Men	464 (40.4)	253 (41.2)	87 (50.3)	
Women	685 (59.6)	361 (58.8)	86 (49.7)	
Smoking status, n (%)				0.361
Never	728 (63.4)	362 (59.0)	105 (60.7)	
Current	260 (22.6)	164 (26.7)	41 (23.7)	
Former	161 (14.0)	88 (14.3)	27 (15.6)	
Educational level, n (%)				0.857
Low	415 (36.1)	221 (36.0)	61 (35.3)	
Medium	436 (37.9)	220 (35.8)	64 (37.0)	
High	298 (25.9)	173 (28.2)	48 (27.7)	
Occupational level, n (%)				0.113
Unemployed	274 (28.1)	155 (29.2)	32 (20.8)	
Low	160 (16.4)	79 (14.9)	27 (17.5)	
Medium	266 (27.3)	124 (23.4)	50 (32.5)	
High	274 (28.1)	172 (32.5)	45 (29.2)	
Physical activity level, n (%)				0.197
Low	193 (19.0)	109 (19.6)	27 (17.1)	
Medium	483 (47.6)	284 (51.1)	89 (56.3)	
High	338 (33.3)	163 (29.3)	42 (26.6)	
BMI status, n (%)				0.280
Normal	499 (46.5)	275 (48.1)	77 (50.2)	
Overweight	392 (36.5)	195 (34.1)	43 (28.1)	
Obese	182 (17.0)	102 (17.8)	33 (21.6)	
Health status, n (%)				
Hypertension	581 (50.6)	300 (48.9)	95 (54.9)	0.367
Type-2 diabetes	92 (8.0)	45 (7.5)	9 (5.2)	0.416
Dislipidemias	224 (19.5)	96 (15.6)	36 (20.8)	0.095
Cardiovascular disease	90 (8.0)	45 (7.5)	19 (11.1)	0.312
Cancer	48 (4.2)	21 (3.4)	9 (5.2)	0.530

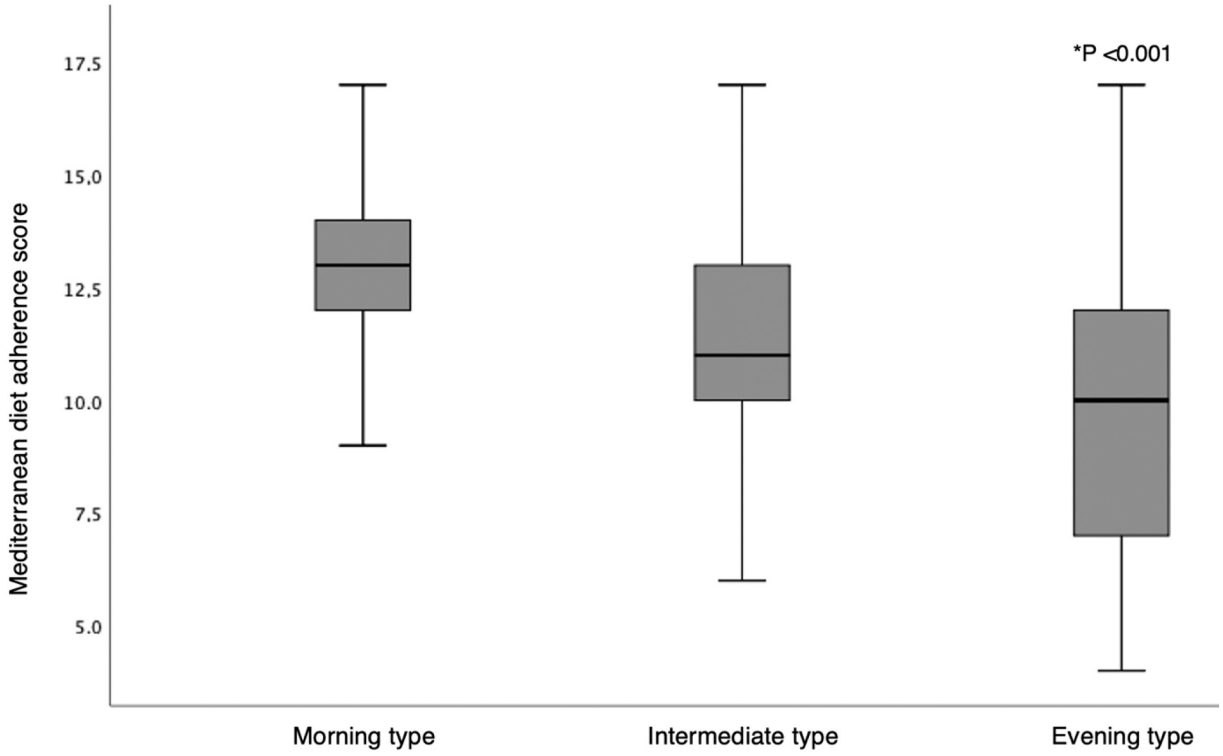

Fig. 1. Mean values of the Mediterranean diet adherence score according to chronotype.

maximum points) to the single food groups composing the Mediterranean diet adherence score reported in Table 2 shows that morning types reported more frequently an optimal consumption of fruit, vegetables, legumes, cereals, fish, and olive oil than subjects with other chronotypes, with opposite trends for dairy products ($p < 0.001$). A very small percentage of participants were in line with alcohol consumption, yet with higher proportion among morning compared to evening types ($p = 0.038$).

The logistic regression analyses exploring the association between chronotypes and high adherence to the Mediterranean diet is reported in Table 3. The univariate and the following multivariate models adjusting for background factors (model 1 adjusted for age, sex, educational and occupational status, smoking habits, physical activity level, BMI status, and alcohol intake) and health status (model 2 further adjusted for previous diagnosis of hypertension, type-2 diabetes, dislipidemias, cardiovascular disease, and cancer) showed that individuals having intermediate and evening chronotypes were less likely to have higher adherence to the Mediterranean diet (in the most adjusted model, OR = 0.28, 95 % CI: 0.18, 0.42 and OR = 0.08, 95 % CI: 0.03, 0.27, respectively; Table 3). When the analysis was conducted in subgroups of age, the results were similar in mid-age (>50 y) participants (for intermediate and evening chronotypes, OR = 0.21, 95 % CI: 0.10, 0.43 and OR = 0.92, 95 % CI: 0.01, 0.69, respectively) while the association with high adherence to the Mediterranean diet of evening compared to morning chronotype lost significance in older (>60 y) participants after adjusting

Table 2
Optimal answers (i.e., choice that gave 2 points) to the questions relating single food groups composing the Mediterranean diet score according to chronotype.

	Morning type (n = 1149)	Intermediate type (n = 614)	Evening type (n = 173)	P-value
Fruit (>2 servings/d), n (%)	672 (58.5)	255 (41.5)	50 (28.9)	<0.001
Vegetables (>2.5 servings/d), n (%)	587 (51.1)	257 (41.9)	62 (35.8)	<0.001
Legumes (>2 servings/week), n (%)	821 (71.5)	332 (54.1)	65 (37.6)	<0.001
Cereals (>1.5 servings/d), n (%)	538 (46.8)	207 (33.7)	57 (32.9)	<0.001
Fish (>2.5 servings/week), n (%)	819 (71.3)	368 (59.9)	79 (45.7)	<0.001
Meat (<1 serving/d), n (%)	410 (35.7)	238 (38.8)	77 (44.5)	0.059
Dairy products (<1 serving/d), n (%)	458 (39.9)	317 (51.6)	95 (54.9)	<0.001
Alcohol (1–2 AU/d), n (%)	97 (8.4)	47 (7.7)	5 (2.9)	0.038
Olive oil (regular use), n (%)	626 (54.5)	282 (45.9)	69 (39.9)	<0.001

AU, alcohol unit.

Table 3
Association between chronotype and high adherence to the Mediterranean diet in the whole sample and in older individuals (>65 y).

	Morning type	Intermediate type	Evening type	P-value
All sample				
Unadjusted	1	0.30 (0.22, 0.43)	0.12 (0.05, 0.30)	<0.001
Model 1	1	0.27 (0.18, 0.41)	0.10 (0.03, 0.33)	<0.001
Model 2	1	0.26 (0.17, 0.39)	0.10 (0.03, 0.32)	<0.001
Mid-age individuals (>50 y)				
Unadjusted	1	0.33 (0.20, 0.55)	0.05 (0.01, 0.39)	<0.001
Model 1	1	0.23 (0.11, 0.48)	0.09 (0.01, 0.73)	<0.001
Model 2	1	0.21 (0.10, 0.43)	0.92 (0.01, 0.69)	<0.001
Older individuals (>65 y)				
Unadjusted	1	0.42 (0.21, 0.85)	0.11 (0.01, 0.84)	0.008
Model 1	1	0.32 (0.11, 0.90)	0.23 (0.03, 1.91)	0.050
Model 2	1	0.27 (0.09, 0.82)	0.22 (0.02, 1.92)	0.038

Model 1 is adjusted for age, sex, smoking status, educational and occupational level, physical activity level, BMI status, and alcohol intake (g/d).
Model 2 is further adjusted for health status (previous diagnosis of hypertension, type-2 diabetes, dislipidemias, cancer, and cardiovascular diseases).

for covariates (for intermediate and evening chronotypes, OR = 0.27, 95 % CI: 0.09, 0.82 and OR = 0.22, 95 % CI: 0.02, 1.92, respectively; Table 3).

3.2. Systematic review

3.2.1. Main characteristics of the included studies

The study search process is presented in Fig. 2. The initial database search identified 259 potential articles, out of which 151 were excluded based on the title evaluation. After screening relevant abstracts, 61 articles were excluded and 47 full-text articles were obtained. After revision of full-text articles, 14 studies were excluded based on the following reasons: children and/or adolescent population (n = 8), no data on chronotype (n = 27), different exposure (n = 1), reporting on pregnant women (n = 1). Finally, 10 articles (Muscogiuri et al., 2020; Muscogiuri et al., 2021; De Amicis et al., 2020; Dinu et al., 2022a; Lotti et al., 2022a; Barrea et al., 2021a; Barrea et al., 2021b; Terschüren et al., 2021; Romero-Cabrera et al., 2022; Barrea et al., 2022) exploring the relation between adherence to the Mediterranean diet and chronotype met eligibility criteria.

The main characteristics of the studies included are presented in Table 4. All but one study had a cross-sectional design. When considering geographic area, all articles were conducted in Europe, out of which one in Germany, one in Spain, and the remaining were conducted in Italy. Only few studies used validated FFQs to assess dietary intakes, while adherence to the Mediterranean diet was tested through the PREDIMED screening tool and the Medi-Lite literature-based score. All studies used the MEQ to assess the participants' chronotypes. The overall quality of the included studies was high, with risk of bias concerning the representativeness of individuals included in the investigations (in most cases volunteers) (Supplementary Table 1).

3.2.2. Mediterranean diet and chronotype

Various studies investigated the possible correlation between chronotype and Mediterranean diet adherence showing mixed results. In two cross-sectional studies conducted in the context of the OPERA (obesity, programs of nutrition, education, research and assessment of the best treatment) Prevention Project involving 172 participants (mean age 52 years) were tested for chronotype through the MEQ and adherence to the Mediterranean diet through the adherence through 14-item MEDAS; the studies showed that those reporting having evening chronotype (12.8 %) had a higher proportion of low adherence to the Mediterranean diet compared to morning and intermediate chronotypes (54.5 % vs. 3 % vs. 12 %, respectively; $p < 0.001$) (Muscogiuri et al., 2020; Muscogiuri et al., 2021). Similar results have been observed in another cross-sectional study involving 416 participants (mean age 50 years), in which chronotype score was assessed through the rMEQ and Mediterranean diet adherence using the 14-item questionnaire: results showed that the adherence to Mediterranean diet was lower in the evening chronotype, represented by 9.1 % of participants with 92.1 % that did not adhere to Mediterranean diet ($p < 0.05$) compared to morning-type (De Amicis et al., 2020). Likewise, in another cross-sectional study conducted on 344 participants with a mean age of 33 years in which chronotype score was evaluated using the MEQ and Mediterranean diet adherence score through Medi-Lite, results showed that the evening chronotype, representing 7.6 % of total participants, had the lowest Mediterranean diet adherence ($p = 0.04$). Furthermore, a positive correlation between MEQ and Medi-lite score was observed ($R = 0.15$, $p = 0.005$) (Dinu et al., 2022a). Also in another cross-sectional study, including 1247 participants (mean age 36 years), it was observed that morning chronotype (represented by 56.7 % of participants) showed higher adherence to Mediterranean diet (adherence score: 10.1 ± 2.2; $p < 0.001$) which was significant even after logistic adjustment (OR = 95

Table 4
Main characteristics of the studies included in the systematic review.

Author, year	Country	Study design, follow-up	Population sex and age	Total population (analyzed sample)	Dietary assessment	Mediterranean diet score	Outcome assessment	Main findings
Muscogiuri, 2020	Italy	Cross-sectional	FM, 52 y	172	NA	14-item MEDAS	MEQ	Individuals with evening chronotype had lower adherence to the Mediterranean diet compared to other chronotypes.
De Amicis, 2020	Italy	Cross-sectional	FM, 50 y	416	NA	14-item MEDAS	rMEQ	Adherence to the Mediterranean diet resulted significantly lower in the evening chronotype compared to morning chronotype.
Barrea, 2021	Italy	Cross-sectional	F, 51 y	123	NA	14-item MEDAS	MEQ	No significant differences were observed between Mediterranean diet adherence and lifestyle.
Barrea, 2021	Italy	Cross-sectional	FM, 37 y	247	NA	14-point MEDAS	MEQ	The morning chronotype was associated with a higher Mediterranean diet adherence.
Muscogiuri, 2021	Italy	Cross-sectional	FM, 52 y	172	NA	14-item MEDAS	MEQ	Subjects with evening chronotype showed a lower Mediterranean diet score compared to the other types.
Terschüren, 2021	Germany	Cross-sectional	FM, 61 y	3513	102-item FFQ	14-item MEDAS	MCTQ	No significant differences between chronotype and adherence to the Mediterranean diet were observed.
Dinu, 2022	Italy	Cross-sectional	FM, 33 y	344	NA	Medi-Lite	MEQ	Individuals with evening chronotype reported lower adherence to the Mediterranean diet.
Lotti, 2022	Italy	Cross-sectional	FM, 36 y	1247	NA	Medi-Lite	MEQ	Morning subjects were more likely to have high adherence to the Mediterranean diet.
Romero-Cabrera, 2022	Spain	Prospective, 4 y	FM, 59 y	857	137-item FFQ	14-item MEDAS	MEQ	No significant differences were observed between chronotype and Mediterranean diet adherence.
Barrea, 2022	Italy	Cross-sectional	F, 24 y	112 PCOS patients	7-d dietary recall	14-item MEDAS	MEQ	Participants with evening chronotype had the lowest MD score.

Abbreviations: F (female); M (male); MEDAS (Mediterranean Diet Adherence Screener); MCTQ (Munich Chronotype Questionnaire); MEQ (Morningness–Eveningness Questionnaire).

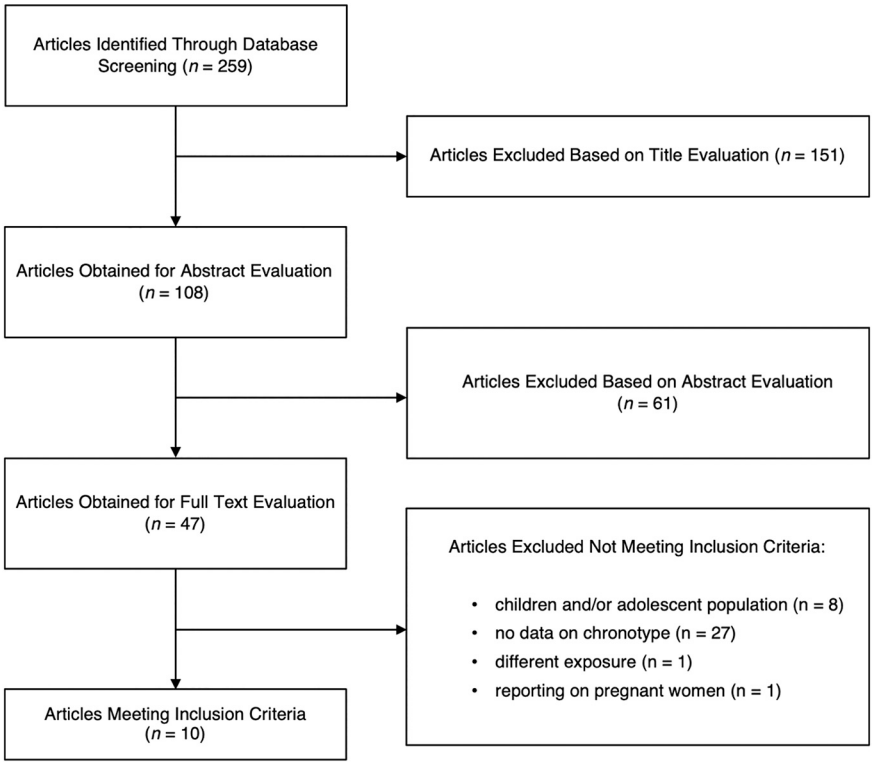

Fig. 2. Flow chart of study selection process.

%, 95 % CI: 1.54: 1.19, 1.99) (Lotti et al., 2022a). Another cross-sectional study including males and females for a total of 247 participants (mean age 37 years) showed that the morning chronotype (representing 62.3 % of population) was associated with a higher adherence to MD (high adherence to the MD: 36.4 %, $p < 0.001$) (Barrea et al., 2021a). However, the same research group obtained mixed results using the same cohort but considering only pre- and post- menopausal women ($n = 123$), with a mean age of 51 years. Mediterranean diet adherence was evaluated using the 14-item PREDIMED questionnaire while the chronotype and sleep quality using the MEQ and PSQI questionnaire, respectively (Barrea et al., 2021b). Other few studies showed null results when Mediterranean diet adherence and chronotype were tested for relationship. In fact, in a cross-sectional study, including 3513 participants with a mean age of 61 years results showed no association between MEDAS score and chronotype (Terschüren et al., 2021). Also the cross-sectional analysis of a prospective, single blind, RCT, conducted on 857 participants (mean age 59 years) reported no significant relation between chronotype and Mediterranean diet adherence (Romero-Cabrera et al., 2022). Finally, a cross-sectional study examined the effects of chronotype on Mediterranean diet adherence in 112 women with polycystic ovary syndrome with a mean age of 24 years. It was detected that participants with lower Mediterranean diet adherence reported the highest percentage of evening chronotype (58.3 %; $p < 0.001$) and, furthermore, no women with evening chronotype showed high Mediterranean diet adherence ($p < 0.001$) (Barrea et al., 2022).

4. Discussion

In this study, the relation between adherence to the Mediterranean diet and chronotype in a sample of southern Italian adults has been explored. Individuals with evening chronotype had lower adherence to the Mediterranean diet. Moreover, a systematic review of the observational studies exploring the association between adherence to the Mediterranean diet and chronotype showed consistent results in the existing scientific literature, with a similar proportion of individuals reporting having an evening chronotype compared to other studies conducted in the Mediterranean area was found. The evaluation of the evidence showed a substantial coherence of the results concerning chronotype, suggesting a clustering of healthy dietary habits and better alignment of circadian rhythms with light-dark cycle.

Various key dietary features of the Mediterranean diet may play a role in sleep hygiene. Given the nature of the study, we cannot define the direction of the association, but we can hypothesize that both chronotype and diet quality may affect each other (Lotti et al., 2023). Plant-based foods, such as fruits and vegetables, but also nuts, seeds, legumes, and olive oil are rich in antioxidant vitamins, minerals, (poly)phenols; specific foods, such as olive oil, seeds, and fish are also sources of healthy fats, including poly- and mono-unsaturated fatty acids (PUFA and MUFA, respectively). All these dietary factors have been demonstrated, to a various extent, to play a role in the human brain and potentially affect sleep features.

Vitamins and minerals exert essential actions in a variety of basic cellular processes, which makes them critical for brain function (Tardy et al., 2020). However, there are a number of specific actions that may affect sleep quality. Among vitamins, vitamin B12 can contribute to melatonin synthesis, while vitamin D and vitamin C may improve sleep through inflammation and oxidative stress inhibition (Zhao et al., 2020). Among minerals, magnesium is involved in gamma-aminobutyric acid production, an inhibitory neurotransmitter for the central nervous system that may favor sleep (Durlach et al., 2002). Zinc may interact with glutamatergic neurons and some inhibitory axon terminals (possibly of the cerebellum and in the spinal cord) acting as cofactor, or directly interact with G protein-coupled receptor 39 (GPR39) (mainly expressed in the amygdala, the hippocampus and the auditory cortex), which may play various roles in the regulation of sleep and wakefulness (Cherasse and Urade, 2017).

Also intake of MUFA and PUFA, which are contained in plant-based foods (among others), such as olive oil, nuts and seeds, but also fish and lean red meat, has been related to modulation of inflammatory pathways in the central nervous system with consequent reduction of pro-

inflammatory cytokine production in microglial and neuronal cells, chronic inflammation, and impairment in the signaling of neurotrophins, such as transforming growth factor beta (Caraci et al., 2011). Moreover, omega-3 PUFA may also interact with the serotonergic and dopaminergic transmission, including metabolism, release, uptake, and receptor function by influencing signal transduction through regulation of G-protein-mediated signal transduction, membrane-bound enzymes, and protein kinase C as well as improving membrane fluidity (Grosso et al., 2014). Finally, higher adherence to the Mediterranean diet is also related to a more favorable omega-3:omega-6 PUFA ratio, which in turn may further support the anti-inflammatory hypothesis toward brain health (Marventano et al., 2015). In contrast, consumption of high-fat meals has been reported to result in a decrease in sleep efficiency. The Mediterranean diet is generally associated with scarce consumption of ultra-processed foods, such as fast foods, fat-rich meats, complex confectionery ready-to-eat meals and snacks, in favor of home cooking, simpler dishes with daily cooked meals and unprocessed foods (such as fruits or nuts) as snacks, overall poor in (long-chain) saturated and hydrogenated trans fats (Godos et al., 2022; Dinu et al., 2022b). These fatty acids may exert pro-inflammatory effects in the central nervous system through various inflammatory pathways, including mitogen-activated protein kinase, nuclear factor-kB, and activator protein-1, resulting in the increased expression of cytokines in macrophages, monocytes, and monocyte-derived dendritic cells (Maki et al., 2021).

(Poly)phenols are secondary metabolites contained in plant-derived foods previously reported to be highly consumed in individuals with high adherence to the Mediterranean diet (Grosso and Galvano, 2016). Food products such as fruit and vegetable, but also olive oil, wine, whole grains, legumes and nuts are valuable sources of a great variety of (poly) phenol molecules exerting different effects on human health (Grosso, 2018). Some (poly)phenol compounds are known to cross the blood-brain barrier and inhibit neuroinflammation and promote neurogenesis and neuronal survival (Caruso et al., 2022). Moreover, dietary (poly)phenols have demonstrated to improve vascular and endothelial function as well as to prevent high blood pressure, which can be associated with REM sleep and sleep latency (Grosso et al., 2022a). Concerning specifically sleep-related properties, (poly)phenols have demonstrated to improve sleep time possibly by acting on gamma-amino butyric acid receptors in synergy with 5-hydroxytryptophan, both of which play a role in sleep quality (Hibi, 2023). Finally, (poly)phenols may support regulating the gut microbiota diversity and prevent dysbiosis and inflammatory process that from the digestive tract may reach the central nervous system through a complex system of signals involving the neural and endocrine systems (Liu et al., 2023).

Another feature of the Mediterranean diet is consumption of whole grains as the main source of daily energy. Aside from their natural richness in fiber (alongside all other vegetable-based foods), a high ratio of carbohydrates in the diet has been associated with better sleep features. Interestingly, results on foods with high and low glycemic index are quite discordant, with early studies supporting high glycemic index as sleep promoters (Afaghi et al., 2007), while newer investigation showing that low glycemic index food consumption was associated with lower prevalence and incidence of insomnia (Gangwisch et al., 2020). Irrespective of the fiber content in the diet, the potential mechanism hypothesized to explain the effects of carbohydrates on sleep features is their role in increasing tryptophan in the brain, which is a precursor of serotonin, a neurotransmitter known to influence various aspects of sleep after transformation in melatonin (Wurtman et al., 2003). However, this hypothesis is still controversial due to the unrealistic doses of melatonin needed to actually exert any effect on the brain, which cannot be credibly provided by the diet (Benton et al., 2022).

Concerning the other way around, the propensity of a person to be more active in the morning rather than afternoon or evening may also affect the adherence to the Mediterranean diet. Daily active individuals have been reported to have a higher diet quality (Suikki et al., 2021) and they are less likely to indulge in recreational foods and empty calorie drinks (Yang and Tucker, 2022; Zuraikat et al., 2021), which do not to characterize the Mediterranean diet. Moreover, higher nutrition knowledge and, more in general, higher education has been consistently associated with higher adherence to the Mediterranean diet: thus, individuals engaging in healthier lifestyles with more active daily life during the morning hours may also be more prone to adopt a healthier diet (Suh et al., 2017), which can be in line with the Mediterranean diet.

The differences observed between the whole sample and the analysis restricted to older individuals can be explained, at least in part, by other factors that may affect the relation between chronotype and high adherence to the Mediterranean diet. It is widely discussed that older individuals living in the Mediterranean area are generally more likely to have a higher adherence to traditional dietary patterns (Tyrovolas et al., 2009). We may hypothesize that the adoption of the Mediterranean diet in such people is more like a cultural trait depending on their natural traditions rather than a factor associated with health consciousness. The original studies conducted in the '60 exploring the common lifestyle habits of the southern Italian rural population emphasize on the active lifestyle of farmers as well as on the frugality of feeding during the day compared to the main early evening meal after the work in the fields (Fidanza et al., 2005). Moreover, the warm climate characterizing the Italian (and in general the southern Mediterranean) area further promotes the engagement in recreational activities at later hours of the day. Thus, there is a recall in the Italian Mediterranean culture to give value to the evenings as a moment of conviviality possibly resulting in a higher adherence to the Mediterranean diet then people with intermediate chronotypes. These are just hypotheses to be further confirmed, but they provide a consistent rationale to understand that investigating the adherence to the Mediterranean diet should be considered in the context of a geographical area and the cultural background of people living in it.

The results presented in this article are supported by inclusion of decent number of studies and good consistency of findings across them. However, some limitations concerning both the original report and the systematic review should be considered when interpreting the presented findings. First, the observational design of the studies does not provide evidence of causality, but only association. Moreover, considering that only cross-sectional studies (except one) have been published on this matter, reverse causality should be taken into account. Second, the methods of dietary assessment were not always gold standard (i.e., FFQs) but in some cases only limited to the tools used to measure the level of adherence to the Mediterranean diet; such a limited approach could undermine the findings by not considering other dietary variables or controlling for some specific dietary factors besides the overall adherence to the Mediterranean diet (i.e., alcohol consumption). Besides, even the use of gold standard methods to retrieve nutritional data may suffer from recall bias and social desirability bias. Third, although most studies adjusted for possible confounding factors, residual confounding (also not related to the diet, such as psychosocial aspects) may still persist. Forth, when the analysis was restricted by age groups, the results were no more significant in participants reporting evening chronotype but this might be the result of a low number of individuals in this group (suggested by the large confidence intervals); thus, a larger number of participants in this category of exposure may also result in significant findings. Finally, the methods to assess the outcomes investigated (such as, chronotypes) are relatively inexpensive tools serving as surrogates of more precise, clinical and biological measurements, which may increase the risk of type II error.

In conclusion, current evidence suggests that a lower adherence to a Mediterranean dietary pattern could be associated with intermediate and evening chronotype. Moreover, this association may be different in older individuals, further complicating the interpretation of the findings. Given the relatively low number of older individuals reporting evening chronotype potential affecting the statistical power of such analysis, future studies with larger samples are needed to confirm the retrieved findings. Considering the cross-sectional nature of the existing studies, the direction of such association cannot be concluded, and the

possibility of an inverse relation, meaning morning chronotype promoting healthy eating, cannot be excluded. However, whether causality would be confirmed in future studies, these findings may support the use of dietary interventions to improve eating habits toward a higher adherence to the Mediterranean diet to improve sleep-related outcomes. The fact that such a dietary pattern is characterized by highly palatable foods with naturally strong organoleptic properties would represent an added value to its adoption if compared to dietary approaches aimed toward food deprivation.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.exger.2023.112284.

Financial support

This work was supported by the Distinguished Scientist Fellowship Program (DSFP) at King Saud University, Riyadh, Saudi Arabia. J.G. was supported by the co-financing of the European Union—FSE-REACT-EU, PON Research and Innovation 2014–2020 DM1062/2021; CUP: E65F21002560001.

CRediT authorship contribution statement

The submission represents the original work of the authors not published previously in the same or substantially similar form and is not currently considered by another journal. The authors declare to have no conflict of interest. No copyright to any other work was breached in the manuscript's creation.

Declaration of competing interest

Authors declare no conflict of interest.

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