Mediterranean Diet on Sleep

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The Mediterranean diet is a plant-based, antioxidant-rich, unsaturated fat dietary pattern that has been consistently associated with lower rates of noncommunicable diseases and total mortality, so that it is considered one of the healthiest dietary patterns. Recent studies have demonstrated that another health parameter favorably influenced by the Mediterranean diet is sleep, which is an essential component of life.

Mediterranean diet sleep quality sleep quantity mental health

1. Introduction

Diet has become a cornerstone in the prevention and treatment of chronic noncommunicable diseases, with clinical areas of influence increasing over time as scientific evidence accumulates [1]. Epidemiological and clinical studies, along with mechanistic findings from cell and animal models, have indeed provided support for causal relationships between specific dietary patterns or foods/nutrients and health outcomes as well as disease development and progression, showing the ability of diet to significantly modify and often determine the lifelong health trajectories and chronic disease risk [2]. Accordingly, a comparative assessment of the disease burden attributable to diet in adult populations among 195 countries showed that suboptimal diets, i.e., diets high in sodium, low in whole grains, low in fruit, low in nuts and seeds, low in vegetables, and low in n-3 fatty acids, are the leading dietary risk factors for deaths and disability-adjusted life-years worldwide [3]. In contrast, diets characterized by increased consumption of vegetables, fruits, legumes, nuts, whole grains, unsaturated vegetable oils, fish, and lean meat or poultry (when meat was included) were associated with decreased risk of all-cause mortality among adults and older adults [4]. This has led to the inclusion of specific dietary recommendations into guidelines by public health entities and their prioritization in the health authority and research agenda to promote health and wellbeing, along with other modifiable lifestyle factors including smoking cessation and physical activity [5].

Among the healthiest diets, the Mediterranean diet is a plant-based dietary pattern that is increasingly become popular worldwide. The traditional Mediterranean diet is the dietary pattern consumed by the populations of the olive tree-growing areas of the Mediterranean basin before the mid-1960s. The traditional Mediterranean diet has entered the medical literature following publications of results from the Seven Countries Study, initiated in the late 1950s and showing that the Mediterranean diet is not simply, or mainly, a cholesterol-lowering diet, but exerts a range of beneficial health effects conferring longevity, better quality of life and preventing major chronic disease such as cardiovascular disease [6][7]. Other observational cohort studies, including the population-based European Prospective Investigation into Cancer and Nutrition (EPIC), confirmed the protection by the Mediterranean diet against chronic diseases, also including cancer. Randomized clinical trials, such as the PREDIMED (PREvencion

con DIeta MEDiterranea) study and the Lyon Diet Heart Study, found impressive benefit of the Mediterranean diet in primary and secondary prevention of cardiovascular disease, respectively [6][7]. Later on, exponentially accumulating scientific evidence has consistently corroborated these findings and extended the health benefits of the Mediterranean dietary pattern against metabolic and neurodegenerative diseases, cognitive impairment as well as overall mortality, which is apparent among younger and older generations across Mediterranean and non-Mediterranean populations [7]. Concomitantly, many investigations have tried to identify the health promoting components(s) within the Mediterranean diet and the mechanisms mediating the beneficial biological effects. Evidence has shown the potential contributory role of some foods and nutrients herein present, such as olive oil, fish, fruits and vegetables, red wine, nuts, grains, and legumes [8]. Although the exact mechanism is not known, many interrelated and overlapping pathways have been hypothesized to play a role including: regulation of lipid and glucose metabolism; improvement of insulin sensitivity; protection against oxidative stress, inflammation, and platelet aggregation; enhancement of endothelial function; inhibition of tumorigenesis; and modulation of the gut microbiota [8].

Peculiar features of the traditional Mediterranean diet are: the abundance of olive oil (25–50 mL/day) as the main culinary fat for cooking and seasoning; the high consumption of vegetables (more than two servings per meal), fruits (one or two servings per meal), nuts (either as part of the recipes or as healthy snacks), cereals (one or two servings per meal), and legumes (more than two servings weekly); the moderate to high consumption of fish and shellfish (two or more servings weekly); the moderate consumption of poultry (two servings weekly), eggs (two to four servings weekly), dairy products (e.g., yogurt, low fat cheese, small portions daily), and alcohol, mainly wine, consumed preferably with meals (for women: ≤one drink/day; for men: one to two drinks/day); the low consumption of red meat and processed meats (less than one serving weekly); occasional consumption of foods rich in sugars and saturated fat (typical of Westernized dietary patterns); and use of herbs and spices as a key ingredient in the unique flavor of many Mediterranean dishes [9][10]. The richness in bioactive components such as vitamins, minerals, and phytochemicals (mostly polyphenols) from fresh fruits, vegetables, nuts, and legumes, contributes with synergistic actions to the health benefits of the Mediterranean diet. Though the intake of total fat is relatively high (30–40% of total energy intake), it mainly comes from virgin olive oil, tree nuts, and fatty fish, and therefore is predominantly unsaturated, mostly monounsaturated fatty acid (MUFA, more than 20% of total energy intake) and polyunsaturated fatty acids (PUFA), mainly n-3 fatty acids: consequently, the ratio of unsaturated to saturated fat is high. Furthermore, carbohydrates in the Mediterranean diet come mostly from unrefined, fiber-rich sources such as whole wheat and beans, while high quality proteins are provided by fish, sea foods, poultry, and legumes [9].

Taking into account adaptations to each country's and region's specific realities, the Mediterranean diet, recognized as Intangible Cultural Heritage of Humanity by UNESCO, is thought not only as a way of eating of the countries surrounding the Mediterranean Sea, but also as an integral part of a preserved social, cultural, and lifestyle sustainable model featured by moderation, biodiversity, local production, conviviality, culinary activities, regular physical activity, and adequate rest including nocturnal sleep and after-meal nap [9].

Besides diet, another essential health-promoting factor is sleep, an active physiological process necessary for life and normally occupying one third of our lives, playing a fundamental role for physical, mental, and emotional health

[11]. Normal sleep architecture is comprised of nonrapid eye movement (NREM) sleep and REM sleep. NREM sleep is divided into three substages: stage N1, stage N2, and stage N3 (slow wave sleep). Older classification had four stages of NREM sleep. In the current rules, NREM stage 3 and NREM stage 4 are combined as stage N3. Sleep stages occur in cycles lasting 90 to 120 min each, with four to five cycles occurring during a typical night of sleep. Shifting of stages occurs over the course of the night, typically with an increased percentage of NREM sleep in the first half of the night and an increased percentage of REM sleep in the second half of the night [12]. Well recognized indicators of sleep quality are sleep latency, i.e., the length of time, in minutes, it takes to transition from wake to sleep (normal range for good sleep quality: 10–20 min), and sleep efficiency, i.e., the percentage of time in bed that is spent asleep (normal value for good sleep quality: above 85%).

Sleep patterns and sleep need are influenced by a complex interplay between genetic, behavioral, environmental, and social factors [13]. Expert consensus recommendations suggest that adults should obtain good sleep quality and duration (a minimum of 7 h per night) to promote optimal health and wellbeing [14][15]. Poor sleep quality and quantity can result from comorbid clinical conditions or sleep disorders, such as insomnia and sleep apnoea, but may also derive from the modern lifestyle with constant social, work, and family commitments, night- and shift-work, and the late-night use of technology (i.e., smartphones, computer, and television), which lead to circadian sleep–wake cycle disruption, chronic insufficient or poor quality sleep among adults as well as children and adolescents [16][17][18][19]. Serious consequences may arise from sleep curtailment ranging from fatigue, excessive daytime sleepiness, depressed mood, poor daytime functioning, and impaired cognitive and safety-related performance, to an increased risk of adverse health outcomes, including weight gain, obesity, type 2 diabetes, hypertension, cardiovascular, and neurodegenerative diseases, cancer as well as all-cause mortality [20][21][22][23]. Plausible biological mechanisms linking poor sleep and chronic disease risk involve endocrine, metabolic, and immune-inflammatory pathways [24], which are physiologically influenced by nocturnal sleep and whose dysfunctions play a determinant role in the development and progression of chronic diseases [25][26].

Sleep is therefore a modifiable risk factor for the development of chronic diseases, making it a target for intervention strategies [27][28]. Interestingly, in a prospective cohort study adding adequate sleep (≥7 h/night) to traditional healthy lifestyle factors, such as physical activity, a healthy diet (Mediterranean diet), moderate alcohol consumption, and nonsmoking, conferred further benefit against cardiovascular disease risk compared with no addition [29].

Besides being both key targetable lifestyle determinants of overall health and chronic disease risk, diet and sleep are linked by a bidirectional relationship. Indeed, qualitatively and/or quantitatively insufficient sleep or mistimed sleep may lead to overfeeding, metabolic impairments with weight gain and obesity, and poor diet quality, and, conversely, diet may influence sleep quality and duration so that nutritionally unbalanced diets or mistimed eating patterns negatively impact sleep parameters [30][31][32].

Accumulating scientific evidence from observational and clinical studies, as synthetized by recent literature reviews [33][34][35][36][37], suggests that dietary factors may impact on—and predict—sleep outcomes in otherwise healthy or clinical populations. In general, it has been shown that foods rich in melatonin (a sleep promoting hormone), or its

precursors tryptophan and serotonin, micronutrients (vitamin D and B, magnesium, zinc), carbohydrate-containing foods, food items including cherries and fish, can improve sleep parameters (e.g., sleep latency, time, efficiency). Contrarily, caffeinated and sugar-rich beverages as well as high fat (mainly saturated fat) and processed foods may negatively affect sleep quality and duration [38][39].

However, nutrients and foods are not consumed in isolation but in combination within dietary patterns (as defined a priori through a validated score or defined a posteriori through data-driven methods) that are expected to more extensively and differentially impact on biological and behavioral processes and hence be more predictive of overall health status and disease risk than individual foods or nutrients [40]. Furthermore, a more sustainable lifestyle approach is thought to be via the modification of the dietary pattern as a whole, instead of simply supplementing or depleting some specific foods or nutrients. However, the influence of dietary patterns on sleep has been less explored [41][42][43][44], and most of the available evidence in this context has been focused on the effects of the Mediterranean diet on sleep and to see whether sleep improvements might be an additional health benefit of this diet. Epidemiological studies, with mainly an obeservational design, have consistently shown that higher adherence to the Mesiterranean diet was associated with better sleep quantity and quality in adolescents as well as adults and older subjects.

2. Potential Mechanisms Underlying the Mediterranean Diet Effects on Sleep

Exploring the mechanisms potentially mediating the beneficial effects of the Mediterranean diet on sleep parameters, several hypotheses have been raised. This dietary pattern has a healthy profile of fat, proteins, and carbohydrates and a peculiar richness in polyphenols and vitamins, mainly provided by the moderate to high intake of fruits, vegetables, nuts, olive oil, cereals, and fish. Mechanisms associated with these foods and nutrients and their possible combinations might explain the benefit of the Mediterranean diet on sleep. On the contrary, a high consumption of red meat, saturated fat, and sugar-rich foods and beverages that are eaten occasionally in the Mediterranean-style diet and characterize unhealthy diets, was associated with negative effects on sleep quality and quantity, and with insomnia symptoms [31][45][46][47][48][49].

Plant-based diets [41][48][50], such as the Mediterranean diet, have been shown to be associated with better sleep quality and/or duration. Indeed, though not consistent, evidence supports the association of intakes of fruits, vegetables, legumes, and their fiber and protein content, with improved sleep parameters [49][51]. These food items as key components of the Mediterranean diet have been found to contribute to the favorable epidemiological association between Mediterranean diet adherence and sleep in both longitudinal [52] and cross-sectional analyses [45][46][47][52]. Interestingly, in some studies [46][47][53] olive oil consumption, which is typical of the Mediterranean diet and a rich source of MUFA (55–83% olive oil fat) and polyphenols (50–800 mg/kg olive oil, about 2% of oil weight), have also emerged as potentially protective for sleep.

Regarding dietary fats, in accordance with cross-sectional findings [31], among major nutrients included in the Mediterranean diet, a higher intake of MUFA to PUFA ratio and of unsaturated fat, predicted better sleep quality at

follow-up [52]. Although with mixed results [54], fatty fish (>150 g three times a week), a major food source of unsaturated fat, as well as plasma concentrations of n-3 fatty acids, including docosahexaenoic acid (DHA), and DHA supplementation were found to be positively associated with sleep quality in adults [47][48][55][56] and pediatric populations [57]. Confirmatory results have been reported in a very recent study in which higher plasma DHA concentrations were related to earlier sleep timing and longer sleep duration on the weekends in Mexican adolescents [58].

One of the most characteristic features and bioactive components of the Mediterranean diet is the richness in polyphenols, which are antioxidant compounds naturally present in plant foods and beverages (**Table 1**). They have gained increasing scientific attention due to their biological activities, their great abundance in human diet, and their role in the prevention of various chronic degenerative diseases, such as cancer, cardiovascular, and neurodegenerative diseases, through mechanisms also independent of their conventional antioxidant activities [59]. Over 500 different molecules having a polyphenol structure (i.e., several hydroxyl groups on aromatic rings) with different properties and bioavailabilities have been identified in edible plants, where they are synthetized as secondary metabolites for defense against biotic and abiotic stresses. They encompass five main groups according to structure: phenolic acids, flavonoids, stilbenes, lignans, and others. The flavonoid class is further divided into six subclasses including flavonols, flavones, isoflavones, flavanones, anthocyanidins, and flavanols [60]. In the European PREDIMED study, the mean total polyphenol intake was 820 ± 323 mg daily, mainly provided by fruits (44%), vegetables (12%), alcoholic (red wine) (6%) and nonalcoholic (coffee) beverages (55%), cereals (5%), olives and olive oil (11%), cocoa products, nuts, and legumes (each food group around 1–2%) [61].

Table 1. Main Mediterranean diet polyphenols, food sources and dietary intake.

Class	Subclass	Main Representatives	Main Food Source	Intake (mg/day)
Flavonoids	Flavanols	Catechin Epicatechin Epigallocatechin	Apples, red wine, tea, peaches, cocoa products, beans	26.7 ± 19.6
	Flavonols	Quercetin Kaempferol Myricetin	Spinach, beans, onions, lettuce	80.4 ± 32.7
	Flavanones	Hesperidin and its aglycone hesperetin Naringenin Didymin	Oranges, orange juice, red wine, tomatoes	132 ± 125
	Flavones	Apigenin Luteolin	Oranges, whole-grain wheat-flour bread, refined-grain wheat-flour bread	41.6 ± 26.1
	Isoflavones	Genistein Daidzen	Beans, beer	0.003 ± 0.003

Class	Subclass	Main Representatives	Main Food Source	Intake (mg/day)
		Glycitein		
	Anthocyanins	Malvidin Cyanidin Delphinidin	Cherries, red wine, olives, strawberries	38.5 ± 37.4
	Phenolic alcohol and secoiridoids	Hydroxytyrosol, tyrosol Oleuropein Oleacein Oleocanthal	Olive oil	39.46 ± 29.37
Non-flavonoids	Stilbenes	Resveratrol	Red wine, white wine, grapes, strawberries	1.84 ± 3.39
	Phenolic acids	Hydroxycinnamic acids (cinnamic, p-coumaric, ferulic, caffeic, chlorogenic, and rosmarinic acids, verbascoside)	Coffee, potatoes, apples, olives	276 ± 146
		Hydroxybenzoic acids (p-hydroxybenzoic, gallic, syringic, protocatechuic, and vanilic acids)	Olives, red wine, walnuts, beer	19.1 ± 16.8
	Lignans	Secoisolariciresinol Pinoresinol 1-Acetoxypinoresinol	Olive oil, whole-grain wheat-flour bread	0.85 ± 0.36
	Tannins	Condensed tannins or proanthocyanidins (oligomers or polymers of flavanols) Hydrolyzable tannins or gallotannins, ellagitannin	Red wine, apples, peaches, plums, orange, green beans, lentils	117 ± 81

Data on polyphenol content were adapted from [61]. Food sources are reported in decreasing order of specific polyphenols content.

also after absorption into the blood [62]. Additionally, a great proportion of nonabsorbed compounds reaches the colon where polyphenols are metabolized by the resident microflora, generating a different array of bioactive metabolites that are absorbed, further transformed, and released into the circulation [62]. Therefore, the bioactivities of ingested polyphenols depend mostly on their metabolites than on the native compounds.

Though experimental animal and in vitro studies have provided some potential mechanisms of sleep regulation by polyphenols (as described below), few human observational studies reported inconclusive results regarding the association of the polyphenol content of the diet and sleep parameters. A prospective study in UK women found that the total polyphenol content (but not polyphenol classes) of fruits and vegetables was inversely associated with sleep duration, in agreement with another study in Chinese adults reporting that soy isoflavone intake was associated with a low risk of long sleep duration [63]. On the contrary, adequate sleep duration and better sleep quality have been documented in association with high intakes of soy isoflavones in a study conducted in Japanese adults [64]. However, soy is not a typical Mediterranean food, and the effect on sleep of isoflavones from specific Mediterranean food items such as legumes has not been assessed. Recently, data from the Italian MEAL

cohort study regarding the energy-adjusted total (poly)phenol intake estimated using the Phenol-Explorer database showed that a higher intake of some flavonoid subclasses (flavanones and flavones, mostly contained in fruits, vegetables, cereals, legumes, olive oil, and tea), phenolic acids, such as hydroxycinnamic acids (contained in fruits, vegetables, coffee, nuts, and cereals), and lignans (present in olive oil, cereals, nuts, legumes, fruits, and vegetables) were associated with a significantly lower likelihood of having inadequate sleep quality, only in normal weight individuals [65].

Human interventional studies also tested the effects of some polyphenol supplements on sleep but, again, the results were inconsistent, and many methodological limitations have been recognized including the small sample size, the health status of the participants, the use of supplements instead of food sources having different bioavailability, and the short duration of supplementation (as reviewed by [51]).

However, the combination of foods and nutrients in the frame of the Mediterranean diet pattern, rather than individual components, seems to better predict the sleep improvements associated with the Mediterranean diet in epidemiologic studies [47][53]. Further research, mostly clinical intervention and mechanistic studies are warranted to uncover efficacy by specific Mediterranean diet key components on sleep features.

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