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Review

Cognitive health and Mediterranean Diet: Just diet or lifestyle pattern?

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ABSTRACT

Mediterranean diet is a term used to describe the traditional eating habits of people in Crete, South Italy and other Mediterranean countries. It is a predominantly plant-based diet, with olive oil being the main type of added fat. There are many observational studies exploring the potential association between adherence to the Mediterranean diet and cognitive decline. The present review focuses on longitudinal studies with repeated cognitive assessments. It also evaluates evidence on behaviors related to the Mediterranean way of living, that have been shown to be associated with cognition, namely social interaction, participation in leisure activities, including physical activities, and sleep quality. The synergistic association-effect of these lifestyle behaviors, including diet, is unknown. Lifestyle patterns may constitute a new research and public health perspective.

Contents

1. Introduction

1.1. What lies behind the Mediterranean diet

The concept of the Mediterranean diet was originally conceived by Ancel Keys, in the Seven Countries Study (Keys, 1970; Nestle, 1995). However, the core foods of the diet of people living around the Mediterranean basin can be recognized in the BC era: bread, olive oil, and wine were the basis of the Greek and Roman diets and, thereafter, important within Christian religions. Bread was symbolic of agriculture and human civilization and olive trees were the identity of Mediterranean lands (Ferrari and Rapezzi, 2011). Following Key's observations that all-cause and coronary heart disease death rates were lower in cohorts with olive oil as the main dietary fat compared to northern European ones (Keys et al., 1986), the notion that the high consumption of olive oil, bread, fruits, vegetables, and cereals may be responsible for profound health benefits was spread in the scientific community (Sofi et al., 2013). Nowadays, the term Mediterranean diet is widely used to describe the traditional dietary habits of people in Crete, South Italy and other Mediterranean countries, and is schematically depicted as a food pyramid (Simopoulos, 2001; Willett et al., 1995). This dietary pattern is characterized by abundance of plant foods: fruits, mainly as the typical after-dinner dessert, vegetables, either as main or side dish, a lot of bread, other forms of cereals, legumes, nuts,

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and seeds. Olive oil is the principal source of fat. Mediterranean diet also includes moderate amounts of dairy products (principally cheese and yogurt), low to moderate amounts of fish and poultry, red meat in low amounts and wine, consumed modestly, normally with meals (Kafatos et al., 2000; Willett et al., 1995).

1.2. Effects on health

In numerous epidemiological studies, greater adherence to the Mediterranean diet has been associated, with longevity and with lower prevalence of several chronic diseases. In specific, greater adherence to the Mediterranean diet has been associated with a significant reduction in total mortality, mortality from cardiovascular disease and cancer mortality, both in Mediterranean and non-Mediterranean populations (Lopez-Garcia et al., 2014; Sofi et al., 2010; Trichopoulou et al., 2003). Furthermore, adherence to the Mediterranean diet has been related to lower cancer risk (Couto et al., 2011; Sofi et al., 2010), to primary and secondary prevention of coronary artery disease (including strokes) (Barzi et al., 2003; de Lorgeril et al., 1999; Estruch et al., 2013; Sofi et al., 2010). Prospective studies and randomized trials have provided consistent evidence regarding the favorable association of the adherence to the Mediterranean diet on type 2 diabetes mellitus risk and management (Abiemo et al., 2013; Esposito et al., 2009; Itsiopoulos et al., 2011; Martinez-Gonzalez et al., 2008; Romaguera et al., 2011; Toobert et al., 2003). Recent meta-analysis has linked greater adherence to the Mediterranean diet with reduced risk of the metabolic syndrome and its resolution (Kastorini et al., 2011). Higher adherence to a Mediterranean-style diet was inversely associated with the development of frailty in community-dwelling older adults (Talegawkar et al., 2012) and with the incidence of hip fracture in a prospective European study (Benetou et al., 2013).

The more prevailing mechanisms underlying the aforementioned health benefits are the anti-inflammatory and anti-oxidative properties of this diet. In specific, adherence to the Mediterranean diet has been consistently associated with decreased biomarkers of subclinical inflammation (Barbaresko et al., 2013; Estruch, 2010) and increased levels of adiponectin, an insulin sensitizing hormone secreted by adipose tissue, affecting glucose and lipid metabolism and exerting distinct antiatherogenic, antidiabetogenic, and antiinflammatory actions (Fragopoulou et al., 2010). Moreover, the Mediterranean diet has been proposed to protect individuals from oxidative stress, as it has been consistently associated with lower blood levels of oxidative molecules and higher blood antioxidant capacity (Bullo et al., 2011; Zamora-Ros et al., 2013).

Much research has been conducted in regards to the potentially beneficial nutrients abundant in the Mediterranean diets, namely monounsaturated fatty acids, a balanced ratio of (n-6):(n-3) essential fatty acids, high amounts of fiber, antioxidants, such as vitamins E and C, resveratrol, polyphenols, selenium, glutathione (Simopoulos, 2001). However, the properties of the whole pattern seem to be well beyond the individual effects of nutrients. By investigating and evaluating the Mediterranean diet as a dietary pattern, we take into account nutrients and foods, their interactions, intercorrelations and cumulative effects. Eating is a complex behavior consisting of several individual behaviors, among others, the choice of specific foods or food groups, the organization of food into meals, and the conditions around or preceding eating. Aim of this review is to evaluate existing evidence on the effect of the Mediterranean diet as a pattern on cognitive function and risk of dementia and to explore potential interactions between this dietary pattern and other behaviors, implying the potential synergistic effect of a lifestyle pattern.

2. Evidence for the effect of the Mediterranean diet on cognition and dementia

There are biological mechanisms that may potentially link Mediterranean diet with cognitive decline and disease. Vascular risk factors, such as dyslipidemia, hypertension, and coronary artery disease, together with white matter lesions, have been related to dementia, Alzheimer disease (AD) and mild cognitive impairment (MCI) (Peters, 2009). Nonvascular biological mechanisms, namely metabolic, oxidative, and inflammatory, have been also proposed to be implicated in the pathophysiology of cognitive decline. Among the foods and nutrients abundant in the Mediterranean Diet, olive oil (through monounsaturated fatty acids and tyrosol, caffeic acid and other phenolic compounds), fish (and n-3 polyunsaturated fatty acids), wine (through alcohol, and phenolic compounds like resveratrol) and fruits and vegetables abundant in flavonoids and vitamins like C and E, have been associated with lower inflammatory and oxidative load and have been inversely associated with cardiometbolic risk factors, cognitive decline and dementia (Frisardi et al., 2010).

Many observational studies explored the hypothesis on the potential relation between adherence to the Mediterranean diet and AD and/or cognitive decline. Cross-sectional approaches have been useful for initial explorations, but due to methodological limitations, interpretations and conclusions deriving from such are tentative. Hence, in the present review, we briefly examine evidence only from longitudinal observational studies with repeated cognitive assessments, as there is essentially no randomized clinical trial with cognitive primary outcomes, so far (Martinez-Lapiscina et al., 2013; Scarmeas, 2013).

In 2006, the potential association between adherence to Mediterranean Diet and cognition was evaluated in a prospective investigation, of 2258 community-based non-demented individuals, aged >65 years in New York. Participants were prospectively evaluated every 1.5 years for an average of 4 years follow-up. One unit increment in the Mediterranean diet score was associated with 9–10% lower risk for development of AD, even after adjustment for potential confounders (Scarmeas et al., 2006). These results were, then, replicated in other US samples (Tangney et al., 2011; Tsivgoulis et al., 2013). A large number of participants ($n = 3790$) in the Chicago Health and Aging Project were evaluated repeatedly during a mean of 7.6 years: a dietary index based on the traditional Mediterranean diet was associated with slower rates of cognitive decline (Tangney et al., 2011). Interestingly, in contrast to the Mediterranean diet, no association between cognition and the Healthy Eating Index 2005 (recommended by the US department of Agriculture) was noted. In the REGARDS study, a very large ($n = 17,478$), geographically dispersed cohort, with oversampling of black subjects, after a mean follow-up period of 4 years, high adherence to the Mediterranean diet was associated with lower likelihood of incident cognitive impairment (Tsivgoulis et al., 2013). Interestingly, in a European cohort of 1410 adults from Bordeaux, 65 years or older, Feart et al. (2009) found that adherence to this dietary pattern was associated with slower decline on the Mini Mental State Examination (MMSE) over 5 years of follow-up; no association with the risk for incident dementia was noted but power for detection of such association was quite limited.

Other studies, on the other hand, failed to detect an association between a score related to adherence to the Mediterranean diet and prospectively assessed measures of cognitive decline. The two US-based, longitudinal studies in women, the Women's Health Study and the Nurses' Health Study, did not detect any association of adherence to the Mediterranean diet with cognitive change (Samieri et al., 2013a,b). In the Mayo Clinic Study of Aging, the reduced risk of mild cognitive impairment or dementia, in subjects in the upper tertile of adherence to the Mediterranean diet at