

COMMENTS & OPINIONS

Whole-Diet Approach, Mediterranean Diet, and Alzheimer Disease

Very recently, Scarmeas and colleagues reported the results of a community-based study involving 2258 nondemented individuals in New York in which adherence to a traditional Mediterranean diet (MeDi) was associated with significant reduction in risk for incident Alzheimer disease.^{1,2} Scarmeas and colleagues used in this report a scale indicating the degree of adherence to the traditional MeDi: a value of 0 or 1 was assigned to each of 9 indicated components with the use of the sex-specific median as the cut-off.³ However, in the study of Scarmeas and colleagues, the ratio of the median daily intake of monounsaturated fatty acids to saturated fatty acids (one of the hallmarks of the MeDi) for individual food categories by MeDi score tertiles was <1 and overall about 2.5 times lower than the same value calculated from other studies on MeDi.^{3,4} In the last years, the study approach was to associate single micronutrients or macronutrients to age-related cognitive decline, mild cognitive impairment, Alzheimer disease, or vascular dementia.^{5,6} Findings from the Italian Longitudinal Study on Aging demonstrated that in a 8.5-year follow-up, high monounsaturated fatty acid, polyunsaturated fatty acid, and total energy intake was significantly associated with a better cognitive performance in time.⁵ Furthermore, in the same sample, high intake of polyunsaturated fatty acids appeared to have a borderline nonsignificant trend for a protective effect against the development of mild cognitive impairment.⁵

We read with great interest the recent article by Scarmeas and colleagues, which in a case-control study nested within a community-based cohort in New York (ie, the same sample of the previous report) found that higher adherence to the MeDi was associated with lower risk for prevalent Alzheimer disease; the introduction of vascular variables (stroke, diabetes mellitus, hypertension, heart disease, lipid levels) in the model did not change the magnitude of the association.¹ The wide diffusion of this methodological approach has undeniable advantages, but some concerns exist. In fact, several devices related to the use of dietary composite score should be considered in evaluating the effects of nutrient intakes in different groups (low and high consumption) in unbiased manner.⁷ In particular, recent findings from the sample from the Italian Longitudinal Study on Aging suggested that a variation in

group heterogeneity, which could be caused by selection of cut-offs, can change in predictable ways the reliability and validity of the scale indicating the degree of adherence to a particular dietary pattern. The effects of change in observed-score variance on reliability can be estimated if it is assumed that error variance remains constant after selection.⁷ On the basis of these considerations, it is not difficult to guess that a “whole-diet” approach such as what the MeDi score measures could not be readily transferred to other populations, including a study population who was traditionally eating according to MeDi pattern. If the findings of Scarmeas and colleagues were successfully replicated,^{1,2} randomized clinical trials should ideally follow to specifically address the question of whether a dietary pattern may have a role in the prevention of cognitive impairment.

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Our study was conducted in a multiethnic urban cohort of New York City, which is unlikely to strictly consume the foods typical of Mediterranean countries. Therefore, and given the ethnic, geographic, and cultural differences in attitude toward olive oil consumption, it is not unexpected that the ratio of monounsaturated fatty acids to saturated fatty acids in our population was significantly lower as compared with that of Mediterranean populations. It is certainly possible that even higher ratios that exceed certain thresholds (such as the ones seen in Mediterranean populations) may have even more beneficial effects in cognition, but that does not negate the benefit of a Mediterranean-type diet in our cohort.

Use of nutrients in continuous forms has clear advantages, including higher power, more direct biological interpretations, and utilization of the data in their original form without use of transformations or cut-offs, which often contain subjective selection elements. However, potential disadvantages may also exist, such as possible underlying, non-normal, skewed distribution (as for example in the case of alcohol that the authors themselves refer to¹ [a large proportion of subjects may need to be assigned a value of 0 since they do not consume it at all]) and absence of monotonic effects. Such potential disadvantages are often dealt with by categorization as in the case of the method used in the MeDi calculation. Clearly the choice of categorization can affect a subject's score assignment (median split being one of the commonest ones in medical literature), but Solfrizzi et al do not clarify (either in this correspondence or in their referenced letter to the editor) how exactly a possible resulting heterogeneity of variance between "high" and "low" groups could negatively affect the reliability and validity of the MeDi score.

Additionally, Solfrizzi et al do not clarify why this possible heterogeneity of variance between high and low groups could negatively affect transferability to other populations. We can appreciate that in our cohort the MeDi may vary from a true MeDi. Subjects with high MeDi adherence in New York may be potentially categorized as subjects with low MeDi adherence if viewed in comparison with Mediterranean populations, but their MeDi-attributable risk in relation to those populations may be difficult to calculate given the multiple genetic, environmental, and other differences among populations. That neither invalidates nor minimizes the significance of our finding since their relative AD risk in comparison with New Yorkers who are even further away from MeDi principles could be still lower.

Finally, transferability of the MeDi (calculated using similar methodology) advantages regarding mortality and other diseases has been clearly demonstrated in multiple previous studies.²⁻⁴ For example, adherence to the principles of the traditional MeDi has been associated with longer survival in both Anglo-Celtic individuals and Greek-Australian residents of Melbourne.³ In another study of 74 607 subjects in 9 European countries, increased adherence to the MeDi was associated with reduced mortality with no evidence of significant heterogeneity among countries in the association of MeDi with overall mortality.⁴

Given the known heterogeneity in diets across the globe, we fully realize that not all diets will fit the true MeDi, but if we can identify those dietary patterns that protect against

diseases such as AD, we have made an important step in public health. We fully agree that successful replication of our findings regarding MeDi and AD in other populations (similarly to what has been already done for mortality²⁻⁴) would be more than desirable.

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New Therapies for Ataxia-Telangiectasia

We read with interest the recent article by Buoni et al¹ in which the authors described a striking improvement in the ataxia in a 3-year-old boy with ataxia-telangiectasia (AT) during treatment with inhaled betamethasone. In spite of the favorable response to the drug, the authors expressed their concern about the adverse effects observed during the trial (weight gain and a cushingoid appearance) and about the safety of betamethasone in an already immunocompromised patient.¹

We recently had the opportunity to treat an adult case of AT, a 34-year-old man born to consanguineous parents.² The neurological exploration revealed gait ataxia with episodic support necessary to walk 10 m, mild distal weakness in the lower extremities, preserved tendon reflexes, and oculomotor apraxia. Administration of a placebo, acetazolamide, and gabapentin rendered no benefit while pregabalin at 225 mg/d improved gait, enabling the patient to walk more than 10 m without support. The posterior addition of tiagabine at 7.5 mg/d increased the unsupported walking distance to more than 20 m, making half turns easier. The amelioration described has been sustained since March 2005.