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File: ■ Extra Virgin Olive (*Olea europaea*) Oil ■ Mediterranean Diet ■ Cognition

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RE: Mediterranean Diet with Added Extra Virgin Olive Oil Improves Cognitive Function

Martínez-Lapiscina EH, Clavero P, Toledo E, et al. Virgin olive oil supplementation and long-term cognition: the PREDIMED-Navarra randomized, trial. *J Nutr Health Aging*. 2013;17(6):544-552.

Included in the Mediterranean diet (MedDiet) are olive (*Olea europaea*) oil as the main culinary fat, high intake of plant-based foods, moderate-to-high consumption of fish and other seafood, low-to-moderate intake of dairy products, low intake of meat, and regular but moderate intake of red wine (from grapes [*Vitis vinifera*]) with meals. The antioxidant, anti-inflammatory, and cerebrovascular protective effects of the MedDiet may have a beneficial impact on cognition. This randomized, primary prevention trial evaluated the effect of 2 MedDiets versus a low-fat diet on cognitive function and mild cognitive impairment (MCI) or dementia.

The multicenter PREDIMED (Prevención con Dieta Mediterránea) study (n=7,447) was conducted in Spain from May 2005 to December 2010 to assess the potential cardiovascular protective effects of a MedDiet supplemented with extra virgin olive oil (MedDiet+EVOO; Fundación Patrimonio Comunal Olivarero and Hojiblanca SA; Spain) or MedDiet+Nuts (almonds [*Prunus dulcis*; Borges SA; Spain], walnuts [*Juglans regia*; California Walnut Commission; California], and hazelnuts [*Corylus avellana*; Morella Nuts SA; Spain]), compared with a control (low-fat) diet. Eligible subjects were community-dwelling men aged 55 to 80 years and women aged 60 to 80 years without cardiovascular disease (CVD) but with a high vascular risk because they had either type 2 diabetes mellitus or ≥ 3 vascular risk factors. Exclusion factors were previous history of CVD, illiteracy, or any severe disease or condition that might limit compliance.

The study population for this smaller, single-center, cognitive sub-study was a randomly drawn sample (n=285) from the 969 participants at one of the PREDIMED recruitment centers (PREDIMED-Navarra) who were alive after 6.5 years of nutritional intervention. Of the 271 participants who gave informed consent, 3 were excluded due to an incomplete neuropsychological examination. The mean age of the 268 participants was 74.1 \pm 5.7 years; 44.8% were men. They had been randomly assigned to the

MedDiet+EVOO (11 allotments weekly) (n=91); MedDiet+Nuts (15 g walnuts, 7.5 g almonds, and 7.5 g hazelnuts daily) (n=88); and control (low-fat) diet (n=89) groups.

At baseline and yearly thereafter, a trained dietitian administered a validated 137-item food frequency questionnaire and a 14-item questionnaire to determine adherence to the MedDiet protocol. A structured in-person neurological and neuropsychological examination was conducted by a neurologist blinded to group allocation. The Mini-Mental State Examination and Clock Drawing Test were used to evaluate global cognition. Over 10 other validated tests were used to evaluate cognitive aspects such as memory, language, attention, executive function, and abstract reasoning. Evidence of impairment in daily living function and in social or occupational function was also assessed. MCI was diagnosed by using the International Working Group on MCI criteria.

Compared with those in the control group, participants in the MedDiet+EVOO group had better post-trial cognitive performance on all cognitive tests, but those differences did not reach statistical significance after correcting for multiple comparisons. Favorable results were also reported for some, but not all, cognitive tasks for participants in the MedDiet+Nuts group.

After adjusting for multiple variables (including age, family history of cognitive impairment or dementia, apolipoprotein E [APOE] genotype, education, physical activity, vascular risk factors, and energy intake), cognitive performance was better in the MedDiet+EVOO group than in the MedDiet+Nuts and control groups. Particularly, the participants in the MedDiet+EVOO group performed significantly better in both visual and verbal memory domains, compared with those in the MedDiet+Nuts group.

At the end of the study, 34 participants were identified with MCI. After adjusting for all confounding factors, the authors found that there was a significantly lower incidence of MCI in the MedDiet+EVOO group compared with the control group. Only 5 cases of dementia were found: 1 in the MedDiet+EVOO group, 3 in the MedDiet+Nuts group, and 1 in the control group.

The authors attribute the MedDiet's protective effects on cognition to several mechanisms. First, inflammatory processes are considered to be an underlying pathogenic mechanism of cognitive decline,¹ and the MedDiet has been associated with lower serum concentrations of inflammatory biomarkers. Second, oxidative stress is related to cognitive impairment,² and typical MedDiets include many antioxidant nutrients. Finally, the beneficial cognitive effects may be mediated through cerebrovascular protection, as the MedDiet seems to improve vascular risk factors.³

The greatest limitation of this study was the lack of baseline cognitive data, although the exclusion criteria, study design, and multivariate analyses countered this drawback to some degree. The authors note that their results are strengthened by the facts that well-established diagnostic criteria were used; the nutritional interventions and neuropsychological evaluations were assessed with validated dietary and neuropsychological instruments; potential confounders were controlled for in the analyses; and the randomized design prevents some of the intrinsic biases of observational studies.

The authors conclude that a 6.5-year intervention with an EVOO-rich MedDiet was associated with better cognition and less MCI compared with a low-fat, control diet.

-Shari Henson

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³Estruch R, Martínez-González MÁ, Corella D, et al.; PREDIMED Study Investigators. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med.* 2006;145(1):1-11.

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