Published in final edited form as:
Mov Disord. 2012 May ; 27(6): 771–774. doi:10.1002/mds.24918.

The Association between Mediterranean Diet Adherence and Parkinson's Disease

RN Alcalay, MD, MSc[1,2], **Y Gu, PhD**[2], **H Mejia-Santana, MSc**[1], **L Cote, MD**[1,3], **KS Marder, MD, MPH**[1,2,3,4], and **N Scarmeas, MD, MS**[1,2,3]

[1]Department of Neurology, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[2]Taub Institute for Research on Alzheimer's Disease and the Aging Brain, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[3]Gertrude H. Sergievsky Center, College of Physicians and Surgeons, Columbia University, New York, NY, USA

[4]Department of Psychiatry, Columbia University Medical Center, NYC, NY, USA

Abstract

Objective—Recent studies demonstrated an association between a Mediterranean-type diet and Alzheimer's risk. We assessed the association between Mediterranean-type diet adherence and PD status.

Methods—257 PD participants and 198 controls completed the Willett semi-quantitative questionnaire that quantifies diet during the past year. Scores were calculated using a 9-point scale; higher scores indicated greater adherence to the Mediterranean-type diet. Logistic regression models were used to assess the association between PD status and Mediterranean-type diet, adjusting for caloric intake, age, gender, education and ethnicity. Adjusted linear regression models were used to examine the association between Mediterranean-type diet adherence and PD age-at-onset.

Results—Higher Mediterranean-type diet adherence was associated with reduced odds for PD after adjustment for all covariates (OR=0.86, 95%CI=0.77–0.97, p=0.010). Lower Mediterranean-type diet score was associated with earlier PD age-at-onset (β=1.09, p=0.010).

Conclusions—PD patients adhere less than controls to the Mediterranean-type diet. Dietary behavior may be associated with age-at-onset.

INTRODUCTION

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease (AD) affecting roughly 1% of individuals overage 60 in North America and Europe.[1] While the role of environmental exposures in the pathogenesis of PD is well established,[2–3] most studies that have investigated associations between PD risk and intake

Corresponding author: Roy N. Alcalay, 710 West 168th Street, New York City, New York. Phone: 212-305-5554. rna2104@columbia.edu.

Authorship contribution:
Conceptualization of the study: Drs. Alcalay, Gu, Marder, Scarmeas. Data collection and design: Dr. Cote, Ms. Mejia-Santana, Dr. Marder. Statistical analyses: Drs. Alcalay, Gu and Scarmeas. Manuscript drafting: Dr. Alcalay. Manuscript revisions: Ms. Mejia-Santana, Drs. Gu, Cote, Marder and Scarmeas

Disclosure: The authors report no conflicts of interest.
Drs. Scarmeas, Gu, and Cote and Mrs. Mejia-Santana have nothing to disclose.

of individual foods and nutrients reported inconsistent results.[4–11] The most consistent data support the association between higher consumption of dairy products and increased PD risk.[8, 12–13] More recently, a prospective analysis of two large cohorts, the Health Professionals Follow-Up Study (HPFS) and the Nurses' Health Study (NHS), revealed an association between PD risk and dietary patterns as assessed by the Alternate Healthy Eating Index (AHEI) and the alternate Mediterranean Diet Score.[14]

The Mediterranean diet (MeDi) has received attention in recent years because of growing evidence associating MeDi with lower risk for AD,[15] cardiovascular disease,[16] several forms of cancer,[17] and overall mortality.[18] The MeDi is characterized by high intake of vegetables, legumes, fruits, and cereals; high intake of unsaturated fatty acids (mostly in the form of olive oil) compared to saturated fatty acids; a moderately high intake of fish; a low-to-moderate intake of dairy products, meat and poultry; and a regular but moderate consumption of ethanol, primarily in the form of wine and generally during meals.[15, 18]

In this case-control study, our aim was to determine whether MeDi adherence is associated with PD and with PD age-at-onset.

PARTICIPANTS AND METHODS

Study population

This study included participants recruited between 1996 and 1998.[19–20] Participants with PD (n=257) were recruited from two sources: 1. The Center for Parkinson's Disease (CPD) at Columbia University in New York (n=209) and 2. A community-based study, the Washington Heights-Inwood Columbia Aging Project (WHICAP,[21–22] n=48). Control participants (n=198) were recruited from three sources: random digit dialing (n=130), WHICAP (n=66) and the CPD (n=2). Four participants were excluded from the analyses because a MeDi score could not be calculated because of missing data on one or more food items. The Columbia University Institutional Review Board approved the protocols and consent procedures. Written informed consent was obtained from all participants in the study.

Exposure - Diet

The Willett semi-quantitative food frequency questionnaire (SFFQ; Channing Laboratory, Cambridge, MA)[23] was used to collect dietary data regarding average food consumption in the past year before the assessment. We previously reported validity and reliability of various components of the SFFQ in WHICAP.[21–22]

We followed the method that Trichopoulou and colleagues[18] described to construct the MeDi score as reported in our previous studies.[15, 24–26] Specifically, we first regressed caloric intake (measured in kilocalories) and calculated the derived residuals of daily gram intake[27] for each of the following seven categories: dairy, meat, fruits, vegetables, legumes, cereals, and fish. Individuals were given one point for each of the following conditions: consumption of a beneficial component (fruits, vegetables, legumes, cereals, and fish) whose caloric-adjusted intake was at or above the sex-specific median; consumption of a detrimental component (meat and dairy products) whose caloric-adjusted consumption was below the sex-specific median; intake ratio of monounsaturated fats to saturated fats above the sex-specific median, and mild to moderate alcohol consumption (>0 to <30 g/d). Participants were given a zero for each of the categories if the caloric-adjusted consumption was outside the range described above.

The MeDi score was generated for each participant by adding the points in the food categories. Thus, the MeDi score ranges from 0–9, with the higher score indicating greater adherence to the MeDi.

Statistical Analyses

Demographics, clinical and dietary characteristics were compared between PD individuals and controls using a *t* test for continuous variables, and Fisher exact or χ^2 test for categorical variables. Similarly, clinical and demographic characteristics were compared according to the tertiles of MeDi adherence. Logistic regression models were used to assess the association between PD status and MeDi adherence (initially as a continuous variable and then in tertiles), in models either unadjusted or adjusted for caloric intake, age, gender, education, and ethnicity. We subsequently tested associations between PD status and the nine food categories used for MeDi derivation (each as a continuous variable, except for alcohol consumption which was dichotomous as above) by including them all simultaneously in a single adjusted model. Finally, we used linear regression models to investigate associations between MeDi adherence and PD age-at-onset after adjusting for PD duration in years, daily caloric intake, gender, and education.

Results

Participants with PD were younger, had higher education, and were less likely to adhere to MeDi than controls (Table 1). The demographics and total daily caloric intake of the participants based on their MeDi adherence are presented in eTable 1 (supplementary). MeDi adherence (tertiles) was not associated with education, gender, race or caloric intake.

The association between PD status and MeDi adherence was significant (p=0.010) after adjustment for demographic characteristics and caloric intake in a logistic model (Table 2). For each additional MeDi point, the odds of having PD were lower by 14%. None of the individual food categories was associated with PD.

Among PD participants, mean PD age-at-onset was 62.1 (Table 1). Greater MeDi adherence was associated with later PD age-at-onset after adjustment for PD duration, daily caloric intake, gender, and education both when MeDi adherence was included in the model as a continuous variable (β=1.09, 95%CI 0.31–1.87; p=0.006) and as tertiles (β=2.3, 95%CI 0.36–4.2; p=0.020).

Discussion

This study suggests that lower adherence to MeDi is associated with PD status. The association persisted after adjustment for multiple potential confounders. The fact that among PD participants, lower adherence was associated with earlier PD age-at-onset further suggests a possible dose-response effect. The relation between MeDi adherence and PD status was not driven by any individual category of the diet but rather the whole pattern.

Previous studies have indicated that environmental factors play a major role in PD;[28] however, most nutritional studies in PD have shown conflicting results.[4–11] A possible explanation for the conflicting data is that most studies have focused on single nutrients, e.g. vitamins C or E,[7, 29] rather than on dietary patterns. Indeed, the largest prospective study of dietary patterns identified a Mediterranean-like diet as protective of PD both in males (HPFS) and females (NHS).[14]Assessing dietary patterns may be more informative than assessing specific nutrients separately. First, this approach is more consistent with individuals' eating habits, and second, it takes into account interactions among nutrients. This approach has been successful in AD and in non-neurological diseases.[15, 30]

The mechanism by which MeDi may be protective in neurodegenerative disorders is largely unknown. Mechanisms that have been hypothesized in the AD literature, include oxidative stress and inflammation.[31]Indeed, oxidative stress has been implicated in the pathogenesis of PD.[32–33] Complex phenols and other substances including vitamin C, vitamin E, and carotenoid may serve as antioxidants,[34] and are found in high concentrations in the typical components of the MeDi. Inflammation has also been implicated in the pathogenesis of PD, and anti-inflammatory non-steroidal medications may be associated with a lower risk for PD.[35]Adherence to the MeDi may attenuate inflammation.[36]In addition, MeDi adherence may be protective because of lower consumption of compounds which are associated with higher PD risk. We and others have shown an association between animal fat consumption and PD,[37] and the association between higher dairy intake and PD was previously reported.[8, 12–13]

The major limitation of our study is its case-control design. It is possible that the association between lack of MeDi adherence and PD is a result of the PD status rather than its cause. Individuals with PD may lose their sense of smell,[38] which in turn may affect their diet. Furthermore, PD medications may also change eating habits. On the other hand, the fact that a similar association between MeDi adherence and PD was reported from a prospective cohort study[14] supports the notion that MeDi adherence protects from PD, rather than the reverse association. Other unmeasured confounders, including (but not limited to) mood and cognitive function of participants with and without PD may have confounded our findings. Another limitation of our study is its sample size. This study may not be large enough for subanalyses assessing which food products (e.g., more vegetables, less dairy) drive this association.

There are also strengths in our study. We used a validated questionnaire and a well-established method for calculating the MeDi score.[18] The outcome measurement of PD was also clear. Participants were evaluated by movement disorders specialists to diagnose PD. We adjusted for multiple potential confounders, including demographic, nutritional and clinical characteristics. Our study was multiethnic which may increase its external validity.

In light of our findings from this retrospective study, larger prospective evaluation of dietary patterns are required to establish a better understanding of nutritional risk factors for PD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was funded by the NIH (RO1-NS32527, AGO7232, R01AG028506, P30 ES009089, 1UL1 RR024156-01) and the Parkinson's Disease Foundation. RNA is supported by the Brookdale Foundation Leadership in Aging Fellowship and the NIH (KL2 RR024157).

Dr. Alcalay is funded by the Brookdale foundation, the Parkinson's Disease Foundation, the Michael J Fox Foundation and the Smart Foundation.

Dr. Marder served on the editorial board of *Neurology* and received research support from NeuroSearch Sweden AB, the NIH [#NS36630 (PI), 1UL1 RR024156-01 (Director PCIR), PO412196- G (Co-I), and PO412196-G (Co-I)], the Parkinson's Disease Foundation, Huntington's Disease Society of America, the Parkinson Study Group, Cure Huntington's Disease Initiative, and the Michael J Fox foundation.

References

1. Nussbaum RL, Ellis CE. Alzheimer's disease and Parkinson's disease. N Engl J Med. 2003; 348:1356–64. [PubMed: 12672864]

2. Tanner CM. Advances in environmental epidemiology. Mov Disord. 25(Suppl 1):S58–62. [PubMed: 20187243]
3. Tanner CM, Ottman R, Goldman SM, et al. Parkinson disease in twins: an etiologic study. JAMA. 1999; 281:341–6. [PubMed: 9929087]
4. Morens DM, Grandinetti A, Waslien CI, Park CB, Ross GW, White LR. Case-control study of idiopathic Parkinson's disease and dietary vitamin E intake. Neurology. 1996; 46:1270–4. [PubMed: 8628465]
5. Paganini-Hill A. Risk factors for parkinson's disease: the leisure world cohort study. Neuroepidemiology. 2001; 20:118–24. [PubMed: 11359079]
6. Zhang SM, Hernan MA, Chen H, Spiegelman D, Willett WC, Ascherio A. Intakes of vitamins E and C, carotenoids, vitamin supplements, and PD risk. Neurology. 2002; 59:1161–9. [PubMed: 12391343]
7. Etminan M, Gill SS, Samii A. Intake of vitamin E, vitamin C, and carotenoids and the risk of Parkinson's disease: a meta-analysis. Lancet Neurol. 2005; 4:362–5. [PubMed: 15907740]
8. Chen H, Zhang SM, Hernan MA, Willett WC, Ascherio A. Diet and Parkinson's disease: a potential role of dairy products in men. Ann Neurol. 2002; 52:793–801. [PubMed: 12447934]
9. Chen H, Zhang SM, Schwarzschild MA, et al. Folate intake and risk of Parkinson's disease. Am J Epidemiol. 2004; 160:368–75. [PubMed: 15286022]
10. de Lau LM, Bornebroek M, Witteman JC, Hofman A, Koudstaal PJ, Breteler MM. Dietary fatty acids and the risk of Parkinson disease: the Rotterdam study. Neurology. 2005; 64:2040–5. [PubMed: 15985568]
11. Chen H, Zhang SM, Hernan MA, Willett WC, Ascherio A. Dietary intakes of fat and risk of Parkinson's disease. Am J Epidemiol. 2003; 157:1007–14. [PubMed: 12777364]
12. Chen H, O'Reilly E, McCullough ML, et al. Consumption of dairy products and risk of Parkinson's disease. Am J Epidemiol. 2007; 165:998–1006. [PubMed: 17272289]
13. Park M, Ross GW, Petrovitch H, et al. Consumption of milk and calcium in midlife and the future risk of Parkinson disease. Neurology. 2005; 64:1047–51. [PubMed: 15781824]
14. Gao X, Chen H, Fung TT, et al. Prospective study of dietary pattern and risk of Parkinson disease. Am J Clin Nutr. 2007; 86:1486–94. [PubMed: 17991663]
15. Scarmeas N, Stern Y, Tang MX, Mayeux R, Luchsinger JA. Mediterranean diet and risk for Alzheimer's disease. Ann Neurol. 2006; 59:912–21. [PubMed: 16622828]
16. Singh RB, Dubnov G, Niaz MA, et al. Effect of an Indo-Mediterranean diet on progression of coronary artery disease in high risk patients (Indo-Mediterranean Diet Heart Study): a randomised single-blind trial. Lancet. 2002; 360:1455–61. [PubMed: 12433513]
17. Trichopoulou A, Lagiou P, Kuper H, Trichopoulos D. Cancer and Mediterranean dietary traditions. Cancer Epidemiol Biomarkers Prev. 2000; 9:869–73. [PubMed: 11008902]
18. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003; 348:2599–608. [PubMed: 12826634]
19. McGuire V, Den Eeden SK, Tanner CM, et al. Association of DRD2 and DRD3 polymorphisms with Parkinson's disease in a multiethnic consortium. J Neurol Sci. 2011
20. Logroscino G, Marder K, Graziano J, et al. Altered systemic iron metabolism in Parkinson's disease. Neurology. 1997; 49:714–7. [PubMed: 9305329]
21. Luchsinger JA, Tang MX, Shea S, Mayeux R. Antioxidant vitamin intake and risk of Alzheimer disease. Arch Neurol. 2003; 60:203–8. [PubMed: 12580704]
22. Luchsinger JA, Tang MX, Shea S, Mayeux R. Caloric intake and the risk of Alzheimer disease. Arch Neurol. 2002; 59:1258–63. [PubMed: 12164721]
23. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol. 1985; 122:51–65. [PubMed: 4014201]
24. Scarmeas N, Luchsinger JA, Schupf N, et al. Physical activity, diet, and risk of Alzheimer disease. JAMA. 2009; 302:627–37. [PubMed: 19671904]
25. Scarmeas N, Stern Y, Mayeux R, Luchsinger JA. Mediterranean diet, Alzheimer disease, and vascular mediation. Arch Neurol. 2006; 63:1709–17. [PubMed: 17030648]

26. Scarmeas N, Stern Y, Mayeux R, Manly JJ, Schupf N, Luchsinger JA. Mediterranean diet and mild cognitive impairment. Arch Neurol. 2009; 66:216–25. [PubMed: 19204158]
27. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. Am J Epidemiol. 1986; 124:17–27. [PubMed: 3521261]
28. Tanner CM. Is the cause of Parkinson's disease environmental or hereditary? Evidence from twin studies. Adv Neurol. 2003; 91:133–42. [PubMed: 12442672]
29. Parkinson Study Group. Impact of deprenyl and tocopherol treatment on Parkinson's disease in DATATOP patients requiring levodopa. Ann Neurol. 1996; 39:37–45. [PubMed: 8572664]
30. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002; 13:3–9. [PubMed: 11790957]
31. Cummings JL. Alzheimer's disease. N Engl J Med. 2004; 351:56–67. [PubMed: 15229308]
32. Barnham KJ, Masters CL, Bush AI. Neurodegenerative diseases and oxidative stress. Nat Rev Drug Discov. 2004; 3:205–14. [PubMed: 15031734]
33. Maguire-Zeiss KA, Short DW, Federoff HJ. Synuclein, dopamine and oxidative stress: co-conspirators in Parkinson's disease? Brain Res Mol Brain Res. 2005; 134:18–23. [PubMed: 15790526]
34. Joshipura KJ, Hu FB, Manson JE, et al. The effect of fruit and vegetable intake on risk for coronary heart disease. Ann Intern Med. 2001; 134:1106–14. [PubMed: 11412050]
35. Gao X, Chen H, Schwarzschild MA, Ascherio A. Use of ibuprofen and risk of Parkinson disease. Neurology. 2011; 76:863–9. [PubMed: 21368281]
36. Chrysohoou C, Panagiotakos DB, Pitsavos C, Das UN, Stefanadis C. Adherence to the Mediterranean diet attenuates inflammation and coagulation process in healthy adults: The ATTICA Study. J Am Coll Cardiol. 2004; 44:152–8. [PubMed: 15234425]
37. Logroscino G, Marder K, Cote L, Tang MX, Shea S, Mayeux R. Dietary lipids and antioxidants in Parkinson's disease: a population-based, case-control study. Ann Neurol. 1996; 39:89–94. [PubMed: 8572672]
38. Gaig C, Tolosa E. When does Parkinson's disease begin? Mov Disord. 2009; 24 (Suppl 2):S656–64. [PubMed: 19877243]

Table 1

Demographic and dietary characteristics of participants with and without PD

		PD (N=257)	Controls (N=198)	p-value*
Age, years (SD)		68.2 (11.0)	72.4 (9.6)	<0.001
Education, years (SD)		14.1 (4.3)	12.2 (5.0)	<0.001
Female, N (%)		115 (44.7%)	96 (48.5%)	0.449
Race, N (%)	White	198 (77.0%)	137 (69.2%)	0.08
	Black	6 (2.3%)	11 (5.6%)	
	Hispanic	49 (19.1%)	49 (24.7%)	
	Other	4 (1.6%)	1 (0.5%)	
Total daily caloric intake (SD), kCal		1505.7 (479.9)	1482.0 (496.2)	0.579
Mediterranean diet score (SD)		4.3 (1.8)	4.7 (1.7)	0.007
PD age-at-onset (SD)		61.7 (11.7)		
PD disease duration from diagnosis (SD)		6.1 (5.1)		
UPDRS-III (SD)		26.8 (13.1)		
Mean levodopa daily dose (SD)		479.5mg (283.6)		

(PD: Parkinson Disease, SD: standard deviation, Kcal: kilocalories, UPDRS-III: Unified Parkinson's Disease Rating Scale)

*P-values from *t* test for continuous variables and Fisher exact or χ^2 test for categorical variables Table 2: The association between PD status and Mediterranean diet adherence and demographics as assessed in logistic regression models

Table 2

The association between PD status and Mediterranean diet adherence and demographics as assessed in logistic regression models

		Univariate model			Multivariate model[1]		
		OR	**95% CI**	**p value**	**OR**	**95% CI**	**p value**
Mediterranean diet adherence (continuous)		0.8	0.78–0.96	0.008	0.86	0.77–0.97	0.010
Mediterranean diet adherence (Tertiles)	Middle versus low	0.61	0.39–0.98	for trend 0.006	0.64	0.39–1.03	for trend 0.008
	Higher versus low	0.49	0.29–0.82		0.48	0.28–0.82	

(PD: Parkinson Disease, OR: odds ratio, CI: confidence interval)

[1]Adjusted for age, education, race