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MIND DIET ASSOCIATED WITH REDUCED INCIDENCE AND DELAYED PROGRESSION OF PARKINSONISM IN OLD AGE

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Abstract

Background: In old age, motor impairments including parkinsonian signs are common, but treatment is lacking for many older adults. In this study, we examined the association of a diet specifically developed to promote brain health, called MIND (Mediterranean-DASH Diet Intervention for Neurodegenerative Delay), to the incidence and progression of parkinsonism in older adults.

Methods: A total of 706 Memory and Aging Project participants aged 59 −97 years and without parkinsonism at baseline were assessed annually for the presence of four parkinsonian signs using a 26-item modified version of the United Parkinson's Disease Rating Scale. Incident parkinsonism was defined as the first occurrence over 4.6 years of follow-up of two or more parkinsonian signs. The progression of parkinsonism was assessed by change in a global parkinsonian score (range: 0–100). MIND, Mediterranean, and DASH diet pattern scores were computed based on a validated food frequency questionnaire including 144 food items. We employed Cox-Proportional Hazard models and linear mixed models, to examine the associations of baseline diet scores with incident parkinsonism and the annual rate of change in global parkinsonian score, respectively.

Results: In models adjusted for age, sex, smoking, total energy intake, BMI and depressive symptoms, higher MIND diet scores were associated with a decreased risk of parkinsonism [(HR=0.89, 95% CI 0.83–0.96)]; and a slower rate of parkinsonism progression [(β= −0.008; SE=0.0037; p=0.04)]. The Mediterranean diet was marginally associated with reduced parkinsonism progression (β= −0.002; SE=0.0014; p=0.06). The DASH diet, by contrast, was not associated with either outcome.

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Ethical standards: The Institutional Review Board of Rush University approved the study, and all participants gave written informed consent.

Conclusion: The MIND diet created for brain health may be a associated with decreased risk and slower progression of parkinsonism in older adults.

Keywords

Parkinsonism; motor decline; dietary pattern; longitudinal; MIND diet

Introduction

It is estimated that by 85 years of age half of the elderly population develops parkinsonian signs which are progressive and associated with disability and mortality (1). Various factors other than Parkinson's disease (PD) pathology (a rare condition) contribute to the development of parkinsonian signs (2, 3). Parkinsonism is a well-defined construct to characterize the loss in motor function that commonly occurs in older adults (4). Currently, there is no known treatment for this condition, and few preventive risk factors have been identified. In this study, we examined whether a diet pattern called MIND (Mediterranean-DASH Diet Intervention for Neurodegenerative Delay) that has been related to lower risk of Alzheimer's disease (5) and slower rate of cognitive decline (6)] might also be associated with reduced incidence and progression of parkinsonism associated with older age. The estimated effects of the MIND diet were compared to estimates for the Mediterranean and DASH diets in identical analyses..

Methods

Study Population

The study was conducted among participants of the Rush Memory and Aging Project (MAP). MAP is an ongoing longitudinal cohort study that recruits elderly from more than 40 retirement communities and subsidized housing facilities in the Chicago area. The cohort details have been published (7). From 2004 to 2017, 1002 participants without dementia at the baseline dietary assessment, had at least one follow-up assessment of parkinsonism. To investigate incident parkinsonism, we excluded baseline cases of parkinsonism (n=286), and PD (n=10), leaving 706 participants for analysis. The Institutional Review Board of Rush University approved the study, and all participants gave written informed consent. .

Assessment and Categorization of Parkinsonism

Parkinsonism was assessed via structured clinical evaluations conducted by trained nurse clinicians using a 26-item modified version of the United Parkinson's Disease Rating Scale to assess four parkinsonian signs: bradykinesia, parkinsonian gait, rigidity and tremors (8, 9). Incident parkinsonism was defined parkinsonism as the presence of two or more parkinsonian signs (1). A sign was present if the clinician assessed two or more of the items for a given sign as having a score of 1 or more. We also assessed diet pattern relations to the rate of progression of parkinsonism score (the average score of all four parkinsonian signs; global parkinsonian score range: 0–100 with higher scores indicating more severe parkinsonism) (8, 9).

Diet assessment

Diet patterns at the baseline were assessed using a modified Harvard food frequency questionnaire (FFQ)validated in older Chicago community residents (10). The FFQ ascertained usual frequency of intake over the previous 12 months of 144 food items. Frequency of consumption of foods were multiplied by either the natural portion size (e.g. one banana) or the typical serving sizes based on the sex-specific mean portion sizes reported by the oldest men and women of national surveys. Diet scores were based on the total frequency of consumption of food items within a food category. Details of the MIND (range: 0 to15), Mediterranean (range: 0 to55), and the DASH (range: 0 to10) diet scores have been published previously (5, 11, 12).

Covariates—Other non-dietary measures were obtained from the participant's annual clinical evaluations including age (in years), smoking history (never, past or current smoker), body mass index (measured height and weight), number of depressive symptoms (modified 10-item version of the Center for Epidemiological Studies-Depression scale (13)), and global cognitive score (composite measure of averaged z-scores of 19 cognitive tests (14)).

Statistical methods

We used Cox proportional hazards models to investigate whether each dietary pattern was associated with the incidence of parkinsonism. Diet pattern associations with parkinsonism progression were analyzed using linear mixed models with random effects in which the continuous parkinsonian score was square root-transformed. The dietary scores were modeled both as continuous variables and in tertiles (to assess non-linear associations). All analyses were performed using ©SAS version 9.4.

Results

The study sample was on average, age 80.3 years, and primarily females (75%). Baseline characteristics were similar across tertiles of MIND diet score, except that the highest tertile group tended to have a lower number of depressive symptoms and higher cognitive scores (Table 1). Diet score means and ranges were 8.0 for MIND (range, 3–13; maximum possible=15), 31.7 for Mediterranean (range, 18–46; maximum possible=55), and 4.2 for DASH (range, 1–8.5; maximum possible=10). A total of 302 of 706 (43 %) MAP participants developed parkinsonism over an average follow-up of 4.6 years and the mean time for developing the first parkinsonian sign was 3.6 years (range 1 to 13 years)..

Associations of Dietary Patterns with Incident Parkinsonism

MIND diet score was associated with lower rate of developing parkinsonism in models adjusted for age, sex, smoking and total energy intake. Each unit increase in MIND score was associated with a 13% reduction in the rate of developing parkinsonism. (Table 2), and those in the second and highest tertiles of scores (median scores of 8 and 10) had reduced risks by 30% (p=0.008) and 42% (p=0.0003), respectively.

In separate analyses, the Mediterranean diet had a modest 3% reduction in risk of developing parkinsonism. however, the DASH score was only marginally (Table 2). Body

Mass Index (BMI) and depressive symptoms have been identified as risk factors of parkinsonism (15), and thus have the potential to confound associations with diet. When we re-analyzed the data with adjustment for BMI and depressive symptoms in the basic models for all three diet scores, only the MIND diet retained its association with incident parkinsonism (Table 2).

In secondary analyses, we investigated education as another potential confounder in the fully adjusted model, but the findings were not materially changed (for MIND model HR=0.90, 95% CI: 0.84–0.97). We also investigated baseline cognitive function as a potential confounder and/or mediator in the associations between the MIND diet pattern and parkinsonism. In these analyses, the hazard ratio for MIND diet score and incident parkinsonism was somewhat reduced but remained statistically significant, indicating a contribution of the diet to the development of parkinsonism that is independent of cognitive status (HR=0.93, 95% CI: 0.86–1.00). There was no evidence of effect modification by age, sex and smoking in separate models that included multiplicative terms with MIND diet score.

Association of Dietary Patterns with the progression of parkinsonism over time

We next examined the associations of the different dietary patterns with the annual rate of change in the severity of parkinsonian signs. Higher scores on only the MIND and MedDiet diet patterns were associated with slower progression of parkinsonism in basic-adjusted models; the DASH diet had no association (Table 3). There were no material differences in the estimated effects for the MIND diet scores when further adjusted for time-varying BMI and depressive symptoms, however, MedDiet association became marginally significant (Table 3). The MIND diet score was slightly more predictive of parkinsonism progression than the MedDiet score (p=0.05); the standardized regression coefficients of the estimated diet effect were −2.16 for MIND and −1.42 for MedDiet.

Discussion

In this community-based study of older adults, we found that higher adherence to the MIND diet was significantly associated with lower rates of developing parkinsonism, and with slower progression of parkinsonian signs. More moderate protective associations were observed for the Mediterranean diet but not for the DASH diet. The stronger, more robust association of the MIND diet with parkinsonism may be due to its emphasis on foods and nutrients that have shown to protect the brain with aging in previous studies (5, 6).

Parkinsonian signs and parkinsonism in older adults can be caused by a wide range of chronic health conditions such as vascular disease, infections, multiple medications and diverse degenerative disorders such as PD and nigral degeneration in the absence of clinical PD (2, 3, 15). While we are unaware of prior studies that examined the relationship of diet patterns with the development of parkinsonism in older adults, our study findings are consistent with studies of diet and Parkinson’s disease intwo large cohorts (Health Professionals Follow-up Study and Nurses’ Health Study) that reported reduced Parkinson’s disease risk with a prudent diet, the alternate Mediterranean score, and the Alternate Healthy Eating Index (16). Two case-control studies also found protective relations to PD with higher

adherence to the Mediterranean diet (17) and a healthy Japanese diet (18). One Finish study reported no association between an Alternate Healthy Eating Index and PD risk, but the null finding could be due to changes in diet over the long follow-up (41 years) without reassessment of diet. (19). In other studies of motor decline, the Mediterranean diet was associated with slower decline in physical function in older adults (e.g. walking speed, chair rise, and balance) (20–22).

In previous studies of the MAP cohort, higher scores of adherence to the MIND diet were associated with slower cognitive decline (6) and with decreased risk of developing Alzheimer's disease (5). These associations were stronger than observed for either the Mediterranean or DASH diets. We speculate that the targeting of brain healthy foods in the MIND diet may be driving its stronger associations with motor and cognitive function. Berries and green leafy vegetables are two specific food components of the MIND diet. Berries were found to enhance motor performance (balance and coordination) in mice (23) as well as marginally improve gait speed and total steps error in older adults (24). Green leafy vegetables, rich in various brain protective nutrients (lutein, folate, beta-carotene, Vitamin E), have not been studied for their effects on the motor or physical function. However, there are mixed findings from various population-based studies looking at the effect of specific nutrients on PD. In a combined analysis of the Harvard studies , dietary intakes of Vitamin E but not carotenoids was associated with lower risk of developing PD (25). A case-control study reported inverse associations of β-carotene and vitamin E (26) with Parkinson's disease risk whereas other studies detected no relationship (27, 28). Dietary Vitamin E is also found to be associated with better physical performance in older adults (29, 30).

The MIND, Mediterranean and DASH diets are all plant-based diets emphasizing fruits and vegetables, legumes, whole grains, nuts, fish, poultry and low intake of saturated fats and red meats. Plant-based diets have been demonstrated to reduce oxidative stress and inflammation (31, 32), two important mechanistic links for neurodegenerative disorders, including Parkinson's disease (33). Oxidative stress promotes Parkinson's disease through alpha-synuclein aggregation, and inflammation causes dopaminergic neuronal loss via microglial activation (34). Thus, a healthy diet rich in nutrients with antioxidants and anti-inflammatory properties may play an important role in preventing the risk for parkinsonism.

Our study has a number of strengths that lend confidence to the findings, including its longitudinal design, community-based cohort, comprehensive dietary assessments, and annual structured assessment of parkinsonian signs. Limitations of the study are the non-diverse study population thus limiting the generalizability of these results to non-Hispanic, white older adults and the observational design that prevents interpretation of causality. In addition, the relatively small sample size may have insufficient power to detect small effects of the Mediterranean and DASH diets on motor changes.

The common condition of parkinsonism in older adults contributes to disability and lower quality of life. The possibility that diet can ameliorate or delay its progression would contribute greatly to the public health, as currently there is no known treatment. Further

studies are required to establish these findings through replication in more diverse populations and ultimately, a randomized diet intervention trial to confirm causality.

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Table 1

Baseline characteristics by tertile of MIND diet score among Memory and Aging Project participants, 2004–2017

		Tertile of MIND diet score		
	N	**T1**	**T2**	**T3**
Median MIND diet score	706	6.5	8.0	10.0
Age, mean ± SD, years	706	80.8 ± 7.5	80.8 ± 6.9	79.4 ± 6.9
Male %	706	30	24	21
Education, mean ± SD, years	706	14.5 ± 3.2	15.2± 2.8	15.6 ± 2.9
Smoking %, never	665	58	60	55
Global Cognitive function, mean ± SD, score	704	0.04 ± 0.64	0.31 ± 0.48	0.32 ± 0.49
Body Mass Index mean ± SD	687	27.5 ± 5.2	27.2 ± 4.6	26.5 ± 5.4
Depressive symptoms, mean ± SD, number	705	1.2 ± 1.7	0.9 ± 1.4	0.8 ± 1.4
Total Energy, mean ± SD, kcal/d	706	1698 ± 561	1785 ± 559	1746 ± 464

Abbreviations: MIND, Mediterranean-DASH diet intervention for neurodegenerative delay; IQR, Inter quartile range

Table 2

Hazard ratios (95% Confidence Intervals) of associations between MIND, Mediterranean and DASH diet scores with incident parkinsonism among participants of the Memory and Aging Project, 2004–2017

Outcomes HR (95% CI)	N	MIND	Mediterranean	DASH
Incident Parkinsonism	706			
Basic model ˜		0.87 (0.81–0.93) *	0.97 (0.95–0.99) *	0.92(0. 85–1.01)
Basic +BMI+Depressive symptoms		0.89 (0.83–0.96) *	0.98 (0.96–1.01)	0.95(0. 87–1.04)

NOTE: Cox-Proportional hazard model was used; Abbreviations: MIND, Mediterranean-DASH diet intervention for neurodegenerative delay; DASH-Dietary approaches to stop hypertension; BMI, Body Mass Index; Basic model includes age, sex, smoking and total energy intake

* p<0.05

Table 3

Beta coefficients (standard error, p-value) of estimated rates of change in the progression of Global Parkinsonian Score according to MIND, Mediterranean and DASH diet scores over a mean 4.6 years among 689 participants of the Memory and Aging Project, 2004–2017

Global Parkinsonian Signs	N	MIND β (SE, p value)	Mediterranean β (SE, p value)	DASH β (SE, p value)
Basic model ˜	689	−0.007 (0.0037, .04)*	−0.003 (0.0014, .04)*	−0.005 (0.0045, .24)
Basic +BMI+Depressive symptoms	670	−0.008 (0.0037, .04)*	−0.002 (0.0014, .06)	−0.006 (0.0045, .19)

NOTE: Linear mixed model with random effects was used; Abbreviations: MIND, Mediterranean-DASH diet intervention for neurodegenerative delay; DASH-Dietary approaches to stop hypertension; BMI, Body Mass Index. ~Basic model includes age, sex, smoking, total energy intake, time and interaction between time and each model covariate. In Basic +BMI+Depressive symptoms model, time varying BMI and depressive symptoms variables were added

*p<0.05