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An exploratory study of diet in childhood and young adulthood and adult-onset multiple sclerosis

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Abstract

There is little evidence on the role of diet in childhood/adolescence and MS in adulthood. The MS Sunshine Study recruited adults with recent-onset MS (n=602) and matched controls (n=653). Of these, 84% provided dietary recall for specific ages between childhood and young adulthood (6–10, 11–15, 16–20 years). We used logistic regression to test associations between age-specific diet and case-control status. Consumption of fruit (all ages), yoghurt (all ages), and legumes (11–15 years) was associated with lower probability of adult-onset MS (all $p < 0.05$). These results suggest that healthy dietary habits between childhood and young adulthood may reduce MS risk.

Keywords

Diet; nutrition; multiple sclerosis; MS Sunshine Study

Introduction

We have previously shown that recent diet is associated with increased probability of association with MS in adults (e.g. (1–4)). Although there is little evidence associating early life diet and later MS, childhood and adolescence have been identified as periods of importance for other environmental risk factors, such as obesity and low sun exposure/low vitamin D status (5). In an Iranian study, higher consumption of various foods (fresh fish,

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Declaration of Competing Interest

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canned tuna, poultry, cheese, yoghurt, butter, fruit, and vegetables) in adolescence (13–19 years) was associated with reduced likelihood of having MS between 15 and 50 years (6). We build on these findings by testing associations between diet in childhood to young adulthood with adult-onset MS using data from the MS Sunshine Study, a United States case-control study examining possible risk factors for MS (7).

Materials and methods

The MS Sunshine Study is described in detail elsewhere (7). In brief, adults aged 18 years were recruited from the Kaiser Permanente Southern California (KPSC) database of over 4 million people. Cases were diagnosed with MS or clinically isolated syndrome in the previous 18 months, or had symptom onset within the past three years. Controls were matched on age, sex, race/ethnicity, and KPSC facility. The participation rate was 74% for cases and 48% for controls (7). Structured in-person interviews were used to collect participant characteristics. Self-administered mail-back questionnaires were used to measure diet according to specific age groups (6–10, 11–15, 16–20 years) for 13 types of foods (see Table 1), chosen to reflect the major food groups (vegetables, fruits, wholegrains, dairy and alternatives, protein foods), plus individual food items where these were thought to have differing nutritional qualities. Frequency of consumption was recorded in eight categories from “never or less than once a month” to “4 or more times a day”. We re-categorised into three groups: “never or less than once a month”, “1–3 times a month” and “weekly or more” to allow for comparison with prior analyses (3). The study was conducted in accordance with the Declaration of Helsinki; the protocol was approved by the KPSC institutional review board (IRB:5962).

We used frequency and percentage to describe categorical variables, and median (interquartile range) for non-normally distributed variables. Pearson chi square was used to test statistical significance of categorical variables and Wilcoxin/Mann-Whitney test for non-normal distributions. We used unconditional logistic regression to estimate adjusted odds ratios (aORs) for the probability of association between frequency of consumption of various food types and adult-onset MS. Prior to analysis, the frequency category responses for the food groups were tested for a linear association with the outcome variables to ensure they could be used as continuous variables in the regression analysis. In addition, tests for randomness in missing values in relation to the outcome variable were conducted to assess any need for imputation (8). Covariates in Model 1 were sex and age; covariates in Model 2 were sex, age, education, race, smoking status, family history of MS and history of infectious mononucleosis. Data were analysed using Stata Software 14 (StataCorp, College Station, TX, USA). Statistical significance was set at $p < 0.05$.

Results

Of the 1255 participants recruited into the study, 84% (1061) provided information on at least some of the foods consumed in childhood and young adulthood. Of those who didn't provide diet information, 97 were controls and 97 were cases. Supplemental Table 1 shows the characteristics of the 1061 eligible participants for this study. Missing values were missing completely at random with respect to the outcome variable; hence, we did not

conduct imputation. A lower percentage of case participants in all age groups consumed fruit weekly or more; a lower percentage consumed yoghurt weekly or more at ages 11–15 years; and a lower percentage consumed legumes weekly or more at ages 11–20 years compared with controls (Supplemental Table 2).

Across all age groups, the three categories of consumption (never or less than once a month, 1–3 times a month, and weekly or more), were related in a linear fashion to whether or not a person had MS. Therefore, the regression analysis was conducted using the frequency of food consumption as a continuous variable. Greater fruit and yoghurt consumption at all ages (6–20 years), and legume consumption at ages 11–15 years, were statistically significantly associated with lower probability of adult-onset MS (Table 1). There was no evidence of any significant association with the frequency of consumption of other foods and adult-onset MS.

Discussion

Consuming fruit, yoghurt and legumes at various ages between childhood and young adulthood was associated with reduced probability of association with adult-onset MS. These foods often load positively on empirically-derived healthy dietary patterns, and feature as healthy foods in the Dietary Guidelines for Americans. Although dietary intake from a full food frequency questionnaire was unavailable, these findings nevertheless suggest a potential link between past diet and adult-onset MS.

There is a growing body of evidence to support current diet as a modifiable risk factor for MS, including a beneficial effect of higher intake of polyunsaturated fatty acids (9). Previous studies support a protective association between recent fish consumption and risk of MS (3, 4, 10). Furthermore, in the aforementioned Iranian study, consuming at least one serving of fresh fish fortnightly (vs. <one serving fortnightly) was associated with lower likelihood of MS (aOR=0.70; 95% confidence interval=0.56, 0.88) (6). We found no such association in our study, although fish consumption across all ages was low, with nearly half the participants consuming no fish at any age.

Childhood obesity (11) and other environmental risk factors during childhood/adolescence have been associated with increased likelihood of adult-onset MS (5). However, it is not clear whether this is due to a longer exposure time or whether childhood/adolescence is a critical age for risk-factor exposure in the genesis of adult-onset MS. Further knowledge about potential environmental risk factors, including diet and its relationship to obesity during these early life stages, is essential for promoting strategies to reduce the risk of adult-onset MS.

A limitation of our study was the limited range of food types and lack of information on typical portion sizes. Retrospective measures of diet from the distant past may be prone to recall error; however, taking a retrospective diet history is considered superior to relying on current diet as an indicator of past diet (12). Case recruitment rates were higher than for controls, which is a common potential source of bias when conducting case-control studies; hence, the low participation rate among the controls makes the study prone to selection

bias. Further, cases may be more likely to recall exposure to risk factors than controls. We cannot rule out the possibility of residual confounding by unmeasured demographic and lifestyle characteristics during childhood/adolescence, such as vitamin D status, body mass index, socioeconomic status and physical activity, or by time since symptom onset for cases (median=3 years; interquartile range =2). Also, since dietary intake was highly correlated across the different age groups (the majority of correlations were between 0.7 and 0.9), we were not able to adjust the models for diet at other ages; therefore, we cannot be confident that risk was associated with exposure in specific age groups.

Limitations notwithstanding, the findings of this exploratory study suggest a potential influence of diet between childhood and young adulthood on the probability of developing MS in adulthood, with higher consumption of foods that are considered healthy (fruit, yoghurt and legumes) associated with reduced probability of adult-onset MS. Hence, further investigation of early diet and likelihood of adult-onset MS is warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Adjusted odds ratios¹ and 95% confidence intervals for frequency of consumption for 13 types of foods by age group (6–10, 11–15 and 16–20 years)

	Model 1 ² aOR [95% CI]	Model 2 ³ aOR [95% CI]	P ⁴
Ages 6–10 years			
Fresh fish	0.91 (0.77,1.08)	0.93 (0.77,1.11)	0.404
Shrimp or canned/dried fish	0.88 (0.74,1.04)	0.87 (0.72,1.03)	0.113
Any fish	0.92 (0.78,1.09)	0.91 (0.77,1.09)	0.312
Milk or soy milk	0.83 (0.65,1.05)	0.84 (0.65,1.08)	0.165
Tofu	0.89 (0.58,1.34)	0.87 (0.52,1.45)	0.600
Red meat	1.01 (0.80,1.27)	0.98 (0.77,1.25)	0.852
Chicken	0.94 (0.68,1.30)	0.86 (0.61,1.21)	0.383
Yoghurt	0.87 (0.76,1.00)	0.82 (0.70,0.96)	0.016
Butter and/or cheese	0.91 (0.68,1.22)	0.83 (0.60,1.14)	0.249
Fruit	0.61 (0.42,0.88)	0.57 (0.39,0.85)	0.006
Vegetables	0.81 (0.59,1.12)	0.77 (0.55,1.07)	0.122
Legumes	0.81 (0.67,0.99)	0.82 (0.67,1.02)	0.070
Wholegrain products	0.93 (0.79,1.08)	0.91 (0.78,1.07)	0.267
Ages 11–15 years			
Fresh fish	1.04 (0.88,1.22)	1.05 (0.88,1.25)	0.598
Shrimp or canned/dried fish	0.98 (0.83,1.16)	0.98 (0.82,1.17)	0.812
Any fish	1.01 (0.85,1.19)	1.01 (0.84,1.21)	0.928
Milk or soy milk	0.94 (0.76,1.16)	0.97 (0.78,1.21)	0.770
Tofu	0.86 (0.60,1.23)	0.84 (0.55,1.30)	0.438
Red meat	1.01 (0.78,1.29)	0.98 (0.76,1.28)	0.901
Chicken	1.03 (0.72,1.49)	0.96 (0.66,1.39)	0.809
Yoghurt	0.84 (0.73,0.96)	0.79 (0.67,0.92)	0.003
Butter and/or cheese	0.95 (0.67,1.33)	0.88 (0.60,1.28)	0.488
Fruit	0.61 (0.41,0.90)	0.58 (0.39,0.87)	0.009
Vegetables	0.78 (0.55,1.12)	0.75 (0.52,1.09)	0.134
Legumes	0.74 (0.60,0.91)	0.74 (0.59,0.92)	0.008
Wholegrain products	0.98 (0.83,1.16)	0.98 (0.83,1.17)	0.853
Ages 16–20 years			
Fresh fish	0.99 (0.85,1.16)	1.02 (0.86,1.20)	0.856
Shrimp or canned/dried fish	0.88 (0.74,1.04)	0.87 (0.72,1.04)	0.116
Any fish	0.99 (0.84,1.17)	1.00 (0.84,1.19)	0.991
Milk or soy milk	0.84 (0.70,1.00)	0.84 (0.70,1.01)	0.062
Tofu	0.96 (0.73,1.25)	0.93 (0.69,1.25)	0.641
Red meat	1.05 (0.83,1.33)	1.04 (0.81,1.33)	0.772
Chicken	1.04 (0.75,1.46)	1.00 (0.70,1.42)	0.995
Yoghurt	0.87 (0.76,1.01)	0.84 (0.72,1.02)	0.033
Butter and/or cheese	1.02 (0.72,1.44)	0.95 (0.66,1.38)	0.802

	Model 1 ² aOR [95% CI]	Model 2 ³ aOR [95% CI]	P ⁴
Fruit	0.64 (0.44,0.93)	0.63 (0.43,0.92)	0.018
Vegetables	0.85 (0.58,1.25)	0.87 (0.58,1.30)	0.495
Legumes	0.80 (0.65,0.99)	0.81 (0.65,1.01)	0.059
Wholegrain products	0.92 (0.76,1.12)	0.91 (0.74,1.12)	0.386

¹ aORs are for frequency of consumption using three groups (never or less than once a month, 1–3 times a month, weekly or more). The categories were used as a continuous variable since the intervals between these three groups were linearly related to the outcome. Compared with never or less than once a month, the aORs represent the amount of decrease or increase in likelihood of being classified as a case for consumption 1–3 times a month and consumption weekly or more.

² Adjusted for sex and age.

³ Adjusted for sex, age, education, race, smoking, family history of multiple sclerosis and history of infectious mononucleosis.

⁴ *p* values for the multivariable regressions were estimated using robust standard errors.

aOR, adjusted odds ratio; CI, confidence interval