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Nutritional factors in the aetiology of multiple sclerosis: a case-control study in Montreal, Canada

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Background It has been suggested that nutrition and food patterns, particularly high consumption of animal fat and low intake of fish products, may play a role in the aetiology of multiple sclerosis (MS).

Methods The relation between nutritional factors and MS was studied among 197 incident cases and 202 frequency matched controls in metropolitan Montreal during 1992–1995. Dietary information was collected by employing a 164-item food frequency questionnaire in a face-to-face interview.

Results An inverse association was observed between high body mass index (BMI) and the risk of MS, with an odds ratio (OR) of 0.76 (95% confidence interval [CI] : 0.61–0.95), per 5-unit increase in BMI, both sexes combined. In addition, taller women showed a greater risk for MS; the OR per 10 cm increase in height was 1.58 (95% CI : 1.06–2.35). In continuous variable analyses, using the difference between the lowest and highest quartile of intake as a unit, a positive association was observed with energy and animal fat intake. The OR per 897 kcal increase was 2.03 (95% CI : 1.13–3.67) and 1.99 (95% CI : 1.12–3.54) per 33 g of animal fat intake above the baseline. A significant protective effect was observed with other nutrients, including vegetable protein, dietary fibre, cereal fibre, vitamin C, thiamin, riboflavin, calcium, and potassium. Similar trends were seen for males and females when analysed separately. With respect to specific foods (as opposed to nutrients), a higher intake of fruit juices was inversely associated with risk (OR = 0.82; 95% CI : 0.74–0.92). A protective effect was also observed with cereal/breads intake for all cases combined (OR = 0.62; 95% CI : 0.40–0.97) and for fish among women only; pork/hot dogs (OR = 1.24; 95% CI : 1.02–1.51) and sweets/candy (OR = 1.29; 95% CI : 1.07–1.55) were positively associated with risk.

Conclusion The study generally supports a protective role for components commonly found in plants (fruit/vegetables and grains) and an increased risk with high energy and animal food intake.

Keywords Multiple sclerosis, case-control, nutrition, epidemiology

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To date, little is known about the aetiology of multiple sclerosis (MS). The onset of this disease is generally after puberty, reaching its peak incidence at age 30.[1] The literature suggests a higher incidence in women than in men (3:2 ratio), in whites compared to blacks (2:1 ratio), and rare occurrence in oriental populations.[1-3] Geographical clusters of MS have been reported in areas where goitre is endemic, in regions with low soil selenium and iodine concentration,[5] exposure to some heavy metals,[6] and a high latitude.[4,5,7]

Although a role for genetic factors is suggested by a 10–50 fold greater incidence of MS in relatives of MS patients,

variations in its prevalence across continents and alteration in the risk of acquiring MS among children of immigrants to reflect the rates of the adoptive country[3,4] suggest a role of lifestyle and local environmental factors.[8] Increased risk has been associated with viral infections,[9] higher socioeconomic status,[10] and dietary habits which characterize over-nutrition.[1,11] Most reports on MS and nutritional factors are based on ecologic correlation studies[12,14–21] and suggest an association with some nutrients and foods such as elevated intakes of energy and animal fats, (particularly saturated fats), milk and oats. In a correlation analysis, Esparza *et al.*[12] using data from the food balance sheets of the United Nations Food and Agriculture Organization (FAO) for the period 1979–1981, found significant positive and independent correlations of MS mortality with saturated fatty acids, animal fat, animal minus fish fat, and latitude. In a case-control study conducted in Italy by Tola *et al.*[13] cases had higher intakes of bread, pasta, butter and lard, legume soup, horse flesh, and caffeine-containing beverages such as coffee and tea, before the age of 15. During adulthood (after 15 years of age), however, eggs (odds ratio [OR] = 5.95), wine (OR = 0.37) and mineral water (OR = 0.30) distinguished cases and controls. Age at exposure has also been reported to be of importance by Hutter[22] who suggested that the influence of sunlight and diet may be of greatest importance during the first two decades of life. There is very little in the literature on observational studies carried out in North America on diet and MS. We have carried out a case-control study of dental amalgam, nutrition and sociodemographic factors and MS. The present article shows the results of this study which was conducted with validated dietary methods, to explore the role of nutritional factors in the aetiology of this disease.

Methods

Case ascertainment

Incident MS cases, resident in greater Montreal and diagnosed between January 1991 to December 1994, were identified with the collaboration of the MS Association of Montreal East, neurologists, and general physician referrals. Announcements were also placed regularly in city newspapers in order to reach other individuals diagnosed with MS during this period. These notices were issued six times during the course of the study, and similar announcements were run on some local radio stations. Eligible incident cases were contacted by phone, and upon informed consent were visited at home and interviewed.

A total of 353 MS cases were identified during the study period. Of these, 87 (24.6%) were not eligible because of incorrect diagnosis or because they were prevalent cases. The remaining 266 (75.4%) eligible subjects were followed up. Of these, 11 (4.1%) declined to participate and 52 (19.5%) were not interviewed because of poor health, loss of contact, or refusal of the physician to issue permission to contact the patient. Finally, six cases (2.3%) were excluded after the interview because of incorrect diagnosis. We were therefore able to interview 197 subjects (74.1%) of the eligible cases.

Control ascertainment

Controls were drawn at random from the general population, and frequency matched to the cases by age (5 years age group), sex and phone number. The controls were identified through random digit dialling (RDD), using the first three digits of the phone number of the cases.[23] Controls were selected from the telephone directory in which the corresponding cases were listed (all patients studied had a listed telephone number: only 1% of families in the Montreal region do not have a telephone). A page from the telephone directory was randomly selected from the sampling frame and the names and addresses of 10 individuals with the same first three-digit telephone numbers as the cases were selected. These residences were then contacted by a letter explaining the aims of the study. Approximately one week later these residences were telephoned to see if they contained an individual who matched the cases for age and sex and who agreed to be interviewed. If so, an interview was arranged at the control's home. If not, the procedure was repeated. If more than one eligible control was reached at a given number, this information was kept in a databank for further use. Non-residential numbers were discarded and a 'no answer' number was redialled up to eight times at various points in time, day and night, weekday and weekend, before being rejected. As with the cases, controls were also contacted by a letter and those who assented were interviewed at home. We contacted a total of 236 population-based controls. Of these, 202 (85.6%) eligible controls were interviewed. The remaining 34 (14.4%) were not interviewed for the following reasons: wrong age group or area of residence, poor health, language problems or refusal to participate (only five subjects).

Questionnaire

Trained interviewers administered a modified version of the health and sociodemographic questionnaire developed in our Unit for numerous case-control studies of diet and chronic disease. The forms have been designed to assess information (about 150 items) on such variables as sociodemographics, anthropometrics, occupational and medical history, family history of several chronic diseases, tobacco and alcohol consumption as well as physical activity. Weight and height at diagnosis were self reported.

A 164-item food frequency questionnaire (FFQ), designed by the Epidemiology Unit of the National Cancer Institute of Canada (NCIC), mainly for epidemiological studies of diet and cancer, was employed to determine usual dietary intakes during the year prior to the interview (prior to diagnosis). This questionnaire was first evaluated by a self-administered method[24,25] and validated more recently against a 7-day food record and a lengthy diet history questionnaire.[26] The questionnaire asks for the accurate frequency of consumption of various foods per day, week or month, in the year before diagnosis of cases, or one year before interview for controls. It contains three sets of pictures of foods in terms of small, medium and large portions of rice, meat and chicken to help visualize portions consumed. Interviews took place at the homes of the participants or at the Hôtel-Dieu Hospital in Montreal. Cases and controls gave their written consent to being interviewed and permission to consult their neurologist to confirm diagnosis, and dentist for their dental amalgam record.

Dietary analysis

Food intakes were calculated by multiplying the reported serving size of each food consumed by its density and daily consumption frequency. Individual nutrient intakes were

calculated using a database based on Handbook No. 8 of the US Department of Agriculture, USDA,[27] modified and expanded for Canadian foods. Dietary variables were restricted to 28 nutrients and alcohol, as well as the separate contributions of 23 individual foods or food groups. These nutrients represented major sources of energy and components of fat as a suggested risk factor, as well as vitamins and minerals. In this study the supplementary vitamins and minerals intake are not included in statistical analysis.

Statistical methods

Odds ratios (OR) were calculated from logistic regression models to estimate the risk of developing MS with each dietary variable and with physical measures of weight and height. Unconditional rather than conditional logistic regression analyses were performed due to frequency matching of controls rather than individual matching. Body mass was computed by weight (kg)/height^2 (m). In continuous variable analyses, the OR represents the risk for each one 'unit' increase in the variable compared to a baseline risk of 1.00 for the same amount of variable. A 'unit' refers to the amount of nutrient per day or the amount of body measure for which risk is estimated. For nutrients, one 'unit' was equivalent to the difference between the 75th percentile and the 25th percentile level of intake. For other variables, unit size is specified in the Tables. For foods and food groups, it was 100 g. Because of the skewed nature of dietary variables, in continuous variable analyses, the 'unit' of variable was log-transformed before performing regression analysis. Arithmetic means of daily nutrient intakes and some other variables are preferably included over geometric means because their standard deviations are more meaningful. Both trends in risk with exposure (parameter estimate of slope), and relative odds by category (in quartiles) for selected nutrients were examined.

All non energy-contributing nutrients were adjusted for 'total energy' in regression models utilizing the standard method of energy adjustment.[28] Energy-contributing nutrients were adjusted by the partition method for 'other sources of energy', that is the calculated difference between total energy and energy from the nutrient being examined.[29] Body mass index (BMI) was included in all dietary models since it was associated with most dietary variables as well as with MS.

Continuous variable analyses were performed for all subjects as well as for males and females separately. However, categorical analysis was undertaken only on all subjects due to the very small number of males in the study.

Results

The study included 197 cases and 202 controls matched for age and sex. Table 1 outlines the mean age, physical characteristics, and daily intakes of various nutrients for cases and controls. In total, 61 male and 136 female cases, and 64 male and 138 female controls were evaluated. There were no statistically significant differences between the mean age, weight and height of cases and controls. The cases had a significantly lower BMI than the controls ($P = 0.01$).

Table 2 shows the risk of developing multiple sclerosis per unit of various nutrients (log-transformed). A higher energy intake (OR = 2.03; 95% CI : 1.13–3.67), and animal fat intake (OR = 1.99; 95% CI : 1.12–3.54) are significantly positively associated with the risk in 'all' subjects. The trend is similar for males and females. Higher intakes of vegetable protein, dietary fibre especially fibre from cereals, vitamin C, thiamin, riboflavin, calcium and potassium were negatively associated with the risk. When any of the three types of fats (saturated fat, animal fat, or total fat) were examined in multivariate analyses, in separate models along with dietary fibre, thiamin, riboflavin, vitamin C, calcium, and potassium, and adjusted for BMI and 'other energy', each remained a significant risk factor. The OR for saturated fat was 3.94 (95% CI : 1.25–12.46, $P = 0.02$), for animal fat it was 5.27 (95% CI : 2.10–13.22, $P = 0.0004$), and for total fat it was 3.37 (95% CI : 1.01–11.23, $P = 0.05$) in separate multivariate models in 'all' subjects. In the same models, calcium and thiamin remained significant protective factors with OR around 0.17 for thiamin and 0.20 for calcium ($P < 0.02$).

Similar findings were observed in the categorical analyses. Table 3 shows the risk of MS associated with the intake of certain nutrients by quartiles for all subjects combined. There was a negative linear trend between dietary fibre intake and the risk of MS (P for trend 0.004). The same pattern was also observed for vitamin E ($P = 0.06$), thiamin ($P = 0.003$), vitamin C ($P = 0.001$), riboflavin ($P = 0.0005$), potassium ($P = 0.008$) and calcium intake ($P = 0.0003$).

Table 4 depicts the risk of MS per 100-g unit intakes of various foods or food groups. The meat group, consisting of pork, ham, luncheon meat, hot dogs, sausages or other processed meats, augmented risk in all subjects (OR = 1.24; 95% CI : 1.02–1.52). Sweets (candy, jam, jelly, chocolate) in females only (OR = 1.29; 95% CI : 1.07–1.55) also appeared to favour an increased risk of MS. However, fruit juices among all participants (OR = 0.82; 95% CI : 0.74–0.92), margarine (OR = 0.73; 95% CI : 0.55–0.96) intake in males, and cereal/bread in all subjects (OR = 0.62; 95% CI : 0.40–0.97), and in males alone (OR = 0.26; 95% CI : 0.10–0.70) were significantly protective.

Discussion

There is insufficient literature on North American observational studies looking at nutrition and MS to permit meaningful comparisons of results with this study. This study was characterized by a low refusal rate by both cases and controls, and listed telephone numbers for the vast majority of the target population in the phone directory, which diminishes the possibility of a selection bias important enough to invalidate our results. The number of cases identified for this study was also close to the numbers expected in the study area for the period of the study. However there are some inherent limitations in the assessment of past diet. Not only are there inaccuracies in recall of past diet by any method but there are large intra-individual variations in diet which make the process of characterizing typical diet for an individual rather difficult. In addition, the presence of disease before its diagnosis may have altered dietary preference among cases. Not much is known about the preferential food habits of MS patients at present. The study, however, employed a validated food frequency questionnaire and standard data collection and processing techniques used by us in several previous studies.

The findings of a lower BMI among cases indicates perhaps individuals with lower BMI are at higher risk of developing MS,

Table 1 Means of age, physical characteristics and daily nutrient intakes for cases and controls, Montreal 1992–1995

	Males				Females			
	Cases (n = 61)		Controls (n = 64)		Cases (n = 136)		Controls (n = 138)	
Variable	Mean	± SD	Mean	± SD	Mean	± SD	Mean	± SD
Age, years	42.2	9.7	41.3	10.1	37.5	9.5	38.1	10.0
Weight, kg	77.5	15.5	79.3	14.9	60.0	11.2	62.3	12.5
Height, cm	175.4	5.4	175.6	6.6	163.2	6.4	161.5	5.8
Body mass index*	25.2	4.9	25.7	4.2	22.5	4.1	23.9	4.7
Energy, kcal	3312	1491	2904	887	2550	918	2358	730
Protein, g	128.3	75.8	108.5	35.2	98.0	36.3	95.6	31.2
Carbohydrates, g	348.0	150.9	335.7	106.3	299.0	115.3	277.6	99.9
Total fat, g	142.0	69.9	120.2	45.3	106.8	43.5	97.4	33.7
Saturated fat, g	54.6	27.8	44.8	18.0	40.6	17.7	36.2	13.3
Oleic acid, g	57.1	28.3	48.6	18.3	41.9	17.0	38.5	13.7
Linoleic acid, g	15.6	10.6	14.7	7.4	12.7	6.4	12.1	5.9
Cholesterol, mg	560.6	285.1	450.1	177.2	404.2	193.6	373.3	143.2
Animal fat, g	97.3	48.5	76.8	34.2	70.2	32.6	62.4	25.0
Vegetable fat, g	44.5	29.8	43.1	20.4	36.0	16.6	34.4	19.2
Animal protein, g	94.4	68.0	75.6	31.3	70.0	31.0	67.2	26.1
Vegetable protein, g	33.5	12.3	32.6	10.0	27.8	9.8	28.1	11.8
Dietary fibre, g	24.2	10.0	24.7	9.2	22.5	8.8	22.8	9.8
Vegetable fibre, g	8.4	4.7	7.7	4.3	8.1	3.7	8.3	3.8
Fruit fibre, g	4.6	4.6	4.9	3.8	5.2	3.7	5.1	3.4
Cereal fibre, g	9.7	4.7	11.1	6.2	8.1	4.3	8.1	4.2
Vitamin A, IU	9730.0	4450.9	9056.4	4678.8	9899.5	4996.9	9898.7	4622.8
Retinol, IU	2593.9	1514.7	2186.2	1746.2	1901.8	1176.8	1953.8	1491.0
Beta carotene, IU	5477.4	2824.5	5333.7	3179.6	6285.3	3763.9	6225.6	3249.6
Vitamin E, mg	25.8	13.7	24.0	9.1	21.8	10.3	20.6	8.7
Vitamin C, mg	210.5	117.9	232.1	143.1	230.1	121.5	253.0	126.8
Thiamin, mg	1.9	0.7	1.8	0.7	1.6	0.6	1.6	0.6
Riboflavin, mg	2.7	1.2	2.5	1.0	2.3	0.9	2.4	0.9
Niacin, mg	31.2	21.4	24.7	7.9	23.0	8.5	22.0	7.7
Calcium, mg	1142.4	577.5	1131.0	462.9	1041.8	498.1	1090.3	465.9
Iron, mg	19.9	7.9	18.5	6.1	16.5	5.4	16.2	5.2
Potassium, mg	4614.4	1815.2	4331.9	1289.0	4120.2	1328.6	4097.3	1323.9
Total sugar, g	124.2	66.4	120.2	51.5	117.8	54.7	109.1	45.8
Alcohol, g	23.1	37.6	12.6	17.2	6.8	15.4	5.6	7.9

* $P = 0.01$.

although the results do not reach statistical significance in men due to small sample size. To what extent this is a real association is not clear. It is possible that the presence of disease may have contributed to a hypermetabolic state and consequent lowering of body weight. However, it is the greater height and not the weight that appears to be the feature distinguishing cases from controls.

A high energy intake appears to be a risk factor for MS in this study, with animal fat contributing to most of this effect. Again, whether this is a real effect or a consequence of a hypermetabolic state, is difficult to say. The subclinical phase of MS may have been present for several years and may have affected the intake of foods among cases in a selective manner. It is possible that high energy and high animal fat foods may have been differentially favoured by cases compared to controls. However, a concomitant increase in animal protein intake (if high energy animal foods were preferred) does not appear to be apparent among all subjects combined or among women. When looking for biological plausibility, attention has been directed specifically at fats since the myelin sheath, the target of disease, is mainly composed of lipids, and the imbalance in the proportion of saturated to unsaturated fatty acids is purported to affect susceptibility to demyelinating agents.[30] The protective effect of polyunsaturated fatty acids, particularly linoleic acid, perhaps due to its immuno-suppressive action, has prompted clinical trials on PUFA supplementation.[31] A non-significant decreased risk was observed in this study with linoleic acid intake in the continuous variable analysis, but none in the categorical

Table 2 Risk of multiple sclerosis per unit of age, physical characteristics and daily nutrient intakes, Montreal 1992–1995

Variable	Unit[a]	All subjects (197 cases/202 controls) Odds ratio[b] (CI)[c]	P	Males (61 cases/64 controls) Odds ratio[b] (CI)[c]	P	Females (136 cases/138 controls) Odds ratio[b] (CI)[c]	P
Age[d], years	10	0.99 (0.81–1.21)		1.10 (0.77–1.58)		0.95 (0.74–1.21)	
Weight[d], kg	10	0.91 (0.79–1.03)		0.92 (0.73–1.67)		0.84 (0.69–1.04)	
Height[d], cm	10	1.15 (0.91–1.44)		0.96 (0.53–1.73)		1.58 (1.06–2.35)	0.02
Body mass index[d]	5	0.76 (0.61–0.95)	0.02	0.88 (0.60–1.31)		0.69 (0.52–0.92)	0.01
Energy, kcal	897	2.03 (1.13–3.67)	0.02	2.59 (0.87–7.73)		1.82 (0.86–3.88)	
Protein, g	37	0.52 (0.18–1.44)		1.53 (0.23–10.11)		0.33 (0.10–1.14)	
Carbohydrates, g	115	0.73 (0.36–1.48)		1.24 (0.05–1.07)		1.11 (0.48–2.59)	
Total fat, g	44	1.71 (0.75–3.90)		2.29 (0.56–9.37)		1.57 (0.55–4.47)	
Saturated fat, g	17	1.88 (0.81–4.36)		2.51 (0.59–10.70)		1.80 (0.61–5.31)	
Oleic acid, g	18.15	1.12 (0.43–2.89)		1.58 (0.31–8.05)		0.99 (0.29–3.39)	
Linoleic acid, g	6.64	0.73 (0.40–1.33)		0.40 (0.12–1.33)		0.89 (0.44–1.79)	
Cholesterol, mg	19	1.55 (0.72–3.34)		3.59 (0.89–14.45)		1.02 (0.40–2.64)	
Animal fat, g	32.64	1.99 (1.12–3.54)	0.02	3.18 (1.09–9.26)	0.03	1.68 (0.83–3.42)	
Vegetable fat, g	22.33	0.84 (0.52–1.36)		0.48 (0.19–1.18)		1.07 (0.59–1.92)	
Animal protein, g	21.6	0.93 (0.47–1.85)		1.77 (0.51–6.12)		0.68 (0.29–1.59)	
Vegetable protein, g	14.3	0.38 (0.17–0.84)	0.02	0.34 (0.07–1.56)		0.38 (0.14–0.99)	0.05
Dietary fibre, g	12.19	0.54 (0.29–1.00)	0.05	0.43 (0.14–1.29)		0.62 (0.28–1.34)	
Vegetable fibre, g	4.75	0.84 (0.53–1.33)		1.15 (0.53–2.52)		0.66 (0.36–1.21)	
Fruit fibre, g	4.81	0.93 (0.76–1.14)		0.87 (0.64–1.18)		1.00 (0.75–1.34)	
Cereal fibre, g	5.57	0.57 (0.36–0.91)	0.02	0.26 (0.09–0.70)	0.008	0.77 (0.44–1.34)	
Vitamin A, IU	5882	0.88 (0.55–1.41)		1.09 (0.47–2.53)		0.80 (0.44–1.45)	
Retinol, IU	1491	1.11 (0.79–1.57)		1.61 (0.86–3.00)		0.96 (0.63–1.46)	
Beta carotene, IU	3849	0.86 (0.58–1.29)		0.88 (0.42–1.86)		0.85 (0.51–1.40)	
Vitamin E, mg	13.24	0.78 (0.41–1.48)		0.53 (0.18–1.58)		0.95 (0.43–2.11)	
Vitamin C, mg	162	0.58 (0.38–0.87)	0.008	0.56 (0.27–1.15)		0.57 (0.34–0.96)	0.03
Thiamin, mg	0.66	0.24 (0.09–0.65)	0.005	0.25 (0.04–1.58)		0.23 (0.07–0.80)	0.02
Riboflavin, mg	1.3	0.33 (0.16–0.68)	0.003	0.52 (0.15–1.81)		0.25 (0.09–0.63)	0.004
Niacin, mg	8.87	1.67 (0.63–4.43)		12.46 (1.67–92.88)	0.01	0.75 (0.23–2.41)	
Calcium, mg	633	0.39 (0.22–0.70)	0.002	0.46 (0.17–1.23)		0.35 (0.16–0.73)	0.006
Iron, mg	6.88	0.40 (0.13–1.28)		0.59 (0.09–3.88)		0.33 (0.07–1.45)	
Potassium, mg	1670	0.29 (0.10–0.86)	0.03	0.41 (0.07–2.54)		0.20 (0.05–0.87)	0.03
Total sugar, g	60.35	0.75 (0.43–1.33)		0.61 (0.25–1.50)		0.85 (0.39–1.86)	
Food weight, g	1075	1.56 (0.66–3.90)		2.59 (0.95–7.14)		1.74 (0.83–3.67)	
Alcohol, g	10.4	1.01 (0.91–1.12)		1.03 (0.87–1.23)		1.01 (0.89–1.15)	

[a] Unit = for nutrients, units are the difference between upper and lower quartile cut points for all controls.

[b] Each line represents a separate model. Odds ratios for all non energy-contributing nutrients are adjusted for total energy and body mass index. Odds ratios for all energy-contributing nutrients are adjusted for 'energy from other nutrients' and body mass index.

[c] CI = 95% confidence intervals.

[d] No log transformation.

Note: items underlined are statistically significant.

analysis. The increasing risk of MS with a high animal and saturated fat intake, as observed in this study, is consistent with findings from other studies.[12] It is postulated that an excess of saturated fatty acids could be responsible for modifying the stability of the myelin sheath or for increasing platelet aggregation, with hypoxia in the microcirculation in the central nervous system and subsequent perivascular demyelinization.[32]

This study shows a protective effect of dietary patterns contributing to higher levels of dietary fibre, vegetable protein, vitamin C, vitamin E, thiamin, riboflavin, calcium, and potassium, which are consistent with benefits of similar dietary patterns in reducing risk for cancer or cardiovascular diseases. These factors may be involved in the regulatory process of the nervous system, or act as an antioxidant. The study generally supports a protective role for components commonly found in plants (fruit/vegetables and grains) and an increased risk with high energy and animal food intake. However, further investigations in similar populations are required to confirm which

Table 3 Risk of multiple sclerosis associated with the intake of selected nutrients by quartiles[a] for all subjects combined, Montreal 1992–1995

Nutrient[b]		Exposure category Q1	Q2	Q3	Q4	*P* for trend
Total energy, kcal	OR	1.00	0.89	0.68	1.65	
	95% CI[c]		(0.50–1.59)	(0.37–1.24)	(0.96–2.82)	0.08
Total fat, g	OR	1.00	1.47	0.89	1.81	
	95% CI		(0.81–2.67)	(0.47–1.71)	(0.88–3.73)	0.30
Saturated fat, g	OR	1.00	0.96	0.96	1.60	
	95% CI		(0.52–1.76)	(0.51–1.82)	(0.77–3.33)	0.25
Animal fat, g	OR	1.00	1.50	1.03	2.11*	
	95% CI		(0.83–2.72)	(0.55–1.93)	(1.09–4.07)	0.08
Total protein, g	OR	1.00	0.73	0.32***	0.70	
	95% CI		(0.41–1.31)	(0.16–0.64)	(0.32–1.53)	0.12
Vegetable protein, g	OR	1.00	0.67	0.66	0.29**	
	95% CI		(0.38–1.21)	(0.36–1.23)	(0.13–0.63)	0.006
Dietary fibre, g	OR	1.00	0.82	0.61	0.38**	
	95% CI		(0.47–1.43)	(0.34–1.11)	(0.19–0.75)	0.004
Vitamin A, IU	OR	1.00	0.94	1.03	0.75	
	95% CI		(0.53–1.67)	(0.58–1.84)	(0.40–1.40)	0.46
Retinol, IU	OR	1.00	0.56	1.19	0.88	
	95% CI		(0.30–1.05)	(0.68–2.10)	(0.48–1.60)	0.76
Beta carotene, IU	OR	1.00	1.16	0.72	0.87	
	95% CI		(0.66–2.04)	(0.40–1.30)	(0.48–1.58)	0.36
Vitamin E, mg	OR	1.00	0.70	0.65	0.49*	
	95% CI		(0.39–1.25)	(0.36–1.19)	(0.24–1.00)	0.06
Thiamin, mg	OR	1.00	0.73	0.40**	0.36**	
	95% CI		(0.41–1.31)	(0.21–0.76)	(0.17–0.78)	0.003
Vitamin C, mg	OR	1.00	0.69	0.55**	0.37***	
	95% CI		(0.40–1.19)	(0.31–0.98)	(0.20–0.69)	0.001
Riboflavin, mg	OR	1.00	0.67	0.44**	0.29***	
	95% CI		(0.38–1.18)	(0.24–0.82)	(0.14–0.61)	0.0005
Niacin, mg	OR	1.00	1.15	0.97	1.02	
	95% CI		(0.63–2.08)	(0.51–1.82)	(0.48–2.17)	0.91
Potassium, mg	OR	1.00	0.32***	0.44**	0 33**	
	95% CI		(0.18–0.61)	(0.24–0.82)	(0.15–0.72)	0.08
Calcium, mg	OR	1.00	0.64	0.43**	0.29***	
	95% CI		(0.36–1.13)	(0.23–0.79)	(0.15–0.59)	0.0003

[a] Cut points for quartiles: total energy 1952, 2427, 2848 kcal; total fat 74.72, 99.37, 122.58 g; saturated fat 27.94, 36.15, 45.46 g; animal fat 46.59, 63.54, 80.79 g; total protein 76.9, 95.6, 114.2 g; vegetable protein 21.7, 27.4, 40.0 g; dietary fibre 16.78, 22.26, 28.80 g; vitamin A 6120, 8949, 12 124 IU; retinol 1067, 1916, 2559 IU; beta carotene 3589, 5569, 7438 IU; vitamin E 14.68, 20.34, 27.71 mg; thiamin 1.28, 1.60, 1.93 mg; vitamin C 156.38, 227.60, 309.87 mg; riboflavin 1.75, 2.27, 3.00 mg; niacin 17.52, 21.71, 26.38 mg; potassium 3317, 3912, 4902 mg, calcium 765, 1047, 1353 mg.

[b] Each line represents a separate model. Odds ratios for all non energy-contributing nutrients are adjusted for total energy and body mass index. Odd ratios for all energy-contributing nutrients are adjusted for 'energy from other nutrients' and body mass index.

[c] CI = 95% confidence intervals.

* $P < 0.05$; ** $P < 0.01$; *** $P < .001$.

factors consistently contribute to increased or decreased risk of developing MS. This study was somewhat exploratory in nature due to a lack of sufficient published studies to generate a priori hypotheses. A large number of findings did not reach statistical significance due to small sample size, but it confirms a possible role of dietary factors in the causation of MS.

Acknowledegments

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Table 4 Risk of multiple sclerosis per 100 grams of foods per day (log transformed), Montreal 1992–1995

	All subjects (197 cases/202 controls)		Males (61 cases/64 controls)		Females (136 cases/138 controls)	
Variable	Odds ratio[a] (CI)[b]	*P*	Odds ratio[a] (CI)[b]	*P*	Odds ratio[a] (CI)[b]	*P*
Milk	0.95 (0.87–1.05)		0.99 (0.84–1.18)		0.93 (0.83–1.05)	
Yogurt	0.96 (0.87–1.06)		0.97 (0.81–1.16)		0.95 (0.84–1.09)	
Coffee	1.07 (0.99–1.16)		1.08 (0.93–1.25)		1.07 (0.98–1.17)	
Juice	0.82 (0.74–0.92)	0.0006	0.70 (0.54–0.90)	0.006	0.87 (0.76–0.98)	0.02
Cheese	0.90 (0.74–1.08)		0.84 (0.59–1.19)		0.92 (0.74–1.16)	
Egg	0.85 (0.69–1.04)		0.94 (0.65–1.38)		0.81 (0.63–1.04)	
Pasta/pizza	1.03 (0.82–1.30)		0.99 (0.58–1.69)		1.05 (0.81–1.36)	
White root veg.	1.13 (0.88–1.44)		0.86 (0.55–1.33)		1.29 (0.95–1.77)	
Red root veg.	0.94 (0.78–1.13)		0.91 (0.66–1.26)		0.95 (0.76–1.19)	
Cruciferous veg.	0.94 (0.80–1.12)		1.04 (0.79–1.37)		0.89 (0.72–1.10)	
Peas	0.95 (0.80–1.13)		1.01 (0.76–1.35)		0.92 (0.75–1.14)	
Other veg.	0.95 (0.76–1.18)		1.10 (0.73–1.67)		0.90 (0.68–1.18)	
Butter	0.96 (0.82–1.12)		1.15 (0.89–1.49)		0.86 (0.71–1.06)	
Margarine	0.96 (0.82–1.12)		0.73 (0.55–0.96)	0.02	1.09 (0.90–1.33)	
Oils	0.89 (0.73–1.10)		1.49 (0.78–1.67)		0.80 (0.62–1.03)	
Beef	1.10 (0.88–1.36)		1.18 (0.81–1.73)		1.05 (0.80–1.37)	
Pork, hot dog, etc.	1.24 (1.02–1.51)	0.03	1.29 (0.93–1.80)		1.21 (0.94–1.55)	
Fish	0.91 (0.78–1.05)		1.08 (0.84–1.40)		0.83 (0.69–1.00)	0.05
Cereal/breads	0.62 (0.40–0.97)	0.04	0.26 (0.10–0.70)	0.008	0.86 (0.50–1.48)	
Cakes	0.88 (0.75–1.04)		0.77 (0.58–1.03)		0.95 (0.77–1.17)	
Fruits	0.97 (0.81–1.15)		0.85 (0.65–1.11)		1.08 (0.84–1.37)	
Sweets	1.12 (0.97–1.30)		0.83 (0.63–1.10)		1.29 (1.07–1.55)	0.007
Chicken	0.86 (0.67–1.10)		0.74 (0.44–1.23)		0.88 (0.67–1.16)	
Stew	0.96 (0.83–1.10)		1.02 (0.81–1.29)		0.92 (0.77–1.09)	

[a] Odds ratios for all foods are adjusted for total energy and body mass index.

[b] CI = 95% confidence intervals

Note: items underlined are statistically significant.

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