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Dietary patterns and schizophrenia: a comparison with healthy controls

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Background: It has been reported that the onset of schizophrenia and the physical complications after its onset are related to diet. Diet has been considered as a variable factor of the pathogenesis of schizophrenia. However, the results of studies on this relationship have been inconsistent. Nutrients are consumed as a mixture in the diet. It is difficult to study them in isolation because they may have mutually complementary effects. The aim of this study was to assess the association between dietary patterns and schizophrenia in Japan.

Methods: The subjects comprised 237 outpatients aged 30–60 years (123 males and 114 females) with diagnoses of either schizophrenia or schizoaffective disorder. The patient diagnoses were determined based on medical records. Patients were recruited between June 2011 and August 2011. As a reference group, 404 healthy volunteers aged 30–60 years (158 males and 246 females) were also included. Demographic data (age, sex, and level of education) were collected by face-to-face method interviews and self-administered questionnaires. We assessed eating habits over the last month using a validated brief self-administered diet history questionnaire. We detected dietary patterns through a principal component analysis of calorie-adjusted intake; two principal components were retained. The principal components for each dietary pattern and for each individual were divided into tertiles by principal component scores.

Results: We derived two dietary patterns by principal component analysis; namely, the "vegetable" dietary pattern and the "cereal" dietary pattern. In the "cereal" dietary pattern, the high tertile was associated with a significantly increased risk of schizophrenia ($P<0.001$).

Conclusion: The "cereal" dietary pattern is associated with schizophrenia. This article is the first to describe a study examining the association of dietary pattern and schizophrenia.

Keywords: schizophrenia, dietary pattern, diet

Introduction

Schizophrenia is a severe mental illness that affects approximately 1% of the population worldwide.[1] Nakane et al[2] reported that prevalence rates for schizophrenia in Japan ranged from 0.19% to 1.79% and morbidity risk rates ranged from 0.35% to 2.48%. They remarked that when compared with mean values from other countries, no significant differences were observed.[2] Unsatisfactory outcomes after pharmacotherapy[3] and physical complications in patients with schizophrenia[4] suggest that the dopamine hypothesis and antipsychotic treatment are not sufficient approaches to understanding the etiology of schizophrenia.

Diet has been considered as a variable factor of the pathogenesis of schizophrenia. Previous studies have shown that physical complications and schizophrenia outcomes are related to diet.[5] Simonelli-Muñoz et al[6] showed that patients who have unhealthy dietary habits have a higher risk of obesity than patients with good dietary habits.

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Sugawara et al[7] suggested that dietary patterns (including a higher intake of protein, fat, n-3 polyunsaturated fatty acids, n-6 polyunsaturated fatty acids, and vitamins) may be related to a decreased prevalence of obesity in patients with schizophrenia. In addition, based on an ecological analysis of nutritional patterns, Peet[8] determined that a higher national dietary intake of refined sugar and dairy products predicted a worse 2-year outcome of schizophrenia.

Nutrients are consumed as a mixture in the diet. It is difficult to study them in isolation because they may have mutually complementary effects. With regard to the risk of schizophrenia, dietary patterns or combinations of foods may have a stronger association than foods or nutrients separately. We hypothesized that dietary patterns may be associated with schizophrenia.

The aim of this study was to assess the relationship between dietary patterns and schizophrenia in Japan. To our knowledge, this is the first study to examine this relationship.

Methods

Participants

The subjects comprised 237 outpatients aged 30–60 years (123 males and 114 females) diagnosed with the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition criteria of either schizophrenia or schizoaffective disorder at four psychiatric hospitals in Japan. Patient diagnoses were determined based on medical records. Patients were recruited between June 2011 and August 2011. As a reference group, 404 healthy volunteers aged 30–60 years (158 males and 246 females) who participated in the Iwaki Health Promotion Project in 2011 were also included. The study was approved by the Ethics Committee of the Hirosaki University School of Medicine, Hirosaki, Japan, and all subjects signed informed consent. Demographic data (age, sex, and level of education) were collected by face-to-face method interviews and self-administered questionnaires.

Measurements

We assessed eating habits over the last month using a validated brief self-administered diet history questionnaire (BDHQ)[9] that consisted of inquiries concerning the consumption frequency of 56 foods and beverages and nine dishes generally consumed in Japanese populations. In order to estimate the intake of calories and of selected nutrients, we used a computer algorithm for the 56 foods and beverages of the BDHQ with the Standard Tables of Food Composition in Japan.[10,11]

Statistical analyses

Dietary patterns were detected through a principal component analysis. We adopted the calorie-adjusted intake that used a density method for the 52 food and beverage items (excluding four items that overlapped with others). We determined the number of principal components to retain by eigenvalues, the scree test, and the interpretability of the factors; two principal components were retained. The principal components for each dietary pattern and for each individual were divided into tertiles by principal component scores.

The subjects with and without schizophrenia were compared using unpaired Student's *t*-tests for continuous variables or chi-squared tests for categorical variables. We assessed trend associations across the tertile categories of each dietary pattern using linear regression analysis for continuous variables and the Cochran–Armitage trend test for categorical variables, with ordinal values ranging from 1 to 3 assigned to the tertile categories of each dietary pattern.

A logistic regression analysis was carried out to evaluate the relationship between dietary patterns and schizophrenia. The model was adjusted for age and sex. The significance level for the results obtained in the hypothesis contrast was $P<0.05$. The data analysis was performed using R for Windows, Version 3.0.2 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

The demographic distribution of the participants is presented in Table 1. The number of subjects of monotherapy is 156, while the number of subjects of polypharmacy (using two or more antipsychotic agents) is 95. The subjects of polypharmacy were receiving risperidone (n=51), aripiprazole (n=25), olanzapine (n=21), blonanserin (n=26), quetiapine (n=25), haloperidol (n=41), levomepromazine (n=31), and other antipsychotic agents.

We derived two dietary patterns by principal component analysis (Table 2). The first component, which loaded green

Table 1 Demographic characteristics of the subjects

	Control (n=404)	Schizophrenia (n=237)	*P*-value
Age (years)	49.1±8.5	44.1±8.4	<0.0001
Sex (n)	Male 158, Female 246	Male 123, Female 114	0.002
Height (cm)	162.0±8.2	170.2±9.0	0.002
Weight (kg)	60.5±10.9	68.9±15.5	<0.0001
Body mass index (kg/m^2)	23.0±3.1	25.5±5.0	<0.001

Notes: The data are expressed as the mean ± standard deviation for categorical variables. The data were analyzed using nonpaired *t*-tests for continuous variables and chi-squared tests.

Table 2 Factor loading matrix for major dietary patterns identified by principal component analysis[a]

	Vegetable dietary pattern	Cereal dietary pattern
Low-fat milk	–	–
Milk	–	–
Chicken	–	–
Pork/beef	–	–
Ham/sausage/bacon	–	–
Liver	–	–
Squid/octopus/shrimp/shellfish	–	–
Small fish with bones	–	–
Canned tuna	–	–
Dried fish/salted fish	–	–
Oily fish	–	–
Lean fish	–	–
Egg	–	–
Tofu/atsuage[b]	0.528	–
Natto[c]	–	–
Potatoes	0.491	–
Picked green leafy vegetables	0.341	–
Other picked vegetables	–	–
Lettuce/cabbage	0.632	–
Green leafy vegetables	0.683	–
Cabbage/Chinese cabbage	0.689	–
Carrots/pumpkin	0.701	–
Japanese radish/turnip	0.652	–
Other root vegetables	0.714	–
Tomatoes	0.413	–
Mushrooms	0.621	–
Seaweed	0.509	–
Western-type confectioneries	–	0.477
Japanese-type confectioneries	–	0.432
Rice crackers/rice	–	0.354
Ice cream	–	0.388
Citrus fruit	–	–
Persimmons/strawberries/ kiwi fruit	0.348	–
Other fruit	–	–
Mayonnaise/dressing	0.338	–
Bread	–	0.426
Buckwheat noodles	–	–
Japanese wheat noodles	–	–
Chinese noodles	–	–
Spaghetti and macaroni	–	–
Green tea	–	–
Black tea/oolong tea	–	–
Coffee	–	–
Cola drink/soft drink	–	–
100% fruit and vegetable juice	–	–
Rice	–	–0.648
Miso soup	–	–0.513
Sake	–	–
Beer	–	–
Spirits	–	–
Whiskey	–	–
Wine	–	–

Notes: [a]Factor loading less than ±0.3 represented by a dash for simplicity; [b]deep-fried tofu; [c]fermented soybeans.

leafy vegetables, lettuce, cabbage, mushrooms, and fruit, was labeled the "vegetable" dietary pattern. The second component, which loaded rice, bread, and confectioneries, was labeled the "cereal" dietary pattern.

The characteristics of the dietary pattern scores categorized by tertiles are shown in Table 3. The subjects with higher scores for the "vegetable" dietary pattern were less likely to have schizophrenia and to be male. The "vegetable" dietary pattern was positively associated with the intake of proteins, carbohydrates, fats, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, n-3 fatty acids, and n-6 fatty acids.

The "cereal" dietary pattern was positively associated with schizophrenia ($P<0.001$). Higher scores for the "cereal" dietary pattern were positively associated with the intake of proteins, fats, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, n-3 fatty acids, and n-6 fatty acids. The "cereal" dietary pattern was negatively associated with carbohydrate intake.

The odds ratios for schizophrenia according to the tertile categories of each dietary pattern score are shown in Table 4. The "vegetable" dietary pattern was not associated with an increased risk of schizophrenia. For the "cereal" dietary pattern, the high tertile was associated with a significantly increased risk of schizophrenia.

Discussion

We designed this cross-sectional study to evaluate the relationship between dietary patterns and schizophrenia in Japan. Two dietary patterns were derived; namely, the "vegetable" and "cereal" patterns. The "vegetable" dietary pattern was characterized by a high consumption of green leafy vegetables, seaweed, potatoes, and soybean products such as tofu and natto, and positively correlated with the intake of fats and proteins. A previous study demonstrated a relationship between fatty acids and schizophrenia.[12] Therefore, we hypothesized that a dietary pattern consuming a large quantity of vegetables would be associated with a lower risk of schizophrenia morbidities. However, an apparent association was not observed between the "vegetable" dietary pattern and schizophrenia. By contrast, the "cereal" dietary pattern, which was characterized by a high consumption of rice, breads, and confectioneries and positively correlated with the intake of fats and proteins, was associated with schizophrenia. In the "cereal" pattern, schizophrenia correlated to fatty acid per calories intake.

Previous studies have demonstrated a relationship between polyunsaturated fatty acids and the pathogenesis of

Table 3 Characteristics according to tertile categories of dietary pattern scores

	Vegetable dietary pattern			Trend *P*-value[a]	Cereal dietary pattern			Trend *P*-value[a]
	Low tertile	Middle tertile	High tertile		Low tertile	Middle tertile	High tertile	
Number of subjects	214	214	213		214	214	213	
Disease (n)	91	75	71	0.049	60	73	104	<0.001
Age (years)	47.0±8.7	46.6±8.7	48.1±9.0	0.199	48.6±8.5	46.7±9.1	46.6±8.8	0.017
Sex (male, n)	151	85	45	<0.001	123	93	65	<0.001
Dietary intake								
Energy (kcal)	1,942±818	1,903±632	1,810±682	0.127	1,848±647	1,888±601	1,920±874	0.359
Protein (g/1,000 kcal)	30.4±6.0	35.7±5.3	40.6±5.7	<0.001	33.5±7.1	36.7±6.7	36.5±6.8	<0.001
Fat (g/1,000 kcal)	23.2±7.2	27.9±5.4	29.8±5.7	<0.001	22.0±5.4	27.6±5.5	31.3±5.7	<0.001
Carbohydrate (g/1,000 kcal)	144.0±22.3	138.8±17.8	135.3±18.5	<0.001	141.8±21.6	139.9±19.3	136.5±18.5	0.0161
Saturated fatty acid (g/1,000 kcal)	6.39±2.76	7.50±1.91	7.63±1.83	<0.001	5.41±1.57	7.13±1.52	8.99±2.09	<0.001
Monounsaturated fatty acid (g/1,000 kcal)	8.25±2.76	9.89±2.17	10.44±2.41	<0.001	7.65±2.04	9.83±2.22	11.10±2.33	<0.001
Polyunsaturated fatty acid (g/1,000 kcal)	5.75±1.69	6.92±1.41	7.73±1.58	<0.001	6.05±1.59	7.05±1.68	7.30±1.76	<0.001
n-3 polyunsaturated fatty acid (g/1,000 kcal)	1.05±0.34	1.38±0.39	1.63±0.43	<0.001	1.22±0.43	1.45±0.48	1.39±0.43	<0.001
n-6 polyunsaturated fatty acid (g/1,000 kcal)	4.69±1.46	5.52±1.18	6.08±1.32	<0.001	4.81±1.29	5.58±1.33	5.89±1.48	<0.001

Notes: [a]On the basis of the Cochran–Armitage trend test for categorical variables and linear regression analysis for continuous variables, ordinal numbers 0–2 were assigned to tertiles of each dietary pattern.

schizophrenia.[12,13] A sudden change in fatty acids can play a role in a wide range of psychiatric, neurological, and developmental disorders in adults.[12] A lack of omega-3 fatty acids in particular is related to the pathogenesis of schizophrenia.[13] The dietary and physical activity habits of individuals with schizophrenia contribute to an unfavorable metabolic profile. The daily calories intake between patients with schizophrenia and control patients was similar; however, individuals with schizophrenia consumed significantly greater amounts of sugar and fat.[14]

A few studies among patients with schizophrenia also reported a significantly increased intake of calories[15–17] and low consumption of both monounsaturated and polyunsaturated fatty acids.[4] Five studies reported no significant difference in the diets of patients with schizophrenia compared with those of healthy subjects.[17–21]

Our study shows that there was a higher ratio of fatty acids in the gross calories of the diet in patients with schizophrenia. This result supports the hypothesis that fatty acids may play a role in schizophrenia pathogenesis. Alternatively, as a result of having compensated for a lack of fatty acids in the nervous system, the human body may consume more fatty acids, leading to this result.

This study also shows that patients with schizophrenia tend to consume meals that contain substantially more oil and fat. In addition, it shows that the ratio of fatty acids in the gross calories of the diet is higher in patients with schizophrenia. This result suggests that schizophrenic patients may be more likely to consume food that contains oil and fat. Roick et al[22] reported that schizophrenic patients have a supper snack and consume fast food more frequently than the general population does. It is concerning that schizophrenic patients in Japan live in an environment in which a diet that contains a substantial amount of fatty acids can be obtained relatively easily and inexpensively.

Only a few studies have investigated which factors may influence the diet of individuals with schizophrenia, and the findings appear to be inconsistent. The results from two such studies suggest that the poor diet associated with schizophrenia is influenced by socioeconomic status.[22,23] Fewer males, compared with the general population, reached acceptable levels for consumption of fruit, vegetables, milk, potatoes, and pulses.[24] Fewer females reached the levels for consumption of milk and potatoes.[24] However, other authors noted that female patients consumed more fat, carbohydrates, and overall calories[17] and less fruit, vegetables, and nuts[25] than females in the general population did. In any case, poor diet may be associated with schizophrenia, and the lifestyle of

Table 4 Odds ratios and 95% confidence intervals (CI) for having schizophrenia, according to tertiles of dietary pattern scores

	No of cases	Crude odds ratio	*P*-value	Adjusted odds ratio[a]	*P*-value
Vegetable dietary pattern					
Low tertile	91	Reference		Reference	
Middle tertile (95% CI)	75	0.66 (0.46–0.96)	0.029	0.74 (0.50–1.10)	0.139
High tertile (95% CI)	71	0.83 (0.54–1.29)	0.41	1.10 (0.67–1.80)	0.701
Cereal dietary pattern					
Low tertile	60	Reference		Reference	
Middle tertile (95% CI)	73	1.19 (0.77–1.83)	0.435	1.15 (0.73–1.81)	0.559
High tertile (95% CI)	104	2.43 (1.67–3.56)	<0.001	2.71 (1.80–4.09)	<0.001

Note: [a]The model was adjusted for age and sex.

people with schizophrenia raises concerns when considering the relationship of this diet with coronary heart disease.[24] In this context, limiting fat intake in patients with schizophrenia may help prevent the onset of metabolic syndrome.

This study has some limitations. First is the cross-sectional nature of the study. We cannot refer to causal determinations to be made between dietary patterns and the onset of schizophrenia. Longitudinal studies are needed to interpret these associations and causalities. Second, the dietary data were collected using the BDHQ. The results may be influenced by potential misclassification of dietary patterns, although the validity and reliability of BDHQ have been estimated.[9,26] Third, we did not examine several potential confounding factors in our study, such as income levels and interpersonal relationships among families. Income levels may be a peculiarly important factor, as the results may have been confounded by low income level. Stratification studies by income levels should be requested in the future. Fourth, in this study, the ages of the participants were limited to 30–60 years. It is known that the onset of schizophrenia commonly occurs between the ages of 10 and 20 years. Our study did not investigate the 10 to 20-year age group; therefore, we could not accurately determine whether there was a relationship between schizophrenia and fatty acids in this younger cohort. Fifth, all of the volunteer participants may have been relatively healthier than the general population because they were more interested in their own health. Thus, the members of the community who did not participate in the study may exhibit different schizophrenia morbidities. Finally, we could not completely eliminate a beta error as the cause of our inability to detect certain associations between dietary patterns and schizophrenia, as our sample size was relatively small.

Conclusion

We hypothesized that a dietary pattern comprising high amounts of vegetables would be associated with a lower risk of schizophrenia. However, no evident association was observed between the "vegetable" dietary pattern and schizophrenia.

By contrast, the "cereal" dietary pattern, which was characterized by a high consumption of rice, bread, and confectioneries and positively correlated with the intake of fats and proteins, was associated with schizophrenia. This result may provide clues regarding the pathogenesis of schizophrenia and the prevention of metabolic syndrome in schizophrenic patients. This article is the first to describe a study of dietary patterns and schizophrenia.

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