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Dietary habits and genetic susceptibility: correlations between nutritional intake and genetic risks for schizophrenia and bipolar disorder

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Dietary habits may impact the prevention and management of schizophrenia (SCZ) and bipolar disorder (BD), and genetic and environmental factors can influence both these habits and these disorders. This study investigated the effects of genetic predispositions to SCZ and BD on current dietary habits among older adults with lifestyle-related diseases, potentially offering insights for preventive mental health strategies. A cohort of 730 older patients who were diagnosed with or suspected of having lifestyle-related diseases was assessed for eight current dietary categories: miso soup, Japanese tea, green and yellow vegetables, light-colored vegetables, fruits, pickles, meats, and soybeans. Polygenic risk scores (PRSs) for the risk of SCZ and BD, including BD types I and II, the shared risk of SCZ and BD, and the differentiation of SCZ from BD, were calculated utilizing data from large-scale genome-wide association studies (GWASs). Our findings revealed that PRSs for SCZ and BD risk significantly influenced specific dietary habits, particularly decreased consumption of nutrient-rich foods such as light-colored vegetables (SCZ, $R^2 = 0.0096$, $p = 3.54 \times 10^{-3}$; BD, $R^2 = 0.0074$, $p = 9.09 \times 10^{-3}$) and soybeans (SCZ, $R^2 = 0.0061$, $p = 0.019$; BD, $R^2 = 0.014$, $p = 8.38 \times 10^{-4}$). Notable differences in dietary effects were observed between PRSs for BD I and BD II, with a more pronounced impact associated with BD I (e.g., light-colored vegetables, BD I, $R^2 = 0.015$, $p = 3.11 \times 10^{-4}$; BD II, $p > 0.05$). Moreover, shared genetic factors for SCZ and BD were correlated with lower intakes of miso soup ($R^2 = 0.013$, $p = 1.21 \times 10^{-3}$), Japanese tea ($R^2 = 0.0092$, $p = 5.59 \times 10^{-3}$), light-colored vegetables ($R^2 = 0.010$, $p = 2.92 \times 10^{-3}$), and soybeans ($R^2 = 0.014$, $p = 3.13 \times 10^{-4}$). No significant correlations were found between PRSs for differentiating SCZ from BD and any dietary patterns ($p > 6.25 \times 10^{-3}$). Genetic risks shared by individuals with SCZ and BD may influence dietary choices in older adults, emphasizing the potential for dietary modifications as part of comprehensive strategies for the prevention of the SCZ and BD onset, as well as for the treatment of individuals at risk of or diagnosed with SCZ and BD.

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INTRODUCTION

Dietary habits and nutritional intake play a crucial role in the management, treatment, and prevention of psychiatric disorders, such as schizophrenia (SCZ) and bipolar disorder (BD) [1, 2]. The dietary patterns observed in these patient groups are influenced by the severity of the illness, side effects of medications, and socioeconomic factors [3–5]. Patients with SCZ often prefer unhealthy food, characterized by a high intake of saturated fat and a lower intake of fruits, vegetables and pulses, leading to a greater risk of metabolic complications, such as obesity and diabetes [3, 6]. Similarly, individuals with BD are prone to consuming unhealthy foods, including sugar, saturated fats, and processed foods, along with irregular eating habits and a low intake of nutrient-rich foods, such as fruits and vegetables, thereby increasing health risks and worsening symptoms [4, 5, 7, 8]. Although direct research on specific dietary habits before the onset of SCZ and BD is limited, unhealthy dietary patterns, such as high sugar and processed food consumption and low omega-3 fatty acid intake, might exist in individuals at high risk for developing psychiatric disorders such as SCZ and BD [9]. These dietary patterns, associated with increased inflammation, oxidative stress, and neurotransmitter imbalances, have been implicated in the pathophysiology of various mental health conditions [1, 10].

Habitual diet is one of many environmental factors that potentially contributes to interindividual differences in physical and mental health. In contrast, habitual dietary intake differences are partly determined by genetic variations influencing olfactory and taste preferences, as well as by the potential risk of psychiatric disorders. Although the proportion of dietary intake variation

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Table 1. Demographic characteristics of older adult patients with cancer, diabetes mellitus, hypertension, or other lifestyle-related diseases across Cohorts 1 and 2.

Variable	Cohort 1 ($n = 300$)	Cohort 2 ($n = 430$)	p values (F, χ^2)
Age (years)	73.3 ± 5.9	72.1 ± 6.8	**0.017 (5.7)**
Sex (male/female)	182/118	347/83	**2.50×10^{-9} (35.5)**[a]
Height (cm)	156.5 ± 9.0	160.2 ± 8.3	0.17 (1.9)[c]
Weight (kg)	55.8 ± 10.4	57.8 ± 9.5	0.73 (0.1)[c]
Body mass index (BMI)	22.7 ± 3.4	22.5 ± 3.0	0.22 (1.5)[c]
Smoker (Current/Past/Never)	50/98/152	91/262/77	**1.80×10^{-20} (90.9)**[a]
Alcohol drinker (Current/Past/Never)	105/40/155	198/68/163	**1.11×10^{-3} (13.6)**[a]
Current cancer (Yes/No/Unknown)	28/262/10	43/371/16	0.75 (0.1)[a,b]
Current diabetes mellitus (Yes/Suspected/No/unknown)	74/7/212/7	55/9/359/7	**2.41×10^{-5} (17.8)**[a,b]
Current hypertension (Yes/No/Unknown)	134/161/5	148/262/20	**0.013 (6.2)**[a,b]
Past cancer (Yes/No/Unknown)	32/265/3	67/358/5	0.055 (3.7)[a,b]
Past diabetes mellitus (Yes/Suspected/No/Unknown)	1/4/288/7	7/10/412/1	0.15 (2.7)[a,b]
Past hypertension (Yes/No/Unknown)	9/286/5	32/394/4	**0.011 (6.5)**[a,b]
Current dietary habits			
Miso soup (0–5 scale)	4.3 ± 1.3	4.3 ± 1.2	0.93 (< 0.1)[c]
Japanese tea (0–5 scale)	4.9 ± 0.8	4.8 ± 0.9	0.47 (0.5)[c]
Green and yellow vegetables (0–5 scale)	4.8 ± 0.6	4.3 ± 1.1	**1.54×10^{-9} (37.4)**[c]
Light-colored vegetables (0–5 scale)	4.8 ± 0.5	4.4 ± 1.0	**9.27×10^{-11} (43.2)**[c]
Fruits (0–5 scale)	4.0 ± 1.3	3.7 ± 1.5	0.11 (2.6)[c]
Pickles (0–5 scale)	3.3 ± 2.0	3.5 ± 1.9	0.074 (3.2)[c]
Meats (0–5 scale)	2.5 ± 1.1	2.3 ± 1.1	0.055 (3.7)[c]
Soybeans (0–5 scale)	4.4 ± 1.1	4.2 ± 1.2	0.080 (3.1)[c]

Complete demographic information was not obtained for all participants (height in Cohort 2, $n = 429$; weight in Cohort 1, $n = 298$ and in Cohort 2, $n = 429$; BMI in Cohort 1, $n = 298$ and in Cohort 2, $n = 428$; alcohol drinker in Cohort 2, $n = 429$; light-colored vegetables in Cohort 2, $n = 429$; fruits in Cohort 1, $n = 299$ and in Cohort 2, $n = 428$; pickles in Cohort 2, $n = 428$; meats in Cohort 2, $n = 429$). The means ± SDs are shown. P values < 0.05 are shown in boldface.
[a]χ^2 or Fisher's exact test.
[b]χ^2 tests in the presence or absence of disease were performed.
[c]ANCOVA with age and sex as covariates.

explained by genetic differences varies among dietary traits, heritability estimates for the majority of these dietary traits range from ~20–50% [11]. Similarly, both genetic and environmental factors contribute to the pathogenesis of SCZ and BD, with these psychiatric disorders demonstrating an estimated heritability of approximately 80% [12, 13]. Large-scale genome-wide association studies (GWASs) conducted on SCZ [14] and BD (including BD I and BD II) [15] by the Psychiatric Genomics Consortium (PGC) Wave 3 have successfully identified multiple genetic loci implicated in these disorders. Additionally, GWASs focusing on the common risk of SCZ and BD (SCZ + BD) and differentiating SCZ from BD (SCZ vs. BD), i.e., SCZ-specific genetic risk, by the SCZ and BD working groups in the PGC Wave 2 have also successfully identified several common and SCZ-specific genetic loci [16]. However, few studies have investigated the influence of genetics on SCZ and BD risk or the influence of common and disorder-specific risk factors for these disorders on the current dietary habits in adults.

In this study, we focused on patients over 60 years of age with lifestyle-related diseases, including cancer, diabetes mellitus, and hypertension. By not limiting our analysis exclusively to individuals with SCZ and BD, we minimized the confounding effects of disorder onset and the use of antipsychotics. This approach allows us to examine the genetic influences on dietary habits within a broader and potentially more genetically diverse population. Furthermore, we did not include evaluations of current or past psychiatric service contacts or psychiatric medication usage. Considering that the hospital where our participants were recruited is a general hospital, not a psychiatric facility, the prevalence of psychiatric disorders among the patients was assumed to approximate that of the general population. Given the observed associations between dietary habits and patients with SCZ and BD and considering the genetic influences on dietary habits and these disorders, we hypothesized that genetic predispositions associated with SCZ, BD or both disorders, captured by polygenic risk scores (PRSs), would influence specific dietary behaviors, such as lower intake of fruits, vegetables, and soybeans and higher meat consumption, in older patients with lifestyle-related diseases. In this study, we investigated the effects of PRSs for SCZ and BD risk, a shared risk of SCZ and BD, and SCZ-specific risk on current dietary habits in 730 older patients who were diagnosed with or suspected of having lifestyle-related diseases.

MATERIALS AND METHODS

Target participants

In this study, 730 older adults were recruited and divided into two groups 300 (Cohort 1) and 430 (Cohort 2) participants aged 60 years and above for independent genotyping arrays (HumanCytoSNP array for Cohort 1, and the HumanCoreExome array for Cohort 2) (Table 1). This division and separate analysis were performed to account for differences in genetic marker coverage between the arrays, which could introduce bias if the datasets were combined. Participants were outpatients at the Department of Clinical Laboratories, Iwata City Hospital, Shizuoka, Japan, who came for

blood sampling. Patients were primarily diagnosed with or suspected of having cancer, diabetes mellitus, hypertension, or other lifestyle-related diseases during the recruitment period from 2003 to 2008. All participants were unrelated, genetically homogeneous Japanese individuals, predominantly residing in the Kanto or Tokai regions of Japan. The detailed participant recruitment procedures have been previously described [17–19]. Eligible patients were over 60 years of age, ambulatory, and capable of verbal communication. The assessment did not include evaluations of current or past psychiatric service contacts or psychiatric medication usage. Given that Iwata City Hospital is a general hospital, not a psychiatric facility, the prevalence of psychiatric disorders among the patients was assumed to approximate that of the general population. Written informed consent was obtained from all subjects. This study adhered to the ethical principles of the World Medical Association's Declaration of Helsinki and was approved by the Institutional Review Boards of Iwata City Hospital and Hamamatsu University School of Medicine (21-8), Gifu University (2019-233), and Tokyo Institute of Psychiatry (now known as Tokyo Metropolitan Institute of Medical Science) (20-23(1)).

Current dietary habits

The dietary habits of the patients were evaluated using a questionnaire [17, 18]. Professional interviewers assisted the patients in completing the questionnaire, which covered eight dietary items: (i) miso soup, (ii) Japanese tea, (iii) green and yellow vegetables (e.g., spinach, carrots), (iv) light-colored vegetables (e.g., cabbage, cauliflower), (v) fruits, (vi) pickles, (vii) meats, and (viii) soybeans. Responses for each item were recorded on a 6-point scale: 0, rarely; 1, 1–3 days a month; 2, 1–2 days a week; 3, 3–4 days a week; 4, 5–6 days a week; and 5, daily consumption.

Genotyping and quality control

A comprehensive overview of the genotyping and quality control (QC) methods used in the study has previously been provided [19]. Briefly, peripheral venous blood and oral mucosa samples were collected from the patients, and genomic DNA was extracted. For Cohort 1, whole-genome genotyping was conducted using the HumanCytoSNP v2.0 BeadChip, while for Cohort 2, the HumanCoreExome v1.0 BeadChip was used (Illumina, San Diego, CA, USA). During the QC process, samples with a genotype call rate of less than 0.95 and SNPs with a genotype call frequency of less than 0.95 or a 'cluster sep' (an index of genotype cluster separation) of less than 0.1 were excluded [19]. After this process, a total of 225,602 SNPs for Cohort 1 and 256,997 SNPs for Cohort 2 were retained.

PRS calculations

We calculated PRSs for our patients—one for the risk of SCZ; one for the risk of BD, including BD types I and II (BD I and BD II); one for the common risk of SCZ and BD (SCZ + BD); and one for differentiating SCZ from BD (SCZ *vs.* BD)—using the following methodology. To identify risk SNPs, along with their p values and odds ratios (ORs) for these psychiatric disorders, we utilized publicly available GWAS datasets as discovery samples: PGC3 for SCZ [14], PGC3 for BD, including BD I and BD II [15], and datasets for SCZ + BD and SCZ *vs.* BD [16] (https://www.med.unc.edu/pgc/results-and-downloads). To eliminate SNPs in linkage disequilibrium (LD) in our target patient, the SNPs were pruned using PLINK v1.9 with a pairwise r^2 threshold of 0.25 and a window size of 200 SNPs. After this pruning process and the exclusion of SNPs located on sex and mitochondrial chromosomes, 72,223 independent SNPs for Cohort 1 and 68,313 independent SNPs for Cohort 2 were retained. The PRSs were calculated using alleles associated with each disorder at varying levels of significance in the discovery GWAS datasets, with the following $P_{T\ cutoff}$ values: $P_T < 0.01$, $P_T < 0.05$, $P_T < 0.1$, $P_T < 0.2$, $P_T < 0.5$, and $P_T \leq 1$. For each target patient, the PRS was determined by weighting the scores of the 'risk SNPs' by the logarithm of the odds ratio (logOR) from each discovery GWAS. The score was the sum of the risk alleles (0, 1, or 2) multiplied by the logOR across all SNPs in the P_T-SNP sets for each patient.

Statistical analyses

All the statistical analyses were conducted using IBM SPSS Statistics 28.0 software (IBM Japan, Tokyo, Japan). Differences in continuous variables, such as age and height, between Cohorts 1 and 2 were analyzed using analysis of variance (ANOVA) or analysis of covariance (ANCOVA), with age and sex as covariates. Differences in categorical variables, such as sex and smoking status, were analyzed using Pearson's χ^2 or Fisher's exact test. Linear regression was used to assess the association between the PRSs for psychiatric disorders based on each $P_{T\ cutoff}$ and current dietary habits in our patients. In this model, current dietary habits were the dependent variable, PRSs for psychiatric disorders were the independent variables, and age, sex, and cohort served as covariates. The proportion of variance in current dietary habits explained by the PRSs is indicated by the adjusted R^2 value. To isolate the variance attributable specifically to the PRSs, we subtracted the adjusted R^2 value for the covariates alone (age, sex, and cohort) from that of the full models. We set the nominal significance level for all the statistical tests at $p < 0.05$. Given that the PRSs at each $P_{T\ cutoff}$ were highly correlated and not independent, p values derived from different $P_{T\ cutoff}$ values were not adjusted for multiple comparisons. To mitigate type I errors, we applied a Bonferroni correction, setting a p value threshold of $p < 6.25 \times 10^{-3}$ ($\alpha = 0.05$ divided by eight, corresponding to the number of current dietary habits).

RESULTS

Demographic characteristics of patients in Cohorts 1 and 2

Although Cohorts 1 and 2 were recruited using the same inclusion and exclusion criteria during the same period, differences were observed in several demographic characteristics between the cohorts (Table 1, $p < 0.05$). Patients in Cohort 1 were older, and this cohort had lower proportions of males, current smokers, alcohol drinkers, and individuals with a history of hypertension and higher proportions of patients with current diabetes mellitus and hypertension than did Cohort 2 ($p < 0.05$). Regarding current dietary habits, patients in Cohort 1 consumed green and yellow vegetables as well as light-colored vegetables more frequently than did those in Cohort 2 ($p < 0.05$). The observed differences in several demographic characteristics between the cohorts are likely attributable to variations in age and sex ratios. Consequently, age, sex, and cohort were included as covariates in the subsequent analyses.

Correlations across dietary habits

We examined partial correlations among eight dietary habits, adjusting for age, sex, and cohort differences, among the participants (Fig. 1). Among current dietary habits, the consumption of green and yellow vegetables had the strongest correlation with the intake of light-colored vegetables ($r = 0.63$, $p = 7.83 \times 10^{-80}$). Similarly, the consumption of miso soup showed a substantial correlation with soybean intake ($r = 0.33$, $p = 8.65 \times 10^{-20}$), and the intake of green and yellow vegetables also correlated significantly with soybean consumption ($r = 0.27$, $p = 4.30 \times 10^{-13}$). Other significant correlations between dietary habits were relatively small ($r \approx 0.12$–0.25, $p < 6.25 \times 10^{-3}$). No significant correlations were identified between meat consumption and any other dietary habits ($p > 6.25 \times 10^{-3}$).

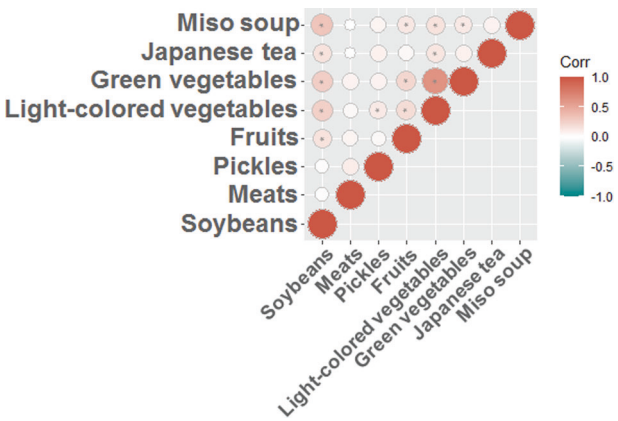

Fig. 1 Partial correlations across eight dietary habits, with age, sex, and cohort as covariates. *$p < 6.25 \times 10^{-3}$.

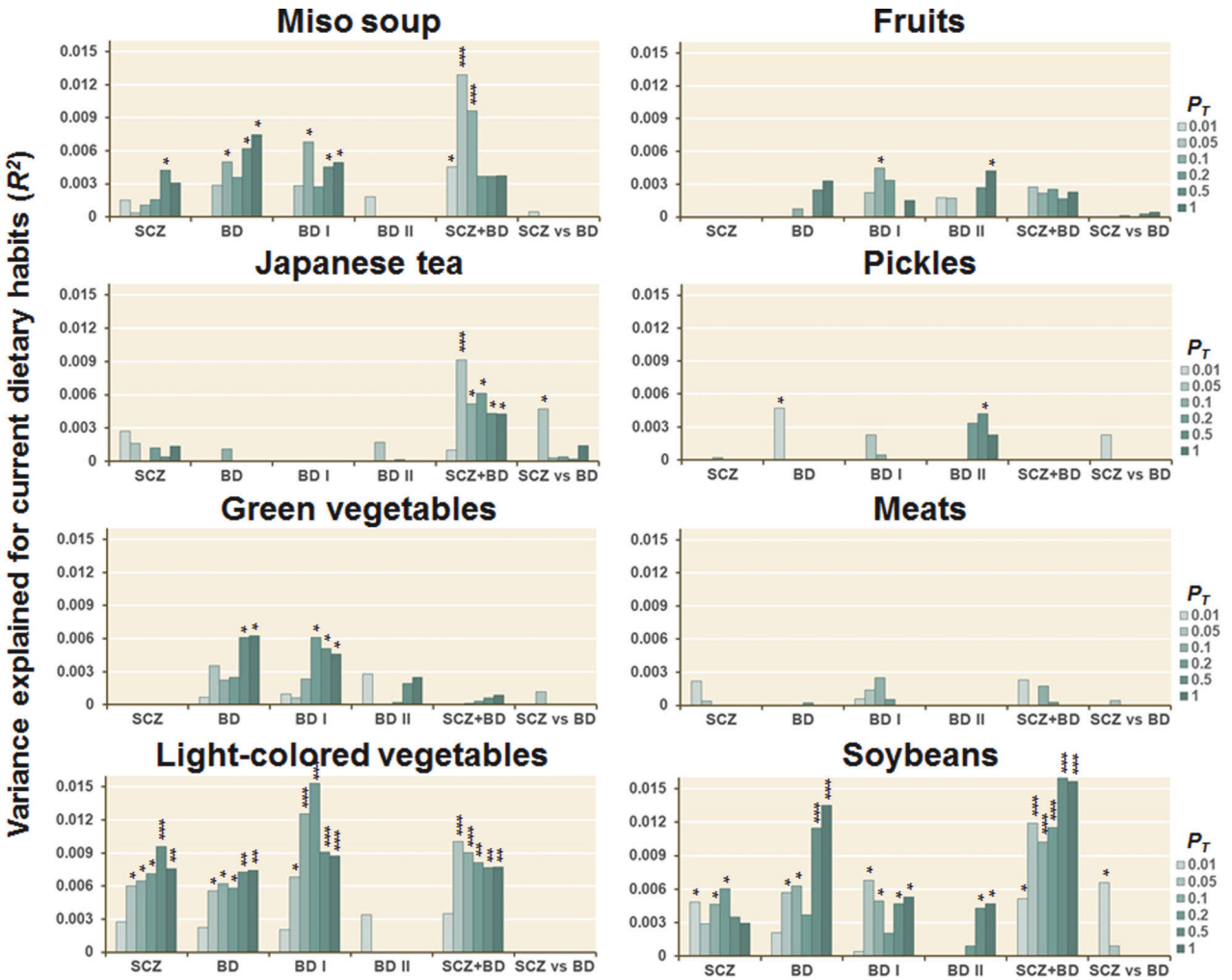

Fig. 2 Influences of polygenic risk scores for the risk of SCZ and BD, including BD types I and II shared SCZ and BD risk (SCZ + BD), and differentiating SCZ from BD (SCZ *vs*. BD) at different P_T levels on eight dietary habits. SCZ schizophrenia, BD bipolar disorder. *$p < 0.05$, **$p < 0.01$, ***$p < 6.25 \times 10^{-3}$.

Effects of PRSs for the risks of SCZ and BD on dietary habits

Our initial analysis investigated the effects of PRSs for the risks of SCZ and BD on eight specific dietary habits at varying P_T levels (Fig. 2). PRSs for SCZ risk showed a significant negative correlation with the frequency of consuming light-colored vegetables (maximum at $P_T < 0.5$: $R^2 = 0.0096$, $p = 3.54 \times 10^{-3}$) and marginally negative correlations with the frequency of miso soup (maximum at $P_T < 0.5$: $R^2 = 0.0042$, $p = 0.043$) and soybean consumption (maximum at $P_T < 0.2$: $R^2 = 0.0061$, $p = 0.019$). Similarly, PRSs for BD risk were significantly negatively correlated with the frequency of soybean consumption (maximum at $P_T \leq 1$: $R^2 = 0.014$, $p = 8.38 \times 10^{-4}$) and marginally negatively correlated with the frequencies of consumption of miso soup (maximum at $P_T \leq 1$: $R^2 = 0.0074$, $p = 0.011$), light-colored vegetables (maximum at $P_T \leq 1$: $R^2 = 0.0074$, $p = 9.09 \times 10^{-3}$), green vegetables (maximum at $P_T \leq 1$: $R^2 = 0.0063$, $p = 0.014$) and pickles (maximum at $P_T < 0.01$: $R^2 = 0.0047$, $p = 0.036$).

Effects of PRSs for BD I and BD II risks on dietary habits

We further explored the effects of PRSs for the risk of BD types I and II on eight current dietary habits (Fig. 2). Correlations between the PRSs for BD risk and current dietary habits were primarily found for the PRSs for BD I risk rather than the PRSs for BD II risk. Specifically, PRSs for BD I risk demonstrated a significant negative correlation with the frequency of consuming light-colored vegetables (Fig. 3 and Supplementary Fig. 1, maximum at $P_T < 0.2$: $R^2 = 0.015$, $p = 3.11 \times 10^{-4}$) and marginally negatively influenced the intake frequency of miso soup (maximum at $P_T < 0.1$: $R^2 = 0.0068$, $p = 0.015$), green vegetables (maximum at $P_T < 0.2$: $R^2 = 0.0061$, $p = 0.016$), fruits (maximum at $P_T < 0.1$: $R^2 = 0.0045$, $p = 0.035$), and soybeans (maximum at $P_T < 0.05$: $R^2 = 0.0068$, $p = 0.014$). Conversely, PRSs for BD II risk showed marginally negative correlations with the intake frequency of fruits (maximum at $P_T \leq 1$: $R^2 = 0.0042$, $p = 0.039$) and soybeans (maximum at $P_T \leq 1$: $R^2 = 0.0047$, $p = 0.033$) but were marginally positively correlated with pickle consumption (maximum at $P_T < 0.5$: $R^2 = 0.0042$, $p = 0.043$).

Effects of PRSs for the shared risk of SCZ and BD and for differentiating SCZ from BD on dietary habits

We next investigated the effects of PRSs on the shared risk for SCZ and BD (SCZ + BD) and for differentiating SCZ from BD (SCZ *vs*. BD) on eight current dietary habits (Fig. 2). PRSs for the common risk for SCZ and BD showed a significant negative correlation with the consumption frequency of miso soup (Fig. 3 and Supplementary Fig. 1, maximum at $P_T < 0.05$: $R^2 = 0.013$, $p = 1.21 \times 10^{-3}$), Japanese tea (Fig. 3 and Supplementary Fig. 1, maximum at $P_T < 0.05$: $R^2 = 0.0092$, $p = 5.59 \times 10^{-3}$), light-colored vegetables (maximum at $P_T < 0.05$: $R^2 = 0.010$,

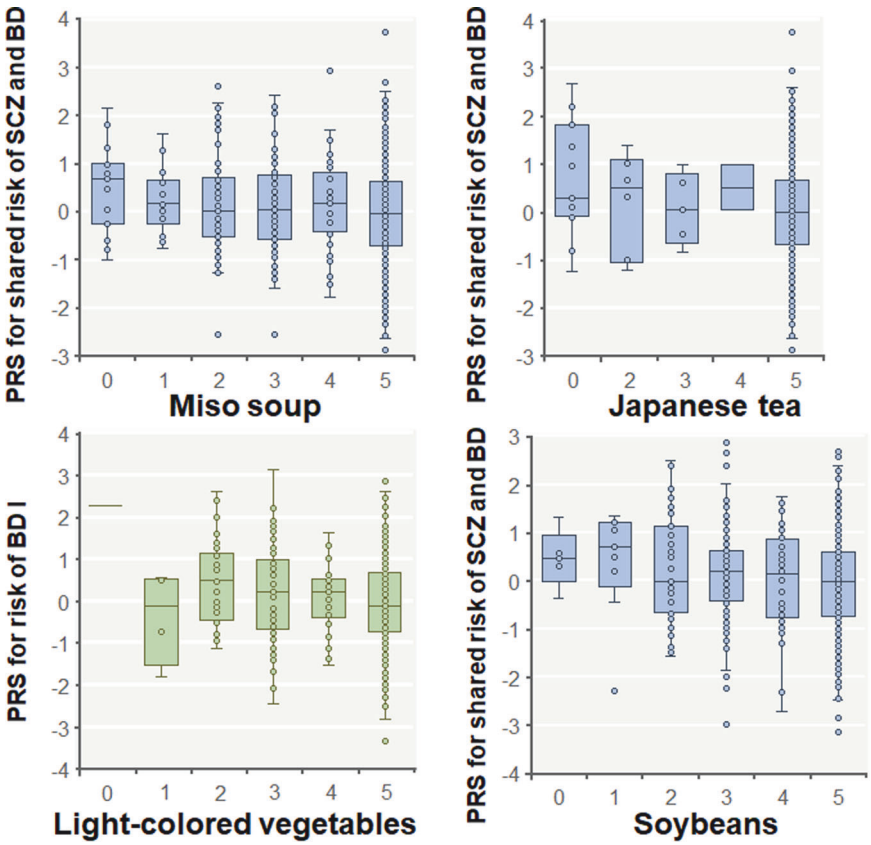

Fig. 3 Effects of PRSs for the shared risk of SCZ and BD and the risk of BD I on consumption frequencies of miso soup, Japanese tea, light-colored vegetables, and soybeans. Box plots among food consumption frequencies based on a questionnaire with a Likert-scale indicate the individual PRSs for the shared risk of SCZ and BD and the risk of BD I in older patients with lifestyle-related diseases. PRSs polygenic risk scores, SCZ schizophrenia, BD bipolar disorder, BD I BD type I. PRSs corrected for cohort were *z*-standardized.

$p = 2.92 \times 10^{-3}$), and soybeans (Fig. 3 and Supplementary Fig. 1, maximum at $P_T < 0.5$: $R^2 = 0.014$, $p = 3.13 \times 10^{-4}$). Conversely, PRSs for differentiating SCZ from BD demonstrated a marginal negative correlation with the frequency of Japanese tea consumption (maximum at $P_T < 0.05$: $R^2 = 0.0047$, $p = 0.035$) and a positive correlation with the consumption frequency of soybeans (maximum at $P_T < 0.01$: $R^2 = 0.0066$, $p = 0.015$).

DISCUSSION

This is the first study to investigate whether polygenetic factors for the risk of SCZ and BD, including BD types I and II, as well as the shared risk of SCZ and BD and SCZ-specific risk, influence current specific dietary habits in older patients diagnosed with or suspected of having lifestyle-related diseases. The PRSs for SCZ and BD risk were found to commonly affect specific dietary habits, such as decreased consumption of light-colored vegetables and soybeans. When differentiating between BD I and BD II, the associations between the PRSs for BD and dietary habits stemmed primarily from the PRSs for BD I rather than BD II. Notably, the PRSs for BD I were associated with reduced consumption of light-colored vegetables. The common genetic risk factors for SCZ and BD were more strongly associated with lower intakes of miso soup, light-colored vegetables and soybeans and were also newly associated with reduced consumption of Japanese tea. Conversely, no significant associations were observed between the PRSs for differentiating SCZ from BD and any dietary habits. These findings indicate that genetic factors for SCZ and BD could commonly affect dietary behaviors even in the older general population.

As shown in Fig. 1, the consumption of light-colored vegetables was more strongly correlated with the intake of green vegetables ($r = 0.63$) than with the consumption of miso soup ($r = 0.16$) or soybeans ($r = 0.25$). Despite these correlations among dietary habits, PRSs for the shared risk of SCZ and BD significantly decreased the consumption of miso soup, light-colored vegetables and soybeans but not green vegetables. Thus, the common genetic risk factors for SCZ and BD appear to impact a dietary pattern composed mainly of miso soup, light-colored vegetables, and soybeans consumption, rather than one consisting of green and light-colored vegetable consumption. In fact, common genetic risk factors were more strongly associated with a principal component consisting of miso soup, light-colored vegetable and soybean consumption (maximum at $P_T < 0.05$: $R^2 = 0.025$, $p = 7.83 \times 10^{-6}$) than with consumption of green and light-colored vegetables (maximum at $P_T \leq 1$: $R^2 = 0.0047$, $p = 0.029$). Increased intake of miso soup, light-colored vegetables, and soybeans may benefit individuals at risk for SCZ and BD, as well as patients with these disorders, as part of comprehensive prevention from the onset and treatment strategies.

Miso soup, light-colored vegetables, and soybeans, which are rich in proteins; dietary fiber; vitamins such as vitamins K and B; and minerals, such as iron, calcium, and magnesium, are associated with positive effects on psychiatric symptoms and disorders. A high protein content is crucial for neurotransmitter synthesis and brain function and is essential for mental health [20]. Dietary fiber plays a significant role in gut health and is increasingly recognized for its impact on mood regulation and mental well-being through the gut-brain axis [21]. Vitamins and minerals found in these foods can support brain health [2], reduce

inflammation, and aid in the prevention of mood disorders [10]. Incorporating these nutrient-rich foods into the diet could be beneficial for managing and potentially improving mental health [4, 7, 10, 22].

In this study, patients who were primarily diagnosed with or suspected of having cancer, diabetes mellitus, hypertension, or other lifestyle-related diseases were recruited at a general hospital. Since the purpose of their visit was not related to psychiatry but to lifestyle-related diseases, we did not assess whether these patients had SCZ or BD. Additionally, SCZ and BD are generally associated with a greater comorbidity rate with these lifestyle-related diseases [23, 24], which might have affected dietary habits. However, our main findings remained significant even after accounting for current and past histories of these lifestyle-related diseases ($p < 6.25 \times 10^{-3}$). Therefore, the PRSs for SCZ and BD risk and dietary habits in these patients appear not to be influenced by the presence of current and past histories of these lifestyle-related diseases.

There are several limitations to the interpretation of our findings. First, our questionnaire does not comprehensively cover all dietary habits, as it excludes grain, rice, fish, eggs, milk, coffee, and snacks, among others. The absence of direct psychiatric assessments means that we could not definitively determine the psychiatric status of our participants, limiting our ability to directly explore the correlation between dietary habits and individuals at risk of or diagnosed with SCZ or BD. Furthermore, focusing on an older population may not fully capture the dietary influences on psychiatric risk in younger individuals, given that dietary habits can change across generations. Additionally, we cannot establish a direct causal relationship between certain dietary habits and genetic risk factors for SCZ and BD. Given that our study did not specifically target patients with SCZ or BD, our findings suggest that dietary habits may be influenced by genetic risks of these disorders rather than changes in lifestyle and medication following the onset of these disorders. Future studies should address these limitations by including participants across a wider age range, implementing direct psychiatric evaluations, and examining the causal relationships between diet, genetic risk, and psychiatric disorders.

In conclusion, our findings suggest that genetic predispositions for SCZ and BD may influence dietary choices, highlighting the potential role of dietary modifications as part of comprehensive prevention from the onset of SCZ and BD and treatment strategies for individuals at risk of or diagnosed with SCZ and BD. Specifically, the reduced consumption of light-colored vegetables, soybeans, and miso soup emphasizes the importance of incorporating nutritional guidance into the management of psychiatric risks associated with SCZ and BD. Increasing the intake of these nutrient-rich foods may provide benefits beyond physical health, potentially contributing to improvements in mental health.

DATA AVAILABILITY

Our data are not publicly available because they contain information that could compromise research participant privacy/consent.

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AUTHOR CONTRIBUTIONS

KO supervised the entire project, wrote the manuscript and was critically involved in the design, analysis and interpretation of the data. KO, TS, TG, IK, TS, DF and TS were responsible for performing the literature review. DN, JH, NS, FT, HS, and KI were heavily involved in the collection of the majority of the data and intellectually contributed to data interpretation. All authors contributed to and have approved the final manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

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