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Sugar-sweetened beverages and cognitive function in children

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Sugar-sweetened beverages and cognitive function in children

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Table of contents

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Sugar-Sweetened Beverages and Depressive and Social Anxiety Symptoms Among Children and Adolescents Aged 7–17 Years, Stratified by Body Composition

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Background: Rare studies investigated the associations between sugar-sweetened beverage (SSB) consumption with depressive and social anxiety symptoms among children and adolescents, particularly in different stratification of body composition, which was our purpose.

Methods: A cross-sectional survey of children and adolescents aged 7–17 years was conducted in Beijing, China, in 2020, with an average age of 12.07 (SD: 3.09) years. Children's Depression Inventory (CDI) questionnaires and social anxiety scale for children (SASC) were completed in the baseline questionnaires. SSB consumption and body composition were assessed using child-reported questionnaires and a GE Healthcare Lunar iDXA dual-energy X-ray bone densitometer. Multivariate logistic regression was used to assess the associations between SSB consumption with depressive and social anxiety symptoms. Confounders were evaluated by child-reported and parental questionnaires, including age, sex, parental educational attainment, maternal smoking status, single-child status, BMI, incomes, fruit consumption, physical activity, screen time, and the frequency of fried food consumption. Stratified analyses were performed to explore whether the associations were influenced by body composition.

Results: A total of 1,311 children and adolescents, including 658 boys and 653 girls, were included in the final analysis. There were 13.96 and 29.75% of the study population with depressive and social anxiety symptoms, respectively. Overall, about 63.77% of the children and adolescents consumed SSB, and the average SSB intake was 0.35 servings per day. In the fully adjusted model, compared to participants who did not consume SSB each day, SSB consumption of ≥1 servings/day was positively associated with depressive symptoms [odds ratio (OR) = 2.28, 95% CI = 1.30–4.01] and social anxiety (OR = 1.10, 95% CI = 0.69–1.77), though the latter did not reach statistical significance. When individuals had higher body fat or lower fat-free mass (FFM) or muscle, the ORs of depressive symptoms were more evident among children and adolescents who drank SSB for ≥1 servings/day ($P < 0.05$).

Conclusion: Higher consumption of SSB could be associated with increased OR of depressive symptoms in children and adolescents. The association remained robust, especially in groups with higher body fat or lower fat-free mass or muscle.

Keywords: sugar-sweetened beverages, depression, social anxiety, body composition, children and adolescents

INTRODUCTION

Depressive and social anxiety symptoms are the most common mental disorders (1), which are important factors affecting children and adolescents' physical and mental development. During the COVID-19 pandemic, the substantial increase in the prevalence of major depressive and anxiety disorders placed a huge burden on the whole society (2). Depressive symptoms feature low mood, slow thinking, decreased mental activity, cognitive impairment, and physical symptoms (3). Social anxiety is defined as persistent fear or avoidance in social occasions, fear or avoidance arising from comments from others, and fear of embarrassment in social occasions, according to the American Psychological Association (1994) (4). At present, the worldwide prevalence of depression and anxiety is increasing (5), and they are still serious problems for the growth and development of Chinese children and adolescents (6). Notably, several evidence indicated that children with obesity were more likely to suffer from depressive and anxiety symptoms compared to peers of normal weight (7, 8), and fat distribution might be a stronger determinant strengthening such relationship (9). It is, therefore, plausible to speculate that body composition might be correlated with psychiatric disturbances, especially in the case of visceral fat deposits.

Sugar-sweetened beverages (SSBs) has been the major contributor of added sugar in the annual diet, which is detrimental to the health and associated with increased risks of weight gain (10), hypertension (11), and metabolic syndrome (12). In parallel to the physical disorders, SSB consumption might be associated with a modestly higher risk of mental health problems, such as depression among adults (13, 14) and children/adolescent population (15). However, only limited epidemiological studies examined this issue among Chinese children and adolescents. To the best of our knowledge, one study conducted in southern China showed that a higher consumption of SSB was associated with poorer performance on executive function in the pediatric population (16). Meanwhile, a school-based nationwide survey conducted in four provinces of China (i.e., Shenzhen, Zhengzhou, Nanchang, and Guiyang) demonstrated that SSB consumption was associated with depressive symptoms in Chinese adolescents (17). However, they did not consider the confounding effects of lifestyle behaviors, such as diet or physical activities; also, they did not measure adolescent body weight. Overall, one previous report suggested that 66.6% of the Chinese children consumed SSB (18), and the per capita and per consumer SSB intake was 2.84 servings/week (∼0.41 servings/day) and 4.26 servings/week (∼0.61 servings/day) (18). Since the percentage of consuming SSBs among Chinese children and adolescents is increasing, it is important to consider the potential effect of SSB intake on the risks of mental disorders in Chinese children and adolescents. Furthermore, addressing the influence of potential effect of body composition on the association between SSB consumption and depression/anxiety should also be important when interpreting this topic, when some studies found that body composition seemed to be a better screening tool than relative rough indicators, such as body mass index (BMI) in the prediction of obesity-related diseases (19, 20). Specifically, BMI may overestimate fatness in children who are shorter or who have higher muscle mass and may underestimate adipose in those with reduced muscle mass (21).

Hypothesizing that Chinese children and adolescents who consumed large quantities of SSBs would tend to report more mental health problems, this study aimed to investigate the association between SSB consumption with depressive and social anxiety symptoms among children and adolescents, and further explore the potential effect of multiple body composition indicators on such associations.

MATERIALS AND METHODS

Study Population

We obtained data from a cross-sectional survey conducted among children and adolescents from Beijing, China, in 2020. We adopted a stratified cluster random sampling method, and selected the original study population from elementary school, junior high school, and high school. According to the sample size calculated, a pre-survey was conducted first, and a total of 1,426 children and adolescents aged 7–17 years were invited to participate in the project. For the inclusion and exclusion criteria, individuals with the missing data of SSB intake, body composition, and the definition of depressive and social anxiety were further excluded. A total of 1,311 children and adolescents aged 7–17 years were included in the final analysis. The research of this project was reviewed and approved by the Ethics Committee of Peking University (number: IRB00001052 20024). The school doctor introduced the research purpose and content of the project to all the children and adolescents and their parents in detail, and the written informed consent was obtained from both students and their parents.

Questionnaire

The questionnaire was distributed by the project team through the school doctors to the students and parents before the physical examination (or through an online questionnaire), with the exception of children in the third grade or under primary school, who completed the questionnaires at home with their primary guardian. Children from or above the fourth grade would fill in the children's questionnaire by themselves while instructed by the class teacher and parents. In addition, trained project members interpreted all the questionnaires in detail. Appropriate guidance would be given by these project members as effectively as possible. The school teacher collected the completed questionnaire on the day of the physical examination and handed it over to our project team members. Child-reported questionnaires included birth date, sex (boys or girls), energy intake behaviors, screen time, and physical activity. Parental questionnaires included information on single-child status (yes or no), parental educational attainment (junior high school or below, high school/secondary or equivalent/junior college or vocational college, undergraduate/postgraduate or above), maternal smoking status (always, quit, and never), and monthly household incomes (<12,000, 12,000–21,000, and ≥21,000 yuan).

For energy intake behaviors, all participants were asked about the frequency (days) and amount of vegetable, fruit, fried food, and SSB consumption. The questions were as follows: "How many days, over the past 7 days, have you drunk SSB, how much have you drunk (serving)?," "How many days, over the past 7 days, have you eaten fruits/vegetables, how much have you eaten (serving)?," and "How many days, over the past 7 days, have you eaten fried food?" One serving of vegetable/fruit was defined as the size of an ordinary adult's closed fist and roughly equaled a medium-sized apple (≈200 g) (22). As set in the questionnaire, only the frequency of fried food consumption was recorded, and fried food included fried chicken, deep-fried dough sticks, fried cakes, French fries, and so on. We classified the frequency of fried food consumption into "0–2 days/week," "3–5 days/week," and "≥6 days/week." SSB included Coca-Cola, Sprite, orange juice, Nutrition Express, Red Bull, and all other sorts of sodas and sugary juices. To better understand SSB consumption, one serving of SSB was determined as a canned beverage (∼250 ml). The average daily consumption was calculated as follows: (days × servings in each of those days)/7. Therefore, the amount of daily SSB consumption was categorized into groups of "=0 servings/day," "<1 servings/day," and "≥1 servings/day."

We recorded the child's physical activity according to the International Physical Activity Questionnaire-Short Form (IPAQ-SF) (23) and defined moderate-to-vigorous physical activity (MVPA) as any kind of aerobic activity which increased heart rate and breathing, such as running, swimming, cycling, basketball, football, table tennis, badminton, and calisthenics. According to the questions, "How many days, over the past 7 days, have you done MVPA? And how much time did you last on average?," children and adolescents were asked to report the frequency (days) and duration (hours and minutes) for MVPA over the past 7 days, and the average daily physical activity was calculated as follows: (days × duration in each of those days)/7.

Screen time was investigated by the following question: "Over the past 7 days, how much time did you spend on watching TV or playing computer or video games on average?," and students, therefore, reported the daily average duration (hours and minutes) of screen time.

Depression and Social Anxiety Symptoms

The Children's Depression Inventory (CDI) was a self-report questionnaire consisting of 27 items, including 5 subscales (i.e., Negative Mood, Interpersonal Problem, Ineffectiveness, Anhedonia, and Negative Self-Esteem) (24), which was the most frequently used scale to measure depression in children and adolescents aged 6–17 years (25). The Negative Mood Scale included sadness, worry, self-blame, crying, irritability, and hesitation, corresponding to items 1, 6, 8, 10, 11, and 13; the Interpersonal Problem Scale included bad behaviors, decreased social interaction, disobedience, and quarrels, corresponding to scale items 5, 12, 26, and 27; the Ineffectiveness Scale included self-deprecation, learning difficulties, poor grades, and self-perceived lower than peers, corresponding to scale items 3, 15, 23, and 24; the Anhedonia Scale included unhappiness, sleep disturbance, fatigue, changes in appetite, physical anxiety, loneliness, hating school, and lack of friends, and the corresponding scale items were 4, 16, 17, 18, 19, 20, 21, and 22; the Negative Self-Esteem Scale included pessimism, self-hatred, suicidal ideation, negative body image, and lack of love, corresponding to items 2, 7, 9, 14, and 25. As previously reported, the subscales also had perfect internal consistency (24). The CDI demonstrated good discriminant validity when classifying children and adolescents with no significant psychopathology vs. those who were depressed (24). The items were rated on a 3-point scale indicating symptom severity (0 = no presence of symptom, 1 = symptom is present and mild, and 2 = highest severity possible). The total scores ranged from 0 to 54, and depressive symptoms were defined as CDI scores > 19 (26), with higher scores indicating more severe depressive symptomatology.

The social anxiety scale for children (SASC) (27) was used to assess the social anxiety level of the research subjects, and the scale was applicable to the age of 7–16 years. The scale included 10 items, mainly examining the two dimensions of fear of negative evaluation, social avoidance, and distress. Items 7 and 9 were social avoidance and distress factors, respectively. Each item used a 3-point scoring system, with 0 for never, 1 for sometimes, and 2 for often, with a total score of 20. A total score of ≥8 indicated the possibility of social anxiety, with higher scores indicating a higher degree of social anxiety.

Physical Examination and Body Composition

Height was measured using a uniform and calibrated mechanical stadiometer (model TZG, Jiangyin No. 2 Medical Equipment Factory, Jiangsu, China), with an accuracy of 0.1 cm. At the same time, the participants were asked to stand straight and barefoot. Weight was measured by a uniform and calibrated electronic scale (model RGT-140, Shanghai Dachuan Electronic Weighing Apparatus Co. Ltd., Shanghai, China) to the nearest 0.1 kg, while subjects were wearing short clothes and standing naturally in the center of the weight measuring plate to keep the body stable. BMI was calculated as the weight (kg) divided by the square of the height (m^2).

We also measured the children and adolescents' body composition using professional medical personnel using a GE Healthcare Lunar iDXA dual-energy X-ray bone densitometer in accordance with the standard use process and program requirements described by the instrument, scanning the whole body and collecting images. The participants were placed as required, lying flat on the scanning bed, with the body in the middle of the instrument, with the thumb facing up, and the palm facing but not touching the leg. All measurements were logically checked before the examination. During each on-site physical examination, a special person was assigned to conduct on-site supervision to ensure that the measurement methods and records of each measurement index were correct and standardized. Fat mass (FM) was calculated by multiplying weight (kg) by the body fat percentage (BF%). To calculate the fat-free mass index (FFMI), the fat-free mass percentage (FFM%) was calculated by subtracting the BF% from 100%. The fat-free mass (FFM) was calculated by multiplying the weight by the FFM%. The FFMI was then calculated as FFM (kg) divided by height squared, and was useful for comparing individuals with different height measurements (28).

For more precise analysis, we divided age into four groups, namely, 7–9, 10–12, 13–15, and 16–17 years, and then stratified the population into two levels based on the age- and sex-specific median values of body fat mass (BFM), BF%, FFMI, muscle rate, and FFM/FM.

Statistical Analysis

Continuous and categorical variables were presented as mean ± standard deviation (SD) and frequency (percentage), respectively. Differences in demographic and lifestyle characteristics by sex were examined by Student's *t*-test for continuous variables and Pearson's chi-squared test for categorical variables. Meanwhile, we calculated odds ratios (ORs) [95% confidence level (95% CI)] in two multivariate logistic models to assess the associations between SSB consumption and depressive and social anxiety symptoms. Model 1 adjusted for age and sex; since physical activity and vegetable consumption were collinear variables, Model 2, therefore, additionally included parental educational attainment, maternal smoking status, single-child status, BMI, incomes, fruit consumption, physical activity, screen time, and the frequency of fried food consumption. Furthermore, the cross-sectional survey design could not generate casual relationships of drinking SSBs and depression or social anxiety; therefore, we also exchanged the independent variables with dependent variables to analyze the reverse correlation, in other words, to explore whether individuals with depressive or social anxiety symptoms were more inclined to drink SSB, which could make the results more realistic in terms of causal inference and meaning generalization. Furthermore, stratified analyses were performed to explore whether the associations between SSB consumption and depressive and social anxiety symptoms were influenced by body composition, such as BFM, BF%, FFMI, muscle rate, and FFM/FM. We performed all statistical analyses using the Statistical Analysis System (SAS) software (version 9.4, SAS Institute, Cary, NC, USA), and a two-sided $P < 0.05$ was considered statistically significant.

RESULTS

Study Population

Table 1 shows the baseline characteristics of the study population. A total of 658 boys (12.01 ± 3.08 years) and 653 girls (12.13 ± 3.10 years) were included in the final analysis. The mean BMI value was 20.67 (SD: 4.74) and 20.47 (SD: 4.67) kg/m^2 for boys and girls, respectively. The majority of the study population (65.65%) was single-child status. For the total population, there were approximately 97.56% of children's mothers without smoking, and 42.28% of children's fathers and 43.49% of children's mothers obtained the high levels of education (undergraduate, postgraduate, or above). For lifestyle behaviors, girls (1.26 servings/day) tended to consume more fruits each day than boys (1.17 servings/day, $P = 0.075$), but boys were more likely to take physical activities (0.24 vs. 0.17 h/day, $P = 0.006$) and drink SSB (0.39 vs. 0.31 servings/day, $P = 0.009$), compared to girls. In terms of body composition, girls had more body adipose and high BF%, while boys owned more muscles, and had higher FFMI and a higher ratio of FFM to FM ($P < 0.0001$). Importantly, 13.96 and 29.75% of the study population had depressive and social anxiety symptoms, respectively; overall, separated by sex, girls had higher rates of depressive (16.39%) and social anxiety symptoms (34.92%) than boys (11.55 and 24.62%) with statistically significant difference ($P < 0.05$).

Rate of Depressive and Social Anxiety Symptoms by SSB Consumption Stratification

The rates of depressive and social anxiety symptoms by SSB consumption stratification are shown in **Figure 1**. In general, the prevalence of depressive and social anxiety symptoms of individuals with SSB intake ≥ 1 servings/day accounted for a large percentage (depression = 27.35%; social anxiety = 36.75%), followed by individuals with <1 servings/day (depression = 14.19%; social anxiety = 29.76%) and 0 serving/day (depression = 10.32%; social anxiety = 28.00%). Separated by sex, the prevalence of social anxiety symptoms was higher among girls than boys in all groups, while only boys drinking SSB for ≥1 servings/day had a slightly higher prevalence of depression (boys = 29.85%, girls = 24.00%).

Association Between SSB Consumption With Depressive and Social Anxiety Symptoms

Table 2 presents the ORs and 95% CI of SSB consumption for depressive and social anxiety symptoms. After adjusting for age and sex, compared to the group with SSB consumption of 0 servings/day, the ORs (95% CI) of depressive symptoms in group with SSB consumption of ≥1 servings/day were 2.83 (1.59–5.02) and 4.65 (2.00–10.82) among the total population and boys, respectively. SSB intake of ≥1 servings/day was also

TABLE 1 | Baseline characteristics of included population.

Characteristics	Total population (*n* = 1,311)	Boys (*n* = 658)	Girls (*n* = 653)	*P*-value
Age, year	12.07 ± 3.09	12.01 ± 3.08	12.13 ± 3.10	0.501
Weight, kg	50.59 ± 18.19	52.64 ± 19.67	48.53 ± 16.32	<0.0001
Height, cm	154.46 ± 15.43	156.90 ± 17.00	152.00 ± 13.23	<0.0001
BMI, kg/m^2	20.57 ± 4.71	20.67 ± 4.74	20.47 ± 4.67	0.452
Single-child status	858 (65.65%)	448 (68.09%)	414 (63.40%)	0.074
Maternal smoking status, *n* (%)				0.546
Always	20 (1.53%)	8 (1.22%)	12 (1.84%)	
Quit	12 (0.92%)	5 (0.76%)	7 (1.07%)	
Never	1,279 (97.56%)	645 (98.02%)	634 (97.09%)	
Paternal educational attainment, *n* (%)				0.393
Junior high school or below	141 (10.84%)	72 (10.94%)	69 (10.57%)	
High school / secondary or equivalent / junior college or vocational college	620 (47.29%)	299 (45.44%)	321 (49.16%)	
Undergraduate / postgraduate or above	550 (42.28%)	287 (43.62%)	263 (40.28%)	
Maternal educational attainment, *n* (%)				0.099
Junior high school or below	119 (9.16%)	60 (9.12%)	59 (9.04%)	
High school/secondary or equivalent/junior college or vocational college	627 (47.83%)	296 (44.98%)	331 (50.69%)	
Undergraduate/postgraduate or above	565 (43.49%)	302 (45.90%)	263 (40.28%)	
Monthly household income, *n* (%)				0.337
<12,000 yuan	668 (50.95%)	343 (52.13%)	325 (49.77%)	
12,000–21,000 yuan	421 (32.59%)	199 (30.24%)	222 (34.00%)	
≥21,000 yuan	222 (17.18%)	116 (17.63%)	106 (16.23%)	
Lifestyle behaviors				
Fruit consumption, servings /day	1.21 ± 0.93	1.17 ± 0.91	1.26 ± 0.95	0.075
Vegetable consumption, servings /day	1.81 ± 1.28	1.78 ± 1.28	1.85 ± 1.27	0.288
Fried food consumption, days /week	1.26 ± 0.49	1.25 ± 0.47	1.28 ± 0.50	0.297
Physical activity, hours /day	0.21 ± 0.45	0.24 ± 0.48	0.17 ± 0.40	0.006
Screen time, minutes /day	165.44 ± 136.37	165.30 ± 134.00	165.60 ± 138.80	0.971
SSB consumption, servings /day	0.35 ± 0.55	0.39 ± 0.63	0.31 ± 0.46	0.009
Group definition				0.007
0 serving /day, *n* (%)	475 (36.23%)	212 (32.22%)	263 (40.28%)	
<1 serving /day, *n* (%)	719 (54.84%)	379 (57.60%)	340 (52.07%)	
≥1 servings /day, *n* (%)	117 (8.92%)	67 (10.18%)	50 (7.66%)	
Body composition, median (IQR)				
BFM	13.68 (10.52)	12.28 (10.45)	14.87 (10.02)	<0.0001
BF%	29.88 (11.63)	26.04 (13.51)	31.96 (9.35)	<0.0001
FFMI	13.91 (3.70)	14.63 (4.19)	13.35 (2.95)	<0.0001
Muscle rate	0.67 (0.12)	0.71 (0.14)	0.65 (0.09)	<0.0001
FFM/FM	2.34 (1.37)	2.85 (1.93)	2.17 (0.92)	<0.0001
Depressive symptoms, *n* (%)	183 (13.96%)	76 (11.55%)	107 (16.39%)	0.012
Social anxiety, *n* (%)	390 (29.75%)	162 (24.62%)	228 (34.92%)	<0.0001

BMI, body mass index; SSB, sugar-sweetened beverage; BFM, body fat mass; BF%, body fat percentage; FFMI, free-fat mass index; FFM/FM, fat-free mass/fat mass. One serving of fruit/vegetable roughly equaled 200 g, and one serving of SSB was determined as ∼250 ml.

positively associated with depressive symptoms in girls but with no statistical difference (OR = 1.63, 95% CI = 0.71–3.73). After additionally adjusting for other covariates in Model 2, the results did not change essentially. In terms of social anxiety, SSB consumption of ≥1 servings/day could also increase the OR of social anxiety but failed to reach statistical significance (Model 1: OR = 1.40, 95% CI = 0.87–2.25; Model 2: OR = 1.10, 95% CI = 0.69–1.77).

We also reported the reverse correlation that whether individuals with depressive and social anxiety symptoms were more inclined to drink SSB ≥ 1 servings/day, as shown in **Supplementary Table 1**. Obviously, adjusting for confounders

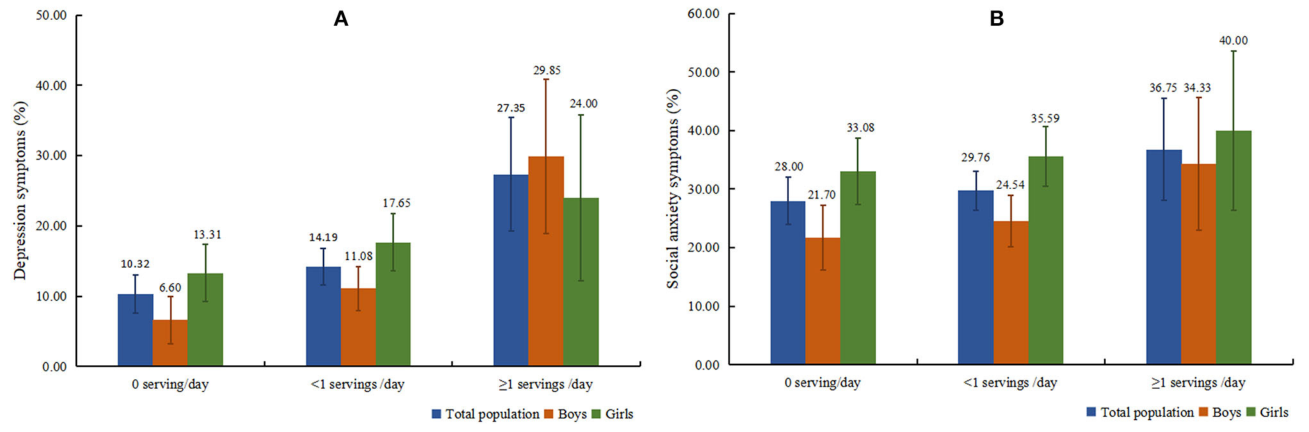

FIGURE 1 | Prevalence of depressive **(A)** and social anxiety **(B)** symptoms among total population and boys and girls, respectively.

TABLE 2 | Multivariate odds ratios (ORs) and 95% confidence intervals (CIs) of SSB consumption for depressive and social anxiety symptoms.

Disorders	**SSB Consumption**		
	0 serving/day	**<1 servings/day**	**≥1 servings/day**
Model 1			
Total population			
Depressive symptoms	1 (Reference)	1.38 (0.90–2.10)	**2.83 (1.59–5.02)**
Social anxiety	1 (Reference)	1.11 (0.83–1.49)	1.40 (0.87–2.25)
Boys (*n* = 658)			
Depressive symptoms	1 (Reference)	1.42 (0.70–2.88)	**4.65 (2.00–10.82)**
Social anxiety	1 (Reference)	0.97 (0.62–1.51)	1.48 (0.77–2.87)
Girls (*n* = 653)			
Depressive symptoms	1 (Reference)	1.39 (0.82–2.35)	1.63 (0.71–3.73)
Social anxiety	1 (Reference)	1.25 (0.85–1.85)	1.23 (0.62–2.46)
Model 2			
Total population			
Depressive symptoms	1 (Reference)	1.21 (0.82–1.79)	**2.28 (1.30–4.01)**
Social anxiety	1 (Reference)	0.99 (0.75–1.30)	1.10 (0.69–1.77)
Boys (*n* = 658)			
Depressive symptoms	1 (Reference)	1.32 (0.68–2.57)	**3.42 (1.47–7.92)**
Social anxiety	1 (Reference)	0.95 (0.62–1.46)	1.14 (0.58–2.24)
Girls (*n* = 653)			
Depressive symptoms	1 (Reference)	1.19 (0.72–1.95)	1.57 (0.70–3.52)
Social anxiety	1 (Reference)	0.96 (0.66–1.39)	1.00 (0.51–1.96)

Model 1: adjusted for age and sex.
Model 2: additionally adjusted for parental educational attainment, maternal smoking status, single-child status, BMI, incomes, fruit consumption, physical activity, screen time and the frequency of fried food consumption. Bold values referred to $P < 0.05$.

in Model 2, boys with depressive symptoms were more likely to drink SSB for ≥1 servings/day (OR = 2.86, 95% CI = 1.45–5.64), compared with their counterparts without depressive symptoms. In addition, boys with social anxiety also presented more SSBs drinking each day (OR = 1.20, 95% CI = 0.65–2.20), though no statistical significance was observed.

Distribution of Body Composition

The distribution of body composition among the total population and each sex group is displayed in **Figure 2**. Based on the age- and sex-specific median value of BFM, BF%, FFMI, muscle rates, and FFM/FM ratios, the total population was divided into two groups almost equally, and the specific percentage of participants in each group was shown in the figure. Overall, in each body composition

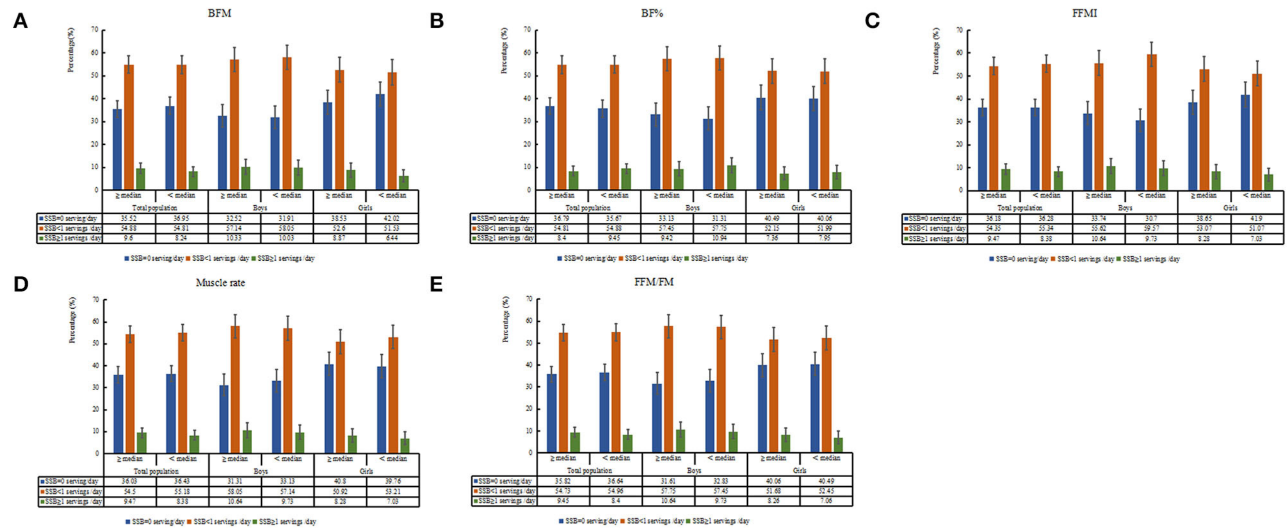

FIGURE 2 | Distribution of sugar-sweetened beverage (SSB) consumption grouped by body composition among total population and boys and girls, respectively (**A**: BFM stratification; **B**: BF% stratification; **C**: FFMI stratification; **D**: Muscle rate stratification; **E**: FFM/FM stratification).

stratification, ∼35–36% of individuals did not drink SSB each day, 54–55% of individuals consumed less than 1 servings/day, and 8–9% of individuals drank equal or over 1 servings/day.

Potential Effect of Body Composition on the Association Between SSB and Depressive and Social Anxiety Symptoms

Figure 3 shows the stratified associations between SSB consumption and depressive and social anxiety symptoms by body composition stratification. Obviously, when individuals had higher BFM and BF%, lower FFMI, muscle rates, and FFM/FM ratios, the ORs of depressive symptoms were more evident among the total population and boys who drank SSB for ≥1 servings/day ($P < 0.05$), compared to their peers who did not drink SSB each day.

As for the reverse correlation, similar results were observed. Children and adolescents with mental disorders who had higher body fat or lower FFM or muscle showed a strong tendency to drink SSB for ≥1 servings/day ($P < 0.05$) (**Supplementary Figure 1**).

DISCUSSION

In the present cross-sectional survey in Beijing, more than one-half of children and adolescents (63.77%) consumed SSB every day and their average SSB intake was 0.35 servings per day. Meanwhile, such population had 13.96% of depressive symptoms and 29.75% of social anxiety. To the best of our knowledge, higher consumption of SSB was positively associated with increased OR of mental disorders, especially depressive symptoms in male children and adolescents. In addition, children and adolescents with high body fat or low FFM or muscle could be a high-risk population.

In view of SSB consumption and mental health problems, limited evidence existed and yielded inconsistent observations. Prospective studies suggested that frequent consumption of SSB might increase a depression risk among older US adults (14) and Japanese adults (29). One meta-analysis also revealed a non-linear dose-response relationship, and the inflection point was the equivalent of about 2 cups/day of cola (13). However, no significant association between SSB consumption and depression risk was found among Spanish university graduates (30). Among the pediatric population, consumption of SSB was positively associated with depressive symptoms in Chinese adolescents (17), and secondary school children of Dhaka city, Bangladesh (31). On the contrary, based on an autoregressive cross-lagged path model, Mrug et al. found that soft drink consumption at age 13 predicted fewer depressive symptoms among US adolescents (32). These inconsistent findings might be attributed to the different sample size, ethnicity, study design, definition of SSB consumption, and depressive symptoms. In addition, we found positive associations between drinking SSBs and social anxiety, though failing to reach statistical significance. Apart from a large quantity of influencing factors, the limited amount of SSB consumption of the Chinese youth might also be the reason for the non-significant result. There were hardly any studies that investigated the association between SSB and social anxiety; therefore, we could not discuss this issue based on the previous findings.

Interestingly, boys might be more vulnerable to SSB-induced depression, and we speculated several potential explanations for the observed sex differences. First, these results might be related to higher consumption of SSB per day as well as less intake of fruits and vegetables among boys, compared to girls. Second, the results might reflect differences in pathways of depression by sex (33) and type of depressive symptomatology (34). Third, women were more in favor of psychotherapy than men (35), which might

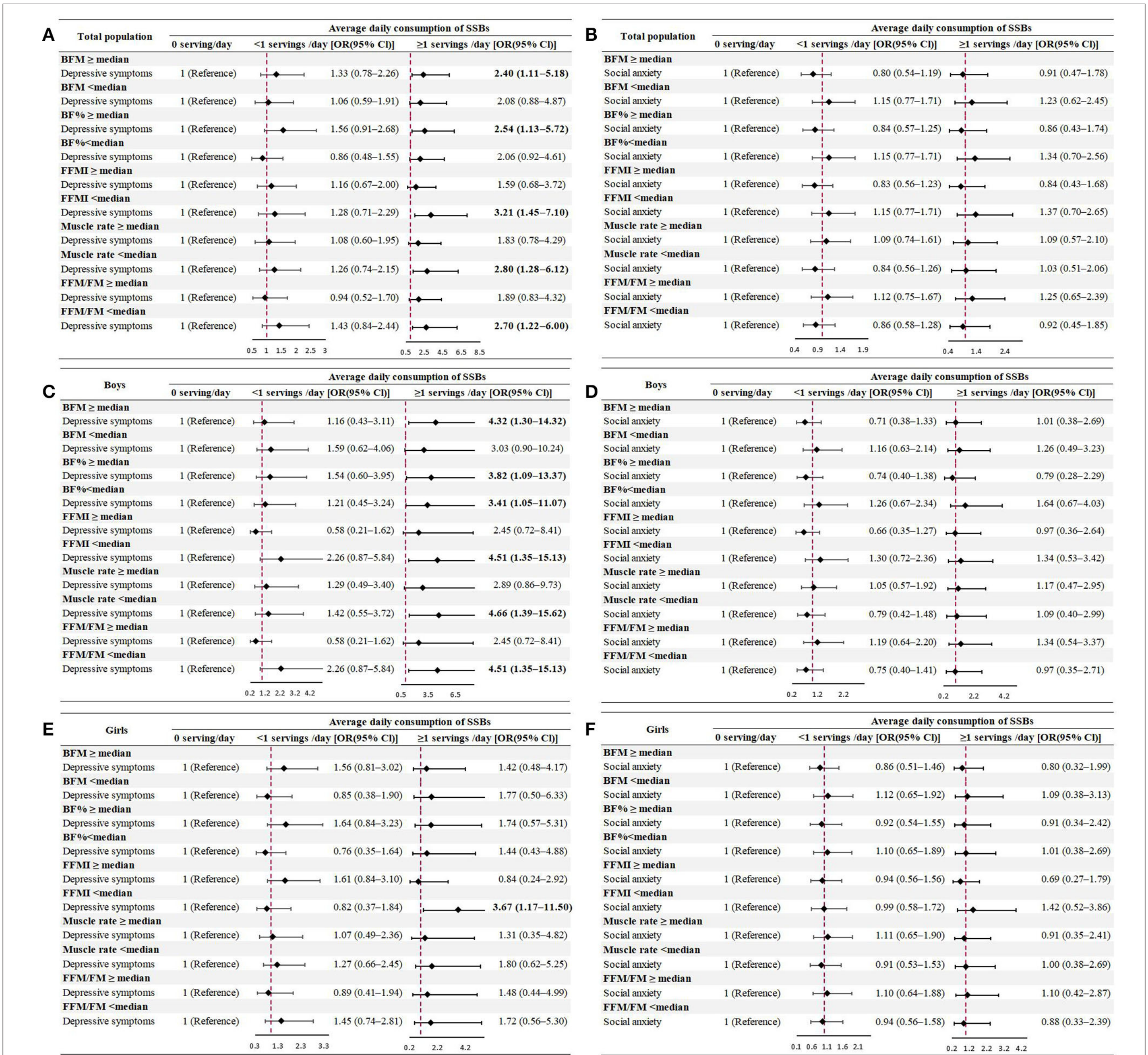

FIGURE 3 | Multivariate odds ratios (OR) and 95% confidence intervals (CI) of SSB consumption for depression (**A,C,E**) and social anxiety (**B,D,F**) symptoms among the total population and each sex group, stratified by body composition (model was adjusted for age, sex, parental educational attainment, maternal smoking status, single-child status, BMI, income, fruit consumption, physical activity, screen time, and the frequency of fried food consumption).

weaken the effects of diet behaviors on mental disorders, to some extent. Besides, differences could also be due to the limitations of the cross-sectional design.

Notably, although the results were typically interpreted in terms of SSB contributing to emotional problems, it was equally likely that mental health problems might be driving the consumption of sugar-sweetened soft drinks. Indeed, experimental studies showed that some individuals consumed more sugary foods in response to stress and negative emotions (36). Our study presented that individuals with mental disorders were more likely to drink SSB. However, a previous study has come to the opposite conclusion and has suggested that depressive symptoms did not contribute to a greater frequency of soft drink consumption over time (32). These differences might be attributed to study population (sex, age, ethnicity, etc.), study design, analytical method, and the definition of SSB or mental health problems. Based on the present evidence, interventions, such as limiting SSB intake, could prove to be beneficial for children's and adolescent's mental health; meanwhile, targeted at high-risk population with mental disorders, restricting the consumption of SSB could also prevent the feedback-induced increases or development of mental illness, since they were more likely to drink SSB.

Not surprisingly, more evident associations between SSB consumption and depressive symptoms were observed among individuals with higher body fat or lower FFM or muscle. Certainly, significant relationships between obesity or high fat and depression appeared, and the magnitude of the association remained stronger in children than adults (37). Weight-related deficits in self-esteem as well as stigma and discrimination were often experienced among children and adolescents with obesity (38), which might contribute to the development of depression (39). This lack of attention to mental health and depression caused by unsatisfied body shape is concerning given our findings.

The physiological mechanisms through which SSB might contribute to mental disorders remained to be established. Obviously, SSB contains a large amount of added sugar, which can increase hypothalamus–pituitary–adrenocortical (HPA) axis reactivity leading to elevations in glucocorticoids (40), and drinking high-level SSB has the potential to promote long-term dysregulation of the stress response. Besides, sugar included in SSB might cause higher secretion of proinflammatory cytokines and lead to inflammation (41), while the latter is positively correlated with the incidence of depression (42). Apart from this, SSB consumption is partly responsible for obesity, while obesity might be associated with the development of mental illness through a stimulation of the HPA axis (43). Although speculative, there are some mechanistic reasons to consider that added sugar contained in SSB might directly impact the development of mental health problems. As for the reverse correlation, one possibility is that individuals with mental disorders might crave sweet beverages, and one might speculate that this might occur even years before receiving a diagnosis of mental illness.

Despite known health risks, reducing SSB consumption is still facing some difficulties. Some possible reasons might be related to sugar-induced addiction through consumption of SSB and attractive marketing strategy (44). Our study provided an important implication for public health. First, governments around the world should implement the SSB taxes, since SSB taxes introduced in jurisdictions appeared to have been effective in reducing SSB purchases and intake (45). Importantly, tax-induced price increases of SSB were associated with reductions in excess weight, especially for adolescent girls (46). However, whether these taxes achieve public health objectives depends, in part, on the extent to which beverage prices increase, known as tax pass-through. For example, given SSB profit margins are relatively high, restaurants or stores may be raising prices of both taxed and untaxed beverages (47, 48). In addition, to increase the sales of SSB, some restaurants employ strategies that may increase consumption, such as offering free refills (49). Second, updating the Nutrition Facts Label to communicate the amount of added sugars included in SSB (50) and introducing warning labels for SSB (51) could effectively dissuade consumers. Meanwhile, the updated or warning label may alter consumers' perceptions about the healthfulness of selected products (52). In addition, the school health team should provide children and adolescents with effective health awareness programs, including providing accurate information, such as appropriate sweet and soft drink amounts, restricting/reducing soft drink consumption in the schools, restricting selling soft drinks from the school premises, and offering a soft drink alternative by providing access to healthy drinks in the schools. In addition, effective social media reaching the younger population to make them aware of potentially harmful consequences of SSB should be applied (44). School health teams should also add the educational information to mental health content. Apart from this, clinicians or parents should not only focus on the diagnosis and treatment of obesity or high fat, and the deleterious effects including mental disorders caused by overweight or obesity need to be further paid attention, especially among children and adolescents.

The strengths of this study deserved to be mentioned. First, children and adolescents aged 7–17 years were included, with a wide age range. Moreover, since obesity might influence the mental disorders, we explored the potential effect of body composition on this issue, using the measure of dual-energy X-ray absorptiometry (DEXA), a previously validated measure in pediatric populations. Compared to BMI, body composition measures could better predict body size dissatisfaction in children and adolescents (53). Certain limitations should also be paid attention. First, the study population was selected in Beijing, and it could not be able to fully represent the Chinese children and adolescent population. Second, we could not rule out that certain types of foods, such as junk food (pastries, chocolates, candies, etc.), and some particular components, including saturated fat content, could also affect our findings. However, as for the information regarding energy intakes, trained project members interpreted all the questionnaires in detail, and appropriate guidance would be given by these project members as effectively as possible. The questionnaires would be rechecked by 3% within 1 week for the same participants. Therefore, the quality of the self-reported data regarding energy intake behaviors should be guaranteed. Third, a cross-sectional survey design could not generate casual relationships of drinking SSBs and depression or social anxiety. However, we also reported the potential "reverse causation" for the observed link between high SSB consumption and depression or social anxiety. In fact, it is not clear whether drinking SSBs or mental disorders occurred first, and a randomized controlled trial is desired to confirm our results. For example, children and adolescents with mental problems and who habitually consume SSB are randomly allocated to a 3-month no SSB provided diet intervention (Diet Group) or a habitual diet control group (Control Group), to investigate whether engaging in a diet intervention can reduce symptoms of mental problems.

CONCLUSION

Children and adolescents in China were still exposed to high levels of depression symptoms and social anxiety, as well as high consumption of SSB. Higher consumption of SSB was positively associated with increased OR of mental health problems in children and adolescents, especially among those with high body fat or low FFM or muscle. This study added to evidence that avoiding soft drinks and beverages as much as possible and keeping a good body shape might be effective approaches to prevent mental disorders among children and adolescents. Thus, taxation of unhealthy foods, particularly sugar-sweetened food and beverage, and promotion of physical activity in keeping a healthy normal weight should be elements of policies to strengthen mental health systems in children and adolescents, which will also inversely support healthy behaviors, promote mental wellbeing, and prevent obesity-related potential metabolic diseases.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics Committee of Peking University (Number: IRB00001052 20024). Written informed consent to participate in this study was provided by students and their parents.

AUTHOR CONTRIBUTIONS

JL: conceptualization and writing—original draft. TC, MC, and YM: data curation. JL and MC: formal analysis. YD and JM: funding acquisition. JL, TM, DG, YL, and LC: methodology. YD and JM: project administration, resources, supervision, and validation. JL, XW, QM, and YZ: software. MC, YM, TM, DG, and YD: visualization. TC, YL, XW, QM, YZ, JM, and YD: writing—review and editing. All authors have read and agreed to the published version of the manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.888671/full#supplementary-material

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ORIGINAL RESEARCH
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Association Between Sugar-Sweetened Beverage Consumption and Executive Function Among Chinese Tibetan Adolescents at High Altitude

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Objective: To estimate the association between sugar-sweetened beverage (SSB) consumption and executive function (EF) among Chinese Tibetan adolescents.

Method: Using three stages by stratified cluster sampling, 1,427 Chinese Tibetan adolescents were recruited from Tibet, China. SSB consumption status was obtained by questionnaires and the three core EFs (inhibition, working memory, and cognitive flexibility) were tested by a modified Eriksen flanker task, N-back shift, and a more-odd shifting task. One-way ANOVA or Chi-square test was used to compare SSB consumption in different categories. Taking the SSB consumption 0 time/week group as the reference, general linear regression (for continuous variable) or Logical regression (classified variable) in three Models was conducted to analyze the relationship between SSB consumption and EF for Chinese Tibetan children and adolescents.

Result: After adjustment of all the covariant in Model 2, all the EF indexes were higher in Chinese Tibetan adolescents with SSB consumption ≥2 times/week than that with SSB consumption of 0 times/week by 21.33 ms (95%*CI*: 6.72, 35.93), 8.21 ms (95%*CI*: 7.06, 9.35), 90.46 ms (95%*CI*: 28.69, 152.23), 147.61 ms (95%*CI*: 81.42, 213.80), 116.18 ms (95%*CI*: 74.48, 157.87), 112.41 ms (95%*CI*: 71.30, 153.52) for incongruent RT, RT difference in incongruent and congruent, 1-back RT, 2-back RT, Heterogeneous RT, RT difference in Heterogeneous and Homogeneous respectively.

Conclusions: The results suggested that SSB consumption was associated with poorer EF in Chinese Tibetan adolescents. SSB consumption should be controlled for healthy brain development of Chinese Tibetan adolescents.

Keywords: Chinese Tibetan adolescents, sugar-sweetened beverages, inhibition, working memory, cognitive flexibility

INTRODUCTION

Located on the Qinghai-Tibet Plateau, Xizang (Tibet) is a remote and low-income area in China, with GDP ranking last in 2021 (1). According to the sixth National census, there are 6.5 million permanent Tibetan residents on the Qinghai-Tibet Plateau, of whom 15% live between 2,500 and 3,000 meters above sea level, 75% live between 3,000 and 4,000 m above sea level, and 10% live above 4,000 m (2). With an average high of 4,000 m above sea level, Chinese Tibetan adolescents are suffering from hypoxia, which affected their body and brain development, including executive function (EF) (3).

Researches on EF has flourished since 2000 in developmental psychology (4). Considered as "air traffic control system of the brain," EF is a collection of top-down control processes used when going on automatic or relying on instinct or intuition would be ill-advised, insufficient, or impossible, such as attentional control, working memory, inhibition, and problem-solving (5). Several studies have found concurrent or longitudinal relations between children's EF and diverse skills, including academic achievement (6), social (7), logical (8), and biological reasoning (9, 10). Several studies have suggested the poor EF of adolescents at high altitudes because of the sensitivity of the brain to environmental hypoxia (11, 12). To our best knowledge, we did not find the data on EF for Chinese Tibetan adolescents in Tibet, China.

As one of the factors influencing EF and underlying brain developmental processes in children, a balanced diet may provide an effective way to promote EF (13). Sugar-sweetened beverages (SSB), a class of very popular non-alcoholic beverages throughout the world, are characterized by high added sugar content, especially fructose-containing sugar (14). SSB was considered to be an important risk factor for obesity, type 2 diabetes mellitus, cardiovascular disease, mortality, and certain cancers worldwide (15, 16). In childhood, evidence supports links between SSB consumption and unhealthy weight gain, as well as other untoward health outcomes, such as dental caries, the earlier timing of puberty, higher blood pressure, and hyperactivity/inattention symptoms (17).

In recent decades, the global production and consumption of SSB have been increasing (18). SSB consumption has declined or plateaued in most western high-income countries since the early 2000s, while in many low-income and middle-income countries, the intake of SSB consumption is increasing, as widespread urbanization and economic development have increased the availability of these beverages (19, 20). In China, it was reported that the production of SSB exceeded 180 million tons in 2017, which was 440 times that of 1992 (21). Compared with 2014, the proportion of SSB non-drinkers among Chinese Tibetan primary school students in Lhasa decreased from 15.16 to 2.47 % in 2019 (22), which was lower than their peers in South China (34.7%) (23). Meanwhile, racial/ethnic disparities in SSB consumption were observed in multi-ethnic areas (24, 25). Verzeletti also emphasized that the ethnic background differences may have an impact on parental beliefs regarding the child's SSB consumption or on rules restricting the intake of SSB by the child (26).

Evidence from a systematic review suggested that less-healthy foods such as SSB were inversely associated with EF (27). The limited studies focusing on this topic has confirmed the association between SSB consumption and poorer EF among children in South China (28). Besides, population-based studies also observed associations between SSB and declined intelligence (29), and poor poorer cognitive performance (30, 31). Nevertheless, the association between SSB consumption and EF among Chinese Tibetan adolescents has been rarely investigated. Given the large population of Chinese Tibetan, the present study aimed to estimate the association between SSB consumption and EF among Chinese Tibetan adolescents.

METHODS

Data Sources and Participants Recruitment

Data were obtained from a cross-sectional study of Chinese Tibetan adolescents in Tibet, China and the research was conducted from August 2019 to December 2020. The participants in this study should be: (1) Chinese Tibetan middle school students with IQ > 90 according to the Wechsler intelligence scale; (2) without physical disability. (3) No color blindness or color weakness; (4) right-handed (32, 33); (5) without depression, anxiety, and other adverse psychological emotions. (6) Born and grew up in Tibet, China with their parents as indigenous Chinese Tibetan.

The recruitment procedure includes three stages by stratified cluster sampling. Firstly, according to altitude, population distribution, geographical distribution, and the situation of economic development of Tibet in China, three cities (Lhasa, Nyingchi, and Nagqu) were selected (**Figure 1**). Secondly, four middle schools in each city were randomly selected for investigation. Thirdly, taking class as the smallest unit of cluster sampling, one class was randomly selected from each grade in each school. All the eligible students in the class were recruited as participants. A total of 1,427 Chinese Tibetan adolescents were recruited and 196 data were excluded because of missing values. Finally, 1,231 data were effective for the present study (86.26%; **Figure 2**).

This study was approved by the Human Experimental Ethics Committee of the East China Normal University (Approval No.: HR0782020). Written informed consent was obtained from the students and their parents before the study. The names of participants were coded to protect their privacy.

Procedure

Before the test, all the team members, composed of graduate students majoring in human sports science, were required to be trained until they were qualified for the test. A self-administered questionnaire collecting demographic information, data on SSB, and dietary intake was completed by the adolescents independently over a 40-min period in classrooms after school. To make sure each item of the questionnaire fully understood, the questionnaire was translated into Tibetan. The team members explained every item in detail to students when they administered the questionnaires and were available all the time

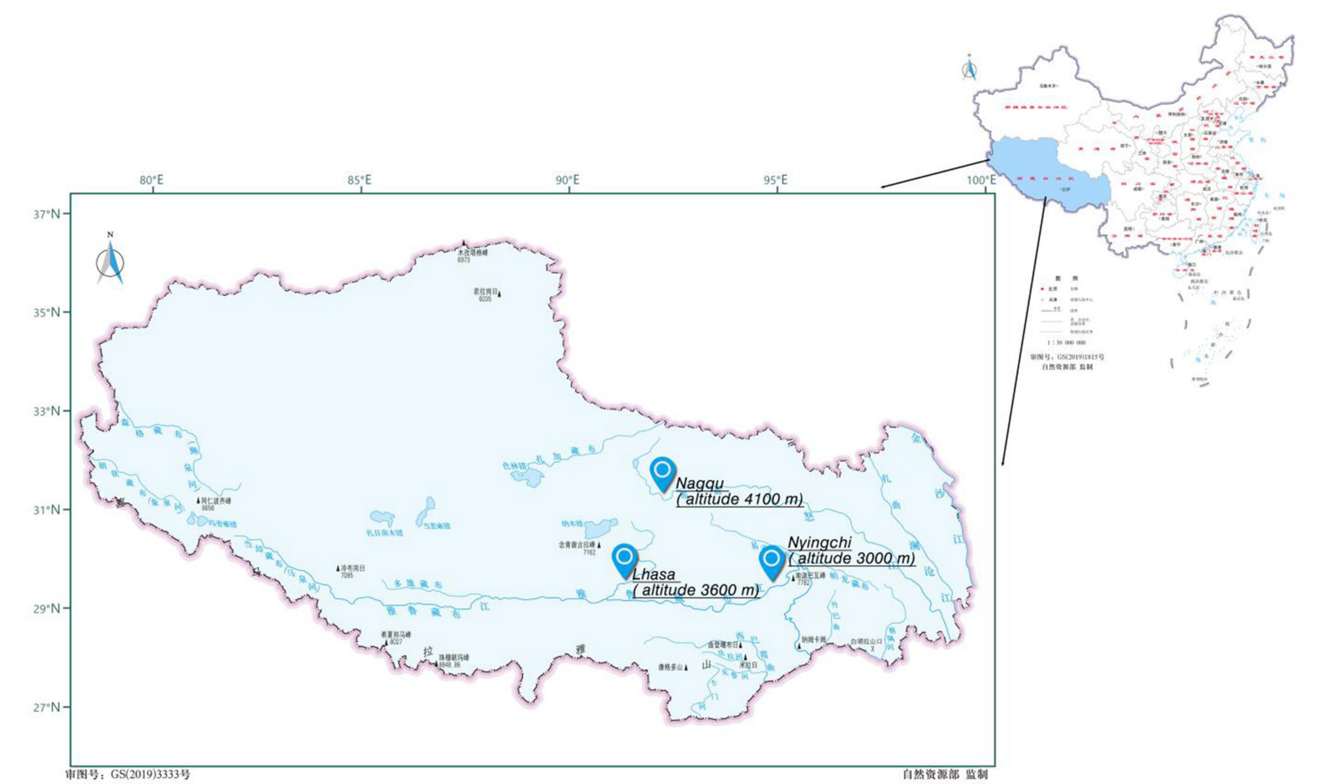

FIGURE 1 | Map of the three cities in Tibet of China.

for any questions raised by students. When completed, the questionnaires were withdrawn on the spot.

Sugar-Sweetened Beverage

Data on SSB consumption were obtained by questionnaires extracted from the Chinese National Survey on Students' Constitution and Health (CNSSCH) (34) and its validation and reliability have been confirmed in previous studies (35, 36). The SSB consumption was assessed by asking them the frequency of SSB consumption from the question "In the past 7 days, how many times did you drink SSB such as Coke, Sprite, Natural fruit juices, Nutrition Express, Red Bull?" (0, 1, 2, 3, 4, $\geq$5). The frequency of SSB consumption was aggregated and categorized into three groups (0 time/week, 1 time/week, and $\geq$2 times/week) to ensure an adequate number of participants in each group.

Executive Function

In the present study, three core EFs (inhibition, working memory, and cognitive flexibility) were tested on the computer by a test tool developed by Chen et al. (37), which has been used in many previous studies (38–41). A modified Eriksen flanker task was used to assess the inhibition aspect of EF (42), and the response times (RT, ms) in the congruent and incongruent trials were recorded as result. The RT difference between incongruent and congruent trials was used as an index of inhibition. Shorter RT and RT differences between incongruent and congruent indicated better performance. The working memory aspect of EF was assessed by 1-back and 2-back tasks. The RT on correct trials was recorded as result and shorter RT reflected better performance. Adapted from Hillman et al. (43) and Salthouse et al. (44), a more-odd shifting task was employed to assess the cognitive flexibility aspect of EF. The RT difference between the heterogeneous and homogeneous blocks was used to estimate cognitive flexibility. Each test was conducted according to the details introduced in the previous paper (45). The stimulus presentation and response data collection were conducted using E-Prime software 1.1 (Psychology Software Tools Inc., Pittsburgh, USA).

The test was conducted in a computer classroom with at least one Chinese Tibetan teacher present for better communication. Before the test, the Chinese Tibetan teachers, who in charge of the test, were trained uniformly until they were qualified. A video explaining how to do the test was also played before the test to make the students better understand until the students were familiar with the test.

Covariant

Results from many studies have demonstrated that EF can be affected by obesity rate (46–48), dietary intake (49), physical activity (50), and VO_{2max} (51, 52). Therefore, the present study took sociodemographic and dietary intake information,

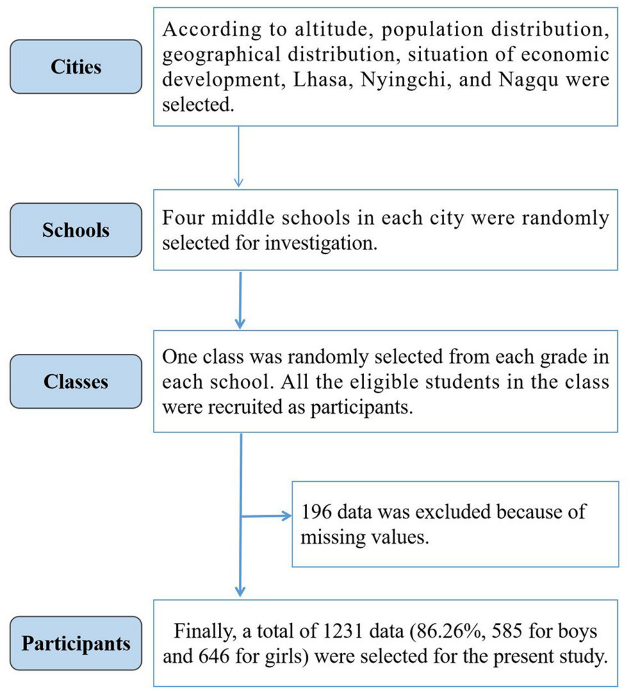

FIGURE 2 | Flowchart of participant inclusion for Chinese Tibetan adolescents.

BMI, WC, Moderate-to-Vigorous Physical Activity (MVPA), and VO_{2max} as covariant.

Sociodemographic information including age (years), sex (boys or girls), siblings (0 or ≥1), father's and mother's education (without education,elementary school,junior middle school, senior middle school, college, or above) was obtained by questionnaires. Information on dietary intake was also collected by questionnaires separately with three questions "In the past 7 days, how many times did you have breakfast? (0, 1, 2, 3, 4, 5, 6, 7)"; "In the past 7 days, how many times did you have eggs or egg products? (0, 1, 2, 3, 4, 5, 6, 7)"; "In the past 7 days, how many times did you have milk or dairy products? (0, 1, 2, 3, 4, 5, 6, 7)". Physical activity status was obtained by the following two questions: "In the past 7 days, how many times did you have physical activity (Moderate-intensity physical activity and Vigorous-intensity physical activity) on school days and weekends, respectively?" The students were asked to respond in the blanks. Moderate-intensity physical activity refers to activity that requires moderate effort, and makes you feel a little breathless, sweaty, or tired, such as cycling at normal speed, brisk walking, skating, etc. Vigorous-intensity physical activity refers to activity that requires a lot of effort, feeling breathless, sweaty, or very tiring, such as heavy lifting, running fast, playing with balls hardly, or cycling fast. If they answered more than 0 times, they were further asked about the duration each time, "On average, how long does each activity last?" Height, weight, and waist circumference (WC) were measured with participants lightly dressed and barely feet. Body mass index (BMI) was calculated as weight (in kilograms) over height (meters) square. The VO_{2max} was estimated by 20 m SRT and the details measurement of 20 m SRT was provided in our previous study (53). All the instruments were calibrated to ensure the accuracy of the test. The test was carried out at the same time every day to reduce the deviation.

Statistical Analyses

For the continuous variables, mean and standard deviation (M ± SD) were used to express the result, and One-way ANOVA was used to compare SSB consumption in different categories. For the classified variable, data were expressed by percentage, and the Chi-square test was used to compare SSB consumption in different categories.

Taking the SSB consumption 0 time/week group as the reference, general linear regression (for continuous variable) or Logical regression (classified variable) was conducted to analyze the relationship between SSB consumption and EF for Chinese Tibetan adolescents. Three models (Crude Model, Model 1, Model 2)were used: Crude Model was conducted without adjustment; Model 1 was conducted after adjusting age, sex, siblings, parental education, BMI, WC, MVPA, and VO_{2max}; Based on Model 1, Model 2 included breakfast, egg or egg products, and milk or dairy-products as additional control variables. We set dummy variables for SSB consumption and took them as continuous variables to estimate the dose-response relationship between SSB consumption and EF. The mean and standard deviation (SD) of RT for the three core EFs were calculated by age and sex. Executive dysfunction was defined as ≥1 SD from the mean.

All analyses were performed using IBM SPSS (version 25.0; IBM Inc., Armonk, NY) and GraphPad Prism 8.0.2 (GraphPad Software, Inc., CA). The level of statistical significance was set at a two-tailed $P < 0.05$.

RESULT

Among 1,231 Chinese Tibetan adolescents aged 13–18 from Tibet of China, 585 (47.5%) were boys with an average age of (15.77 ± 1.68) years. There are 634 (51.50%) adolescents with SSB consumption 1 time/week, and 409 (33.23%) adolescents with SSB consumption ≥2 time/week. Compared with non-SSB consumption, adolescents with SSB consumption ≥1 time/week have lower parental education, fewer breakfast times per week, higher BMI and waist circumference, and lower MVPA and VO_{2max} levels ($P < 0.05$; **Table 1**).

All the EF index (including congruent RT, incongruent RT, RT difference in incongruent and congruent, 1-back RT, 2-back RT, Heterogeneous RT, Homogeneous RT, RT difference in Heterogeneous and Homogeneous) of Chinese Tibetan adolescents with different SSB consumption are significantly different ($F = 20.44$, 29.32, 174.78, 20.72, 43.87, 67.25, 9.77, and 60.23, respectively, $P < 0.001$; **Table 2**). Compared with non-SSB consumption, adolescents with SSB consumption ≥1 time/week have a longer reaction time, that is, the worse performance of EF (**Table 2**).

There is a significant correlation between SSB consumption and EF for Chinese Tibetan adolescents in Tibet of China

TABLE 1 | The SSB consumption status of Chinese Tibetan adolescents in Tibet, China.

Characteristics	Total sample	SSB consumption			χ^2/F	*P*-Value
		0 time/week	1 time/week	≥2 time/week		
N	1,231	188 (15.27)	634 (51.50)	409 (33.23)	363.58	<0.001
Age	15.77 ± 1.68	15.95 ± 1.81	15.93 ± 1.65	15.44 ± 1.61	12.13	<0.001
Sex						
Boys	585 (47.5)	102 (54.3)	262 (41.3)	221 (54.0)	20.14	<0.001
Girls	646 (52.5)	86 (45.7)	372 (58.7)	188 (46.0)		
Siblings						
0	198 (16.1)	29 (15.4)	97 (15.3)	72 (17.6)	1.05	0.59
≥1	1,033 (83.9)	159 (84.6)	537 (84.7)	337 (82.4)		
Father's education						
Elementary school and below	683 (63.2)	95 (58.3)	366 (64.7)	222 (63.2)	13.16	0.01
Middle school	268 (24.8)	36 (22.1)	135 (23.9)	97 (27.6)		
College and above	129 (11.9)	32 (19.6)	65 (11.5)	32 (9.1)		
Mother's education						
Elementary school and below	775 (72.2)	93 (57.8)	432 (75.9)	250 (72.9)	38.95	<0.001
Middle school	164 (15.3)	25 (15.5)	78 (13.7)	61 (17.8)		
College and above	134 (12.5)	43 (26.7)	59 (10.4)	32 (9.3)		
Breakfast						
≤1 time/week	35 (2.8)	9 (4.8)	12 (1.9)	14 (3.4)	13.85	0.01
2–4 times/week	67 (5.4)	9 (4.8)	25 (3.9)	33 (8.1)		
≥5 times/week	1,129 (91.7)	170 (90.4)	597 (94.2)	362 (88.5)		
Eggs or egg products						
≤1 time/week	356 (28.9)	54 (28.7)	192 (30.3)	110 (26.9)	4.58	0.33
2–4 times/week	562 (45.7)	79 (42.0)	281 (44.3)	202 (49.4)		
≥5 times/week	313 (25.4)	55 (29.3)	161 (25.4)	97 (23.7)		
Milk or dairy-products						
≤1 time/week	349 (28.4)	68 (36.2)	179 (28.2)	102 (24.9)	9.21	0.06
2–4 times/week	619 (50.3)	79 (42.0)	321 (50.6)	219 (53.5)		
≥5 times/week	263 (21.4)	41 (21.8)	134 (21.1)	88 (21.5)		
BMI	20.49 ± 2.37	19.74 ± 1.79	20.4 ± 2.46	20.98 ± 2.37	19.31	<0.001
WC	68.56 ± 7.22	67.38 ± 8.00	67.97 ± 6.90	70.01 ± 7.12	13.06	<0.001
MVPA	41.81 ± 23.48	60.21 ± 18.45	40.25±23.26	35.76±21.69	82.26	<0.001
VO_{2max}	37.19 ± 5.58	38.96 ± 5.48	36.85 ± 5.52	36.90 ± 5.58	11.35	<0.001

Descriptive statistics are presented as (mean ± standard deviation) and number (percentage) for continuous and categorical.
SSB, sugar-sweetened beverages; BMI, body mass index; MVPA, moderate-to-vigorous physical activity; VO_{2max}, maximal oxygen uptake; WC, waist circumference.

(**Table 3**). After adjustment in Model 2, all the EF index were higher in Chinese Tibetan adolescents with SSB consumption ≥2 time/week than that with SSB consumption 0 time/week by 21.33 ms (95%*CI*: 6.72, 35.93), 8.21 ms(95%*CI*: 7.06, 9.35), 90.46 ms (95%*CI*: 28.69, 152.23), 147.61 ms (95%*CI*: 81.42, 213.80), 116.18 ms (95%*CI*: 74.48, 157.87), 112.41 ms (95%*CI*: 71.30, 153.52) for incongruent RT, RT difference in incongruent and congruent, 1-back RT, 2-back RT, Heterogeneous RT, RT difference in Heterogeneous and Homogeneous, respectively ($P < 0.05$).

Table 4 shows the logistic regression of executive dyfunction for Chinese Tibetan adolescents with different SSB consumption. After adding additional control variables in Model 2, Chinese Tibetan adolescents with SSB consumption ≥2 times/week perform poorer on the three core EFs (inhibition, working memory, cognitive flexibility) than that with SSB consumption 0 time/week [$OR = 5.91$, (95%*CI*: 2.78, 12.59)], [2.98, (95%*CI*: 1.40, 6.34)], [2.80, (95% *CI*:1.16, 6.74)], respectively ($P < 0.05$).

DISCUSSION

The present study cross-sectionally analyzed the association between SSB consumption and EF in Chinese Tibetan adolescents in high-altitude areas of China. The result showed that the SSB consumption of Chinese Tibetan adolescents in high-altitude areas was related to the poor performance of the EF. After adjusting for demographic factors, sociodemographic information, dietary behaviors, and some physical status, there was still a significant correlation between SSB consumption and EF in Chinese Tibetan adolescents. At the same time, our study

TABLE 2 | The status of executive function for Chinese Tibetan adolescents with different SSB consumption in Tibet of China.

RT (ms)	SSB Consumption	*N*	Mean	SD	*F*-Value	*P*-Value
Inhibition						
Congruent	0 time/week	188	745.65	94.22	20.44	<0.001
	1 time/week	634	772.52	76.96		
	≥2 times/week	409	791.86	86.64		
Incongruent	0 time/week	188	760.80	93.67	29.32	<0.001
	1 time/week	634	792.35	76.12		
	≥2 times/week	409	815.67	86.43		
Difference incongruent and congruent	0 time/week	188	15.15	3.28	174.78	<0.001
	1 time/week	634	19.84	6.31		
	≥2 times/week	409	23.81	4.53		
Working memory						
1-back	0 time/week	188	927.03	351.95	20.72	<0.001
	1 time/week	634	938.24	311.75		
	≥2 times/week	409	1,056.71	290.49		
2-back	0 time/week	188	960.10	360.41	43.87	<0.001
	1 time/week	634	1,075.45	380.06		
	≥2 times/week	409	1,226.01	275.48		
Cognitive flexibility						
Heterogeneous	0 time/week	188	1,017.51	209.75	67.25	<0.001
	1 time/week	634	1,100.70	253.78		
	≥2 times/week	409	1,236.58	221.42		
Homogeneous	0 time/week	188	737.48	133.50	9.77	<0.001
	1 time/week	634	741.79	114.80		
	≥2 times/week	409	771.56	107.75		
Difference in heterogeneous and homogeneous	0 time/week	188	280.04	179.29	60.23	<0.001
	1 time/week	634	358.90	228.52		
	≥2 times/week	409	465.02	178.77		

Descriptive statistics are presented as (mean ± SD).
SSB, sugar-sweetened beverages; N, number of the sample; SD, standard deviation.

also observed that SSB consumption was associated with a higher risk of executive dysfunction.

Our study showed that 84.73% of Chinese Tibetan adolescents consumed at least one time of SSB in the past week, which was higher than American adolescents (60.7%) (54). Over the past decades, excessive SSB consumption is spreading into low and middle-income countries, leading to an increase in chronic non-communicable diseases, cancer, and all-cause mortality, bringing a huge medical burden to the country (55, 56). It was reported that SSB consumption of children and adolescents was associated with parental SSB consumption patterns and accessibility of SSB consumption (57), frequency of fast-food consumption (58), and time spent watching television or viewing advertisements (59). Rodent studies suggest that SSB consumption may activate a glucocorticoid-metabolic-brain-negative feedback pathway, which may turn off the stress response and thereby reinforce habitual SSB overconsumption (60). Hence, targeted efforts such as taxing SSB and increasing knowledge of SSB are needed to reduce intake of SSB consumption are needed.

Similar to our findings, Gui et al. also found out that SSB consumption was associated with poorer EF among children in Guangzhou, China, and the global executive index of children with SSB consumption ≥2 times/week increased by 1.62 times compared with non-SSB consumption children (28). A study of children and adolescents in the United States showed that an increase in daily SSB consumption was associated with a 2.4-point decline in the intelligence of children and adolescents as assessed by the Kaufman Brief Intelligence Test (29). Though the association was observed between SSB consumption and EF, the bi-directional associations between them remain unclear. Obesity researchers emphasize the significance of executive-control systems for explaining the occurrence of non-homeostatic forms of dietary behavior and modulating cravings for and consumption of high-calorie foods (61). While research from other disciplines suggested SSB was inversely associated with EF (27). Hence, more longitudinal studies are needed to explore the causal relationship between them.

A systematic review suggested that the relation between EF and dietary intake is equivocal (49). In addition, a study focused on school-aged children aged 8–10 years in the United States found no association between SSB consumption and working memory, academic performance, cognition, and inhibitory

TABLE 3 | The multiple linear regression of executive function for Chinese Tibetan adolescents with different SSB consumption (n = 1,231).

RT (ms)	Estimates (95% Confidence Interval)		
	Crude Model	**Model 1**	**Model 2**
Inhibition			
Congruent			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	26.87 (13.33, 40.40)[a]	7.56 (−5.67, 20.79)	6.59 (−6.64, 19.82)
≥2 times/week	46.21 (31.85, 60.57)[a]	14.16 (−0.58, 28.89)	13.12 (−1.59, 27.83)
P for trend	<0.001	<0.001	<0.001
Incongruent			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	31.55 (18.11, 44.99)[a]	12.15 (−0.98, 25.28)	11.21 (−1.92, 24.34)
≥2 times/week	54.87 (40.61, 69.13)[a]	22.32 (7.69, 36.95)[a]	21.33 (6.72, 35.93)[a]
P for trend	<0.001	<0.001	<0.001
RT difference in incongruent and congruent			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	4.69 (3.81, 5.56)[a]	4.60 (3.57, 5.62)[a]	4.62 (3.59, 5.65)[a]
≥2 times/week	8.66 (7.73, 9.59)[a]	8.16 (7.02, 9.30)[a]	8.21 (7.06, 9.35)[a]
P for trend	<0.001	<0.001	<0.001
Working memory			
1-back			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	11.20 (−39.54, 61.95)	−14.32 (−69.75, 41.12)	−14.28 (−69.81, 41.25)
≥2 times/week	129.67 (75.83, 183.51)[a]	89.91 (28.15, 151.67)[a]	90.46 (28.69, 152.23)[a]
P for trend	<0.001	<0.001	<0.001
2-back			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	115.35 (59.04, 171.66)[a]	53.24 (−5.95, 112.43)	53.48 (−6.02, 112.99)
≥2 times/week	265.92 (206.17, 325.66)[a]	147.40 (81.46, 213.34)[a]	147.61 (81.42, 213.80)[a]
P for trend	<0.001	<0.001	<0.001
Cognitive flexibility			
Heterogeneous			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	83.18 (44.56, 121.80)[a]	14.69 (−22.70, 52.07)	14.54 (−22.94, 52.03)
≥2 times/week	219.06 (178.09, 260.04)[a]	116.93 (75.28, 158.57)[a]	116.18 (74.48, 157.87)[a]
P for trend	<0.001	<0.001	<0.001
Homogeneous			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	4.32 (−14.52, 23.15)	−11.77 (−30.82, 7.29)	−11.71 (−30.76, 7.35)
≥2 times/week	34.09 (14.10, 54.07)[a]	3.57 (−17.66, 24.79)	3.76 (−17.43, 24.95)
P for trend	<0.001	<0.001	<0.001
RT difference in Heterogeneous and Homogeneous			
0 time/week	0 (Reference)	0 (Reference)	0 (Reference)
1 time/week	78.87 (45.30, 112.43)	26.46 (−10.33, 63.25)	26.25 (−10.71, 63.21)
≥2 times/week	184.98 (149.37, 220.59)	113.36 (72.37, 154.34)[a]	112.41 (71.30, 153.52)[a]
P for trend	<0.001	<0.001	<0.001

Crude Model: without adjustment; Model 1: adjusting age, sex, siblings, parental education, BMI, WC, MVPA, and VO_{2max}*; Model 2: based on Model 1, including breakfast, egg, or egg products, and milk or dairy products as additional control variables.*

[a]*Indicate* $P < 0.001$.

control (62). The wide variety of measures used to assess EF and dietary intake may play in the relation between EF and dietary intake, making the overall interpretation of the literature more complicated. For example, EF can be used by questionnaires such as Behavior Rating Inventory of Executive Function or computerized tests (Computerized Dots Task, Computerized Neuro-psychological Test). Dietary intake can be measured by Food Frequency Questionnaire or Lab-Based Food Task. Besides,

TABLE 4 | The logistic regression of executive function for Chinese Tibetan adolescents with different SSB consumption ($n = 1,231$).

Executive dysfunction	Odds ratio (95% Confidence Interval)		
	Crude Model	Model 1	Model 2
Inhibition dysfunction			
0 time/week	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
1 time/week	4.20 (2.16, 8.18)[a]	3.12 (1.51, 6.48)[a]	3.10 (1.49, 6.44)[a]
≥2 times/week	7.22 (3.69, 14.13)[a]	5.93 (2.79, 12.61)[a]	5.91 (2.78, 12.59)[a]
P for trend	<0.001	<0.001	<0.001
Working memory dysfunction			
1-back			
0 time/week	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
1 time/week	0.82 (0.54, 1.24)	0.68 (0.41, 1.13)	0.71 (0.42, 1.19)
≥2 times/week	1.45 (0.95, 2.21)	1.29 (0.75, 2.22)	1.37 (0.79, 2.36)
P for trend	<0.001	<0.001	<0.001
2-back			
0 time/week	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
1 time/week	2.91 (1.68, 5.02)[a]	2.67 (1.30, 5.47)[a]	2.75 (1.34, 5.65)[b]
≥2 times/week	3.30 (1.88, 5.78)[a]	2.89 (1.36, 6.14)[a]	2.98 (1.40, 6.34)[a]
P for trend	<0.001	<0.001	<0.001
Cognitive flexibility dysfunction			
0 time/week	1.00 (Reference)	1.00 (Reference)	1.00 (Reference)
1 time/week	4.31 (2.06, 9.03)[a]	2.22 (0.96, 5.16)	2.32 (0.99, 5.46)
≥2 times/week	6.90 (3.28, 14.53)[a]	2.67 (1.12, 6.36)[b]	2.80 (1.16, 6.74)[b]
P for trend	<0.001	<0.001	<0.001

Crude Model: without adjustment; Model 1: adjusting age, sex, siblings, parental education, BMI, WC, MVPA, and VO_{2max}; Model 2: based on Model 1, including breakfast, egg, or egg products, and milk or dairy products as additional control variables.
[a]*Indicate $P < 0.01$.*
[b]*Indicate $P < 0.05$.*

the non-uniform covariant may also affect the result. In sum, the relation between EF and SSB needs to be further confirmed.

This study has some strengths and limitations. The strength is that we controlled several covariant such as sociodemographic information (age, sex, siblings, father's and mother's education), information on dietary intakes (eggs, milk, breakfast), and physical status (BMI, WC, MVPA, $VO_{2max,}$). However, the cross-sectional analysis of the present study can't decide a causal relationship. A prospective cohort study is needed in the future. Besides, we used self-report SSB consumption, which are inevitably affected by the recall ability. Meanwhile, the information on volumes of SSBs consumption by adolescents were not collected. At last, the impact of confounding variables on EF was not included in the study.

CONCLUSIONS

In conclusion, this study analyzed the relationship between SSB consumption and EF for Chinese Tibetan adolescents at high altitudes and concluded that SSB consumption is associated with poorer EF performance and executive dysfunction. Given the large population of Chinese Tibetan and the brain damage caused by hypoxia at high altitudes, it is necessary to make targeted efforts to reduce SSB consumption of Chinese Tibetan adolescents in high altitude, such as taxing SSB, increasing knowledge of SSB, or environmental interventions that alter the physical or social environment in which individuals make beverage choices. Longitudinal studies and clinical trials are further needed to clarify the direction of causality and to investigate the underlying mechanism.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Human Experimental Ethics Committee of the East China Normal University (Approval No.: HR0782020). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

Conceptualization: FZ, XY, and CB. Methodology: YL and ML. Validation, supervision, and funding acquisition: XY. Formal analysis and visualization: FZ. Investigation: FZ and ML. Resources, writing—original draft preparation, and project administration: ML. Data curation: XG. Writing—review and editing: FZ and YL. All authors have read and agreed to the published version of the manuscript.

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Association Between Dairy Intake and Executive Function in Chinese Children Aged 6–12 Years

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Association between dairy intake and executive function remains controversial, especially among children, a population with fast-developing executive functions. This study aimed to explore this topic. Additionally, we further distinguished the role of dairy intake types (full- or low-fat milk or yogurt) in this relationship. This survey included 5,138 children aged 6–12 years. Dairy intakes were assessed by validated questionnaires. Executive function was measured by the behavior rating inventory of executive function (BRIEF; Parent Version), and lower T-scores of BRIEF indices indicated superior executive function performance. Results showed that children with higher dairy intake had statistically better performance in Shift (46.58 ± 7.48 vs. 45.85 ± 7.10), Initiate (48.02 ± 8.58 vs. 47.14 ± 8.33), and Working Memory (50.69 ± 8.82 vs. 49.89 ± 8.73). In the analysis of multivariate linear regression, we found that for every one unit increase in full-fat dairy intake, T-scores for Shift (β = −0.350 (95% confidence interval [CI]: (−0.660, −0.039) and Initiate (β = −0.486 (95% CI: (−0.845, −0.127) were decreased and for every one unit increase in low-fat dairy intake, T-score for Organizations of Materials (β = −0.940 (95% CI: (−1.690, −0.189) was decreased. After distinguishing dairy into milk and yogurt, we observed that only milk intake, not yogurt, was significantly associated with better executive function performance in Shift (β = −0.390 (95% CI (−0.745, −0.035) and Initiate (β = −0.509 (95% CI (−0.917, −0.101) after adjusting for potential confounding factors. This study shows that a higher intake of dairy, irrespective of fat content, is related to better executive function performance among children aged 6–12. In addition, a significantly positive relationship between dairy intake and executive function's indices of Shift and Initiate only was observed in milk, not in yogurt.

Keywords: children, dairy intake types, executive function, BRIEF-parent version, cross-sectional study

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INTRODUCTION

Executive function, a particularly crucial domain within cognitive processing, consists of the mental capacity to make goal-directed behaviors, including inhibitory control, working memory, attention, and planning (1). Executive function skills develop significantly throughout childhood, with ongoing maturation continuing into adolescents and adulthood (2). A higher level of executive function plays an important role in both academic achievement (3) and health-related decision-making among children and adolescents (4–6). Thus, identifying modifiable factors, such as dairy intake, is generally considered to play an important role in children's executive function development.

A milk-derived tripeptide, Tyr-Leu-Gly (YLG), has been shown in animal experiments to contribute to executive function development by promoting the growth of nerve growth factor (NGF) and glial cell line-derived neurotrophic factor in the hippocampus (7). Milk is a great source of high-quality protein, minerals, vitamins, insulin-like growth factors, polyunsaturated fatty acids, and bioactive peptides (8). Previous studies have documented that more milk intake was beneficial to childhood growth and physical health (8, 9). Evidence shows that dairy intake, which includes liquid milk, such as milk and yogurt, is associated with executive function in the elderly (10–14). Unlike elderly individuals whose cognitive level is declined, children are in a stage of rapid development of executive functions (15). The difference in the development process of executive function implies that associations of dairy intake with executive function among the elderly may not be extrapolated to children. It has become a public consensus that dairy intake can promote the physical development of children and adolescents (16), but studies investigating the association between dairy intake and executive function in children are still limited and controversial (9, 17–20). Two school-based trials have shown that children who drink milk or more milk have better learning and executive function performance than those with no milk or less milk (9, 20), although the studies did not distinguish types of dairy intake, such as full- or low-fat milk or yogurt. Inconsistently, results of a review reported that only one-third of studies agree that milk intake would affect the cognitive function-related abilities (intelligence, academic performance, etc.) of school-age children (19). Studies conducted among adults indicated that the impacts of dairy intake on cardiovascular and metabolic health are mainly due to sugar content and not just fat content (21, 22). Yogurt sold on the market contains more sugar than regular milk (23). Based on this, we speculate that the possible reason for the inconsistent relationship between dairy intake and children's executive function is different types of dairy intake. However, as far as we know, there is still a lack of direct evidence that distinguishes dairy intake from milk and yogurt to explore their relationship with children's executive function.

Therefore, there is a need for an extensive and comprehensive assessment of the impact of dairy intake on executive function among children to help better inform future recommendations regarding dairy intake and developing executive function among children. In the present study, we hypothesize that those with higher dairy intake will have better executive function performance, and this relationship varies depending on the types of dairy intake.

MATERIALS AND METHODS

Study Design and Participants

The data were from the baseline examination of a school-based prospective cohort study (Clinical Trial Registration Number: NCT03582709). This study was approved by the Ethics and Human Subject Committee of Sun Yat-sen University, and the design has been described in detail elsewhere (24). Briefly, the multistage stratified random cluster sampling method was adopted to recruit study participants from March to May 2017. First, we randomly selected five districts from Guangzhou city. Second, we randomly selected one elementary school from each study district. All children of the five schools were invited to participate and complete the questionnaire. Children who were younger than 6 years or older than 12 years and diagnosed with visceral diseases, abnormal growth and development, or mental health problems were excluded from the study. All children and their parents voluntarily participated in this project with informed consent forms. The final sample consisted of 5,138 children and their parents completed questionnaires and anthropometric measurements, and the response rate was 90.1% (5,138/5,704). We excluded those who had missing information about dairy intake ($n = 262$) or on the behavior rating inventory of executive function (BRIEF; $n = 315$) and children with diseases ($n = 8$; **Figure 1**).

Questionnaire Survey

Dairy Intake

A validated self-reported questionnaire, completed by children and their parents together, was used to assess the consumption of dairy (25). The questions were put forth as: "In the past 7 days, how many times did you consume dairy products in total (such as full-, low-, and skimmed-fat milk, yogurt, or milk powder)? and how many milliliters (ml) of them did you consume each time?" (1 box of milk is equivalent to 250 ml, 1 bottle of yogurt is equivalent to 150 ml, and 1 scoop of milk powder is equivalent to 30 ml). In order to obtain information on dairy intake of different types, we further investigated separately the frequency and quantity of full-, low-, and skimmed-fat milk or yogurt intake in the past 7 days. The questions were as follows: "How many times did you drink full-, low-, and skimmed-fat milk and yogurt during the days you consumed dairy products? How many milliliters did you drink each time?" Finally, we calculated the

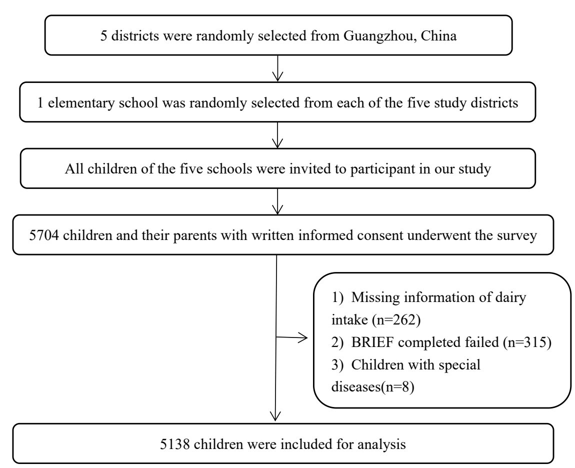

FIGURE 1 | Flowchart of participants' inclusion.

total milliliters of daily dairy intake and the daily dairy intake of full-, low-, and skimmed-fat milk and yogurt, respectively. In the analysis, we combined skimmed-fat dairy and low-fat dairy into the group of low-fat dairy intake. Full-fat dairy includes full-fat milk and full-fat yogurt, low-fat dairy includes low-fat milk and low-fat yogurt, milk includes full- and low-fat milk, and yogurt includes full- and low-fat yogurt.

Executive Function

We used the parents-rated BRIEF to assess children's executive function during the past 6 months, which is widely used in epidemiological studies (26, 27). The BRIEF is an 86-item report with a 4-point response scale (response for each is "No" [1 point]), "Sometimes" [2 points], or "Often" [3 points]) (28). It contains eight clinical domains (Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor) that comprise two index scores: Behavioral Regulation Index (BRI) and Metacognition Index (MI). Inhibit, Shift, and Emotional Control constitute the BRI, with the remaining domains constituting the MI. BRI and MI combine to form the global executive function score (GEC). **Supplementary Table 1** shows the detailed description of the indicator of the BRIEF scale. The T-scores of the BRIEF were adjusted for age and sex according to previously published normative values (27). Higher T-score indicates greater degrees of executive dysfunction. T-scores of 65 or higher are considered "clinically increased" levels. This inventory is confirmed to have a good internal consistency of 0.74–0.96, a good convergent validity of 0.41–0.64, and a good test-retest of 0.68–0.89 in school-aged children in China (29) and other countries (30) according to previous studies.

Assessment of Covariates

The physical examination included height and weight, which were tested by professionals. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Sociodemographic factors (e.g., children's birth date, sex, paternal and maternal educational level, and household

TABLE 1 | Descriptive characteristics of study children by dairy intake.

	All (*n* = 5,138)	<300 ml/day (*n* = 4,506)	≥300 ml/day (*n* = 632)	*P*
Age, years	9.08 ± 1.73	9.06 ± 1.73	9.19 ± 1.75	0.03
Gender				<0.001
Boy	2,706 (52.7)	2,310 (51.3)	396 (62.7)	
Girl	2,432 (47.3)	2,196 (48.7)	236 (37.3)	
Paternal educational level				<0.001
High school or below	1,226 (24.2)	1,112 (25.1)	114 (18.3)	
Junior college	1,238 (24.5)	1,100 (24.8)	138 (22.2)	
College or above	2,596 (51.3)	2,225 (50.1)	371 (59.6)	
Maternal educational level				<0.001
High school or below	1,325 (26.2)	1,199 (27.0)	126 (20.2)	
Junior college	1,375 (27.2)	1,212 (27.3)	163 (26.2)	
College or above	2,360 (46.6)	2,026 (45.7)	334 (53.6)	
Household monthly income				0.144
<5,000, CNY	1,071 (21.2)	940 (21.2)	131 (21.2)	
5,000∼7,999, CNY	1,299 (25.8)	1,127 (25.5)	172 (27.9)	
8,000∼11,999, CNY	891 (17.7)	785 (17.7)	106 (17.2)	
≥12,000, CNY	1,088 (21.6)	946 (21.4)	142 (23.0)	
No answer	695 (13.8)	629 (14.2)	66 (10.7)	
BMI	17.05 ± 3.22	17.00 ± 3.22	17.23 ± 3.09	0.043
MVPA, min/day	43.49 ± 36.43	43.17 ± 28.92	45.09 ± 29.74	0.076
After-school ST, min/day	170.13 ± 82.88	170.44 ± 82.73	166.42 ± 81.47	0.163
Fruits, servings/day	2.21 ± 1.99	2.14 ± 1.93	2.62 ± 2.20	<0.001
Vegetables, servings/day	3.98 ± 3.63	3.86 ± 3.52	4.63 ± 4.08	<0.001
Cereals, servings/day	0.89 ± 1.21	0.87 ± 1.18	0.94 ± 1.24	0.064
Fish, servings/day	1.15 ± 1.50	1.13 ± 1.47	1.24 ± 1.57	0.04
Red meat, servings/day	2.27 ± 2.49	2.16 ± 2.38	2.82 ± 2.90	<0.001
Fried food, times/day	0.56 ± 0.74	0.55 ± 0.73	0.57 ± 0.76	0.4
Sugar-sweetened beverages, cups/day	0.17 ± 0.26	0.16 ± 0.25	0.18 ± 0.30	0.013
dairy intake, ml/day	180.81 ± 123.36	146.86 ± 83.57	420.60 ± 87.96	<0.001
Full-fat dairy	113.10 ± 115.75	100.65 ± 102.36	205.00 ± 156.21	<0.001
Low-fat dairy	27.66 ± 60.58	26.96 ± 58.83	33.38 ± 72.07	0.004
Milk	89.66 ± 103.35	80.13 ± 93.79	160.31 ± 138.75	<0.001
Yogurt	50.18 ± 65.83	46.61 ± 62.60	75.09 ± 79.66	<0.001

CNY, Chinese yuan; BMI, body mass index; MVPA, moderate-to-vigorous intensity physical activity; after-school ST, after-school sedentary time.

monthly income) were reported by parents. Paternal and maternal educational level was categorized into three groups (high school or below, junior college, and college or above). Monthly household income was divided into five groups (<5,000, 5,000–7,999, 8,000–11,999, ≥ 12,000, and "No answer"). Physical activities and sedentary time were reported by children and their parents according to the International Physical Activity Questionnaire Short Form. For other dietary behaviors, including the consumption of fruit, vegetable, cereals, fish, and red meat, children and their parents were required to report data on the frequency and quantity in the past 7 days, and the average daily food consumption was calculated. We obtained information about fried food through a question: "In the past 7 days, how many times have you eaten fried food?" Regarding sugar-sweetened beverages, we asked children the number of times and cups of sugar-sweetened beverages in the past 7 days and calculated the average daily amounts of sugar-sweetened beverages.

TABLE 2 | Performance of children with different dairy intake on the scale of the BRIEF.

Scale/Index	All	<300 ml/day	≥300 ml/day	P
Inhibit	46.67 ± 7.42	46.67 ± 7.39	46.45 ± 7.48	0.458
Shift	46.52 ± 7.46	46.58 ± 7.48	45.85 ± 7.10	0.017
Emotional control	43.22 ± 7.15	43.25 ± 7.12	42.84 ± 7.07	0.16
BRI	44.55 ± 7.23	44.57 ± 7.22	44.17 ± 7.09	0.182
Initiate	47.95 ± 8.57	48.02 ± 8.58	47.14 ± 8.33	0.013
Working memory	50.62 ± 8.81	50.69 ± 8.82	49.89 ± 8.73	0.028
Plan/organize	52.15 ± 9.64	52.16 ± 9.59	51.74 ± 10.45	0.409
Organization of materials	46.53 ± 9.03	46.49 ± 9.04	46.67 ± 8.91	0.621
Monitor	52.21 ± 10.36	52.26 ± 10.33	51.74 ± 10.45	0.220
MI	50.04 ± 9.48	50.07 ± 9.47	49.63 ± 9.45	0.269
GEC(BRI + MI)	47.83 ± 8.60	47.85 ± 8.58	47.42 ± 8.57	0.237

BRI, Behavioral Regulation Index; MI, Metacognition Index; GEC, global executive function score.

Statistical Analysis

Continuous variables were reported as the mean ± standard deviation (SD), whereas categorical variables were shown as numbers and percentages. Children were divided into subgroups based on whether their daily dairy intake reached 300 ml. The differences in participant characteristics among dairy intake groups were compared using independent groups t-tests for continuous variables and Pearson's chi-squared tests for categorical variables. Multivariate linear regression was carried out to evaluate the associations between dairy intake and executive function. Model 1 was adjusted for age, gender, paternal and maternal educational level, household monthly income, and BMI. Model 2 was further adjusted for moderate-to-vigorous intensity physical activity and after-school sedentary time. Model 3 was additionally adjusted for other dietary intakes, including fruits, vegetables, cereals, fish, red meat, fried food, and sugar-sweetened beverages. All the variables were entered simultaneously into multivariate linear models. All analyses were conducted using SPSS version 21.0 (IBM, Armonk, NY, United States) and a 2-sided $p < 0.05$ indicated statistical significance.

RESULTS

The analytic sample included 5,138 children, with a mean (SD = 1.73) age was 9.08 years and 2,706 (52.7%) were boys. The average children's daily dairy intake is 180.81 ± 123.36 ml, of which 113.10 ± 115.75 ml was full-fat dairy intake and 27.66 ± 60.58 ml was low-fat dairy intake. Daily intake of milk and yogurt is 89.66 ± 103.35 ml and 50.18 ± 65.83 ml, respectively. The characteristics of children according to dairy intake levels are summarized in **Table 1**. Children who consumed a higher level of dairy were older, had higher BMI, had parents with a higher level of education, and consumed more fruits, vegetables, red meat, and sugar-sweetened beverages ($p < 0.001$).

Table 2 presents the BRIEF scores across different dairy intake groups. The results showed that children with higher dairy intake had statistically lower T-scores of BRIEF for Shift (46.58 ± 7.48 vs. 45.85 ± 7.10), Initiate (48.02 ± 8.58 vs. 47.14 ± 8.33), and Working Memory (50.69 ± 8.82 vs. 49.89 ± 8.73). Preliminary analysis revealed a reduction of BRIEF indices in the significant association between dairy intake and executive function with increasing adjustment for covariates (**Table 3**). In the analysis of multivariate linear regression, we found that for every one unit (150 ml) increase in dairy intake, the T-scores for GEC (β = −0.308 (95% confidence interval [CI] (−0.618, −0.004)), Shift (β = −0.404 (95% CI (−0.672, −0.137), BRI (β = −0.278 (95% CI (−0.537, −0.020), and Initiate (β = −0.443 (95% CI (−0.751, −0.137) were decreased when we adjusted for potential confounding factors (Model 3).

To clarify whether there are differences in the relationship between different types of dairy intakes and executive functions, we further analyzed the association of full- and low-fat dairy intake, milk, and yogurt with indices of executive function. Children who consumed more full-fat dairy had lower scores in Shift (β = −0.350 (95% CI (−0.660, −0.039) and Initiate (β = −0.486 (95% CI (−0.845, −0.127) after adjusting for covariates (**Table 4**). However, the intake of low-fat dairy was significantly negatively correlated with the T-score for Organizations of Materials (β = −0.940 (95% CI (−1.690, −0.189). After distinguishing dairy into milk and yogurt (**Table 5**), we observed that only milk intake, not yogurt, was significantly associated with better executive function performance in Shift (β = −0.390 (95% CI (−0.745, −0.035) and Initiate (β = −0.509 (95% CI (−0.917, −0.101). Furthermore, **Supplementary Table 2** shows that the statistically significant negative associations between milk intake and the T-scores of BRIEF mainly existed in the type of full-fat milk ($p < 0.05$).

DISCUSSION

Considering different types of dairy intake (full- and low-fat, milk, and yogurt), we provided a comprehensive evaluation of the associations of dairy intake with children's executive

TABLE 3 | Multivariate linear regression for analyzing associations of dairy intake with executive function.

Scale/Index	Dairy intake unstandardized β (95% CI) Model 1	Model 2	Model 3
Inhibit	–0.220 (–0.470, 0.029)	–0.165 (–0.429, 0.100)	–0.165 (–0.429, 0.101)
Shift	–0.424 (–0.674, –0.174)**	–0.404 (–0.672, –0.136)*	–0.404 (–0.672, –0.137)*
Emotional control	–0.230 (–0.470, 0.010)	–0.241 (–0.499, 0.018)	–0.241 (–0.499, 0.019)
BRI	–0.295 (–0.539, –0.052)*	–0.278 (–0.537, –0.019)*	–0.278 (–0.537, –0.020)*
Initiate	–0.552 (–0.839, –0.265)**	–0.443 (–0.751, –0.136)*	–0.443 (–0.751, –0.137)*
Working memory	–0.333 (–0.630, –0.037)*	–0.221 (–0.534, 0.092)	–0.221 (–0.534, 0.093)
Plan/Organize	–0.333 (–0.654, –0.011)*	–0.301 (–0.641, 0.038)	–0.301 (–0.641, 0.039)
Organization of materials	–0.295 (–0.597, 0.007)	–0.196 (–0.521, 0.129)	–0.196 (–0.521, 0.130)
Monitor	–0.389 (–0.736, –0.041)*	–0.266 (–0.639, 0.108)	–0.266 (–0.639, 0.109)
MI	–0.423 (–0.746, –0.099)*	–0.322 (–0.663, 0.019)	–0.322 (–0.663, 0.020)
GEC (BRI + MI)	–0.391 (–0.686, –0.096)*	–0.308 (–0.618, –0.003)*	–0.308 (–0.618, –0.004)*

*BRI, Behavioral Regulation Index; MI, Metacognition Index; GEC, global executive function score. Model 1 is adjusted for age, gender, paternal and maternal educational level, household monthly income, and BMI. Model 2 is further adjusted for moderate-to-vigorous intensity physical activity and after-school sedentary time plus variables in Model 1. Model 3 is additionally adjusted for other dietary intakes, such as fruits, vegetables, cereals, fish, red meat, fried food, and sugar-sweetened beverages plus variables in Model 2. *p < 0.05, **p < 0.001.*

TABLE 4 | Multivariate linear regression for analyzing associations of full- or low-fat dairy intake with executive function.

Scale/Index	Full-fat dairy unstandardized β (95% CI)			Low-fat dairy unstandardized β (95% CI)		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Inhibit	–0.240 (–0.513, 0.033)	–0.158 (–0.448, 0.131)	–0.188 (–0.494, 0.118)	0.002 (–0.527, 0.532)	0.081 (–0.481, 0.643)	0.204 (–0.404, 0.812)
Shift	–0.386 (–0.662, –0.110)*	–0.358 (–0.652, –0.064)*	–0.350 (–0.660, –0.039)*	–0.426 (–0.961, 0.110)	–0.299 (–0.869, 0.271)	–0.110 (–0.727, 0.506)
Emotional control	–0.199 (–0.463, 0.065)	–0.110 (–0.392, 0.172)	–0.117 (–0.417, 0.182)	–0.137 (–0.644, 0.370)	–0.252 (–0.795, 0.292)	–0.143 (–0.734, 0.448)
BRI	–0.296 (–0.564, –0.028)*	–0.221 (–0.505, 0.064)	–0.231 (–0.532, 0.069)	–0.157 (–0.677, 0.362)	–0.164 (–0.716, 0.387)	0.010 (–0.587, 0.606)
Initiate	–0.605 (–0.923, –0.287)**	–0.497 (–0.836, –0.157)*	–0.486 (–0.845, –0.127)*	–0.525 (–1.135, 0.085)	–0.259 (–0.911, 0.394)	–0.020 (–0.728, 0.688)
Working memory	–0.343 (–0.670, –0.016)*	–0.150 (–0.493, 0.194)	–0.134 (–0.496, 0.229)	–0.352 (–0.985, 0.280)	–0.209 (–0.874, 0.457)	–0.050 (–0.766, 0.665)
Plan/Organize	–0.322 (–0.679, 0.035)	–0.138 (–0.513, 0.236)	–0.096 (–0.492, 0.300)	–0.387 (–1.080, 0.305)	–0.155 (–0.884, 0.573)	–0.017 (–0.802, 0.767)
Organization of materials	–0.260 (–0.594, 0.074)	–0.082 (–0.440, 0.277))	–0.086 (–0.465, 0.294)	–0.989 (–1.633, –0.345)*	–0.884 (–1.576, –0.192)*	–0.940 (–1.690, –0.189)*
Monitor	–0.279 (–0.665, 0.107)	–0.062 (–0.473, 0.350)	–0.001 (–0.437, 0.436)	–0.540 (–1.283, 0.203)	–0.388 (–1.818, 0.406)	–0.221 (–1.083, 0.641)
MI	–0.340 (–0.699, 0.019)	–0.130 (–0.508, 0.248)	–0.093 (–0.491, 0.305)	–0.707 (–1.402, –0.011)*	–0.499 (–1.233, 0.236)	–0.370 (–1.155, 0.415)
GEC (BRI + MI)	–0.327 (–0.655, –0.001)*	–0.148 (–0.492, 0.195)	–0.130 (–0.492, 0.232)	–0.456 (–1.093, 0.181)	–0.318 (–0.989, 0.352)	–0.190 (–0.906, 0.527)

*BRI, Behavioral Regulation Index; MI, Metacognition Index; GEC, global executive function score. Model 1 is adjusted for age, gender, paternal and maternal educational level, household monthly income, and BMI. Model 2 is further adjusted for moderate-to-vigorous intensity physical activity, and after-school sedentary time plus variables in Model 1. Model 3 is additionally adjusted for other dietary intakes, such as fruits, vegetables, cereals, fish, red meat, fried food, and sugar-sweetened beverages plus variables in Model 2. *p < 0.05, **p < 0.001.*

function assessed by BRIEF. Generally, results showed that higher dairy intake is associated with a lower T-score for BRIEF, indicating superior executive function performance. In particular, negative associations were observed between full-fat dairy intake and Initiate and Working Memory, and low-fat dairy intake and Organization of Materials, indicating that a higher intake of dairy, irrespective of fat content, is correlated with superior executive function performance. In addition, a positive relationship between dairy intake and indices of Shift and Initiate only was observed in milk, not in yogurt.

Dairy products have been advertised for a long time as being excellent sources of nutritional components and as a part of a well-balanced diet, but there are still large regional differences in dairy consumption (31). In the present study, the average total dairy intake of children was 180.81 ml/day, which was higher than the average dairy intake of 126.7 g in 2019 (32). The possible reason is that the sample of this study was sampled from Guangzhou, China, which has relatively good economic development. In addition, whether dairy intake is beneficial or detrimental to executive function is controversial (19, 33, 34). In general, our analysis supported that a higher intake of dairy was related to superior executive function in children, which was consistent with several studies (9, 17, 20). Interventional studies on children have reported that increasing the intake of certain dairy products could promote executive function (9), those with higher dairy intake performed better in academics (17), and they scored higher on cognitive tests than those with lower dairy intake (20). Meanwhile, some studies conducted among adults and the elderly found that higher dairy intake is likely to have a protective effect against cognitive impairment, such as Dementia (11, 35). On the contrary, there are some inconsistent reports of associations between dairy intake and executive function (19, 33). No association was observed between dairy intake and cognitive ability assessed by the Wechsler Intelligence Scales in a 6-year longitudinal study (18). Additionally, several studies carried out on older adults suggested that greater dairy intake is related

TABLE 5 | Multivariate linear regression for analyzing associations of milk or yogurt with executive function.

Scale/Index	Milk unstandardized β (95% CI)			Yogurt unstandardized β (95% CI)		
	Model 1	**Model 2**	**Model 3**	**Model 1**	**Model 2**	**Model 3**
Inhibit	–0.263 (–0.572, 0.045)	–0.189 (–0.518, 0.140)	–0.130 (–0.479, 0.219)	–0.166 (–0.640, 0.308)	–0.077 (–0.578, 0.423)	–0.160 (–0.696, 0.375)
Shift	–0.459 (–0.771, –0.146)*	–0.427 (–0.762, –0.093)*	–0.390 (–0.745, –0.035)*	–0.433 (–0.912, 0.046)	–0.332 (–0.840, 0.176)	–0.262 (–0.804, 0.280)
Emotional control	–0.365 (–0.662, –0.068)*	–0.271 (–0.590, 0.048)	–0.210 (–0.551, 0.131)	0.079 (–0.379, 0.537)	0.066 (–0.421, 0.552)	0.019 (–0.503, 0.542)
BRI	–0.380 (–0.684, –0.077)*	–0.310 (–0.633, 0.014)	–0.237 (–0.580, 0.107)	–0.183 (–0.650, 0.283)	–0.129 (–0.620, 0.363)	–0.160 (–0.686, 0.366)
Initiate	–0.655 (–1.103, –0.298)**	–0.518 (–0.901, –0.135)*	–0.509 (–0.917, –0.101)*	–0.582 (–1.131, –0.033)*	–0.369 (–0.953, 0.215)	–0.107 (–0.731, 0.517)
Working memory	–0.408 (–0.777, –0.040)*	–0.223 (–0.611, 0.166)	–0.168 (–0.581, 0.245)	–0.384 (–0.950, 0.182)	–0.158 (–0.751, 0.435)	–0.028 (–0.661, 0.604)
Plan/Organize	–0.465 (–0.870, –0.060)*	–0.226 (–0.653, 0.202)	–0.169 (–0.621, 0.283)	–0.204 (–0.821, 0.413)	–0.015 (–0.660, 0.631)	0.128 (–0.562, 0.818)
Organization of materials	–0.634 (–1.011, –0.257)**	–0.455 (–0.861, –0.048)*	–0.428 (–0.860, 0.005)	–0.164 (–0.744, 0.416)	0.032 (–0.587, 0.651)	0.024 (–0.639, 0.687)
Monitor	–0.524 (–0.960, –0.088)*	–0.260 (–0.727, 0.207)	–0.150 (–0.647, 0.347)	–0.073 (–0.739, 0.593)	0.084 (–0.625, 0.792)	0.193 (–0.568, 0.955)
MI	–0.576 (–0.984, –0.169)*	–0.339 (–0.769, 0.091)	–0.259 (–0.713, 0.195)	–0.239 (–0.858, 0.381)	–0.020 (–0.670, 0.631)	0.108 (–0.585, 0.801)
GEC (BRI + MI)	–0.487 (–00.859, –0.115)*	–0.293 (–00.685, 0.099)	–0.212 (–00.626, 0.202)	–0.233 (–00.799, 0.334)	–0.061 (–00.654, 0.532)	–0.011 (–0.643, 0.621)

BRI, Behavioral Regulation Index; MI, Metacognition Index; GEC, global executive function score. Model 1 is adjusted for age, gender, paternal and maternal educational level, household monthly income, and BMI. Model 2 is further adjusted for moderate-to-vigorous intensity physical activity, and after-school sedentary time plus variables in Model 1. Model 3 is additionally adjusted for other dietary intakes, such as fruits, vegetables, cereals, fish, red meat, fried food, and sugar-sweetened beverages plus variables in Model 2. *$p < 0.05$, **$p < 0.001$.

to poorer memory performance and cognitive function (36, 37). The pieces of literature with these inconsistent conclusions pointed out that the failure to distinguish between high- and low-fat dairy intakes is a possible reason (18, 36). Based on the above, the current study explored the role of dairy fat content in this relationship. We observed that intake of full-fat dairy was negatively correlated to Initiate and Working Memory, and low-fat dairy was negatively related to Organization of Materials, indicating that both full- or low-fat dairy higher intake are correlated with superior children's executive function. Some evidence supported our research conclusions. Moderate intake of milk fat can improve neurodevelopment, which has been confirmed in animal experiments and interventional population studies, as most milk fats are rich in phospholipids and sphingolipids (38). On the other hand, the heterogeneity of the study population may also partially explain the inconsistency of results. The sample population for this study is children aged 6–12, who are at the age of rapid brain development (6, 15). However, the sample population for these studies (36, 39) is adults or elderly people who are in a period of plateau or decline in cognitive function.

Growing evidence indicated that the effects of dairy intake on cardiovascular and metabolic health appear to vary by type (i.e., milk, yogurt, etc.) and not just by fat content (40, 41). Thus, analysis of further types of dairy intake may provide insightful information on how dairy intake modifications likely affect children's executive function. Indeed, it was determined that associations between dairy intake and children's executive function may vary depending on the types of milk or yogurt in the current study. Specifically, a significantly positive association exists only in milk with executive function, whereas it disappears in yogurt with executive function. Previous studies conducted in Australia, England, and South Africa reported that sugar content in yogurt is generally higher than that in milk (23). Yogurt was often added with sugar to improve its taste (42). According to the survey, yogurt with 10% sugar content is more popular than those with 7% sugar content (43). The above results highlighted the possibility that those who frequently consume yogurts could be at increased risk of exceeding their recommended daily intake of sugar (23). In particular, studies have confirmed that excessive sugar intake will affect the synaptic connections and neurotransmitter transmission in the developing brain (44). Considering the unfavorable contribution of excessive sugar content to children's brain development, we speculate that it is a possible reason for the inconsistency in the relationship between the two (milk and yogurt) and children's executive function performance.

The biological mechanisms linking dairy intake to cognitive function are plausible. Dairy products are rich in β-lactolin, which is a β-lactoglobulin-derived Gly-Thr-Trp-Tyr tetrapeptide (45). A previous study using a mouse model demonstrated that β-lactolin can increase monoamine levels in the cortex and hippocampus regions (46). Moreover, it can also promote spatial working memory and attention in mice with pharmacologically induced amnesia (46). A randomized, double-blind study on humans also reported that supplementation with β-lactolin increases neural activity, as indicated by the P300 amplitude, in the parietal area during auditory tasks that require attention (47). Thus, higher intake of dairy may lead to changes in the brain structure and function, particularly in the frontal cortical regions involved, through synapse formation, in neurogenesis, myelination, and glucose control.

To the best of our knowledge, this is the first study based on a large sample to provide an evaluation of the associations of dairy intake with children's executive function assessed by BRIEF, a highly reliable tool for measuring capacity for everyday skills. Findings from this novel study contribute to an important foundation, more rigorous investigations in associations between types of dairy intake and children's executive function to identify potential targets for intervention to improve children's executive function through diet modification. However, several study shortcomings should be considered in regard to the generalizability of our data. First, a cross-sectional study lacks the ability to demonstrate causality. Second, although this study adjusted for many confounders, we could not entirely exclude some underlying factors, such as intelligence quotient (48), which may mediate the observed associations. Third, our research did not include all types of dairy products, such as cheese, milk-containing beverages, and milk-containing ice cream. Although the children in this study had extremely low intakes of these dairy products, the lack of consideration for them may still affect the stability of the relationship. Fourth, alternatives to cow's milk intake, such as goat's milk intake, were not considered in this study, and future research should take them into account.

CONCLUSION

This study shows that a higher intake of dairy, irrespective of fat content, is related to better executive function performance among children aged 6–12. In addition, a significantly positive relationship between dairy intake and executive function's indices of Shift and Initiate only was observed in milk, not in yogurt. This study might contribute to identifying potential targets for intervention to improve children's executive function through dairy intake modification.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethics and Human Subject Committee of Sun Yat-sen University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

YC and QC designed the experiments. XZ and ZG carried out the experiments. XZ performed the statistical analysis and drafted the manuscript. TS, WY, and QC critically revised the manuscript. LC and ZG provided suggestions in the statistical analysis and revised manuscript. All authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.879363/full#supplementary-material

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Sugar-Sweetened Beverage Intake and Motor Function Among Autistic and Typically Developed Children

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Background and Objectives: The relationship between brain function and sugar-sweetened beverages (SSBs) is widely explored, but the motor function was not included. We aim to explore the relationship between SSBs and motor function among children with or without autism.

Methods: Participants were a representative autism sample (ASD, $n = 106$) comprising ages ranging 6–9 years and their age-matched typical counterparts (TD, $n = 207$), recruited in the research center of Guangzhou, China. Valid questionnaires of parent-reported including weekly SSBs intake, physical activity (PA), sedentary time (ST), and motor coordination function was used to collect relevant information. SSBs intake was further classified as no intake (no habit of taking SSBs), small to medium intake (<375 ml/week), and large intake (375 ml/week or more). Physical activity, sedentary time, and motor coordination function among the mentioned three groups as well as ASD *vs*. TD was compared *via* general linear models.

Results: Compared with TD children, ASD children showed less vigorous PA (4.23 ± 0.34 h *vs*. 2.77 ± 0.49 h, $p = 0.015$) as well as overall sedentary time (5.52 ± 1.89 h *vs*. 3.67 ± 0.28 h, 3.49 ± 0.16 h *vs*. 2.68 ± 0.24 h, and 34.59 ± 1.15 h *vs*. 23.69 ± 1.69 h, TD *vs*. ASD, sedentary time at weekdays, weekends and total ST in a week, respectively, all $p < 0.05$), lower scores in the developmental coordination disorder questionnaire (fine motor and handwriting: 14.21 ± 0.26 *vs*. 12.30 ± 0.38, general coordination: 28.90 ± 0.36 *vs*. 25.17 ± 0.53, control during movement: 24.56 ± 0.36 *vs*. 18.86 ± 0.53, and total score: 67.67 ± 0.75 *vs*. 56.33 ± 1.10, TD *vs*. ASD, all $p < 0.05$). Stratified by SSBs intake, TD children with small to medium SSBs intake showed the lowest sedentary time both on weekdays and weekends (all $p < 0.05$), they also performed worst in fine motor and handwriting skills ($p < 0.05$).

Conclusion: The association between SSBs and motor function was observed in typical development children, but not autistic children. A larger sample size study with a longitudinal design is warranted to confirm the association between SSBs and sedentary time among typically developed children and the potential causation direction.

Keywords: sugar-sweetened beverage, motor function, autism, physical activity, sedentary time

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INTRODUCTION

The intake of sugar-sweetened beverages (SSBs) is well explored in regard to the metabolic status of children (1). According to reports published in recent years, SSBs are also associated with brain function (2). For instance, both research conducted on humans and rodents (3, 4) showed a negative impact of excessive sugar intake on the brain, especially on executive (5) and memory function (6), which indicated a potentially negative effect on overall brain function.

However, motor function, as an important domain of brain function, has been neglected in the research pertaining to SSBs and the brain. Motor function is the basis of physical activity and fitness in children; thus, it plays a vital role in the long-term health and well-being of children. The current evidence regarding SSBs and motor function is limited, as it only focuses on physical activity and sedentary time (7). Although research has predominantly reported that long durations of ST are associated with increased SSB intake (8–11), the relationship between PA and SSB intake is still debated. Ranjit et al. and Gan et al. reported that high PA was associated with more SSB intake (8, 11); however, a study conducted on African Americans showed that high PA was associated with both healthy and unhealthy diets (12), indicating that the findings regarding the relationship between motor function and SSB intake are inconsistent (7). Animal studies have also supported the association between SSBs and motor function (13), as excessive sugar intake was shown to activate the oxidative stress pathway in the human brain (13). During the key period of brain development, oxidative stress may affect the myelinization of white matter (14), thus potentially leading to motor function impairment. Both PA and ST could reflect motor competence, as individuals who lack motor skills are also less motivated to partake in PA and are more likely to be sedentary (15). In this case, it is necessary to directly clarify the relationship between SSBs and motor skills and motor competence.

The previous research regarding SSBs and motor function has focused on typically developed children, while there is a lack of evidence from children with developmental disorders. Autism, a developmental disorder that impairs social function, also impacts motor function in children, thus posing high risks to their physical health in their future life (16). In addition, children with autism tend to show peculiar food preferences, such as particular interests in consuming sugary or high-calorie food (17), which may also affect their SSB-intake behavior. Clarifying the relationship between motor function and SSB intake in children with autism could aid in providing a better description of the lifestyle of these children and in addressing the potential health risks imposed by this lifestyle. In this regard, we propose that it is worth exploring the association between SSBs and lifestyles in both ASD and TD children, to support a targeted intervention for SSB-related negative health outcomes. In this research, we explored the association between SSB intake and PA, ST, and the motor coordination function of children. Both typically developed children (who are described as possessing normally developed motor function) and children with autism (ASD) (who have partially impaired brain function) were included, in order to examine the association between SSBs and motor function in the overall child population. Considering the fact that executive function (EF) is impaired in children with autism (18), and that EF is related to both PA and motor coordination function (19), we employed EF as a covariate in the adjusted model. According to the literature review, we hypothesize that (a) children who consume more SSBs are more likely to adopt a low PA and high ST behavior pattern, and their motor competence will also be lower; (b) children with ASD exhibit lower PA, higher ST, and worse motor coordination function, compared with TD children, while increased SSB intake is associated with less PA and more ST, as well as lower motor coordination function, among both ASD and TD children.

METHODS

Study Population and Procedure

Children with ASD (aged 6–9 years, $n = 108$) were obtained from an ongoing study, "The Guangzhou Longitudinal Study of Children with ASD," examining the developmental trajectories of children with ASD in Guangzhou, China. These children were recruited between 2017 and 2021 from the Center for Child and Adolescent Psychology and Behavioral Development at Sun Yat-sen University. Each child had a historical diagnosis of ASD, which was further confirmed by a Childhood Autism Rating Scale (CARS) assessment, as well as an assessment conducted by two professional child psychiatrists in the research team (JJ and XL), using the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5). Simultaneously, age- and gender-matched typically developed children (TD, $n = 207$) were recruited *via* online media. We excluded children with a physical handicap as well as those with neurodevelopmental disorders other than ASD (e.g., attention-deficit/hyperactivity disorder, ADHD). Parent-reported questionnaires were employed to obtain information on the children, including demography, sugar-sweetened beverage intake, physical activity, sedentary time, motor coordination, and executive function. If one family had more than one child who fitted the inclusion criteria, we only included the eldest child. This study was approved by the Ethics Committee of Sun Yat-sen University and written informed consent was obtained from the parents of the child.

Sugar-Sweetened Beverage Intake

Information regarding the sugar-sweetened beverage intake of the child was obtained by the question, "In the last 7 days, how many times did your child have sugar-sweetened beverages? Sugar-sweetened beverages included those beverages containing sugar, such as Coke, Sprite, bottled juice with sugar, Red Bull, etc. Please specify the exact number, and at each time, how many cups did your child have these sugar-sweetened beverages? One cup equals 250 ml." The parents of the children were asked to specify the frequency and volume of SSB intake.

Physical Activity and Sedentary Time

Physical Activity

Vigorous physical activity (VPA) was assessed by the question, "In the last 7 days, how many days did your child have vigorous physical activity? Vigorous physical activity means an activity that causes people to be out of breath, perspire and experience extreme exhaustion, such as basketball, football, carrying a heavy load, etc. Please specify the number of days. These days, how long did your child usually spend in these physical activities? Please specify the accurate time (hours and minutes)."

Moderate physical activity (MPA) was assessed by the question, "In the last 7 days, how many days did your child have moderate intensively physical activity? Moderate physical activity means an activity that causes people to mildly perspire and experience slight exhaustion, such as bicycling, playing table tennis, badminton, etc., but not including walking. Please specify the number of days. These days, how long did your child usually spend in these physical activities? Please specify the accurate time (hours and minutes)."

Walking was assessed by the question, "In the last 7 days, how many days did your child have walked (please only include and accumulate those walking that lasted 10 min or longer)? Walking includes those that happened at school, home, commute between school and home, and for exercise. Please specify the number of days. These days, how much time did your child usually spend in these walking? Please specify the accurate time (hours and minutes)."

Sedentary Time

Sedentary time was assessed by the question, "In the last 7 days, how long did your child have usually spend sitting or lying still each day (sedentary time includes sitting still at school, home, or other places, but does not include sleeping time)? Please specify the daily sedentary time and report the time of workdays (Monday to Friday) and holidays (Saturday and Sunday, other legal holidays) separately."

Motor Coordination Assessment

Motor coordination was assessed using the Developmental Coordination Disorder Questionnaire (DCDQ, Chinese version) (20), which is a 17-item parent-reported questionnaire consisting of three subscales that measure three domains of motor coordination, i.e., fine motor/handwriting, general coordination, and control during movement. This questionnaire provides a total score ranging from 17 to 85, as well as three subscale scores, with higher scores indicating better motor coordination function. The Chinese version of DCDQ covered the age range from kindergarten children to primary school-aged children (3–12 years) (21); it could be employed to assess, with acceptable reliability and validity, both typically developed children who have suspected motor coordination problems and children with neurodevelopmental disorders, such as ASD (22) or ADHD (23).

Potential Cofounders

The following characteristics were included as potential confounders: sociodemographic information, such as the child's gender, age, maternal/paternal age, maternal/paternal education, family's household income, and executive function. Sociodemographic information was collected using a parent-reported questionnaire and executive function was evaluated by the Behavior Rating Inventory of Executive Function (BRIEF) (24).

Statistical Analysis

Data analyses were conducted in February 2022, and statistical analyses were performed using Statistic Package for Social Science 25.0 (SPSS 25.0, IMB, U.S., 2017). Continuous variables and categorical variables are presented as mean (standard deviation [*SD*]) values and percentages, respectively. The T-tests (for continuous variables) or chi-square tests (for categorical variables) were employed to explore the differences between ASD and TD children. A general linear model with several potential adjusted cofounders was used to evaluate the differences between ASD and TD children, and SSB intake was grouped and treated as one fixed factor, in order to test the potential interaction effect between SSB intake and ASD/TD group. All the tests employed were two-sided tests, and $p < 0.05$ was considered statistically significant.

RESULTS

A total of 107 ASD children and 209 TD children were included in the final analysis. The basic characteristics of both groups are described in **Table 1**. Compared with the TD group, there were a higher proportion of males in the ASD group (84.1 *vs*. 54.5%, ASD *vs*. TD, respectively, $p < 0.001$; **Table 1**). In addition, the ASD group had a lower maternal education level (college degree: 58.9 *vs*. 75.1%, ASD *vs*. TD, respectively, $p = 0.003$; **Table 1**) and a lower proportion of per capita family income over CNY 8000/month (43.0 *vs*. 74.6%, ASD *vs*. TD, respectively, $p < 0.001$; **Table 1**). We also observed a lower score on the executive function test among ASD children (54.08 ± 8.71 *vs*. 63.35 ± 9.16, ASD *vs*. TD, respectively, $p < 0.001$; **Table 1**), compared with TD children. No differences were observed in terms of child's age, maternal and paternal age, paternal education level, and SSB intake between the two groups (**Table 1**).

Compared with TD children, ASD children were shown to spend less time performing high-intensity physical activity each week (2.77 ± 0.49 h *vs*. 4.23 ± 0.34 h, ASD *vs*. TD, respectively, $p = 0.015$) and less time being sedentary on weekdays (3.67 ± 0.28 h *vs*. 5.52 ± 1.89 h, ASD *vs*. TD, respectively, $p < 0.001$), weekends (2.68 ± 0.24 h *vs*. 3.49 ± 0.16 h, ASD *vs*. TD, respectively, $p = 0.005$), and per week (23.69 ± 1.69 *vs*. 34.59 ± 1.15, ASD *vs*. TD, respectively, $p < 0.001$). In terms of motor coordination function, ASD children showed lower scores for both the total scale (56.33 ± 1.10 *vs*. 67.67 ± 0.75, ASD *vs*. TD, respectively, $p < 0.001$) and the three subdomains of the scale: fine motor/handwriting (12.30 ± 0.38 *vs*. 14.21 ± 0.26, ASD *vs*. TD, respectively, $p < 0.001$), general coordination (25.17 ± 0.53 *vs*. 28.90 ± 0.36, ASD *vs*. TD, respectively, $p < 0.001$), and control during movement (18.86 ± 0.53 *vs*. 24.56 ± 0.36, ASD *vs*. TD, respectively, $p < 0.001$). In addition, more children in the ASD group were classified as having motor coordination problems (abnormal: 47.3 *vs*. 15.4%, ASD *vs*. TD, respectively, $p < 0.001$). No statistical differences were observed in the time spent performing moderate- or low-intensity physical activity each week (**Table 2**, all $p > 0.05$), between ASD and TD children.

TABLE 1 | Basic characteristics of autism spectrum disorder (ASD) children and typically developed (TD) children ($n = 315$).

	ASD ($n = 107$)	TD ($n = 208$)	*P*-value
Child characteristics			
Age (mean ± SD)	7.71 ± 1.30	7.76 ± 1.32	0.745
Gender (%)			<0.001*
Boys	84.1%	54.5%	
Girls	15.9%	45.5%	
Family characteristics			
Maternal age (mean ± SD)	36.92 ± 3.42	37.06 ± 3.51	0.749
Paternal age (mean ± SD)	39.3 ± 4.7	39.2 ± 4.2	0.883
Maternal college degree (%)			0.003*
No	41.1%	24.9%	
Yes	58.9%	75.1%	
Paternal education (%)			0.752
Junior college or below	37.4%	35.6%	
College or higher	62.6%	64.4%	
Per capita monthly household income (%)			<0.001*
Less than CNY 8,000/month	57.0%	25.4%	
More than CNY 8,000/month	43.0%	74.6%	
Executive Function	63.35 ± 9.16	54.08 ± 8.71	<0.001*
Sugar-Sweetened beverage intake (ml/week)	335.86 ± 40.36	300.57 ± 28.88	0.487
Sugar-Sweetened beverage intake (%)			0.591
No intake	36 (33.6)	83 (39.7)	
Small to medium intake	37 (34.6)	66 (31.6)	
High intake	34 (31.8)	60 (28.7)	

ASD, autism spectrum disorder; TD, typically developed; SD, standard deviation.
**P < 0.05.*

TABLE 2 | Comparison of physical activity, sedentary time, and developmental coordination disorder (DCD) score [mean ± standard deviation (SD)] between ASD and TD children[a].

	ASD ($n = 107$)	TD ($n = 208$)	*P*-value
Physical activity (h/per week)			
Time of high-intensity physical activity	2.77 ± 0.49	4.23 ± 0.34	0.015*
Time of moderate-intensity physical activity	3.64 ± 0.42	3.96 ± 0.29	0.540
Time of low-intensity physical activity	4.24 ± 0.43	4.50 ± 0.31	0.522
Sedentary time (h/per day)			
Weekdays	3.67 ± 0.28	5.52 ± 1.89	<0.001*
Weekends	2.68 ± 0.24	3.49 ± 0.16	0.005*
Total (h/per week)	23.69 ± 1.69	34.59 ± 1.15	<0.001*
DCD score			
Fine motor and handwriting	12.30 ± 0.38	14.21 ± 0.26	<0.001*
General coordination	25.17 ± 0.53	28.90 ± 0.36	<0.001*
Control during movement	18.86 ± 0.53	24.56 ± 0.36	<0.001*
DCD Total score	56.33 ± 1.10	67.67 ± 0.75	<0.001*
Motor coordination abnormal			<0.001*
Yes	47.3%	15.4%	
No	52.7%	84.6%	

ASD, autism spectrum disorder; TD, typically developed; DCD, developmental coordination disorder; SD, standard deviation.
[a]The model adjusted for gender, maternal education, and executive function.
**P < 0.05.*

Stratified by SSB intake volume (**Table 3**), we found that, in TD children, there was a significant difference in sedentary time among the three SSB intake groups. TD children with small to medium SSB intake spent the least time being sedentary on weekdays (5.83 ± 0.28, 4.54 ± 0.31, and 6.09 ± 0.31—no intake, small to medium intake, and high intake, respectively; $p < 0.05$), weekends (3.57 ± 0.24, 2.9 ± 0.26, and 3.94 ± 0.27 – no intake, small to medium intake, and high intake, respectively; $p < 0.05$), and during the entire week (36.31 ± 1.68, 28.48 ± 1.87, and 38.33 ± 1.89—no intake, small to medium intake, and high intake, respectively; $p < 0.05$). In addition, TD children with small to medium SSB intake showed the lowest fine motor and handwriting scores (14.72 ± 0.39, 13.37 ± 0.43, and 14.38 ± 0.44—no intake, small to medium intake, and high intake, respectively; $p < 0.05$).

We observed an interaction effect between groups and SSB intake in terms of weekday sedentary time ($p = 0.044$, **Table 3**). In this case, a simple effect has been tested. In the ASD group, the weekday sedentary time remained relatively stable among children with different SSB intake levels (3.86 ± 0.42, 3.60 ± 0.41, and 3.41 ± 0.45—no intake, small to medium intake, and high intake, respectively; $p > 0.05$; **Table 3**), while the children with small to medium SSB intake in the TD group showed the lowest weekday sedentary time (5.83 ± 0.28, 4.54 ± 0.31, and 6.09 ± 0.31—no intake, small to medium intake, and high intake, respectively; $p < 0.05$; **Table 3**). No significant interactions between physical activity and DCD score were observed (**Table 3**, all $p > 0.05$).

DISCUSSION

This study aimed to gain insights into SSB intake and motor function among autistic and typically developed children. Firstly, we observed a relatively lower vigorous PA time, overall sedentary time, and motor coordination function among ASD children, relative to TD children. Secondly, TD children with small to medium SSB intake showed less sedentary time and lower motor coordination function, relative to TD children with no SSB intake or high SSB intake. However, children with ASD did not exhibit the same trend.

This research is significant and possesses many strengths; it provides (1) new information regarding the association between SSBs and brain health, especially motor coordination function among children with or without neural disorder (autism in this

TABLE 3 | Relationship of intake of SSBs (mean ± SD) to physical activity, sedentary lifestyle, DCD score, and sleeping status among ASD and TD children[#].

	ASD (n = 107)			**TD (n = 208)**			P_{group}	P_{intake}	$P_{group*intake}$
	No intake (n = 36)	**Small to medium intake (n = 37)**	**High intake (n = 34)**	**No intake (n = 83)**	**Small to medium intake (n = 66)**	**High intake (n = 59)**			
Physical activity (h/per week)									
VPA	2.86 ± 0.75[a]	3.02 ± 0.74[a]	2.27 ± 0.81[a]	4.53 ± 0.5[a]	4.15 ± 0.56[a]	3.97 ± 0.57[a]	0.013	0.639	0.875
MPA	4.08 ± 0.65[a]	3.12 ± 0.64[a]	3.78 ± 0.7[a]	3.86 ± 0.44[a]	4.09 ± 0.48[a]	3.92 ± 0.49[a]	0.567	0.792	0.521
Walking	3.48 ± 0.78[a]	4.56 ± 0.77[a]	4.47 ± 0.84[a]	5 ± 0.52[a]	4.17 ± 0.58[a]	4.48 ± 0.59[a]	0.544	0.937	0.293
Sedentary time									
Week days (h/per day)	3.86 ± 0.42[a]	3.60 ± 0.41[a]	3.41 ± 0.45[a]	5.83 ± 0.28[a]	4.54 ± 0.31[b]	6.09 ± 0.31[a]	<0.001	0.048	0.044
Weekends (h/per day)	3.14 ± 0.35[a]	2.27 ± 0.35[a]	2.62 ± 0.38[a]	3.57 ± 0.24[a]	2.9 ± 0.26[b]	3.94 ± 0.27[a]	0.005	0.015	0.302
Total (h/per week)	25.57 ± 2.52[a]	22.53 ± 2.49[a]	22.29 ± 2.7[a]	36.31 ± 1.68[a]	28.48 ± 1.87[b]	38.33 ± 1.89[a]	<0.001	0.017	0.062
DCD score									
Fine motor and handwriting	13.03 ± 0.58[a]	11.66 ± 0.57[a]	12.06 ± 0.62[a]	14.72 ± 0.39[a]	13.37 ± 0.43[b]	14.38 ± 0.44[a]	<0.001	0.016	0.770
General coordination	25.25 ± 0.82[a]	25.43 ± 0.80[a]	24.69 ± 0.88[a]	29.17 ± 0.54[a]	29.1 ± 0.61[a]	28.39 ± 0.62[a]	<0.001	0.517	0.979
Control during movement	18.93 ± 0.81[a]	18.91 ± 0.80[a]	18.67 ± 0.87[a]	24.56 ± 0.54a	23.78 ± 0.6a	25.34 ± 0.62a	<0.001	0.631	0.427
DCD total score	57.21 ± 1.67[a]	56 ± 1.65[a]	55.42 ± 1.8[a]	68.45 ± 1.12[a]	66.25 ± 1.24[a]	68.11 ± 1.28[a]	<0.001	0.456	0.691
DCD (abnormal%)	38.6%[a]	51.4%[a]	55.0%[a]	13.8%[a]	17.0%[a]	15.7%[a]	<0.001	0.451	0.786

VPA, vigorous physical activity; MPA, moderate physical activity; DCD, developmental coordination disorder; ASD, autism spectrum disorder, TD, typically developed; SD, standard deviation.

[#]*The model adjusts for gender, maternal education, and executive function.*

[ab]*Data with different upper letters had statistically significant differences in the pairwise comparisons ($P < 0.05$).*

**P* < 0.0.5.

case), (2) an improved understanding of SSBs and the risks they may pose to a child's health, and, thus, (3) a potential intervention target for assessing motor function in school-aged children.

Research that has addressed the accelerometer-measured PA of ASD children has predominately shown that it is lower relative to TD children (25), while we only showed lower VPA among ASD children. This could be attributed to the parent-reported assessment of PA in our study. Relatively lower VPA could represent a neural basis for the social difficulties experienced by ASD children (26), as most VPA requires cooperation with peers and strong volition to complete; however, ASD children lack both these characteristics. Therefore, children with ASD could experience great difficulty in performing VPA. Low motor competence in ASD children has been widely observed in the previous research (27), as well as in our study (**Table 2**). The lack of necessary motor skills could directly impede the ability of a child with ASD to partake in physical activity, which is also a potential reason for the decreased time spent performing PA. In the previous research, the sedentary time of ASD children has been debated, as some researchers reported no significant difference in ST between ASD and TD children (28, 29), while other researchers reported more ST among ASD children than TD children (30). However, these researchers failed to consider the potential repetitive symptoms of ASD, which are widely observed among ASD children (31). Repetitive behavior includes aimless wandering, turning around, and other behaviors involving activity (31) that are not considered to be PA or ST. Thus, ASD children could show less PA as well as ST.

The abundance of fine sugar contained in SSBs was concluded to be the reason for the rapid increase in blood glucose. It may explain the *U*-shape in the association between SSB intake and ST. Relatively high glucose levels are proven to be linked with low (32) - grade inflammation in humans (33), the latter of which could cause fatigue (34); consequently, an individual with relatively high glucose levels shows less active and more sedentary behavior. On the other hand, relatively low glucose levels may have a similar effect, as bodily activity is energy supplementary dependent; therefore, low glucose levels can hardly support the activity of the human body.

In TD children, those with small to medium SSB intake or high SSB intake showed relatively lower scores in fine motor and handwriting skills, which could support the SSB–brain function hypothesis. The relationship between motor coordination function and SSBs has been confirmed by an animal study, and the causation was attributed to oxidative stress originating from excessive SSB intake (35). Motor skills, particularly fine motor and handwriting skills, require white matter integrity during the child's cerebrum–cerebellum development (36), while excessive fine sugar intake affects the internal environment of white matter myelination, by increasing the level of inflammation (33). On the other hand, regardless of the fine sugar present in SSBs, caffeine and additives could be bioactive and damage motor function (37), which is potentially related to fine motor and handwriting skills.

A study in the U.S.A. showed that individuals with autism had a low-quality diet and high-SSB intake, compared with nationally representative data (38). In addition, ASD children had unique food preferences (39), which may have also affected their diet, particularly SSB intake. The previous research reported that individuals with the developmental disabilities were more susceptible to the negative health outcomes associated with SSBs (40); however, this also depends on the education level of the child's mother. A relatively highly educated mother may decrease their child's SSB intake (41), therefore, reducing the associated risks, considering the fact that over 50% of the mothers in the ASD group had a bachelor's degree or above, which may explain the lack of differences in SSB intake between ASD and TD children in our study.

This research has a few limitations. Firstly, the data collection was conducted using parent-reported questionnaires, which compromised the reliability. Secondly, the relatively small sample size in the ASD group also limited the statistical power. Moreover, we only included sugar-sweetened beverages, but the consumption of other sweet products also provided sugar in the children's daily diets; thus, the sugar intake in our study is underestimated. The recruitment of TD children *via* online media may have affected the representativity of the control group. It is also worth mentioning that the relatively low intake of SSBs in the research population decreased discrimination among the groups; this may affect the results of this research. A population with higher average SSB intake should be identified in future studies, to confirm our findings. In addition, the cross-sectional design of the study means that the causation can hardly be tested. Future research should focus on a longitudinally designed, large sample-sized study, as well as objective measurements of activity.

CONCLUSION

In this research, we described the PA, ST, and motor coordination function of both typically developed children and children with autism, and confirmed the relatively low PA and low ST lifestyles in children with autism. The association between SSBs and motor function in typically developed children is also addressed. The results showed the necessity of supporting children with lifestyle interventions and promoting early lifestyle interventions, therefore, decreasing the risk of long-term health problems.

This study also provided important evidence showing that children with special conditions should be supported with lifestyle interventions, including the promotion of motor function training to encourage a healthier lifestyle.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by the Ethical Review Committee for Biomedical

Research, Sun Yat-sen University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

Concept and design and drafting of the manuscript: MC. Acquisition, analysis, or interpretation of data: TG, CJ, and MC. Critical revision of the manuscript for important intellectual content: XL and JJ. Statistical analysis: TG. Obtained funding: JJ. All authors contributed to the article and approved the submitted version.

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Association between dietary quality and executive functions in school-aged children with autism spectrum disorder

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Background: It is well known that children with autism spectrum disorder (ASD) had executive functions deficit. However, it is still unclear whether the poor dietary quality is related to the impairment of executive functions. The current study aimed to explore the association between dietary quality and executive functions in children with ASD.

Methods: A total of 106 children with ASD (7.7 ± 1.3 years) and 207 typically developing (TD) children (7.8 ± 1.3 years) were enrolled from Guangzhou, China. The Chinese version of Behavior Rating Scale of Executive function (BRIEF), the working memory subscales of the Chinese version of Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV), and the Stroop Color-Word Test (SCWT) were used to measure the participant's executive functions. The food frequency questionnaire (FFQ) was used to collect the dietary intake information, and the Chinese Diet Balance Index (DBI_16) was used to evaluate the dietary quality. Generalized linear models were used to estimate the association between dietary quality and executive functions.

Results: In children with ASD, Low Bound Score (LBS) was positively correlated with the working memory subscale score of BRIEF ($\beta = 0.23$, 95% CI: 0.02–0.44, $P < 0.05$), while High Bound Score (HBS) and LBS were positively correlated with the organizable subscale score of BRIEF ($\beta = 0.44$, 95% CI: 0.11–0.77, $P < 0.01$; $\beta = 0.19$, 95% CI: 0.01–0.37, $P < 0.05$). Compared to TD children, children with ASD had a higher proportion of moderate and high levels of insufficient dietary intake (moderate level, 37.7% vs. 23.2%, high level, 4.7% vs. 1.4%) and moderate level of unbalanced dietary intake (36.8% vs.21.3%), higher scores on all subscales of BRIEF ($P < 0.01$), and lower score on the working memory (81.3 ± 32.3 vs. 104.6 ± 12.5, $P < 0.01$), while there was no difference on the SCWT.

Conclusion: Poor dietary quality was associated with the impairment of working memory and organizational capacity in children with ASD. This study emphasized the importance of dietary quality in executive functions among children with ASD, and attention should be paid to improving their dietary quality.

KEYWORDS

autism spectrum disorder, dietary quality, executive function, Diet Balance Index, children

Introduction

Autism spectrum disorder (ASD) is a developmental disorder characterized by social communication deficits and repetitive/unusual sensory-motor behaviors (1), with a median prevalence of 1% (2). ASD is highly disabling, resulting in a heavy public health burden (3). Numerous studies have shown that children with ASD had abnormal executive functions. Executive functions refer to a set of cognitive abilities responsible for goal-directed behavior (e.g., working memory, attention, planning, response inhibition, mental flexibility, and self-monitoring) (4, 5). Executive functions have an important role in everyday behaviors across the life span (6). Literature showed that the impairment of executive functions might associate with worse core symptoms (7, 8), poor quality of life (9), and impaired mental and physical health (10–12) in children with ASD. Thus, exploring the risk factors for the impairment of executive functions in children with ASD is become increasingly important and will help to propose feasible treatment intervention plans for children with ASD in the future.

Although there were many studies on dietary problems in children with ASD, the traditional dietary evaluation was based on specific foods or nutrient intake, with inconsistent results. Evans et al. (13) compared dietary patterns among American children and found that children with ASD consumed significantly more sweetened beverages and snack foods and fewer fruits and vegetables than typically developing (TD) children. Meguid et al. (14) found that Egyptian children with ASD consumed more carbohydrates but lower protein than healthy controls. Tsujiguchi et al. (15) found that children with ASD consumed more carbohydrates but slightly less protein, fat, minerals, and vitamins than children without ASD in Japan. A nutritional survey in Chongqing, China suggested that Children with ASD consumed fewer macronutrients and vitamin A (16). Because of dietary quality's support on the morphological development, neurochemistry, and neurophysiology of the human brain (17), effects on synaptic plasticity (18), influence on the gut microbiome (19), it was suggested that dietary quality might be associated with executive functions (20).

Up to now, there are many studies exploring the relationship between dietary quality and executive functions in TD children (see Supplementary Table S1). Riggs et al. (21) found that the overall executive function measured by Behavior Rating Scale of Executive function (BRIEF) was negatively correlated with the intake of high-calorie snacks, and positively correlated with the intake of fruits and vegetables. Guerrieri et al. (22) measured inhibitory control using the stop-signal task and found that there was no relationship between inhibition and calorie intake. However, another longitudinal study showed that there was a positive relationship between inhibitory control measured by BRIEF and the intake of "high-calorie, low nutrient snacks" (23). Such inconsistent conclusions also exist in working memory, cognitive flexibility, and other components of executive functions.

Notably, comparatively little is known about the association between dietary quality and executive functions among children with ASD. Firstly, few studies have focused on children with ASD. Secondly, the dietary assessment methods used in previous studies cannot accurately reflect the complexity of dietary quality. Thirdly, there was a lack of overall assessment of the executive functions in children. To address these gaps, we used the revised Chinese Diet Balance Index (DBI_16) to comprehensively evaluate the dietary quality of Children with ASD, including indices of insufficient, excessive, or imbalanced dietary intake. We also used the parent-reported questionnaire of BRIEF and face-to-face experimental tasks to comprehensive evaluate the executive functions. BRIEF included 2 indices: the Behavioral Regulation Index (BRI) and the Metacognition Index (MI). BRI reflects the ability of the child to shift cognitive set and modulate emotions and behaviors *via* appropriate inhibitory control. MI indicates the child's ability to initiate, plan, organize, and sustain future-oriented problem-solving in working memory. Corresponding to the two indices, the face-to-face experimental tasks used in the current study included working memory subscales of the Chinese version of Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) and the Stroop Color-Word Test (SCWT), a classic inhibitory control task.

In short, the purpose of the study was to explore the relationship between dietary quality and executive function in children with ASD.

Methods

Participants

We used the baseline data of the ongoing cohort of "the Guangzhou Study of Children with ASD" in Guangzhou, China. We selected a subsample of 107 children with ASD and 209 TD children from Jan, 2021 to Sep, 2021. One child with ASD missed data from subscales of BRIEF and 2 TD children with Intelligence Quotient (IQ) below 80 were excluded. Finally, 106 children with ASD (89 boys and 17 girls) and 207 TD children (113 boys and 94 girls) were included in the final analysis. All the 313 participants took part in SCWT. But only 76 children with ASD and 173 TD children finished SCWT, because it was based on literacy. We obtained working memory index and a full-scale intelligence quotient (FSIQ) of 99 children with ASD and 207 TD children, who completed WISC-IV. All the children with ASD were diagnosed by a combination of the Childhood Autism Rating Scale (CARS) and an expert clinician. Their diagnosis was further confirmed by two professional child psychiatrists using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Revision (DSM-5) criteria. Detailed inclusion criteria for both groups were as follows: (1) chronological age between 6 years 0 months and 12 years 0 months; (2) voluntary participation of the children's parents. Exclusion criteria included: (1) dyslexia, seizures, head trauma, cerebral palsy, severe visual or auditory impairment, other movement disorders; (2) genetic or chromosomal abnormalities.

Procedure

Children underwent face-to-face measures performed by trained psychometrists or research assistants at the research center. Information on demographic, physical activity, executive functions, and dietary intake status was obtained through in-person interviews with primary caregivers or validated tools/questionnaires. All the parents of the participants signed informed consent forms. The study was approved by the Ethical Review Committee for Biomedical Research, Sun Yat-Sen University (2015-No.29).

Measures

Assessment of executive functions

We assessed executive functions by parent-reported questionnaire and face-to-face experimental tasks. The rating scale we used was the Chinese version of BRIEF for children aged 6 to 18 years. The BRIEF is a validated 86-item questionnaire with the Cronbach α coefficient ranging from 0.74 to 0.96 (24). It includes the following subscales: inhibit, shift, emotional control, initiate, working memory, plan/organize, organization of materials, and monitor. The subscales form 2 indices: BRI and MI. The Global Executive Composite (GEC) combines the 2 indices and represents the summary measure of executive functions. The 86 items are rated using the following responses: never, sometimes, or often, coded 1, 2, or 3, respectively. A higher score indicates greater perceived impairment of executive functions. The subscales and total scores were calculated and standardized into Z-scores.

Children's executive functions were also assessed by face-to-face experimental tasks including working memory subscales of the Chinese version of WISC-IV, and the classical inhibitory control tasks (i.e., SCWT). The WISC-IV's working memory index is a commonly index to test working memory of executive functions. Working memory subscales include Digit Span and Letter-Number Sequencing subtests; Digit Span assesses short-term working memory by asking the child to repeat a series of increasingly long number sequences forward and then backward; Letter-Number Sequencing is a well-validated measure of manipulation working memory. The tester read a series of numbers and letters, then asked the child to recall the numbers in ascending order and the letters in alphabetical order. The SCWT is a classical test of inhibition (25), which was computerized using E-Prime 2.0 in current study. This test consisted of three subtasks, namely reading the color words, naming the colors, and naming the color of the ink rather than the words. Each subtask consisted of 10 trials, and each trial presented a color or a color word. The interviewer manipulated buttons on the keyboard to record responses and asked the participants to respond as accurately and quickly as possible. We calculated the differences between the incongruent and neutral conditions in terms of mean reaction time (I-NRT) and correct rate (N-I %Cor).

Assessment of dietary quality

The dietary intake information of children was collected by a parent-reported Food Frequency Questionnaire (FFQ). The FFQ contains 20 kinds of food such as cereal, vegetables, fruit, animal food, condiments. The questionnaire had been validated before the study (26), the average Intraclass Correlation Coefficient (ICC) for test-retest reliability was 0.398. The respondent of FFQ (i.e., the participant's parent or primary caretaker) needed to indicate how many times last seven days the participant ate a given food and to describe the size of the usual serving relative to a standard serving on the days they had eaten the food (1 serving = 1 egg size). Then we calculated the daily intake of various foods [intake frequency (times/week) × average intake per time /7].

We assessed dietary quality by the DBI_16 revised by He et al. (27), which consisted of eight food group-level indicators including cereals, vegetable and fruit, dairy and soybean, animal food, empty energy food (cooking oil, alcoholic beverage), condiments (addible sugar, salt), variety and water. The DBI_16 indicators were calculated by the insufficient, appropriate and excessive dietary intake based on the recommendations of Dietary Guidelines for Chinese Residents-2016. Being evaluated to insufficient, excessive or imbalanced dietary intake according to the recommendations is considered to be poor dietary quality. For foods that are emphasized as "appropriate amount" in the Dietary Guidelines, the index value should reflect both insufficient intake and excessive intake, so there are positive and negative bidirectional values, such as cereals and animal foods (including red meat and products, poultry and game, fish and shrimp, and eggs); For foods that are emphasized as "more to eat" in the Dietary Guidelines, the index value mainly evaluates the degree of insufficient, so the index value is negative, such as vegetable and fruit, dairy and soybean, variety and water; The index values are positive for foods that are highlighted as "less to eat" in the Dietary Guidelines, such as cooking oil and salt, because they focus on assessing the degree of excess. According to the DBI_16 standard, the dietary intake of children with ASD and TD children was calculated to obtain the scores of each single index of DBI_16 and combine to values of the high bound score (HBS), low bound score (LBS), and diet quality distance (DQD). HBS is the positive-sum value of all the DBI_16 index scores, reflecting the situation of children's excessive dietary intake, with the score ranging from 0 to 44. LBS is the absolute value of the sum of all negative values in the DBI_16 index score, which reflects the insufficient dietary intake of children, with the score ranging from 0 to 72. DQD is the absolute value of all the DBI_16 index scores, which comprehensively reflects the overall situation of children's dietary intake, and the score ranges from 0 to 96. And HBS, LBS, and DQD were divided into five levels: no problem (= 0), almost no problem (HBS: 1∼9, LBS: 1∼14, DQD: 1∼19), low level (HBS: 10∼18, LBS: 15∼29, DQD: 20∼38), moderate level (HBS: 19∼27, LBS: 30∼43, DQD: 39∼57) and high level (HBS: 28∼44, LBS: 44∼72, DQD: 58∼96). (The detail of DBI_16 was shown in Supplementary Table S2).

Assessment of covariates

Demographic information

The children's age, gender, maternal age and education level, paternal age and education level, and per capita monthly household income were reported by parents *via* questionnaire.

Anthropometric measurements

Anthropometric measurements were taken by trained staff according to the standard procedure of anthropometric procedures and data collection developed by WHO. The weight and height were averaged by two measurements, and the body mass index (BMI) was estimated by dividing weight (kg) by height^2 (m^2). The definitions of overweight and obesity were using the screening thresholds for overweight and obesity in Chinese school-age children and adolescents released by the National Health and Family Planning Commission in 2018 (28).

Physical activity

Physical activity was assessed by the International Physical Activity Questionnaire short format which included vigorous physical activity, moderate physical activity, and walking. For the above activities, respondents were asked to review the activities of at least 10 min each time in the past 7 days and answer the number of days of activities and the average daily duration. Based on the total metabolic equivalent (MET), physical activity status was classified into three categories: low, moderate, and high (29).

Intelligence quotient

IQ was assessed *via* the Chinese Version of WISC-IV, which provides a full-scale intelligence quotient (FSIQ) based on the sum of scores from the 10 core subtests (30). FSIQ < 70 was defined as intellectual disorder (ID).

Statistical analyses

To compare the differences in characteristics between ASD and TD children, we calculated means and standard deviations for continuous variables using independent sample *t*-tests, and calculated percentages for categorical variables using chi-square tests. We used generalized linear models to compare the differences in dietary quality and executive functions between the two groups and to investigate the associations between dietary quality and executive functions in both groups. We fitted the crude model without any adjustments and adjusted the model by adjusting for child's age, sex, maternal education level, paternal education level, family income, category of physical activity, BMI, and with or without ID (FSIQ ≥ 70 /<70). The results were presented as coefficient estimates (β) with a 95% confidence interval (CI). For all analyses, the statistical significance was set at *P*-value < 0.05 (two-sided). We conducted all statistical analyses with R 4.0.3 statistical software (31).

Results

Demographic characteristics

The demographic characteristics of the included children are shown in Table 1. The mean age of children with ASD was 7.7 ± 1.3 years. There were 84.0% of children with ASD were boys. Compared with TD children, children with ASD had lower scores in the FSIQ (92.0 ± 18.8 vs. 112.9 ± 12.8, $P < 0.01$), a higher proportion of the low and moderate levels of physical activity (10.4% vs. 3.4% and 43.4% vs. 36.2%, $P < 0.01$), and lower maternal education level (41.5% vs. 24.6%, $P < 0.01$) and family economic situation (57.5% vs. 25.1%, $P < 0.01$). There were no differences between groups in children's age, category of BMI, or paternal education level.

TABLE 1 Demographic characteristics of children with ASD and TD children.

Characteristics	ASD Means (SD)/*N* (%) N = 106	TD Means (SD)/*N* (%) N = 207	*P* value
Age	7.7 (1.3)	7.8 (1.3)	0.86
Sex			
Boy	89 (84.0)	113 (54.6)	**< 0.01**
Girl	17 (16.0)	94 (45.4)	
FSIQ	92.0 (18.8)	112.9 (12.8)	**< 0.01**
BMI			0.07
Underweight	10 (9.4)	26 (12.7)	
Normal	68 (64.2)	146 (71.6)	
Overweight	12 (11.3)	19 (9.3)	
Obesity	16 (15.1)	13 (6.4)	
Level of physical activity			**< 0.01**
Low	11 (10.4)	7 (3.4)	
Moderate	46 (43.4)	75 (36.2)	
High	49 (46.2)	125 (60.4)	
Maternal education level			**< 0.01**
Below bachelor	44 (41.5)	51 (24.6)	
Bachelor degree or above	62 (58.5)	156 (75.4)	
Paternal education level			
Below bachelor	40 (37.7)	73 (35.4)	0.69
Bachelor degree or above	66 (62.3)	133 (64.6)	
Per capita monthly household income			**< 0.01**
≤ ¥8,000 /month	61 (57.5)	52 (25.1)	
> ¥8,000 /month	45 (42.5)	155 (74.9)	

ASD, autism spectrum disorder; TD, typically developing; SD, standard deviation; FSIQ, full scale intelligence quotient; BMI, body mass index.
The bold values represented statistically significant difference between children with ASD and TD children.

The association of DBI_16 indicators with executive functions in children with ASD and TD children

Table 2 shows the association between DBI_16 indicators and executive functions in children with ASD. LBS was positively associated with the working memory subscale score of BRIEF ($\beta = 0.23$, 95% CI: 0.02–0.44, $P < 0.05$). HBS and LBS had positive associations with the organizable subscale score of BRIEF ($\beta = 0.44$, 95% CI: 0.11–0.77, $P < 0.01$; $\beta = 0.19$, 95% CI: 0.01–0.37, $P < 0.05$) in the adjusted model, while other indicators had no association with other components of executive functions.

In addition, there was a null association between DBI_16 indicators and all executive function scores in the adjusted models in TD children (see Table 3).

The comparison of DBI_16 indicators and components between children with ASD and TD children

As shown in Figure 1 (detailed data are shown in Supplementary Table S3), the distribution of LBS and DQD had a significant difference between children with ASD and TD children. Children with ASD had a higher proportion of the moderate and high levels of insufficient dietary intake (moderate level, 37.7% vs. 23.2%, high level, 4.7% vs. 1.4%) and the moderate level of unbalanced dietary intake (36.8% vs.21.3%) comparing with TD children. As shown in Figure 2 (detailed data are shown in Supplementary Table S4), children with ASD had more insufficient dietary intake in the fruit (-3.8 ± 1.4 vs. -3.4 ± 1.5, $P < 0.01$), dairy (-2.3 ± 1.8 vs. -1.9 ± 1.6, $P < 0.05$) and dietary variety (-4.1 ± 1.9 vs. -3.7 ± 1.9, $P < 0.05$) categories than TD children.

The comparison of executive functions between children with ASD and TD children

Table 4 shows the comparison of executive functions in children with ASD and TD children. Compared to TD children, children with ASD had higher BRIEF total score (66.3 ± 9.2 vs. 53.9 ± 8.6, $P < 0.01$), dimensions scores (BRI, 60.8 ± 10.5 vs. 48.6 ± 7.8, MI, 67.9 ± 9.1 vs. 56.8 ± 9.3, $P < 0.01$) and all subscale scores, lower working memory score (81.3 ± 32.3 vs. 104.6 ± 12.5, $P < 0.01$). There was no difference in reaction time and correct rate of SCWT between the two groups.

Discussion

The current study showed that higher HBS was associated with worse organizable ability, while higher LBS was associated with worse organizable ability and working memory in children with ASD. Children with ASD had more problems of insufficient and unbalanced dietary intake compared to TD children. Children with ASD also had lower scores of BRIEF and working memory than TD children, while there was no significant difference in SCWT. To our knowledge, it was the first study using the DBI_16 scores to evaluate the dietary quality of Chinese children with ASD and explore the association of dietary quality with executive functions in children with ASD.

The most important finding of this study was that excessive and insufficient dietary intake in children with ASD was both positively correlated with impairment of organizable ability and

TABLE 2 The association of DBI_16 indicators with executive functions in children with ASD.

Executive functions	HBS		LBS		DQD	
	Crude model β (95% CI)	Adjust model β (95% CI)	Crude model β (95% CI)	Adjust model β (95% CI)	Crude model β (95% CI)	Adjust model β (95% CI)
BRIEF						
GEC	0.15 (−0.20, 0.51)	0.24 (−0.14, 0.62)	0.07 (−0.13, 0.26)	0.10 (−0.11, 0.31)	−0.01 (−0.21, 0.20)	−0.02 (−0.23, 0.18)
BRI	−0.02 (−0.43, 0.39)	0.01 (−0.42, 0.45)	−0.08 (−0.30, 0.15)	−0.09 (−0.32, 0.15)	0.09 (−0.15, 0.33)	0.08 (−0.16, 0.31)
Inhibit	0.06 (−0.41, 0.54)	0.13 (−0.39, 0.65)	0.08 (−0.18, 0.34)	0.09 (−0.19, 0.37)	−0.05 (−0.32, 0.23)	−0.07 (−0.35, 0.20)
Shift	−0.20 (−0.61, 0.21)	−0.19 (−0.62, 0.24)	−0.22 (−0.44, 0.00)	−0.21 (−0.44, 0.03)	0.15 (−0.09, 0.38)	0.18 (−0.06, 0.41)
Emotion control	0.04 (−0.37, 0.45)	0.05 (−0.39, 0.48)	−0.22 (−0.44, 0.00)	−0.13 (−0.37, 0.10)	0.13 (−0.10, 0.37)	0.11 (−0.12, 0.35)
MI	0.24 (−0.11, 0.59)	0.36 (−0.02, 0.73)	−0.09 (−0.31, 0.14)	0.20 (−0.00, 0.40)	−0.06 (−0.27, 0.14)	−0.08 (−0.28, 0.12)
Initiate	−0.01 (−0.41, 0.39)	−0.01 (−0.45, 0.43)	0.06 (−0.16, 0.28)	0.13 (−0.11, 0.36)	−0.08 (−0.32, 0.15)	−0.07 (−0.30, 0.16)
Working memory	0.11 (−0.28, 0.50)	0.28 (−0.11, 0.68)	0.16 (−0.05, 0.38)	**0.23 (0.02, 0.44)***	−0.13 (−0.36, 0.09)	−0.15 (−0.37, 0.08)
Plan/organize	0.24 (−0.15, 0.63)	0.36 (−0.06, 0.79)	0.10 (−0.12, 0.31)	0.15 (−0.08, 0.38)	0.00 (−0.23, 0.23)	−0.02 (−0.25, 0.20)
Organize	**0.44 (0.14, 0.74)*****	**0.44 (0.11, 0.77)****	**0.21 (0.04, 0.38)***	**0.19 (0.01, 0.37)***	−0.04 (−0.22, 0.14)	−0.09 (−0.27, 0.09)
Monitor	0.26 (−0.14, 0.65)	0.40 (−0.03, 0.83)	0.11 (−0.10, 0.33)	0.19 (−0.08, 0.39)	−0.03 (−0.26, 0.20)	−0.04 (−0.27, 0.19)
SCWT[a]						
N–I %Cor	−0.00 (−0.01, 0.00)	−0.00 (−0.01, 0.00)	0.00 (−0.00, 0.00)	0.00 (−0.00, 0.00)	−0.00 (−0.00, 0.00)	−0.00 (−0.00, 0.00)
I–NRT	3.73 (−16.53, 23.99)	−0.40 (−23.52, 22.72)	−2.38 (−13.28, 8.51)	−5.25 (−16.95, 6.45)	3.39 (−8.57, 15.35)	6.14 (−6.63, 18.91)
Working memory test[b]	0.80 (−0.46, 2.07)	−0.09 (−1.07, 0.89)	0.44 (−0.25, 1.13)	0.06 (−0.47, 0.59)	−0.08 (−0.81, 0.65)	−0.09 (−0.64, 0.46)

DBI_16, The Chinese Dietary Balance Index_16; LBS, Low Bound Score; HBS, High Bound Score; DQD, Diet Quality Distance; CI, confidence interval; GEC, Global executive component; BRI, Behavioral regulation index; MI, Metacognition index; SCWT, Stroop Color-Word test; I-NRT, the difference between the incongruent and neutral conditions in terms of mean reaction time; N-I %Cor, the difference between the incongruent and neutral conditions in terms of correct rate.
Crude model: without adjustment.
Adjust model: adjusted for child's age, sex; maternal education level, paternal education level, family income, level of physical activity, BMI category and with or without intellectual disorder (FSIQ≥ 70/ <70).
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.
[a]76 autistic children finished SCWT; [b]99 autistic children finished Working memory test.
The bold values represented statistically significant association between executive functions and the DBI_16 indicators.

working memory. These two components of executive function were all belong to Metacognition Index, which indicated that diet quality might have more effect on the ability of initiate, plan, organize, and sustain future-oriented problem-solving in working memory. The possible reason was that MI is particularly sensitive to brain-based deficits and disruptions in brain connectivity (32), and poor diet quality might associate with impairment of brain function (17). In future, more studies are needed to explore the underlying mechanisms involved. It is worth noting that the associations between dietary quality and executive functions were only observed in BRIEF, not in working memory test of WISC-IV. A possible reason is that

TABLE 3 The association of DBI_16 indicators with executive function in TD children.

Executive functions	HBS		LBS		DQD	
	Crude model β (95% CI)	Adjust model β (95% CI)	Crude model β (95% CI)	Adjust model β (95% CI)	Crude model β (95% CI)	Adjust model β (95% CI)
BRIEF						
GEC	0.04 (−0.21, 0.30)	0.09 (−0.17, 0.36)	−0.12 (−0.27, 0.03)	−0.08 (−0.23, 0.07)	0.14 (−0.01, 0.28)	0.12 (−0.04, 0.27)
BRI	−0.07 (−0.30, 0.17)	−0.02 (−0.26, 0.22)	−0.09 (−0.22, 0.05)	−0.06 (−0.19, 0.08)	0.06 (−0.07, 0.20)	0.05 (−0.09, 0.19)
Inhibit	0.09 (−0.18, 0.35)	0.11 (−0.16, 0.38)	−0.06 (−0.22, 0.09)	−0.04 (−0.19, 0.12)	0.09 (−0.06, 0.25)	0.07 (−0.08, 0.23)
Shift	−0.19 (−0.43, 0.05)	−0.18 (−0.43, 0.08)	−0.07 (−0.21, 0.07)	−0.03 (−0.18, 0.11)	0.01 (−0.13, 0.15)	−0.02 (−0.17, 0.12)
Emotion control	−0.12 (−0.37, 0.12)	−0.05 (−0.31, 0.20)	−0.08 (−0.22, 0.06)	−0.07 (−0.21, 0.08)	0.04 (−0.11, 0.18)	0.05 (−0.10, 0.20)
MI	0.13 (−0.15, 0.40)	0.17 (−0.11, 0.46)	−0.13 (−0.29, 0.03)	−0.09 (−0.25, 0.07)	**0.18** **(0.02, 0.34)***	0.15 (−0.01, 0.32)
Initiate	0.08 (−0.20, 0.36)	0.08 (−0.22, 0.38)	−0.14 (−0.30, 0.02)	−0.10 (−0.27, 0.07)	**0.16** **(0.00, 0.32)***	0.14 (−0.04, 0.21)
Working memory	0.08 (−0.20, 0.36)	0.14 (−0.15, 0.42)	**−0.16** **(−0.32, −0.00)*****	−0.11 (−0.27, 0.05)	**0.19** **(0.03, 0.35)***	0.16 (−0.01, 0.32)
Plan/organize	0.13 (−0.17, 0.43)	0.20 (−0.11, 0.51)	−0.10 (−0.27, 0.08)	−0.06 (−0.24, 0.12)	0.14 (−0.03, 0.31)	0.13 (−0.05, 0.31)
Organize	0.12 (−0.14, 0.39)	0.11 (−0.17, 0.40)	−0.09 (−0.26, 0.08)	−0.08 (−0.24, 0.08)	0.13 (−0.03, 0.28)	0.12 (−0.04, 0.29)
Monitor	0.08 (−0.21, 0.38)	0.15 (−0.15, 0.45)	−0.09 (−0.26, 0.08)	−0.04 (−0.22, 0.13)	0.12 (−0.05, 0.29)	0.10 (−0.08, 0.27)
SCWT[a]						
N–I %Cor	0.00 (−0.00, 0.00)	0.00 (−0.00, 0.00)	0.00 (−0.00, 0.00)	−0.00 (−0.00, 0.00)	0.00 (−0.00, 0.00)	0.00 (−0.00, 0.00)
I–NRT	−2.75 (−15.03, 9.52)	−0.10 (−13.20, 12.99)	1.16 (−6.30, 8.61)	1.48 (−6.31, 9.28)	−2.17 (−9.61, 5.28)	−1.56 (−9.45, 6.33)
Working memory test[b]	0.15 (−0.22, 0.52)	−0.08 (−0.36, 0.19)	0.13 (−0.09, 0.34)	−0.08 (−0.24, 0.08)	−0.08 (−0.29, 0.14)	0.05 (−0.11, 0.22)

DBI_16, The Chinese Dietary Balance Index_16; LBS, Low Bound Score; HBS, High Bound Score; DQD, Diet Quality Distance; CI, confidence interval; GEC, Global executive component; BRI, Behavioral regulation index; MI, Metacognition index; SCWT, Stroop Color-Word test; I-NRT, the difference between the incongruent and neutral conditions in terms of mean reaction time; N-I %Cor, the difference between the incongruent and neutral conditions in terms of correct rate.
Crude model: without adjustment; Adjust model: adjusted for child's age, sex; maternal education level, paternal education level, family income, level of physical activity, BMI category and FSIQ.
*$P < 0.05$, ***$P < 0.001$.
[a]173 TD children finished SCWT; [b]207 TD children finished Working memory test.
The bold values represented statistically significant association between executive functions and the DBI_16 indicators.

BRIEF has higher ecological effect compared to psychometric tests (33), it is based on more representative environmental situations (34). But as an objectively psychometric tests, working memory test of WISC-IV may better reflect the state of brain development (33). Consistent with previous animal experiments and interventional study in ASD, Zilkha, N. et al. (35) found that a high-fat and imbalanced diet exacerbates cognitive rigidity and social deficiency in the BTBR mouse model of autism. A randomized controlled trial showed that diet modification based on the *Chanyi* approach in 1 month had positive effects on improving mental flexibility, response inhibition, and planning in children with ASD (36). However, it is controversial on the correlation between dietary quality and specific components of executive functions in normal population. Some studies (37–42) suggested that dietary quality was associated with inhibitory control, while the other studies (22, 43–46) showed that there

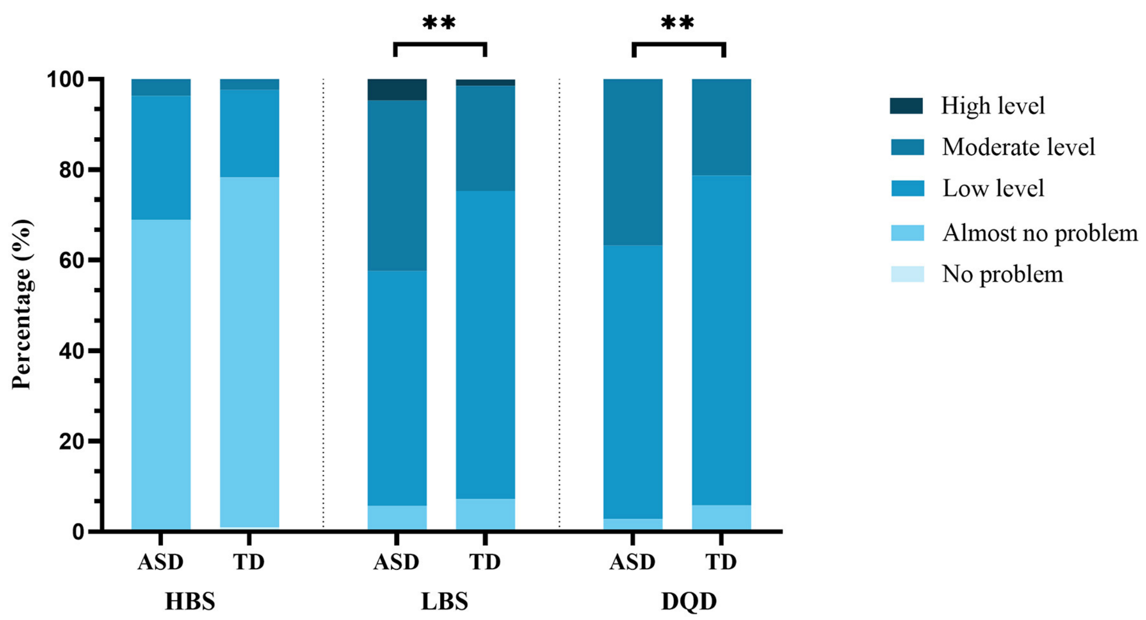

FIGURE 1
Comparison of DBI_16 indicators among children with ASD and TD children. ASD, autism spectrum disorder; TD, typically developing; LBS, Low Bound Score; HBS, High Bound Score; DQD, Diet Quality Distance. ** $P < 0.01$.

was no association between dietary quality and inhibitory control. On the other hand, some studies (47–49) suggested that dietary quality was associated with working memory, while the other studies (47, 50–54) showed that there was no association between dietary quality and working memory. We speculated that compared to the TD children, the organizable ability and working memory in children with ASD may be more susceptible to dietary quality.

A moderate supply of nutrients could support the morphological development, neurochemistry, and neurophysiology of the human brain (17). First, the transfer of energy from foods to neurons might be fundamental to the control of brain function. Processes related to the management of energy in neurons can affect synaptic plasticity and have the potential to affect cognitive function (18). Second, some dietary components have been identified as having positive effects on cognitive ability (18, 55), such as minerals (e.g., Zn) and certain vitamins (e.g., B vitamins) are cofactors for enzymes that synthesize neurotransmitters, which could influence the development of cognition throughout childhood (56, 57); Dietary lipids (e.g., Omega-3 polyunsaturated fatty acids) can affect myelin sheath integrity and nerve cell membranes, so as to impact the brain function (18). Third, growing evidence indicated the importance of dietary components in influencing non-genetic events (e.g., DNA methylation, transcriptional activation, translational control, and posttranslational modifications), which cause a potentially heritable phenotypic change. In addition, there was evidence that dietary quality can influence the gut microbiome (58), and changes in the gut microbiome may impact executive functions through the "gut-brain axis" (19). Therefore, poor dietary quality may lead to changes in the brain structure and function, particularly in the brain regions associated with cognitive function (i.e., frontal cortical regions) involved, through synapse formation, in neurogenesis, myelination. The dimension of working memory refers to the ability to hold information in their mind and manipulate this information to achieve task completion, and it has been related to the frontal regions including the bilateral superior and middle frontal gyri, bilateral frontal polar regions, and precuneus gyrus (59). The dimension of organization represents the individual's organization within their environment and extends to the state of their work, living, and storage spaces (60), which involved the brain region including the dorsolateral prefrontal cortex, the anterior and posterior cingulate areas, and the parietal cortex (59, 61). The brain function of working memory and organization involved might be sensitive to the insufficient specific nutrients or energy which caused by insufficient dietary intake (i.e., cereals, animal foods, vegetable and fruit, dairy product). On the other hand, excessive dietary intake refers to the excess of foods that are emphasized as "less to eat" and "appropriate amount" in the Dietary Guidelines (i.e., cereals, animal foods, empty energy food and condiments), which might affect the function of brain regions involved by organizable ability through energy metabolism and other pathways. But the direction of the effects could also be reversed. Another

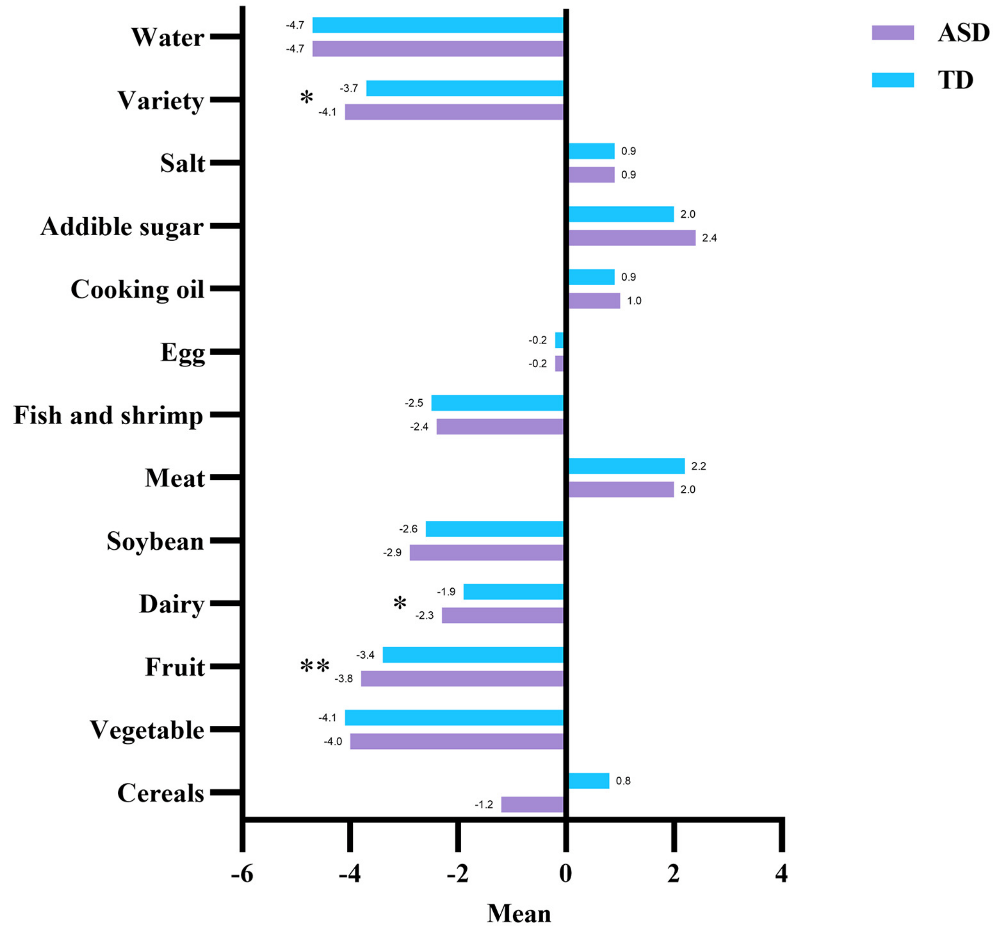

FIGURE 2
Comparison of DBI_16 components among children with ASD and TD children. ASD, autism spectrum disorder; TD, typically developing; LBS, Low Bound Score; HBS, High Bound Score; DQD, Diet Quality Distance. *$P < 0.05$; **$P < 0.01$.

possibility is that the impairment of executive function results in poor dietary quality. For example, studies have shown that inhibitory control may play a role in inhibiting dietary-related ideas or appetitive behaviors, and working memory may help children with better dietary quality by maintaining and updating dietary-related strategy (62). In future, more studies are needed to explore the underlying mechanisms involved.

Furthermore, we have compared the difference on the dietary quality and executive function between children with ASD and TD children to understand the association among them well. We found that compared to TD children, children with ASD had more problems of dietary quality including overall insufficient and unbalanced dietary intake. Further analysis showed that children with ASD had more insufficient dietary intake in the fruit, dairy and dietary variety categories than TD children. A few studies showed that there was no difference in dietary intake between children with ASD and TD children (63–65), however, the majority of studies showed similar results to ours (66–68). Insufficient and unbalanced dietary intake problems may be caused by the following factors, First, children with ASD often exhibit repetitive and stereotypical behaviors, and other uncontrolled behaviors at mealtimes (69, 70). These behaviors put them at higher risk for eating problems such as food rejection, high frequency of single food intake, pica (71–73). Second, dietary quality generally improved with the increase of income level and education level (74–77). However, children with ASD in the current study had lower family income and maternal education levels compared to TD children. Third, children with ASD are more likely to present with food allergies include especially milk/dairy, nuts, and fruits (78–81), which may lead to insufficient and unbalanced dietary intake. It is well known that dietary quality is a vital determinant of physical growth and mental development, poor dietary quality can contribute to non-communicable diseases (82), lead to worse mental health (83), and impair brain integrity and functionality (84), therefore, more attention should pay to the

TABLE 4 The comparison of executive function in children with ASD and TD children.

Executive function	ASD/Mean (SD) ($N = 106$)	TD/Mean (SD) ($N = 207$)	P value
BRIEF			
GEC	66.3 (9.2)	53.9 (8.6)	**< 0.01**
BRI	60.8 (10.5)	48.6 (7.8)	**< 0.01**
Inhibit	66.0 (12.3)	50.2 (9.0)	**< 0.01**
Shift	57.6 (10.5)	48.9 (8.2)	**< 0.01**
Emotion control	54.8 (10.6)	47.5 (8.3)	**< 0.01**
MI	67.9 (9.1)	56.8 (9.3)	**< 0.01**
Initiate	61.4 (10.4)	52.6 (9.4)	**< 0.01**
Working memory	67.9 (10.1)	54.4 (9.4)	**< 0.01**
Plan/Organize	68.7 (10.2)	58.9 (10.1)	**< 0.01**
Organization	57.1 (8.0)	54.1 (9.0)	**< 0.01**
Monitor	71.1 (10.2)	58.8 (9.9)	**< 0.01**
SCWT[a]			
I-NRT/ ms	401.1 (464.3)	407.9 (384.1)	0.91
N-I %Cor	0.9 (0.1)	0.9 (0.1)	0.09
Working memory test[b]	81.3 (32.3)	104.6 (12.5)	**< 0.01**

SD, Standard deviation; GEC, Global executive component; BRI, Behavioral regulation index; MI, Metacognition index; SCWT, Stroop Color-Word test; I-NRT, the difference between the incongruent and neutral conditions in terms of mean reaction time; N-I %Cor, the difference between the incongruent and neutral conditions in terms of correct rate.

[a]76 autistic children and 173 TD children finished SCWT; [b]99 autistic children and 207 TD children finished Working memory test.

The bold values represented statistically significant difference between children with ASD and TD children.

dietary management of children with ASD. Besides, we found that compared to TD children, children with ASD performed significantly worse on all subscales of BRIEF and working memory test, but had intact performance in SCWT. Executive function has long been considered to play a role in the specific impairments of ASD, such as social impairment, restricted and repetitive behavior patterns. However, the characteristic of executive function in ASD remains unclear because different studies used different assessment tool (33). Most studies used BRIEF to assess manifestations of executive function in everyday life of children, and showed that children with ASD had the impairment of executive functions, which suggested that children with ASD might have specific difficulties in complex, unstructured everyday problem-solving situations. However, it should be considered that BRIEF was parents- or teachers-reported which was sensitive for rater bias (85). Conversely, experimental tests (e.g., working memory test and SCWT) were administered directly to children with more objective. Most studies indicated that working memory in children with ASD had impairment (86). However, the impairment of inhibitory control in autistic children without ID was less prominent compared to the impairment of working memory (87). Most of the children with ASD in the current study were without ID, and most of them were recruited from mainstream educational schools, these might be why we found that children with ASD had relatively normal inhibitory control ability but poor working memory.

The current study had several strengths. First, it was the first study using the DBI_16 scores to evaluate the dietary quality of Chinese children with ASD and explore the association of dietary quality with executive functions in children with ASD. Second, the executive function of children with ASD was evaluated by both objective and subjective measures (i.e., BRIEF, working memory subscale of WISC-IV, and SCWT) to comprehensively reflect children's reality-based executive functions. Third, the dietary quality was assessed by DBI_16 rather than single food intake, which can represent the overall dietary information of children with ASD. However, some limitations should be considered. First, the current study was a cross-sectional design, thus it was impossible to determine the causal nature of the association between dietary quality and executive function in children with ASD. Further longitudinal studies or interventional studies are needed to confirm the relationship. Second, ASD represents a heterogeneity group of disorders, and most of the children with ASD in the current study were without ID, so the results couldn't reflect the association in autistic children with ID directly. Third, the study did not explore the relationship between dietary quality and cognitive flexibility which was an important component of executive function, and more studies were needed. Fourth, the dietary assessment in the current study was subjective reported, which could not accurately calculate the specific amounts of macronutrients and determine the intrinsic nutrient levels. Furthermore, the self-reported investigation might be influenced by parents' recall bias and personal expectations. Therefore, more objective investigations are needed to comprehensively collect children's dietary intake information.

Conclusion

Poor dietary quality was associated with the impairment of working memory and organizational capacity in children with ASD. Compared to TD children, children with ASD had poorer dietary quality and executive functions. This study emphasized the importance of dietary quality in executive functions among children with ASD, and attention should be paid to improving their dietary quality.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and was approved by the Ethical Review Committee for Biomedical Research, Sun Yat-Sen University (2015-No.29). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

JJ and XL: conceptualization, supervision, project administration, and funding acquisition. XW and XS: methodology, formal analysis, and writing-original draft preparation. XW: study design, manuscript revise, and data curation. XW, XS, YJ, XZ, MC, XG, SL, XO, and TG: data collection. XS, XW, LC, and XL: writing - review and editing. All authors read and revised the manuscript, and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.940246/full#supplementary-material

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The association between sugar-sweetened beverages and milk intake with emotional and behavioral problems in children with autism spectrum disorder

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Background: Emotional and behavioral problems are common in children with autism spectrum disorder (ASD). It's still unclear whether children with ASD have abnormal sugar-sweetened beverages (SSBs) and milk intake and whether this abnormality will affect their emotions and behavior remains unclear. The current study aims to investigate the association of SSBs and milk intake with emotional and behavioral problems in children with autism spectrum disorder (ASD).

Methods: 107 children with ASD and 207 typical developing (TD) children aged 6-12 years old were recruited for the study. The frequency of SSBs and milk intake was assessed by a self-designed questionnaire. Emotional and behavioral problems were assessed by Strength and Difficulties Questionnaire (SDQ). Then, the linear regression model was produced to evaluate the association of SSBs and milk intake with emotional and behavioral problems.

Results: In the current study, there was no difference in frequency of SSBs intake between children with ASD and TD children ($p > 0.05$), and children with ASD consumed less milk compared to TD children ($p < 0.05$). After adjusting sex, age, maternal and paternal education, and monthly family income, we found a significant difference in each subscale score of SDQ in the two groups ($p < 0.05$). In children with ASD, higher frequent SSBs intake was positively associated with the scores of the emotional problem (p for trend < 0.05), and lower frequent milk intake was inversely associated with the scores of prosocial behavior (p for trend < 0.05). No interactive effects were found on SSBs and milk intake with emotional and behavioral problems (p for trend > 0.05).

Conclusion: In children with ASD, frequency of SSBs and milk intake was associated with the emotional problem and prosocial behavior, respectively. Children with ASD should increase the frequency of milk intake and decrease the frequency of SSBs intake.

KEYWORDS

sugar sweetened beverages, milk, autism spectrum disorder, emotional and behavioral problems, children

Introduction

Autism spectrum disorder (ASD) is a serious neurodevelopmental disorder characterized by social communication deficits and repetitive behaviors (1). Children with ASD are more likely to develop substantial comorbidities, including emotional (e.g., depression and anxiety mood) and behavioral (e.g., hyperactivity and opposed behavior) problems (2). Literature showed that 72∼86% of children with ASD had at least one emotional or behavioral problem (3). Emotional and behavioral problems may discourage the development of social communication and interaction in children with ASD. Moreover, it also leads to isolation, interferes with educational and therapeutic intervention, and limits participation in social and community activities (4). Therefore, emotional and behavioral problems are non-negligible problems in children with ASD.

Interestingly, some studies showed that there was a relationship between SSBs intake with emotional and behavioral problems in typically developing (TD)children (5), such as depression (6), and hyperactivity/inattention (7). Sugar-sweetened beverages (SSBs) refer to beverages with added artificial sugar or sugar content of more than 5% added in the process, such as tea drinks, carbonated drinks, sweetened milk tea, coffees, sweetened fruit juices, and sports drinks (8). It has been well documented that SSBs intake has harmful effects on children health, such as obesity, dental caries, high blood pressure, metabolic syndromes, diabetes and cardiovascular diseases (9), and emotional and behavioral problems (5). Some studies have shown that compared to TD children, children with ASD tend to intake more SSBs and sugars due to refuse bitter taste during the period of preschool and primary school (10, 11). Unfortunately, children with ASD were vulnerable to diet (12), so we speculated that higher frequent SSBs intake was positively associated with emotional and behavioral problems in the children with ASD.

In addition, literature studies have indicated that SSBs intake was associated with milk intake (13), but the association was inconsistent. Some studies showed that increased SSBs intake was associated with reduced milk intake in TD children aged 3–13 years (14–16), while another study showed that SSBs intake was positively associated with milk intake among low family income preschool-age children (17). Milk is considered beneficial for child growth and development as it is an excellent source of essential nutrients (18). Previous studies showed that milk intake might reduce the risk of chronic diseases such as overweight and obesity (19), metabolic syndrome (20), high-blood pressure (21), as well as improve bone health (22) and sleep satisfaction (23). A few studies showed that compared to TD children, children with ASD aged 4–10 years have less frequent milk intake (24, 25). Two studies indicated that meeting recommendations for milk and alternative in childhood was associated with fewer health care encounters for mental illnesses, such as depressive episodes, mood disorder, general anxiety disorder, attention-deficit/hyperactivity disorder (ADHD), and so on (26, 27). Therefore, it's reasonable to speculate that milk intake was negatively associated with emotional and behavioral problems, and there were interactive effects between SSBs and milk intake on emotional and behavioral problems in children with ASD.

In summary, the present study aimed to explore: (1) compared TD children, whether children with ASD had a different frequency of SSBs and milk intake; (2) whether there was an association between SSBs and milk intake with emotional and behavioral problems in children with ASD; (3) whether there were interactive effects between SSBs and milk intake on emotional and behavioral problems in children with ASD.

Materials and methods

Study population and procedure

The data in the current study were from the baseline data of an ongoing study "the Guangzhou Longitudinal Study of Children with ASD", which examined the developmental trajectories of 6- to 12-year-olds children with ASD in Guangzhou, China. In this study, the children with and without ASD were diagnosed by the Childhood Autism Rating Scale (CARS), and two professional child psychiatrists further confirmed their diagnosis using the Diagnostic and Statistical Manual of Mental Disorders, Fifth Revision (DSM-5) criteria. The additional inclusion criteria for both groups were as follows: (1) chronological age was from 6 years 0 months to 12 years 11 months; (2) children's parents voluntarily participated in the study; (3) all participants reported without dyslexia, seizures, head trauma, cerebral palsy, or other movement disorders; (4) all participants reported without known genetic or chromosomal abnormalities or severe visual or hearing impairment. All children came from different families. Finally, a total of 107 children with ASD (90 boys and 17 girls) and 207 TD children (113 boys and 94 girls) were enrolled in this study (the flow chart of subject screening is shown in Supplementary Figure S1).

Sugar-sweetened beverages and milk intake

The question about SSBs and milk frequency was designed according to a parent-reported Food Frequency Questionnaire (FFQ). The average Intraclass Correlation Coefficient (ICC) for test-rest reliability of the questionnaire was 0.398 (28). The questions included: "In the past 7 days, how many times did your child drink SSBs/milk?" if they answered more than one time, they were further asked about cups of SSBs/milk each time consumed from the question "How many cups of

SSBs/milk did your child drink per time on average? (One cup is equal to 250 mL)". All of these questions were responded to by parents of children. Total weekly SSBs/milk intake was calculated as (weekly times of SSBs or milk intake) × (cups of SSBs or milk intake each time). Finally, the frequency of SSBs intake was categorized as: "0 times/week", "1-2 times/week", "> 2 times/week", and the frequency of milk intake was also categorized as, "0-3 times/week", "4-7 times/week", ">7 times/week".

Strengths and difficulties questionnaire

The parent-reported Strengths and Difficulties Questionnaire (SDQ) was used to assess children's emotional and behavioral problems (29). The parent-reported SDQ is widely used to screen multidimensional mental health for children aged 3–16 years. The SDQ consists of 25 items and is divided into five sub-scales, including emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behavior. Based on the child's performance in the last 6 months, each item was answered on a three-point response scale (0= not true,1= somewhat true, 2= certainly true). The higher scores for difficult parts mean having serious emotional and behavioral problems, except for the prosocial behavior subscale, where lower scores indicated greater difficulties. Previous studies demonstrated that the internal consistency of the sub-scales of SDQ was good (Cronbach's α, 0.50–0.74) (30).

Covariates

The covariates were collected in the current study, including individual factors and family factors (31). Individual factors included sex (boys and girls), age (years), physical activity (intensity of exercise: high, moderate, low), full scale intelligence quotient (FSIQ) (score), screen times (< 2h/day, > 2h/day), body mass index (BMI) (underweight, normal, overweight); family factors included maternal education (high school or below, university or above), paternal education (high school or below, university or above) and monthly family income (<8,000 RMB/month, >8,000 RMB/month), which indicated the family socioeconomic status. Owing to the "females protect effect", where females would require the greater etiologic load to manifest the same degree of affectedness as males (32), females had lower autism prevalence than males (33). Thus, we controlled the sex as covariates in the following analysis. All of the demographic information was collected from the children's parents. The FSIQ of the participants was measured by the Chinese version of the Wechsler IV Intelligence Test (34).

Physical activity was assessed by the International Physical Activity Questionnaire (IPAQ) short format (35). All participants were asked to report the days and times in which they performed physical activity during the last 7 days at three intensities: high, moderate, and low. Examples of high activities like heavy lifting, digging, aerobics, or fast bicycling, moderate activities included carrying light loads, bicycling at a regular pace or doubles tennis, and low activities included walking. Metabolic Equivalent of Tasks (METs) is a standard unit of measurement for expressing the intensity of physical activity. The total weekly physical activity was calculated as a continuous variable by weighting the time performing each activity intensity with its metabolic equivalent (MET). Based on the total METs, the participants were classified into low ($0 \leq$ METs $<$ 600), moderate ($600 \leq$ METs < 3000), and high (METS $\geq$ 3,000) groups.

The BMI was estimated by dividing weight (kg) by height^2 (m^2), and the measurements of weight and height were taken by trained staff according to the standard procedure of anthropometric procedures and data collection developed by the World Health Organization (WHO). We adopted the age- and gender-specific BMI cutoff points for Chinese school-age children and adolescents released by the National Health and Family Planning Commission in 2018, underweight and overweight were defined as ≤5th percentile and ≥85th percentile, then classified BMI into underweight, normal, and overweight (36).

Statistical analysis

R core team version 4.0. was used for the statistical analysis. Data were presented as mean ± standard deviation (SD) for continuous variables and percentage for categorical variables. Next, in order to assess the differences between the children with ASD and TD children, the two-sided t test and chi-square tests were used for consecutive data and categorical variables, respectively (37). Then, we adopted a linear regression model to construct three models to analyze the association of SSBs, milk intake, and their interactive effect on SDQ sub-scales. Owing to the interactive effects of SSBs intake within the group, milk intake in the group was significant, we further analyzed the association of SSBs intake and SDQ sub-scales, milk intake, and SDQ sub-scales in the group of children with ASD and TD children respectively. The 0 time/week and 0–3 times/week were, respectively, treated as a reference for SSBs and milk intake, and model estimates were presented by estimates (β) and 95% confidence interval (CI). We performed trend tests by entering the median value of SSBs/milk intake as continuous variables in the models. The adjusted model included demographic factors, such as sex, age, physical activity, FSIQ, screen times, BMI, family income, and maternal and paternal education. All criteria for statistical significance were set at a two-tailed $p < 0.05$.

TABLE 1 Demographic characteristics of the study participants.

	ASD ($N = 107$)	TD ($N = 207$)	Total ($N = 314$)	*p*-value
Age, y	7.72 ± 1.30	7.77 ± 1.32	7.75 ± 1.31	0.791
Sex, %				<0.001
Boys	90 (84.11)	113 (54.59)	203 (64.65)	
Girls	17 (15.89)	94 (45.41)	111 (35.35)	
Maternal education, %				0.003
High school or below	44 (41.12)	51 (24.64)	95 (30.25)	
University or above	63 (58.88)	156 (75.36)	219 (69.75)	
Paternal education[a], %				0.054
High school or below	40 (37.38)	73 (35.44)	113 (36.10)	
University or above	67 (62.62)	133 (64.56)	200 (63.90)	
Monthly family income, %				<0.001
<RMB 8000	61 (57.01)	52 (25.12)	113 (35.99)	
≥RMB 8000	46 (42.99)	155 (74.88)	201 (64.01)	
FSIQ[b]	92.01 ± 18.76	112.88 ± 12.77	106.51 ± 17.67	<0.001
BMI[c], %				0.059
Underweight	10 (9.35)	26 (12.75)	36 (11.58)	
Normal	68 (63.55)	146 (71.57)	214 (68.81)	
Overweight	13 (12.15)	19 (9.31)	32 (10.29)	
Obesity	16 (14.95)	13 (6.37)	29 (9.32)	
Screen time, %				<0.001
<2 h/day	57 (53.27)	181 (87.44)	238 (75.80)	
≥2 h/day	50 (46.73)	26 (12.56)	76 (24.20)	
Physical activity, %				0.003
High	38 (35.51)	109 (52.66)	147 (46.82)	
Low	23 (21.50)	21 (10.14)	44 (14.01)	
Moderate	46 (42.99)	77 (37.20)	123 (39.17)	

[a]1 TD children with missing data on the paternal education.
[b]16 children with ASD failed to complete the Wechsler IV intelligence test due to their low cognitive ability.
[c]3 TD children with missing data on the BMI (body mass index).
ASD, Autism Spectrum Disorder; TD, Typical Developing; FSIQ, Full Scale Intelligence Quotient; BMI, Body Mass Index.

Result

The demographic characteristics of all participants

Table 1 summarized the demographic characteristics of the participants. From a total of 314 participants, 107 were diagnosed with ASD (90 boys, 84.11%) and 207 were normal controls (113 boys, 54.59%). Compared to children with TD, children with ASD were more likely to be boys, a mother with lower education degrees, a family with lower monthly incomes, lower FSIQ, longer screen time, and lower frequent physical activity (all $p < 0.05$).

TABLE 2 The comparison of SSBs and milk intake and SDQ scores between ASD and TD.

	ASD ($N = 107$)	TD ($N = 207$)	Total ($N = 314$)	*p*-value
SSBs intake, %				0.274
0 time/week	36 (33.64)	83 (40.10)	119 (37.90)	
1–2 times/week	51 (47.66)	98 (47.34)	149 (47.45)	
>2 times/week	20 (18.69)	26 (12.56)	46 (14.65)	
Milk intake, %				0.033
0–3 time/week	32 (29.91)	37 (17.87)	69 (21.97)	
4–7 times/week	54 (50.47)	112 (54.11)	166 (52.87)	
>7 times/week	21 (19.63)	58 (28.02)	79 (25.16)	
Emotional symptom[a]	2.78 (1.80)	2.39 (2.01)	2.52 (1.95)	0.007
Conduct problem[a]	2.59 (1.99)	2.06 (1.41)	2.24 (1.65)	0.037
Hyperactivity/Inattention[a]	6.64 (2.29)	4.49 (2.59)	5.22 (2.69)	<0.001
Peer relationship problem[a]	5.21 (1.91)	1.82 (1.45)	2.98 (2.28)	<0.001
Prosocial behavior[a]	4.57 (2.26)	6.68 (2.11)	5.96 (2.38)	<0.001

[a]The comparison of SDQ scores was adjusted for the following covariates: sex, age, maternal education, paternal education, monthly family income.
SSBs, Sugar-sweetened Beverages; ASD, Autism Spectrum Disorder; TD, Typical Developing; SDQ, Strength and Difficulty Questionnaire.

SSBs, milk intake and emotional and behavioral problems (Strength and Difficulties Questionnaire Scores)

As shown in Table 2 (Supplementary Figure S2), approximately half of the children in both the ASD and TD children consumed at least one time of SSBs each week (66.35 and 59.9%, respectively), there was no significant difference between the two groups in SSBs intake. However, compared to TD children, children with ASD consumed less times of milk ($p < 0.05$). In children with ASD, the scores of the other subscales of SDQ except for prosocial behavior were higher than TD children ($p<0.05$). The distribution of SSBs, milk intake, and SDQ sub-scales scores in children with ASD and TD children were shown in Supplementary Figures S2, S3.

Association of SSBs, milk intake, and their interactive effects on emotional and behavioral problems among all participants

As shown in Table 3, higher frequent milk intake was positively associated with prosocial behavior (p for trend <0.05) among all participants. The interactive effects of SSBs intake and group in emotional symptom ($\beta = -1.58$, 95%CI: −2.93, −0.23, $p = 0.022$) and conduct problem ($\beta = -1.21$, 95% CI: −2.35, −0.07, $p = 0.038$) among all participants was

TABLE 3 Adjusted model of association of SSBs, milk intake and their interactive effects on emotional and behavioral problems among all participants.

Adjust model	Emotional symptom β (95%CI)	Conduct problem β (95%CI)	Hyperactivity/ Inattention β (95%CI)	Peer relationship problem β (95%CI)	Prosocial behavior β (95%CI)
SSBs					
SSBs intake (N = 314) [a]					
1–2 times/week	−0.14 (−0.97, 0.69)	0.69 (−0.01, 1.38)	0.11 (−0.96, 1.18)	−0.25 (−0.96, 0.45)	0.56 (−0.38, 1.49)
>2 times/week	1.04 (−0.04, 2.12)	0.89 (−0.02, 1.80)	0.02 (−1.38, 1.42)	0.10 (−0.82, 1.03)	−0.35 (−1.57, 0.86)
p for trend	0.857	0.830	0.727	0.436	0.960
Group (N = 314)[b]	−0.42 (−1.26, 0.43)	−0.27 (−0.99, 0.44)	−1.90 (−2.99, −0.80)	−3.33 (−4.05, −2.60)	2.27 (1.32, 3.22)
p value	0.332	0.450	0.001	**<0.001**	**<0.001**
SSBs*Group (N = 314)[c]					
1–2 times/week*Group times/ week*Group	−0.15 (−1.15, 0.85)	−0.39 (−1.23, 0.45)	0.33 (−0.96, 1.63)	0.36 (−0.50, 1.22)	−0.92 (−2.05, 0.21)
p-value	0.769	0.365	0.616	0.410	0.110
>2 times/week*Group	−1.58 (−2.93, −0.23)	−1.21 (−2.35, −0.07)	0.49 (−1.26, 2.24)	−0.24 (−1.39, 0.92)	0.39 (−1.14, 1.91)
p-value	**0.022**	**0.038**	0.583	0.688	0.621
Milk					
Milk intake (N = 314)[d]					
4–7 times/week	−0.16 (−1.01, 0.70)	0.70 (−0.02, 1.43)	−0.10 (−1.21, 1.00)	−0.02 (−0.75, 0.71)	0.20 (−0.75, 1.15)
>7 times/week	−1.02 (−2.10, 0.06)	0.31 (−0.62, 1.23)	0.06 (−1.34, 1.47)	−0.70 (−1.62, 0.23)	1.68 (0.47, 2.89)
p for trend	0.514	0.954	0.513	0.358	**0.022**
Group (N = 314)[b]	−0.71 (−1.75, 0.34)	−0.12 (−1.01, 0.77)	−1.03 (−2.39, 0.32)	−3.30 (−4.19, −2.41)	2.73 (1.57, 3.90)
p-value	0.185	0.794	0.136	**<0.001**	**<0.001**
Milk*Group (N = 314)[e]					
4–7 times/week*Group times/ week*Group	−0.46 (−1.59, 0.66)	−0.81 (−1.76, 0.15)	−0.65 (−2.10, 0.81)	−0.10 (−1.06, 0.86)	−0.77 (−2.03, 0.48)
p-value	0.418	0.099	0.385	0.844	0.227
>7 times/week*Group	1.00 (−0.36, 2.37)	−0.48 (−1.64, 0.68)	−0.80 (−2.57, 0.96)	0.65 (−0.52, 1.81)	−1.69 (−3.21, −0.17)
p-value	0.149	0.418	0.373	0.275	**0.029**
SSBs*Milk					
SSBs*Milk (N = 314)	−0.01 (−0.08, 0.06)	0.01 (−0.05, 0.07)	0.03 (−0.06, 0.13)	−0.01 (−0.07, 0.05)	0.01 (−0.06, 0.09)
p-value	0.762	0.780	0.459	0.803	0.716
Group (N = 314)[b]	−0.35 (−1.48, 0.77)	−0.14 (−1.10, 0.82)	−1.31 (−2.76, 0.14)	−3.11 (−4.06, −2.15)	2.19 (0.93, 3.44)
p-value	0.538	0.776	0.076	**<0.001**	**0.001**
SSBs*Milk*Group (N = 314)[f]	0.09 (−0.00, 0.18)	0.03 (−0.05, 0.11)	0.02 (−0.10, 0.14)	0.07 (−0.01, 0.14)	−0.07 (−0.18, 0.03)
p-value	0.061	0.447	0.740	0.095	0.164

β value (95% Confidence Interval) from linear regression represented the correlation between variables and emotional and behavioral problems. Adjusted model was adjusted for sex, age, physical activity, FSIQ, screen time, BMI, maternal education, paternal education, monthly family income.
[a]0 time/week of SSBs intake is the reference group.
[b]ASD group is the reference group.
[c]0 time/week*Group is the reference group.
[d]0–3 times/week of milk intake is the reference group.
[e]0–3 times/week*Group is the reference group.
[f]SSBs*milk* Group is the reference group.
SSBs, Sugar-sweetened Beverages; FSIQ, Full Scale Intelligence Quotient; BMI, Body Mass Index; ASD, Autism Spectrum Disorder.
The bold values indicate statistically significant association between variables and emotional and behavioral problems.

significant, and the interactive effects of milk and group in prosocial behavior ($\beta = -1.69$, 95% CI: −3.21, −0.17, $p = 0.029$) among all participants was significant. Thus, we further analyzed the association of SSBs, and milk intake with emotional and behavioral problems in the group of children with ASD and TD children respectively. Besides, the crude model showed the same results as the adjust model (See Supplementary Table S1).

TABLE 4 Association of SSBs, milk intake and their interactive effects on emotional and behavioral problems in children with ASD.

	Emotional symptom β (95%*CI*)	Conduct problem β (95%*CI*)	Hyperactivity/ Inattention β (95%*CI*)	Peer relationship problem β (95%*CI*)	Prosocial behavior β (95%*CI*)
SSBs intake					
Crude model ($N = 107$)[a]					
1–2 times/week	−0.18 (−0.94, 0.57)	0.72 (−0.12, 1.56)	0.10 (−0.88, 1.08)	−0.21 (−1.03, 0.61)	0.58 (−0.38, 1.54)
>2 times/week	0.91 (−0.06, 1.88)	0.87 (−0.21, 1.94)	0.32 (−0.94, 1.58)	0.35 (−0.70, 1.40)	−0.36 (−1.59, 0.87)
p for trend	**0.045**	0.260	0.614	0.692	0.824
Adjusted model ($N = 107$)[a]					
1–2 times/week	−0.08 (−0.85, 0.70)	0.58 (−0.29, 1.45)	0.08 (−0.99, 1.15)	−0.15 (−1.04, 0.73)	0.47 (−0.56, 1.50)
>2 times/week	0.98 (−0.05, 2.00)	0.92 (−0.23, 2.08)	0.05 (−1.36, 1.47)	0.06 (−1.11, 1.23)	−0.66 (−2.02, 0.70)
p for trend	**0.048**	0.146	0.957	0.876	0.259
Milk intake					
Crude model ($N = 107$)[b]					
4–7 times/week	−0.31 (−0.94, 0.57)	0.78 (−0.09, 1.65)	0.01 (−1.00, 1.03)	−0.09 (−0.93, 0.75)	0.18 (−0.78, 1.15)
>7 times/week	−0.99 (−1.98, 0.00)	0.30 (−0.79, 1.39)	−0.25 (−1.53, 1.03)	−0.80 (−1.85, 0.25)	1.60 (0.38, 2.82)
p for trend	0.054	0.687	0.704	0.126	**0.009**
Adjusted model ($N = 107$)[b]					
4–7 times/week	−0.22 (−1.14, 0.70)	0.21 (−0.99, 1.41)	0.56 (−0.49, 1.60)	0.16 (−0.83, 1.16)	0.38 (−0.73, 1.50)
>7 times/week	−0.89 (−1.31, 1.55)	0.12 (−1.99, 0.21)	0.12 (0.43, 3.10)	−0.60 (−1.79, 0.59)	1.76 (−1.13, 1.37)
p for trend	0.071	0.616	0.969	0.213	**0.006**
Interaction					
Crude model ($N = 107$)					
SSBs*Milk	−0.00(−0.03,0.03)	0.02(−0.02,0.05)	−0.00(−0.04,0.04)	−0.01(−0.04,0.03)	0.01 (−0.04,0.05)
p value	0.936	0.372	0.967	0.698	0.775
Adjusted model ($N = 107$)					
SSBs*Milk	−0.00 (−0.04,0.03)	0.02 (−0.02,0.05)	−0.01(−0.06,0.03)	−0.02 (−0.06,0.02)	0.01 (−0.04,0.05)
p-value	0.834	0.433	0.638	0.368	0.721

β value (95% Confidence Interval) from linear regression represented the correlation between variables and emotional and behavioral problems. Adjusted model was adjusted for sex, age, physical activity, FSIQ, screen time, BMI, maternal education, paternal education, monthly family income.
[a]0 time/week of SSBs intake was the reference group.
[b]0–3 times/week of milk intake was the reference group.
SSBs, Sugar-sweetened Beverages; ASD, Autism Spectrum Disorder; FSIQ, Full Scale Intelligence Quotient; BMI, Body Mass Index.
The bold values indicate statistically significant association between variables and emotional and behavioral problems.

Association of SSBs, milk intake and their interactive effects on emotional and behavioral problems in children with ASD

The relationship between SSBs, milk intake, and their interactive effects on emotional and behavioral problems in children with ASD was presented in Table 4. More frequent of SSBs intake was significantly associated with emotional symptoms in children with ASD, and there were significant dose-response relationships between SSBs intake and emotional symptoms (all *p* for trend <0.05). The crude model estimates (95% *CI*) for emotional symptom across the SSBs categories were −0.18 (−0.94, 0.57) for 1–2 times of SSBs per week, 0.91 (−0.06, 1.88) for >2 times per week. After adjusting covariates, the dose-response relationships between SSBs intake and emotional symptoms still remained, the estimates (95% *CI*) for emotional symptoms across the SSBs categories were −0.08 (−0.85, 0.70) for 1–2 times of SSBs per week, 0.98 (−0.05, 2.00) for >2 times per week.

Less frequent milk intake was positively associated with prosocial behavior. In children with ASD, there were significant dose-response relationships between milk intake and prosocial behavior (all *p* for trend <0.05). The crude model estimates (95%*CI*) for prosocial behavior across the milk categories were 0.18 (-0.78, 1.15) for 4–7 times of milk intake per week, 1.60 (0.38, 2.82) for >7 times per week. After adjusting covariates, the dose-response relationships between milk intake and prosocial behavior still remained, the estimates (95% *CI*) for prosocial behavior across the milk categories were 0.38 (−0.73, 1.50) for 4–7 times of milk intake per week, 1.76 (−1.13, 1.37) for >7 times per week.

TABLE 5 Association of SSBs, milk intake and their interactive effects on emotional and behavioral problems in TD children.

	Emotional symptom β (95%*CI*)	Conduct problem β (95%*CI*)	Hyperactivity/ Inattention β (95%*CI*)	Peer relationship problem β (95%*CI*)	Prosocial behavior β (95%*CI*)
SSBs intake					
Crude model ($N = 207$)[a]					
1–2 times/week	−0.29 (−0.88, 0.29)	0.32 (−0.09, 0.73)	0.57 (−0.19, 1.33)	0.12 (−0.31, 0.55)	0.30 (−0.92, 0.32)
>2 times/week	−0.47 (−1.36, 0.41)	−0.34 (−0.95, 0.28)	0.62 (−0.51, 1.76)	0.14 (−0.50, 0.78)	0.08 (−0.86, 1.01)
p for trend	0.288	0.308	0.616	0.669	0.877
Adjusted model ($N = 203$)[a]					
1–2 times/week	−0.32 (−0.92, 0.29)	0.30 (−0.12, 0.72)	0.43 (−0.33, 1.18)	0.05 (−0.39, 0.49)	−0.31 (−0.96, 0.33)
>2 times/week	−0.60 (−1.55, 0.35)	−0.42 (−1.09, 0.23)	0.33 (−0.86, 1.52)	−0.20 (−0.89, 0.49)	0.11 (−0.90, 1.13)
p for trend	0.218	0.217	0.580	0.569	0.835
Milk intake					
Crude model ($N = 207$)[b]					
4–7 times/week	−0.83 (−1.58, −0.08)	0.78 (−0.09, 1.65)	−0.07 (−0.61, 0.47)	−0.10 (−0.65, 0.46)	−0.74 (−1.54,0.06)
>7 times/week	−0.34 (−1.17, 0.50)	0.30 (−0.79, 1.39)	−0.05 (−0.64, 0.55)	−0.04 (−0.65, 0.57)	−0.21 (−1.09,0.67)
p for trend	0.927	0.953	0.450	0.993	0.738
Adjusted model ($N = 203$)[b]					
4–7 times/week	−0.70 (−1.48, 0.08)	−0.13 (−0.69, 0.43)	−0.78 (−1.76, 0.21)	−0.12 (−0.69, 0.45)	−0.64 (−1.47,0.20)
>7 times/week	−0.04 (−0.91, 0.84)	−0.19 (−0.82, 0.43)	−0.78 (−1.89, 0.32)	−0.02 (−0.66, 0.62)	0.00 (−0.94, 0.93)
p for trend	0.435	0.583	0.320	0.909	0.454
Interaction					
Crude model ($N = 107$)					
SSBs*Milk	0.00 (−0.03, 0.02)	0.00 (−0.01, 0.02)	0.02 (−0.01, 0.04)	0.01 (−0.00, 0.03)	−0.01 (−0.03, 0.01)
p-value	0.730	0.964	0.264	0.162	0.321
Adjusted model ($N = 107$)					
SSBs*Milk	0.00 (−0.03, 0.02)	0.00 (−0.02, 0.01)	0.01 (−0.02, 0.04)	0.00 (−0.01, 0.02)	−0.01 (−0.04, 0.01)
p-value	0.717	0.798	0.604	0.623	0.349

β value (95% Confidence Interval) from general linear models represented the correlation between variables and emotional and behavioral problems. Adjusted model was adjusted for sex, age, physical activity, FSIQ, screen time, BMI, maternal education, paternal education, monthly family income.
SSBs, Sugar-sweetened Beverages; TD, Typical Developing; FSIQ, Full Scale Intelligence Quotient; BMI, Body Mass Index.
[a]0 time/week of SSBs intake was the reference group.
[b]0–3 times/week of milk intake was the reference group.

We further assessed the interactive effects of SSBs and milk intake on emotional and behavioral problems in children with ASD. However, no significant interactive effects of SSBs and milk intake on emotional and behavioral problems were observed.

Association of SSBs, milk intake, and their interactive effects on emotional and behavioral problems in TD children

Table 5 provided detailed information about the association of SSBs, milk intake, and their interactive effects on emotional and behavioral problems in TD children. The results showed no significant differences both in SSBs and milk intake with emotional and behavioral problems. At the same time, there were no interaction effects of SSBs and milk intake on emotional and behavioral problems in TD children.

Discussion

We found that compared to TD children, children with ASD had a higher frequency of milk intake, more serious emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and less prosocial behavior. Among all participants, the interactive effects of SSBs intake with the group, and milk intake with the group were significant. Thus, we further analyzed the association of SSBs, and milk intake with emotional and behavioral problems in the two groups respectively. In children with ASD, higher frequent SSBs intake was associated with more serious emotional symptoms, and higher frequent milk intake was associated with better prosocial behavior, while there were no significant interactive effects of SSBs and milk intake on emotional and behavioral problems in children with ASD and TD. It was the first study to explore the relationships between SSBs and milk intake with emotional and behavioral problems in children with ASD, which could provide an important basis for clinical nutritional intervention for children with ASD.

In the current study, there was no significant difference in the frequency of SSBs intake between children with ASD and TD children. Inconsistent with our study, some studies showed that compared to TD children, children with ASD tended to intake more SSBs and sugars (10, 11, 38). A study with a large sample among Chinese children aged 6–17 years showed that only 24.50% of the children consumed SSBs <1 time /week, and 25.90% consumed SSBs ≥ 5 times/week (39). However, in the current study, approximately 40.10% of children with TD never consumed SSBs in the past week, and 12.56% consumed >2 times/week. Most of the population in the current study were from the urban area of Guangzhou in China. Studies showed that due to the warm and humid climate and cultural differences, most people in Guangzhou tend to consume less strong flavored food, which may result in a lower frequency of SSBs intake in the current study population (40). Furthermore, compared to other studies conducted in China, the parental education level in the current population was relatively higher (5). Studies showed that a higher parental education level was associated with a lower frequency of SSBs intake (41).

Interestingly, we found that a higher frequency of SSBs intake was positively associated with emotional problems in children with ASD. A growing body of persuasive evidence posed a positive correlation between SSBs intake and emotional and behavioral problems (5), common mental disorders, and depression (6, 42). Several potential biological mechanisms might explain the association. Because SSBs were the principal source of added sugar in diets (43), it was reasonable to propose that the mechanism for explaining the association between SSBs intake and the emotional symptom was relevant to sugar content. First, several studies indicated that sugar intake resulted in a high risk of inflammation (44, 45). A cohort study indicated that long-term inflammation increased the risk of common mental disorders (46), such as depression. What's more, studies showed that inflammation was positively associated with psychological problem and autism symptoms (47). Thus, sugar intake triggered inflammation in children with ASD, which might be responsible for the association between SSBs intake and emotional symptom. Additionally, additives in SSBs, such as artificial food colors (AFCs) and caffeine, might somewhat explain the association between SSBs intake and emotional problem. Researches showed that AFCs had deleterious effects on children' s behavior (48) and caffeine intake was positively correlated with the severity of depression and insomnia in adolescents (49). In TD children, we found no association between SSBs intake with emotional and behavioral problems, however, there was no significant difference in SSBs intake between children with ASD and TD children. The results showed that compared to TD children, children with ASD were more vulnerable to the SSBs. Literature indicated that as one of the major environmental factors influencing children with ASD, diet may influence gastrointestinal microbiota composition and nutrients deficiency, then lead to the disorder of intestinal brain axis (50).

Unfortunately, consistent with previous studies (24, 25, 51, 52), results of our study indicated that children with ASD displayed lower milk intake than TD children. It's unclear why children with ASD had lower milk intake than TD children. Potential explanations might be included: first, compared to TD children, the children with ASD had lower socioeconomic status (parental education, monthly family income) in this study. Studies showed that higher family income and parental education levels have a positive relationship with milk intake (53, 54). Second, the literature showed that approximately 90% of children with ASD experienced a string of feeding-related problems (55), and they were more likely to experience food allergies including milk/dairy, nuts, and fruits (56). Therefore, the parents of children with ASD might take the initiative to reduce their milk intake for autistic children.

The current study showed that higher frequent milk intake was positively associated with better prosocial behavior in children with ASD but not in TD children. The positive association between milk intake and prosocial behavior might be explained by several mechanisms. First, milk is an important source of macronutrients and micronutrients in the diets of children and adolescents, including protein, vitamins, and minerals (57), and plays important role in meeting multiple nutrient recommendations (58). Compared to TD children, children with ASD had less frequent milk intake, which might further result in a lack of macronutrients and micronutrients in these children. Children with ASD have impaired development and are more vulnerable to nutrient deficiencies (59). A meta-analysis showed that vitamin/mineral supplementation can reduce anti-social behavior (60). Secondly, calcium and dairy products in milk may decrease inflammation in children with ASD. Evidence from mice and human demonstrated that dietary calcium decreased oxidative and inflammatory stress *in vivo* and dairy products contain additional factors, such as angiotensin-converting enzyme inhibitors, which might further suppress oxidative and inflammatory stress (61). In addition, studies indicated that higher frequent milk intake was associated with better perceived happiness, and sleep satisfaction (62), which may help children increase prosocial behavior. We found that higher frequent milk intake showed relatively lower risk of prosocial problem in children with ASD, while there were no significant correlation between milk intake and prosocial problem in TD children. Future studies may be needed to further explore the benefits of milk for children and the effects of dietary patterns on emotional and behavioral problems in addition to milk.

Several studies showed the association between SSBs and milk intake, reporting that the increased frequency of SSBs intake was coupled with the decreased intake of milk among school-aged children (14, 63). The current study showed that there were no interactive effects of SSBs and milk intake on emotional and behavioral problems in children with ASD and TD, which suggested that SSBs and milk intake have independent effects on emotional and behavioral problems. It was the first study conducted on the interactive effects of SSBs and milk intake on emotional and behavioral problems in children with ASD and TD, more researches need to further explore the interactive effects of SSBs and milk intake on emotional and behavioral problems in the future.

However, this study had several limitations. First, the current study was cross-sectional and cannot verify a causal relationship between SSBs and milk intake with emotional and behavioral problems. Future studies should investigate the longitudinal effects of SSBs and milk intake on emotional and behavioral problems in children with ASD. Secondly, the data concerning the SSBs and milk intake, SDQ, and questionnaire-based sociodemographic factors were reported by parents and guardians, which might be influenced by recall bias. Furthermore, there were many factors influencing SDQ and we only have explored a part of them, so further researches need to pay attention to other factors.

In summary, this study suggested that compared to TD children, children with ASD have less frequent milk intake and worse performance on all SDQ subscales. Furthermore, in children with ASD but not in TD children, higher frequency of SSBs intake was positively associated with an emotional problem, higher frequent milk intake was associated with better prosocial behavior, and there were no interactive effects of SSBs and milk intake on emotional and behavioral problems both in children with ASD and TD. We speculated that compared to TD children, the emotional problem and prosocial behavior of children with ASD were more vulnerable due to the SSBs and milk intake. However, the current study was a cross-sectional design, and prospective research is needed to verify our hypothesis in the future.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Sun Yat-sen University. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

LL designed the study. NP, XX, HL, JC, CJ, and SP performed the survey research. NP and ST analyzed the data. ST drafted the manuscript. XL and JJ were critical revision of the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.927212/full#supplementary-material

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Association between patterns of eating habits and mental health problems in Chinese adolescents: A latent class analysis

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Objective: We aimed to investigate the association between different eating habit patterns and mental health problems among Chinese middle and high school students, and further to estimate the interaction effect of different grouping variables on eating habits.

Methods: One thousand three hundred and forty-eight adolescents from Jilin Province in China were involved in this cross-sectional study. Mental health and eating habits were assessed using General Health Questionnaire and questions on Nutrition Knowledge, Attitude and Practice, respectively. Latent class analysis (LCA) was performed to identify eating habit patterns. Binary logistic regression and generalized linear models were used to explore the association between eating habit patterns, energy-adjusted nutrient intakes and mental health problems. Interaction analysis was performed to analyze the association between eating habits and mental health in different groups.

Results: Based on the LCA results, a 3-class parallel model was identified: 648 adolescents (48.1%) were classified in class-1 "Healthy Eating Behavior/Eating at Home," 452 adolescents (33.5%) in class-2 "Healthy Eating Behavior/Eating at School" and 248 adolescents (18.4%) in class-3 "Unhealthy Eating Behavior/Random Place." Compared with class-1, participants in class-2 and class-3 were at higher risk of mental health problems, especially for class-3 ($p < 0.05$). The energy and nutrient intakes by different latent classes showed that adolescents who ate unhealthy had lower daily intake of energy, protein, carbohydrate, fiber, Vitamins and minerals ($p < 0.05$). The interaction between age, sleep duration and different eating habits was statistically significant (p for interaction < 0.1).

Conclusion: "Unhealthy eating behavior/random place pattern" was positively correlated with mental health problems of adolescents. The adolescents with health diet were accompanied by fewer mental health problems, especially for that eating at home. And there were interactions between eating habits and age, sleep duration on the mental health problems.

KEYWORDS

eating habit, mental health, adolescent, latent class analysis, energy intake

Introduction

Mental health problems affect 10–20% of young people around the world (1). Adolescence is a period of great and rapid changes in students' physiology and habit (2). Many health-related bad behaviors would appear in this period, which increased the risk of mental health problems (3). Mental health status was closely related to health-related problems of young people, especially the decline of academic performance, poor interpersonal relationship, violence and drug abuse. Mental disorders also placed a heavy burden on young people's mortality, mainly due to significantly higher suicide rates among youth with mental health problems. And suicide was the leading cause of death among people aged 15–24 (1). The factors that affected mental health problems were complex and diverse, such as physical health, unhealthy lifestyle and family factors (3–5).

Although the determinants of mental health were complex, more and more studies showed that unhealthy eating habits were related to mental health (6–8). Teenagers were often exposed to unhealthy foods, such as takeout and high calorie snacks, and their meals were irregular. Research showed that people who regularly ate snacks at midnight (4) and skipped breakfast (9) were more likely to have psychological problems such as depression and increased psychological stress. And some studies pointed out that there were significant differences in dietary nutrition intake between students who ate at home and those who ate at school (10). However, the relationship between dietary patterns including eating locations and mental health status was unclear among adolescents (11–14).

Previous studies on mental health and nutrition of adolescents mainly focused on specific nutrients and foods or specific eating habits. The high correlation between various foods or eating habits made it difficult to attribute the impact to a single independent component, which limited the interpretation and application of the results (15). Due to the presence of dietary patterns, the association between diet and mental health outcomes was simplified and robust. The influence of overall diet on mental health may be more likely to translate into dietary advice and public health information (16). Moreover, most diet studies focus on the food types of "dietary patterns." For example, a study in Norway divided the eating patterns into three types: varied Norwegian/junk or convenient/snacking (17). However, few studies integrated adolescent eating habit and eating environment into different patterns.

Although various methods were used to cluster different eating patterns, there were still great differences in accuracy. Recently, latent class analysis (LCA) has been applied to nutritional epidemiology (18). Compared with factor analysis, LCA is a human-centered analysis method, which classifies samples into several mutually exclusive categories to explore the latent variables behind the categorical explicit variables with statistical correlation (19). And a Chinese study showed that LCA was more suitable for the study of dietary structure and disease risk than factor analysis (20).

Therefore, this study used LCA to analyze the eating habit patterns of adolescents in Jilin Province of China, to explore the association between different potential categories of eating habits and mental health problems, and further to estimate the interaction effect of different grouping variables on eating habits, so as to provide a scientific basis for the development of targeted health intervention measures.

Methods

Data source and study population

This cross-sectional study was questionnaire-based, which was conducted from August 2019 to December 2020 in Jilin Province, China, funded by the Department of Science and Technology of Jilin Province, China. A total of 1,875 adolescents were investigated in this survey. We excluded participants who had missing data on GHQ score or covariates, those who reported extreme total energy intake (outside the mean ± 3 standard deviations [SD]). Finally, a total of 1,348 adolescents were involved in our study, with an average age of 14.49 ± 1.99 years. This study covered students from 6 high schools and 6 middle schools in 9 cities in Jilin Province, and adopted the principle of multi-stage stratified random sampling and the form of face-to-face interview.

The study protocol was approved by the Ethics Committee of Jilin University (batch number: 20180515). All participants provided written informed consent. Research was conducted in accordance with the Helsinki Declaration as revised 1989.

Data collection

Data collection occurred in two steps. The first step was to measure anthropometric parameters. Body composition analyzer of Tsinghua Tongfang BAC-2A was used to measure body weight and body mass index (BMI). Height measurements (without shoes) were taken with a height ruler. In our study, IOTF criteria for Asian children and adolescents were selected to determine BMI cut-off values of 23 and 27 kg/m^2 for overweight and obesity (21).

The second step was the questionnaire. Students were asked to complete a nutrition status questionnaire, which was divided into four main parts referred to as follows: Section A was the basic information questionnaire, including gender, age, grade, nation and other information. Section B was the General Health Questionnaire (GHQ), which was originally designed by Goldberg in 1972 to examine the mental health status of respondents in community settings and non-psychiatric clinical settings (22). In this study, the Chinese version of GHQ-20 revised by Li was used to reflect the mental health status of subjects in the past month, including 20 items from three dimensions of self-identity, depression and anxiety, which was a useful scale to measure the mental health of students (23). Each item has a score of 0 or 1, and the sum of self-affirmation, depression, and anxiety sub-score is the GHQ total score, ranging from 0 to 20. The higher the total GHQ score, the worse the individual's mental health. The cut-off point for "case" recognition in GHQ-20 is between 3 and 4, with sensitivity and specificity of 78 and 85%, respectively, compared to the DSM-IL criteria (24). Section C included questions on nutrition knowledge, attitude and practices (KAP). The data we used on eating habits was from the nutritional practices section of the KAP questionnaire, which contained 5 questions, as shown in Table 1. The contents of the questionnaire were formulated on the basis of previous studies (25). Section D was the food frequency questionnaire (FFQ), which was a validated semi-quantitative food questionnaire and included more than 170 kinds of food in 11 categories, including cereals, beans, fungi and algae, vegetables and fruits. Both the reproducibility (r value = 0.5–0.8) and validity (r value = 0.3–0.6) of the instrument were acceptable, as reported elsewhere (26, 27). The intake frequency of each food should be filled in according to times/day, times/week, times/month, or times/year. Meanwhile, the consumption of each food should be recalled and recorded to obtain the daily intake of each food, and the food intake level and nutrients of the subjects were estimated based on the results of dietary frequency questionnaire. Under the guidance of nutrition experts from the School of Public Health, Jilin University, China, before the widespread use of this questionnaire, quality investigators conducted pre-experiments to verify the feasibility and comprehensiveness of the questionnaire and survey process.

Statistical analyses

This study clustered eating behaviors by LCA to form different eating habits patterns of adolescents. LCA was conducted using MPlus 8.3 as indicators for each item of eating habits. LCA is a finite mixed model that identifies meaningful homogeneous groups of individuals in a population given a set of measurement variables. We compared LCA for 2–5 categories, these criteria were used to determine the best model: (1) The lower Bayesian Information Criterion (BIC) or the lower Akaike Information Criterion (AIC) values indicate that the model fits well. (2) The p-values corresponding to the Lo-Mendell-Rubin adjusted likelihood ratio test (LMR) and bootstrapped likelihood ratio test (BLRT) indicators reach a significant level ($p < 0.05$), indicating that the models of the k classes are significantly superior to the models of the (k−1) classes. (3) The Entropy value ranges from 0 to 1. When Entropy ≥ 0.80 indicates that the classification accuracy reaches 90%. The higher the Entropy value, the higher the classification accuracy (28).

Continuous variables were presented as mean and standard deviation (SD) or Median (25–75th Percentile). Wilcoxon signed rank test was used for comparison between the two groups. Categorical variables were presented as case and percentage and were compared using Pearson's Chi-square test. We took the total score of GHQ-20 from 3 to 4 as the cut-off point to form a binary variable. Next, we used binary logistic regression to evaluate the association between eating habit patterns and mental health problems. Model 2 was adjusted for age and gender; Model 3 was adjusted for variables in model 2 plus physical activity, sleep duration and passive smoking. Generalized linear models were applied to investigate the comparison of energy and nutrient intakes by latent classes with *post-hoc* pairwise comparisons conducted using the Bonferroni correction. Generalized linear models were controlled for covariates including age, gender physical activity, sleep duration and passive smoking. When interactions were significant (p for interaction < 0.1), stratified analyses were performed. $P < 0.05$ was considered statistically significant. The analysis was performed using SPSS24.0.

Results

The demographic characteristics of the participants were presented in Table 2. In total, 704 (52.2%) adolescents had mental health problems and 644 (47.8%) adolescents did not, of whom 47.8% were male and 52.2% were female. The average age of the sample was 14.49 years old, of whom 59.1% were junior middle school students. And most of the students were Han nationality (83.4%). The proportion of female with mental health problems was higher than that of male adolescents ($p = 0.006$). In addition, compared with the adolescents without mental health problems, most of the adolescents with mental

TABLE 1 Participants' responses to questions related to nutritional practices.

Questions	Male ($n = 643$)	Female ($n =7 03$)	Total ($n = 1,346$)	p-value
1. Do you have breakfast				0.033
Never	15 (2.3)	24 (3.4)	39 (2.9)	
Sometimes	106 (16.5)	126 (17.9)	232 (17.2)	
Often	122 (19.0)	168 (23.9)	290 (21.5)	
Everyday	400 (62.2)	385 (54.8)	785 (58.3)	
2. What is your main way of eating lunch?				0.045
Take-out food	11 (1.7)	12 (1.7)	23 (1.7)	
Dining hall	324 (50.4)	398 (56.6)	722 (53.6)	
Fast food	39 (6.1)	43 (6.1)	82 (6.1)	
Brown bag	17 (2.6)	28 (4.0)	45 (3.3)	
Eating at home	252 (39.2)	222 (31.6)	474 (35.2)	
3. What is your main way of eating dinner?				0.002
Take-out food	12 (1.9)	12 (1.7)	24 (1.8)	
Dining hall	183 (28.5)	252 (35.8)	435 (32.3)	
Fast food	22 (3.4)	30 (4.3)	52 (3.9)	
Brown bag	6 (0.9)	18 (2.6)	24 (1.8)	
Eating at home	420 (65.3)	391 (55.6)	811 (60.3)	
4. Do you like to eat off-campus street food?				0.036
Like	278 (43.2)	344 (48.9)	622 (46.2)	
Dislike	365 (56.8)	359 (51.1)	724 (53.8)	
5. Do you eat the night snack?				0.001
Everyday	46 (7.2)	21 (3.0)	67 (5.0)	
Often	63 (9.8)	55 (7.8)	118 (8.8)	
Sometimes	350 (54.4)	428 (60.9)	778 (57.8)	
Never	184 (28.6)	199 (28.3)	383 (28.5)	

health problems had fewer physical activities, shorter sleep duration and were passive smokers ($p < 0.05$).

The association between eating habits and GHQ scores and their subscales has shown in Table 3. The total score of GHQ, as well as the scores of self-affirmation, depression and anxiety sub-score had statistical significance in different breakfast frequency, preference for roadside stall and frequency of night snack ($p < 0.05$). Regular breakfast eating was positively associated with mental health. And the mental health status of people who ate take out and fast food for lunch and dinner was poor ($p < 0.05$). In addition, people who liked to eat roadside stalls and often ate night snack had higher GHQ scores ($p < 0.001$).

Model fit indicators for solutions with 2 through 5 classes were summarized in Table 4, and three eating habit pattern classes were chosen. To determine the most optimal classification, we first assumed that there were only two classes for all subjects, and gradually increased the number of classes until we found the best model to fit the data. BLRT significance test showed that increasing the number of classifications might improve the model, but LMR showed no statistical significance for 4-class model, indicating that there was no significant improvement in model fitting between 3-class model and 4-class model. When the model class was 3, LMR and BLRT had $p < 0.05$, and the entropy was 0.745. For these reasons, the 3-class model was selected as the optimal models in terms of suitability, simplicity and interpretability for further analysis. This solution created 3 mutually exclusive and collectively exhaustive groups into which an individual was assigned to one class based on their greatest likelihood. The different eating habits conditional probability from the selected eating habit patterns for the three classes was presented in Table 5.

Figure 1 showed the project probabilities for each of the three categories of solutions, and we provided subjective labels for each category. Class 1, accounting for 48.1% of the sample ($n = 648$), was termed "healthy eating behavior/eating at home," because adolescents in this class had regular breakfast, mostly ate at home for lunch and dinner, and did not often eat roadside stalls and night snacks. The class 2 accounted for 33.5% of the sample ($n = 452$), and were termed "healthy eating behavior/eating at school." Adolescents in this class had regular breakfast, and most of them had lunch and dinner in the school canteen. These people did not eat night snacks very often, and nearly half of them didn't like to eat roadside stalls. Class 3, accounting for 18.4% of the sample ($n = 248$), was

TABLE 2 Major characteristics of study population.

Variables	Total (n = 1,348)	No mental health problems (n = 644, 47.8%)	With mental health problems (n = 704, 52.2%)	t/χ^2	p-value
Age (Mean ± SD)	14.49 ± 1.99	14.67 ± 2.04	14.71 ± 1.95	−0.347	0.729
Gender (n, %)				7.647	0.006
Male	644 (47.8)	333 (51.7)	311 (44.2)		
Female	704 (52.2)	311 (48.3)	393 (55.8)		
Grade (n, %)				2.662	0.103
Junior high school	796 (59.1)	395 (61.3)	401 (57.0)		
Senior high school	552 (40.9)	249 (38.7)	303 (43.0)		
Nation (n, %)				0.341	0.559
Han	1,124 (83.4)	533 (82.8)	591 (83.9)		
Minorities	224 (16.6)	111 (17.2)	113 (16.1)		
Physical activity (n, %)				19.123	<0.001
More than 4 times a week	388 (28.8)	198 (30.7)	190 (27.0)		
2∼3 times a week	723 (53.6)	343 (53.3)	380 (54.0)		
1 time a week	185 (13.7)	93 (14.4)	92 (13.1)		
None	52 (3.9)	10 (1.6)	42 (6.0)		
Sleep duration (n, %)				45.628	<0.001
More than 8 h	242 (18.0)	144 (22.4)	98 (13.9)		
6–8 h	776 (57.6)	392 (60.9)	384 (54.5)		
<6 h	330 (24.4)	108 (16.8)	222 (31.5)		
Passive smoking (n, %)				8.929	0.003
Yes	332 (24.6)	135 (21.0)	197 (28.0)		
No	1 016 (75.4)	509 (79.0)	507 (72.0)		
Monthly household income (RMB) (n, %)				2.247	0.523
<1,000	40 (3.0)	19 (3.0)	21 (3.0)		
1,000∼5,000	691 (51.2)	334 (51.9)	357 (50.7)		
5,000∼10,000	430 (31.9)	211 (32.8)	219 (31.1)		
≥10,000	187 (13.9)	80 (12.3)	107 (15.2)		
BMI (n, %)				4.169	0.124
Normal	974 (72.3)	450 (69.9)	524 (74.4)		
Overweight	255 (18.9)	136 (21.1)	119 (16.9)		
Obese	119 (8.8)	58 (9.0)	61 (8.7)		

SD, standard deviation; BMI, body mass index.

termed as "unhealthy eating behavior/random place," because the teenagers in this class did not have regular eating habits and eating places, most of them skipped breakfast and school meals, preferred roadside stalls, and had a higher rate (34.1%) of eating late-night snacks than the other two classes. This pattern was deemed unhealthy.

Table 6 summarized binary logistic regression analysis using class-1 (healthy eating behavior/eating at home) as the reference. Univariate analysis showed that class-2 (healthy eating behavior/eating at school) and class-3 (unhealthy eating behavior/ random place) were associated with a higher mental health risk ($p < 0.05$), and the harmful effect of class-3 [adjusted Odds Ratio (OR) = 2.15, 95% Confidence Interval (CI) =1.59, 2.91] on mental health was higher than that of class-2 (adjusted OR = 1.59, 95% CI = 1.25, 2.02). After further adjusting for age, gender, physical activity, sleep duration, and passive smoking in model 3, the ORs (95% CIs) of class-2 (healthy eating behavior/eating at school) and class-3 (unhealthy eating behavior/random place) for mental health problems comparing with class-1 (healthy eating behavior/eating at home) were 1.73 (1.27, 2.38) and 2.23 (1.62, 3.08). The correlation between the two variables did not change ($p < 0.05$).

Table 7 presented the comparison of energy and nutrient intakes by different latent classes. After adjustment for

TABLE 3 Nutritional behavior based on GHQ total score, self-affirmation sub-score, anxiety sub-score, and depression sub-score of the sample.

Variable	GHQ total score		Self-affirmation sub-score		Depression sub-score		Anxiety sub-score	
	M (P25, P75)	*p*-value	M (P25, P75)	*p*-value	M (P25, P75)	*p*-value	M (P25, P75)	*p*-value
Frequency of breakfast								
Never	7.0 (4.0, 12.0)	<0.001	4.0 (2.0, 5.0)	<0.001	1.0 (1.0, 3.0)	<0.001	2.0 (0, 5.0)	<0.001
Sometimes	5.0 (2.0, 9.0)		3.0 (2.0, 5.0)		0 (0, 1.0)		1.0 (0, 3.0)	
Often	4.0 (2.0, 8.0)		2.0 (1.0, 4.0)		0 (0, 1.0)		1.0 (0, 2.0)	
Everyday	3.0 (1.0, 6.0)		2.0 (1.0, 4.0)		0 (0, 1.0)		0 (0, 2.0)	
Lunch way								
Take-out	5.0 (3.0, 10.0)	0.005	3.0 (2.0, 5.0)	0.005	1.0 (0, 2.0)	0.171	1.0 (0, 3.0)	0.289
Dining hall	4.0 (2.0, 7.0)		2.0 (1.0, 4.0)		0 (0, 1.0)		1.0 (0, 2.0)	
Fast food	4.0 (2.0, 8.0)		3.0 (1.0, 4.0)		1.0 (0, 1.0)		1.0 (0, 2.0)	
Brown bag	3.0 (2.0, 8.0)		2.0 (1.0, 4.0)		1.0 (0, 1.0)		1.0 (0, 2.2)	
Eat home	3.0 (1.0, 7.0)		2.0 (0, 4.0)		0 (0, 1.0)		0 (0, 2.0)	
Dinner way								
Take-out	5.0 (3.0, 10.0)	0.037	2.5 (1.3, 5.0)	0.021	1.0 (0, 2.0)	<0.001	0.5 (0, 3.0)	0.638
Dining hall	4.0 (2.0, 7.0)		3.0 (1.0, 4.0)		0 (0, 1.0)		1.0 (0, 2.0)	
Fast food	5.0 (2.0, 9.0)		3.0 (0.3, 5.0)		1.0 (0, 2.0)		1.0 (0, 2.0)	
Brown bag	4.0 (1.3, 8.8)		3.0 (1.0, 4.8)		1.0 (0, 2.8)		1.0 (0, 2.0)	
Eat home	3.0 (1.0, 7.0)		2.0 (1.0, 4.0)		0 (0, 1.0)		0 (0, 2.0)	
Roadside stall								
Like	5.0 (2.0, 8.0)	<0.001	3.0 (1.0, 4.0)	<0.001	1.0 (0, 1.0)	<0.001	1.0 (0, 3.0)	<0.001
Dislike	3.0 (1.0, 6.0)		2.0 (1.0, 4.0)		0 (0, 1.0)		0 (0, 2.0)	
Frequency of night snack								
Everyday	4.0 (2, 10)	<0.001	2.0 (1.0, 5.0)	0.001	1.0 (0, 2.0)	<0.001	0 (0, 2.0)	<0.001
Often	5.0 (2, 10)		3.0 (1.0, 5.0)		1.0 (0, 2.0)		1.0 (0, 4.0)	
Sometimes	4.0 (2.0, 8.0)		2.0 (1.0, 4.0)		0 (0, 1.0)		1.0 (0, 2.0)	
Never	3.0 (1.0, 6.0)		2.0 (0, 4.0)		0 (0, 1.0)		0 (0, 2.0)	

GHQ, general health questionnaire.

TABLE 4 Fit indices for LCA between 2 and 5 classes.

Number of classes	AIC	BIC	aBIC	Entropy	LMR	BLRT
2C	12441.793	12603.191	12504.717	0.758	<0.0001	<0.0001
3C	12288.496	12533.196	12383.897	0.745	0.006	<0.0001
4C	12237.969	12565.971	12365.874	0.796	0.975	<0.0001
5C	12194.428	12606.732	12354.783	0.789	0.843	<0.0001

AIC, Akaike information criterion; BIC, Bayesian information criterion; aBIC, adjusted BIC; LMR, Lo-Mendell-Rubin adjusted likelihood ratio test; BLRT, bootstrap likelihood ratio test.

multiple covariates, adolescents with an "unhealthy eating behavior/random place pattern" had lower daily intakes of energy, protein, dietary fiber, vitamins and minerals, and higher intakes of total fat ($p < 0.05$). Compared with "healthy eating behavior/eating at home" adolescents, adolescents who ate at school had higher intakes of minerals ($p < 0.05$), but there was no statistically significant difference in nutrient intakes ($p \geq 0.05$). The results of pairwise comparisons showed that there was no statistically significant difference in the percentage (%) of energy provided by carbohydrates among the three groups ($p \geq 0.05$).

Table 8 showed the interaction between eating habits and adolescents' mental health problems in different subgroups, and we performed subgroup analyses by different variables. The results showed that adolescents aged <14 years old had a better correlation between eating habits and mental health problems (p for interaction = 0.003). The ORs (95% CIs) of class-3 (unhealthy eating behavior/random place pattern) for mental health problems comparing with class-1 (healthy eating

TABLE 5 Latent class conditional probabilities for 3 classes of Nutrition Practices.

	Class 1 (*n* = 6 48, 48.1%)	Class 2 (*n* = 4 52, 33.5%)	Class 3 (*n* = 248, 18.4%)
Frequency of breakfast			
Never	0.013	0.013	0.090
Sometimes	0.123	0.174	0.276
Often	0.153	0.243	0.305
Everyday	0.711	0.570	0.329
Lunch way			
Take-out food	0	0.011	0.064
Dining hall	0.358	0.908	0.302
Fast food	0.063	0.026	0.115
Brown bag	0.052	0.015	0.022
Eat home	0.527	0.040	0.496
Dinner way			
Take-out food	0.002	0	0.081
Dining hall	0.008	0.924	0
Fast food	0.044	0.011	0.073
Brown bag	0.015	0.032	0
Eat home	0.931	0.034	0.846
Roadside stall			
Like	0.234	0.539	0.824
Dislike	0.766	0.461	0.176
Midnight snack frequency			
Everyday	0.019	0.043	0.126
Often	0.016	0.104	0.215
Sometimes	0.513	0.651	0.596
Never	0.452	0.202	0.062

behavior/eating at home pattern) were 2.37 (1.52, 3.69). There was also a significant difference in the association between eating habit patterns and mental health problems among different sleep duration groups (p for interaction = 0.001). In the group with sleep duration of 6–8 h, unhealthy eating behavior was strongly associated with mental health problems (adjusted OR = 2.91, 95% CI = 1.88, 4.51). And we did not find an association between eating habit patterns and mental health in groups with adequate sleep duration (≥8 h) and short sleep duration (<6 h). Furthermore, gender (p for interaction = 0.387) and passive smoking (p for interaction = 0.290) did not significantly alter the association between eating habits and mental health problems.

Discussion

In this study, we used LCA to analyze the association between eating habits and mental health problems among adolescents in Jilin Province. Our study identified three patterns, "healthy eating behavior/eating at home," "healthy eating behavior/eating at school" and "unhealthy eating behavior/random place." Participants in the "unhealthy eating behavior/random place pattern" had lower daily intake of energy, protein, carbohydrate, fiber, Vitamins and minerals. Unhealthy eating habits were associated with higher mental health risks. The adolescents with health diet were accompanied by fewer mental health problems, especially for that eating at home. Subgroup analysis showed that the association still persisted in age <14 years and participants with less sleep duration (6–8 h).

The incidence of mental health problems among Chinese adolescents in our study was high (52.2%), which was consistent with recent reports (29, 30). There were several factors that may lead to changes in mental health, such as the increase of academic pressure, the change of relationship with classmates or parents, bad behavior (5). Previous reports have pointed out that many people choose to relieve stress by overeating or eating unhealthy food (31). However, studies pointed out that unhealthy diet had no benefit in reducing psychological stress (32). The conclusion was controversial. But study examining eating habit patterns in relation to mental health was lacking. In line with these findings, our study explored the impact of eating habits on adolescents' mental health. We observed that the "unhealthy eating behavior/random place pattern" observed in the present study was associated with higher mental health risk, compared with the "healthy eating behavior/eating at home pattern" and "healthy eating behavior/eating at school pattern," after adjusting for sociodemographic and lifestyle factors. This finding was consistent with literature reporting a positive association between unhealthy eating behavior and mental health problems.

Epidemiological studies suggested adolescents who didn't eat breakfast were more likely to have elevated stress, depression and emotional distress (7). An earlier study among Chinese teenagers found that college students who ate breakfast almost every day tended to choose healthier food all day (33). A study showed that skipping breakfast was associated with increased cortisol (34), which in turn increased the risk of mental health problems such as anxiety and depression (35). A survey of four provinces in China pointed out that the increased consumption of fast food and sugary drinks had a great impact on teenagers' psychological symptoms (36). The possible explanation was that takeout, fast food and roadside stalls were related to pro-inflammatory diet. Studies pointed out that there was a significant positive correlation between pro-inflammatory diet and the risk of depression (37). In addition, compared with

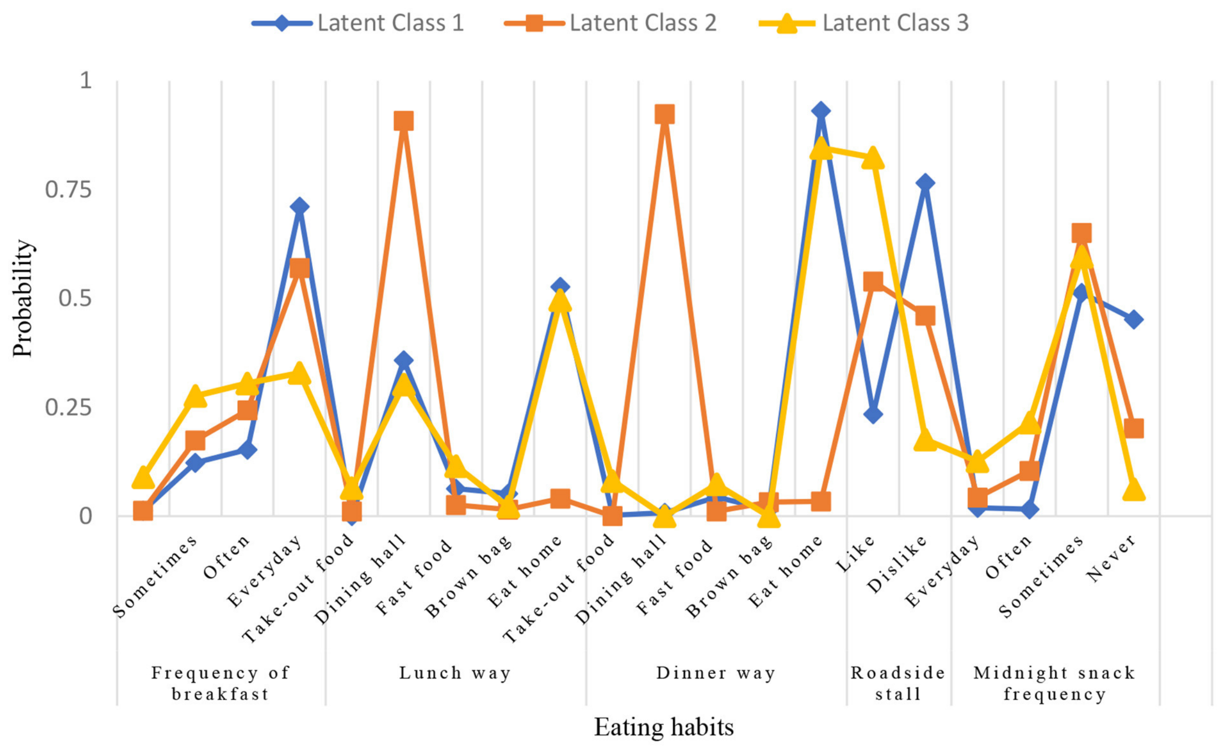

FIGURE 1
Conditional item probability plots.

TABLE 6 Association between latent class membership and mental health problems.

	Model 1		Model 2		Model 3	
	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value	OR (95%CI)	*p*-value
Class 1: healthy eating behavior/eating at home	Ref		Ref		Ref	
Class 2: healthy eating behavior/eating at school	1.59 (1.25, 2.02)	<0.001	1.78 (1.13, 2.41)	<0.001	1.73 (1.27, 2.38)	0.001
Class 3: unhealthy eating behavior/random place	2.15 (1.59, 2.91)	<0.001	2.38 (1.74, 3.25)	<0.001	2.23 (1.62, 3.08)	<0.001

OR, odds ratio; CI, confidence interval.
Model 1: univariate analysis; Model 2: adjusted for age and gender; Model 3: Model 2 + physical activity, sleep duration, and passive smoking.

the food at home, fast food and roadside stalls were often less healthy, because these foods contained higher fat, salt and sugar and less nutrients, which were related to various negative health outcomes (38, 39).

Previous studies formed different eating patterns based on dietary intake and eating habits (15–17), but these studies did not consider the impact of eating place on adolescents' mental health. We incorporated eating location into eating patterns, which emphasized that direct food environment might have an impact on adolescents' mental health. Our research results indicated that eating at home had a higher protective effect on adolescents' mental health than eating at school. Children who ate at home had higher intake of core foods (grains, vegetables, fruits, fish, meat, nuts and dairy products) (10). Studies on nutritional intake of children and adolescents in Europe showed that eating at home was associated with higher nutritional intake and lower dietary energy density (40). A study pointed out that regular family meals might promote healthier eating habits, improve parent-child relationship and reduce the risk of depressive symptoms in adolescents (5). Children eating with their parents helped to improve their life satisfaction and emotional stability, and reduced high-risk behaviors such

TABLE 7 Comparison of energy and nutrient intakes by latent classes.

Variables	Healthy eating behavior/eating at home ($n = 648$)	Healthy eating behavior/eating at school ($n = 452$)	Unhealthy eating behavior/random place ($n = 248$)	*p*-value
Energy, kcal	3543.63 ± 41.39[a]	3509.39 ± 67.30[a]	2931.91 ± 49.30[b]	<0.001
Protein, g	145.70 ± 2.15[a]	146.59 ± 3.49[a]	115.30 ± 2.56[b]	<0.001
Protein (% energy)	16.37 ± 0.14[a]	16.40 ± 0.23[a]	15.66 ± 0.17[b]	0.002
Total fat, g	107.42 ± 1.79[a]	110.56 ± 2.91[a]	96.46 ± 2.13[b]	<0.001
Total fat (% energy)	27.36 ± 0.35[b]	28.96 ± 0.57[a]	29.32 ± 0.42[a]	0.001
Carbohydrate, g	515.20 ± 6.62[a]	509.09 ± 10.76[a]	423.45 ± 7.88[b]	<0.001
Carbohydrate (% energy)	66.23 ± 0.66	59.73 ± 1.08	58.21 ± 0.79	0.140
Fiber, g	29.81 ± 0.63[a]	30.67 ± 1.02[a]	23.81 ± 0.75[b]	<0.001
Vitamin C, mg	212.50 ± 5.93[a]	201.97 ± 9.64[a]	145.50 ± 7.06[b]	<0.001
Calcium, mg	1517.93 ± 38.22[b]	1703.32 ± 62.13[a]	1204.56 ± 45.52[c]	<0.001
Iron, mg	58.08 ± 1.37[b]	63.32 ± 2.23[a]	50.16 ± 1.63[c]	<0.001
Sodium, mg	3615.91 ± 81.70[ab]	3856.61 ± 132.83[a]	3441.56 ± 97.31[b]	0.040
Potassium, mg	4510.14 ± 78.28[a]	4707.14 ± 127.27[a]	3511.53 ± 93.24[b]	<0.001

Data are the mean ± standard deviation adjusted for age, gender, physical activity, sleep duration, and passive smoking. Different superscript letters indicate pairwise comparisons of the mean using Bonferroni correction, with adjustment for multiple comparisons, between latent classes (p< 0.0167). [a,b,c]Represent latent classes with the highest, medium and lowest mean values.

TABLE 8 Multivariable-adjusted odds ratios for the association between eating habits and mental health problems by subgroups.

	Class 1: healthy eating behavio/eating at home	Class 2: healthy eating behavior/eating at school	Class 3: unhealthy eating behavior/random place	*p* for interaction
Age				0.003
<14	Ref	1.16 (0.48, 2.83)	2.37 (1.52, 3.69)	
≥14	Ref	1.44 (1.04, 1.97)	1.73 (1.09, 2.73)	
Gender				0.387
Male	Ref	1.68 (1.05, 2.69)	1.93 (1.25, 3.00)	
Female	Ref	1.83 (1.19, 2.81)	2.70 (1.67, 4.38)	
Passive smoking				0.290
Yes	Ref	1.13 (0.64, 2.03)	1.24 (0.59, 2.61)	
No	Ref	2.02 (1.37, 2.96)	2.55 (1.78, 3.64)	
Sleep duration				0.001
More than 8 h	Ref	2.43 (0.75, 7.81)	1.56 (0.77, 3.15)	
6–8 h	Ref	2.35 (1.58, 3.51)	2.91 (1.88, 4.51)	
<6 h	Ref	0.96 (0.51, 1.80)	1.46 (0.72, 2.97)	

Data are presented as odds ratio (95% confident interval).
Models are adjusted for age, gender, physical activity, sleep duration, and passive smoking except the subgroup variable itself.

as suicide attempts, antisocial behavior, violence and extreme dieting (14).

Previous research pointed out that limited food and vegetable variety in school cafeterias may lead to inadequate vitamin and mineral intake among teens, and adolescents preferred to buy energy-dense foods in the cafeteria (41, 42). But we did not find similar results in our study. Our results found no significant differences in energy and nutrient intake between home and school meals among adolescents eating healthy eating behaviors. School diets and mental health often involve the interaction of multiple influences and factors. The reason for the poor mental health of adolescents who ate at school may be that most of these students live in dormitories, and they were more likely to encounter problems such as peer influence, school atmosphere pressure, and interpersonal relationships (43, 44). This prompted us to pay more attention to the mental health of students who ate at school.

In the subgroup analysis of this study, we found that the association between unhealthy eating habits and mental health problems was present in younger participants, which was consistent with previous research (11). A potential reason for the age difference may be that younger children were not as good at dealing with mental health issues as older children (45). Furthermore, the relationship was also related to sleep duration. Eating habits had a significant effect on the mental health of participants with a sleep duration of 6–8 h, but there was no correlation when the duration was <6 h. This may be because shorter sleep had a greater impact on mental health status (46), but the relationship between the three need to be further studied. In the findings of this study, girls were more likely to experience mental health problems, and gender differences in mental health risks during adolescence were widely recognized (12). However, we did not find an interaction between gender and eating habits. This was also consistent with results from previous studies showing no signs of gender differences between eating habits and mental health (12, 13).

Our findings have clinical and policy implications. First of all, schools should pay attention to the assessment of students' mental health, and suggest to carry out mental health promotion activities for parents. Educators should promptly identify high-risk groups for early psychological intervention. In addition, we promote strategies for families to eat together. More importantly, schools should strengthen supervision over the sale of unhealthy foods in the surrounding environment, strengthen nutrition and health education for youth schools and families, and cultivate students to form healthy eating habits.

The advantages of this study included the use of LCA as a novel method to obtain three different eating habit patterns according to teenagers' eating places and eating characteristics. The dietary patterns of adolescents were assessed from the overall level, which was more conducive to macro-regulation of diets and more easily translated into dietary recommendations and public health information. And the sample size of the study was relatively large and representative, which can well-reflect the dietary situation of middle school students in Northeast China. Finally, our study explored the association between eating habits and mental health problems stratified by age, sex, and sleep duration, which was conducive to the timely detection of the adverse mental state and take measures.

There were some limitations that should be considered in interpreting the study results. First of all, this study was a cross-sectional study, we cannot judge the causal association between eating habits and mental health status. However, a longitudinal research results did not support the hypothesis of reverse causality (47). Another limitation was that the mental health scale used in this study was not a clinical diagnostic standard scale, so the interpretation of the results should be more cautious. Finally, study outcomes were assessed using self-reported questionnaires and were susceptible to recall bias and misreporting.

Conclusion

Our results supported the hypothesis that eating habit affected adolescents' mental health. "Unhealthy eating behavior/random place pattern" was positively correlated with mental health problems of adolescents. The protective effect of healthy eating behavior/eating at home on mental health was higher than that of healthy eating behavior/eating at school. And there were interactions between eating habits and age, sleep duration.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Author contributions

YL and XL made the study design. BL, NY, and JL conducted the study. XL, MS, and RG analyzed the data and wrote the manuscript. LW, WH, and YY attended the manuscript revision. All authors agreed with the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Association of consumption of sugar-sweetened beverages with cognitive function among the adolescents aged 12–16 years in US, NHANES III, 1988–1994

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Objective: As a major source of added sugar, the consumption of sugar-sweetened beverages (SSBs) continues to increase worldwide. The adverse health effects associated with SSBs are also risk factors for cognitive development, but studies on the relationship between SSBs and adolescents' cognitive function are limited. We used data released by the National Health and Nutrition Examination Survey (NHANES) III (1988–1994) to explore the association between the consumption of SSBs and cognitive function among children and adolescents aged 12–16 years in the United States.

Methods and procedures: A nationally representative population sample included 1,809 adolescents aged 12–16 years who participated in the United States NHANES from 1988 to 1994 and provided samples for the dietary intake frequency questionnaire and measures of cognitive function. Binary logistic regression was used to estimate the association between the frequency of SSB consumption and scores on cognitive function tests.

Results: This study of 1,809 adolescents aged 12–16 years comprised 963 girls (weighted proportion, 48.17%) and 846 boys (weighted, 51.83%), with a weighted mean (SE) age of 13.99 (0.05) years. Compared with adolescents who intake SSBs 0–1 times per week, those who drank 4–7 times per week had better scores in arithmetic, reading, and digit span tests, with odds ratios (ORs) of 0.36 (95% CI = 0.16–0.82), 0.35 (95% CI = 0.18–0.70), and 0.19 (95% CI = 0.08–0.44), respectively. The ORs for abnormal block design scores increase with the frequency of SSB intake after being adjusted for potential confounders (*P* for trend 0.02). Stratified analyses showed that compared with normal or below BMI, among overweight or obese individuals, the frequency of SSB intake had significant ORs for abnormal digit span scores (OR = 4.76, 95% CI = 1.19–18.96 vs. 0.35, 95% CI = 0.10–1.25; *P* for interaction = 0.01).

Conclusion: The positive associations of SSBs at moderate level intake with better scores in arithmetic, reading, and digit span were observed, but no dose-response relationship was identified at the overall level. Additionally, with the increasing frequency of SSB consumption, the risk of anomalous block design scores increased among US adolescents. Further investigation is warranted to confirm the association and mechanism between SSBs and cognitive function among adolescents.

KEYWORDS

sugar-sweetened beverages, cognition, adolescent, NHANES III, WISC-R, WRAT-R

Introduction

Sugar-sweetened beverages (SSBs) are the major source of added sugar, representing a nutritionally poor, calorie-dense but palatable type of drink that is appealing to children and adolescents (1). The consumption of SSBs continues to increase worldwide. Similarly, American children and adolescents of all ages are increasingly consuming SSBs (2), and the proportion of calories consumed from SSBs also increased significantly (3).

Current studies indicated that increased consumption of SSBs is associated with a number of health risks, including cardiometabolic burden, increased risk of obesity, type 2 diabetes, hypertension, and metabolic syndrome among people of all age groups (4–7). Moreover, regarding its impact on brain function, findings from previous studies suggested that SSBs are associated with the responsive release of dopamine and opioids in the striatum (8), which is related to value-based learning, encoding hedonic valuation, and motivated behavior (9, 10).

During adolescence, the brain is undergoing rapid structural and functional development, and the neurofunction of adolescents can easily be disturbed by external factors during the special period (11, 12). Although the evidence is limited, there are studies relating SSB consumption to mental health problems (13, 14), dysfunction of executive ability (15), and behavioral adaptation (16) in adolescents. Nevertheless, very few studies have focused on the impact of SSB consumption on cognitive function, and the findings remain inconsistent and insufficient, especially in adolescents.

The cognitive function plays an essential role in learning, daily life, and academic performance in early life, which is affected by multifactor including diet (17). It has been widely recognized that excessive sugar or simple carbohydrate intake is linked with impaired cognitive functions (18). A study on adolescent rats showed that excessive consumption of added sugars, especially HFCS-55 (high fructose corn syrup-55), during adolescence, adversely affects hippocampal function and metabolic outcomes and promotes neuroinflammation (19). Regular consumption of sweets or sweeteners, even at low dosages, can significantly alter brain neurochemistry, especially dopamine levels and its turnover rate, as well as high cognitive function (20). A recent cross-sectional study in China showed that SSB consumption was positively associated with all subscales and composite scores of the Behavior Rating Inventory of Executive Function (BRIEF, for assessment of executive function impairment) and a higher risk of increased executive difficulty (21). Another study reported that increased consumption of SSBs was associated with significantly lower test scores in reading and numeracy in Australian school-aged children (22). Therefore, it is reasonable to hypothesize that SSBs may negatively impact cognitive function beyond a certain level of intake.

However, an early meta-analysis from the 90s concluded that sugar did not affect children's behavioral or cognitive performance (23). In addition to that, a double-blinded controlled trial showed that neither sucrose nor aspartame had significant cognitive or behavioral effects on normal preschoolers or school-age children who were considered sugar-sensitive (24). We aimed to address the inconsistency over the potential impact of SSBs on the cognitive function of adolescents.

Therefore, in this study, we used data published by NHANES III (1988–1994) to examine the association between the consumption of SSBs and cognitive function among adolescents aged 12–16 years in the United States.

Methods

Study population

Our analysis was based on 1988–1994 cross-sectional data from the NHANES III database, a nationally representative survey regularly conducted by the US Centers for Disease Control and Prevention. A stratified multistage clustered probability design involving two 3-year phases was used to select a sample of the civilian noninstitutionalized US population at and above 2 months of age. Detailed descriptions for the survey are available elsewhere (25).

NHANES III included medical and cognitive examinations and interviews conducted with survey children and proxy respondents. The primary purpose of this study was to examine the relationship between SSB intake and cognitive function in adolescents. In the original study, cognitive examinations were administered to children and adolescents aged 6–16 years, and dietary intake frequency questionnaires were administered to adolescents aged 12–16 years, therefore, restricted our study population to those aged 12–16 years and had cognitive function test results and SSB consumption data (N = 1,825). After excluding 9 intellectually disabled and 7 children and adolescents who attended or needed special schools due to health conditions, 1,809 adolescents remained for the primary analysis.

Measurements and variable definitions

Cognitive function assessment

Cognitive function was evaluated using subcomponents of two tests, namely, the Wechsler Intelligence Scale for Children-Revised (WISC-R) and the Wide Range Achievement Test-Revised (WRAT-R). The Mobile Examination Center (MEC) interviewers were trained to conduct the WISC/WRAT examination. During annual site visits, test administration was evaluated, and retraining was performed where necessary. Two subcomponents of the WISC-R test, namely, a verbal component (Digit Span) and a performance exam (Block Design), were administered and are considered relatively culturally unbiased. In addition, two subcomponents of the WRAT-R test, namely, math and reading, were conducted. The WISC-R test was administered first and was followed by the WRAT-R. The scores for all four subcomponents used a common scale and were derived for each child relative to his/her age group based on test-specific standardization samples created by the test developers. This study used scaled scores, which were determined using calculations provided in the WISC-R Manual and WRAT-R Administration Manual (26, 27). The scaled score for the four tests allows comparison between the WRAT-R and WISC-R exams (25). Since the data distribution type is non-normal, bounded by 5th percentile scores, adolescents whose scores are lower than 5th percentile scores and higher than or equal to 5th percentile scores are divided into abnormal group and normal group, respectively (28).

Consumption of sugar-sweetened beverages

During the home interview, intakes of SSBs were determined from responses to the food-frequency questionnaire that was administered to participants to assess their usual consumption over the prior month (25). Food-frequency questionnaire assessment of dietary intake has been shown to be a valid and reliable method for assessing average dietary consumption (29–31). Flavored drink such as ginger ale and tonic water was considered SSBs, and mixed drink containing SSBs was also counted for, but carbonated drink without sugar (e.g., club soda or Seltzer) was not included (32). The frequency of SSB intake was converted according to 1 month = 4.3 weeks (values were unrounded) (25), we combined the quartile situation of the data distribution (3.8, 12.7, and 29.2 times/month are approximately equal to 1, 4, and 7 times/week) and the classification method of the other study (33), and the SSB classification for this study also used 1 and 4 as cutoff points. Finally, we selected three nodes (1, 4, and 7 times/week) as the dividing points to divide the SSBs into four groups with average weekly consumption frequency being: [0, 1), [1, 4), [4, 7), and [7, 182) times/week.

Assessment of covariates

Information about participant age, gender, race/ethnicity, family income, marital status and educational level of adult reference person [defined as one of the persons in the household who owned or rented the home (most often the parent)], physical activity, and dietary intake was collected using questionnaires. Race/ethnicity was categorized as non-Hispanic white, non-Hispanic black, Mexican-American, and other races/ethnicity. Family income was classified as the ratio of family income to the federal poverty level ($\leq$ 1.30, 1.31–3.50, and $>$ 3.50) (34). The education level of the family reference person was grouped as below high school, high school, and college or above. The marital status of the family reference person was grouped as married/living and as married or not. The adolescents were asked "How many times per week do you play or exercise enough to make you sweat or breathe hard?." According to the Surgeon General's Report on Physical Activity and Health (35), if adolescents reported participating in physical activity at least five times per week, these adolescents were classified as being physically active most days of the week. Based on the studies linking obesity to cognitive function (36), we examined whether the relationship between frequency of SSB consumption and cognitive function differed by sex, race/ethnicity, and BMI. BMI was calculated in kilogram per meter square and then converted to sex- and age-specific BMI percentile values using a computerized formula derived from the 2,000 Centers for Disease Control Growth Charts (37). We assigned each participant to an obesity BMI stratum ($\geq$95th percentile), an overweight BMI stratum (85th to 94th percentile), or a normal BMI stratum (<85th percentile). The grams of total carbohydrates include sugars and complex carbohydrates. The total carbohydrate figure is the difference between 100 and the sum of the protein, fat, ash, and water (25). According to the 2015–2020 Dietary Guidelines for Americans, the recommended carbohydrate intake for adolescents aged 12–16 years is 45%-65% kcal (38). Therefore, carbohydrate intake was categorized into three groups (< 45%, 45–65%, and > 65% kcal).

TABLE 1 Mean (continuous variables) and proportion (categorical variables) differences in cognitive function, socioeconomic status, and demographics of adolescents aged 12–16 years are presented by consumption of sugar-sweetened beverages (SSBs) in NANESIII, 1988–1994.

Characteristics[a]	Total	Frequency of intake of SSBs				χ^2/F	*P*-value
		[0, 1) times/week	[1, 4) times/week	[4, 7) times/week	[7, 182] times/week		
No. of participants (%)	1,809 (100)	492 (27.20)	669 (35.83)	419 (24.04)	229 (12.93)		
Age, y [mean (SE)]	13.99 (0.05)	13.84 (0.09)	13.89 (0.07)	14.03 (0.06)	14.50 (0.13)	13.88	<0.001
Sex, *N* (%)							
Male	846 (51.83)	198 (41.26)	332 (54.70)	211 (59.28)	105 (52.29)	13.66	0.01
Female	963 (48.17)	294 (58.74)	337 (45.30)	208 (40.70)	124 (47.71)		
Race/ethnicity, *N* (%)							
Non-Hispanic white	486 (67.74)	120 (62.86)	173 (65.73)	126 (71.65)	67 (76.27)	22.88	0.01
Non-Hispanic black	636 (14.48)	194 (16.16)	214 (14.01)	140 (12.86)	88 (15.28)		
Mexican-American	601 (7.92)	149 (7.93)	250 (9.23)	132 (6.87)	70 (6.22)		
Other	86 (9.86)	29 (13.06)	32 (11.02)	21 (8.62)	4 (2.23)		
Family reference person married/living as married, *N* (%)							
Yes	1,242 (74.81)	350 (75.77)	463 (73.55)	284 (77.27)	145 (71.74)	1.22	0.75
No	567 (25.19)	142 (24.23)	206 (26.45)	135 (22.73)	84 (28.26)		
Family reference person education level, *N* (%)							
Below high school	510 (15.84)	124 (15.52)	198 (12.63)	113 (17.94)	75 (21.50)	6.24	0.38
High school	815 (43.56)	229 (42.32)	293 (43.55)	193 (44.34)	100 (44.72)		
College or above	484 (40.61)	139 (42.16)	178 (43.82)	113 (37.73)	54 (33.78)		
Family income to poverty ratio, *N* (%)							
≤ 1.30	772 (27.33)	219 (31.72)	285 (25.79)	167 (23.33)	101 (29.79)	16.51	0.06
1.31–3.50	696 (46.39)	183 (42.96)	253 (43.52)	178 (54.20)	83 (47.05)		
> 3.50	194 (20.63)	57 (18.10)	76 (26.21)	36 (15.24)	25 (20.47)		
Missing	147 (5.66)	33 (7.23)	55 (4.48)	38 (7.23)	21 (2.68)		
Residence, *N* (%)							
Urban residence	835 (46.18)	240 (52.70)	302 (44.66)	205 (47.56)	88 (34.10)	6.25	0.10
Rural residence	974 (53.82)	252 (47.30)	367 (55.34)	214 (52.45)	141 (65.90)		
Physical activity[b], *N* (%)							
Yes	970 (58.09)	232 (52.92)	368 (61.53)	237 (59.02)	133 (57.72)	3.61	0.31
No	839 (41.91)	260 (47.08)	301 (38.47)	182 (40.98)	96 (42.28)		
BMI[c], kg/m^2, *N* (%)							
Normal or below	1,209 (70.49)	330 (70.77)	448 (69.67)	276 (69.63)	155 (73.80)	1.31	0.97
Overweight	333 (18.34)	92 (17.68)	117 (18.41)	77 (19.01)	47 (18.27)		
Obesity	267 (11.17)	70 (11.55)	104 (11.93)	66 (11.37)	27 (7.93)		
Carbohydrate intake, %kcal, *N* (%)							
<45	392 (17.24)	120 (21.13)	152 (16.67)	78 (15.49)	42 (13.86)	4.03	0.67
45–65	1,252 (70.30)	325 (65.72)	459 (72.19)	298 (73.03)	170 (69.62)		
>65	165 (12.46)	47 (13.15)	58 (11.14)	43 (11.48)	17 (16.52)		
WRAT-R							
Arithmetic, *N* (%)							
<5% percentile scores	107 (4.13)	37 (6.00)	33 (3.32)	24 (2.16)	13 (6.10)	4.07	0.25
≥5% percentile scores	1,702 (95.87)	455 (94.00)	636 (96.68)	395 (97.84)	216 (93.90)		
Reading, *N* (%)							
<5% percentile scores	122 (3.89)	37 (5.35)	40 (3.18)	27 (2.10)	18 (6.16)	5.00	0.17
≥5% percentile scores	1,687 (96.11)	455 (94.65)	629 (96.82)	392 (97.90)	211 (93.84)		

(Continued)

TABLE 1 Continued

Characteristics[a]	Total	Frequency of intake of SSBs [0, 1) times/week	[1, 4) times/week	[4, 7) times/week	[7, 182] times/week	χ^2/F	*P*-value
WISC-R							
Block design, *N* (%)							
<5% percentile scores	94 (3.18)	31 (3.91)	22 (1.88)	19 (2.52)	22 (6.47)	6.02	0.11
≥5% percentile scores	1,715 (96.82)	461 (96.09)	647 (98.12)	400 (97.48)	207 (93.53)		
Digit span, *N* (%)							
<5% percentile scores	94 (3.30)	35 (5.45)	28 (2.30)	18 (1.18)	13 (5.50)	8.35	0.04
≥5% percentile scores	1,715 (96.70)	457 (94.55)	641 (97.79)	401 (98.82)	216 (94.50)		

Data source: NHANES III, National Health Interview Survey III, 1988-1994.
[a]All means and SEs for continuous variables and percentages and SEs for categorical variables were weighted, with the exception of the number of participants. Since all numbers were rounded, percentages may not total 100%. Data are presented as weighted means and standard errors in parentheses for continuous variables and frequencies and weighted percentages in parentheses for categorical variables. BMI, body mass index; SE, standard error.
[b]The adolescents were classified as being physically active most days of the week if adolescents reported participating in physical activity at least five times per week.
[c]Overweight: 85th to less than the 95th percentile; obesity: equal to or greater than the 95th percentile.

Statistical methods

Following the NHANES III analytic guidelines (39), we applied sampling weights, strata, and primary sampling units in the analyses to account for the unequal probability of selection, oversampling of certain subpopulations, and non-response adjustment.

Means and proportions of baseline characteristics were compared using ANOVA for continuous variables and chi-square tests for categorical variables. We used binary logistic regression to estimate the association between the frequency of SSB consumption and four cognitive functions. Model 1 adjusted for adolescent sex and age, whereas model 2 additionally adjusted for sociodemographic and lifestyle characteristics. In a fully adjusted model, we adjusted for age, sex, race/ethnicity, education level and marital status of family reference person, household income level, physical activity, BMI, and carbohydrate intake. Furthermore, we performed a stratified analysis to examine whether this association differed by sex, ethnicity, and BMI.

All statistical analyses were conducted using the survey modules of SAS software, version 9.4 (SAS Institute). A 2-sided *P*-value < 0.05 was considered statistically significant.

Results

The characteristics of participants according to their frequency of SSB consumption are described in Table 1. The study population of 1,809 adolescents aged 12–16 years comprised 963 girls (weighted proportion, 48.17%) and 846 boys (weighted, 51.83%), with a weighted mean (SE) age of 13.99 (0.05) years; 486 participants (weighted, 67.74%) of non-Hispanic white, 636 (weighted, 14.48%) of non-Hispanic black, 601 (weighted, 7.92%) of Mexican-American, and 86 (weighted, 9.86%) of other race/ethnicity. Weighted mean (SE) scores for arithmetic, reading, block design, and digit span were 8.54 (0.17), 8.69 (0.16), 9.32 (0.12), and 8.56 (0.11), respectively (not shown in table). There were no differences between the four frequency classes of SSB consumption among those cognitive functions (arithmetic, reading, and block design) in regard to normal and abnormal scores. But, there was a difference in four levels of SSB intake among adolescents with normal and abnormal digit span scores (Table 1).

The odds ratios (ORs) of SSB consumption with cognitive function in adolescents are listed in Table 2. In the crude model, compared with adolescents who drank SSBs 0–1 times per week, those who drank 4–7 times per week had better scores in arithmetic, reading, and digit span tests, with OR values of 0.35 (95% CI = 0.14–0.86), 0.38 (95% CI = 0.20–0.71), and 0.21 (95% CI = 0.09, 0.49), respectively. In the final model (model 3) additionally adjusted for age, sex, race/ethnicity, family reference person education years and marital status, poverty-income ratio, residence, physical activity, BMI, and carbohydrate intake, the ORs and 95% CIs (arithmetic, reading, and digit span tests) were not substantially changed. The ORs of SSB consumption and block design scores were invalid, but the risk of abnormal block design scores increased with the frequency of SSB intake after adjustment for three models (the *P*-values for trend were 0.049, 0.04, and 0.02, respectively).

Stratified analyses showed that compared with normal or below BMI, among overweight or obese individuals, the frequency of SSB intake was a risk factor for abnormal digit span scores [(OR = 4.76, 95% CI = 1.19–18.96) vs. (OR = 0.35, 95% CI = 0.10, 1.25); *P* for interaction = 0.01]. The association did not significantly differ by sex or ethnicity (Table 3).

TABLE 2 Association of intake of SSBs with cognitive tests in adolescents aged 12–16 years in the United States: NHANES III, 1988–1994.

Scaled score	Frequency of intake of SSBs, OR (95%CI)				
	[0, 1) times/week	[1, 4) times/week	[4, 7) times/week	[7, 182] times/week	*P* for trend
Arithmetic					
Cases/Total	37/492	33/669	24/419	13/229	
Crude model	Reference	0.54 (0.30–0.95)*	0.35 (0.14–0.86)*	1.02 (0.29–3.55)	0.47
Model 1	Reference	0.53 (0.31–0.90)*	0.33 (0.15–0.76)*	0.97 (0.34–2.79)	0.45
Model 2	Reference	0.58 (0.30–1.11)	0.34 (0.14–0.80) *	1.02 (0.35–2.99)	0.42
Model 3	Reference	0.59 (0.31–1.10)	0.36 (0.16–0.82)*	1.05 (0.37–2.97)	0.41
Reading					
Cases/Total	37/492	40/669	27/419	18/229	
Crude model	Reference	0.58 (0.26–1.28)	0.38 (0.20–0.71) *	1.16 (0.42–3.24)	0.27
Model 1	Reference	0.57 (0.26–1.25)	0.36 (0.20–0.67) *	0.99 (0.33–2.93)	0.43
Model 2	Reference	0.63 (0.30–1.32)	0.34 (0.17–0.69) *	1.21 (0.39–3.80)	0.27
Model 3	Reference	0.64 (0.33–1.24)	0.35 (0.18–0.70) *	1.22 (0.42–3.60)	0.26
Block design					
Cases/Total	31/492	22/669	19/419	22/229	
Crude model	Reference	0.47 (0.19–1.18)	0.64 (0.25–1.60)	1.70 (0.56–5.21)	0.05
Model 1	Reference	0.55 (0.22–1.36)	0.82 (0.31–2.12)	2.08 (0.62–7.04)	0.05*
Model 2	Reference	0.62 (0.25–1.56)	0.90 (0.33–2.47)	2.45 (0.66–9.04)	0.04*
Model 3	Reference	0.66 (0.27–1.61)	0.96 (0.38–2.41)	2.82 (0.82–9.71)	0.02*
Digit span					
Cases/Total	35/492	28/669	18/419	13/229	
Crude model	Reference	0.41 (0.16–1.04)	0.21 (0.09–0.49)*	1.01 (0.44–2.31)	0.17
Model 1	Reference	0.39 (0.16–0.94)*	0.19 (0.08–0.44) *	0.88 (0.36–2.15)	0.30
Model 2	Reference	0.40 (0.16–1.02)	0.20 (0.09–0.46)*	0.85 (0.37–2.00)	0.28
Model 3	Reference	0.40 (0.16–1.01)	0.19 (0.08–0.44)*	0.82 (0.34–1.98)	0.32

*$P < 0.05$.
Model 1: adjusted for age and sex.
Model 2: Model 1 plus race/ethnicity, education level and marital status of family reference person, poverty–income ratio, residence, and physical activity.
Model 3: Model 2 plus body mass index and carbohydrate intake.

TABLE 3 Stratified analysis of the association of intake of SSBs with cognitive tests in adolescents aged 12–16 years in the United States: NHANES III, 1988–1994.

Scaled score	Frequency of intake of SSBs, OR (95%CI)					
	[0, 1) times/week	[1, 4) times/week	[4, 7) times/week	[7, 182] times/week	*P* for trend	*P* for Interaction
Arithmetic						
Cases/Total	37/492	33/669	24/419	13/229		
Sex						
Male	Reference	1.89 (0.57–6.22)	0.60 (0.21–1.75)	2.91 (0.67–12.67)	0.23	0.11
Female	Reference	0.24 (0.06–0.94)*	0.28 (0.07–1.12)	0.38 (0.08–1.73)	0.58	
Race/ethnicity						
Non-Hispanic white/Other	Reference	0.66 (0.22–1.96)	0.17 (0.03–0.89)*	1.25 (0.31–4.97)	0.30	0.96
Non-Hispanic black	Reference	0.34 (0.12–0.95)*	0.72 (0.35–1.48)	0.42 (0.18–0.98)*	0.27	
Mexican-American	Reference	1.23 (0.58–2.61)	0.97 (0.23–4.05)	0.65 (0.10–4.28)	0.48	
BMI						
Normal or below	Reference	0.69 (0.27–1.77)	0.25 (0.09–0.71) *	1.18 (0.42–3.35)	0.31	0.59
Overweight or obesity	Reference	0.34 (0.09–1.30)	0.44 (0.12–1.67)	0.79 (0.10–6.43)	0.77	
Reading						
Cases/Total	37/492	40/669	27/419	18/229		
Sex						
Male	Reference	0.88 (0.33–2.30)	0.63 (0.18–2.20)	1.71 (0.32–9.26)	0.28	0.88
Female	Reference	0.48 (0.17–1.31)	0.16 (0.04–0.62) *	1.33 (0.29–6.25)	0.30	
Race/ethnicity						
Non-Hispanic white/Other	Reference	1.10 (0.38–3.17)	0.10 (0.02–0.58)	0.96 (0.21–4.37)	0.64	0.97
Non-Hispanic black	Reference	0.43 (0.11–1.64)	0.98 (0.37–2.60)	1.32 (0.40–4.36)	0.21	
Mexican-American	Reference	0.63 (0.29–1.35)	0.66 (0.24–1.81)	0.72 (0.18–2.84)	0.92	
BMI						
Normal or below	Reference	0.84 (0.36–1.92)	0.42 (0.18–0.98) *	1.80 (0.51–6.38)	0.17	0.27
Overweight or obesity	Reference	0.23 (0.08–0.66) *	0.17 (0.03–0.80) *	1.01 (0.14–7.17)	0.47	
Block design						
Cases/Total	31/492	22/669	19/419	22/229		
Sex						
Male	Reference	1.34 (0.21–8.68)	0.96 (0.22–4.19)	4.41 (0.72–27.03)	0.04*	0.97

(Continued)

TABLE 3 Continued

Scaled score	Frequency of intake of SSBs, OR (95%CI)					
	[0, 1) times/week	[1, 4) times/week	[4, 7) times/week	[7, 182] times/week	*P* for trend	*P* for Interaction
Female	Reference	0.54 (0.20–1.44)	1.00 (0.36–2.79)	2.98 (0.66–13.45)	0.05	
Race/ethnicity						
Non-Hispanic white/Other	Reference	0.80 (0.18–3.57)	1.56 (0.33–7.28)	5.98 (0.81–44.08)	0.02*	0.65
Non-Hispanic black	Reference	0.47 (0.17–1.27)	0.32 (0.11–0.94)*	0.91 (0.39–2.12)	0.22	
Mexican-American	Reference	0.85 (0.24–3.04)	1.25 (0.20–7.88)	1.38 (0.23–8.30)	0.53	
BMI						
Normal or below	Reference	0.67 (0.22–2.03)	0.69 (0.16–2.97)	2.37 (0.38–14.68)	0.16	0.89
Overweight or obesity	Reference	0.48 (0.11–2.02)	1.11 (0.24–5.12)	4.47 (0.67–29.86)	0.02*	
Digit span						
Cases/Total	35/492	28/669	18/419	13/229		
Sex						
Male	Reference	0.47 (0.16–1.41)	0.23 (0.07–0.71) *	1.02 (0.30–3.45)	0.20	0.66
Female	Reference	0.34 (0.11–1.04)	0.13 (0.04–0.45) *	1.01 (0.23–4.33)	0.48	
Race/ethnicity						
Non-Hispanic white/Other	Reference	0.33 (0.08–1.46)	–**	0.78 (0.21–2.87)	0.28	0.20
Non-Hispanic black	Reference	0.57 (0.21–1.51)	0.35 (0.10–1.24)	0.22 (0.03–1.67)	0.25	
Mexican-American	Reference	0.48 (0.17–1.37)	1.40 (0.61–3.25)	0.69 (0.25–1.88)	0.87	
BMI						
Normal or below	Reference	0.37 (0.14–1.04)	0.09 (0.03–0.32) *	0.35 (0.10–1.25)	0.74	0.01*
Overweight or obesity	Reference	0.24 (0.07–0.85)*	0.52 (0.22–1.23)	4.76 (1.19–18.96)*	0.01*	

*$P < 0.05$.
All sample sizes have been adjusted for weight. Stratified variables were not included in the model.
**The case of anomalous digit span scores is 0.

Discussion

To the best of our knowledge, this is the first study examining the association of SSB intake with the subset score of WISC-R and WRAT. Based on a nationally representative population sample of the United States, we observed no significant association between the frequency of SSB intake and the scores of arithmetic, reading, and digit span at the overall level in adolescents. However, consuming SSBs 4–7 times per week was positively associated with arithmetic, reading, and digit span scores, with increasing frequency of SSB consumption, the risk of anomalous block design scores increased (*P* for trend = 0.02), and even after full adjustment, the association remained significant.

Although our findings were not in line with the hypothesis, these findings had some support from existing research. First, SSB consumption was found to be associated with improved cognitive function in the low and moderate intake groups but was negatively associated with higher intake levels. The Dietary Guidelines Advisory Committee in the United States have published a review in 2020 highlighting the harmful effects of high-level SSBs, by 2020, but the effect of low or moderate levels of SSB intake on health is yet to be determined (40). It has also been reported numerous times that there was no association between SSB consumption and cognitive function in children and adolescents (23, 24, 41, 42). For instance, the zero impact of sugar intake has been reported in lab-based laboratory studies of "sugar-responsive" children (41). Besides, a review by Benton concluded that there was no evidence of any negative effects of sugar on behavior (42).

The positive associations between lower consumption of SSBs and cognitive function observed in this study may be attributed to brain energy metabolism. The brain is metabolically demanding, and the weight of it only counts for 2% of total body weight but requires 20% of total energy intake due to its complex structure and processing needs (43). The preferred source of energy in the brain is glucose (44). The dynamic utilization of glucose by the cerebral cortex over the course of development suggests that the relative apportionment of glucose must also be dynamic (45), and since the glucose cannot be stored in the brain, at the right level of sugar intake, SSBs may raise the blood sugar level in the brain and boost brain metabolism, leading to higher cognitive scores (46). The result of a systematic review and meta-analysis of interventional studies also revealed modest beneficial effects of glucose on cognition, particularly recognition memory and attention processes (47).

Point estimates showed a negative relationship in the high SSB intake groups, although the ORs did not reach a statistically significant level. This suggests that excessive consumption of SSBs may damage cognitive function, and most studies have pointed out that excessive consumption of SSBs was related to neurological decline (21, 22, 48). A study has reported that consumption of sugary beverages in early childhood is negatively associated with KBIT-II language scores in middle childhood [−2.4 points per serving/day, 95% CI (−4.3, −0.5)] (48). Notably, in our study, it was found that block design scores reflecting short-term memory and attentional function decreased with increasing consumption of SSBs, showing a significant dose-response relationship, which may be related to SSBs affecting memory-related brain regions. Studies in animal models have shown that deleterious effects of long-term sugar intake on memory deficits and hippocampal neurogenesis (49), 2 months of an HFS (high-fat, refined sugar) diet, were sufficient to reduce hippocampal levels of BDNF and spatial learning performance (50), and excessive consumption of added sugars, especially HFCS-55, during the adolescent period of development, negatively affect hippocampal function, metabolic outcomes, and neuroinflammation (19). In addition, Jacobson et al. found an independent association between cognitive changes and time-weighted HbA_{1c} in diabetic people, which they believed may reflect the deleterious effects of high brain glucose levels on neuronal integrity (51). Glucose metabolism increased the glutamate-glutamine cycle (52); therefore, higher cerebral blood glucose may lead to increased prefrontal Glx (an excitatory neurotransmitter that causes neuronal damage at high concentrations) concentrations (53), which was associated with reduced cognitive performance (54). This might explain the increased risk of abnormal block design scores with consumption of SSBs as observed in our study.

The relationship between sugar intake and cognitive function in adolescents is not well understood to date. Existing literature had inconsistent and unclear cutoff values for SSB consumption and failed to reveal the true association between SSBs and cognitive function, and this should be addressed in further studies along with investigation regarding the potential underlying mechanism.

This study has some strengths. To the best of our knowledge, this is the first report of an association of SSB intake with cognitive function in adolescents. In addition, the NHAENS is a nationally representative survey that provides reliable data to explore this association. There are also several limitations to be noted. First, this is a cross-sectional observational study, and we cannot infer the causal relationship between SSB consumption and cognitive function of adolescents. Second, the consumption of SSBs was assessed on a frequency basis, making it impossible to determine specific intake volume, which may affect the correlation of outcomes. Finally, the use of self-reported FFQ to obtain dietary intake data may be subject to recall bias, thus introducing errors into our estimation model.

Conclusion

In this study, no association was found between the frequency of consumption of SSBs and arithmetic, reading, and digit span at the overall level in adolescents. The positive associations of SSBs at moderate level intake with better scores in arithmetic, reading, and digit span, but with increasing frequency of SSB consumption, the risk of anomalous block design scores increased among US adolescents. Further investigation is warranted to confirm the association and mechanism between SSBs and cognitive function among adolescents.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found at: https://www.cdc.gov/nchs/nhanes/index.htm.

Ethics statement

The studies involving human participants were reviewed and approved by the National Center for Health Statistics Research Ethics Review Board. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

WY has full access to all the data in this study and assumes responsibility for study supervision. WY and QC conceptualized and designed the study, collected and analyzed data, carried out the initial analyses, and reviewed and revised the manuscript. XY, YX, and JZ acquired, analyzed, interpreted the data, and drafted the initial manuscript. All authors critically revised manuscripts of significant intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Association of sugar-sweetened beverages with executive function in autistic children

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The association between sugar-sweetened beverages (SSBs) consumption and executive function (EF) among typically developing (TD) children has been investigated in previous studies but with inconsistent results. Furthermore, this relationship has been less investigated among autistic children who perform worse in EF compared with TD children. In this study, we aimed to investigate the association between SSB consumption and EF in autistic children, and whether the association between SSB and EF in autistic children is different from that in TD children. We recruited 106 autistic children and 207 TD children aged 6–12 years in Guangzhou, China. Children's EF was assessed by using the Chinese version of parent-reported Behavior Rating Inventory of Executive Function, Stroop Color–Word Test, and working memory subscales of the Chinese version of Wechsler Intelligence Scale for children, Fourth edition. Meanwhile, we assessed children's dietary intake and SSB consumption with a validated Food Frequency Questionnaire. In this study, 70 (66.0%) autistic children consumed SSB and 20 (18.9%) of them consumed more than two servings SSB a week. Among autistic children, over two servings per week SSB consumption was associated with poorer performance in emotional control [$\beta = 7.20$, 95% confidence interval (CI): 0.94–13.46] and plan/Organize ($\beta = 6.45$, 95% CI: 0.27–12.63). The association between over two servings/week SSB consumption and emotional control among autistic children was significantly different from that among TD children ($\beta_{ASD} = 7.20$; $\beta_{TD} = -3.09$, $Z = 2.72$, $p = 0.006$). Results of this study show that SSB consumption was associated with an impairment in some subscales of EF in autistic children. Furthermore, the association between SSB and EF in autistic children might be different from that in TD children.

KEYWORDS

sugar-sweetened beverage, children, autism spectrum disorder, executive function, cross-sectional study

Introduction

Consumption of sugar-sweetened beverages (SSBs) among children remains at a high level, especially in low- and middle-income countries, including China (1–3). SSBs such as carbonated beverages and sugar-sweetened fruit juice beverages, were suggested to have an association with an increased risk of children's physical health problems, including dental caries, obesity(s) and other metabolic diseases (4, 5). Some previous studies suggested that SSB consumption was linked with mental problems, such as impaired cognitive function (6, 7), executive function (EF) (8), as well as behavioral problems, including hyperactivity problems and emotional symptoms (9, 10).

Executive function is an umbrella term for functions that include two dimensions and associate with a child's cognitive functioning, behavior, emotional control, and social interaction (11). Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental disorder with impaired social communication and interaction, repetitive behaviors, and varying levels of intellectual disability (12). Compared with typically developing (TD) children, children with ASD performed significantly worse in EF (13–16). Although EF impairment commonly exists in autistic children, high-order EF will have sustainable development and is sensitive to environmental factors [e.g., nutrition (17), air pollution (18), lifestyle (19, 20), and socioeconomic status (21)] during school age. Therefore, it is of significance to improve EF or reduce impairment of EF in autistic children by controlling some environmental factors, especially the highly modifiable dietary factors including SSB.

Studies in healthy animals have shown that fructose consumption could adversely influence synaptic plasticity and cognition (22–28). In population studies, previous reports have investigated the association of SSB consumption with EF among school-aged TD children, but with inconsistent findings. Some studies indicated that SSB had an inverse relationship with all the indexes of EF (8, 9, 29–32), but a few of them indicated that SSB had no relationship with some of the indexes or could be beneficial for children's cognition EF (29, 33, 34). Inconsistencies in the findings could be partly explained by difference in assessments of EF, ethnicity, and economic development levels.

Although previous studies indicated that SSB consumption was inversely related with EF in school-aged TD children, few studies investigated the relationship of SSB with EF in autistic children (35, 36). Furthermore, several studies suggested that autistic children had a high preference for energy-dense foods, leading to a high consumption of sugar, juice, and sweetened beverages (37–41). Since the food preference and EF of autistic children was different from TD children, it is reasonable to hypothesize that the association between SSB and EF in autistic children may be different from that in TD children. Therefore, we aimed to investigate (1) the association between SSB consumption and EF of autistic children; and (2) whether the association between SSB and EF in autistic children is different from that in TD children.

Materials and methods

Study design and participants

In this cross-sectional study, a total of 107 autistic children and 209 TD children aged 6–12 years were recruited from a study entitled "the Guangzhou Longitudinal Study of Children with ASD" in Guangzhou, China. The autistic children had to have a historical diagnosis of ASD, autism, or Asperger's syndrome and be confirmed by two professional child psychiatrists (Xiuhong Li and Jin Jing) according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Revision (DSM-5) criteria.

Both groups conformed to the additional inclusion criteria as follows: (1) chronological age between 6 years 0 month and 12 years 11 months 30 days; (2) voluntarily participation of the children's parents; (3) without known genetic or chromosomal abnormalities or severe visual or hearing impairment; and (4) without any other medical diagnosis of neuropsychiatric disorders such as ADHD, seizures, Tourette syndrome, head trauma, cerebral palsy, or other movement disorders that would interfere with study assessment.

In the current study, one autistic child had missed data from subscales score of the Behavior Rating Inventory of Executive Function (BRIEF) and two TD children had an Intelligence Quotient (IQ) below 70. They were not included in any of the analysis. A subsample of 106 autistic children (89 boys and 17 girls) and 207 TD children (113 boys and 94 girls) were included for final analysis. All 313 participants took part in the Stroop Color–Word Test (SCWT). Because of its presupposition of literacy, only 76 autistic children and 173 TD children finished SCWT. At the research center, 99 autistic children and 207 TD children finishing the IQ test. They had complete scores of four index scores and a full score of IQ (the flowchart was in **Supplementary Figure 1**).

Procedure

Children underwent face-to-face measures performed by well-trained psychologists and research assistants at the research center. All the parents of the participants were provided with written consent. This study was approved by the Ethical Review Committee for Biomedical Research at Sun Yat-sen University (2015-No.29).

Measures

Assessment of executive function

We evaluated EF of children *via* parent-reported questionnaire and behavioral experiment.

Behavior Rating Inventory of Executive Function

Behavior Rating Inventory of Executive Function is a parent-reported questionnaire for parents of children aged 6–18 years. Parents were asked to rate the 86 items by evaluating how often the problem bothered their child in the past 6 months. The 86 items are rated into three ranks, which are "never," "sometimes," and "often," corresponding to the scores "1," "2," and "3," respectively. The BRIEF comprises three composite indexes (i.e., behavioral regulation index, BRI; metacognition index, MI; and global executive composite, GEC). The BRI reflects the ability to shift cognitive set and modulate emotions and behaviors *via* appropriate inhibitory control, containing three subscales (i.e., inhibit, shift, and emotional control). The MI reflects the ability to initiate, plan, organize, and sustain future oriented problem-solving in working memory, containing initiate, working memory, plan/organize, organization, and monitor subscales. The GEC represents a sum of all the eight subscale scores. The BRI, MI, and GEC were converted into T-scores (mean = 50, standard deviation = 10) and standardized by gender and age. Higher scores indicate greater impairment in EF. Among the school-aged children in China, the subscales and total scores have good internal consistency (0.74–0.96), except for the initial subscale (0.61), and good test-retest reliability (0.68–0.89) (42).

Stroop Color–Word Test

The SCWT is a widely used neuropsychological measure that can assess inhibitory control (43). Due to its presupposition of literacy, the test is limited to school-aged children. In the current study, this test consists of three subtasks, namely, reading names of colors serially, naming the colors, and naming the color of ink instead of the words. Each subtask contains 10 trials, and each trail presents one kind of color or a color word. The E-Prime 2.0 on computer was used to run the task and record the response. The participants were asked to respond by pressing buttons on the keyboard as quickly and accurately as possible. The average reaction times (RTs) of all the correct answers would replace the RT of all the wrong answers. Stroop interference (SI) is the difference in RTs between naming the color and naming the color of the ink instead of the words. We recorded the correct rate of Stroop and SI to assess the participants' performance on SCWT.

Working Memory Index

We also used Working Memory Index (WMI) in the Chinese version of Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) to assess children's EF (44). WISC-IV has an internal consistency ranging from 0.98 to 0.99 and test-retest reliability ranging from 0.71 to 0.86. The WMI is made up of Digit Span (DS) and Letter-Number Sequencing (LNS) subtests. DS includes Digit Span Forward (DSF) and Digit Span Backward (DSB), and scoring combines the total number of correctly repeated digit strings. The LNS subtests require children to repeat the sequence of letters and numbers provided randomly in a predetermined order. An arithmetic subtest may be used as a replacement if a participant cannot finish one of the two aforementioned subtests. In this subtest, children are required to answer verbally presented arithmetic problems. A higher score of WMI indicates greater working memory ability.

Dietary intake and sugar-sweetened beverage consumption

Dietary intake was assessed by using a validated Food Frequency Questionnaire (FFQ) (45). Parents of children were required to report the frequency and amount of food their children consumed during the past 7 days. The list of foods included cereals, vegetables, fruits, dairy foods, soybeans, red meat and products, poultry and game, fish and shrimp, nuts, eggs, salt, SSBs, cooking oil, and water. To assist the interview, we provided food photographs with standard portion sizes.

For SSB consumption, parents were asked to answer the questions "During the past seven days, how many times had your child drunk SSB (e.g., Coca-Cola, Sprite, orange juice, etc.)?" and "How many glasses (250 milliliters per glass) of SSB had your child consumed on average each time?" In this study, we used the term "servings" to describe the intake of SSB, and 250 ml of SSB was defined as one serving. We also classified the SSB servings per week into three categories as "0 servings/week, >0–2 servings/week, and >2 servings/week."

Assessment of covariates

Social demography factors

Demographic information such as children's gender, age, maternal and paternal education level, and per capita monthly household income was obtained *via* questionnaires.

Physical activity and sedentary time

Physical activity (PA) and sedentary time (ST) during the past 7 days were assessed *via* the International Physical Activity Questionnaire Short Form (IPAQ-SF). Parents were required to report the weekly frequency and duration of vigorous-intensity activities (VPA), moderate activities (MPA), and walking. ST includes after-school homework time and screen time of the participants (including watching television and taking online courses). Three levels of PA were classified as "HEPA active," "Minimally active," and "Inactive" according to the criteria based on different energy requirements of activities (46). We also classified the screen time per day into two categories as "<2 hours/day" and "≥2 hours/day."

Anthropometric measurements

Anthropometric measurements were taken according to the standard protocol of the National Standard Test Method for Students' Physical Health. The body mass index (BMI) of each participant was calculated as weight (kg) divided by height squared (m^2). According to the Chinese Standards, we classified the BMI of the children into four categories, namely, underweight, healthy weight, overweight, and obese (47, 48).

Statistical analyses

Means and standard deviations were calculated to describe continuous variables and percentages to describe categorical variables. We compared demographic information between children with ASD and TD children using *t*-tests and Chi-square tests.

We used generalized linear models to investigate the associations of EF and SSB consumption. Crude models were fitted without any adjustments. Adjusted model 1 was fitted by adjusting the child's age, gender, maternal and paternal education level, and per capita monthly household. Adjusted model 2 was fitted by further adjusting screen-exposure time, category of PA, category of BMI, and water intake. Adjusted model 3 further adjusted the category of IQ (<70 and ≥70). To investigate whether the association between SSB and EF of autistic children is different from that of TD children, we further implemented a test for coefficient estimate (β), based on the point estimate and standard error (SE):

$$Z = \frac{\beta_{ASD} - \beta_{TD}}{\sqrt{se(\beta_{ASD})^2 + se(\beta_{ASD})^2}}$$

All statistical analysis was conducted with the R 4.1.3 statistical software (R Core Team) (49). Coefficient estimate (β) with a 95% confidence interval (CI) were presented as the results. A two-sided *p*-value < 0.05 was considered statistically significant.

Results

Characteristics of autistic children and typically developing children

A total of 106 autistic children and 207 TD children aged 6–10 years participated in the investigation (Table 1).

TABLE 1 Demographic characteristics of children with ASD and TD children.

	ASD (N = 106) N (%)/mean (SD)	TD (N = 207) N (%)/mean (SD)	*P-value*
Age (years)	7.7 (1.3)	7.8 (1.3)	0.854
Gender			<0.001***
Boys	89 (84.0)	113 (54.6)	
Girls	17 (16.0)	94 (45.4)	
BMI	16.6 (2.6)	15.8 (2.4)	0.007**
BMI category			0.060
Underweight	10 (9.4)	26 (12.6)	
Healthy weight	68 (64.2)	149 (71.9)	
Overweight	12 (11.3)	19 (9.2)	
Obese	16 (15.1)	13 (6.3)	
Physical activity category			0.009**
Inactive	11 (10.4)	7 (3.4)	
Minimally active	46 (43.4)	75 (36.2)	
HEPA active	49 (46.2)	125 (60.4)	
Maternal education			0.002**
High school degree or less	44 (41.5)	52 (24.9)	
Bachelor's degree or above	62 (58.5)	157 (75.1)	
Paternal education			0.730
High school degree or less	40 (37.7)	74 (35.7)	
Bachelor's degree or above	66 (62.3)	133 (64.3)	
Per capita monthly household income			<0.001***
<¥8000	61 (57.5)	52 (25.1)	
≥¥8000	45 (42.5)	155 (74.9)	

ASD, autism spectrum disorder; TD, typically developing; SD, standard deviation; BMI, body mass index.
$^{**}p < 0.01$; $^{***}p < 0.001$.

Among autistic children, the majority of children (84.0%) were boys. Among TD children, approximately half of the children were boys (54.6%).

Autistic children had a significantly higher average BMI (16.6 ± 2.6 vs. 15.8 ± 2.4; $p < 0.01$) compared with TD children. Autistic children showed higher rates of obesity (15.1 vs. 6.3%) and lower rates of healthy weight (64.2 vs. 71.9%). The PA category also had a significant difference between children with ASD and TD children (inactive: 10.4 vs. 3.4%; minimally active: 43.4 vs. 36.2%; HEPA active: 46.2 vs. 60.4%; $p < 0.01$). Lower maternal education level and lower monthly household income (both $p < 0.01$) were noted in children with ASD.

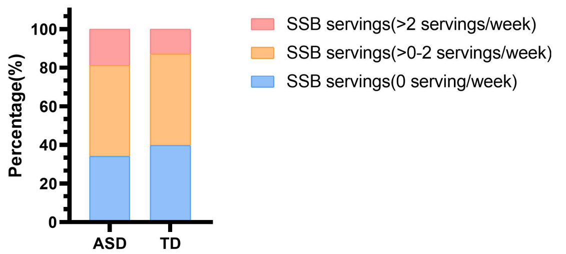

FIGURE 1
Sugar-sweetened beverage consumption in children with ASD and TD children. SSB, sugar-sweetened beverage; ASD, autism spectrum disorder; TD, typically developing.

Comparison of sugar-sweetened beverage in children with autism spectrum disorder and typically developing children

The mean (SD) of servings of SSB consumption per week was 1.3 (1.6) among autistic children and 1.2 (1.7) among TD children. A total of 20 (18.9%) autistic children and 26 (12.6%) TD children reported consuming no less than two servings of SSB per week. Thirty-six (34.0%) autistic children and 83 (40.1%) TD children reported consuming 0 servings of SSB per week (Figure 1). However, there was no statistically significant difference between the SSB consumption of autistic children and TD children (Supplementary Table 1).

Executive function of autistic children and typically developing children

The scores of BRIEF in autistic children and TD children are shown in Figure 2. In parent-report BRIEF, the mean (SD) score of GEC in autistic children was 66.3 (9.2), while that in TD children was 53.9 (8.6). Besides, the mean (SD) of BRI and MI in autistic children was 60.8 (10.5) and 67.9 (9.1), while that in TD children was 48.6 (7.8) and 56.8 (9.3), respectively. In behavioral experiment, the mean (SD) of correct rate of Stroop was 0.9 (0.1) in both the groups. And the mean (SD) of SI and WMI in autistic children was 401.1 (464.3) and 90.1 (18.8), while that in TD children was 407.9 (384.1) and 104.6 (12.5), respectively.

Association between sugar-sweetened beverage consumption and executive function in autistic children

The association between SSB consumption and EF in autistic children is summarized in Tables 2, 3 and Supplementary Table 2. In model 3, autistic children who consumed more than two servings of SSB per week were associated with significantly higher scores of emotional control (β = 7.20, 95% CI: 0.94 to 13.46, $p = 0.024$) and plan/organize (β = 6.45, 95% CI: 0.27 to 12.63, $p = 0.041$), compared with those who consumed none. The results indicated that autistic children who have more than two servings of SSB per week might have worse performance in emotional control and plan/organize than those who did not drink SSB. There was no significant association between SSB consumption and EF among TD children (Tables 2, 3 and Supplementary Table 3).

Comparison of the correlation between sugar-sweetened beverage consumption and executive function in two groups

We further investigated the difference between the correlation (β) between SSB and EF in the two groups (Tables 2, 3). The relationship between >2 servings/week SSB consumption and emotional control in autistic children significantly differed from that in TD children ($Z = 2.72$, $p = 0.006$). And the correlation between >2 servings/week SSB consumption and BRI was significantly different from that in TD children ($Z = 2.58$, $p = 0.010$). Besides, the correlation between SSB consumption and other subscales of BRIEF in autistic children, as well as the correlation between SSB consumption and their behavioral experiment results had no significant difference compared with that in TD children.

Discussion

In the current study, about two-thirds of autistic children consumed SSB. About one in five autistic children consumed an average of two servings of SSB per week. Higher SSB consumption was associated with worse performance on the BRIEF subscale of emotional control and plan/organize in autistic children. In addition, we observed that the relationship between >2 servings/week SSB consumption and EF in autistic children was different from that in TD children. However, we did not find significant associations of SSB consumption with inhibition-control ability measured by the SCWT and WMI measured by WISC-IV test.

Some of our findings were consistent with previous studies among TD children. Most of the previous studies investigated the association between consumption of SSB and EF in TD children (6–8, 29). A randomized, cross-over study of 29 school-aged children assessed children's EF by using a selection of tests from the Cognitive Drug Research (CDR) computerized assessment system (29). This study reported that the glucose drink was associated with great declines in attention and episodic secondary memory but had no association with

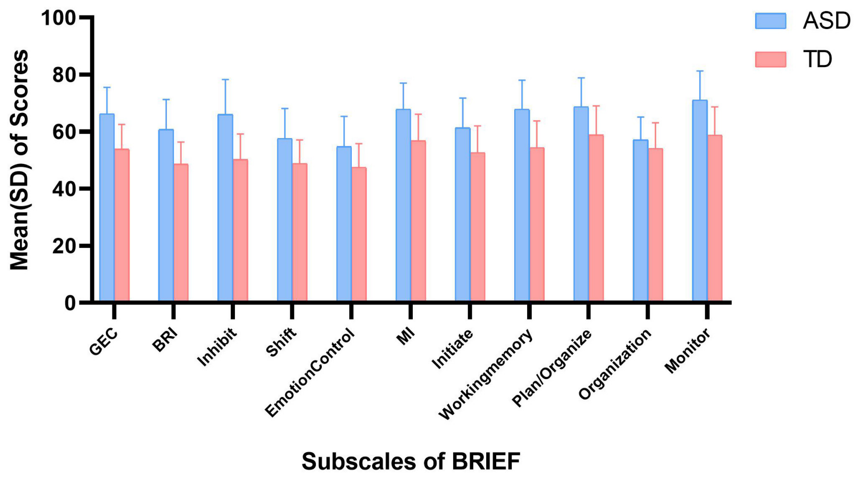

FIGURE 2
Scores of BRIEF in ASD and TD children. ASD, autism spectrum disorder; TD, typically developing; SD, standard deviation; GEC, global executive component; BRI, behavioral regulation index; MI, metacognition index.

working memory. In a cross-sectional analysis of over 6,000 children in Guangzhou, higher SSB consumption was associated with poorer performance in all the subscales and composite scores of parent-reported BRIEF (8). In addition, a cohort study of 1,234 children in the United States used Kaufman Brief Intelligence Test (KBIT-II) to assess verbal and non-verbal global intelligence and the Wide Range Assessment of Memory and Learning for visual memory (7). The results revealed that additional SSB consumption in early childhood was associated with poorer verbal intelligence at mid-childhood. These studies all indicated that SSB consumption had an association with impairment of EF in children. The findings may vary in the indexes or strength of the association due to different assessment of EF, adjusted covariates, study population, and methods in quantifying SSB consumption.

Although the previous studies indicated that SSB consumption was inversely related with EF in school-aged TD children, few studies investigated the relationship of SSB with EF in autistic children. In our study, we focused on autistic children in China. We assessed children's EF with the SCWT, WMI of WISC-IV, and the Chinese version of the parent-reported BRIEF. Besides social demography and economic factors, we also adjusted for the screen time category, water intake, and IQ category, which had a relationship with children's EF or SSB consumption (50–52). After adjustment for the covariates, our findings showed that having more than two servings of SSB per week was associated with increasing scores of emotional control and plan/organize in autistic children. Emotional control subscale describes children's ability to modulate emotional responses appropriately. Plan/organize subscale describes the ability to anticipate future events, set goals, and understand and communicate key concepts. This finding indicated that in autistic children, a higher level of SSB consumption might have an inverse association with performance on appropriately modulating emotional responses and anticipating future events. Findings of our study add to the literature on the adverse associations of SSB consumption and EF in autistic children. More studies from different regions are needed to confirm this relationship in this population. In addition, the association between emotional control and SSB consumption in autistic children was significantly different from that in TD children. Some previous studies indicated that sensory sensitivity was commonly found in autistic population (12, 53). This kind of sensory sensitivity was associated with autistic person's intolerance of uncertainty and subsequent anxiety (53). In this study, autistic children might be more sensitive to a higher level of SSB consumption and performed worse in emotional control and BRI. The BRI also reflects the ability to modulate emotions. This finding indicated that autistic children's emotional control ability might be more susceptible to high SSB consumption than that of TD children.

According to previous studies, the biological mechanism underlying the relationship between SSB consumption and EF is plausible. Most of these studies proposed that a high level of sucrose or fructose would increase inflammation and oxidative stress and decrease neurotrophins, which may be one of the pathways to explain the relationship. Animal evidence from general rat models indicated that 4 weeks of sucrose–fructose drinks feeding would induce increased expression of pro-inflammatory mediator genes such as IL-1β and IL-6 (22, 28). In the hypothalamus of sucrose–fructose fed rats, Toll-like receptor 4 (TLR4) as well as nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) have higher levels than the control group. As for autism, many studies indicated that levels of brain cytokines, including IL-6 and

TABLE 2 Association between SSB consumption and scores of BRIEF among the two groups, and the comparison between the coefficient estimate (β) of the two groups.

	Coefficient estimate (β, adjust model 3[α])				Z^{δ}	p^{ε}
	ASD		TD			
	β_{ASD} (95% CI)	p^{β}	β_{TD} (95% CI)	p^{γ}		
Inhibit						
0 serving/week	Reference		Reference			
>0–2 servings/week	−0.53 (−6.34, 5.27)	0.857	−0.71 (−3.41, 1.98)	0.604	0.06	0.956
>2 servings/week	3.83 (−2.58, 11.24)	0.311	−3.37 (−7.63, 0.89)	0.121	1.65	0.099
Shift						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.46 (−4.55, 5.46)	0.858	−1.32 (−3.79, 1.15)	0.295	0.62	0.533
>2 servings/week	4.43 (−1.97, 10.82)	0.175	−2.83 (−6.74, 1.07)	0.155	1.90	0.057
Emotional control						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.91 (−3.99, 5.82)	0.715	−1.00 (−3.49, 1.49)	0.431	0.68	0.496
>2 servings/week	7.20 (0.94, 13.46)	0.024*	−3.09 (−7.03, 0.84)	0.123	2.72	0.006**
Initiate						
0 serving/week	Reference		Reference			
>0–2 servings/week	−0.28 (−5.33, 4.78)	0.915	−0.00 (−2.85, 2.85)	0.999	−0.71	0.480
>2 servings/week	−0.27 (−6.72, 6.18)	0.935	3.04 (−1.46, 7.54)	0.185	−1.16	0.245
Working memory						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.03 (−4.53, 4.58)	0.991	0.90 (−1.83, 3.62)	0.520	−0.32	0.748
>2 servings/week	3.62 (−2.19, 9.44)	0.222	−0.41 (−4.71, 3.89)	0.852	1.09	0.276
Plan/organize						
0 serving/week	Reference		Reference			
>0–2 servings/week	1.46 (−3.37, 6.30)	0.553	1.19 (−1.77, 4.16)	0.431	0.09	0.926
>2 servings/week	6.45 (0.27, 12.63)	0.041*	2.37 (−2.31, 7.06)	0.321	1.03	0.302
Organization						
0 serving/week	Reference		Reference			
>0–2 servings/week	−1.25 (−5.15, 2.65)	0.530	1.05 (−1.68, 3.77)	0.452	−0.95	0.343
>2 servings/week	0.88 (−4.10, 5.87)	0.728	−0.09 (−4.39, 4.21)	0.967	0.29	0.772
Monitor						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.77 (−4.25, 5.79)	0.764	−0.73 (−3.66, 2.21)	0.628	0.51	0.613
>2 servings/week	2.56 (−3.85, 8.97)	0.434	−2.92 (−7.55, 1.71)	0.216	1.35	0.174
BRI						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.28 (−4.63, 5.19)	0.911	−1.00 (−3.34, 1.34)	0.401	0.46	0.644
>2 servings/week	6.04 (−0.22, 12.31)	0.059	−3.53 (−7.22, 0.16)	0.061	2.58	0.010*
MI						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.25 (−4.12, 4.61)	0.912	0.63 (−2.13, 3.40)	0.653	−0.14	0.885
>2 servings/week	3.50 (−2.06, 9.07)	0.218	0.64 (−3.73, 5.00)	0.775	0.79	0.438
GEC						
0 serving/week	Reference		Reference			
>0–2 servings/week	0.35 (−3.97, 4.66)	0.875	0.02 (−2.54, 2.58)	0.989	0.13	0.897
>2 servings/week	4.85 (−0.66, 10.35)	0.084	−0.86 (−4.86, 3.33)	0.691	1.64	0.101

[α] Adjusted for age, sex, maternal education, paternal education, family income, screen time category, physical activity category, BMI category water, and IQ.
[β] p-Value of the correlation between SSB consumption and BRIEF in autistic children.
[γ] p-Value of the correlation between SSB consumption and BRIEF in TD children.
[δ] $Z = \frac{\beta_{ASD} - \beta_{TD}}{\sqrt{se(\beta_{ASD})^2 + se(\beta_{ASD})^2}}$.
[ε] P value of the comparison between the β_{ASD} and β_{TD}.
*$p < 0.05$; **$p < 0.01$.

TABLE 3 Association between SSB consumption and behavioral experiments among the two groups, and the comparison between the β of the two groups.

	Coefficient estimate (β, adjust model 3[α])				Z^{δ}	p^{ε}
	ASD		TD			
	β_{ASD} (95% CI)	p^{β}	β_{TD} (95% CI)	p^{γ}		
Correct rate of Stroop						
0 serving/week	Reference		Reference			
>0–2 servings/week	−0.02 (−0.08, 0.05)	0.593	0.01 (−0.03, 0.04)	0.703	−0.83	0.405
>2 servings/week	0.00 (−0.08, 0.09)	0.954	0.02 (−0.03, 0.08)	0.426	−0.40	0.689
SI						
0 serving/week	Reference		Reference			
>0–2 servings/week	−13.11 (−282.12, 255.90)	0.924	−65.50 (−194.84, 63.83)	0.321	0.34	0.731
>2 servings/week	−148.01 (−502.67, 206.65)	0.413	−134.19 (−336.36, 67.99)	0.193	−0.07	0.947
WMI						
0 serving/week	Reference		Reference			
>0–2 servings/week	2.41 (−4.83, 9.65)	0.514	−1.06 (−3.74, 1.62)	0.439	0.88	0.378
>2 servings/week	−3.82 (−13.17, 5.53)	0.423	−1.41 (−5.65, 2.82)	0.513	−0.46	0.645

[α] Adjusted for age, sex, maternal education, paternal education, family income, screen time category, physical activity category, BMI category water, and IQ.
[β] *p*-Value of the correlation between SSB consumption and BRIEF in autistic children.
[γ] *p*-Value of the correlation between SSB consumption and BRIEF in TD children.
[δ] $Z = \frac{\beta_{ASD} - \beta_{TD}}{\sqrt{se(\beta_{ASD})^2 + se(\beta_{ASD})^2}}$.
[ε] *p*-Value of the comparison between the β_{ASD} and β_{TD}.

IL-1β, were significantly higher in autistic children compared with TD controls (54–59). Some studies demonstrated that brain IL-6 could mediate autism-like behaviors including heightened anxiety and deficits (60, 61). In an animal study, the researchers developed a mouse model that overexpresses IL-6 in the brain, and they discovered that the elevation of IL-6 in the mouse brain could produce autistic features, including impaired cognitive abilities, deficits in learning, decreased social interactions, as well as abnormal anxiety-like traits and habituation (60). Another study in 223 pre-school aged children indicated that stereotypical behavior and impaired social interactions in autistic children were more pronounced, as certain cytokine (IL-1β, IL-6, and IL-8) levels increased (62). Therefore, SSB consumption may further elevate the level of autistic children's brain IL-6 and cause severer EF impairment. Compared with TD children, autistic children might be more sensitive to increased brain IL-6 level because of the original IL-6 dysregulation (62, 63). In addition, several studies indicated that IL-6 was associated with emotional problems (64–70). Many studies found elevated IL-6 levels and its membrane-bound receptors in depressed individuals (67–70). Therefore, we might be able to speculate that sucrose–fructose drinks could impair children's EF by increasing the levels of brain IL-6 and IL-1β and this impairment would be greater in autistic children.

In this study, there were about one-fifth of autistic children who consumed no less than two servings of SSB per week, which contained about 50 g of sugar. However, children are advised to drink less or no SSB according to the current dietary guideline for Chinese (71) or Americans (72). Therefore, autistic children are suggested to decrease the consumption of SSB and improve adherence to nutrition guidelines. Parents, community, and schools should help these children to achieve better dietary quality. There were some limitations in this study. First, it is not possible to infer the causality of SSB consumption and EF based on the cross-sectional study design. Prospective cohort studies would be needed to confirm the long-term associations. Second, recall bias and information bias were inevitable because SSB consumption, children's performance on EF, and demographic factors were based on parent-reported questionnaires in our study. However, the face-to-face interview and other quality control method may help us to reduce the recall bias. Third, although we adjusted for many individual confounders in the models, we cannot rule out the effects of other unmeasured potential confounding factors such as parental smoking and parental mental status.

Conclusion

We found that SSB consumption was inversely related to EF in autistic children, and the emotional control ability of autistic children might be more susceptible to SSB. These findings highlight the necessity of limiting autistic children's SSB consumption.

Data availability statement

The generated datasets are available by request to the corresponding author JJ, jingjin@mail.sysu.edu.cn.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethical Review Committee for Biomedical Research, Sun Yat-sen University (2015-No.29). Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

LC and JJ: conceptualization, supervision, project administration, and funding acquisition. SP: methodology and formal analysis, and writing—original draft preparation. XW and LC: study design and manuscript revision. SP, XW, JC, XZ, CJ, XO, and TG: data collection. XW: data curation. SP, XW, LL, JC, XZ, CJ, XO, TG, LC, and JJ: writing—review and editing. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.940841/full#supplementary-material

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Association between maternal sugar-sweetened beverage consumption and the social-emotional development of child before 1 year old: A prospective cohort study

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Background: Excessive consumption of sugar-sweetened beverages (SSBs) has become an international public health issue. Adverse effects of sugary beverage consumption on both mother and child during pregnancy continue to be found. However, evidence regarding maternal SSB consumption and social-emotional development of children is lacking.

Methods: Based on the Shenzhen Birth Cohort Study (loss rate: 10.97%), we included 985 mother-infant pairs from 2018 to 2022. All mothers had a singleton live birth without hypertension, diabetes, tumor, or serious immune system disease before pregnancy. We used a chart of frequency distribution to show maternal SSB consumption, including non-diet soda, tea drinks (not 100% tea), fruit drinks, Sugar-sweetened coffee, bubble tea, or cocoa drinks, and total SSBs. A multivariate logistic regression model was used to estimate the odds ratios of the potential delay on social-emotional development of each child was monitored at both 6 months and 12 months of age based on maternal SSB consumption.

Results: Among the mothers, 728 (73.91%) drank SSBs <1 time per week, 194 (19.70%) drank SSBs 1–2 times per week, 43 (4.37%) drank SSBs 3–4 times per week, and 20 (2.03%) drank SSBs 5 or more times per week. Children aged 12 months with mothers who drank SSBs five or more times per week during pregnancy had an increased risk of potential delay on social-emotional development compared to those with mothers who drank SSBs less than once per week [odds ratio: 3.08 (1.13–8.39)]. Regarding the specific kinds of SSBs, we found that tea drinks (not 100% tea) were positively associated with potential delay on social-emotional development in children aged 6 months.

Conclusion: Nearly three-quarters of mothers consumed almost no SSBs during pregnancy. High SSB intake during pregnancy was associated with an increased risk of the potential delay on social-emotional development of a child at 6 and 12 months of age.

KEYWORDS

sugar-sweetened beverages (SSB), social-emotional functioning/development, birth cohort study, pregnancy, ASQ-SE

Introduction

Sugar-sweetened beverages (SSBs) refer to beverages with added artificial sugar or beverages with more than 5% of added sugar content (1), according to the Food Guide Pagoda for Chinese Residents (2022). SSBs have become an international public health issue since their intake frequency and portion size have increased (2, 3). In China, SSBs were ranked in the top three contributors of total fluid intake (TFI). The median daily intake of SSBs in adult females (18–55 years) was reported as 163 mL/day (4). The contribution of water intake from SSBs among Chinese pregnant women in 2018 accounted for 1.4% (5). Many reports have revealed the role of SSBs in obesity, cardiovascular disease, type 2 diabetes, and chronic diseases (6–8). There is also evidence that the negative consequences of soft drinks can be linked to cognitive impairment, such as stroke and dementia, oxidative stress, and poorer sleep quality and duration of sleep (9, 10). Potential mechanisms include an increase in glutathione-6-dehydrogenase levels, increased levels of gamma-aminobutyric acid (GABA), and glutamate and dopamine alteration in brain waves using electroencephalography (EEG) (10).

During pregnancy, sugar-sweetened beverage intake was also associated with an increased risk of pre-eclampsia, preterm delivery, and other pregnancy complications (11). In addition, accumulating evidence has linked SSB intake during pregnancy to birth size, allergic disease, obesity risk, and other developmental problems of offspring in later life (12–16). Further, Berger et al. revealed that infant neurodevelopmental outcomes at 24 postnatal months can be adversely affected by maternal fructose intake in early lactation (17).

However, there seem to be no human studies describing the relationship between prenatal SSB intake and cognitive function development of offspring. Social emotion is a representative part of neurobehavioral development. Previous reports suggested that children who received social-emotional intervention had better academic achievements and lower emotional stress (18). These children also showed better self-attitude, behavior, and ability to manage stress (19). Since China is a populous country, this has become a question worthy of further study. According to China's national census data, the population growth of Shenzhen ranks first in China, in which the fertility policy has played a continuous and effective role.

In this study, we describe maternal SSB consumption in Shenzhen, China and explore the relationship between maternal SSB consumption and the social-emotional development of child before 1 year old.

Methods

Participants

Mother-infant pairs were recruited from Shenzhen Birth Cohort Study (SZBC, NCT03830879), a population-based prospective cohort study at Nanshan Maternity and Child Healthcare Hospital of Shenzhen. SZBC was designed to identify early environmental and genetic causes of normal and abnormal growth, development, and health from fetal life until young adulthood. Briefly, pregnant women were recruited by SZBC staff at the first antenatal visit around gestational weeks 6–12. Enrolled participants completed three face-to-face interviews in all three trimesters during pregnancy. When the children were born, a serious of follow-up interviews including questionnaires, bio-sample collecting, and developmental assessment were carried out with the mother and child.

In this study, we included all mothers with a live singleton birth, and whose SSB information during pregnancy and Ages & Stages Questionnaire: Social-Emotional (ASQ-SE) for the child at 6 months and 12 months of age was available, and we excluded mothers with hypertension, diabetes, tumor, and serious immune system disease before pregnancy. Our study finally consisted of 985 mother-infant pairs. This study followed the guidelines for reporting observational studies—Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (Supplemental materials 1)—and were approved by ethics committees at Nanshan Maternity & Child Healthcare Hospital of Shenzhen (NSFYEC-KY-2020031) and Sun Yat-sen university (2018-054).

Exposure: Maternal SSB intake during pregnancy

Considering possible loss of appetite, nausea, and vomiting in the first trimester, the second trimester was selected to collect dietary intake information. Information on maternal SSBs was collected using a self-administered questionnaire between the 20th and 28th gestational week. Food photographs with standard portions sizes were provided to the mothers. SSBs consisted of non-diet soda, fruit drinks (not 100% fruit juice), sugar-sweetened coffee, bubble tea, or cocoa drink, and tea drinks (not 100% tea). Mothers needed to answer how often they had drunk SSBs in the past month (< 1 time per week, 1–2 times per week, 3–4 times per week, or 5 or more times per week).

Outcome: Social-emotional development of child

Child social-emotional development was measured by the Chinese version of the ASQ-SE, based on children at 6 months and 12 months of age. The ASQ-SE is a screening tool to capture the potential delay of child social-emotional development and assesses self-regulation, compliance, social-communication, adaptive functioning, autonomy, affect, and interaction with people. The score was assigned according to the answers provided by the caregiver, and lower scores indicate better social-emotional development in the child. The total score ranges from 0 to 120 for children at 6 months, and 0 to 160 for children at 12 months. According to the ASQ-SE instruction (20), the potential delay on social-emotional development at 6 or 12 months of age was defined as a total score of ≥40. Cronbach's alpha coefficient was 0.8 for the Chinese version of ASQ-SE, and sensitivity and specificity were 87.50 and 84.48%, respectively (21).

Covariates

Covariates were selected according to previous studies and preliminary studies of our research, including socio-demographics, environmental factors during pregnancy, obstetric conditions, and child feeding. Information on mother's age (< 25 years old, 25–34 years old, ≥35 years old), education level (lower than college, college, higher than college), monthly income level (<5,000 yuan, 5,000–10,000 yuan, 10,000–15,000 yuan, 15,000–20,000 yuan, ≥20,000 yuan), parity (0, ≥1), smoking or drinking before pregnancy (yes, no), and initiation of prenatal care was collected by SZBC First Trimester Questionnaire when the study participants joined the cohort before their 19th gestational week. Information on threatened abortion (yes, no), preterm birth (yes, no), and maternal complications (yes, no)—which were defined as gestational diabetes, gestational hypertension, hyperthyroidism, or hypothyroidism—was collected directly from mothers' medical records. Information on breastfeeding more than 6 months (yes, no) and initiation of complementary feeding was collected by the SZBC Child Questionnaire at 12 months.

Statistical analysis

We assessed the distribution of sociodemographic and maternal characteristics according to maternal SSB consumption. Comparisons between categorical variables were tested using chi-square tests. We used chart of frequency distribution to show maternal SSB consumption. Mothers were divided into four groups based on how often they drank SSBs, <1 time per week, 1–2 times per week, 3–4 times per week, and 5 or more times per week.

Multivariate logistic regression models were used to estimate the odds ratios (ORs) and 95% CI of the potential delay on social-emotional development of the child at 6 and 12 months of age based on maternal SSB consumption. Covariates listed above were adjusted in these models. The <1 time per week group was used as the reference group when maternal SSB consumption was evaluated as a rank variable in these models.

We also performed a sensitivity analysis by taking four kinds of SSBs (non-diet soda, tea drinks (not 100% tea), fruit drinks (not 100% fruit juice), and sugar-sweetened coffee, bubble tea, or cocoa drinks) as continuous variables into multivariate logistic regression models.

Two-sided $P < 0.05$ were considered statistically significant. All statistical analyses were conducted using survey modules of SAS software version 9.4 (SAS Institute, Cary, North Carolina).

Results

This study comprised 985 mothers-child pairs. A total of 13.71% (n = 135) and 15.74% (n = 155) children showed potential delay in social-emotional development at 6 months and 12 months, respectively. Among the mothers, 728 (73.91%) drank SSBs <1 time per week, 194 (19.70%) drank SSBs 1–2 times per week, 43 (4.37%) drank SSBs 3–4 times per week, and 20 (2.03%) drank SSBs 5 or more times per week. Table 1 presents a comparison of socio-demographics, environmental factors during pregnancy, obstetric conditions, and child-feeding characteristics of the mothers in four SSB groups. Women who were younger or had complications drank SSBs more often than their counterparts (Table 1).

There were L-shaped frequency distributions on the consumption of total SSBs and four kinds of SSBs, non-diet soda, tea drinks (not 100% tea), fruit drinks (not 100% fruit juice), and sugar-sweetened coffee, bubble tea, cocoa drinks during pregnancy. In our research, many mothers consumed almost no SSBs during pregnancy. The frequencies of non-diet soda were 94.62, 4.87, 0.41, and 0.10% in the < 1 time per week group, 1–2 times per week group, 3–4 times per week group, and 5 or more times per week group, respectively; while the frequencies of tea drinks (not 100% tea) were 93.71, 5.38, 0.40, and 0.51%; of fruit drinks (not 100% fruit juice) were 92.59, 6.80, 0.41, and 0.20%; and of sugar-sweetened coffee, milk, bubble tea, cocoa drinks

TABLE 1 Characteristics of the study population, according to maternal total sugar-sweetened beverage consumption.

Variables	N	Total sugar-sweetened beverage consumption			
		<1 time per week	1–2 times per week	3–4 times per week	5 or more times per week
Overall	985 (100%)	728 (73.91%)	194 (19.70%)	43 (4.37%)	20 (2.03%)2.0 (.03%)
Age, years, *n* (%)[a]					
<25	54 (5.48%)	33 (4.53%)	14 (7.22%)	4 (9.30%)	3 (15.00%)
25–34	731 (74.21%)	530 (72.80%)	155 (79.90%)	32 (74.42%)	14 (70.00%)
≥35	200 (20.30%)	165 (22.66%)	25 (12.89%)	7 (16.28%)	3 (15.00%)
Education levels, *n* (%)					
Lower than college	397 (40.30%)	287 (39.42%)	88 (45.36%)	15 (34.88%)	7 (35.00%)
College	483 (49.04%)	365 (50.14%)	88 (45.36%)	21 (48.84%)	9 (45.00%)
Higher than college	105 (10.66%)	76 (10.44%)	18 (9.28%)	7 (16.28%)	4 (20.00%)
Income (RMB), *n* (%)					
<5,000	169 (17.16%)	119 (16.35%)	36 (18.56%)	8 (18.60%)	6 (30.00%)
5,000–9,999	460 (46.70%)	342 (46.98%)	92 (47.42%)	19 (44.19%)	7 (35.00%)
10,000–14,999	206 (20.91%)	150 (20.60%)	45 (23.20%)	9 (20.93%)	2 (10.00%)
15,000–19,999	80 (8.12%)	67 (9.20%)	9 (4.64%)	2 (4.65%)	2 (10.00%)
≥20,000	70 (7.11%)	50 (6.87%)	12 (6.19%)	5 (11.63%)	3 (15.00%)
Parity, *n* (%)					
0	561 (56.95%)	410 (56.32%)	116 (59.79%)	23 (53.49%)	12(60.00%)
≥1	424 (43.05%)	318 (43.68%)	78 (40.21%)	20 (46.51%)	8 (40.00%)
Smoking or drinking before pregnancy, *n* (%)[a]					
Yes	279 (28.32%)	190 (26.10%)	70 (36.08%)	11 (25.58%)	8 (40.00%)
No	706 (71.68%)	538 (73.90%)	124 (63.92%)	32 (74.42%)	12 (60.00%)
Pregnancy complications, *n* (%)					
Yes	471 (47.82%)	344 (47.25%)	94 (48.45%)	23 (53.49%)	10 (50.00%)
No	514 (52.18%)	384 (52.75%)	100 (51.55%)	20 (46.51%)	10 (50.00%)
Threatened abortion, *n* (%)					
Yes	254 (25.79%)	194 (26.65%)	52 (26.80%)	7 (16.28%)	1 (5.00%)
No	731 (74.21%)	534 (73.35%)	142 (73.20%)	36 (83.72%)	19 (95.00%)
Preterm birth, *n* (%)					
Yes	35 (3.55%)	23 (3.16%)	10 (5.15%)	1 (2.33%)	1 (5.00%)
No	950(96.45%)	705 (96.84%)	184 (94.85%)	42 (97.67%)	19 (95.00%)
Breastfeeding more than 6 months, *n* (%)					
Yes	793(80.51%)	600 (82.42%)	144 (74.23%)	33 (76.74%)	16 (80.00%)
No	192(19.49%)	128 (17.58%)	50(25.77%)	10(23.26%)	4 (20.00%)
Initiation of prenatal care, mean ± SD					
Weeks	5.46 ± 0.69	5.49 ± 0.68	5.37 ± 0.73	5.37 ± 0.66	5.25 ± 0.64
Potential delay on social-emotional development at 6 months, *n* (%)					
Yes	135 (13.71%)	93 (12.77%)	36 (18.56%)	3 (6.98%)	3 (15.00%)
No	850 (86.29%)	635(87.23%)	158(81.44%)	40 (93.02%)	17 (85.00%)
Potential delay on social-emotional development at 12 months, *n* (%)					
Yes	155 (15.74%)	107 (14.70%)	35 (18.04%)	6 (13.95%)	7 (35.00%)
No	830 (84.26%)	621 (85.30%)	159 (81.96%)	37 (86.05%)	13 (65.00%)

[a]$P < 0.05$.
The percentage in brackets was the composition ratio of each horizontal item.

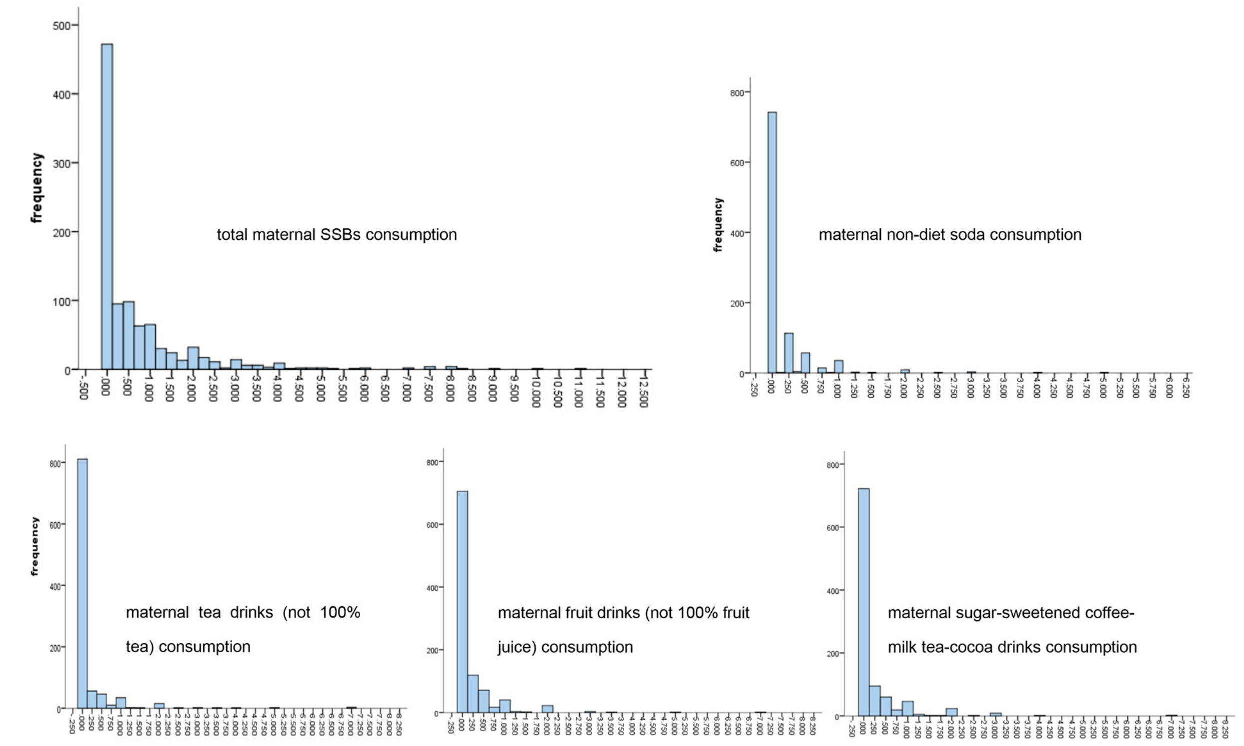

FIGURE 1
Frequency distribution of maternal SSBs consumptions.

were 90.96, 7.82, 1.02, and 0.20% in the four groups, respectively (Figure 1).

By using the multivariate logistic regression, we found that mothers who drank SSBs five or more times per week during pregnancy had increased odds of potential delay on the social-emotional development of their child at 12 months of age compared to mothers who drank SSBs <1 time per week. The adjusted OR was 3.08 (95% CI, 1.13–8.39) (Table 2).

As shown in Table 3, there was a positive association between the consumption of tea drinks (not 100% tea) during pregnancy and the social-emotional development of the child at 6 months of age [OR:1.39 (95% CI, 1.06–1.82)]. The frequency of drinking different kinds of SSBs during pregnancy had a nonsignificant relationship with children's social-emotional development at 12 months of age, with the ORs ranging from 1.03 to 1.27.

Discussion

With data from SZBC, we found 73.91% women in China drink SSBs <1 time per week, especially soda, during pregnancy. There might be a link between high maternal SSB consumption and a potential delay on social-emotional development of a child at 6 and 12 months of age.

Previous studies found that 49.3% of US adults consumed ≥ 1 SSBs on a given day (2011–2014) (12), with a total of 21.9 and 9.7% of pregnant women consuming SSBs ≥1 time/day and ≥2 times/day, respectively (2017) (22). In China, 47% of adults consumed ≥1 servings of SSB/day (2016), and SSBs were the third most common type of water intake during pregnancy (2018) (9, 17). However, our study showed that nearly three-quarters of mothers consumed SSBs < 1 time/day during pregnancy. The habits of SSB consumption by these mothers are more in line with the Dietary Guidelines for Chinese Residents (2022). The potential causes for the difference may be that the mothers in our study had higher education levels (60% college and above) and are more likely to have received systematic and comprehensive education about healthy diets (17, 23).

To the best of our knowledge, this is the first study regarding the association between maternal sugar-sweetened beverage intake and the social-emotional development of children. A prospective birth cohort study in Boston, US, found that greater prenatal sucrose and SBB intake by mothers were associated with poorer cognition among offspring. However, this study focused on cognition, such as intelligence, memory, and learning, in children aged three to seven years old, and it is difficult to distinguish between pre- and postnatal effects on children neurodevelopmental outcomes, because children's own eating or drinking habits and acquired environmental

TABLE 2 Associations between maternal total sugar-sweetened beverage consumption and social-emotional development at child at 6 months and 12 months of age.

		Potential delay on social-emotional development (ASQ-SE ≥ 40)	
		6-month OR (95%CI)	12-month OR (95%CI)
Total sugar-sweetened beverages consumption [a]		1.02 (0.88–1.17)	1.11 (0.98–1.25)
Total sugar-sweetened beverages consumption [b]	<1 time per week	1.00	1.00
	1–2 times per week	1.50 (0.97–2.33)	1.15 (0.74–1.78)
	3–4 times per week	0.53 (0.16–1.78)	0.91 (0.37–2.25)
	5 or more times per week	1.26 (0.34–4.65)	**3.08 (1.13–8.39)**

[a]Evaluated as a continuous variable.
[b]Evaluated as a rank variable, and <1 time per week group was used as the reference group.
Age, education, income, parity, smoking or drinking before pregnancy, pregnancy complications (e.g., gestational diabetes, gestational hypertension, hyperthyroidism, hypothyroidism), threatened abortion, preterm birth, breastfeeding more than 6 months, and initiation of complementary food were adjusted in models.
The bold values indicate that the ORs are statistically different.

TABLE 3 Associations of four kinds of maternal sugar-sweetened beverages consumption on social-emotional development at child at 6 and 12 months.

Specific kinds of sugar-sweetened beverages	Potential delay on social-emotional development	
	6-month OR (95%CI)	12-month OR (95%CI)
Non-diet soda	1.23 (0.77–1.96)	1.10 (0.72–1.68)
Tea drinks (not 100% tea)	**1.39 (1.06–1.82)**	1.03 (0.77–1.37)
Fruit drinks (not 100% fruit juice)	0.64 (0.38–1.08)	1.27 (0.93–1.73)
Sugar-sweetened coffee, bubble tea, cocoa drinks	0.82 (0.54–1.26)	1.06 (0.79–1.43)

Age, education, income, parity, smoking or drinking before pregnancy, pregnancy complications (e.g., gestational diabetes, gestational hypertension, hyperthyroidism, hypothyroidism), threatened abortion, preterm birth, breastfeeding more than six months, and initiation of complementary food were adjusted in models.
The bold values indicate that the ORs are statistically different.

factors have a great influence on their neurodevelopmental development (9, 24). Overall, our results are consistent with the findings of the study in Boston, which support the varying degrees of adverse associations of maternal SSB consumption on child development.

Although the detailed mechanisms underlying the association between maternal sugar-sweetened beverage intake and social-emotional development remain to be understood, placental and fetal growth and metabolism are thought to be the leading factors (12). An animal study revealed that a maternal high-sugar diet can disrupt the N-methyl-D-aspartic acid (NMDA) receptor composition and regulation in the medial prefrontal cortex and the hippocampus, which might influence the social-emotional function of offspring (25). Further research found that fructose, the content of SSBs, was partly responsible for cognitive damage (14).

This study has important clinical and public health implications. The increasing consumption of SSBs is a worldwide problem. The low intake of SSBs for the majority of mothers in our study might be due to the positive impact of promotion of various nutrition and health programs. Researchers found that dietary intervention for adolescents combined with dietary guidelines for Americans has achieved certain favorable results in the US in recent years (13). How to combine the latest version of Dietary Guidelines for Chinese residents with health education and health intervention during pregnancy is worth further discussion. Furthermore, we found that maternal SSB consumption poses a risk to the potential delay of social-emotional development of children under 1 year old despite the low overall intake of SSBs in this population, which could explain the value of nutrition and health projects from another aspect. This finding can also help physicians who provide preconception or prenatal care. According to the latest Dietary Guidelines for Chinese Residents, adults are advised to drink fewer or no SSBs. Our study found that more than 25% of pregnant women consume one serving or more of SSBs per week, indicating more efforts are needed from different aspects, including governments, medical care institutions, the food industry, community groups, media, and individuals.

This study benefits from using longitudinal statistical modeling of data drawn from a prospective Shenzhen birth cohort study. However, there are several limitations to note. First, we only focused on the frequency of beverage intake and not on the amount consumed. Second, at lower intake of SSBs, we did not have enough power to perform stratified analyses, such as by age group. Third, there was recall bias in the survey of SSB intake. However, we tried to reduce the bias by providing food photographs with standard portion sizes, one-to-one surveys, and other quality control methods. Fourth, we could not include all potential covariates associated with children's outcomes, leading to potential for residual or unmeasured confounding bias. Lastly, the findings should be interpreted conservatively because of the observational nature of the study.

Conclusions

In this population-based prospective birth cohort study, we found nearly three-quarters of mothers consume almost no SSBs during pregnancy. High SSB intake during pregnancy was associated with an increased risk of potential delay to the social-emotional development of children aged 6 and 12 months. Further investigation is needed to understand the underlying mechanisms.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Nanshan Maternity and Child Healthcare Hospital in Shenzhen, China, Sun Yat-sen University, Guangzhou, China. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

RG and LC conceived and designed the study. XLiu and RG conducted the statistical analysis and drafted the manuscript. XLi supervised the study and provided technical support. All authors acquired, analyzed, or interpreted the data, and critically revised the article for important intellectual content. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.966271/full#supplementary-material

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