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Mini-Review

Dietary Nutrients May Contribute to Increasing Mental Health Disorders in Japan

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Abstract

The global incidence of mental health disorders, including autism spectrum disorder, anxiety disorder, and bipolar disorder, continues to rise, with etiologies involving both genetic and environmental risk factors. This mini-review examines dietary nutrients as an environmental risk factor for mental health disorders, with a focus on recent trends in Japan. National survey data indicate an increasing prevalence of psychiatric disorders in Japan, accompanied by dietary shifts toward a more Westernized pattern. These changes, particularly among younger generations, include decreased intake of folate, a key nutrient for one-carbon metabolism involved in epigenetics and neurotransmitter, alongside increased consumption of meat and reduced intake of fish, vegetables, and fruits. Despite high awareness of the importance of folic acid in preventing neural tube defects, supplementation rates among pregnant Japanese women remain low compared with other countries. Given the rising trends in mental health disorders, greater attention should be paid to the role of parental (both maternal and paternal) preconception nutrition in promoting offspring mental health..

Keywords: Mental Health Disorders; Folate; One-Carbon Metabolism; Epigenetics; Parental Preconception Nutrition

Introduction

Mental health disorders, including depression, anxiety, bipolar disorder, and schizophrenia, affect thinking, feeling, mood, or behavior, often leading to significant distress or disability in social, occupational, or other important activities [1]. The incidence of mental health disorders has been increasing worldwide and is projected to continue rising [2]. In Japan, while the number of patients using mental health services increased from the 2000s to the 2010s, the prevalence of common mental disorders, such as mood, anxiety, and substance-related disorders, remained relatively stable and lower than in other high-income countries [3]. Both genetic and environmental/behavioral factors contribute to the etiology of mental health disorders [4-6]. In this mini-review, we focus on dietary nutrients as an environmental risk factor for mental health disorders, with particular attention to their situation in Japan.

Increase in mental health disorders in Japan

Figure 1 shows annual changes in the number of psychiatric outpatients, stratified by age groups, based on surveys by the Ministry of Health, Labour and Welfare of Japan every three years from 2002 to 2023. The total number of outpatients increased more than 2.5-fold over this period, although the estimation method changed in 2020. The largest increases were observed among individuals aged 0–24 years, 45–54, and 75 years and older. The same survey indicated notable increases in behavioral disorders, mood disorders and dementia (particularly Alzheimer's disease) during the survey period [7]. It is reasonable to infer that the sharp rise in outpatient numbers among older adults is linked to dementia in Japan's super-aged society. Among younger generations, attention-deficit/hyperactivity disorder (ADHD), one of the most common neurobehavioral disorders in childhood, increased from 2010 to

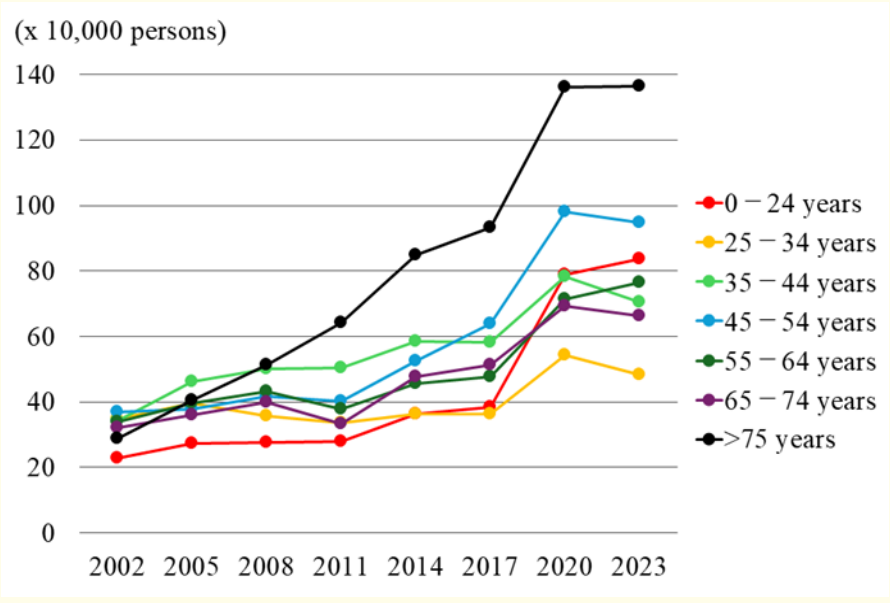

Figure 1: Annual changes in the number of psychiatric outpatients in Japan, stratified by age group, based on surveys conducted every three years from 2002 to 2023. Note: the estimation method was revised in 2020.

2019 across children, adolescents, and adults. The notably increase among adults may be partly attributable to greater awareness of the disorder [8]. *Hikikomori*, often accompanied by major depressive disorder and social phobia, has been regarded as a culture-bound syndrome in Japan but is now increasingly recognized internationally [9]. Its prevalence in Japan rose between the World Mental Health Japan Surveys conducted in 2002–2006 and in 2013–2015 [3].

The prevalence of common mental disorders in Japan is about one-third that of the United States [10]. However, large community-based interview surveys found that the prevalence of severe and moderate psychological distress in Japan (4.0%-4.2% and 24.2%-24.9%) was higher in the United States (2.9%-3.3% and 14.6%-16.5%) [11]. Nishi, *et al.* [3] suggested that Japanese individuals may underreport psychiatric symptoms due to stigma and that psychiatric disorders in Japan may not be accurately diagnosed using the International Classification of Diseases or the Diagnostic and Statistical Manual of Mental Disorders. They emphasized that while community-based surveys are essential for estimating prevalence, patient surveys are necessary to assess the actual conditions of both inpatients and outpatients.

Potential contribution of a westernized diet to mental health disorders

Peper [6] described the development of mental health disorders using the analogy that "genetics loads the gun; epigenetics, behavior, and environment pull the trigger." Among environmental and lifestyle factors, nutritional status has been increasingly recognized as relevant to the etiology and progression of mental health disorders, potentially via mechanisms involving inflammation, oxidative stress, the gut microbiome, epigenetic modifications, and neuroplasticity [12-14]. A recent systematic review and meta-analysis [15] found that a Western dietary pattern, characterized by high consumption of red or processed meat, refined grains, sugar-sweetened beverage, high-fat dairy products, butter, potatoes, and high-fat gravy, and low consumption of fruits and vegetables, was associated with an increased risk of anxiety, depression, and depressive symptoms (with the exception of high-fat dairy products). In Japanese working adults, low intake of seaweed, fish and shellfish, and vegetables was associated with more severe autistic traits [16].

The traditional Japanese diet is rich in soy products, seafood, and vegetables, followed by rice and miso soup. While generally considered healthy, it has become increasingly Westernized in recent years [17]. Using national dietary data from the Ministry of Health, Labour and Welfare of Japan, we previously showed that intakes of seaweed, fish and shellfish, fruits, and vegetables decreased steadily from 2001 to 2019 among Japanese women, particularly in the younger generations, while meat intake increased, reflecting a shift toward a more Westernized pattern [18]. Figure 2 presents actual changes in mean daily intakes of meat, fish & shellfish, vegetables, and fruits among Japanese men and women in 2003, 2013 and 2023. The increase in meat consumption and the decrease in consumption of fish & shellfish, vegetables, and fruits among people aged 7 to 59 years represent nutritional trends of concern. Given the observed associations between nutrition and mental health disorders as mentioned above, the prevalence of some kinds of mental health disorders, these dietary shifts may contribute to the rising prevalence of certain mental health conditions in Japan. Furthermore, the role of ultra-processed foods, a key component of Western or unhealthy dietary patterns, warrants consideration in evaluating the dietary contribution to mental health disorders [3,19].

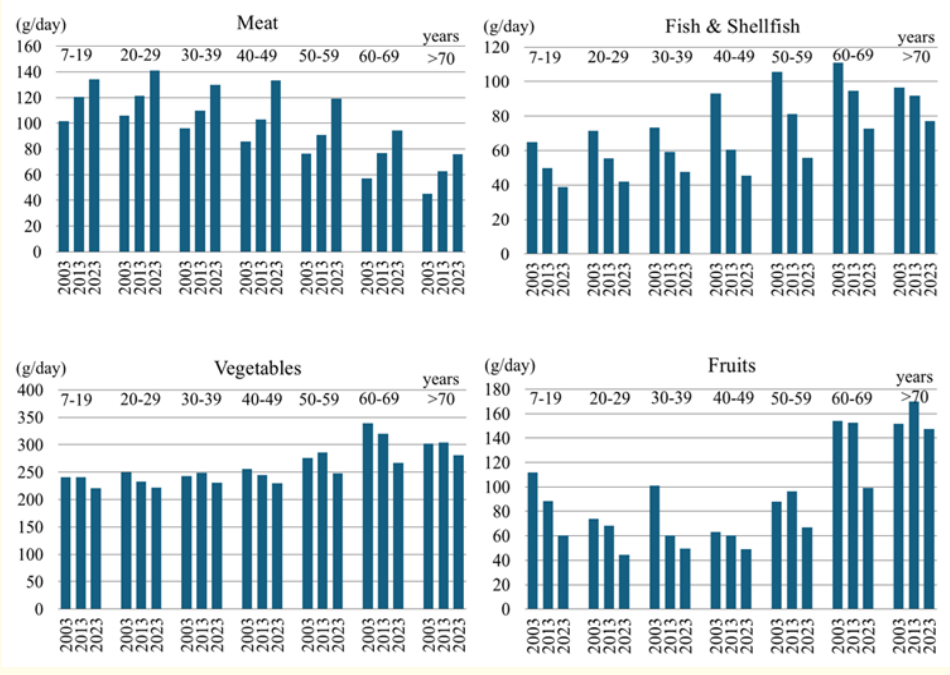

Figure 2: Mean daily intakes of meat, fish and shellfish, vegetables and fruits among Japanese people, stratified by age group, in 2003, 2013, and 2023.

Associations between nutrients and mental health disorders

Among nutritional factors, vitamins D, B9 (folate), and B12 have drawn particular attention because of their roles in neurological function [14,20]. Vitamin D is involved in the key neurological pathways beyond its traditional role in bone homeostasis, including modulation of neuroinflammation, neurotransmitter regulation, neuroplasticity and DNA methylation [20-25]. Folate and vitamin B12 are essential cofactors in one-carbon metabolism (Figure 3), which supports DNA methylation, neurotransmitter synthesis, and homocysteine regulation, all of which are critical for maintaining proper brain function [20,26-28]. The link between folate deficiency and depression is well-known [20,29]. Folate deficiency during pregnancy is also associated with neural tube defects in the fetus and with autism spectrum disorders in children [27,30,31]. Vitamin B12 deficiency can cause demyelination, leading to slowed cognitive processing, memory impairment, and executive dysfunction [32,33].

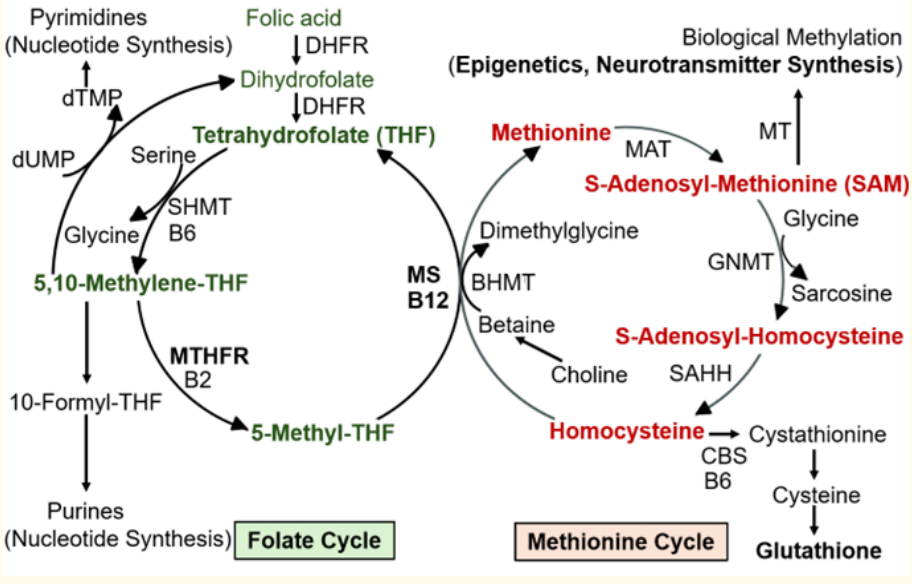

Figure 3: Overview of one-carbon metabolism, comprising the folate and methionine cycles. Abbreviations: DHFR, dihydrofolate reductase; SHMT, serine hydroxymethyltransferase; MTHFR, methylenetetrahydrofolate reductase; MS, methionine synthase; MAT, methionine adenosyltransferase; MT, multiple methyltransferases; GNMT, glycine-N-methyltransferase; SAHH, S-adenosylhomocysteine hydrolase; BHMT, betaine-homocysteine S-methyltransferase; CBS, cystathionine beta-synthase.

A cross-sectional study among Japanese adults aged 21 to 67 years found that higher dietary folate intake was associated with a lower prevalence of depressive symptoms in men only; no statistically significant linear associations were found for riboflavin (B2), pyridoxine (B6), cobalamin (B12), or omega-3 polyunsaturated fatty acids in either sex [34]. Another study among young Japanese women aged 18 to 28 years found that folate intake exceeding the recommended dietary allowance (RDA) of 240 µg/day was associated with a reduced incidence of depression [35]. Figure 4 presents mean daily folate intake in 2023 by age group, showing that more than half of women aged 15–39 years consumed less than the RDA. In the Hokkaido Study on Environment and Children's Health Cohort, low folate status during the first trimester was associated with younger maternal age, lower educational level, and lower annual income [36]. Another Japanese report indicated that among women of childbearing age, an increasing prevalence of spina bifida (a typical manifestation of neural tube defects) paralleled decreases in body mass index and dietary energy intake, likely due to distorted body image, as well as an increased smoking rate [37]. In a study of 58 healthy female university students in Tokyo, mean folate intake was 262±111 (range: 112-734) µg/day and 12.1% of participants had low serum folate levels (<3.0 ng/ml) [38].

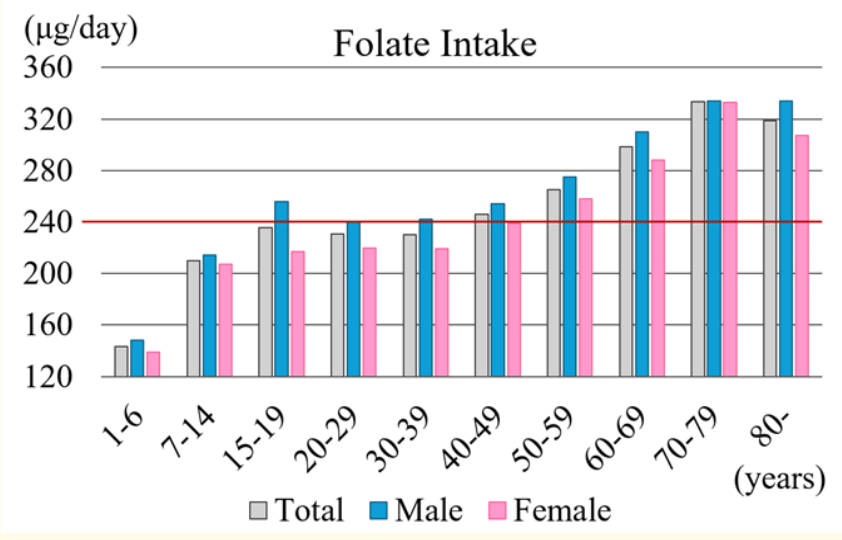

Figure 4: Mean daily folate intake (μg/day) among Japanese people, stratified by age group, in 2023, based on a national survey by the Ministry of Health, Labour and Welfare of Japan. The recommended dietary allowance and estimated average requirement for folate are 240 and 200 μg/day, respectively, for individuals aged ≥15 years, and 130–230 and 110–190 μg/day, respectively, for children aged 6–14 years.

Contributions of parental folate status to offspring mental health

The preventive role of synthetic folic acid supplementation before and during pregnancy (400 μg/day recommended in Japan) against neural tube defects is well established [39,40]. First-trimester maternal folic acid supplementation, but not multivitamin use, has also been linked to a substantially lower risk of congenital heart diseases [41]. Interestingly, both folate deficiency and excess folate intake during pregnancy may influence the risk of autism spectrum disorders (ASD) in offspring, suggesting a U-shaped association [31,42]. Extremely high maternal plasma folate and vitamin B12 levels at birth have been associated with increased ASD risk [42].

In Japan, where food fortification with folic acid is not mandatory, effective public health strategies to encourage supplement use among women of childbearing age are urgently needed [39]. Table 1 summarizes reports from several countries on the prevalence of folic acid supplementation during pregnancy and/or awareness of its necessity. Compared with other countries, supplementation rates among pregnant women in Japan are relatively low despite high awareness of its importance. According to Quinn, *et al.* [51], as of July 2023, Australia and Ghana have implemented mandatory folic acid fortification; Japan, Italy, India, China, and the United Arab Emirates have implemented voluntary fortification; and Lebanon has no fortification. Among 193 countries studied, 69 had mandatory fortification (mean plasma folate level: 36 nmol/L), 47 had voluntary fortification (21 nmol/L), and 77 had no fortification (17 nmol/L). In 75 countries with neural tube defect prevalence data, mean rates per 10,000 population were 4.19, 7.61 and 9.66 for mandatory, voluntary and no fortification, respectively.

While the role of maternal folate status in preventing fetal neural tube defects is well known, its broader influence on offspring neurodevelopment and brain health is less clearly established [52].

Authors(Year)	Country	Study design	Population/Period and Main findings	Ref.
Yamamoto., *et al*. (2017)	Japan	Cross-sectional	1,862 pregnant women attending a perinatal center in Osaka (2014-2015) 20.5% took folic acid supplements periconceptionally; 70.4% were aware of its protective effect.	39
Nishigori., *et al*. (2019)	Japan	Pro-spective cohort	92,269 pregnant women recruited nationwide (2011-2014) 8.27% used preconception folic acid supplementation; 74 neural tube defect cases were reported (32 spina bifida, 24 anencephaly, 19 encephalocele).	43
Nilsen., *et al*. (2016)	Italy	Cross-sectional	2,189 women visiting 7 clinics during or after pregnancy (2012) Preconception folic acid use was reported by 23.5% of the participants, and was associated with higher maternal age, higher education, marriage, lower parity, infertility treatments, and chronic disease.	44
Livock., *et al*. (2016)	Australia	Cross-sectional	2,146 pregnant women visiting 7 maternity hospitals (2011–2012) Approximately 40% of women consumed a folic acid preparation preconceptionally, with this figure rising to 62% after pregnancy awareness.	45
Medawar., *et al*. (2019)	Lebanon	Cross-sectional	413 women interviewed by 5 gynecologists during their postnatal visits (2014) 76 % of the participants reported having knowledge about folic acid during pregnancy; 93.9% took folic acid supplements during pregnancy; 33.6% took folic acid supplements before becoming aware of their pregnancy.	46
Patel., *et al*. (2023)	India	Cross-sectional	399 women visiting antenatal clinics in their trimester of pregnancy (2019) 49.8% of women were taking folic acid during pregnancy; Only 45.6% of pregnant women were aware of the importance of folic acid supplementation; The majority (77.9%) had poor knowledge, and only 1.3% knew folic acid should be taken preconceptionally.	47
Zhou., *et al*. (2024)	China	Retro-spective cohort	567,547 women planning a pregnancy within 6months (2010-2012) 74.7% of women took folic acid supplementation; 599 birth defects were self-reported (folic acid taking vs not taking, 0.102% vs 0.116%, $P < 0.001$); Neural tube defects were lower in maternal folic acid supplementation (OR = 0.56, P = 0.003).	48
Seidu., *et al*. (2024)	Ghana	Cross-sectional	400 pregnant women attending randomly selected health facilities (2021) 84.5% of women were adhered to iron and folic acid supplementation (self-reported); Knowledge of iron and folate supplementation was associated with adherence.	49
Mutare., *et al*. (2025)	United Arab Emirates	Cross-sectional	54 pregnant women within their first trimester out of 312 eligible participants. 98% of participants took supplementation (57%) before and (44%) during pregnancy; 56% took a multivitamin containing folic acid, and 43% took a folic acid-only supplement.	50

Table 1: Summary of reports on the prevalence of folic acid supplement intake among pregnant women and/or awareness of its necessity.

Emerging research also highlights the role of paternal nutrition, including age-related epigenetic changes in sperm, in shaping offspring mental health [53,54]. Animal studies show that paternal folate deficiency can delay offspring neurobehavioral development, in addition to the effects of maternal deficiency [55,56]. Thus, the importance of parental preconception nutrition for offspring outcomes, including mental health disorders, is gaining recognition [57]. Although direct human evidence linking paternal folate deficiency to psychiatric disorders remains limited, converging animal and human findings support the hypothesis that paternal folic acid intake and age are important factors in offspring neurodevelopment.

Conclusions

The increasing prevalence of psychiatric disorders in Japan may be partly attributable to the further Westernization of the diet, potentially leading to nutrient insufficiencies associated with mental illness. Among these, folate, a key nutrient in one-carbon metabolism involved in epigenetics and neurotransmitter synthesis, has shown an apparent decline in intake, especially younger generations. Compared with other countries, the prevalence of folic acid supplementation among pregnant Japanese women remains low despite high awareness of its role in preventing neural tube defects. Given the rising trends in mental health disorders, greater attention should be paid to the role of parental (both maternal and paternal) preconception nutrition in promoting offspring mental health.

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Author Contributions

YA designed the study and wrote the manuscript. MN contributed to the section "Increasing Mental Health Disorders in Japan"; SS contributed to the section "Epigenetic Risk of Mental Health Disorders". All authors approved the final version of the manuscript.

Conflicts of Interest

The authors have declared that they have no potential conflicts of interest.

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