



Research paper

Association between habitual tryptophan intake and depressive symptoms in young and middle-aged women



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ABSTRACT

Background: The intake of tryptophan, the precursor of serotonin, is assumed to affect serotonin availability and depression onset. Nevertheless, a definitive relationship between dietary tryptophan intake and depressive symptoms has not been established. We examined the association between tryptophan intake and depressive symptoms screened in a group of 4272 first-year female dietetic students and 3651 their mothers.

Methods: Dietary tryptophan intake during the preceding month was assessed with a validated, self-administered diet history questionnaire. Depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale (CES-D) using two cutoff scores: CES-D score ≥ 16 and CES-D score ≥ 19 (the optimal cutoff score for Japanese people). The multivariate adjusted prevalence ratio (PR) and 95% confidence interval (CI) for depressive symptoms were calculated using Poisson regression analysis.

Results: The prevalence of depressive symptoms (CES-D score ≥ 16) was 50.0% for young women and 26.5% for middle-aged women. The adjusted PR (95% CI) for depressive symptoms in the highest versus lowest quintile of tryptophan intake was 0.84 (0.75, 0.93) in young women (P for trend < 0.0001) and 0.83 (0.64, 1.01) in middle-aged women (P for trend < 0.0001). These associations were stable even when depressive symptoms were defined as a CES-D score ≥ 19 .

Limitations: This is a cross-sectional study. Depressive symptoms were assessed using a self-reported questionnaire.

Conclusions: This cross-sectional study showed that a higher tryptophan intake was independently associated with a lower prevalence of depressive symptoms in young Japanese women.

1. Introduction

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration. Depression is a leading cause of disease burden and an important source of lost years of healthy life for women aged 15–44 years (World Health Organization, 2008). In 2017, the World Health Organization (WHO) reported that the number of patients with depression in the world was 322 million (World Health Organization, 2017). The 12-month prevalence of depression in Japan is 3.08% for women and 1.17% for men (Kawakami, 2007). These prevalence values are relatively low compared to those of Western countries. However, according to the report from the WHO, the suicide rate of Japanese women aged 15–49 years is the second highest among the high-income

countries after the Republic of Korea (World Health Organization, 2014). Since depression is an important risk factor for suicide (Hirokawa et al., 2012), it is critical to investigate factors that cause depression.

Several risk factors have been reported for depression, including female sex, older age, low income, widowed or divorced marital status, and worse perceived health status (Lehtinen and Joukamaa, 1994; Oliver-Quetglas et al., 2013). In addition, nutritional factors have been examined as a risk factor for depression in many studies (Murakami and Sasaki, 2010; Sanhueza et al., 2013). Among these factors, tryptophan, an essential amino acid, has been proposed as a nutrient that is associated with the onset and progress of depression (Hakkarainen et al., 2003; Lieberman et al., 2016; Parker and Brotchie, 2011).

Tryptophan is a precursor of serotonin, which is a monoamine neurotransmitter and regulates mood, emotion, wakefulness, sleep, and

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appetite in humans (Shabbir et al., 2013). Low brain serotonin levels or suppression of serotonin-stimulated function is considered a mechanism of pathogenesis of depression (Markus, 2008). Although a number of foods contain serotonin, including cheese, meat, fruits, and vegetables, its passage into the brain is inhibited by the blood-brain barrier (Shabbir et al., 2013). Serotonin synthesized in the gastrointestinal tract is also unable to cross the blood-brain barrier. Thus, the amount of serotonin produced in the brain depends on the amount of tryptophan in plasma (Yuwiler et al., 1977). Since tryptophan cannot be synthesized *de novo* and must be supplied from the daily diet, low tryptophan intake has been assumed to cause lower brain serotonin levels and to be an important risk factor involved in the onset and course of a variety of affective disorders, including depression (Markus, 2008).

The relationship between tryptophan intake and mood status has been examined mainly in intervention studies using tryptophan supplementation, restriction, or dietary intervention (Lindseth et al., 2015; Shaw et al., 2001; Young, 2013). Few previous studies, however, have investigated the relationship between habitual dietary tryptophan intake and depression (Hakkarainen et al., 2003; Lieberman et al., 2016). From a preventive perspective, the relationship between dietary tryptophan intake and depression in a free-living setting should also be examined.

In this study, we examined the relationship between dietary tryptophan intake and depressive symptoms in a large group of young and middle-aged Japanese women.

2. Methods

2.1. Participants

This cross-sectional study was conducted as a part of the Three-generation Study of Women on Diets and Health. The Three-generation Study of Women on Diets and Health is a cross-sectional study examining associations between dietary habits and health problems in young, middle-aged, and old women. It was conducted among dietetic students who were pursuing a major in dietetics or nutritional science and enrolled in a university, college, or vocational school in Japan (a total of 85 institutions in 35 of 47 prefectures), as well as their mothers, and grandmothers (Kobayashi et al., 2013).

This survey was conducted in northern (four institutions in one prefecture [Hokkaido]) and western (54 institutions in 22 prefectures) Japan from April to May 2011, and in eastern Japan (27 institutions in 12 prefectures) from April to May 2012. We recruited institutions that offer coursework in dietetics and were ready to participate in this study. All measurements at each institution were conducted according to the survey protocol (Kobayashi et al., 2013). Collaborators at each institution explained the purpose and outline of the survey to 7016 potential participants (all newly enrolled students) and recruited participants to participate in the survey. The collaborators asked the students who agreed to participate in the survey to answer questionnaires on dietary habits and lifestyle. The collaborators also asked the students to invite their mothers and grandmothers to participate in the survey and to distribute the questionnaires to their mothers and grandmothers. The students explained the purpose and outline of the study to their mothers and grandmothers using written and oral explanations. The mothers and grandmothers who agreed to participate were asked to answer the dietary and lifestyle questionnaires.

In this study, we analyzed the datasets of the students and their mothers. Among the eligible 7016 students and 7016 mothers recruited to participate in this survey, 5132 students and 4236 mothers agreed to participate in this survey. Of the mothers, 459 agreed to participate while their children did not. Among the participants, 4933 students (70.3%) and 4044 mothers (57.6%) answered both the dietary and lifestyle questionnaires. Participants who lived in eastern Japan and answered the questionnaires in 2011 were excluded because their lifestyles and habitual diets in April and May 2011, were likely to have

been influenced by the Great East Japan Earthquake that occurred on March 11, 2011 (45 students and 63 mothers). Two students and two mothers from an institution with an extremely low response rate (2%) were also excluded. In addition, we excluded male students (277 students); those who answered the questionnaires on May 20 or later (85 students); those who did not complete the survey questionnaire (seven students and four mothers); those who had extremely low or high reported energy intakes (< 500 or > 4000 kcal/day; 48 students and 21 mothers); those with a medical history of mental disorders or who were currently under treatment for mental disorders (85 students and 125 mothers); those with chronic digestive diseases (six students); those who use dietary supplements that may contain tryptophan (four mothers); students aged 21 years old and over (145 students); and mothers aged 65 years and older (10 mothers). We also excluded participants with endometabolic diseases such as diabetes or thyroid disease (23 students and 104 mothers) or those with estrogen preparation use at the time of the survey (24 students and 84 mothers). These participants were excluded because these diseases and the use of estrogen preparation can cause insulin resistance and affect the bioavailability of tryptophan in the central nervous system (Gierach et al., 2014; Godsland et al., 1992). After exclusion according to these criteria, 4272 students and 3651 mothers remained in the analysis.

This study was conducted according to the latest version of the Declaration of Helsinki, and the protocol of this survey was approved by the ethics committee of the University of Tokyo (approval no. 3249; approval date: November 29, 2010). Written informed consent was obtained from each participant and also from a parent of participants aged < 20 years after the nature of the procedures had been fully explained.

2.2. Dietary measurements

Dietary nutrient intake during the preceding month was assessed using a modified version of a self-administered diet history questionnaire (DHQ) developed by Sasaki et al. (Sasaki et al., 1998). Responses to the DHQ were checked once for completeness by trained research staff at the survey center, and if necessary, returned to the participant for review and clarification of ambiguous responses.

The original version of the DHQ is a 16-page structured self-administered questionnaire that includes questions about the consumption frequency and portion size of 150 foods and beverages during the preceding month (Kobayashi et al., 2011). A total of 150 food and beverage items were selected to represent food consumed commonly in Japan, and their standard portion sizes were determined based on several cookbooks for Japanese dishes (Sasaki et al., 1998). For consumption frequency of food and beverage items, participants chose from eight possible responses: never, once per month, two or three times per month, once per week, two or three times per week, four to six times per week, once per day, or twice per day or more. In addition, respondents chose a relative portion size consumed, compared with a standard portion size, from five categories: ranging from 50% or less to 150% or more (Sasaki et al., 2000). Details of the modification of the DHQ are as follows: one food item, skim milk, was deleted from the original DHQ; two food items, soybean milk and salted green and yellow vegetable pickles, were added to the original version; and questions about dietary supplement use were removed and added to the lifestyle questionnaire.

The estimates of dietary nutrient and tryptophan intake were calculated using a computer algorithm developed specifically for the DHQ, based on the Standard Tables of Food Composition in Japan, 2010 (Science and Technology Agency, 2010) and the amino acid database developed by Suga et al. (Suga et al., 2013). Although dietary supplement use was queried in the lifestyle questionnaire, the intake of supplements was not included in the analysis because there is no reliable composition table of dietary supplements in Japan.

The validity of nutrients and amino acids estimated from the DHQ

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