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Research paper

Association of total zinc, iron, copper and selenium intakes with depression in the US adults

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ABSTRACT

Background: The aim of present study was to examine the associations of total zinc, iron, copper and selenium intakes from diet and supplements with depression.

Methods: Cross-sectional study used data from the National Health and Nutrition Examination Survey (NHANES) 2009–2014 in the present study. Logistic regression models and restricted cubic spline models were applied to examine the associations of total zinc, iron, copper and selenium intakes with depression.

Results: A total of 14834 adults aged 18 years or older (7399 men and 7435 women) were included in the present study. Total zinc, iron, copper and selenium intakes were inversely associated with depression in unadjusted model and age- and gender-adjusted model. The multivariate adjusted odds ratios (ORs) with 95% confidence intervals (CIs) of depression were 0.68 (0.49–0.94) and 0.46 (0.32–0.67) for the highest versus lowest quartile of copper and selenium intakes, respectively. The inverse associations of depression were statistically significant for the quartile 3 versus lowest quartile of total zinc (OR: 0.70; 95% CI: 0.49–0.99) and iron intake (OR: 0.66 95% CI: 0.50–0.87). Compared to those below the RDA (Recommended Dietary Allowance), participants who met the RDA for zinc (OR: 0.74; 95% CI: 0.56–0.99), copper (OR: 0.68; 95% CI: 0.56–0.82) and selenium (OR: 0.52; 95% CI: 0.39, 0.71) had significantly lower odds of depression.

Limitations: This was a cross-sectional study, limiting causal inferences. Assessment of depression was based on a self- report scale.

Conclusion: Total zinc, iron, copper and selenium intakes may be inversely associated with depression.

1. Introduction

Depression is a common illness worldwide, with more than 300 million people affected (WHO, 2017). The lifetime prevalence of depression is approximately 15% among adults in high-income countries worldwide (Bromet et al., 2011). Depression is associated with significant disability, disease burden, and health care costs. It is expected to be the leading cause of disability (Ferrari et al., 2013; WHO, 2014) and the world's second leading cause of disease burden by 2030 (Mathers and Loncar, 2006). At present, there are adequate treatment options for depression, but a significant proportion of people still fail to achieve remission (Mauskopf et al., 2009). Hence, it is necessary to investigate the modifiable risk factors and effective preventive methods for depression.

Extensive research efforts have been done in past decades; however, the etiology of depression has not been fully explained. Physical inactivity (Rebar et al., 2015; Zhai et al., 2015) and dietary factors, including fish (Li et al., 2016), fruit, vegetables (Liu et al., 2016) and coffee (Wang et al., 2016) may play important roles in the development of depression. In recent years, there has been a growing interest in the role of nutrients in depression. Magnesium, vitamin D and folate have been assessed to be associated with depression (Anglin et al., 2013; Li et al., 2017a; Petridou et al., 2016). Zinc, iron, copper, and selenium as essential microelements, have essential roles in growth and development. Zinc and iron are important in regulating of cellular function and neuromodulation (Dusek et al., 2012; Momcilovic et al., 2010). As components of enzymes, copper and selenium have crucial roles in antioxidant protection (Heninger et al., 1996; Roman et al., 2014). Studies have suggested that oxidative stress may contribute to depression (Lee et al., 2013). However, epidemiological studies on the

Abbreviations: BDNF, brain derived neurotrophic factor; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CI, confidence interval; NHANES, National Health and Nutrition Examination Survey; MEC, mobile examination center; NCHS, National Centers for Health Statics; NMDA, N-methyl-D-aspartate; OR, odds ratio; PHQ, Patient Health Questionnaire; RDA, Recommended Dietary Allowance

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associations between zinc, iron, copper, and selenium intakes and depression are limited or controversial.

The results of the associations between dietary zinc and iron intakes and depression remained controversial. For zinc intake, an inverse association between dietary zinc intake and depression was found in some studies (Amani et al., 2010; Jacka et al., 2012; Kim et al., 2015; Miki et al., 2015), whereas no significant association was found in other studies (Lehto et al., 2013; Maserejian et al., 2012; Vashum et al., 2014). However, only one cross-sectional study evaluated the association between zinc intake and depression in the US among these studies (Maserejian et al., 2012). With regard to iron intake, two studies suggested that higher iron intake was associated with lower prevalence of depressive symptoms (Kim et al., 2015; Miki et al., 2015), while Fulkerson et al. found no significant association (Fulkerson et al., 2004). Regarding copper intake, one case-control study in Korean adolescent girls found an inverse relationship between copper intake and depression (Kim et al., 2015). Regarding selenium intake, one nested case-control study in Australia suggested that lower dietary selenium intake was associated with an increased risk of *de novo* depression (Pasco et al., 2012). Nevertheless, most previous studies did not include intakes from supplements. To date, epidemiological study on zinc, iron, copper and selenium intakes and depression is scarce in the US population. Accordingly, we performed analyses on a subsample of National Health and Nutrition Examination Survey (NHANES) 2009–2014 to investigate the associations of total zinc, iron, copper and selenium intakes from diet and supplements with depression in the US adults. In addition, this study assessed the association between zinc to copper ratio and depression, because zinc and copper compete at the level of intestinal absorption and there is a strong interaction between zinc and copper (Abdel-Mageed and Oehme, 1991; Lonnerdal, 1996; Wu et al., 2015).

2. Materials and methods

2.1. Data collection and study population

The NHANES is a nationally representative sample of the non-institutionalized US civilians, selected by using a complex, stratified, multistage sample design to assess the health and nutritional status of adults and children in the US. The NHANES is an ongoing, 2-year-cycle program administrated by the National Centers for Health Statics (NCHS) at the Centers for Disease Control and Prevention (CDC). The study protocol was approved by the NCHS Institutional Review Board and all informed consent was obtained from all participants. Data of the NHANES are collected by a household interview and an examination conducted in a mobile examination center (MEC) (Centers for Disease Control and Prevention). The data from 3 cycles of NHANES (2009–2010, 2011–2012 and 2013–2014) were combined for the present analyses. The response rates were 79.4%, 72.6% and 71.0% of interviewed sample and 77.3%, 69.5% and 68.5% of examined sample for 2009–2010, 2011–2012 and 2013–2014, respectively (Centers for Disease Control and Prevention, 2009–2014). A total of 30468 individuals participated in the NHANES during 2009–2014, and our analyses were limited to 18,504 adult participants 18 years of age or older. Of these, 15,844 completed the depression questionnaire. Pregnant or lactating females (n = 256) and participants with incomplete or unreliable 24-h recall data (n = 583) were excluded. Furthermore, participants whose total energy intake was more than mean ± 3 SDs were excluded (n = 171). Finally, 14834 participants aged 18 years or older (7399 men and 7435 women) were included in the analyses.

2.2. Depression assessment

Depression was assessed by a nine-item Patient Health Questionnaire (PHQ-9) which is a reliable and valid diagnostic tool for detecting depression in both clinical and research settings (Kroenke et al., 2010; Spitzer et al., 1999). DSM-IV based symptom criteria for the nine-item instrument "not at all," "several days," "more than half the days," and "nearly every day" were given a point ranging from 0 to 3. A total score was based on the sum of the points in each item ranging from 0 to 27. The PHQ-9 score ≥ 10 was used as the cut-off point to identify depression which had a sensitivity of 88% and a specificity of 88% for the diagnosis of major depression (Kroenke et al., 2001).

2.3. Dietary and supplemental intake assessment

Dietary intakes data were assessed by using a 24-h recall survey. The 24-h recall is a retrospective dietary assessment method that provides information on the respondent's food intake during the previous 24-h period. Given evidence from biomarker-based validation studies that 24-h dietary recalls capture dietary intake with less bias than do food-frequency questionnaires (Prentice et al., 2011; Subar et al., 2003). The dietary intake data were used to estimate the types and amounts of foods and beverages (including all types of water) consumed during the 24-h period prior to the interview (midnight to midnight). Daily aggregates of food energy, nutrients and other food components from all foods and beverages were calculated using US Department of Agriculture (USDA) Food and Nutrient Database for Dietary Studies (FNDDS 2009–2010, 2011–2012 and 2013–2014, respectively). Two 24-h dietary recalls were administered. The first dietary recall interview was collected in-person in the MEC and the second interview is collected by telephone 3–10 days later, but not on the same day of the week as the MEC interview. If a participant completed both 24-h recalls, we used the average dietary intake data of both. Otherwise, we used the single reliable dietary recall (among all, 90% participants completed both the 24-h recalls).

The dietary supplements were obtained during the household interview. Participants were asked what supplements, how often and how much they had taken in the past 30 days. The average daily amount of supplemental nutrients were calculated by summing across all supplemental nutrients and dividing it by 30.

The total daily nutrient intake was calculated by summing each participant's nutrient intake from diet and the average daily amount from supplements.

2.4. Covariates

Demographic characteristics included age, gender, ethnicity (Mexican American, other Hispanic, Non-Hispanic White, Non-Hispanic Black, and other race), education (less than 9th grade, 9th–11th grade, high school graduate/GED or equivalent, some college or AA degree, and college graduate or above), and annual family income were obtained from in-person household interviews. Total energy intake was obtained from 24-h dietary recall. Body mass index (BMI) was calculated as weight (in kg) divided by height squared (in meter) which were measured in the MEC and divided into < 25.0, 25.0 to < 30.0 and ≥ 30.0 kg/m^2. Educational level was divided into < high school, high school, and > high school. Participants were considered as smokers if they had smoked ≥ 100 cigarettes in their life. History of hypertension or diabetes was defined as self-reported physician diagnosis of hypertension or diabetes.

2.5. Statistical analysis

All statistical analyses were performed with Stata 12.0 to account for the complex sampling design. Appropriate sampling weights, primary sampling unit and strata information were included in the analyses. When combining two or more 2-year cycles of the continuous NHANES data, new sample weights must be constructed before beginning any analyses. In the present study, we combined three 2-year survey cycles of the continuous NHANES (2009–2010, 2011–2012 and 2013–2014). New special 6-year dietary weights were created by taking one-third of the 2-year dietary weights following the NHANES