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Research report

Dietary zinc is associated with a lower incidence of depression: Findings from two Australian cohorts



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ABSTRACT

Background: Several animal and human studies have shown that zinc plays a role in reducing depression, but there have been no longitudinal studies in both men and women on this topic. The aim of this study was to investigate dietary zinc, and the zinc to iron ratio, as predictors of incident depression in two large longitudinal studies of mid-age and older Australians.

Methods: Data were self-reported, as part of the Australian Longitudinal Study on Women's Health (women aged 50–61 years) and Hunter Community Study (men and women aged 55–85 years). Validated food frequency questionnaires were used to assess dietary intake. Energy-adjusted zinc was ranked using quintiles and predictors of incident depression were examined using multivariate logistic regression.

Results: Both studies showed an inverse association between dietary zinc intake and risk of depression, even after adjusting for potential confounders. Compared to those with the lowest zinc intake those with the highest zinc intake had significantly lower odds of developing depression with a reduction of about 30–50%. There was no association between the zinc to iron ratio and developing depression in either study.

Limitations: Dietary assessment was carried out only at baseline and although adjustments were made for all known potential confounders, residual confounding cannot be entirely excluded.

Conclusions: Low dietary zinc intake is associated with a greater incidence of depression in both men and women, as shown in two prospective cohorts. Further studies into the precise role of zinc compared to other important nutrients from the diet are needed.

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1. Introduction

Depression is a mental disorder with high morbidity and mortality; more than 350 million people of all ages worldwide suffer from depression (WHO, 2012). Depression is a major risk factor for self-inflicted injury and, at its worst, can lead to suicide. It has been estimated that suicide is responsible for 1 million deaths every year (WHO, 2012). Depression is also associated with

decreased productivity, poor psychosocial outcomes, and decreased quality of life and wellbeing. In Australia, mental disorders were identified as the leading cause of healthy years of life lost due to disability in 2003 (AIHW, 2008). Depression-associated disability costs the Australian economy \$14.9 billion annually and depression is forecast to come second only to heart disease as the leading medical cause of death and disability within 20 years (The Department of Health, 2009).

Even though there are treatments for depression, pharmacotherapy is usually costly. Medications have the potential for adverse side effects (Gartlehner et al., 2007) and a significant proportion of people fail to achieve a reduction in their depressive symptoms (Mauskopf et al., 2009). Hence, there is a need to investigate alternative treatments and prevention strategies. In recent years, there has been an increasing interest in the role of nutrition in depression (Lai et al., 2014). Micronutrients of particular interest in depression are zinc and magnesium (Jacka et al.,

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2012a; Szwedczyk et al., 2008). Zinc is an immunomodulatory trace mineral found in abundance in the human brain where it is required to regulate numerous aspects of cellular metabolism. It has been suggested that zinc supplementation enhances antidepressant therapy by lowering depressive scores in patients (Lai et al., 2012). Zinc may produce antidepressant-like effects through modulating the functions of serotonergic and N-methyl-D-aspartate (NMDA) receptors and increasing levels of brain derived neurotrophic factor (BDNF) (Szwedczyk et al., 2009, 2011; Takeda and Tamano, 2009). In animal models of depression, zinc induces an antidepressant-like effect that appears to be mediated through its interaction with NMDA receptors (Krocicka et al., 2001; Rosa et al., 2003; Sowa-Kucma et al., 2008) and enhances the effect of antidepressant medication (Krocicka et al., 2001). In humans, recent population-based studies have shown an association between low dietary zinc intake and depression (Jacka et al., 2012a; Maserejian et al., 2012; Roy et al., 2010) in women and men (Lehto et al., 2013).

Although animal and human studies have demonstrated a role for zinc in reducing depression, there have been no longitudinal studies looking at the link between dietary intake of zinc and depression in both men and women. To date there has been only one prospective study carried out to look at dietary zinc intake and risk of incident depression (Lehto et al., 2013); however, this was only carried out in men. Therefore, the aim of this study was to determine if dietary zinc is associated with depression using Centre for Epidemiological Studies Depression Scale (CESD) scores in both men and women from two large Australian cohorts. In addition, this study examined the association of dietary zinc to iron ratio with depression, because minerals with similar physical or chemical properties such as iron and zinc may compete with each other biologically (Hill and Matrone, 1970) and previous studies in humans have shown that iron interferes with the absorption of zinc (Solomons, 1986).

2. Methods

2.1. The Hunter Community Study (HCS)

Data for this study was obtained from the Hunter Community Study (HCS), a cohort of community-dwelling men and women aged 55–85 years of age in Newcastle, NSW, Australia. Approval to conduct the research was granted by the University of Newcastle Human Research Ethics Committees. This study has been described in detail elsewhere (McEvoy et al., 2010). In brief, participants were randomly selected from the NSW State Electoral Roll and contacted between December 2004 and May 2007. Data collection was carried out simultaneously during this period. Participants were asked to complete a series of self-reported postal questionnaires that included socio-demographics, self-reported medical and surgical history, complementary and alternative medicines use, medication use, and Centre for Epidemiological Studies Depression Scale (CESD) after written consent was obtained. In addition to completing the postal questionnaires, participants were invited to attend the HCS data collection centre (clinic) to collect measures of blood pressure, height, weight, waist-circumference and a blood sample.

The cohort was followed-up with repeat questionnaires and clinical assessment from 2010 to 2011 to update exposure and outcome information. Out of the 3281 participants, 2918 completed the food frequency questionnaire (FFQ) at baseline and 2092 participants completed the follow-up after 5 years.

2.2. Dietary assessment for HCS

At baseline, dietary data were collected using a twice-validated 145-item self-administered semi-quantitative FFQ. The Older

Australian's FFQ was originally developed for the Blue Mountains Eye Study to measure the dietary intakes of older community-dwelling older adults in Australia (Smith et al., 1998) and was modelled on an early FFQ by Willett et al. (1988). The Older Australians' FFQ was originally validated against three separate 4-day food records (Smith et al., 1998), and has recently been further validated using objective folate and carotenoid biomarkers (Lai et al., manuscript to be published). The Older Australians' FFQ shows high reproducibility in the short term, with correlations for most nutrients including zinc and iron at about 0.70–0.80. It is acceptably reproducible in the longer term, with correlations of mostly 0.60–0.70, and less than 1% of the subjects grossly misclassified, indicating good validity (Smith et al., 1998). Dietary data from the Older Australians' FFQs were coded into a custom-made nutrient analysis program based on NUTTAB 2006, an Australian nutrient composition database (FSANZ, 2007). Nutrient supplement information was obtained from manufacturers and added to the database.

2.3. The Australian Longitudinal Study on Women's Health (ALSWH)

The Australian Longitudinal Study on Women's Health (ALSWH) is national cohort examining the health and wellbeing of women of different ages. This paper uses data from 1946 to 1951 cohort, who were 45–50 years at the Survey 1 (baseline) in 1996. Ethical clearance for ALSWH was obtained from the University of Newcastle and University of Queensland. Details of ALSWH's methods and recruitment have been previously published (Brown et al., 1999; Lee et al., 2005). Briefly, women were randomly selected from Medicare, the National Health Insurance Database, which includes all permanent residents of Australia. ALSWH collects self-reported data using mailed and online surveys at roughly 3-year intervals and has linked the study data with administrative records after the women gave their consent to participate in the study. The surveys include questions about: health conditions, symptoms, and diagnoses; use of health services; health-related quality of life; social circumstances, including work and time use; demographic factors; and health behaviours.

The response rate for the 1946–1951 cohort at Survey 3 in 2001 (then aged 50–55 years) was 83% of those who had completed Survey 1 (1996) and had not died ($n=115$) or become too ill to complete further surveys ($n=21$). Complete FFQ data were available for 11,196 women aged 50–55 years (Survey 3, 2001) and 9738 of these had data available for analysis when they were 56–61 years (Survey 5 in 2007).

2.4. Dietary assessment for ALSWH

ALSWH uses the Dietary Questionnaire for Epidemiological Studies (DQES) Version 2 FFQ. Both the development of the questionnaire (Ireland et al., 1994) and its validation in young Australian women has been previously reported (Hodge et al., 2000). This questionnaire asks respondents to report their usual consumption of 74 foods and six alcoholic beverages over the preceding 12 months using a 10-point frequency scale. Additional questions are asked about the number of serves or type of fruit, vegetables, bread, dairy products, eggs, fat spreads and sugar and further details are provided in Hodge et al. (2000). Nutrient intakes were computed from NUTTAB 1995, a national government food composition database of Australian foods NUTTAB95 (Lewis et al., 1995), using software developed by the Cancer Council of Victoria. The validation of the FFQ against a 7-day weighted food record showed Pearson correlation coefficient=0.40 for dietary zinc and 0.44 for dietary iron. The FFQ validation study deemed the correlation coefficient acceptable as it is of similar magnitude to those previously reported (Hodge et al., 2000).

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