Journal of Affective Disorders 141 (2012) 79–85

Contents lists available at SciVerse ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research report

Nutrient intakes and the common mental disorders in women

Felice N. Jacka [a,b,*], Michael Maes [c], Julie A. Pasco [d,e], Lana J. Williams [a,b], Michael Berk [a,b,f,g]

[a] Barwon Psychiatric Research Unit, School of Medicine, Deakin University, Australia
[b] Department of Psychiatry, The University of Melbourne, Australia
[c] Piyavate Hospital, Bangkok, Thailand, Thailand
[d] Barwon Epidemiology & Biostatistics Unit, School of Medicine, Deakin University, Australia
[e] NorthWest Academic Centre, Department of Medicine, The University of Melbourne Australia
[f] Orygen Youth Health, The University of Melbourne, Australia
[g] Mental Health Research Institute, Australia

ARTICLE INFO

Article history:
Received 17 November 2011
Received in revised form 10 February 2012
Accepted 10 February 2012
Available online 6 March 2012

Keywords:
Depression
Anxiety
Psychiatric
Diet
Nutrients
Nutrition

ABSTRACT

Background: There is an increasing recognition of the role of nutrition in depression and anxiety. Magnesium, folate and zinc have all been implicated in depressive illness, however there are few data on these nutrients in anxiety disorders and the data from population-studies are limited.
Aims: In a large, randomly-selected, population-based sample of women, this study aimed to examine the relationship between the dietary intakes of these three micronutrients and clinically determined depressive and anxiety disorders and symptoms.
Methods: Nutrient intakes were determined using a validated food frequency questionnaire. The General Health Questionnaire-12 measured psychological symptoms, and a clinical interview (Structured Clinical Interview for DSM-IV-TR, non-patient edition) assessed current depressive and anxiety disorders.
Results: After adjustments for energy intake, each standard deviation increase in the intake of zinc, magnesium and folate was associated with reduced odds ratio (OR) for major depression/dysthymia (zinc: OR = 0.52, 95% confidence interval (CI) 0.31 to 0.88; magnesium: OR = 0.60, 95% CI 0.37 to 0.96; folate: OR = 0.66, 95% CI 0.45 to 0.97). There was also an inverse association between the intake of magnesium and zinc and GHQ-12 scores (zinc: $z\beta = -0.16$, 95% CI −0.29 to −0.04; magnesium: −0.14, 95% CI −0.26 to −0.03). These relationships were not confounded by age, socioeconomic status, education or other health behaviours. There was no relationship observed between any nutrient and anxiety disorders.
Conclusion: These results demonstrate an association between the dietary intakes of magnesium, folate and zinc and depressive illnesses, although reverse causality and/or confounding cannot be ruled out as explanations.

1. Introduction

In recent years, there has been an increasing interest in the role of nutrition in depression. Apart from the extensive investigations focused on long-chain omega-3 fatty acids (for review see Parker et al., 2006), three micronutrients in particular have been examined in depression: zinc, magnesium and folate. Zinc is a trace mineral involved in modulating the function of NMDA receptors (Takeda, 2000), which in turn play a critical role in synaptic plasticity in areas of the brain salient to depressive illness, such as the hippocampus and amygdala (Nestler et al., 2002). In animal models of depression, zinc treatment produces antidepressant-like effects (Kroczka et al., 2000, 2001; Nowak et al., 2003b; Rosa et al., 2003) and enhances the efficacy of common antidepressant medications (Kroczka et al., 2001). In humans, decreased serum zinc is described in individuals with MDD

* Corresponding author at: Barwon Psychiatric Research Unit, School of Medicine, Deakin University. Tel.: +61 3 52603084; fax: +61 3 52465165.
E-mail addresses: felice@barwonhealth.org.au, felicejacka@gmail.com (F.N. Jacka).

0165-0327/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2012.02.018

(Maes et al., 1994, 1997b; McLoughlin and Hodge, 1990), while serum zinc levels are negatively correlated with illness severity (Maes et al., 1994) and treatment resistance (Maes et al., 1997b). Moreover, zinc supplementation has been shown to enhance the efficacy of antidepressant therapy (Nowak et al., 2003a), while two very recent studies have shown inverse relationships between the dietary intake of zinc and self-reported depression in pregnant women (Roy et al., 2011) and female students (Amani et al., 2011).

Magnesium is another micronutrient thought to play role in depression. A magnesium-deficient diet has been shown to increase depression- and anxiety-related behaviour in mice (Singewald et al., 2004), while magnesium treatment appears to improve such behaviours in animal models (Poleszak et al., 2004, 2005). In humans, Jacka et al. (2009) have reported an inverse relationship between dietary magnesium intake and self-reported depression, but not anxiety, in a large sample of community-dwelling men and women in Norway. However, to date there have been no comprehensive studies investigating the link between the dietary intake of either zinc or magnesium and clinically-determined depressive and anxiety disorders in humans.

Finally, folate deficiencies have been associated with depression in a range of clinical and epidemiological studies. Symptoms of depression such as apathy, fatigue, insomnia, irritability and impaired concentration, are commonly seen in various states associated with deficiencies of folate and the results of more than 20 clinical studies have indicated that serum folate deficiency affects as many as one-third of psychiatric patients (Alpert et al., 2000). Serum folate levels are related to treatment response in major depression (Fava et al., 1997; Papakostas et al., 2005), while folate supplementation appears to enhance antidepressant treatments (Taylor et al., 2004). A relationship between low serum folate and depression is also seen in both cross-sectional (Morris et al., 2003) and prospective (Kim et al., 2008) population-based studies, while the dietary intake of folate is also related to self-reported depression cross-sectionally (Tolmunen et al., 2003) and to the risk for clinical depression over time (Tolmunen et al., 2004a), although the findings are equivocal (Hakkarainen et al., 2004).

In this study, we aimed a priori to examine the dietary intake of those three micronutrients that are supported by extant evidence and the common mental disorders and symptoms in a large, randomly-selected, population-based sample of adult women. Our hypothesis was that women with lower dietary intakes of each of these micronutrients would be more likely to have clinical depressive and anxiety disorders and higher levels of psychiatric symptomatology.

2. Methods

2.1. Participants

The Geelong Osteoporosis Study (GOS) is an ongoing epidemiological study based in south-eastern Australia. An age-stratified, randomly-selected, population-based sample of 1494 women aged 20–94 years was recruited between 1994 and 1997, with a participation of 77.1% (Pasco et al., in press). These women have continued to return for biennial follow-up assessments that include comprehensive measures of lifestyle, medical and family history, medication use, as well as anthropometric, body composition and bone fragility measures. At the ten-year GOS assessments, a psychiatric component was introduced to the study. Of the 1127 women who participated in the GOS 10-year follow-up (Pasco et al., in press), participants for whom psychiatric or dietary data were not available at the time of the study ($n = 81$) were excluded from the analyses, resulting in a sample of 1046 women aged 20–93 years available for analysis. The Barwon Health Human Research Ethics Committee approved the study, and written informed consent was obtained from all participants.

2.2. Dietary assessments

Habitual diet was assessed using the Cancer Council Victoria dietary questionnaire (Giles and Ireland, 1996). This is a comprehensive, computer-read, food frequency questionnaire (FFQ), validated for assessing habitual dietary intake in the Australian population (Hodge et al., 2000). This questionnaire reports participant's usual consumption of 74 foods and six alcoholic beverages over the preceding 12 months using a 10-point frequency scale. Nutrient intakes, including energy, were computed from the dietary data using NUTTAB95 nutrient composition data.

2.3. Psychiatric assessments

The Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition (SCID-I/NP) (First et al., 2002) was the primary diagnostic instrument for the common mental disorders. This is the gold-standard assessment tool comprising a validated, semi-structured clinical interview for the major axis one psychiatric disorders in DSM-IV-TR. Diagnoses of current major depressive disorder, dysthymia and anxiety disorders were our outcomes of interest, as they comprise the high prevalence mental disorders. Researchers trained in psychology and administration of the SCID-I/NP conducted these interviews. Psychiatric symptoms were measured with the self-reported General Health Questionnaire (GHQ-12) (Goldberg and Hillier, 1979).

2.4. Covariates

Socioeconomic status was determined using Socioeconomic Index For Areas (SEIFA) index scores based on the 2006 Australian Bureau of Statistics census data. It was decided a priori to use the Index of Relative Socioeconomic Advantage and Disadvantage, which accounts for high and low income and the type of occupation from unskilled employment to professional positions. A low score on this index identifies the most disadvantaged (quintile 1), and a high score identifies the most advantaged (quintile 5). Information regarding the highest educational level attained was derived from baseline assessments, and comprised four categories, from primary schooling only (1), to (4) university or other tertiary qualification. Physical activity was assessed by self-report questionnaire and ranged from (1) chair or bedridden, or limited activity throughout the home, through to (4) very active. Alcohol consumption in grams per day was ascertained from the dietary questionnaire and was subsequently categorised according to 2001 recommendations for women ((NHMRC), 2001) as the following: zero consumption (1), 1–14 standard drinks per week (2),

and 15 or more standard drinks per week (3). Current cigarette smoking, yes/no, was self-reported. Height was measured to the nearest 0.1 cm and body weight was measured to the nearest 0.1 kg. Body mass index (BMI) was calculated from these measurements as weight/height^2 (kg/m^2). Although nutritional supplement use was self-reported by participants, the data were of insufficient detail or quality to adequately determine intakes of the investigated nutrients. However, supplement use (yes/no) was also tested as a potential confounder, as those taking nutrient supplements were more likely to have a common mental disorder ($p = 0.02$).

2.5. Statistical analyses

In calculating the intakes of individual nutrients such as zinc, nutrients in alcohol were added to those calculated from food intake in the FFQ to calculate a total intake amount for each nutrient per day. All nutrient and GHQ-12 scores were positively skewed and were normalised using a natural log transformation. All exposure variables and GHQ-12 scores were subsequently standardised using z-scores and expressed as standard deviation units.

Multivariate linear regression analyses were used to assess the relationship of nutrient intakes as exposures and GHQ-12 scores as outcomes. Logistic regression models were also developed to estimate odds ratios with 95% confidence intervals using current major depressive disorder/dysthymia and anxiety disorders as the outcomes of interest. For each analysis, the following covariates were entered sequentially in order to test their contribution to the mental health outcomes: age, socioeconomic factors (SEIFA scores and education), health behaviours (physical activity, alcohol consumption and smoking); and energy intake. BMI and supplement use were also tested in the models as explanatory variables. These models took into account potential non-linear associations and interactions.

There were no missing data on dietary variables. There were missing data for GHQ-12 scores ($n = 23$) and listwise exclusions were used when GHQ-12 was the outcome variable, resulting in a sample of 1000 women for these analyses. There were 24 participants with missing data on BMI. There were no missing data on any other variables.

3. Results

Table 1 presents characteristics of the study participants with and without depressive and anxiety disorders. Comparisons revealed no evident differences between those with and without these disorders on any of the included variables.

Median intakes and interquartile ranges of nutrients were as follows: zinc (9.6 mg/day, IQR 7.5 to 12.2); magnesium (240.9 mg/day, IQR 189.5 to 304.4); and folate (261.6 μ/day, IQR 322.8 to 210.7). While 70% of women in the sample met or exceeded the recommended daily intake (RDI) for zinc (8 mg/day), only 26% of women met or exceeded the RDI of magnesium (320 mg/day), and 8% met or exceeded the RDI for folate (400 μ/day). The correlations between nutrients were high (all $r > 0.7$, $p < 0.001$), precluding the inclusion of all nutrients in the same statistical models.

Table 2 presents the results of linear regression analyses with nutrient intakes as exposures and GHQ-12 scores as the outcome variable of interest. After adjustment for all covariates, the intake of both zinc and magnesium was inversely related to GHQ-12 scores. Each standard deviation increase in zinc and magnesium was associated with an approximate 0.15 standard deviation decrease in GHQ-12 scores. There tended to be an inverse relationship between folate intake and GHQ-12 scores.

Table 3 presents the results of logistic regression analyses. Age, socioeconomic status, health behaviours and BMI did not confound the relationships examined. The only identified confounder was energy intake, and all figures cited are concordantly adjusted. For each standard deviation increase in nutrient intakes, the likelihood of current depressive disorders was reduced by between a third and a half. The relationship between nutrient intakes and anxiety disorders was not statistically significant (all $p > 0.05$).

4. Discussion

Hypotheses regarding the association between the nutrients magnesium, folate and zinc and mental health were largely supported by the data, with the intake of each of these nutrients from food associated with reduced psychiatric symptomatology and the likelihood of depressive disorders. However, the relationship between nutrient intakes and anxiety disorders, while in the same direction, was not significant.

4.1. Magnesium

The inverse relationship between magnesium intake and GHQ-12 scores was in the same direction, and of almost identical magnitude to that previously demonstrated in a large community-based study undertaken in Norway (Jacka et al., 2009). In that study of nearly 6000 adults, after adjustments for a wide range of lifestyle, socioeconomic and medical variables, each one standard deviation decrease in magnesium intake was associated with a 0.11 standard deviation increase in depression score on the Hospital Anxiety and Depression Scale. Also in common with the Norwegian study (Jacka et al., 2009) was the relationship of nutrient intakes to anxiety disorders, wherein the associations were in the same direction as to depression but failed to reach statistical significance. It is unclear as to why the relationship between nutrient intakes and anxiety disorders may be less apparent. One explanation is that biological pathways that underpin depression and anxiety differ, with differential mechanisms influenced by the presence or absence of nutrients. Another explanation is that of reverse causality, wherein the influence of depression on dietary habits is different to that of anxiety.

We have previously proposed that one pathway by which magnesium may be linked to depression is via its contribution to immune system functioning (Jacka et al., 2009). Systemic inflammation and cell-mediated immune activation are prominent features of major depression (Maes, 2011). Magnesium has strong anti-inflammatory effects (Almoznino-Sarafian et al., 2007) and studies in animal models have shown that induced magnesium deficiency in rats results in a systemic pro-inflammatory/pro-oxidant state (Weglicki et al., 1992). In humans, large community studies such as the National Health and Nutrition Survey (NHANES) in the US have reported an inverse relationship between magnesium intake and systemic

Table 1
Characteristics of study sample: comparisons between those with and without depressive/anxiety disorders.

		Depressive/anxiety disorders				p-Value
		No		Yes		
		(n = 905)		(n = 118)		
			IQR		IQR	
Age	(years)	52	34–67	49	34–60	0.11
BMI	(kg/m^2)	26	23–31	27	24–31	0.64
Energy	(kJ/day)	6561	5208–8055	6880	5562–8489	0.13
Socioeconomic status			%		%	
	1 (low)	140	16	20	17	0.38
	2	197	22	22	19	
	3	207	23	29	25	
	4	171	19	29	25	
	5	190	21	18	15	
Education						
	Primary	36	4	7	6	0.76
	Some secondary	380	42	48	41	
	Completed secondary	224	25	27	23	
	Post-secondary	265	29	36	30	
Physical activity						
	Chair or bedridden/limited activity	46	5	7	6	0.48
	Sedentary	144	16	24	20	
	Active	477	53	62	53	
	Very active	238	26	25	21	
Current smoker						
	Yes	116	13	23	20	0.05
	No	789	87	95	80	
Alcohol consumption						
	Zero consumption	173	19	24	20	0.89
	1–14 standard drinks per week	601	66	79	67	
	15 or more standard drinks per week	131	15	15	13	

inflammation (King et al., 2005; Song et al., 2005). Pro-inflammatory states are also implicated in a range of health conditions comorbid with depression, such as cardiovascular disease, osteoporosis, obesity and the metabolic syndrome (Shoelson et al., 2007; Sutherland et al., 2004), and the low intakes of magnesium reported in our study may have implications for these diseases in addition to depression.

4.2. Folate

The relationship between folate intake and the mental health measures was less prominent than that of magnesium and zinc, with only a trend towards an association between dietary folate and reduced GHQ-12 scores. It is may be that this is a result of the consistently very low levels of intake in the sample obscuring this relationship. However, the relationship between higher folate intake and a lower likelihood for major depression/dysthymia is in accordance with previous community-based studies showing a relationship between folate intake and the likelihood of depression in cross-sectional studies (Murakami et al., 2008; Tolmunen et al., 2003), and over time (Tolmunen et al., 2004a). For example, in a study of 2313 middle-aged Finnish men, intakes of folate were measured at baseline and discharge diagnoses of clinical depression over approximately 10 years were ascertained from national registries. After controlling for numerous covariates, including depressive symptoms at baseline, the dietary

Table 2
Linear regression analyses examining food-derived nutrient intakes and GHQ-12 scores (all transformed and z-score standardised, to be interpreted as standard deviations)[a].

	GHQ-12 scores		
	$_{zf}\beta$	95% CI	p-Value
Zinc	−0.16	−0.29 to −0.04	0.01
Magnesium	−0.14	−0.26 to −0.03	0.02
Folate	−0.09	−0.18 to 0.01	0.06

[a] Adjusted for age, SES, education, PA, alcohol consumption, smoking and energy intake.

Table 3
Logistic regression analyses examining food-derived nutrient intakes and categorical depressive and anxiety disorders (odds ratios and 95% confidence intervals)[a].

	MDD/Dysthymia (n = 60)			Anxiety Disorders (n = 80)		
	OR	95% CI	p-value	OR	95% CI	p-value
Zinc	0.52	0.31 to 0.88	0.01	0.76	0.48 to 1.19	0.23
Magnesium	0.60	0.37 to 0.96	0.03	0.81	0.54 to 1.23	0.32
Folate	0.66	0.45 to 0.97	0.03	0.81	0.58 to 1.13	0.21

[a] Adjusted for energy intake.

consumption of folate below the median was associated with a 2.5-fold increased risk of MDD after all adjustments (Tolmunen et al., 2004a). In the Finnish sample, the average intakes of folate were below the recommended daily intake and this is concordant with our study, wherein the large majority of women consumed less than the RDI of folate.

It is thought that disturbed one-carbon metabolism, which is a consequence of folate deficiency, may be an important factor in depression (Coppen and Bolander-Gouaille, 2005). As methylfolate is required for the synthesis of methionine from homocysteine, folate deficiencies result in increased plasma levels of homocysteine (Tolmunen et al., 2003). Increased total plasma homocysteine is a marker of allostatic load, and high levels have been repeatedly shown in individuals with depression (Bjelland et al., 2003; Bottiglieri et al., 2000; Tolmunen et al., 2004b). Moreover, methionine is a precursor of S-adenosylmethionine (SAM), which is essential for numerous methylation processes in the brain involving monoamines, neurotransmitters and membrane phospholipids (Bottiglieri, 2005). Folate also interacts with inflammatory processes, with folate supplementation demonstrating anti-inflammatory effects in humans (Solini et al., 2006).

4.3. Zinc

Of the nutrients studied, it was zinc intake that demonstrated the strongest relationship to both psychological symptoms and depressive disorders. These results complement previous studies showing a significant reduction in serum zinc levels in patients with MDD compared to controls. For example, Maes et al. (1994) examined levels of zinc in the serum of 48 patients with differing degrees of depression: minor depression, MDD without melancholia and MDD with melancholia, compared to 32 healthy controls. The authors reported that serum zinc was decreased in these patients in a dose–response manner, wherein those with MDD had the lowest levels of zinc (approximately 12% lower than controls) and those with minor depression had intermediate values compared to controls. There was also an inverse relationship between depression severity and zinc levels. Importantly, these decreases were not attributable to either depression-associated anorexia, or to HPA axis hyperactivity, as measured using the dexamethasone test. This finding was replicated in two other studies of patients with MDD, wherein those with MDD had lower levels of serum zinc compared to healthy controls (Maes et al., 1997b, 1999b). In these studies, no relationship between zinc status and either severity or duration of illness, depression-related anorexia, or cortisol levels after dexamethasone challenge (Maes et al., 1997b, 1999b) was observed. However, there were significant assocations between serum zinc and markers of systemic immune system activation, including inverse correlations with plasma interleukin-6, serum neopterin and the CD4/CD8 T cell ratio (Maes et al., 1994, 1997a, b) and positive correlations with serum albumin and trasnferrin, two negative acute phase proteins (Maes et al., 1997b). Therefore, the authors proposed that the observed decreases in serum zinc were secondary to the inflammatory response in depressive illness. In these studies, habitual diet was not measured, and it is not possible to rule out differences in dietary intake as a factor in these findings.

This study is the first to examine the dietary consumption of zinc and its relationship to clinically determined depressive and anxiety disorders and the results support a role for dietary zinc in depressive illnesses, although not in anxiety disorders. There are many reasons to consider zinc as an important component of habitual diet in regards to depressive illness. As well as playing a role in modulating the function of NMDA receptors (Takeda, 2000), and in the stabilisation of cellular membranes (Maes et al., 1997b), adequate zinc is required for the functioning of cells involved in mediating immunity, such as neutrophils and Natural Killer (NK) cells, while zinc deficiency affects cytokine production and the functioning of macrophages and T and B cells (Prasad, 2008). Chronic zinc deficiency also activates the HPA axis, leading to the chronic overproduction of cortisol (Fraker and King, 2004). Moreover, zinc is known to possess anti-inflammatory properties, down-regulating the gene expression of pro-inflammatory cytokines such as TNF-α and IL-1ß (Prasad et al., 2004). Zinc is also an essential factor in polyunsaturated fatty acid (PUFA) metabolism, e.g. zinc is required for the activity of desaturase enzymes, which are responsible for the conversion of essential fatty acids to PUFAs (Russo et al., 1997). In depression, lower serum zinc is associated with reduced levels of EPA and DHA, suggesting that reduced zinc may contribute to the depletion of n-3 PUFAs commonly observed in depression (Maes et al., 1999a). Another important aspect of zinc is the role it plays as a neuro-protector. Zinc is a potent antioxidant as it protects cellular membranes from lipid peroxidation (Maes et al., 1997b); induces the production of metallothionein, which has the ability to scavenge hydroxide — a component of reactive oxygen species (ROS) (Prasad et al., 2004); and protects against DNA damage in humans (Prasad et al., 2004). Zinc also upregulates the expression of the brain derived neurotrophic factor (BDNF) gene in the cortex and hippocampus (Nowak et al., 2005). BDNF is a neuroprotective agent — protecting neurons from oxidative stress and promoting neurogenesis (Duman et al., 1997). In acting as an anti-inflammatory and neuroprotective agent, zinc may thus play a role in depressive illness. In this study, 30% of women consumed less than the RDI of zinc, which may have implications for a range of disease outcomes in addition to that of mental health.

4.4. Limitations

This study is limited by a cross-sectional design, which does not afford a determination of the direction of the relationship between dietary nutrient intakes and mental health. Reverse causality, wherein dietary intakes are a consequence of mental ill health, is another potential explanation for our findings, and there may also be differences in the reporting of diet between those with and without depressive and anxiety disorders. Reverse causality has been examined in studies examining the link between mental health and diet, and the available, although limited, data do not support this explanation (Akbaraly et al., 2009; Jacka et al., 2011; Sanchez-Villegas et al., 2009). Although we adjusted statistically for other potential confounding factors, such as health behaviours and socioeconomic status, we may not have fully captured relevant aspects of those factors. Furthermore, there may be other, unidentified confounding variables that we have not accounted

for. We could not determine the intake of nutrients from supplements, although these may not be nutritionally equivalent. Finally, it may be the case that these nutrients are simply markers of dietary quality. Our previous study identified a dietary pattern ('Traditional'), comprising vegetables, fruits, lean red meats, fish and wholegrains, as being inversely associated with these mental health outcomes (Jacka et al., 2010), and each of these nutrients were moderately to highly correlated with this dietary pattern and each other, precluding the inclusion of each in the same statistical models (McGee et al., 1984) (data not shown). Strengths of the study include the use of gold-standard assessment tools for both nutritional intakes and psychiatric outcomes, the large sample size, the inclusion of a range of potential confounding variables, and a randomly-selected sample of women across the adult age range.

5. Conclusion

The results of this study support the contention that the consumption of nutrient-dense foods plays a role in depression, but not anxiety. Magnesium and folate are prominent components of foods recommended as part of the Australian National Healthy Eating guidelines ((NHMRC), 2003), such as leafy green vegetables, nuts, legumes and wholegrains, while zinc is found in lean meats and seafoods, which are also important components of a healthy diet. Of concern are the very low intakes of magnesium and folate recorded in women in our study. This is in line with findings from the 2008 Victorian Population Health Survey, wherein only 10.5% of women met the recommended five or more serves of vegetables per day (Department of Human Services, 2008). Promoting an increased consumption of nutrient-dense foods may be a useful strategy in the prevention and treatment of depression in the community.

Conflict of interest

All authors have no conflict to declare.

Acknowledgments

This study was funded by the National Health and Medical Research Council of Australia (Project Grants # 454356, 251638) and an unrestricted educational grant from Eli Lilly. The University of Melbourne, Faculty of Medicine, Dentistry and Health Sciences and Australian Rotary Health provided postgraduate scholarships to FNJ and LJW. FNJ is supported by an NHMRC Post-doctoral Training Fellowship (#628912). The funding providers played no role in the design or conduct of the study; collection, management, analysis, and interpretation of the data; or in preparation, review, or approval of the manuscript.

References

Akbaraly, T.N., Brunner, E.J., Ferrie, J.E., Marmot, M.G., Kivimaki, M., Singh-Manoux, A., 2009. Dietary pattern and depressive symptoms in middle age. The British Journal of Psychiatry 195, 408–413.

Almoznino-Sarafian, D., Berman, S., Mor, A., Shteinshnaider, M., Gorelik, O., Tzur, I., Alon, I., Modai, D., Cohen, N., 2007. Magnesium and C-reactive protein in heart failure: an anti-inflammatory effect of magnesium administration? European Journal of Nutrition 46, 230–237.

Alpert, J.E., Mischoulon, D., Nierenberg, A.A., Fava, M., 2000. Nutrition and depression: focus on folate. Nutrition 16, 544–546.

Amani, R., Saeidi, S., Nazari, Z., Nematpour, S., 2011. Correlation between dietary zinc intakes and its serum levels with depression scales in young female students. Biological Trace Element Research 137, 150–158.

Bjelland, I., Tell, G.S., Vollset, S.E., Refsum, H., Ueland, P.M., 2003. Folate, vitamin B12, homocysteine, and the MTHFR 677C->T polymorphism in anxiety and depression: the Hordaland Homocysteine Study. Archives of General Psychiatry 60, 618–626.

Bottiglieri, T., 2005. Homocysteine and folate metabolism in depression. Progress in Neuro-Psychopharmacology & Biological Psychiatry 29, 1103–1112.

Bottiglieri, T., Laundy, M., Crellin, R., Toone, B.K., Carney, M.W., Reynolds, E.H., 2000. Homocysteine, folate, methylation, and monoamine metabolism in depression. Journal of Neurology, Neurosurgery & Psychiatry 69, 228–232.

Coppen, A., Bolander-Gouaille, C., 2005. Treatment of depression: time to consider folic acid and vitamin B12. Journal of Psychopharmacology 19, 59–65.

Department of Human Services, 2008. Victorian population health survey 2008. Health surveillance and evaluation section.

Duman, R.S., Heninger, G.R., Nestler, E.J., 1997. A molecular and cellular theory of depression. Archives of General Psychiatry 54, 597–606.

Fava, M., Borus, J.S., Alpert, J.E., Nierenberg, A.A., Rosenbaum, J.F., Bottiglieri, T., 1997. Folate, vitamin B12, and homocysteine in major depressive disorder. The American Journal of Psychiatry 154, 426–428.

First, M., Spitzer, R., M, G., Williams, J., 2002. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition. (SCID-I/NP). Biometrics Research, New York State Psychiatric Institute, New York.

Fraker, P.J., King, L.E., 2004. Reprogramming of the immune system during zinc deficiency. Annual Review of Nutrition 24, 277–298.

Giles, C., Ireland, P., 1996. Dietary Questionnaire for Epidemiological Studies 555 (Version 2). Cancer Council of Victoria, Melbourne.

Goldberg, D.P., Hillier, V.F., 1979. A scaled version of the General Health Questionnaire. Psychological Medicine 9, 139–145.

Hakkarainen, R., Partonen, T., Haukka, J., Virtamo, J., Albanes, D., Lonnqvist, J., 2004. Food and nutrient intake in relation to mental wellbeing. Nutrition Journal 3, 14.

Hodge, A., Patterson, A.J., Brown, W.J., Ireland, P., Giles, G., 2000. The Anti Cancer Council of Victoria FFQ: relative validity of nutrient intakes compared with weighed food records in young to middle-aged women in a study of iron supplementation. Australian and New Zealand Journal of Public Health 24, 576–583.

Jacka, F.N., Overland, S., Stewart, R., Tell, G.S., Bjelland, I., Mykletun, A., 2009. Association between magnesium intake and depression and anxiety in community-dwelling adults: the Hordaland Health Study. The Australian and New Zealand Journal of Psychiatry 43, 45–52.

Jacka, F.N., Pasco, J.A., Mykletun, A., Williams, L.J., Hodge, A.M., O'reilly, S.L., Nicholson, G.C., Kotowicz, M.A., Berk, M., 2010. Association between western and traditional diets and depression and anxiety in women. The American Journal of Psychiatry 167, 305–311.

Jacka, F., Kremer, P.J., Berk, M., De Silva-Sanigorski, A., Moodie, M., Leslie, E., Pasco, J., Swinburn, B., 2011. A prospective study of diet quality and mental health in adolescents. PLoS One 6, e24805.

Kim, J.M., Stewart, R., Kim, S.W., Yang, S.J., Shin, I.S., Yoon, J.S., 2008. Predictive value of folate, vitamin B12 and homocysteine levels in late-life depression. The British Journal of Psychiatry 192, 268–274.

King, D.E., Mainous III, A.G., Geesey, M.E., Woolson, R.F., 2005. Dietary magnesium and C-reactive protein levels. Journal of the American College of Nutrition 24, 166–171.

Kroczka, B., Zieba, A., Dudek, D., Pilc, A., Nowak, G., 2000. Zinc exhibits an antidepressant-like effect in the forced swimming test in mice. Polish Journal of Pharmacology 52, 403–406.

Kroczka, B., Branski, P., Palucha, A., Pilc, A., Nowak, G., 2001. Antidepressant-like properties of zinc in rodent forced swim test. Brain Research Bulletin 55, 297–300.

Maes, M., 2011. Depression is an inflammatory disease, but cell-mediated immune activation is the key component of depression. Progress in Neuro-Psychopharmacology & Biological Psychiatry 35, 664–675.

Maes, M., D'haese, P.C., Scharpe, S., D'hondt, P., Cosyns, P., De Broe, M.E., 1994. Hypozincemia in depression. Journal of Affective Disorders 31, 135–140.

Maes, M., Bosmans, E., De Jongh, R., Kenis, G., Vandoolaeghe, E., Neels, H., 1997a. Increased serum IL-6 and IL-1 receptor antagonist concentrations in major depression and treatment resistant depression. Cytokine 9, 853–858.

Maes, M., Vandoolaeghe, E., Neels, H., Demedts, P., Wauters, A., Meltzer, H.Y., Altamura, C., Desnyder, R., 1997b. Lower serum zinc in major depression is a sensitive marker of treatment resistance and of the immune/inflammatory response in that illness. Biological Psychiatry 42, 349–358.

Maes, M., Christophe, A., Delanghe, J., Altamura, C., Neels, H., Meltzer, H.Y., 1999a. Lowered omega3 polyunsaturated fatty acids in serum phospholipids and cholesteryl esters of depressed patients. Psychiatry Research 85, 275–291.

Maes, M., De Vos, N., Demedts, P., Wauters, A., Neels, H., 1999b. Lower serum zinc in major depression in relation to changes in serum acute phase proteins. Journal of Affective Disorders 56, 189–194.

Mcgee, D., Reed, D., Yano, K., 1984. The results of logistic analyses when the variables are highly correlated: an empirical example using diet and CHD incidence. Journal of Chronic Diseases 37, 713–719.

Mcloughlin, I.J., Hodge, J.S., 1990. Zinc in depressive disorder. Acta Psychiatrica Scandinavica 82, 451–453.
Morris, M.S., Fava, M., Jacques, P.F., Selhub, J., Rosenberg, I.H., 2003. Depression and folate status in the US Population. Psychotherapy and Psychosomatics 72, 80–87.
Murakami, K., Mizoue, T., Sasaki, S., Ohta, M., Sato, M., Matsushita, Y., Mishima, N., 2008. Dietary intake of folate, other B vitamins, and omega-3 polyunsaturated fatty acids in relation to depressive symptoms in Japanese adults. Nutrition 24, 140–147.
National Health and Medical Research Council (NHMRC), 2001. Australian Alcohol Guidelines: Health Risks and Benefits.
National Health and Medical Research Council (NHMRC), 2003. Dietary Guidelines for Australian Adults. A Guide to Healthy Eating.
Nestler, E.J., Barrot, M., Dileone, R.J., Eisch, A.J., Gold, S.J., Monteggia, L.M., 2002. Neurobiology of depression. Neuron 34, 13–25.
Nowak, G., Siwek, M., Dudek, D., Zieba, A., Pilc, A., 2003a. Effect of zinc supplementation on antidepressant therapy in unipolar depression: a preliminary placebo-controlled study. Polish Journal of Pharmacology 55, 1143–1147.
Nowak, G., Szewczyk, B., Wieronska, J.M., Branski, P., Palucha, A., Pilc, A., Sadlik, K., Piekoszewski, W., 2003b. Antidepressant-like effects of acute and chronic treatment with zinc in forced swim test and olfactory bulbectomy model in rats. Brain Research Bulletin 61, 159–164.
Nowak, G., Szewczyk, B., Pilc, A., 2005. Zinc and depression. An update. Pharmacological Reports 57, 713–718.
Papakostas, G.I., Petersen, T., Lebowitz, B.D., Mischoulon, D., Ryan, J.L., Nierenberg, A.A., Bottiglieri, T., Alpert, J.E., Rosenbaum, J.F., Fava, M., 2005. The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine. The International Journal of Neuropsychopharmacology 8, 523–528.
Parker, G., Gibson, N.A., Brotchie, H., Heruc, G., Rees, A.M., Hadzi-Pavlovic, D., 2006. Omega-3 fatty acids and mood disorders. The American Journal of Psychiatry 163, 969–978.
Pasco, J., Nicholson, G. & Kotowicz, M. in press. Cohort profile: Geelong Osteoporosis Study (GOS). International Journal of Epidemiology. doi:10.1093/ije/dyr148.
Poleszak, E., Szewczyk, B., Kedzierska, E., Wlaz, P., Pilc, A., Nowak, G., 2004. Antidepressant- and anxiolytic-like activity of magnesium in mice. Pharmacology Biochemistry and Behavior 78, 7–12.
Poleszak, E., Wlaz, P., Kedzierska, E., Radziwon-Zaleska, M., Pilc, A., Fidecka, S., Nowak, G., 2005. Effects of acute and chronic treatment with magnesium in the forced swim test in rats. Pharmacological Reports 57, 654–658.
Prasad, A.S., 2008. Zinc in human health: effect of zinc on immune cells. Molecular Medicine 14, 353–357.
Prasad, A.S., Bao, B., Beck, F.W., Kucuk, O., Sarkar, F.H., 2004. Antioxidant effect of zinc in humans. Free Radical Biology & Medicine 37, 1182–1190.
Rosa, A.O., Lin, J., Calixto, J.B., Santos, A.R., Rodrigues, A.L., 2003. Involvement of NMDA receptors and L-arginine–nitric oxide pathway in the antidepressant-like effects of zinc in mice. Behavioural Brain Research 144, 87–93.
Roy, A., Evers, S.E., Avison, W.R., Campbell, M.K., 2011. Higher zinc intake buffers the impact of stress on depressive symptoms in pregnancy. Nutrition Research 30, 695–704.
Russo, C., Olivieri, O., Girelli, D., Guarini, P., Pasqualini, R., Azzini, M., Corrocher, R., 1997. Increased membrane ratios of metabolite to precursor fatty acid in essential hypertension. Hypertension 29, 1058–1063.
Sanchez-Villegas, A., Delgado-Rodriguez, M., Alonso, A., Schlatter, J., Lahortiga, F., Majem, L.S., Martinez-Gonzalez, M.A., 2009. Association of the Mediterranean dietary pattern with the incidence of depression: the Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. Archives of General Psychiatry 66, 1090–1098.
Shoelson, S.E., Herrero, L., Naaz, A., 2007. Obesity, inflammation, and insulin resistance. Gastroenterology 132, 2169–2180.
Singewald, N., Sinner, C., Hetzenauer, A., Sartori, S.B., Murck, H., 2004. Magnesium-deficient diet alters depression- and anxiety-related behavior in mice — influence of desipramine and Hypericum perforatum extract. Neuropharmacology 47, 1189–1197.
Solini, A., Santini, E., Ferrannini, E., 2006. Effect of short-term folic acid supplementation on insulin sensitivity and inflammatory markers in overweight subjects. International Journal of Obesity 30, 1197–1202.
Song, Y., Ridker, P.M., Manson, J.E., Cook, N.R., Buring, J.E., Liu, S., 2005. Magnesium intake, C-reactive protein, and the prevalence of metabolic syndrome in middle-aged and older U.S. women. Diabetes Care 28, 1438–1444.
Sutherland, J.P., Mckinley, B., Eckel, R.H., 2004. The metabolic syndrome and inflammation. Metabolic Syndrome and Related Disorders 2, 82–104.
Takeda, A., 2000. Movement of zinc and its functional significance in the brain. Brain Research. Brain Research Reviews 34, 137–148.
Taylor, M.J., Carney, S.M., Goodwin, G.M., Geddes, J.R., 2004. Folate for depressive disorders: systematic review and meta-analysis of randomized controlled trials. Journal of Psychopharmacology 18, 251–256.
Tolmunen, T., Voutilainen, S., Hintikka, J., Rissanen, T., Tanskanen, A., Viinamaki, H., Kaplan, G.A., Salonen, J.T., 2003. Dietary folate and depressive symptoms are associated in middle-aged Finnish men. Journal of Nutrition 133, 3233–3236.
Tolmunen, T., Hintikka, J., Ruusunen, A., Voutilainen, S., Tanskanen, A., Valkonen, V.P., Viinamaki, H., Kaplan, G.A., Salonen, J.T., 2004a. Dietary folate and the risk of depression in Finnish middle-aged men. A prospective follow-up study. Psychotherapy and Psychosomatics 73, 334–339.
Tolmunen, T., Hintikka, J., Voutilainen, S., Ruusunen, A., Alfthan, G., Nyyssonen, K., Viinamaki, H., Kaplan, G.A., Salonen, J.T., 2004b. Association between depressive symptoms and serum concentrations of homocysteine in men: a population study. American Journal of Clinical Nutrition 80, 1574–1578.
Weglicki, W.B., Bloom, S., Cassidy, M.M., Freedman, A.M., Atrakchi, A.H., Dickens, B.F., 1992. Antioxidants and the cardiomyopathy of Mg-deficiency. American Journal of Cardiovascular Pathology 4, 210–215.