Low dietary intake of magnesium is associated with increased externalising behaviours in adolescents

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Abstract

Objective: Adequate zinc and magnesium intakes may be beneficial for the prevention and treatment of mental health problems, such as depression, anxiety and attention-deficit hyperactivity disorder. We aimed to investigate the prospective association between dietary intakes of zinc and magnesium and internalising and externalising behaviour problems in a population-based cohort of adolescents.

Design: Prospective analysis (general linear mixed models) of dietary intakes of zinc and magnesium assessed using a validated food frequency questionnaire and mental health symptoms assessed using the Youth Self-Report (YSR), adjusting for sex, physical activity, family income, supplement status, dietary misreporting, BMI, family functioning and energy intake.

Setting: Western Australian Pregnancy Cohort (Raine) Study.

Subjects: Adolescents (*n*=684) at the 14 and 17 year follow-ups.

Results: Higher dietary intake of magnesium (per standard deviation) was significantly associated with reduced externalising behaviours (β -1.45; 95% CI -2.40, -0.50; p = 0.003). There was a trend towards reduced externalising behaviours with higher zinc intake (β -0.73; 95% CI -1.57, 0.10; p = 0.085).

Conclusions: This study shows an association between higher dietary magnesium intake and reduced externalising behaviour problems in adolescents. We observed a similar trend, although not statistically significant, for zinc intake. Randomised controlled trials are necessary to determine any benefit of micronutrient supplementation in the prevention and treatment of mental health problems in adolescents.

Introduction

Zinc and magnesium are essential minerals involved in functioning of the central nervous system. Dietary sources of zinc include red meat, poultry, legumes, nuts and seeds, certain types of seafood (e.g. oysters, crab and lobster), whole grains, fortified breakfast cereals and dairy products. Magnesium is widely distributed in plant foods, particularly green leafy vegetables, legumes, nuts, seeds and whole grains. Zinc is a co-factor of many enzymes that play a role in brain function[(1)] and is present in regions of the brain associated with the pathophysiology of mood disorders, including the amygdala, hippocampus and cerebral cortex[(2)]. Zinc modulates neuronal excitability by inhibiting both the *gamma*-aminobutyric acid (GABA) and N-methyl-D-aspartate (NMDA) receptors[(3)] and has shown antidepressant-like activities in animal models[(4-6)]. Magnesium is another potent antagonist of the NMDA receptor complex[(7)] and magnesium deficiency has been related to symptoms such as agitation, anxiety, irritability and hyperexcitability[(8)]. In rodent models, magnesium depletion increases anxiety and depression-like behaviours[(9, 10)], and mice with low erythrocyte magnesium levels have been found to exhibit more aggressive behaviour than those with high magnesium levels[(11)].

Recently, Jacka and colleagues (2012) reported that dietary intakes of zinc and magnesium were inversely and cross-sectionally associated with depressive and anxiety scores in a population-based sample of women (n = 1046)[(12)]. Other studies have shown inverse relationships between dietary zinc intakes and depression in women[(13-16)]. Furthermore, research suggests that zinc supplementation as an adjunct to antidepressant drug treatment significantly lowers depressive symptoms in depressed patients compared to antidepressant treatment alone [(17-19)]. Research on magnesium with depressive and anxiety symptoms is less conclusive. Although energy-adjusted magnesium intakes were inversely associated with depression scores in a sample of Norwegian community-dwelling men and women (n = 5708)[(20)], this finding was not supported in a cohort (n = 12,939) of Spanish university graduates[(21)]. Zinc and magnesium supplementation have both been shown to be beneficial in the treatment of attention-deficit hyperactivity disorder (ADHD) in children, as a stand-alone treatment and as an adjunct to medication[(22-24)]; however, limited research exists in this area.

While there is increasing recognition of the role of magnesium and zinc in mental health, most of the evidence to date has focused on adult participants, often with a cross-sectional design or in the context of a clinical trial. In this study, we aimed to examine the prospective association between dietary intakes of zinc and magnesium and internalising (withdrawn, somatic complaints, anxious/depressed) and externalising (attention problems, aggressive/delinquent) behaviour problems in a population-based cohort of adolescents at the 14 and 17 year follow-ups. Our hypothesis was that lower dietary intakes of zinc and magnesium would be associated with increased internalising and externalising behaviour problems.

Methods

Participants

The Western Australian Pregnancy Cohort (Raine) Study methodology has been described previously[25]. In brief, a total of 2900 pregnant women attending the public antenatal clinic at King Edward Memorial Hospital, or nearby private practices, were recruited into the Raine Study between May 1989 and November 1991 and gave birth to 2868 children. These children underwent assessment at birth and at regular intervals. Recruitment and all follow-ups were approved by the ethics committees of King Edward Memorial Hospital for Women and the Princess Margaret Hospital for Children, Perth, Western Australia. Informed and written consent was obtained from the participant and/or their primary caregiver for all follow-ups. Data collection for the 14 and 17 year follow-ups occurred between 2003-2005 and 2006-2008, respectively.

Assessment of mental health

Mental health at 14 and 17 years was assessed using the Youth Self Report (YSR), which is a version of the Child Behaviour Checklist for Ages 4-18 (CBCL/4-18) and is designed specifically for self-report in adolescents. The YSR is a 118-item empirically-validated and reliable measure of emotional and behavioural problems in children and adolescents[26, 27]. The YSR generates an externalising problem score that describes uncontrolled and anti-social behaviour (attention problems, aggressive/delinquent) and an internalising problem score that describes over-controlled and inhibited behaviour (withdrawn, somatic complaints, anxious/depressed), with higher scores indicating a higher level of emotional and behavioural problems. We calculated standardised T-scores for total, externalising and internalising problem scales, normalised separately for boys and girls by age.

Assessment of zinc and magnesium intakes

A semi-quantitative food frequency questionnaire (FFQ) developed by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Adelaide, Australia was used to assess zinc and magnesium intakes[28]. This 212-item FFQ assessed usual dietary intake over the previous year, collecting information on the frequency of consumption of individual foods, mixed dishes and beverages, along with information on usual serving sizes in relation to a standard serving size in household units. Seasonal differences were accounted for by asking how often foods were eaten in summer and winter. At the 14 year follow-up, the primary caregiver was asked to complete the FFQ in association with the adolescent. At the 17 year follow-up, the FFQ was completed by the adolescent. The questionnaire has been validated against a 3-day food record in the same cohort at the 14 year follow-up[29].

All questionnaires were checked by a research nurse and queries were clarified with the adolescent or primary caregiver. Food intake data were entered into a database and verified by CSIRO. Estimated daily micronutrient intakes were provided by CSIRO using nutrient composition derived from four sources: the Australian nutrient database (NUTTAB95)[30]; the British Food Composition Tables[31]; the US Department of Agriculture food tables; and manufacturers' data. Questionnaires were excluded if the daily energy intake reported was implausible (< 3000 or > 20 000 kJ per day).

Potential confounding variables

Participants were weighed to the nearest 100 g using a Wedderburn Digital Chair Scale and height was determined to the nearest 0.1 cm with a Holtain Stadiometer. Body Mass Index (BMI) was calculated as weight in kilograms divided by height in metres squared. Dietary misreporting was estimated using the Goldberg method[32], which is widely used to estimate the cut-off levels for under-reporters, plausible reporters and over-reporters in dietary surveys. Current use of nutritional supplements (yes/no) was collected from a self-reported questionnaire.

Physical activity was assessed using a self-reported questionnaire based on exercise outside of school hours per week, with exercise defined in three categories for activity causing breathlessness or sweating (≥ 4 times per week, 1-3 times per week and < once per week). Annual family income before tax was completed by the primary caregiver and reported in three categories (≤ $40,000, $40,001-78,000 and > $78,000). Family functioning was included in order to account for a number of related family factors, including communication and parental conflict, allowing for a parsimonious model whilst also considering the importance of family in offspring mental health. Family functioning was measured using the 12-item general functioning scale (GFS) from the

McMaster Family Assessment Devise[33]. The scale has been shown to be reliable and internally consistent [34], with lower scores on the GFS representing poorer family functioning and higher scores representing better family functioning.

Statistical analysis

Characteristics of participants who completed the FFQ and the YSR at both 14 and 17 years were compared with non-participants from the original cohort. Sex, race, family income during pregnancy, maternal age at birth, maternal education and maternal pre-pregnancy BMI were compared using Chi-square tests. Baseline characteristics were described for participants in the current study, including sex, YSR T-scores (total, internalising and externalising), zinc and magnesium intakes, energy intake, dietary misreporting, supplement use, BMI, physical activity, family income and family functioning.

Zinc and magnesium intakes at 14 and 17 years were converted to z-scores within each follow-up separately. General linear mixed models were used to investigate the prospective univariate relationships between zinc and magnesium intakes and YSR T-scores (total, internalising and externalising). Models were then adjusted for sex, physical activity, family income, supplement status, dietary misreporting, BMI, family functioning and energy intake. Interactions between time and zinc or magnesium intakes were explored in order to determine whether the effect of intakes on the YSR-T scores were different at the two follow-ups. Similarly, interactions between sex and zinc or magnesium intakes were investigated in order to determine whether there were sex differences in the effect of zinc and magnesium intakes on YSR T-scores. Analyses were performed using IBM SPSS Statistics Release Version 19.9.9.1 (IBM SPSS Inc., 2010, Chicago, IL). Statistical significance was defined as $p < 0.05$.

Results

A total of 684 adolescents completed the YSR and FFQ at both follow-ups (Figure 1). Compared with those from the original cohort who did not participate in the current study ($n = 2184$), participants were more likely to be female, Caucasian, to come from families with a higher income during pregnancy and to have mothers with a higher age, higher education during pregnancy and healthier pre-pregnancy body mass index ($p < 0.05$).

Mean YSR total, internalising and externalising T-scores were approximately 50 at both follow-ups (Table 1), which is consistent with population norms. Dietary zinc and magnesium intakes were similar at 14 and 17 years: mean zinc intake was approximately 12 mg/day and magnesium intake was approximately 310 mg/day. The mean intakes in this population were in line with the Estimated Average Requirements for zinc and magnesium (zinc, 11 mg/day for males and 6 mg/day for females; magnesium, 340 mg/day for males and 300 mg/day for females).

In univariate analyses (*n* = 684), zinc and magnesium intakes (per SD) were not significantly associated with internalising or externalising behaviours over the three-year study period (Table 2). However, after adjusting for potential confounders (*n* = 667 at 14 years and *n* = 607 at 17 years), including sex, physical activity, family income, supplement use, dietary misreporting, BMI, family functioning and energy intake, there was a significant inverse association between magnesium and externalising behaviour problems. Although there was a trend towards improved externalising behaviour problems with increased zinc intake, the association did not reach the statistically significant level we had specified. There were no significant interactions between time and zinc or magnesium intakes, and between sex and zinc or magnesium intakes. Further, there were no significant associations between zinc and magnesium intakes and internalising behavior problems or total YSR T-scores.

Discussion

This study examined the prospective associations between zinc and magnesium intakes and internalising and externalising behaviour problems in adolescents. The results support our hypothesis that dietary magnesium intakes are inversely associated with externalising behaviour problems in adolescents. Although we found no significant associations between zinc and internalising or externalising behaviours, there was a trend towards higher zinc intake and reduced externalising behaviour problems. Externalising behaviour problems include attention problems, rule-breaking behaviours and aggressive behaviours, meaning that there is some overlap between our findings and previous research that found beneficial effects of magnesium supplementation on symptoms of ADHD[22-24]. However, we did not find a significant association between zinc or magnesium intake and internalising behaviour problems, which contrasts with previous literature[12-15, 17, 18, 20].

There are several reasons why magnesium intake may relate to externalising behaviour problems in adolescents. Some insight is provided by considering symptoms of ADHD, which share characteristics of externalising behaviours and may also be influenced by intake magnesium. Magnesium plays a role in the function of the serotonergic, noradrenergic and dopaminergic receptors, which are related to the pathophysiology of ADHD[35]. Improved ADHD symptoms have been reported in children after magnesium supplementation[24, 36].

We found no prospective association between dietary zinc and internalising behaviour problems (withdrawn, somatic complaints, anxious/depressed) in our study, which is consistent with results from a longitudinal study of 2317 middle-aged Finnish men[37]. In contrast, dietary intakes of zinc have repeatedly shown an inverse relationship with depressive symptoms in cross-sectional analyses, particularly in women[12-15, 38-40]. We also found no association between dietary magnesium intakes and internalising behaviour problems, which is consistent with a study in 12,939 Spanish university graduates[21]. However, a number of cross-sectional studies have found an inverse association between dietary magnesium intakes and depressive symptoms[12, 20, 38, 41, 42]. Differences between our results and those reported elsewhere may stem, at least in part, from differences in the age of participants, and the nature and duration of follow-up. Our study included population-based adolescents followed from 14 to 17 years, whereas most of the previous literature has included adult participants, often assessed cross-sectionally (in the case of population-based studies) or in the context of a clinical trial. Further research is warranted to determine if zinc and magnesium intakes relate to internalising problems in some age or demographic groups and not others.

The equivocal results in studies examining dietary zinc and magnesium intakes and mental health may also relate to the use of different mental health assessment tools. An advantage of our study is the use of the YSR, since it distinguishes between internalising and externalising behaviour problems - a differentiation that is not captured by all mental health measures. At the same time, the YSR does not generate clinical diagnoses and we cannot comment on associations between dietary intakes and clinically significant depression, anxiety or ADHD. Differences in how mental health problems are conceptualised and assessed may contribute to differences in results across studies, again speaking to the need for further research in this area.

Strengths of our study were the prospective study design, use of a validated food frequency questionnaire, and extensive characterisation of a population-based cohort. The latter allowed us to assess the effect of dietary zinc and magnesium intakes on mental health while accounting for a wide range of potential confounding factors. A limitation of our study was the use of self-reported questionnaire, rather than clinical diagnosis, to assess mental health problems. While self-report assessment of mental health may lead to more truthful reporting than face-to-face assessment, self-report measurements are subject to reporting bias. It can also be difficult to accurately assess nutrient intakes using an FFQ. However, the FFQ used in this study was validated against a 3-day food record in the same cohort and the mean daily intakes of zinc and magnesium were similar when measured by the FFQ and the 3-day food record[29].

It is possible that behaviour problems result in altered appetite and eating habits, including increased consumption of processed foods, which are lower in minerals such as zinc and magnesium. Furthermore, growing evidence suggests that obesity may be related to numerous psychiatric disorders, and several behavioural and biological pathways have been proposed to explain this potential relationship, which are outside the realm of nutrition[43]. In adjusting for confounders, we have attempted to present evidence for a causative relationship; however, we cannot rule out the possibility of reverse causality or residual confounding. A further limitation of the study was the loss to follow-up. Participants included in the current study were more likely to be from families with higher socioeconomic status relative to participants from the original cohort and care should be taken when generalising results to the wider community. However, although attrition may have been higher for those participants suffering mental health difficulties, the YSR T-scores in the current study reflect the population norm.

Given that dietary magnesium intake can be optimised through the consumption of nutrient-dense foods and supplementation, our study has important public health implications. Promoting increased consumption of magnesium-rich foods, such as green leafy vegetables, legumes, nuts, seeds and whole grains, along with supplementation to address identified micronutrient deficiencies, may be a useful strategy to prevent mental health and behavioural problems in adolescents. In order to determine any benefit of magnesium and/or zinc supplementation in the prevention and treatment of externalising behaviour problems, further randomised controlled trials using optimal doses are necessary.

Table 1. Characteristics of the Raine Study participants for whom Youth Self Report and micronutrient intakes were available at both the 14 and 17 year follow-ups (n = 684)

	14 year follow-up		17 year follow-up	
	n		*n*	
Sex (%)				
Male	*319*	46.6	*319*	46.6
Female	*365*	53.4	*365*	53.4
Youth Self Report T-scores (mean, SD)				
Total	*684*	49.6 (9.0)	*684*	51.0 (9.7)
Internalising	*684*	47.3 (9.4)	*684*	48.9 (10.6)
Externalising	*684*	49.2 (9.5)	*684*	50.7 (10.1)
Zinc [mg/day (mean,SD)]	*684*	12.4 (4.2)	*684*	12.6 (5.5)
Magnesium [mg/day (mean, SD)]	*684*	308.3 (103.8)	*684*	311.8 (135.6)
Energy intake [kcal/day (mean, SD)]	*684*	2253.5 (726.7)	*684*	2305.5 (1012.1)
Dietary reporting (%)				
Under-reporter	*286*	41.8	*372*	54.5
Plausible-reporter	*352*	51.5	*272*	39.9
Over-reporter	*46*	6.7	*38*	5.6
Supplement status (%)				
Supplement user	*94*	13.7	*177*	25.9
Supplement non-user	*590*	86.3	*507*	74.1
Body mass index [kg/m^2 (median, IQR)]	*683*	20.1 (4.3)	*682*	21.9 (4.2)
Physical activity (%)				
≥ 4 times per week	*219*	32.1	*169*	25.8
1-3 times per week	*397*	58.1	*349*	53.4
< once per week	*67*	9.8	*136*	20.8
Family income (%)				
≤ $40,000 per year	*160*	23.7	*93*	14.5
$40,001-78,000 per year	*272*	40.4	*194*	30.2
> $78,000 per year	*242*	35.9	*355*	55.3
Family functioning (mean, SD)	*676*	1.8 (0.4)	*648*	1.8 (0.5)

SD, standard deviation; IQR, interquartile range

Table 2. General linear mixed model coefficients for Youth Self Report T-scores and zinc and magnesium intakes at ages 14 and 17 years

	Zinc		Magnesium	
	β (95% CI)[1]	*p*	β (95% CI)[1]	*p*
		Unadjusted		
Total	0.35 (-0.25, 0.96)	0.256	0.31 (-0.16, 0.80)	0.191
Internalising	0.09 (-0.58, 0.76)	0.796	0.01 (-0.51, 0.54)	0.961
Externalising	0.35 (-0.28, 0.98)	0.273	0.39 (-0.11, 0.89)	0.126
		Adjusted[2]		
Total	-0.48 (-1.29, 0.32)	0.241	-0.44 (-1.35, 0.47)	0.342
Internalising	-0.07 (-0.97, 0.84)	0.887	0.52 (-0.50, 1.53)	0.316
Externalising	-0.73 (-1.57, 0.10)	0.085	-1.45 (-2.40, -0.50)	0.003

[1]Estimated difference in Youth Self Report T-scores per standard deviation increase in zinc and magnesium intakes

[2]Adjusted for sex, physical activity, family income, supplement status, dietary misreporting, BMI, family functioning and energy intake; n = 667 at 14 years, n = 607 at 17 years

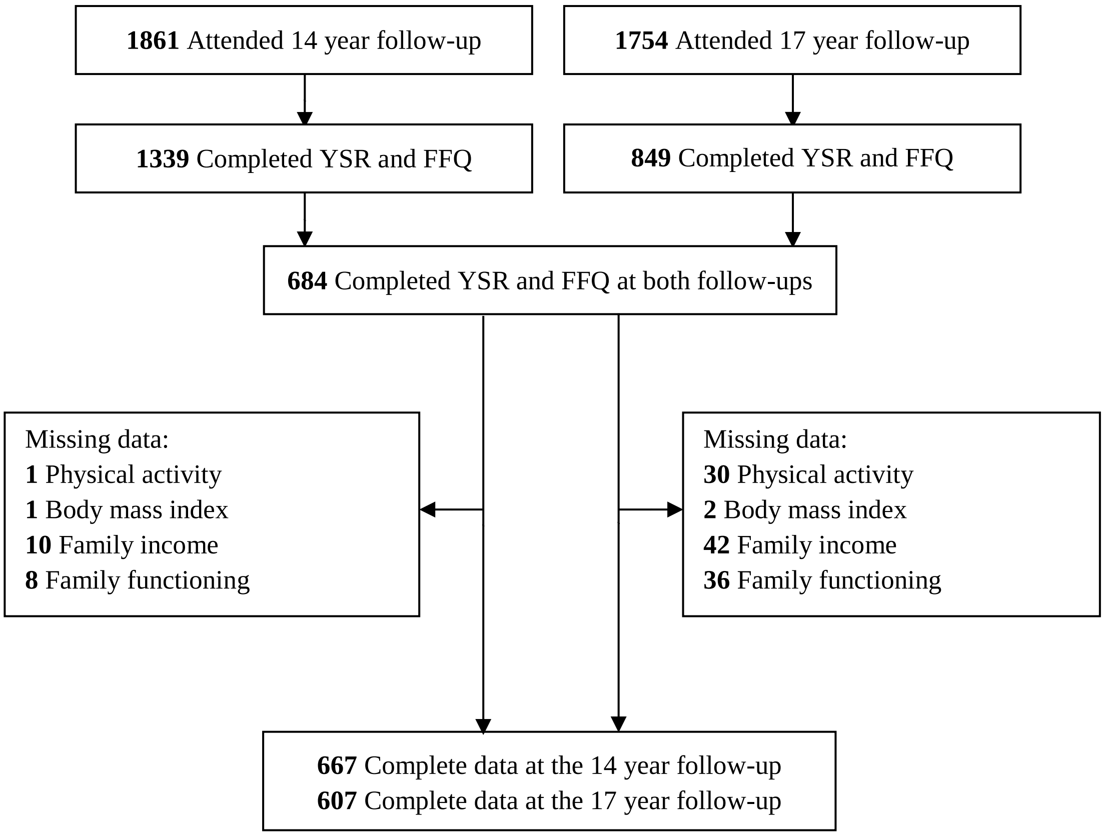

Figure 1. Flow diagram of adolescents attending the 14 and 17 year follow-ups

YSR, Youth Self-Report; FFQ, food frequency questionnaire

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