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

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Abstract

Objective: Adequate Zn and Mg 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 Zn and Mg and internalising and externalising behaviour problems in a population-based cohort of adolescents.
Design: Prospective analysis (general linear mixed models) of dietary intakes of Zn and Mg assessed using a validated FFQ 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 Mg (per SD increase) was significantly associated with reduced externalising behaviours ($\beta = -1{\cdot}45$; 95 % CI −2·40, −0·50; $P = 0{\cdot}003$). There was a trend towards reduced externalising behaviours with higher Zn intake (per SD increase; $\beta = -0{\cdot}73$; 95 % CI −1·57, 0·10; $P = 0{\cdot}085$).
Conclusions: The study shows an association between higher dietary Mg intake and reduced externalising behaviour problems in adolescents. We observed a similar trend, although not statistically significant, for Zn intake. Randomised controlled trials are necessary to determine any benefit of micronutrient supplementation in the prevention and treatment of mental health problems in adolescents.

Keywords
Magnesium
Dietary intake
Raine Study
Mental health

Zn and Mg are essential minerals involved in functioning of the central nervous system. Dietary sources of Zn 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. Mg is widely distributed in plant foods, particularly green leafy vegetables, legumes, nuts, seeds and whole grains. Zn is a cofactor 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]. Zn modulates neuronal excitability by inhibiting both the GABA (γ-aminobutyric acid) and NMDA (*N*-methyl-D-aspartate) receptors[3] and has shown antidepressant-like activities in animal models[4–6]. Mg is another potent antagonist of the NMDA receptor complex[7] and Mg deficiency has been related to symptoms such as agitation, anxiety, irritability and hyperexcitability[8]. In rodent models, Mg depletion increases anxiety and depression-like behaviours[9,10], and mice with low erythrocyte Mg levels have been found to exhibit more aggressive behaviour than those with high Mg levels[11].

Recently, Jacka *et al.* reported that dietary intakes of Zn and Mg 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 Zn intakes and depression in women[13–16]. Furthermore, research suggests that Zn supplementation as an adjunct to antidepressant drug treatment significantly lowers depressive symptoms in depressed patients compared with antidepressant treatment alone[17–19]. Research on Mg with depressive and anxiety symptoms is less conclusive. Although energy-adjusted Mg 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

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cohort (*n* 12 939) of Spanish university graduates[21]. Zn and Mg 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 Mg and Zn 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 the present study we aimed to examine the prospective association between dietary intakes of Zn and Mg 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 Zn and Mg 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 antisocial 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 FFQ developed by the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Adelaide, Australia was used to assess Zn and Mg 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 d 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: (i) the Australian nutrient database (NUTTAB95)[30]; (ii) the British food composition tables[31]; (iii) the US Department of Agriculture food tables[32]; and (iv) manufacturers' data. Questionnaires were excluded if the daily energy intake reported was implausible (<3000 or >20 000 kJ/d).

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. BMI was calculated as weight in kilograms divided by the square of height in metres. Dietary misreporting was estimated using the Goldberg method[33], 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/week, 1–3 times/week and <1 time/week). Annual family income before tax was completed by the primary caregiver and reported in three categories (≤$AUS 40 000, $AUS 40 001–78 000 and >$AUS 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 while also considering the importance of family in offspring mental health. Family functioning was measured using the twelve-item General

Functioning Scale (GFS) from the McMaster Family Assessment Device[34]. The scale has been shown to be reliable and internally consistent[35], 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 χ^2 tests. Baseline characteristics were described for participants in the current study, including sex, YSR T-scores (total, internalising and externalising), Zn and Mg intakes, energy intake, dietary misreporting, supplement use, BMI, physical activity, family income and family functioning.

Zn and Mg 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 Zn and Mg 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 Zn or Mg 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 Zn or Mg intakes were investigated in order to determine whether there were sex differences in the effect of Zn and Mg intakes on YSR T-scores. Analyses were performed using the statistical software package IBM SPSS Statistics Release Version 19·9·9·1. Statistical significance was defined as $P < 0{\cdot}05$.

Results

A total of 684 adolescents completed the YSR and FFQ at both follow-ups (Fig. 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 BMI ($P < 0{\cdot}05$).

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

In univariate analyses (*n* 684), Zn and Mg intakes (per SD increase) were not significantly associated with internalising or externalising behaviours over the 3-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,

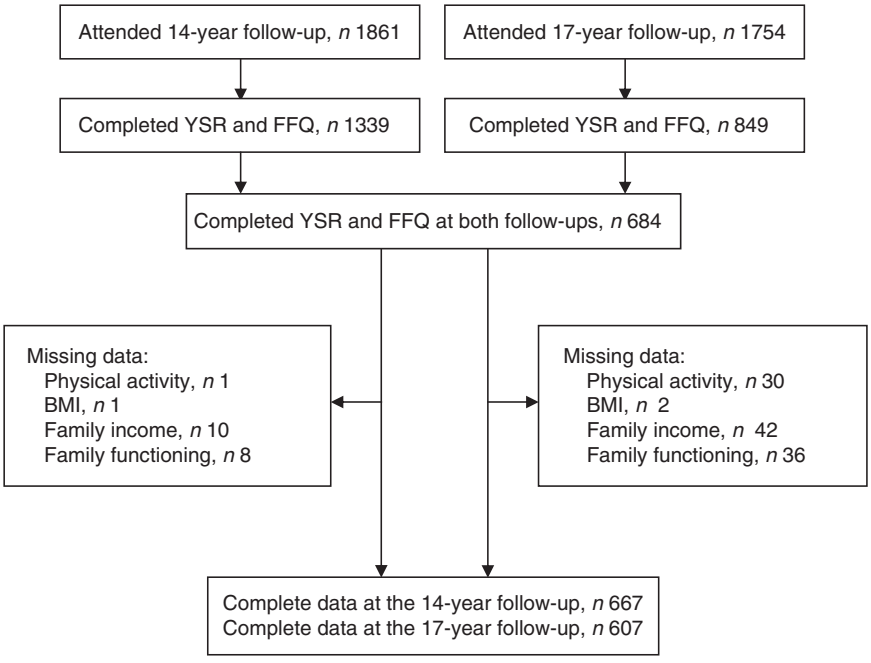

Fig. 1 Flow diagram of adolescents attending the 14- and 17-year follow-ups, Western Australian Pregnancy Cohort (Raine) Study (YSR, Youth Self-Report)

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Table 1 Characteristics of the Western Australian Pregnancy Cohort (Raine) Study participants for whom YSR 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	%, mean or median	SD or IQR	*n*	%, mean or median	SD or IQR
Sex (%)						
Male	319	46·6	–	319	46·6	–
Female	365	53·4	–	365	53·4	–
YSR T-scores, mean and 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
Zn (mg/d), mean and SD	684	12·4	4·2	684	12·6	5·5
Mg (mg/d), mean and SD	684	308·3	103·8	684	311·8	135·6
Energy intake (kJ/d), mean and SD	684	9428·6	3040·5	684	9646·2	4234·6
Energy intake (kcal/d), mean and 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	–
BMI (kg/m^2), median and IQR	683	20·1	4·3	682	21·9	4·2
Physical activity (%)						
>4 times/week	219	32·1	–	169	25·8	–
1–3 times/week	397	58·1	–	349	53·4	–
<1 time/week	67	9·8	–	136	20·8	–
Annual family income (%)						
<$AUS 40 000	160	23·7	–	93	14·5	–
$AUS 40 001–78 000	272	40·4	–	194	30·2	–
>$AUS 78 000	242	35·9	–	355	55·3	–
Family functioning, mean and SD	676	1·8	0·4	648	1·8	0·5

YSR, Youth Self-Report; IQR, interquartile range.

Table 2 General linear mixed model coefficients for YSR T-scores and zinc and magnesium intakes at ages 14 and 17 years, Western Australian Pregnancy Cohort (Raine) Study

	Zn			Mg		
	*β**	95 % CI	*P*	*β**	95 % CI	*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†						
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

YSR, Youth Self-Report.
*Estimated difference in YSR T-scores per SD increase in Zn and Mg intakes.
†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.

dietary misreporting, BMI, family functioning and energy intake, there was a significant inverse association between Mg and externalising behaviour problems. Although there was a trend towards improved externalising behaviour problems with increased Zn intake, the association did not reach the statistically significant level we had specified. There were no significant interactions between time and Zn or Mg intakes, or between sex and Zn or Mg intakes. Further, there were no significant associations between Zn and Mg intakes and internalising behaviour problems or total YSR T-scores.

Discussion

The current study examined the prospective associations between Zn and Mg intakes and internalising and externalising behaviour problems in adolescents. The results support our hypothesis that dietary Mg intakes are inversely associated with externalising behaviour problems in adolescents. Although we found no significant associations between Zn and internalising or externalising behaviours, there was a trend towards reduced externalising behaviour

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problems with higher Zn intakes. 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 Mg supplementation on symptoms of ADHD[22–24]. However, we did not find a significant association between Zn or Mg intake and internalising behaviour problems, which contrasts with previous literature[12–15,17,18,20].

There are several reasons why Mg 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 of Mg. Mg plays a role in the function of the serotonergic, noradrenergic and dopaminergic receptors, which are related to the pathophysiology of ADHD[36]. Improved ADHD symptoms have been reported in children after Mg supplementation[24,37].

We found no prospective association between dietary Zn 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[38]. In contrast, dietary intakes of Zn have repeatedly shown an inverse relationship with depressive symptoms in cross-sectional analyses, particularly in women[12–15,39–41]. We also found no association between dietary Mg 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 Mg intakes and depressive symptoms[12,20,39,42,43]. Differences between our results and those reported elsewhere may stem, at least in part, from differences in the age of the 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 Zn and Mg intakes relate to internalising problems in some age or demographic groups and not others.

The equivocal results in studies examining dietary Zn and Mg 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 FFQ and extensive characterisation of a population-based cohort. The latter allowed us to assess the effect of dietary Zn and Mg intakes on mental health while accounting for a wide range of potential confounding factors. A limitation of our study was the use of a 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 the present study was validated against a 3 d food record in the same cohort and the mean daily intakes of Zn and Mg were similar when measured by the FFQ and the 3 d 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 Zn and Mg. 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[44]. 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 socio-economic 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 Mg intake can be optimised through the consumption of nutrient-dense foods and supplementation, our study has important public health implications. Promoting increased consumption of Mg-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 Mg and/or Zn supplementation in the prevention and treatment of externalising behaviour problems, further randomised controlled trials using optimal doses are necessary.

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