



Applied nutritional investigation

Dietary intake of minerals in relation to depressive symptoms in Japanese employees: The Furukawa Nutrition and Health Study



Takako Miki M.P.H.^{a,b,*}, Takeshi Kochi M.D.^c, Masafumi Eguchi M.D.^c,
 Keisuke Kuwahara Ph.D.^{a,d}, Hiroko Tsuruoka R.N., P.H.N.^c, Kayo Kurotani Ph.D.^a,
 Rie Ito R.N., P.H.N.^c, Shamima Akter Ph.D.^a, Ikuko Kashino Ph.D.^a,
 Ngoc Minh Pham M.D., Ph.D.^e, Isamu Kabe M.D., Ph.D.^c,
 Norito Kawakami M.D., Ph.D.^b, Tetsuya Mizoue M.D., Ph.D.^a, Akiko Nanri Ph.D.^a

^a Department of Epidemiology and Prevention, Center for Clinical Sciences, National Center for Global Health and Medicine, Tokyo, Japan

^b Department of Mental Health, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

^c Department of Health Administration, Furukawa Electric Corporation, Tokyo, Japan

^d Teikyo University Graduate School of Public Health, Tokyo, Japan

^e Department of Epidemiology, Faculty of Public Health, Thai Nguyen University of Medicine and Pharmacy, Thai Nguyen Province, Vietnam

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ABSTRACT

Objective: Although intake of minerals has been suggested to be beneficial against depression, epidemiologic data from free-living settings are limited. The aim of this study was to determine the cross-sectional associations between the intake of magnesium, calcium, iron, and zinc and the prevalence of depressive symptoms in Japanese employees.

Methods: Participants were 1792 men and 214 women ages 19 to 69 y. Dietary intake was assessed using a validated, brief self-administered diet history questionnaire. Participants with depressive symptoms were defined as those with a scale score of ≥ 16 on the Center for Epidemiologic Studies Depression Scale.

Results: The prevalence of depressive symptoms was 27.8%. Intakes of magnesium, calcium, iron, and zinc were inversely associated with the prevalence of depressive symptoms. The multivariate adjusted odds ratios (95% confidence interval) of having depressive symptoms were 0.63 (0.44–0.91), 0.64 (0.47–0.88), 0.59 (0.40–0.87), and 0.63 (0.45–0.87) in the highest versus lowest tertiles of magnesium, calcium, iron, and zinc, respectively.

Conclusion: Results suggest that higher dietary intake of magnesium, calcium, iron, and zinc is associated with lower prevalence of depressive symptoms in Japanese employees.

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Introduction

Depression is a common mental health problem in the general population and causes great loss to society with respect to

reduction in work productivity and quality of life, as well as an increase in mortality [1]. An emerging body of evidence suggests that dietary factors are associated with the emergence of depressive symptoms; however, to our knowledge, relatively few studies have focused on these associations in free-living settings, especially in terms of mineral intake [2].

Several hypothesized mechanisms have been proposed to explain the associations between mineral intake and prevalence of depression. Minerals, including magnesium, calcium, iron, and zinc, are essential to many brain coenzyme systems and might be responsible for the full activation of enzymes that synthesize mood-regulating neurotransmitters [3]. Previous population-based studies showed that dietary zinc intake was inversely associated with depressive symptoms [4–8]; however, findings

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* Corresponding author. Tel.: +81 3 5841 3522; fax: +81 3 5841 3592.

E-mail address: Takakomiki-tyk@umin.ac.jp (T. Miki).

for magnesium, calcium, and iron were inconsistent [4,9–15]. With regard to the association between magnesium intake and depressive symptoms, most [4,9,10] but not all [11] cross-sectional studies reported an inverse association, whereas one prospective study failed to confirm any association [12]. Regarding calcium intake, one study [11] found an inverse association with depressive symptoms, but two others [13,14] showed no associations between the two. Regarding iron intake, one study [15] showed an inverse association with depressive symptoms, but another [13] found no significant association.

These studies [4–6,8–15], however, did not consider other potentially important nutrients for mood, such as folate, vitamin C, vitamins B₆ and B₁₂, and ω -3 polyunsaturated fatty acids [14, 16–18], and some were relatively small in size (population <500 participants) [5,6,10,11,14]. Furthermore, diet habit differs markedly between Eastern and Western populations, and some data showed a lower mineral intake (magnesium, calcium, and iron) in Japanese populations compared with those in the United Kingdom and the United States [19]. Epidemiologic evidence on mineral intake and depression is scarce in East Asia [11,14,15]; therefore, we conducted cross-sectional examination of the association of magnesium, calcium, iron, and zinc intakes with prevalence of depressive symptoms in Japanese employees.

Materials and methods

Study design and participants

As part of the Japan Epidemiology Collaboration on Occupational Health Study, the Furukawa Nutrition and Health Study, a nutritional epidemiologic survey, was conducted at the time of the periodic health examination among workers of a manufacturing company and its affiliates in Chiba and Kanagawa Prefectures, Japan, in April 2012 and May 2013. Before the health checkup, 2800 workers were asked to participate in the survey and fill out two types of survey questionnaires (one specifically designed for diet and another for overall health-related lifestyle). Of these, 2162 employees (1930 men and 232 women, ages 18–70 y) participated in the survey (response rate: ~77%). On the day of the health checkup, research staff checked questionnaires for completeness and, where necessary, clarified responses with the participants.

We obtained health checkup data, including results of anthropometric and biochemical measurements and disease history. The protocol of the study was approved by the ethics committee of the National Center for Global Health and Medicine, Japan, and the secondary analysis of the data (the Furukawa Nutrition and Health Study) was approved by the ethics committee of the University of Tokyo. Written informed consent was obtained from each participant.

We excluded 100 participants with a history of cancer (n = 20), cardiovascular diseases (n = 25), chronic hepatitis (n = 2), kidney disease including nephritis (n = 11), pancreatitis (n = 3), and mental disorder including depression and neurotic disorder (n = 45). Some participants had two or more conditions for exclusion. These participants were excluded because such diseases might affect dietary habits or depressive symptoms and may cause reverse causality. Of the remaining 2062, we further excluded 11 individuals who did not return the study questionnaire and 33 who had missing data on outcome and covariates used in the present analysis. We additionally excluded 12 participants with outliers, where total energy intake was more than mean \pm 3 SDs, leaving 2006 participants (1792 men and 214 women) for analysis.

Dietary intake

Dietary habits during the preceding 1-mo period were assessed using a validated brief self-administered diet history questionnaire (BDHQ) [20] consisting of five sections:

1. Intake frequency of 46 food and nonalcoholic beverage items;
2. Daily intake of rice and miso soup;
3. Frequency of alcoholic consumption and the amount of consumptions for five alcoholic beverages per typical drinking occasion;
4. Usual cooking method; and
5. General dietary behavior.

Dietary intake for energy and selected nutrients, such as magnesium, calcium, iron, and zinc, were estimated using an ad hoc computer algorithm for the

BDHQ [21], with reference to the Standard Tables of Food Composition in Japan [22,23]. According to the validation study of the BDHQ using 16-d weighted dietary records as the gold standard, Pearson correlation coefficients in 92 women (31–69 y old) and 92 men (32–76 y old) for energy-adjusted intake of magnesium, calcium, iron, and zinc were 0.56 and 0.59, 0.51 and 0.66, 0.53 and 0.57, and 0.32 and 0.43, respectively [20]. Because only a small number of participants (6.7%) used dietary supplements at least weekly (calcium, iron, and other supplements), the amount of mineral intake from dietary supplements was not incorporated into each dietary mineral intake.

Depressive symptoms

Depressive symptoms were assessed using the Japanese version [24] of the Center for Epidemiologic Studies Depression (CES-D) scale [25]. This scale consists of 20 items addressing six symptoms of depression, including depressed mood, guilt or worthlessness, helplessness or hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance experienced during the preceding week. Each item is scored on a scale of 0 to 3 according to the frequency of the symptom and summed up to the total CES-D score, ranging from 0 to 60. The criterion validity of the CES-D scale has been well established in both Western [25] and Japanese [24] individuals. Prevalent cases of depressive symptoms were defined as having a CES-D score of \geq 16. A cut-off value of \geq 19 was also used, as a value that might be suitable for the Japanese working population [26].

Other variables

The survey questionnaire asked about marital status, night and rotating shift work, job grade, smoking, alcohol consumption, physical activity during work and housework or while commuting to work, and leisure-time physical activity. Physical activity during work and housework or while commuting and during leisure-time was expressed as the sum of metabolic equivalent (MET) [27] multiplied by the duration of time (in hours) across all levels of physical activity.

Statistical analysis

Differences in characteristics between participants with and without depressive symptoms were assessed using an independent *t* test (continuous variable) and a χ^2 -test (categorical variable). Participants were divided into tertiles of energy-adjusted intake (using a density method) of selected nutrients, including magnesium, calcium, iron, and zinc. To examine the association between the intake of dietary minerals and depressive symptoms, we performed a multiple logistic regression analysis and calculated the odds ratios (ORs) and 95% confidence intervals (CIs) of depressive symptoms for the tertiles of selected nutrient intake, using the lowest tertile category as reference. The first model was adjusted for age (year, continuous), sex, and site (survey in April 2012 or May 2013); the second model was further adjusted for marital status (married or other), job grade (low, middle, or high), night or rotating shift work (yes or no), monthly overtime work (<10, 10 to <30, or \geq 30 h), daily physical activity at work and housework or on commuting to work (<3, 3 to <7, 7 to <20, or \geq 20 MET/h), weekly leisure-time physical activity (not engaged, >0 to <3, 3 to <10, or \geq 10 MET/h), smoking (never-smoker, former smoker, current smoker consuming <20 cigarettes/d, or current smoker consuming \geq 20 cigarettes/d), alcohol consumption (nondrinker, drinker consuming 1 to 3 d/mo, weekly drinker consuming <1, 1 to <2, or \geq 2 go/d), total energy intake (kcal/d, continuous), and intake of folate (μ g/1000 kcal, continuous), vitamin C (mg/1000 kcal, continuous), vitamin B₆ (mg/1000 kcal, continuous), vitamin B₁₂ (μ g/1000 kcal, continuous), and ω -3 polyunsaturated fatty acids (% energy, continuous). One go (a traditional Japanese unit of alcohol beverage [180 mL]) of sake (Japanese rice wine, with ethanol concentrations of 10%–14%) contains ~23 g of ethanol. The nutrients we for which we adjusted have been frequently linked to depression [14,16–18]. Due to the high intercorrelation of minerals such as magnesium, calcium, iron, and zinc found in the present study population (Pearson correlation coefficients ranging from 0.46 to 0.72), we decided not to further adjust for other three minerals. The statistical significance of trend association was tested by assigning ordinal numbers (1–3) to tertile categories of selected nutrient intake. We additionally analyzed the data stratified by age (<42 or \geq 42 y, based on median age). Two-sided *P*-values <0.05 were regarded as statistically significant. All analyses were performed using Stata version 12.1 (StataCorp, College Station, TX, USA).

Results

Participant characteristics are presented in Table 1. The prevalence of depressive symptoms (CES-D scale \geq 16) was 27.8%. Corresponding value was 18.1% when a higher cutoff (CES-D scale \geq 19) was used. Compared with participants without depressive symptoms, those with depressive symptoms were younger and

Table 1
Characteristics of study participants

	Depressive symptoms* (n = 557)	No depressive symptoms† (n = 1449)	P value‡
Age (mean ± SD, y)	40.5 ± 9.3	42.9 ± 10.3	<0.001
Sex (women, %)	10.6	10.7	0.95
Site (April 2012 survey, %)	51.0	57.6	0.007
Marital status (married, %)	55.5	70.1	<0.001
Job grade (low, %)	75.6	66.5	<0.001
Night or rotating shift work (yes, %)	24.2	18.6	0.005
Overtime work (≥30 h/mo, %)	28.4	25.9	0.13
Physical activity at work and housework or while commuting to work (≥20 METs-h/d, %)	26.9	21.5	0.01
Leisure-time physical activity (≥10 METs-h/wk, %)	20.8	28.2	<0.001
Smoking status (current, %)	35.2	26.4	<0.001
Alcohol drinking (current‡, %)	51.4	53.6	0.36
Daily dietary intake (mean ± SD)			
Total energy (kcal)	1827 ± 518	1785 ± 478	0.09
Magnesium (mg/1000 kcal)	123 ± 28	127 ± 26	0.004
Calcium (mg/1000 kcal)	220 ± 88	239 ± 86	<0.001
Iron (mg/1000 kcal)	3.7 ± 1.0	3.8 ± 1.0	0.001
Zinc (mg/1000 kcal)	4.1 ± 0.7	4.2 ± 0.6	0.001
Folate (μg/1000 kcal)	158 ± 64	166 ± 59	0.007
Vitamin C (mg/1000 kcal)	47 ± 24	52 ± 24	<0.001
Vitamin B ₆ (mg/1000 kcal)	0.60 ± 0.15	0.61 ± 0.15	0.054
Vitamin B ₁₂ (μg/1000 kcal)	4.4 ± 2.4	4.4 ± 2.0	0.92
ω-3 polyunsaturated fatty acids (% energy)	1.2 ± 0.3	1.2 ± 0.3	0.11

C-ESD, Center for Epidemiologic Studies Depression; MET, metabolic equivalent

* Participants with a C-ESD scale score ≥16.

† Participants with a C-ESD scale score <16.

‡ For continuous variables, independent *t* test was used; for categorical variables, χ^2 test was used.

§ Alcohol consumption of at least 1 d/wk.

more likely to be smokers, unmarried, night or rotating shift workers, and in a low-ranking job position; had higher physical activity levels at work and housework or while commuting to work but lower physical activity during leisure time.

Table 2
Odds ratios and 95% confidence intervals for depressive symptoms according to tertile of dietary intake of magnesium, calcium, iron, and zinc

	CES-D (15/16)				CES-D (18/19)			
	T1 (low)	T2	T3 (high)	<i>P</i> _{trend}	T1 (low)	T2	T3 (high)	<i>P</i> _{trend} *
Magnesium (median, mg/1000 kcal)	101.5	123.2	148.5		101.5	123.2	148.5	
With/without depressive symptoms	232/437	167/502	158/510		146/523	115/554	102/566	
Model 1 [†]	1.00 (ref)	0.65 (0.52–0.83)	0.64 (0.50–0.82)	<0.001	1.00 (ref)	0.78 (0.60–1.03)	0.73 (0.55–0.97)	0.03
Model 2 [‡]	1.00 (ref)	0.64 (0.49–0.84)	0.63 (0.44–0.91)	0.009	1.00 (ref)	0.79 (0.58–1.08)	0.73 (0.48–1.11)	0.13
Calcium (median, mg/1000 kcal)	156.2	220.2	311.2		156.2	220.2	311.2	
With/without depressive symptoms	229/440	180/489	148/520		144/525	116/553	103/565	
Model 1 [†]	1.00 (ref)	0.73 (0.58–0.93)	0.58 (0.46–0.75)	<0.001	1.00 (ref)	0.81 (0.61–1.06)	0.73 (0.55–0.97)	0.03
Model 2 [‡]	1.00 (ref)	0.77 (0.60–1.00)	0.64 (0.47–0.88)	0.006	1.00 (ref)	0.88 (0.65–1.19)	0.85 (0.59–1.22)	0.38
Iron (median, mg/1000 kcal)	2.9	3.7	4.7		2.9	3.7	4.7	
With/without depressive symptoms	223/446	182/487	152/516		141/528	124/545	98/570	
Model 1 [†]	1.00 (ref)	0.77 (0.61–0.97)	0.63 (0.49–0.81)	<0.001	1.00 (ref)	0.89 (0.68–1.16)	0.71 (0.53–0.95)	0.02
Model 2 [‡]	1.00 (ref)	0.79 (0.60–1.04)	0.59 (0.40–0.87)	0.008	1.00 (ref)	0.93 (0.68–1.27)	0.67 (0.42–1.05)	0.10
Zinc (median, mg/1000 kcal)	3.6	4.1	4.7		3.6	4.1	4.7	
With/without depressive symptoms	210/459	193/476	154/514		140/529	123/546	100/568	
Model 1 [†]	1.00 (ref)	0.89 (0.70–1.12)	0.66 (0.52–0.85)	0.001	1.00 (ref)	0.86 (0.65–1.13)	0.68 (0.51–0.91)	0.01
Model 2 [‡]	1.00 (ref)	0.94 (0.72–1.23)	0.63 (0.45–0.87)	0.006	1.00 (ref)	0.93 (0.68–1.26)	0.66 (0.45–0.97)	0.04

CES-D, Center for Epidemiologic Studies Depression Scale; ref, reference; T, tertile

* Based on multiple logistic regression analyses, assigning ordinal numbers 1–3 to the tertile categories of the independent variable.

† Adjusted for age (y, continuous), sex, and site (survey in April 2012 or May 2013).

‡ Adjusted for age (y, continuous), sex, site (survey in April 2012 or May 2013), marital status (married or other), job grade (low, middle, or high), night or rotating shift work (yes or no), overtime work (<10 h/mo, 10 to <30 h/mo, or ≥30 h/mo), physical activity at work and housework or while commuting to work (<3 METs-h/d, 3 to <7 METs-h/d, 7 to <20 METs-h/d, or ≥20 METs-h/d), leisure-time physical activity (not engaged, >0 to <3 METs-h/wk, 3 to <10 METs-h/wk, or ≥10 METs-h/wk), smoking (never-smoker, former smoker, current smoker consuming <20 cigarettes/d, or current smoker consuming ≥20 cigarettes/d), alcohol consumption (nondrinker, drinker consuming 1–3 d/mo, weekly drinker consuming <1 go/d, 1 to <2 go/d, or ≥2 go/d; one go contains ~23 g of ethanol), total energy intake (kcal/d, continuous), and intake of folate (μg/1000 kcal, continuous), vitamin C (mg/1000 kcal, continuous), vitamin B₆ (mg/1000 kcal, continuous), vitamin B₁₂ (μg/1000 kcal, continuous), and ω-3 polyunsaturated fatty acids (% energy, continuous).

As shown in Table 2, in the multivariate model, the ORs of depressive symptoms tended to decrease with increasing level of minerals, with statistically significant trend associations being observed for magnesium, calcium, iron, and zinc (*P*_{trend} = 0.009, 0.006, 0.008, and 0.006, respectively). The multivariate adjusted ORs (95% CI) for having depressive symptoms in the highest versus lowest tertiles of magnesium, calcium, iron, and zinc were 0.63 (0.44–0.91), 0.64 (0.47–0.88), 0.59 (0.40–0.87), and 0.63 (0.45–0.87), respectively. Similar associations were observed when a higher cutoff point (CES-D scale score ≥19) was used in the definition of depressive symptoms, although the association was not statistically significant except for zinc intake. Additionally, inverse associations were observed in both groups stratified by age (data not shown).

Discussion

In this cross-sectional study among Japanese employees, we found that a higher dietary intake of magnesium, calcium, iron, and zinc was associated with a lower prevalence of depressive symptoms, even after adjustment for potentially important confounding factors.

To date, four cross-sectional studies and one prospective study have explored the association between magnesium intake and depressive symptoms in a general population, and their findings have been generally consistent among cross-sectional studies; three observed a significant inverse association [4,9,10], and another small study also found an inverse, albeit statistically nonsignificant, association [11]. The present study, where a range of dietary (including folate; vitamins B₆, B₁₂, and C; and ω-3 polyunsaturated fatty acids) and non-dietary potential confounders was adjusted for, confirmed the findings of previous cross-sectional studies.

In a large cohort study with Spanish university graduates, however, higher magnesium intake was not associated with a decreased risk for depression [12]. The authors of that study

ascribed the null finding to relatively high magnesium intake in the study population (median intake 404 mg/d). The median magnesium intake in our study was 216 mg/d, which was below the Japanese recommended dietary allowance for magnesium [28]. The results of population-based studies that measured blood levels of magnesium are inconsistent; one found a significant inverse association [29], whereas another found no association [11]. Such discrepancy might be due to differences in the assessment of depressive symptoms and the selection of covariates.

In the present study, calcium intake was associated with decreased odds of depressive symptoms, a finding consistent with that of a study with Korean women [11]. However, two other studies with U.S. adolescents [13] and an elderly Japanese population [14] found no association between calcium intake and depressive symptoms. Such inconsistencies may be due in part to the difference in calcium intake levels according to study population. Mean calcium intake in the Korean women's study [11] and the present study was 456 mg/d and 419 mg/d, respectively. In the other two studies that found no association, mean calcium intake was relatively high: >1000 mg/d in U.S. adolescents [13] and 825 mg/d for men and 876 mg/d for women in the elderly Japanese population [14]. Studies that measured serum calcium concentrations found no association with depressive symptoms [11,29], probably due to tight regulation by homeostasis of circulating calcium concentrations [30].

The present study showed a significant and inverse association between iron intake and depressive symptoms, consistent with a finding of a cross-sectional study of an elderly Chinese population [15]. Another study in U.S. adolescents, where energy intake was not adjusted for, however, found no significant association between them [13]. Inconsistency among these dietary studies may be partly ascribed to poor correlation between dietary iron intake and body iron status [31]. However, studies that measured blood ferritin concentrations, a good marker of systemic iron storage in healthy individuals [32], also have shown inconsistent results. Of five community studies that measured ferritin concentrations [33–37], three showed a significant inverse association between serum ferritin and depressive symptoms [33–35], but the other two found no significant association [36,37]. Brain iron uptake may be constitutive and independent of plasma transferrin, transferrin saturation, or regional brain iron concentration [38]. Additionally, serum ferritin is increased in the setting of inflammatory conditions [39]. These issues might account for the inconsistent results among blood studies.

Four population-based, cross-sectional studies and one prospective study have consistently shown an inverse association between zinc intake and depressive symptoms [4–8]. Furthermore, a biomarker study found a linear, inverse association between Beck depression scores and serum zinc concentrations [5]. The present finding, together with those of previous studies [4–7] in the community setting support the notion that elevated zinc intake is associated with a reduction in prevalence of depressive symptoms.

The mechanism linking magnesium, calcium, iron, and zinc to depressive symptoms is unclear, but several have been suggested. Magnesium is a cofactor of tryptophan hydroxylase and is necessary for serotonin receptor binding *in vitro* [40]. Magnesium is a potent antagonist of the *N*-methyl-D-aspartate receptor complex [41]. Additionally, magnesium may contribute to lowering systemic inflammation [42], which has been associated with depression [43]. Calcium activates tryptophan hydroxylase in the biosynthetic pathway leading to serotonin synthesis [44]. Additionally, dopamine synthesis in the brain is enhanced by a

calcium/calmodulin-dependent system [45]. Iron plays a role in the oxygenation of brain parenchyma and the synthesis of neurotransmitters, such as dopamine and serotonin [46], and iron deficiency decreases dopamine receptor density in animals [47]. Zinc might increase levels of brain-derived neurotrophic factor by enhancing the function of the serotonergic system and by inhibiting the activity of glycogen synthase kinase-3 [48].

The prevalence of depressive symptoms (CES-D scale score ≥ 16) in the present study population (27.8 %) was higher than those in Western populations (e.g., 11.9 % in a British study [49]), but similar to that of a Japanese study (29.9%) [50]. This is probably due to the fact that the Japanese tend to express their positive emotion in a modest manner, leading to a high score on depression scales [51]. We confirmed, however, that results did not materially change when we used a higher cutoff point (CES-D scale score ≥ 19).

The major strengths of this study include its high participation rate and adjustment for known and suspected risk factors of depressive symptoms. However, our study also had several limitations. First, an association derived from a cross-sectional study does not necessarily indicate causality. Second, although we adjusted for a variety of potential confounding variables, we cannot rule out the possibility that the observed associations are due to unmeasured confounders and residual confounding. Third, we were unable to disentangle the effect of each mineral intake from that of other minerals because the correlation between minerals was high. Fourth, mineral intake does not necessarily reflect body mineral status, which is determined not only dietary intake but also other factors including absorption, metabolism, and excretion. Thus, studies using reliable biomarkers of minerals are needed to confirm our results. Finally, because the study participants were Japanese manufacturing employees, caution is required in generalizing the present findings.

Conclusion

Higher intake of magnesium, calcium, iron, and zinc was associated with a lower prevalence of depressive symptoms in Japanese employees. The inverse association in this cross-sectional observation requires confirmation in prospective study among populations with different background in terms of ethnics, sex, age, anthropometry, physical activity, and physiological and psychological conditions. Additionally, intervention trials are required to confirm the effect of mineral supplements on mood.

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