Substitution of whole grains for refined grains: a means to avoid excess B-vitamin intake

Dear Editor:

We read with interest the article by Karl et al. (1) in a recent issue of the Journal. The authors studied the effects of the substitution of whole grains for refined grains on energy-balance metrics in healthy men and postmenopausal women. The results showed that stool energy excretion was higher and prospective consumption and glycemia after an oral-glucose-tolerance test trended toward being lower in the whole grain–rich diet group than in the refined grain–based diet group. The authors attributed these effects to increased fiber intake. However, the authors have not provided information with regard to changes in the intake of B vitamins from grains, which may cast doubt on their explanation.

It has long been known that B vitamins promote appetite and weight gain (2), whereas B-vitamin deficiency decreases appetite. A good example is that pellagra, a disease due to deficiency of niacin (vitamin B-3, including nicotinic acid and nicotinamide), is associated with loss of appetite and body weight (3). Therefore, particular attention should be paid to changes in the intake of appetite-enhancing B vitamins in the development of diseases that are correlated with an enhanced appetite, such as obesity and type 2 diabetes.

In the United States, one of the biggest differences between refined grains and whole grains is that refined grains are mandatorily fortified with high levels of appetite-promoting B vitamins (52.9 mg niacin, 6.4 mg thiamin, and 4 mg riboflavin/kg flour) (4). The implementation of mandatory grain fortification began in the early 1940s, and the fortification standards were increased in 1974. This was followed by 2 sharp increases in the mean BMI of the US population, which occurred in 1944–1950s (5) and in 1976 and 1980 (6), respectively, which cannot be explained by grain fiber intake (7). It was found that the increased prevalence of obesity and diabetes in the United States is strongly correlated with the increased per capita consumption of the appetite-promoting B vitamins, which is mainly due to the increased consumption of refined and fortified grains (7). By contrast, European countries that restrict grain fortification with B vitamins have a significantly lower prevalence of obesity than does the United States (4, 8). More importantly, despite the absence of B-vitamin fortification, there was very low prevalence of B-vitamin deficiency diseases in general populations in the European countries in the past several decades. Therefore, when studying the role of grains in metabolic disorders, the factor of vitamin fortification should be taken into account.

Among the B vitamins fortified in refined grains, niacin is known to induce insulin resistance and impair glucose tolerance (4), which are hallmarks of obesity and type 2 diabetes. Thus, it is likely that the mandatory fortification–induced sustained high intake of appetite-promoting B vitamins is a more plausible explanation for the association between refined grains and diseases that are correlated with an increased appetite.

With regard to the changes in stool energy excretion after the substitution of whole grains for refined or fortified grains, B vitamins may also play a role. Early studies showed that B vitamins increase intestinal absorption and food utilization (9). It is common knowledge that a decrease in niacin intake increases stool excretion or even causes diarrhea, a hallmark of pellagra (3). Given that the substitution of whole grains for refined or fortified grain in foods may decrease B-vitamin intake, it is possible that the observed increase in stool energy excretion by Karl et al. (1) may be related to changes in B-vitamin intake.

In addition to B vitamins, iron has also been mandatorily fortified in refined grains (44 mg/kg flour in the United States). It needs to be pointed out that Denmark implemented iron fortification (30 mg/kg flour) from 1954 to 1986 and abolished fortification in 1987, and there was no significant difference in the prevalence of iron deficiency anemia between the 2 surveys before (in 1984) and after the abolishment of (in 1994) iron fortification (10). Obviously, the substitution of unfortified whole grains for refined or fortified grains can avoid excess intake of micronutrients. Unfortunately, this important factor has long been glossed over.

In summary, given that *1*) B vitamins stimulate appetite, *2*) B-vitamin intake is increased by the consumption of B-vitamin–fortified grains but decreased by substitution of unfortified whole grains for refined or fortified grains, and *3*) B-vitamin fortification is associated with increased prevalence of obesity and diabetes, to avoid misleading interpretations clinical trials related to refined and fortified grains must consider the intake and role of B vitamins before reaching a conclusion.

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Reply to S-S Zhou and Y Zhou

Dear Editor:

We thank Zhou and Zhou for their interest in our recent work (1), which reported favorable effects of consuming a whole grain–rich diet compared with a refined grain–rich diet on energy-balance metrics in healthy adults. Zhou and Zhou speculate that our findings could be the result of higher B-vitamin intakes in the refined-grain diet group because refined grains are enriched with several B vitamins within the United States. As supporting evidence, they state that B vitamins promote appetite and weight gain, and that B-vitamin deficiencies result in loss of appetite and weight loss. They also state as supporting evidence that niacin induces insulin resistance and impairs glucose tolerance and that B vitamins increase intestinal absorption and utilization of nutrients. We appreciate the opportunity to respond to these comments.

Although synergy among multiple nutrients likely underlies many of the putative health effects of whole grains (2, 3), including those observed in our report, we believe that our data support a dominant role of the higher fiber content of the whole-grain diet relative to the refined-grain diet. As described in our report (1), this assertion is supported by a large evidence base with regard to the role of dietary fiber in energy-balance regulation. In contrast, we find little evidence to support Zhou and Zhou's assertion that differences in B-vitamin intake were likely to underpin between-group differences in study outcomes.

B vitamins play an important role in metabolism, and we agree that deficiencies may impair metabolic function, energy absorption and utilization, and appetite (4). However, the observation that a nutrient deficiency degrades a particular function and that nutrient sufficiency restores (i.e., normalizes) that function does not mean that the nutrient, when consumed at an adequate level, stimulates that function above and beyond a normal baseline. Furthermore, we caution against inferring causal relations between changes in B-vitamin intake and obesity from the ecological associations cited by Zhou and Zhou, because many other factors change in parallel. To our knowledge, there is no credible evidence from randomized controlled trials that B-vitamin intakes within recommended ranges in healthy, nondeficient subjects affect appetite, nutrient absorption, or body weight. Although the consumption of high amounts of niacin (vitamin B-3) has been associated with impaired glucose tolerance and decreased insulin sensitivity in some studies (5, 6), these associations have been reported for pharmacologic doses of niacin (>1000 mg/d). We note that in the case of our study, as published elsewhere (7), B-vitamin intakes met the Dietary Reference Intakes (4) and were relatively comparable between groups (**Table 1**).

In summary, the suggestion that B-vitamin fortification of refined-grain foods was responsible for the between-group differences in energy-balance metrics observed in this study is not supported by the evidence base or the actual B-vitamin intakes within the study groups. Furthermore, our data do not support the suggestion of Zhou and Zhou that B-vitamin fortification is a causal factor in changes in rates of obesity over time across different countries.

Any opinions, findings, conclusions, or recommendations expressed in this letter are those of the authors and do not necessarily reflect the views of the USDA, the US Army, or the US Department of Defense. None of the authors had a conflict of interest.

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TABLE 1
Intake of B vitamins during a provided 2-wk run-in diet and while consuming a provided refined grain–rich diet or a whole grain–rich diet for 6 wk[1]

	Refined-grain diet (n = 40)		Whole-grain diet (n = 41)		
	Run-in	Intervention	Run-in	Intervention	P^2
Thiamin, mg/d	2.3 ± 0.05	2.3 ± 0.05	2.3 ± 0.05	1.9 ± 0.04	<0.001
Riboflavin, mg/d	2.6 ± 0.1	3.0 ± 0.1	2.7 ± 0.1	2.7 ± 0.1	<0.001
Niacin, mg/d	35 ± 0.9	34 ± 0.9	38 ± 1.3	34 ± 0.8	0.08
Pantothenic acid, mg/d	5.8 ± 0.1	6.1 ± 0.2	5.9 ± 0.1	7.3 ± 0.2	<0.001
Vitamin B-6, mg/d	2.5 ± 0.1	2.4 ± 0.1	2.6 ± 0.1	2.8 ± 0.1	<0.001
Folate, μg/d	736 ± 16	781 ± 17	742 ± 16	661 ± 18	<0.001
Vitamin B-12, μg/d	6.5 ± 0.1	5.7 ± 0.1	6.6 ± 0.2	5.8 ± 0.2	0.93

[1] Values are means ± SEMs.
[2] Derived by using independent-samples t test of the differences (change within the whole-grain diet compared with change within the refined-grain diet).