Body Mass Index and Dietary Intake of Thiamin: Evidence for a Sexually Dimorphic Relation

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INTRODUCTION

The concept of body mass index (BMI) originated with Quetelet's 19th century proposed relation between stature and body weight (Ross et al., 1988). BMI is correlated not only with body fat, but also with lean mass, and different body proportions such as leg length (Ross et al., 1988). On a population scale, it has been used as an estimator of body fat (e.g., Gallagher et al., 1996). Based on monozygotic and dizygotic twin studies, the heritability of BMI has been estimated to be 50-90% in different studies (Maes et al., 1997; Keller et al., 2003 and references therein).

Thiamin (vitamin B1) has a central regulatory role as co-enzyme in energy metabolism as well as in metabolic pathways involving carbohydrates, amino acids, and lipids. Thiamin functions as a coenzyme for several dehydrogenases (e.g., Bender 1999), branched chain keto-acid dehydrogenase in amino acid metabolism, pyruvate dehydrogenase in carbohydrate metabolism and α-ketoglutarate dehydrogenase in the citric acid cycle; and it is a coenzyme for transketolase in the pentose phosphate pathway of carbohydrate metabolism. More recently, thiamin has also been proposed as coenzyme for 2-hydroxyphytanoyl-CoA lyase in fatty acid alpha-oxidation (Casteels et al., 2003).

In this report, relations between intake of thiamin and BMI in age-matched (+/- average of 1 yr) and BMI-matched (+/- average of 2 units) male (n = 58) and female (n = 59) adults are presented. A 3-day recall method was used to assess intake of vitamins and minerals. Previous studies have established that thiamin intake exhibits a direct proportionality with some biochemical indicators of thiamin levels in the body (Powers et al., 1993; Bailey et al., 1997; Smidt et al., 1990). Thiamin intake may, thus, be an important contributor to overall thiamin status in the body.

RESULTS AND DISCUSSION

The relation of BMI and thiamin intake exhibited the strongest correlation with the greatest gender difference among all the macronutrient and micronutrients examined (see below). Because of the central role of thiamin in energy metabolism and the strong relationship between thiamin status and carbohydrate intake (Elmadfa et al., 2001), correlations of BMI were made not only with *thiamin* (data not shown, see below for correlation coefficients), but also with *thiamin intake(g)/kcal* (Fig. 1) and *thiamin intake(g)/carbohydrate intake (% total calories)* (Fig. 2).

Statistically significant ($P < 0.05$) positive and negative correlations of *thiamin intake/kcal* with BMI were found for males ($r = 0.274$) and females ($r = -0.246$), respectively (Fig. 1). Such strong correlations for both sexes were not observed for two other vitamins involved in energy metabolism, riboflavin (e.g., female BMI vs. riboflavin, $r = 0.041$) and niacin (e.g., male BMI vs. niacin, $r = 0.118$), nor for the other vitamins and minerals examined (A, B6, C, E, folate, calcium, iron, sodium, potassium, zinc; data not shown). Similar positive ($r = 0.215$) and negative ($r = -0.185$) correlations of BMI with *thiamin intake* were also found for males and age-matched females, respectively (data not shown); but these were not statistically significant ($a = 0.05$). A previous study, in which correlations of thiamin intake with biochemical erythrocyte thiamin levels were examined, also indicated stronger correlations if *thiamin intake/kcal* was used instead of *thiamin intake* (Bailey et al., 1997).

Correlation of BMI with *thiamin intake (g) divided by % total caloric from carbohydrate* was much higher for females ($r = -0.225$, strong negative correlation of borderline statistical significance, $P \sim 0.05$) than for males ($r = 0.087$, very poor positive correlation without statistically significant, $P >> 0.05$) (Fig. 2). Gender differences in the relation between thiamin intake and glucose metabolism have also been noted in other studies (e.g., Bakker et al., 1998).

In the context of thiamin's central role in energy metabolism, the contribution of the three macronutrient energy sources (each as % total

calories) relative to thiamin intake was assessed (Figure 3). For ease of comparison and because of the recommendation that thiamin status be considered relative to carbohydrate intake, the data in figure 3 are shown relative to carbohydrate.

The results suggest that in males, *thiamin intake (g)/% total caloric from protein* and *thiamin intake (g)/% total caloric from fat* are strongly (~ 2X carbohydrate) and very weakly (~0.2 X carbohydrate) correlated with BMI, respectively.

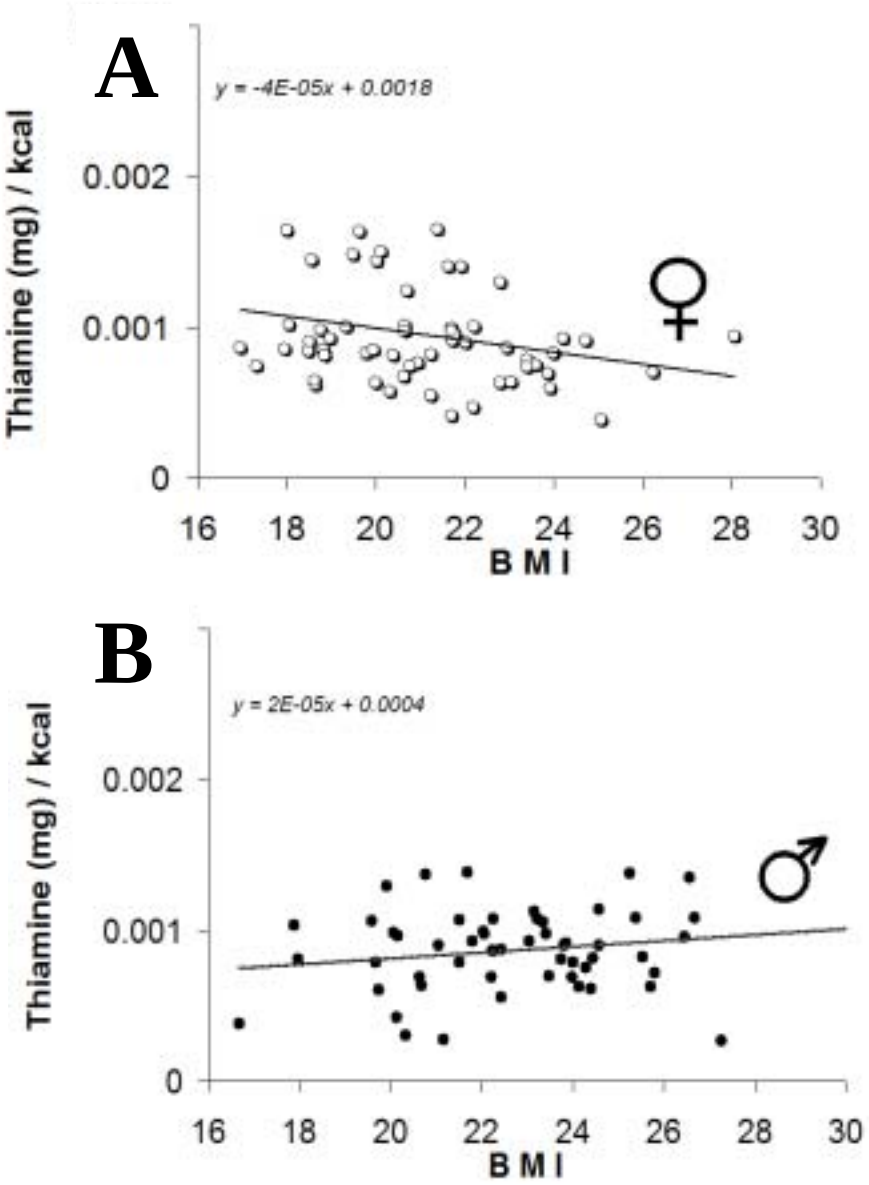

Fig. 1. Correlation analysis of thiamin *intake (mg/day) per kilocalorie* with *body mass index (BMI)* for females (A) and males (B).
The trendlines and respective linear equations are shown. The correlations for females (r = -0.246) and males (r = 0.274) are both statistically significant, P d" 0.05 (a = 0.05).

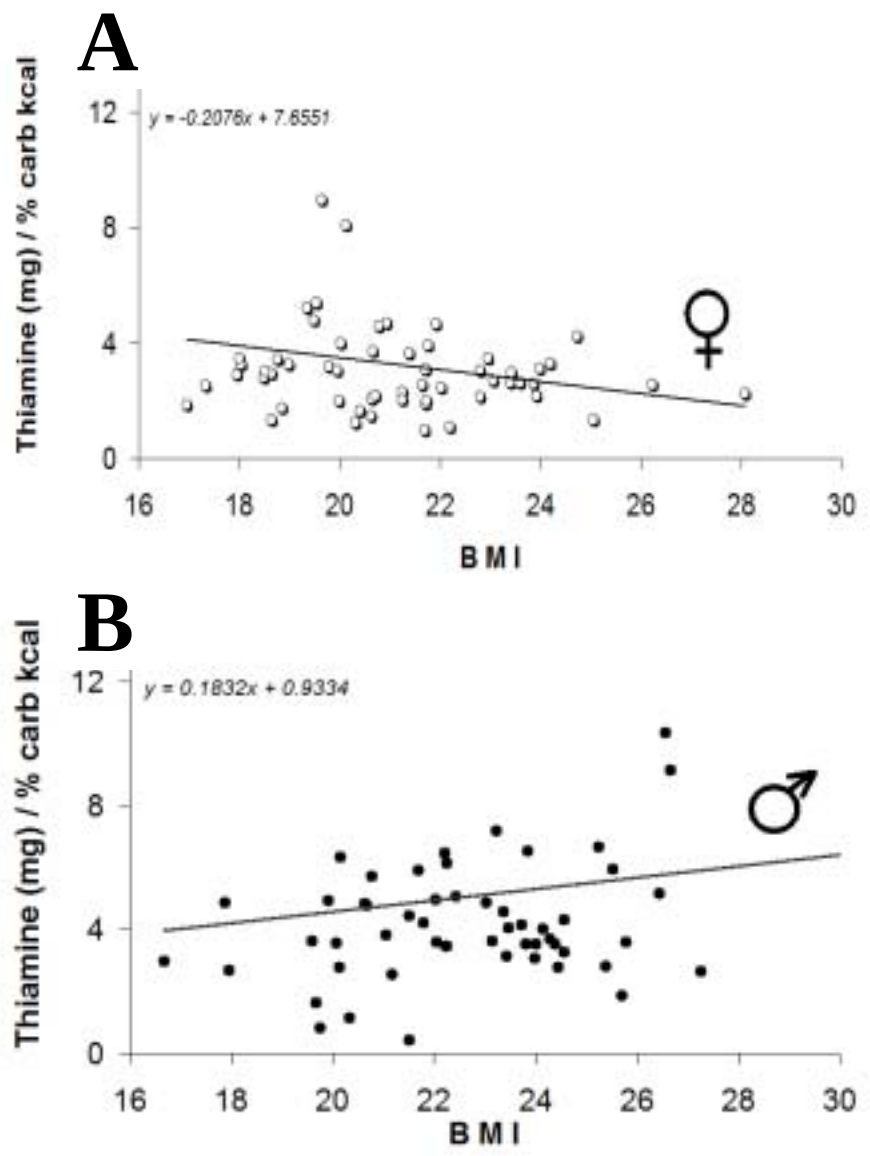

Fig. 2. Correlation analysis of *thiamin intake (mg/day) divided by percent of total calories from carbohydrate* with *body mass index (BMI)* for females (A) and males (B).
The trendlines and respective linear equations are shown. The correlation for females (r = -0.225) is of borderline statistical significance, P ~ 0.05. The correlation for males (r = 0.087) is not statistically significant, P >> 0.05 (a = 0.05).

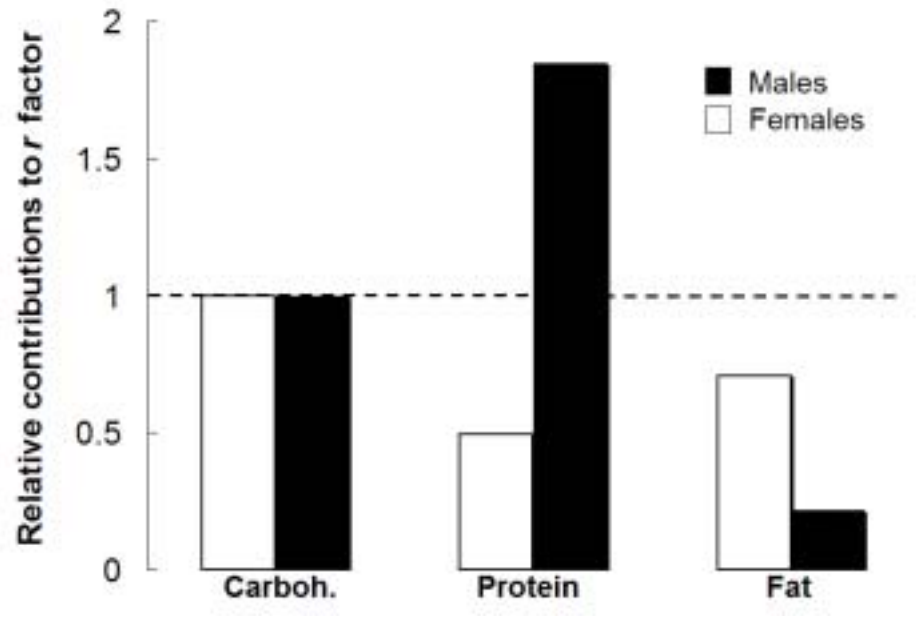

Fig. 3. Relative contributions of the indicated macronutrient to the absolute value of the correlation coefficient, r.

The correlation in question is that of '*BMI*' with '*thiamin intake divided by percent total calories for a given macronutrient.*' For both males and females, data were standardized relative to carbohydrate (see text for further details of standardization and related discussion).

For females, in contrast, thiamin intake relative to protein calories, or relative to fat calories, makes a relatively weaker contribution (~ 0.5-0.7 X carbohydrate) to the correlation with BMI than thiamin intake relative to carbohydrate calories. Because such correlations with BMI are negative for females, the relative data in Figure 3 suggest that gender differences in thiamin-dependent fat metabolism are the greatest contributors to the observed sexual dimorphism for the observed correlations of BMI with the three parameters involving thiamin (i.e., thiamin intake, thiamin intake/kcal, and thiamin intake /% total caloric from carbohydrate). In this context, a variety of sexually dimorphic responses in terms of energy metabolism have been documented: e.g., β-adrenergic inhibition results in increases in fat oxidation (lipolysis) in women, but corresponding decreases in men; and such inhibition also increases energy metabolism from specific amino acids (e.g., leucine) in men but not women (Lamont et al., 2003). The authors of this study suggest the possibility of gender dimorphism in the regulation of branched-chain α-keto-acid dehydrogenase, an enzyme that has thiamin (diphosphate) as a cofactor (reviewed in Chuang et al., 2006).

Through impaired α-ketoglutarate dehydrogenase activity in the citric acid cycle, thiamin deficiency may increase flux through the gamma-aminobutyrate (GABA) shunt (e.g., Page et al., 1989). GABA is also known to affect feeding; and sexual dimorphisms in GABA receptor subtypes are known (e.g., Wolfe et al., 2005; Lovick et al., 2005). Changes in GABA levels could be an important contributor to the established relation between thiamin deficiency and anorexia (Page et al., 1989, and references therein); and these responses may be sexually dimorphic (cf. Reddy and Kulkarni, 1999). Thiamin deficiency may also affect neuronal responses to GABA by decreasing GABA-mediated neural transmission (Dodd et al., 1996).

In terms of the sexual dimorphism observed for the relation between BMI and thiamin intake there are additional or alternative possible explanations. For example, there is some evidence for gender differences in thiamin-dependent

transketolase activities (Han et al., 2005), and a putative novel human transketolase gene on the X chromosome has been reported (Coy et al., 1996). Studies of dry beriberi cases in developing countries have suggested that males are more affected than females (San Sebastian and Jativa 1998; Barrett and Browne 1992). If transketolase activity/subtype has a major influence on the severity of the symptoms (cf. Bender 1999), then the above gender differences in beriberi may relate to differences in transketolase activation.

In addition to the activities proposed above, other general aspects to be considered in the context of this report include influences of gender on macronutrient energy metabolism (e.g., Lamont et al., 2003; Nagy et al., 1996; review by Tarnapolsky 2000; see also above) and energy expenditure (e.g., thermic effect of food component, Gougeon et al., 2005), sex hormone influences on thiamin transport (including extracellular carrier proteins and cell membrane transporters), and influences of thiamin status on hepatic lipogenesis and flux through the hexosamine pathway (cf., Babaei-Jadidi et al., 2004 and references therein). Future studies along these lines may reveal more into sexually dimorphic mechanisms that contribute to the possible relation between the body's thiamin status and BMI.

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REFERENCES

Babaei-Jadidi, R., Karachalias, N., Kupich, C., Ahmed, N. and Thornalley, P.J.: High-dose thiamine therapy counters dyslipidaemia in streptozotocin-induced diabetic rats. *Diabetologia,* **47:** 2235-46 (2004).

Bailey, A.L., Maisey, S., Southon, S., Wright, A.J., Finglas, P.M. and Fulcher, R.A.: Relationships between micronutrient intake and biochemical indicators of nutrient adequacy in a "free-living' elderly UK population. *Br. J. Nutr.,* **77:** 225-42 (1997).

Bakker, S.J., Hoogeveen, E.K., Nijpels, G., Kostense, P.J., Dekke,r J.M., Gans, R.O. and Heine, R.J.: The association of dietary fibres with glucose tolerance is partly explained by concomitant intake of thiamine: the Hoorn Study. *Diabetologia,* **41:** 1168-75 (1998).

Barret, H.R.,and Browne, A.W.: Beri Beri: age-gender bias in The Gambia. *Soc. Sci. Med.,* **34:** 1295–1297 (1992).

Bender, D.A.: Optimum nutrition: thiamin, biotin and pantothenate. *Proc. Nutr. Soc.* ,**58:** 427-33 (1999).

Casteels, M., Foulon, V., Mannaerts, G.P. and Van Veldhoven, P.P.: Alpha-oxidation of 3-methyl-substituted fatty acids and its thiamine dependence. *Eur. J. Biochem.,* **270:** 1619-27 (2003).

Chuang, D.T., Chuang, J.L. and Wynn, R.M.: Lessons from genetic disorders of branched-chain amino acid metabolism. *J. Nutr.,* **136:** 243S-9S (2006).

Coy, J.F., Dubel, S., Kioschis, P., Thomas, K., Micklem, G., Delius, H. and Poustka, A.: Molecular cloning of tissue-specific transcripts of a transketolase-related gene: implications for the evolution of new vertebrate genes. *Genomics,* **32:** 309-16 (1996).

Dodd, P.R., Thomas, G.J., McCloskey, A., Crane, D.I. and Smith, I.D.: The neurochemical pathology of thiamine deficiency: GABAA and glutamateNMDA receptor binding sites in a goat model. *Metab. Brain Dis.,* **11:** 39-54 (1996).

Elmadfa, I., Majchrzak, D., Rust, P. and Genser, D.: The thiamine status of adult humans depends on carbohydrate intake. *Int. J. Vitam. Nutr. Res.,* **71:** 217-21 (2001).

Gougeon, R., Harrigan, K., Tremblay, J.F., Hedrei, P., Lamarche, M. and Morais, J,A.: Increase in the thermic effect of food in women by adrenergic amines extracted from citrus aurantium. *Obes. Res.,* **13:** 1187-94 (2005).

Han, J., Xu, J., Epstein, P.N. and Liu, Y.Q.: Long-term effect of maternal obesity on pancreatic beta cells of offspring: reduced beta cell adaptation to high glucose and high-fat diet challenges in adult female mouse offspring. *Diabetologia,* **48:** 1810-8 (2005).

Lamont, L.S., McCullough, A.J. and Kalhan, S.C.: Gender differences in the regulation of amino acid metabolism. *J. Appl. Physiol.,* **95:** 1259-65 (2003).

Nagy, T.R., Goran, M.I., Weinsier, R.L., Toth, M.J., Schutz, Y. and Poehlman, E.T.: Determinants of basal fat oxidation in healthy Caucasians. *J. Appl. Physiol.,* **80:** 1743-8 (1996).

Page, M.G., Ankoma-Sey, V., Coulson, W.F., and Bender. D.A.: Brain glutamate and gamma-aminobutyrate (GABA) metabolism in thiamin-deficient rats. *Br. J. Nutr.,* **62:** 245-53 (1989).

Powers, J.S., Zimmer, J., Meurer, K., Manske, E., Collins, J.C. and Greene, H.L.: Direct assay of vitamins B1, B2, and B6 in hospitalized patients: relationship to level of intake. *JPEN J Parenter Enteral Nutr.,* **17:** 315-6 (1993).

Reddy, D.S. and Kulkarni, S.K.: Sex and estrous cycle-dependent changes in neurosteroid and benzodiazepine effects on food consumption and plus-maze learning behaviors in rats. *Pharmacol. Biochem. Behav.,* **62:** 53-60 (1999).

Ross, W.D.: Relationship of body mass index with skinfolds, girths, and bone breadths in Canadian men and women aged 20-70 year. *Am. J. Phys. Anthrop.,* **77:** 169-173 (1988).

San Sebastian, M. and Jativa, R.: Beriberi in a well-nourished Amazonian population. *Acta Trop.,* **70:** 193-6 (1998).

Smidt, L.J., Cremin, F.M., Grivetti, L.E. and Clifford, A.J.: Influence of thiamin supplementation on the health and general well-being of an elderly Irish population with marginal thiamin deficiency. *J. Gerontol.,* **46:** M16-22 (1991).

Tarnopolsky, M.A.: Gender differences in substrate

metabolism during endurance exercise. *Can. J. Appl. Physiol.*, **25:** 312-27 (2000).
Wolfe, C.A., Van Doren, M., Walker, H.J., Seney, M.L., McClellan, K.M., and Tobet, S.A.: Sex differences in the location of immunochemically defined cell populations in the mouse preoptic area/anterior hypothalamus. *Brain Res. Dev. Brain Res.*, **157:** 34-41 (2005).

KEYWORDS BMI. Thiamin. Body Composition. Energy Metabolism. Sexual Dimorphism

ABSTRACT Body mass index (BMI) correlates with several anthropometric parameters including body adiposity. Comparisons of genetic and environmental factors have resulted in a heritability estimate for BMI of about 70%. Thiamin is a vitamin involved in energy metabolism and metabolic pathways for carbohydrates, amino acids, and fatty acids. This vitamin functions as a coenzyme for transketolase and three dehydrogenases that catalyze decarboxylation of a-ketoacids; it has also been proposed as a fatty acid-CoA lysase. Herein, we report on the association of thiamin intake with BMI, and the observed opposite gender effects. A significant positive ($P < 0.05$) correlation of thiamin intake/kcal with BMI was found among adult males; and a significant negative correlation ($P < 0.05$) was found among adult females. Based on reports that physiological levels for this vitamin can reflect dietary intake, possible metabolic reasons are presented for influences of thiamin on BMI and for the observed sexual dimorphism of this relation.

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