

# Plasma Adiponectin Concentrations Are Associated with Body Composition and Plant-Based Dietary Factors in Female Twins<sup>1</sup>

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## Abstract

Circulating adiponectin is emerging as an important link between obesity, type 2 diabetes, and cardiovascular disease (CVD). However, the spectrum of lifestyle factors that modulate the adiponectin concentration remains to be elucidated, particularly among women. We conducted a cross-sectional study of 877 female twin pairs from the TwinsUK adult twin registry. Using a co-twin design, we examined dietary and body composition influences on adiponectin by conducting matched, within-pair analyses to eliminate confounding. Following multivariable adjustment within-twin pairs, significant influences on adiponectin (log-transformed, percent change per SD of the dietary/body composition variable) were observed for nonstarch polysaccharides (3.25%; 95% CI: 0.06, 6.54;  $P < 0.05$ ) and magnesium intake (3.80%; 95% CI: 0.17, 7.57;  $P < 0.05$ ), with a trend toward an association for fruit and vegetable (F&V) intakes (2.55%; 95% CI: -0.26, 5.45;  $P = 0.08$ ). These modest positive associations cannot be explained by confounding through other lifestyle factors shared by the twins. A significant relationship between adiponectin and 3 derived dietary patterns (F&V, dieting, traditional English), carbohydrate, protein, trans fat, and alcohol intake was also observed. Strong inverse associations with adiponectin were observed for BMI (-10.72%; 95% CI: -13.78, -7.55), total (-6.89%; 95% CI: -10.34, -3.30;  $P < 0.05$ ), and central fat mass (-12.50%; 95% CI: -15.82, -9.05;  $P < 0.05$ ); these relationships were significant both when twins were analyzed as individuals and when characteristics were contrasted within-twin pairs, suggesting a direct effect. We observed modest associations between dietary factors and adiponectin in female twins, independent of adiposity, and report strong inverse associations with body composition. These data reinforce the importance of weight maintenance and increasing consumption of diets rich in plant-based foods to prevent CVD and type 2 diabetes. *J. Nutr.* 139: 353–358, 2009.

## Introduction

Adiponectin, a circulating adipose tissue-specific adipokine that is produced in visceral, subcutaneous, and bone marrow fat depots (1), plays an important role in modulating insulin sensitivity and lipid metabolism (2–5). Although adiponectin expression is almost exclusively restricted to adipocytes, plasma concentrations are paradoxically downregulated in obese subjects (1,6,7). Both total fat mass and distribution of adipose tissue determine adiponectin levels; higher central adiposity is associated with lower levels (7,8).

Circulating adiponectin is emerging as an important link among obesity, type 2 diabetes, and cardiovascular disease

(CVD)<sup>6</sup> (3,4,6,9–13), but to date, the spectrum of lifestyle factors that are predictors of adiponectin concentrations remains to be elucidated. A better understanding of the control of adiponectin expression may be important, because dietary components may directly influence the molecular events that govern gene expression of adipokine synthesis and interrelated lipid and glucose metabolism. Limited available data suggest energy restriction, weight loss, and activation of PPAR $\gamma$  are potential modifiers of adiponectin concentrations (14–18). In healthy men, moderate alcohol intake is associated with increased levels (2,19) and a carbohydrate-rich diet with a high glycemic load is associated with decreased adiponectin concentrations (19). In diabetic women, adherence to a Mediterranean-

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<sup>6</sup> Abbreviations used: CVD, cardiovascular disease; DZ, dizygotic; F&V, fruit and vegetable; IMD, index of multiple deprivation score; MZ, monozygotic; NSP, nonstarch polysaccharide; PA, physical activity.

type diet is associated with increased levels (20). However, at present, little is known about dietary predictors of adiponectin concentrations in healthy women.

The present study examines dietary and body composition associations with adiponectin in healthy female twins derived from the U.K. population. Studying associations in twins is the equivalent of a matched case-control design, in which pairs are matched for their genetic background and a range of factors in their shared environment, all of which may influence the association between adiponectin, diet, and body composition. This provides a unique level of control over confounding by lifestyle factors, which is a major limitation in the interpretation of many dietary association studies. Our aim was to use a co-twin design to examine the associations of body composition, dietary patterns, foods, and nutrients on adiponectin concentrations in female twins.

## Methods

**Subjects and study design.** The TwinsUK adult twin registry is an ongoing study examining a wide range of age-related phenotypes. The volunteer population comprises ~5000 twin pairs [35% monozygotic (MZ), 65% dizygotic (DZ)], most of whom have undergone extensive clinical investigations as part of previous studies. Participants were not aware of the hypotheses being tested in this study and were not selected on the basis of variables being studied. No significant differences have been found for a range of traits when this group was compared with U.K. adult singleton populations, suggesting that they are representative (21,22). Zygosity was derived by questionnaire and confirmed by multiplex-DNA fingerprinting (PE Applied Biosystems). Ethical approval was obtained from the St. Thomas's Hospital Research Ethics committee and informed consent was obtained from all subjects.

The twins included in this study were female, aged 18–80 y, and were a sample of the total population group who attended for dual-energy X-ray absorptiometry scans and clinical assessment between 1996–2000. Complete data for this study were available for 1754 individuals, representing 723 DZ pairs and 154 MZ pairs. Height and weight were measured and BMI calculated. A venous blood sample was drawn following an overnight fast and the resulting serum stored at  $-40^{\circ}\text{C}$  until analysis. For both twins of each pair, blood was taken 5 min apart. At assessment, twins completed a questionnaire detailing their medical history and lifestyle factors. Physical activity (PA) was recorded as inactive, light, moderate, and heavy exercise during leisure time. This previously validated measure of activity correlates well with an in-depth measure of PA in the Dunbar Health Survey (23). Smoking was categorized as current, ex, or never smoker. Index of multiple deprivation scores (IMD) were derived for all subjects with valid U.K. postcodes, as a measure of social class (22).

**Assessment of body composition and dietary intake.** Body composition was measured using dual-energy X-ray absorptiometry (Hologic QDR). Total body fat (mass and percent body weight) was then determined using standard software calculations. Central abdominal fat was measured by a single blinded investigator and was defined as the abdominal region extending from the top of the 2nd lumbar to the bottom of the 4th lumbar vertebrae and laterally to the inner aspect of the ribs (24); this region relates strongly to central abdominal fat measured by computed tomography (25,26). Central abdominal fat is expressed as mass of fat tissue in the defined region (in kilograms).

Subjects completed a 131-item validated FFQ (27,28) and nutrient composition was determined using McCance and Widdowson Food tables (29). To examine effects of dietary patterns and food and nutrient intake on adiponectin, we first examined the relationship between the dietary patterns previously described in our cohort (22): fruit and vegetable (F&V): frequent intakes of fruit, allium, and cruciferous vegetables and low intakes of fried potatoes; high alcohol: frequent intakes of beer, wine, and allium vegetables and low intakes of high-fiber breakfast cereals and fruit; traditional English: frequent intakes of fried fish and potatoes, meats, savory pies and cruciferous vegetables; dieting:

frequent intakes of low-fat dairy products, low-sugar soda and low intake of butter and sweet baked products; and low meat: frequent intakes of baked beans, pizza, and soy foods and low intakes of meat, other fish and seafood, and poultry. We then looked to confirm previous findings from men and diabetic women (19,20) in relation to adiponectin concentrations. To investigate the relative contribution of components of F&V to circulating adiponectin concentrations, we conducted separate analyses specifically to examine the relative contributions of magnesium and nonstarch polysaccharide (NSP) intake to adiponectin levels.

**Assessment of plasma adiponectin concentrations.** Fasting serum total adiponectin levels were measured with a 2-site DELFIA assay using antibodies and standards from R&D Systems as described previously (30). Adiponectin assays were performed by the Core Biochemical Assay Laboratory, National Institute for Health Research Cambridge Biomedical Research Centre, UK.

The day-to-day CV for plasma adiponectin was 9.9% at a concentration of 3.2 mg/L, 7.8% at 8.5 mg/L, and 5.2% at 14.7 mg/L (30).

**TABLE 1** Characteristics of the study population<sup>1</sup>

	All twins	MZ only	DZ only	P-value <sup>4</sup>
<i>n</i>	1754	308	1446	
Plasma adiponectin, <sup>2</sup> mg/L	7.4 ± 1.6	7.3 ± 1.6	7.5 ± 1.6	0.44
Age, y	47.8 ± 12.3	47.0 ± 13.4	47.9 ± 12.0	0.28
BMI, <sup>3</sup> kg/m <sup>2</sup>	24.9 ± 1.2	24.4 ± 1.2	25.0 ± 1.2	0.02
Lean mass, % total body weight	64.3 ± 7.3	65.2 ± 7.2	64.1 ± 7.3	0.01
Fat mass, % total body weight	35.7 ± 7.3	34.8 ± 7.2	35.9 ± 7.3	0.01
Central fat mass, % total body weight	5.5 ± 1.6	5.3 ± 1.7	5.5 ± 1.6	0.13
Fat mass:lean mass	0.6 ± 0.2	0.6 ± 0.2	0.6 ± 0.2	0.01
Total energy intake, kJ/d	481 ± 129	483 ± 125	505 ± 130	0.76
Carbohydrate, % total energy	49.6 ± 6.3	49.4 ± 6.7	49.6 ± 6.3	0.68
Protein, % total energy	16.7 ± 2.8	16.5 ± 2.6	16.7 ± 2.8	0.40
Total fat, % total energy	30.2 ± 5.4	30.3 ± 5.4	30.1 ± 5.4	0.67
Saturated fat, % total energy	11.2 ± 2.8	11.3 ± 3.0	11.2 ± 2.8	0.77
Monounsaturated fat, % total energy	10.1 ± 2.1	10.1 ± 2.1	10.0 ± 2.1	0.58
Polyunsaturated fat, % total energy	6.7 ± 1.7	6.7 ± 1.6	6.7 ± 1.7	0.99
Trans fat, % total energy	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	0.54
NSP, g/d	20.5 ± 7.7	20.3 ± 7.7	20.6 ± 7.7	0.55
F&V consumption, <sup>5</sup> portions/d	6.7 ± 3.6	6.8 ± 3.7	6.7 ± 3.5	0.47
Alcohol, g/d	10.4 ± 14.2	10.9 ± 13.2	10.3 ± 14.4	0.47
Magnesium, mg/d	366 ± 99.3	363 ± 102	367 ± 98.8	0.51
Current smokers, %	30.7	26.6	31.6	0.06
Moderate PA, %	54.8	56.8	54.4	0.33
IMD quintile, <sup>5</sup> %	33.8	36.0	33.3	0.13

<sup>1</sup> Values are means ± SD or % unless otherwise indicated.

<sup>2</sup> Nongeometric values for adiponectin: mean = 8.32, SD = 4.03, minimum = 1.69, maximum = 28.5.

<sup>3</sup> Values transformed back from the logarithmic of the original distribution.

<sup>4</sup> P-values are from independent *t* tests for continuous variables or chi-square test for categorical variables.

<sup>5</sup> 80 g/portion.

**Analytical approach.** The relationship between plasma adiponectin, body composition, and dietary intake was assessed by fitting linear regression. Dietary variables were standardized giving a mean of 0 and a SD of 1. Plasma adiponectin concentrations were log-transformed to achieve a normal distribution. Analyses were conducted by first examining associations in twins as individuals:

$$E(Y_{ij}) = \beta_0 + \beta_c X_{ij},$$

where  $Y_{ij}$  and  $X_{ij}$  represent the plasma adiponectin (Y) value and dietary variable of interest (X) of twin  $j$  from pair  $i$ , respectively.  $\beta_c$  represents the expected change in plasma adiponectin per SD increase in the dietary/body composition variable in individuals (the individual specific effect), with values expressed as  $\beta$  (95% CI) in tables. The influence of confounding variables was assessed by fitting a sequence of models, including (1) BMI and (2) BMI, energy intake, PA, smoking, and social class. For magnesium, NSP, and F&V, further dietary covariates were added to the models.

To examine associations within twin pairs, the model was extended to take into account the twin pair mean:

$$E(Y_{ij}) = \beta_0 + \beta_i(X_{ij}) + \beta_t \bar{X}_i$$

where  $\bar{X}_i$  is the mean value of X for twin pair  $i$ . The  $\beta_i$  gives the expected mean in Y for a 1-unit deviation from the pair change in the outcome variable (within-pair). The  $\beta_t$  gives the expected change in Y for a 1-unit change in the twin pair average X (between-pair) while holding constant the individual deviation from the average. Thus,  $\beta_i$  (the within-pair effect) represents the strength of the association within pairs and is free from the confounding influence of factors that are common to the twin pair.  $\beta_t$  (the between-pair effect) reflects further variation in Y that is accounted for by factors in the shared environment or genetic background of twins and which do not account for individual differences. In general, a strong within-pair effect with a small or absent between-pair effect is consistent with an individual specific mechanism/causal mechanism or a direct/real effect (31). Heritability of plasma adiponectin has previously been determined (32). Our analyses focused on the direct effects of dietary exposure and body composition using a matched co-twin design. We also examined MZ and DZ twin pairs separately, but there were no important differences in the magnitude of either the within- or between-pair coefficients (data not shown). Data from MZ and DZ twin pairs were pooled in the analysis, because no important differences were detected in the magnitude of the within- or between-pair coefficients (data not shown). Differences between MZ and DZ twins were investigated using  $t$  tests for continuous variables and chi-square tests for categorical variables. Results are presented as means  $\pm$  SD. All statistical analyses were performed using STATA version 9 (Stata Corp).

## Results

In all participants, plasma adiponectin concentrations were  $7.43 \pm 1.62$  mg/L and there were no differences between MZ and DZ twin pairs. DZ twins had moderately but significantly higher BMI and fat mass and lower lean mass than MZ twins, but food and nutrient intakes did not differ between the MZ and DZ twin pairs (Table 1).

In the individual-level analysis, following adjustment, a 1 SD increase in BMI, total fat mass, and central fat mass was associated with decreases in plasma adiponectin ( $P < 0.05$ ) (Table 2). These inverse associations remained significant in the within-pair analyses. These body composition measures were significantly correlated (range from 0.38 for lean mass and central fat to 0.89 for BMI and total fat) and it is therefore hard to disentangle their relative contributions to plasma adiponectin concentrations.

In individual-level analyses, the magnitude of the associations with dietary variables and plasma adiponectin were modest (2–3% change in plasma adiponectin for every SD change in the diet variable) relative to the body composition measures (Table 3). We observed a significant positive relationship for both the F&V and dieting patterns with plasma adiponectin after adjustment for age and BMI, which remained significant following multivariate adjustment for the dieting pattern (Table 3).

Following multivariable adjustment for age, BMI, energy intake, PA, smoking, and social class, negative associations between the traditional English and dietary patterns (2.3% decrease in plasma adiponectin per 1 SD increase in pattern score) with plasma adiponectin were observed in individual-level analyses (Table 3). There were no significant within-pair relationships in any of the models, but results approached significance ( $P = 0.052$ ) for between-pair associations, suggesting that shared lifestyle factors other than diet were driving this apparent relationship.

**Carbohydrate, protein, and trans fat intake.** In the age-adjusted analyses (model 1), negative associations with plasma adiponectin were observed for dietary intakes of carbohydrate, protein, and trans fat intake. After further adjustment (models 2 and 3), these relationships were attenuated and no longer significant (Table 3). There were no significant within-pair or between-pair relationships.

**TABLE 2** Associations between plasma adiponectin concentrations and measures of body composition in the twin cohort and within and between-pair differences<sup>1–3</sup>

	Model	$B_c^1$		$B_i^2$ (within-pair)		$B_t^3$ (between-pair)	
		$\beta$ (per SD change)	(95% CI)	$\beta$ (per SD change)	(95% CI)	$\beta$ (per SD change)	(95% CI)
BMI, kg/m <sup>2</sup>	1 <sup>4</sup>	-11.57*	(-13.66, -9.42)	-10.81*	(-13.87, -7.65)	-1.70	(-6.06, 2.86)
	2 <sup>5</sup>	-11.47*	(-13.60, -9.29)	-10.72*	(-13.78, -7.55)	-1.71	(-6.04, 2.82)
Total fat mass, kg	1 <sup>4</sup>	-10.71*	(-12.85, -8.53)	-9.06*	(-12.10, -5.86)	-3.53	(-7.87, 1.02)
	2 <sup>5</sup>	-8.58*	(-11.19, -5.89)	-6.81*	(-10.24, -3.25)	-3.66	(-7.95, 0.82)
	3 <sup>6</sup>	-8.59*	(-11.24, -5.85)	-6.89*	(-10.34, -3.30)	-3.56	(-7.81, 0.88)
Central fat mass, kg	1 <sup>4</sup>	-15.32*	(-17.42, -13.17)	-13.49*	(-16.61, -10.24)	-4.07	(-8.51, 0.59)
	2 <sup>5</sup>	-14.45*	(-16.84, -11.99)	-12.54*	(-15.85, -9.09)	-4.17	(-8.57, 0.44)
	3 <sup>6</sup>	-14.46*	(-16.88, -11.96)	-12.50*	(-15.82, -9.05)	-4.31	(-8.65, 0.23)
Lean mass, kg	1 <sup>4</sup>	-8.71	(-0.78, -6.58)	-10.77*	(-13.8, -7.60)	4.500	(-0.37, 9.61)
	2 <sup>5</sup>	-12.00	(-4.25, -9.62)	-13.56*	(-16.7, -10.3)	3.658	(-1.08, 8.62)
	3 <sup>6</sup>	-11.86	(-14.2, -9.47)	-13.40*	(-16.5, -10.1)	3.582	(-1.13, 8.52)

<sup>1</sup> Expected change in plasma adiponectin (%) for a 1 SD change in the body composition measure, multivariate regression analysis. \*  $P < 0.05$

<sup>2</sup> Expected change in plasma adiponectin (%) for a 1 SD change in body composition measure, allowing for twin effects (within-pair), multivariate regression analysis.

<sup>3</sup> Expected change in plasma adiponectin (%) for a unit change in the family (twin pair mean) body composition measure, expressed on a scale of SD (between-pair), multivariate regression analysis.

<sup>4</sup> Adjusted for age.

<sup>5</sup> Adjusted for age and lean mass (lean mass adjusted for total fat mass).

<sup>6</sup> Adjusted for age, lean mass (lean mass adjusted for total fat mass), energy intake, PA, smoking, and IMD.

**TABLE 3** Associations between plasma adiponectin concentrations and dietary intake in the entire twin cohort and within- and between-pair differences<sup>1–3</sup>

	Model	B <sub>c</sub> <sup>1</sup>		B <sub>i</sub> <sup>2</sup> (within-pair)		B <sub>t</sub> <sup>3</sup> (between-pair)	
		β (per SD change)	(95% CI)	β (per unit change)	(95% CI)	β (per unit change)	(95% CI)
F&V pattern	1 <sup>4</sup>	2.56	(0.31,4.86)	1.82	(−1.20,4.94)	1.62	(−2.86,6.30)
	2 <sup>5</sup>	2.59*	(0.35,4.88)	1.87	(−1.14,4.98)	1.57	(−2.90,6.24)
	3 <sup>6</sup>	2.32	(−0.01,4.70)	1.55	(−1.49,4.69)	1.72	(−2.78,6.43)
Traditional English pattern	1 <sup>4</sup>	−2.33*	(−4.53,−0.07)	−0.81	(−3.40,1.84)	−4.22	(−8.26,0.00)
	2 <sup>5</sup>	−2.34*	(−4.55,−0.07)	−0.77	(−3.37,1.89)	−4.36	(−8.41,−0.13)
	3 <sup>6</sup>	−2.41*	(−4.63,−0.14)	−0.91	(−3.50,1.74)	−4.27	(−8.36,0.00)
Dieting pattern	1 <sup>4</sup>	2.36*	(0.21,4.57)	1.50	(−1.33,4.43)	2.31	(−2.46,7.30)
	2 <sup>5</sup>	2.36*	(0.21,4.56)	1.53	(−1.31,4.45)	2.24	(−2.55,7.26)
	3 <sup>6</sup>	2.36*	(0.21,4.55)	1.50	(−1.33,4.43)	2.31	(−2.56,7.43)
Carbohydrate, g/d	1 <sup>4</sup>	−2.14*	(−4.19,−0.05)	−1.92	(−4.61,0.85)	−0.59	(−5.17,4.21)
	2 <sup>5</sup>	−1.61	(−3.64,0.47)	−1.48	(−4.13,1.25)	−0.34	(−4.85,4.39)
	3 <sup>6</sup>	−3.58	(−7.93,0.98)	−3.36	(−8.11,1.63)	−0.55	(−5.10,4.22)
Protein, g/d	1 <sup>4</sup>	−2.56*	(−4.58,−0.49)	−1.56	(−4.01,0.96)	−2.84	(−6.85,1.35)
	2 <sup>5</sup>	−1.46	(−3.47,0.58)	−0.74	(−3.16,1.75)	−2.05	(−5.98,2.05)
	3 <sup>6</sup>	−2.00	(−5.46,1.59)	−1.34	(−5.03,2.50)	−2.02	(−6.00,2.13)
Trans fat, g/d	1 <sup>4</sup>	−2.44*	(−4.45,−0.39)	−1.24	(−3.97,1.57)	−3.20	(−7.64,1.45)
	2 <sup>5</sup>	−1.80	(−3.76,0.19)	−0.91	(−3.55,1.81)	−2.37	(−6.64,2.09)
	3 <sup>6</sup>	−1.59	(−4.41,1.31)	−0.64	(−4.01,2.87)	−2.47	(−6.76,2.02)
NSP, g/d	1 <sup>4</sup>	0.68	(−1.51,2.92)	1.01	(−1.78,3.88)	−0.84	(−5.16,3.69)
	2 <sup>5</sup>	1.24	(−0.92,3.45)	1.78	(−0.98,4.62)	−1.35	(−5.63,3.13)
	3 <sup>6</sup>	2.63	(−0.02,5.36)	3.25 <sup>1</sup>	(0.06,6.54)	−1.55	(−5.84,2.95)
F&V, <sup>7</sup> portions/d	1 <sup>4</sup>	1.32	(−0.84,3.52)	1.05	(−1.67,3.83)	0.66	(−3.62,5.13)
	2 <sup>5</sup>	1.87	(−0.21,3.99)	1.90	(−0.78,4.65)	−0.07	(−4.33,4.37)
	3 <sup>6</sup>	2.35*	(0.14,4.60)	2.55	(−0.26,5.45)	−0.49	(−4.76,3.98)
Alcohol, g/d	1 <sup>4</sup>	2.41	(0.36,4.50)	1.03	(−1.66,3.79)	3.39	(−0.93,7.91)
	2 <sup>5</sup>	1.85	(−0.18,3.91)	0.93	(−1.70,3.63)	2.22	(−1.79,6.40)
	3 <sup>6</sup>	2.36 <sup>1</sup>	(0.35,4.42)	1.47	(−1.11,4.10)	2.23	(−1.78,6.39)
Magnesium, g/d	1 <sup>4</sup>	0.08	(−2.02,2.24)	0.39	(−2.20,3.05)	−0.83	(−5.10,3.64)
	2 <sup>5</sup>	0.53	(−1.57,2.66)	1.03	(−1.55,3.68)	−1.34	(−5.48,2.99)
	3 <sup>6</sup>	3.31*	(0.00,6.74)	3.80 <sup>1</sup>	(0.17,7.57)	−1.33	(−5.50,3.02)

<sup>1</sup> Expected change in plasma adiponectin (%) for a 1 SD change in the body composition measure, multivariate regression analysis. \*  $P < 0.05$  from particular regression model.

<sup>2</sup> Expected change in plasma adiponectin (%) for a 1 SD change in body composition measure, allowing for twin effects (within-pair), multivariate regression analysis.

<sup>3</sup> Expected change in plasma adiponectin (%) for a unit change in the family (twin pair mean) body composition measure, expressed on a scale of SD (between-pair), multivariate regression analysis.

<sup>4</sup> Adjusted for age.

<sup>5</sup> Adjusted for age and lean mass.

<sup>6</sup> Adjusted for age, lean mass (except for lean mass regression, which was adjusted for total fat mass), energy intake, PA, smoking and IMD.

<sup>7</sup> 80 g/portion.

**Alcohol.** In individual-level analyses, significant positive associations were observed between alcohol consumption and plasma adiponectin concentrations after adjustment for energy intake, BMI, PA, smoking, and social class.

**NSP.** In individual-level analyses, there was no significant relationship between NSP intake and plasma adiponectin. However, a significant within-pair association was observed after adjustment for energy intake, BMI, PA, smoking, and social class (model 3).

**F&V.** In individual-level analyses, there were significant positive associations between F&V intake and plasma adiponectin concentrations after multivariate adjustment.

**Magnesium.** In individual-level analyses, magnesium and plasma adiponectin were positively associated following adjustment for energy intake, BMI, PA, smoking, and social class (model 3). There was also a significant positive within-pair relationship.

There were no important differences in the magnitude of either the within- or between-pair coefficients when we examined MZ and DZ twin pairs separately (data not shown). This suggests that the significant relationships were not primarily mediated through genetic factors. Results include data from 46 subjects who were taking diabetic medication or antihypertensive or lipid-lowering drugs. Exclusion of these subjects from the analyses did not affect the results. Furthermore, when analyses were restricted to either pre- or postmenopausal women, no significant differences appeared and the addition of hormone replacement therapy to the model made no significant difference to the results (data not shown).

## Discussion

In the present study, using a co-twin design, significant within-pair relationships were observed between plasma adiponectin and both NSP and magnesium intake, with a trend toward an association for F&V intakes following multivariable adjustment ( $P = 0.08$ ). Our data support the notion that F&V or another

**TABLE 4** The relative importance of magnesium and NSP and F&V intake on plasma adiponectin concentrations<sup>1</sup>

	Model <sup>3</sup>	Bc <sup>1</sup>	
		$\beta$ (per SD change)	(95% CI)
F&V, <sup>2</sup> portions/d	3	2.35*	(0.14, 4.60)
	3 + Mg	1.65	(-0.75, 4.10)
	3 + NSP	1.49	(-2.06, 5.17)
	3 + Mg + NSP	1.64	(-1.92, 5.34)
Magnesium, g/d	3	3.31*	(0.00, 6.74)
	3 + F&V	2.33	(-1.26, 6.05)
	3 + NSP	2.20	(-1.78, 6.33)
	3 + F&V + NSP	2.33	(-1.66, 6.48)
NSP, g/d	3	2.63	(-0.02, 5.36)
	3 + Mg	1.55	(-1.65, 4.84)
	3 + F&V	1.28	(-2.94, 5.68)
	3 + Mg + F&V	0.01	(-4.63, 4.86)

<sup>1</sup> Expected change in plasma adiponectin (%) for a 1 SD change in the dietary variable, multivariate regression analysis. \*  $P < 0.05$  from multivariate regression model.

<sup>2</sup> 80 g/portion.

<sup>3</sup> Model 3: Adjusted for age, BMI, energy intake, PA, smoking, and IMT.

unquantified component of plant-based foods (e.g. glycemic index but not NSP) explain the observed relationship between magnesium and plasma adiponectin (Table 4).

Our observed positive relationship between magnesium and plasma adiponectin in female twins agrees with previous data from diabetic men (33). This modest positive association also agrees with recent epidemiological, clinical, and experimental data that have demonstrated an inverse relationship between dietary magnesium intake and systemic inflammation (34) and risk of CVD and type 2 diabetes (35). The relationship is plausible, because magnesium is a cofactor for several enzymes involved in glucose metabolism; participates in intracellular signaling systems, insulin receptor activity, and phosphorylation reactions; and affects platelet aggregation and vascular smooth muscle tone (35).

The positive relationship between the dieting pattern and the inverse relationship with the traditional English pattern support previous research showing that long-term weight loss is associated with increased plasma adiponectin (2,16,36,37). For carbohydrate intake, the inverse relationship following adjustment for age was attenuated following additional adjustment for other confounders. The within-pair coefficient was similar but was not significant ( $P = 0.12$ ), in part because we measured only total carbohydrate intake and not more accurate measures of carbohydrate quality or glycemic load, which were unavailable in our food composition database. This is consistent with previous data in diabetic men, where dietary glycemic index and glycemic load were inversely associated with plasma adiponectin concentrations (33).

For protein and trans fat intake, the inverse relationship with age was also attenuated following adjustment. For trans fat intake, the lack of association following the addition of BMI to the model may be because of the mediating effect of BMI, given the strong relationship between BMI and plasma adiponectin (Table 2) or, more likely, the direct effects of long-term trans fat consumption on weight gain with specific increases in intra-abdominal fat deposition (38). Using a controlled animal feeding model with a long-term intervention with trans fats, monkeys gained significant weight and this was associated with increased insulin resistance (38).

We observed inverse associations between plasma adiponectin and BMI, total fat mass, and central fat mass similar in magnitude

to those of previous singleton studies (1,7,8). By using the twin model, we showed that these differences are mediated within and not between pairs, suggesting that this is a real association. Although the few previous studies examining factors influencing plasma adiponectin concentrations made adjustments for sociodemographic and other risk factors, no study to our knowledge has previously accounted for familial or genetic influences that may be shared.

Heritable and familial determinants affect plasma adiponectin concentrations, BMI (24,32,39), and food preferences (22) and have been the subject of other studies. Quantitative genetic analysis of plasma adiponectin levels detected an additive genetic heritability of 88% (32,39). An alternative explanation for the association between these variables is that it might be mediated genetically, but we found no evidence of this. The associations we observed in MZ twins and the similarity of the strength of the association in DZ twins suggests the associations are environmentally mediated, although we cannot formally exclude the possibility of gene  $\times$  environment interactions (40).

One of the well-recognized limitations of the use of FFQ relates to the potential influence of reporting food intake by weight status. The matched nature of the study and adjustment for BMI minimizes these influences and by modeling within-pairs, we could take these factors into account. When we compared twins within-pairs and conducted matched analysis, we found that NSP, magnesium intake, and plasma adiponectin associations were not diminished, which suggests a pure effect.

Other potential limitations include the cross-sectional nature of the study and the focus on female twin pairs; although they are representative of the U.K. population for a range of characteristics (21,22), the results may differ in men. It has been suggested that measurement error with FFQ is greater than with more precise record methods (28), but under the assumption of random measurement error, our observed effects might be attenuated. Our nutrient composition database did not allow us to differentiate between cereal and soluble fiber, which is a limitation of the current study. Clearly, these findings require replication in other cohort studies. Our analytical method assessed total plasma adiponectin levels, which does not account for the different complexes of adiponectin in plasma. The high molecular weight form is the most biologically active form but is highly correlated with total plasma adiponectin levels (41,42).

Using twins, we have demonstrated that shared environmental and genetic factors do not confound the associations between body composition and plasma adiponectin concentrations. Although we observed modest associations with dietary factors, when considered together, these data provide a plausible biological mechanism and point to the importance of maintaining optimal weight and increasing consumption of plant-based foods to prevent CVD and the development of visceral obesity.

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