

Food Preference Patterns in a UK Twin Cohort

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Food liking-disliking patterns may strongly influence food choices and health. Here we assess: (1) whether food preference patterns are genetic/environmentally driven; and (2) the relationship between metabolomics profiles and food preference patterns in a large population of twins. 2,107 individuals from TwinsUK completed an online food and lifestyle preference questionnaire. Principle components analysis was undertaken to identify patterns of food liking-disliking. Heritability estimates for each liking pattern were obtained by structural equation modeling. The correlation between blood metabolomics profiles (280 metabolites) and each food liking pattern was assessed in a subset of 1,491 individuals and replicated in an independent subset of monozygotic twin pairs discordant for the liking pattern (65 to 88 pairs). Results from both analyses were meta-analyzed. Four major food-liking patterns were identified (Fruit and Vegetable, Distinctive Tastes, Sweet and High Carbohydrate, and Meat) accounting for 26% of the total variance. All patterns were moderately heritable (Fruit and Vegetable, h^2 [95% CI]: 0.36 [0.28; 0.44]; Distinctive Tastes: 0.58 [0.52; 0.64]; Sweet and High Carbohydrate: 0.52 [0.45; 0.59] and Meat: 0.44 [0.35; 0.51]), indicating genetic factors influence food liking-disliking. Overall, we identified 14 significant metabolite associations (Bonferroni $p < 4.5 \times 10^{-5}$) with Distinctive Tastes (8 metabolites), Sweet and High Carbohydrate (3 metabolites), and Meat (3 metabolites). Food preferences follow patterns based on similar taste and nutrient characteristics and these groupings are strongly determined by genetics. Food preferences that are strongly genetically determined ($h^2 \geq 0.40$), such as for meat and distinctive-tasting foods, may influence intakes more substantially, as demonstrated by the metabolomic associations identified here.

■ **Keywords:** food preference, metabolomics, twins, heritability

Food preferences are formed by myriad of factors, including environmental (e.g., food exposure during childhood (Ventura & Worobey, 2013), economics (Novakovic et al., 2014) and genetic determinants (particularly related to tasting; Feeney et al., 2011; Pirastu et al., 2012). Individual food preferences have shown to be correlated with reported food intakes (Drewnowski et al., 1999; Duffy et al., 2009), suggesting they are prominent determinants of food intake and subsequently may have implications for the development of long-term chronic diseases that are increasingly prevalent in Western countries today.

The employment of statistical methods for food intake data reduction to population-specific dietary patterns and connecting these patterns with metabolic health and disease outcomes has surged in recent years. However, application of these methods to food hedonic (i.e., the degree of 'lik-

ing' or 'wanting' a food) questionnaires is limited within the literature. Recently, subject hedonic ratings of food images were reduced to seven components through PCA and then assessed against BMI and reported intakes (Johnson et al., 2014). Drewnowski et al. (1999) evaluated food preferences in young women and utilized factor analysis to reduce food preferences to categories and subcategories, and assessed these against reported nutrient intakes. These studies demonstrate that food liking tends to cluster into

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statistically reliable groupings based on nutritional value and/or taste characteristics, offering a potentially powerful tool to assess the genetic influence on these traits.

Studies including our UK and Finnish twin cohorts have identified groupings of food hedonics based on taste tend to be significantly and strongly heritable (Keskitalo et al., 2007; Tornwall et al., 2012a; 2012b). Using multiple measures of chemosensory traits, additive genetic effects have been found to explain variation in hedonic ratings between 0.49 and 0.53 for sweet foods (Keskitalo et al., 2007), 0.18 and 0.58 for oral pungency (spicy foods) (Tornwall et al., 2012a), and 0.34 and 0.50 for sour foods (Tornwall et al., 2012b). Although well designed, these studies have provided a narrow assessment of the heritability of chemosensory traits by focusing on a subset of taste phenotypes rather than food preferences based on the whole diet. Moreover, the impact of these strongly genetically determined traits on metabolic health, potentially through modifying food intake, has rarely been examined.

The degree to which food preferences influence intake has been evaluated by examining the correlations between preference of foods and reported intakes previously (Drewnowski et al., 1999; Duffy et al., 2007; 2009; Johnson et al., 2014; Peracchio et al., 2012), although the validity and precision of intake measurements is affected by self-reporting (Westerterp & Goris, 2002). The food preference questionnaire developed by Duffy et al. (2007) and utilized for the current study has been shown to produce statistically reliable food groups (Duffy et al., 2007; 2009) and to correlate well with objective measures, including consistent associations between adiposity with sweet-and-fatty food liking (Duffy et al., 2007; 2009; Peracchio et al., 2012) and carotenoid status with fruit and vegetable liking (Scarmo et al., 2012). Further assessment of the food preference questionnaire against objective biomarkers would provide greater insight into the degree to which food preferences influence metabolic health and food consumption habits. In this instance, metabolomics, the global measurement of metabolites in a biological sample at one time point would provide a strong advantage. Novel candidate biomarkers of dietary intake have been identified by assessing tissue metabolomic profiles against intake frequency-derived dietary patterns (Altmaier et al., 2011; Menni et al., 2013c; O'Sullivan et al., 2011), validating this approach for use in epidemiological studies. However, replicating results in independent populations is challenging due to the wide-ranging genetic influence on metabolite levels (Shin et al., 2014); therefore, usage of the co-twin control method (first used to investigate the impact of smoking on mortality; Friberg et al., 1970) provides an advantage through segregating the non-genetic component and adjusting for known and unknown biases including age and cohort effects.

The objectives of this article were to identify food preference patterns in a UK twin population, to determine if these food preference patterns are primarily genetic or envi-

ronmentally determined and to identify if patterns of food liking influence the long-term blood metabolomics profiles of individuals.

Materials and Methods

Subjects

Subjects included in the analysis were twins enrolled in the TwinsUK registry, a national register of UK adult, predominantly female twins (Moayyeri et al., 2013). In this study, we included twins who had completed the food preference questionnaire and had blood metabolomic profiling available. The study was approved by the St. Thomas' Hospital Research Ethics committee and all subjects provided informed written consent. Measured BMI (kg/m^2) was taken by trained research assistants at the visit time nearest to questionnaire completion. Income was evaluated by asking subjects to estimate their total yearly household income before taxes according to the following categories: (1) Less than £10,000; (2) £10,000–£14,999; (3) £15,000–£19,999; (4) £20,000–£24,999; (5) £25,000–£49,999; (6) £50,000–£74,999; (7) £75,000–£99,999; 8, £100,000 or more.

Food and Lifestyle Preference Questionnaire

Figure 1 contains the study pipeline. Male and female twins ($n = 2569$), aged 19 to 88 years, provided responses to the food and lifestyle preference questionnaire between July and August 2014 via Qualtrics, an online questionnaire platform. Twins were sent an email and asked to complete the questionnaire by following an anonymized link. The questionnaire was adapted from Duffy (2007) to suit the large UK twin cohort. Modifications to the questionnaire included: conversion from a paper to online survey format, modification of the food items to suit a UK diet, and the addition of a box to the left of the scale for the subject to indicate if they had not tried a food or non-food. In our study, degrees of liking-disliking for 87 foods and beverages and 18 non-foods (9 activities and 9 experiences/sensations) were rated on a horizontal continuous line scale labeled with five faces (Peracchio et al., 2012). The scale ranged from ± 100 (0 = neutral/ neither like nor dislike; +100 = strongest liking of any kind; -100 = strongest disliking of any kind). A picture of each food was placed to the left of the scale. Subjects with incomplete questionnaires were excluded from the analysis ($n = 76$).

Metabolomics

Non-targeted metabolomics mass spectrometry profiling was conducted by the metabolomics provider Metabolon, Inc. (Durham, NC) on 1,491 fasting blood samples, as previously described (Menni et al., 2013a; 2013b). Blood samples were taken an average of 7 years (SD : 3 years; range: 4–17 years) prior to food preference questionnaire completion. In this study, we analyzed 280 structurally named biochemicals (known metabolites) categorized into the following

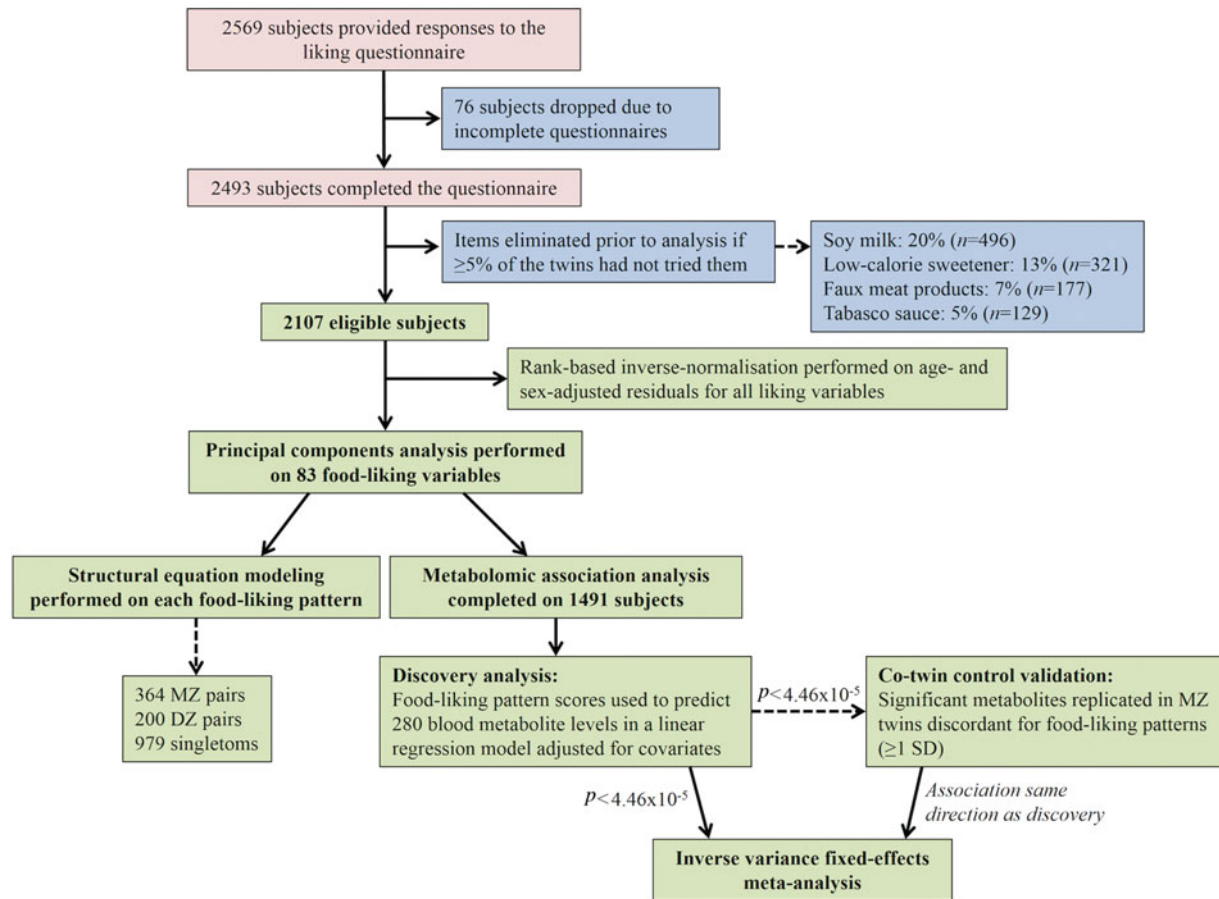


FIGURE 1

(Colour online) Pipeline of study design.

broad groups: amino acids, carbohydrates, vitamins, lipids, nucleotides, peptides, and xenobiotics.

Statistical Analysis

All statistical analyses were conducted in Stata, unless otherwise noted. We inverse normalized the metabolite data as the metabolite concentrations were not normally distributed. Metabolites were excluded from the analysis if more than 20% of the values were missing to avoid false-positive associations. Missing values for the remaining metabolites were imputed using minimum run day measures.

Dietary pattern generation. We removed foods from the analysis if 5% or more of the respondents had not tried them (Figure 1). Due to the wide age range included in the sampling population, all food items were residual adjusted for age prior to analysis. A small portion of the subjects were male (11%) and ratings were found to differ significantly by sex for many foods so all ratings were also residual adjusted for sex. Ratings of liking-disliking for most foods did not follow a normal distribution and therefore all items were transformed by rank-based inverse normalization. Principal component analysis (PCA) was conducted

on liking-disliking ratings for 83 foods, and only twins who had tried all of these foods were included in the analysis ($n = 2,107$). Components were retained by reviewing the inflection point of the scree plot and rotated using varimax rotation.

Heritability. Heritability of the food liking-disliking scores was determined using linear structural equation modeling in Mx (Neale & Cardon, 1992; Neale et al., 2003). Univariate ACE models decompose the phenotypic variance into additive genetic effects (A), common (C) environmental effects, and non-shared environmental effects (E). Additive genetic influences are indicated when MZ twins are significantly more similar than DZ twins. The common environmental component estimates the contribution of family environment, which is assumed to be equal in both MZ and DZ twin pairs (Kyvik, 2000). By comparison, the unique environmental component does not contribute to twin similarity; rather, it estimates the effects that apply only to each individual and includes measurement error. Any greater similarity between MZ twins than DZ twins is attributed to greater sharing of genetic influences. Heritability is defined

TABLE 1
Characteristics of the Study Population and Trends With Food-Liking Patterns^a

	All subjects (N = 2,107)	Fruit and vegetable		Distinctive tastes		Sweet and high carbohydrate		Meat	
		Beta (SE)	p	Beta (SE)	p	Beta (SE)	p	Beta (SE)	p
Age (years)	57.4 (12.5)								
Sex (M:F)	238:1869								
BMI (kg/m ²)	26.0 (4.8)	-0.03 (0.04)	0.465	-0.13 (0.04)	0.004	0.27 (0.05)	7.02 × 10 ⁻⁹	0.34 (0.05)	2.55 × 10 ⁻¹⁰
Smoking-liking	-82.0 (41.7)	-0.05 (0.01)	1.96 × 10 ⁻¹⁰	0.03 (0.01)	8.88 × 10 ⁻⁵	0.02 (0.01)	0.020	-0.01 (0.01)	0.874
Physical activity-liking ^b	15.4 (36.8)	1.12 (0.08)	1.21 × 10 ⁻³⁹	0.70 (0.08)	1.70 × 10 ⁻¹⁷	-0.07 (0.08)	0.361	-0.07 (0.07)	0.315
Age finished education (years)	18.2 (3.3)	-0.01 (0.02)	0.602	0.08 (0.02)	4.16 × 10 ⁻⁵	-0.09 (0.02)	5.25 × 10 ⁻⁶	-0.04 (0.02)	7.38 × 10 ⁻³
Household income level ^c	4.9 (1.7)	-0.02 (0.04)	0.610	0.16 (0.04)	1.18 × 10 ⁻⁴	-0.13 (0.04)	0.001	0.02 (0.04)	0.592
Ever followed a diet to lose weight? (Y:N)	910:1161	0.003 (0.004)	0.452	0.003 (0.004)	0.512	0.01 (0.004)	0.025	0.02 (0.005)	0.001

Note: ^aCharacteristics are expressed in mean (SD) for age, BMI, smoking-liking, physical activity-liking, age finished education and household income level, the male to female ratio (M:F) for sex (1, male; 2, female) and the yes to no (Y:N) ratio of subjects who had ever followed a diet to lose weight (0, no; 1, yes). Smoking-liking and physical activity-liking were assessed on a scale ranging from -100 to +100. A simple linear regression was conducted between each food-liking score and descriptive phenotype. ^bSubject reported liking for seven physical activities (taking the stairs, going to the gym, exercising alone, playing sports, exercising with others, bicycling and working up a sweat) formed a statistically reliable group (Cronbach's alpha: 0.83) and were summed. ^cSubjects were asked their level of yearly household income as follows: (1) Less than £10,000; (2) £10,000–£14,999; (3) £15,000–£19,999; (4) £20,000–£24,999; (5) £25,000–£49,999; (6) £50,000–£74,999; (7) £75,000–£99,999; (8) £100,000 or more.

as the proportion of the phenotypic variation attributable to genetic factors and is given by the equation, $h^2 = (A)/(A + C + E)$. Akaike's information criterion (AIC) was used to determine the best fitting model (among ACE, AE, CE, and E models). The model with the lowest AIC reflects the best balance of goodness of fit and parsimony (Neale & Cardon, 1992). All variables were residual-adjusted for age and sex.

Liking pattern-metabolite associations. For each metabolite, random intercept linear regression analysis was first undertaken by excluding MZ twin pairs discordant for each food preference pattern (MZ twins with measures one SD apart in scores for the relevant food preference pattern) adjusting for age, metabolite batch, sex, BMI, and family relatedness:

$$Y_i = \beta_0 + \beta_i X_{ij} + \gamma_i \text{age}_{ij} + \delta_i \text{BMI}_{ij} + \zeta_j + \varepsilon_{ij}$$

where Y_i is the metabolite and X_{ij} the food preference pattern of twin j from pair i , ζ_j is the family-specific error component that captures the unobserved heterogeneity or family characteristics.

We used a Bonferroni correction to adjust for multiple testing, which gave a significant threshold of 4.5×10^{-5} ($0.05/[280 \text{ detected metabolites} \times 4 \text{ food preference patterns}]$). For each significant metabolite-food preference pattern association from the discovery sample, the same linear regression analysis was undertaken in the MZ discordant twin pair population. The MZ discordant twin pair design provides a powerful means to examine the impact of environmental and lifestyle exposures, while controlling for age, sex, baseline genetic sequence, and shared upbringing (van Dongen et al., 2012). Associations from the discordant MZ pair analysis in the same direction as the discovery set were considered replicated. Finally, we combined the results using an inverse variance fixed effect meta-analysis.

To determine if food preference pattern-associated metabolites were driven by the liking of single foods, we repeated the same linear regression analysis as described for the liking pattern associations (above) for all food-liking variables against each significant metabolite (Bonferroni $p < 5.5 \times 10^{-5}$ ($0.05/[11 \text{ metabolites} \times 83 \text{ food liking variables}]$)).

Results

Demographic Characteristics

The demographic characteristics of the study population are included in Table 1. Food liking-disliking data was complete for 2,107 twins, of which a subset of 1,491 had blood metabolomics profiling available. The mean age of the study sample was 57.4 years (12.5 years SD; 19–88 years), and the mean BMI was 26.0 kg/m² (4.8 kg/m² SD) and in the overweight range (>25 kg/m²).

Food Liking-Disliking Patterns

The first 20 components presented in the scree plot (Figure 2) show an inflection point after the fourth component, so only the first four components were retained. The total variance explained by the first four components was 26%. Figure 3 shows the component loadings for each of the four components; the full rotated component matrix with all variable component loadings can be found in Supplementary Table S1. The four patterns were designated as follows according to their top food preference loadings:

Fruit and vegetable (12.2% variance). High liking of strawberries, spinach/greens, melon, raw carrot, banana, pineapple, pear, cherries, fresh tomatoes, tuna or salmon, beetroot, porridge, and broccoli.

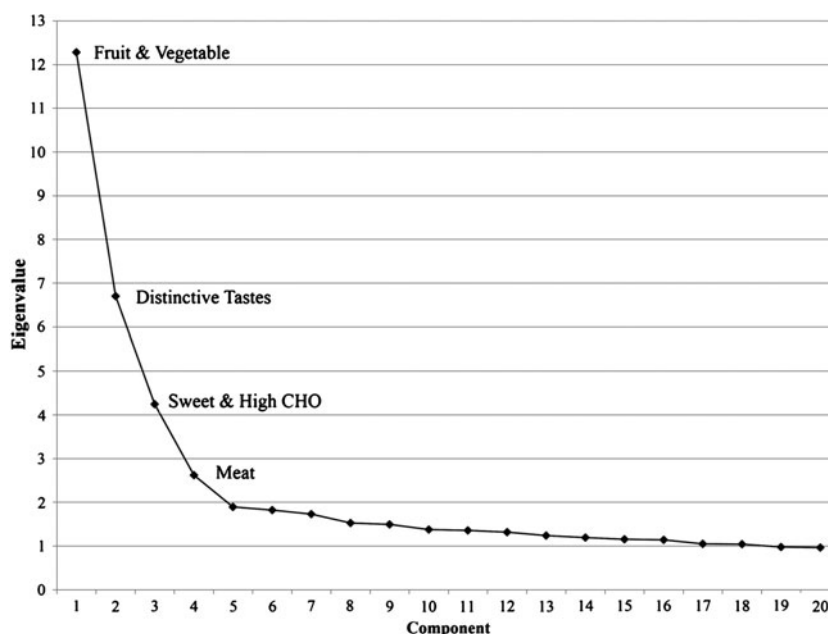


FIGURE 2

Eigenvalues for the first 20 principle components derived from the liking-disliking ratings for 83 foods from 2,107 subjects.

Distinctive tastes (6.7% of variance). High liking of chili pepper, the burn of spicy foods, horseradish/wasabi, olives, gherkins, blue cheese, curries, garlic, red wine, aubergine, soy sauce, fresh coriander, beer, salty pretzels, vodka/gin/scotch, and black pepper.

Sweet and high carbohydrate (4.2% of variance). High liking for biscuits, cakes or pastries, carbonated drinks and sweet drinks, cake icing, jam/jelly, cheesecake, ice cream, bagels/rolls, sweet coffee drinks and whipped cream, diet carbonated soft drinks, pizza, chips, cornflakes, and ketchup.

Meat (2.6% of variance). High liking for beef steak, chargrilled meats, pork chops, ham, crispy bacon, baked chicken, sausage, fried chicken, prawns and shellfish, and fried fish.

Pattern Scores and Population Characteristics

Trends for each pattern score and BMI, liking for smoking and physical activities, age finished education, household income level, and whether twins had ever followed a diet to lose weight are presented in Table 1. Scoring highly on the Fruit and Vegetable-liking pattern was strongly associated with higher physical activity liking (Beta[SE]: 1.12[0.08], $p = 1.21 \times 10^{-39}$), while associated with a lower liking for cigarette smoking ($-0.05[0.01]$, $p = 1.96 \times 10^{-10}$). Scoring highly on the Distinctive Tastes pattern was associated with higher scores for liking of cigarette smoking ($0.03[0.01]$, $p = 8.88 \times 10^{-5}$) and physical activities ($0.70[0.08]$, $p = 1.70 \times 10^{-17}$), a higher age finished education ($0.08[0.02]$,

$p = 4.16 \times 10^{-5}$) and household income ($0.16[0.04]$, $p = 1.18 \times 10^{-4}$), and mildly associated with having a lower BMI ($-0.13[0.04]$, $p = .004$). Scoring highly on the Sweet and High Carbohydrate pattern was associated with having a higher BMI ($0.27[0.05]$, $p = 7.02 \times 10^{-9}$), mildly associated with higher ratings for liking of cigarette smoking ($0.02[0.01]$, $p = .02$) and ever following a diet for weight loss ($p = .01[0.004]$, 0.025). Higher scores on the Sweet and High Carbohydrate pattern were associated with a lower age finishing education ($-0.09[0.02]$, $p = 5.25 \times 10^{-6}$) and household income ($-0.13[0.04]$, $p = .001$). Higher scores on the Meat-liking pattern were associated with having a higher BMI ($0.34[0.05]$, $p = 2.55 \times 10^{-10}$) and ever following a diet for weight loss ($0.02[0.005]$, $p = .001$), and finishing education at a lower age ($-0.04[0.02]$, $p = .007$).

Heritability

Heritability estimates for the four food preference scores are presented in Table 2. The AE model was the best fitting model for all liking-disliking groups. Variation in food liking-disliking scores for the Distinctive Tastes ($h^2[95\% \text{ CI}]: 0.61[0.53; 0.68]$), Sweet and High Carbohydrate ($0.52[0.44; 0.60]$) and Meat-liking ($0.45[0.35; 0.54]$) components were each strongly and significantly determined by additive genetic effects ($a^2 \geq 0.40$) or non-shared environmental factors. Variation in liking-disliking scores for the Fruit and Vegetable group was less strongly determined by additive genetic effects ($0.38[0.28; 0.48]$).

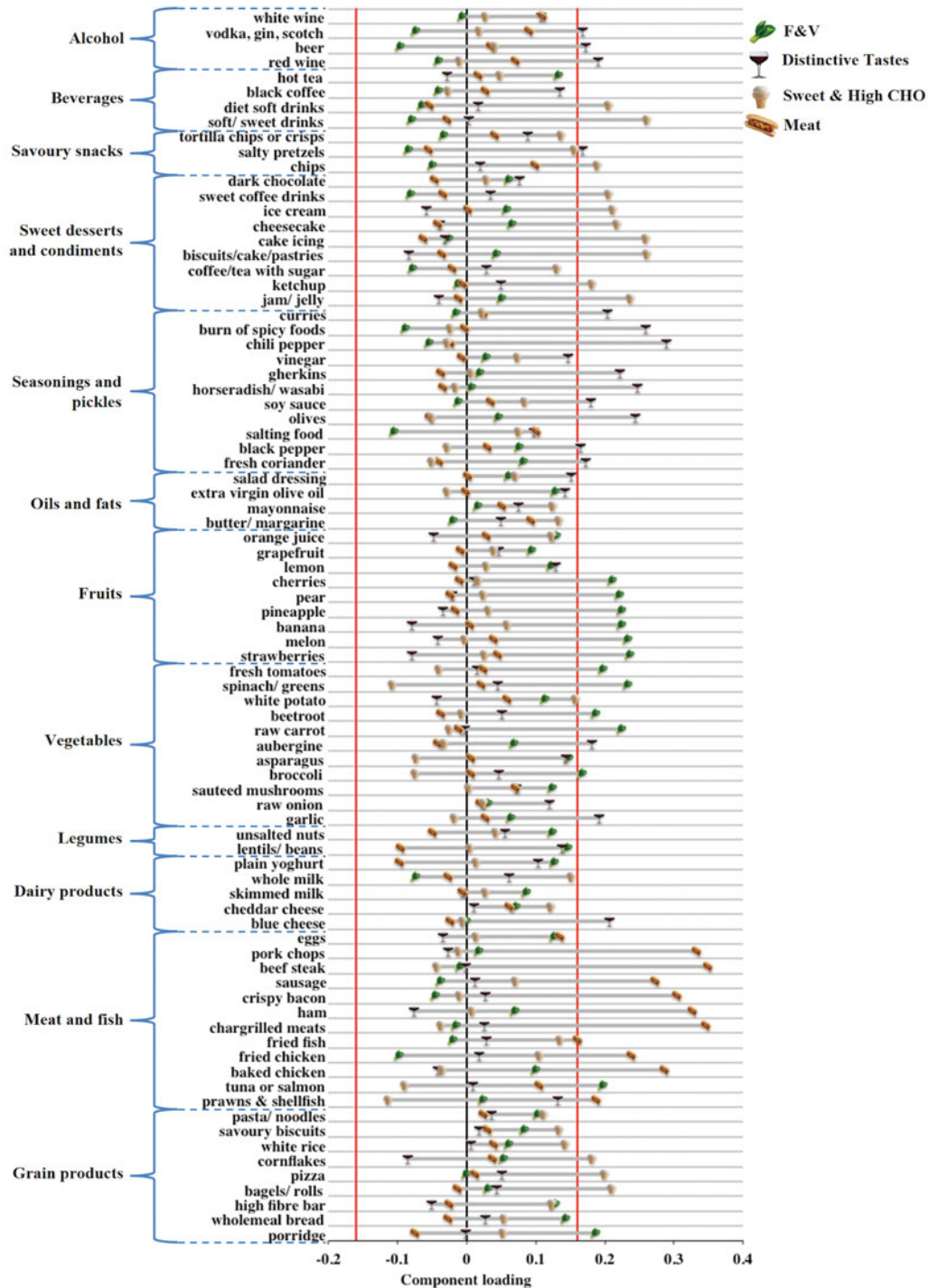


FIGURE 3

(Colour online) Rotated component loadings for liking-disliking ratings of foods. Loadings for each food liking-disliking pattern are presented by food with each food pattern represented by a symbol: F&V (Fruit and Vegetable), green lettuce; Distinctive Tastes, glass of red wine; Sweet and High CHO (carbohydrate), ice cream cone; Meat, hot dog. The red line indicates the top loadings (≥ 0.16 ; ≤ -0.16); loadings that pass this line were used to assign names and decipher the pattern.

Metabolomic Associations

We identified 14 significant metabolite associations with the food-liking patterns after adjusting for covariates and multiple testing (Bonferroni $p < 4.5 \times 10^{-5}$) and repli-

cated them in the MZ discordant group (Table 3). Having replicated these metabolites associated with food-liking patterns using identical twins discordant for the corresponding pattern, this substantiates the influence of food intake,

TABLE 2

Heritability Estimates for the Food Liking-Disliking Patterns (364 MZ Pairs, 200 DZ Pairs and 979 Singletons)

Variable	MZ		DZ		Best model	A [95%CI]	C [95%CI]	E [95%CI]
	Mean (SD)	ICC [95% CI]	Mean (SD)	ICC[95% CI]				
Fruit & vegetable	0.08 (2.83)	0.39 [0.30; 0.47]	-0.12 (2.64)	0.10 [-0.04; 0.24]	AE	0.36 [0.28; 0.44]	—	0.64 [0.56; 0.72]
Distinctive tastes	0.11 (2.61)	0.58 [0.51; 0.65]	-0.17 (2.68)	0.33 [0.20; 0.45]	AE	0.58 [0.52; 0.64]	—	0.42 [0.36; 0.48]
Sweet & high CHO	-0.01 (2.56)	0.53 [0.45; 0.60]	0.01 (2.48)	0.33 [0.20; 0.45]	AE	0.52 [0.45; 0.59]	—	0.48 [0.41; 0.55]
Meat	0.01 (2.23)	0.46 [0.38; 0.54]	-0.003 (2.17)	0.12 [-0.02; 0.25]	AE	0.44 [0.35; 0.51]	—	0.56 [0.49; 0.64]

Note: MZ = monozygotic; DZ = dizygotic; ICC = intra class correlation coefficient. Values in the three rightmost columns indicate the amount of variance attributed to the compartment of additive genetic factors (A or heritability), common environmental factors (C) and unique environmental factors.

as a product of food liking and an environmental effect, on metabolite levels, independent of the genetic effects. The Distinctive Tastes pattern was significantly associated with 8 metabolites (5 lipids, 1 xenobiotic, 1 amino acid, and 1 cofactor/vitamin). The furan fatty acid 3-carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF) was most strongly associated with this pattern (meta-analysis result: 0.084[0.009]; $p = 5.24 \times 10^{-19}$). The Sweet and High Carbohydrate pattern was associated with three metabolites and most strongly with CMPF (-0.051[0.010]; $p = 1.72 \times 10^{-7}$). Three metabolites were significantly associated with the Meat-liking group, including three amino acids. The amino acid involved in glutamate metabolism, pyroglutamine, was most strongly associated with meat-liking scores (-0.088[0.011]; $p = 1.76 \times 10^{-15}$). No association passed multiple testing correction for correlations between the Fruit and Vegetable group and blood metabolites.

To determine if food preference pattern associated metabolites were driven primarily by the liking of single foods, we repeated the same linear regression analysis for all food-liking variables against each significant metabolite (Bonferroni $p < 5.5 \times 10^{-5}$ (0.05/ [11 metabolites \times 83 food liking variables])). We identified 76 associations between single food-liking variables and the pattern associated metabolites after adjusting for covariates and replicated these in the MZ discordant twin group (Table 4). Overall, CMPF was associated with 17 food-liking variables (top association, prawns and shellfish: 0.276[0.025]; $p = 2.40 \times 10^{-28}$), DHA with 14 foods (top association, tuna or salmon: 0.238[0.026]; $p = 1.85 \times 10^{-19}$), EPA with 10 foods (top association, prawns & shellfish: 0.184[0.026]; $p = 5.35 \times 10^{-13}$), tryptophan betaine with 6 foods (top association, lentils/ beans: 0.199[0.030]; $p = 2.93 \times 10^{-11}$), scyllo-inositol with 5 foods (top association, red wine: 0.247[0.026]; $p = 8.03 \times 10^{-21}$), myo-inositol with 1 food (fresh coriander: 0.103[0.025]; $p = 4.98 \times 10^{-5}$), piperine with 7 foods (top association, black pepper: 0.207[0.027]; $p = 1.62 \times 10^{-14}$), gamma-tocopherol with 1 food (biscuits/cake/pastries: -0.125[0.030]; $p = 2.81 \times 10^{-5}$, pyroglutamine with 7 foods (top association, chargrilled meats: 0.143[0.025]; $p = 6.49 \times 10^{-9}$), creatine with 6 foods (top association, pork chops: 0.164[0.025]; $p = 7.46 \times 10^{-11}$),

and trans-4-hydroxyproline with 2 foods (top association, pork chops: 0.143[0.026]; $p = 6.13 \times 10^{-8}$).

Discussion

This is the first UK study and the largest globally to examine patterns of reported food liking-disliking in adults based on an assessment of the whole diet. Here, we show that reports of food liking-disliking fall into unique patterns each defined by similar types of foods. Moreover, we found that patterns of food-liking defined by strong tastes (particularly pungent and sour), sweet and high carbohydrate foods, and meats are strongly heritable, thus justifying further examination into the genetic determinants of food and taste preferences. In particular, we are the first to report a strong heritability for meat liking in adults. Finally, individuals who report high liking for foods characterized by distinctive tastes or meat have higher levels of multiple circulating metabolites independent of the genetic influence on levels of these metabolites.

Our results are in agreement with findings of previous studies where food hedonic patterns tend to vary according to taste and/or nutrient value (Drewnowski et al., 1999; Johnson et al., 2014). Recently, Johnson and collaborators (Johnson et al., 2014) applied PCA to subject hedonic ratings ($n = 129$) of 104 foods and identified similar patterns to our population, such as the groupings of high liking for vegetables (Light Main Courses), fruits (Fruits), meats (Meats), or sweet foods (Desserts). The Distinctive Tastes pattern we identified characterized by strong tasting foods appears to be somewhat novel. Though liking scores for spicy food in Finnish twins has been shown to form a statistically reliable group previously (Tornwall et al., 2012a; 2014), to our knowledge it has not been shown that individuals who like salty/sour fermented foods (olives, gherkins, horseradish, and soy sauce) tend to also like spicy food, as depicted by the loadings for the Distinctive Tastes component. Higher scores on the Distinctive Tastes and lower scores on the Sweet and High CHO components were associated with increased household income and age finished education, implying food costs, education, and/or social environment may have influenced ratings; these areas require further analysis.

TABLE 3**Significant Food-Liking Pattern-Metabolomic Associations After Adjusting for Age, BMI, Batch Effects, Family Relatedness and Sex (n = 1,491)**

Pattern	Metabolite	Sup-p	Sub-p	Discovery		Discordant MZ replication		Meta-analysis	
				Beta (SE)	p	Beta (SE)	p	Beta (SE)	p
Distinctive tastes	Tryptophan betaine	a-a	Tryptophan metabolism	0.07(0.01)	6.16×10^{-9}	0.08(0.03)	1.00×10^{-2}	0.07(0.01)	1.20×10^{-10}
	3-Carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	l	Fatty acid, dicarboxylate	0.09(0.01)	3.66×10^{-17}	0.06(0.02)	9.00×10^{-3}	0.08(0.01)	5.24×10^{-19}
	Scyllo-inositol	l	Inositol metabolism	0.07(0.01)	1.20×10^{-10}	0.09(0.03)	2.00×10^{-3}	0.07(0.01)	3.41×10^{-13}
	Myo-inositol	l	Inositol metabolism	0.05(0.01)	2.88×10^{-5}	0.02(0.03)	4.86×10^{-1}	0.04(0.01)	3.34×10^{-5}
	Docosahexaenoate (DHA; 22:6n3)	l	Essential fatty acid	0.08(0.01)	3.79×10^{-12}	0.05(0.02)	4.50×10^{-2}	0.07(0.01)	4.61×10^{-13}
	Eicosapentaenoate (EPA; 20:5n3)	l	Essential fatty acid	0.08(0.01)	1.67×10^{-11}	0.03(0.03)	3.72×10^{-1}	0.07(0.01)	3.58×10^{-11}
	Piperine	x	Food component, Plant	0.08(0.01)	6.94×10^{-13}	0.04(0.03)	2.07×10^{-1}	0.08(0.01)	3.01×10^{-13}
Sweet and high CHO	Gamma-Tocopherol	c&v	Tocopherol metabolism	0.05(0.01)	1.49×10^{-5}	0.05(0.03)	4.40×10^{-2}	0.05(0.01)	1.47×10^{-6}
	3-Carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	l	Fatty acid, dicarboxylate	-0.05(0.01)	4.21×10^{-5}	-0.07(0.02)	1.00×10^{-3}	-0.05(0.01)	1.72×10^{-7}
	Docosahexaenoate (DHA; 22:6n3)	l	Essential fatty acid	-0.05(0.01)	1.39×10^{-6}	-0.03(0.02)	1.62×10^{-1}	-0.05(0.01)	7.20×10^{-7}
	Eicosapentaenoate (EPA; 20:5n3)	l	Essential fatty acid	-0.06(0.01)	1.12×10^{-6}	-0.02(0.02)	4.45×10^{-1}	-0.05(0.01)	2.55×10^{-6}
Meat	Pyroglutamine*	a-a	Glutamate metabolism	-0.09(0.01)	2.66×10^{-14}	-0.06(0.03)	3.50×10^{-2}	-0.09(0.01)	1.76×10^{-15}
	Creatine	a-a	Creatine metabolism	0.10(0.01)	6.58×10^{-14}	0.05(0.03)	6.90×10^{-2}	0.09(0.01)	1.69×10^{-14}
	Trans-4-Hydroxyproline	a-a	Urea cycle; arginine-, proline-, metabolism	0.07(0.02)	5.00×10^{-7}	0.08(0.03)	6.00×10^{-3}	0.08(0.01)	6.73×10^{-9}

Note: a-a = amino-acid; c&v = cofactor and vitamin; l = lipid; x = xenobiotic; beta coefficients presented for the results of each linear regression analysis represent the food liking pattern score that corresponds to a 1 SD increase in the metabolite level.

TABLE 4

Significant Single Item Food-Liking Metabolomic Associations after Adjusting for Age, BMI, Batch Effects, Family Relatedness, and Sex (n = 1,491) for Food-Liking Pattern Associated Metabolites

Pattern	Metabolite	Food-liking variable	Discovery		Discordant MZ replication		Meta-analysis			
			Beta(SE)	p	Beta(SE)	p	Beta(SE)	p		
Distinctive tastes/Sweet and high CHO	3-Carboxy-4-methyl-5-propyl-2-furanpropanoate (CMPF)	Prawns and shellfish	0.30(0.03)	3.35 × 10 ⁻²⁷	0.13(0.07)	6.09 × 10 ⁻²	0.28(0.03)	2.40 × 10 ⁻²⁸		
		Tuna or salmon	0.26(0.03)	7.55 × 10 ⁻¹⁸	0.21(0.07)	2.71 × 10 ⁻³	0.25(0.03)	1.63 × 10 ⁻²⁰		
		Olives	0.22(0.03)	6.34 × 10 ⁻¹⁶	0.03(0.07)	6.74 × 10 ⁻¹	0.19(0.03)	6.43 × 10 ⁻¹⁵		
		Aubergine	0.18(0.03)	1.03 × 10 ⁻¹⁰	0.15(0.06)	2.53 × 10 ⁻²	0.17(0.03)	5.04 × 10 ⁻¹²		
		Extra virgin olive Oil	0.17(0.03)	1.21 × 10 ⁻¹⁰	0.11(0.05)	1.97 × 10 ⁻²	0.16(0.02)	7.26 × 10 ⁻¹²		
		Garlic	0.16(0.03)	6.89 × 10 ⁻¹⁰	0.15(0.06)	1.06 × 10 ⁻²	0.16(0.02)	1.42 × 10 ⁻¹¹		
		Blue cheese	0.16(0.03)	6.61 × 10 ⁻⁹	0.11(0.05)	4.19 × 10 ⁻²	0.15(0.03)	7.88 × 10 ⁻¹⁰		
		Fresh coriander	0.16(0.03)	4.93 × 10 ⁻⁹	0.11(0.07)	1.16 × 10 ⁻¹	0.16(0.03)	1.33 × 10 ⁻⁹		
		Plain yoghurt	0.14(0.03)	5.82 × 10 ⁻⁸	0.16(0.07)	1.86 × 10 ⁻²	0.15(0.02)	2.42 × 10 ⁻⁹		
		Asparagus	0.16(0.03)	4.59 × 10 ⁻⁹	0.08(0.06)	1.95 × 10 ⁻¹	0.15(0.03)	2.91 × 10 ⁻⁹		
		Red wine	0.15(0.03)	8.96 × 10 ⁻⁸	0.03(0.05)	5.15 × 10 ⁻¹	0.13(0.03)	4.72 × 10 ⁻⁷		
		Horseradish/wasabi	0.13(0.03)	8.48 × 10 ⁻⁷	0.07(0.06)	2.96 × 10 ⁻¹	0.12(0.03)	6.59 × 10 ⁻⁷		
		Cornflakes	-0.13(0.03)	9.00 × 10 ⁻⁷	-0.04(0.06)	5.34 × 10 ⁻¹	-0.11(0.02)	2.11 × 10 ⁻⁶		
		Dark chocolate	0.13(0.03)	7.93 × 10 ⁻⁷	0.02(0.07)	7.28 × 10 ⁻¹	0.12(0.02)	2.14 × 10 ⁻⁶		
		Chili pepper	0.13(0.03)	4.82 × 10 ⁻⁶	0.09(0.08)	2.28 × 10 ⁻¹	0.13(0.03)	2.24 × 10 ⁻⁶		
		Soft/sweet drinks	-0.12(0.03)	2.29 × 10 ⁻⁵	-0.13(0.08)	7.63 × 10 ⁻²	-0.12(0.03)	3.96 × 10 ⁻⁶		
		Soy sauce	0.12(0.03)	1.61 × 10 ⁻⁵	0.01(0.07)	8.98 × 10 ⁻¹	0.11(0.03)	4.17 × 10 ⁻⁵		
	Docosahexaenoate (DHA; 22:6n3)	Tuna or salmon	0.25(0.03)	2.39 × 10 ⁻¹⁷	0.18(0.06)	6.01 × 10 ⁻³	0.24(0.03)	1.85 × 10 ⁻¹⁹		
		Prawns and shellfish	0.24(0.03)	3.26 × 10 ⁻¹⁸	0.15(0.07)	4.10 × 10 ⁻²	0.23(0.03)	1.85 × 10 ⁻¹⁹		
		Olives	0.18(0.03)	3.39 × 10 ⁻¹⁰	0.05(0.06)	3.47 × 10 ⁻¹	0.16(0.03)	1.18 × 10 ⁻⁹		
		Aubergine	0.17(0.03)	3.98 × 10 ⁻⁹	0.09(0.06)	1.14 × 10 ⁻¹	0.15(0.03)	1.54 × 10 ⁻⁹		
		Asparagus	0.14(0.03)	1.91 × 10 ⁻⁶	0.14(0.07)	4.07 × 10 ⁻²	0.14(0.03)	1.75 × 10 ⁻⁷		
		Plain yoghurt	0.13(0.03)	2.89 × 10 ⁻⁶	0.17(0.08)	2.43 × 10 ⁻²	0.14(0.03)	1.90 × 10 ⁻⁷		
		Extra virgin olive oil	0.14(0.03)	3.53 × 10 ⁻⁷	0.07(0.06)	2.24 × 10 ⁻¹	0.13(0.03)	2.32 × 10 ⁻⁷		
		Dark chocolate	0.14(0.03)	1.36 × 10 ⁻⁶	0.11(0.06)	7.25 × 10 ⁻²	0.14(0.03)	2.39 × 10 ⁻⁷		
		Fresh coriander	0.15(0.03)	3.43 × 10 ⁻⁷	0.06(0.07)	3.77 × 10 ⁻¹	0.14(0.03)	4.65 × 10 ⁻⁷		
		Garlic	0.13(0.03)	6.70 × 10 ⁻⁶	0.1(0.05)	6.43 × 10 ⁻²	0.13(0.03)	1.09 × 10 ⁻⁶		
		Biscuits/cake/pastries	-0.11(0.03)	5.39 × 10 ⁻⁵	-0.14(0.06)	1.30 × 10 ⁻²	-0.12(0.03)	1.99 × 10 ⁻⁶		
		Red wine	0.15(0.03)	1.69 × 10 ⁻⁶	0.05(0.06)	4.43 × 10 ⁻¹	0.12(0.03)	3.69 × 10 ⁻⁶		
		White wine	0.12(0.03)	2.98 × 10 ⁻⁵	0.07(0.05)	1.40 × 10 ⁻¹	0.11(0.03)	1.31 × 10 ⁻⁵		
		Spinach/ greens	0.13(0.03)	1.97 × 10 ⁻⁵	0.04(0.06)	5.75 × 10 ⁻¹	0.11(0.03)	3.77 × 10 ⁻⁵		
		Eicosapentaenoate (EPA; 20:5n3)	Prawns and shellfish	0.21(0.03)	1.79 × 10 ⁻¹³	0.06(0.06)	3.58 × 10 ⁻¹	0.18(0.03)	5.35 × 10 ⁻¹³	
			Tuna or salmon	0.20(0.03)	1.59 × 10 ⁻¹¹	0.12(0.07)	9.15 × 10 ⁻²	0.19(0.03)	3.99 × 10 ⁻¹²	
			Olives	0.19(0.03)	3.58 × 10 ⁻¹⁰	0.04(0.06)	5.14 × 10 ⁻¹	0.15(0.03)	3.22 × 10 ⁻⁹	
			Aubergine	0.15(0.03)	3.14 × 10 ⁻⁷	0.07(0.05)	1.76 × 10 ⁻¹	0.13(0.03)	2.39 × 10 ⁻⁷	
			Asparagus	0.15(0.03)	7.33 × 10 ⁻⁷	0.07(0.06)	2.45 × 10 ⁻¹	0.14(0.03)	5.68 × 10 ⁻⁷	
			Plain yoghurt	0.14(0.03)	1.97 × 10 ⁻⁶	0.11(0.08)	1.59 × 10 ⁻¹	0.13(0.03)	6.33 × 10 ⁻⁷	
	Fresh coriander		0.15(0.03)	1.81 × 10 ⁻⁶	0.01(0.07)	9.47 × 10 ⁻¹	0.13(0.03)	1.10 × 10 ⁻⁵		
	Extra virgin olive Oil		0.13(0.03)	1.42 × 10 ⁻⁵	0.04(0.06)	4.47 × 10 ⁻¹	0.11(0.03)	2.64 × 10 ⁻⁵		
	Dark chocolate		0.13(0.03)	4.39 × 10 ⁻⁵	0.07(0.06)	2.42 × 10 ⁻¹	0.12(0.03)	2.83 × 10 ⁻⁵		
	Red wine		0.13(0.03)	2.79 × 10 ⁻⁵	0.04(0.05)	4.35 × 10 ⁻¹	0.11(0.03)	4.95 × 10 ⁻⁵		
	Lentils/ beans		0.22(0.03)	8.85 × 10 ⁻¹²	0.04(0.08)	6.07 × 10 ⁻¹	0.20(0.03)	2.93 × 10 ⁻¹¹		
	Distinctive tastes		Tryptophan betaine	Unsalted nuts	0.18(0.03)	9.51 × 10 ⁻⁹	0.19(0.07)	5.70 × 10 ⁻³	0.18(0.03)	1.01 × 10 ⁻¹⁰
				Curries	0.17(0.03)	1.81 × 10 ⁻⁶	0.07(0.08)	3.78 × 10 ⁻¹	0.15(0.03)	2.02 × 10 ⁻⁶
		Chili pepper		0.15(0.03)	4.56 × 10 ⁻⁶	0.06(0.11)	6.09 × 10 ⁻¹	0.14(0.03)	4.73 × 10 ⁻⁶	
Ham		-0.15(0.03)		2.21 × 10 ⁻⁶	-0.03(0.08)	7.12 × 10 ⁻¹	-0.13(0.03)	5.34 × 10 ⁻⁶		
Fresh coriander		0.14(0.03)		2.57 × 10 ⁻⁵	0.08(0.08)	3.04 × 10 ⁻¹	0.13(0.03)	1.61 × 10 ⁻⁵		
Scyllo-inositol		Red wine	0.25(0.03)	1.75 × 10 ⁻¹⁷	0.26(0.07)	8.58 × 10 ⁻⁴	0.25(0.03)	8.03 × 10 ⁻²¹		
		White wine	0.21(0.03)	1.64 × 10 ⁻¹²	0.03(0.07)	6.77 × 10 ⁻¹	0.18(0.03)	1.13 × 10 ⁻¹¹		
		Beer	0.16(0.03)	1.95 × 10 ⁻⁷	0.09(0.07)	1.62 × 10 ⁻¹	0.15(0.03)	9.14 × 10 ⁻⁸		
		Chili pepper	0.14(0.03)	3.60 × 10 ⁻⁶	0.14(0.08)	8.12 × 10 ⁻²	0.14(0.03)	6.10 × 10 ⁻⁷		
		Burn of spicy foods	0.13(0.03)	2.00 × 10 ⁻⁵	0.18(0.08)	2.30 × 10 ⁻²	0.14(0.03)	1.32 × 10 ⁻⁶		
Myo-inositol		Fresh coriander	0.11(0.03)	4.50 × 10 ⁻⁵	0.05(0.06)	4.26 × 10 ⁻¹	0.10(0.03)	4.98 × 10 ⁻⁵		
		Black pepper	0.22(0.03)	1.89 × 10 ⁻¹³	0.14(0.06)	3.43 × 10 ⁻²	0.21(0.03)	1.62 × 10 ⁻¹⁴		
		Chili pepper	0.22(0.03)	1.28 × 10 ⁻¹³	0.13(0.09)	1.44 × 10 ⁻¹	0.21(0.03)	3.00 × 10 ⁻¹⁴		
		Burn of spicy foods	0.18(0.03)	8.67 × 10 ⁻¹⁰	0.14(0.09)	1.14 × 10 ⁻¹	0.18(0.03)	1.69 × 10 ⁻¹⁰		
		Curries	0.15(0.03)	2.10 × 10 ⁻⁷	0.11(0.07)	1.29 × 10 ⁻¹	0.15(0.03)	5.99 × 10 ⁻⁸		
Piperine		Garlic	0.13(0.03)	1.31 × 10 ⁻⁵	0.06(0.08)	4.78 × 10 ⁻¹	0.12(0.03)	1.33 × 10 ⁻⁵		
		Vodka/gin/scotch	0.13(0.03)	4.19 × 10 ⁻⁵	0.09(0.07)	1.79 × 10 ⁻¹	0.12(0.03)	1.64 × 10 ⁻⁵		
		Biscuits/cake/pastries	-0.13(0.03)	2.40 × 10 ⁻⁵	-0.05(0.08)	5.09 × 10 ⁻¹	-0.12(0.03)	2.96 × 10 ⁻⁵		
		Biscuits/cake/pastries	-0.13(0.03)	4.96 × 10 ⁻⁵	-0.09(0.08)	2.83 × 10 ⁻¹	-0.13(0.03)	2.81 × 10 ⁻⁵		
		Gamma-Tocopherol								

TABLE 4
Continued.

Pattern	Metabolite	Food-liking variable	Discovery		Discordant MZ replication		Meta-analysis	
			Beta(SE)	p	Beta(SE)	p	Beta(SE)	p
Meat	Pyroglutamine*	Chargrilled meats	-0.18(0.03)	3.01×10^{-10}	-0.02(0.05)	7.49×10^{-1}	-0.14(0.03)	6.49×10^{-9}
		Beef steak	-0.17(0.03)	3.66×10^{-9}	-0.06(0.05)	2.42×10^{-1}	-0.14(0.02)	1.09×10^{-8}
		White wine	-0.15(0.03)	2.11×10^{-8}	-0.07(0.05)	1.38×10^{-1}	-0.13(0.02)	1.70×10^{-8}
		Ham	-0.14(0.03)	1.96×10^{-7}	-0.10(0.06)	1.12×10^{-1}	-0.14(0.03)	5.08×10^{-8}
		Pork chops	-0.13(0.03)	3.06×10^{-6}	-0.12(0.05)	1.16×10^{-2}	-0.13(0.02)	8.60×10^{-8}
	Creatine	Prawns and shellfish	-0.13(0.03)	2.70×10^{-6}	-0.15(0.08)	7.09×10^{-2}	-0.13(0.03)	4.18×10^{-7}
		Sausage	-0.13(0.03)	2.59×10^{-5}	-0.06(0.04)	1.75×10^{-1}	-0.10(0.03)	2.33×10^{-5}
		Pork chops	0.18(0.03)	6.42×10^{-10}	0.11(0.05)	3.62×10^{-2}	0.16(0.03)	7.46×10^{-11}
		Ham	0.17(0.03)	6.84×10^{-9}	0.06(0.06)	3.34×10^{-1}	0.15(0.03)	1.27×10^{-8}
		Baked chicken	0.18(0.03)	3.44×10^{-9}	0.05(0.06)	3.99×10^{-1}	0.15(0.03)	1.47×10^{-8}
	Trans-4-Hydroxyproline	Beef steak	0.17(0.03)	4.39×10^{-8}	0.07(0.06)	2.63×10^{-1}	0.15(0.03)	5.93×10^{-8}
		Bacon	0.14(0.03)	1.38×10^{-6}	0.10(0.06)	7.42×10^{-2}	0.13(0.03)	2.84×10^{-7}
		Sausage	0.14(0.03)	3.22×10^{-6}	0.07(0.05)	1.57×10^{-1}	0.13(0.03)	2.00×10^{-6}
		Pork chops	0.16(0.03)	2.75×10^{-8}	0.05(0.06)	4.15×10^{-1}	0.14(0.03)	6.13×10^{-8}
		Beef steak	0.15(0.03)	4.44×10^{-7}	0.05(0.06)	3.92×10^{-1}	0.13(0.03)	7.76×10^{-7}

Note: Beta coefficients presented for the results of each linear regression analysis represent the food liking rating that corresponds to a 1 SD increase in the metabolite level.

The high heritability of the Distinctive Tastes component reflects findings from the Finnish twin group ($n = 328$) where, through the usage of multiple ratings, heritability of the preference for oral pungency (spicy foods) was found to range from 18% to 58% (Tornwall et al., 2012a). In the same cohort, investigations into the genetics of preference for sour foods determined up to one half (34–50%) of the variation in the pleasantness and use-frequency of factor analysis derived sour food groups, although this was based on ratings for sour fruits and berries and dairy products, not fermented vegetables or vinegar (Tornwall et al., 2012b). In our group, previously ($n = 663$) additive genetic effects explained 49%, 54%, and 53% of the variation in liking for a sweet solution, liking for sweet foods, and use-frequency of sweet foods respectively (Keskitalo et al., 2007). The Fruit and Vegetable pattern was less strongly heritable; as discussed below, this group appears to be a health-related pattern more influenced by the environment.

The Distinctive Tastes liking pattern, defined by a high liking for foods with strong tastes (particularly fermented and pungent foods), was marked by significant increases in eight metabolites: CMPF, docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), scyllo-inositol, myo-inositol, piperine, tryptophan betaine, and γ -tocopherol. Each of these metabolites has been associated with habitual consumption of particular foods in previous metabolomic studies (Guertin et al., 2014; Zheng et al., 2014). The furan fatty acid CMPF is a potent uremic toxin (Miyamoto et al., 2012) formed from the consumption of vegetables and fish/shellfish and potential marker of habitual consumption of these foods (Guertin et al., 2014; Zheng et al., 2014); moreover, we confirmed liking of prawns and shellfish to be most strongly associated with CMPF in blood. The essential fatty acids DHA and EPA are lipids found in characteristically high-concentrations in fatty fish and

consistent markers of habitual fish and seafood consumption (Guertin et al., 2014; Zheng et al., 2014), which we found to be the most strongly associated with liking of fatty fish and shellfish. Myo and scyllo-inositol are lipid compounds found in particularly high-concentrations in wine (Carlavilla et al., 2006) and citrus fruits (Mucci et al., 2013) that have been associated with high intakes of these foods (Guertin et al., 2014; Zheng et al., 2014) in other metabolomics studies, we confirmed liking of red and white wines to be most strongly associated with scyllo-inositol. Piperine is the component responsible for the taste of black pepper (Dutta & Bhattacharjee, 2015), which we found to associate most strongly with black pepper liking; increased alcohol intake in African Americans has previously been associated with elevated levels of this metabolite (Zheng et al., 2014). We found a significant association with liking of vodka/gin/scotch, suggesting subjects who consume more alcohol may consume more spiced foods. Tryptophan betaine has been associated with nut consumption previously (Guertin et al., 2014), and we confirmed the strongest associations with this metabolite were with lentils/beans and unsalted nuts. The vitamin E form γ -tocopherol is utilized in corn and soybean oils to prevent PUFA oxidation. Higher intakes of vitamins and supplements and increased scores on the US Healthy Eating Index were inversely associated with serum levels of γ -tocopherol (Guertin et al., 2014). Liking of sweet baked products (biscuits/cake/pastries) was inversely associated with blood γ -tocopherol; the origin of this association requires further investigation.

The Sweet and High Carbohydrate food-liking pattern was associated with lower levels of fish and seafood-derived metabolites: CMPF, DHA, and EPA (Guertin et al., 2014; Zheng et al., 2014). Liking of these items had very low loadings on this component, suggesting individuals who like sweet foods consume less fish. No metabolite

associations were related to sugar or carbohydrate consumption although the significant association with BMI alludes to an increased consumption of such energy-dense foods. Validated blood biomarkers of habitual sugar intake have yet to be defined in the literature, though one recent metabolomic study using the same platform found increased consumption of sugar-rich foods and beverages, dietary sucrose and carbohydrate to associate negatively with metabolites related to glutathione synthesis (Zheng et al., 2014); these results have yet to be replicated.

Scores for the Meat-liking pattern were strongly associated with amino acids potentially derived from compounds contained in meat. For instance, increased meat liking was associated with higher levels of creatine, which red meat contains in high quantities. Vegetarians have presented with lower blood levels of this metabolite (Delanghe et al., 1989). The urea cycle amino acid, *trans*-4-hydroxyproline is a major component of connective tissue (Bienkowski, 1984) that has been demonstrated to increase in the blood following oral gelatin ingestion (Ohara et al., 2007) and was elevated with increasing Meat-liking scores. Reduced levels of the amino acid pyroglutamine was found with higher scores on the Meat-liking group; serum levels previously have shown to be reduced with increased consumption of poultry (Guertin et al., 2014). In our single association analysis with these metabolites we confirmed top associated liking variables to be meat items, although the Meat-liking pattern was more strongly associated with circulating levels of these amino acid metabolites than any of these items alone, alluding to the power of the group to identify meat consumers.

The Fruit and Vegetable pattern factor score was not associated with any blood metabolite levels. We speculate this may have occurred for a number of reasons. For one, intakes of the foods loading highly on this pattern characterized by bland, 'healthy' foods may be less reliant on liking. For instance, reported liking and intake of less sour fruits have been in lower agreement than intake and liking of sour fruits, whereas a pattern of high liking of Light Main Courses (e.g., liking of mixed vegetables, salads, and soup) was in low agreement with reported vegetable intake compared with other food groups (Johnson et al., 2014). Additionally, within the time-between measurement of blood metabolites and administration of the questionnaire (mean 7 years after blood sample), subjects scoring highly on this component may have modified their habits to adopt a healthier lifestyle. Supporting this reasoning, the liking of tuna or salmon loads highest on this pattern and is strongly associated with seafood-derived metabolites (EPA and DHA) independently, though this pattern is not significantly associated with these metabolites. Thus, this relationship requires further exploration.

Our study has some limitations. First, utilizing liking-disliking patterns against blood metabolomics profiles may have been less powerful for identifying potential metabolite

associations than examining liking-disliking of single foods or food groups. For instance, when applied to FFQs, single exhaustive food analyses are more successful at strengthening diet-disease associations than dietary patterns derived from principal components (Bakolis et al., 2014); this observation may translate into diet-metabolite associations as well. Therefore, in our future work we aim to assess this. Fasting blood samples were taken on average 7 years (*SD*: 3 years; range: 4–17 years) before the food preference questionnaire was administered, and the food environment or eating habits and preferences of the twins may have changed to some degree in this amount of time. Despite this time difference and while using conservative testing methods, we identified significant associations, suggesting food preferences have a pervasive impact on food intake through time; in particular, those we showed to be strongly genetically determined. Moreover, metabolite levels have been shown to have long-term stability (Yousri et al., 2014). Using a predominantly female sample we were not able to investigate sex differences. Administration of the questionnaire in an online format may have resulted in responder bias, especially considering that TwinsUK is an aging cohort. The underlying cultural, economic, educational, and geographical determinants of the food preference patterns were not extensively considered in this study but are areas for future investigations. Moreover the questionnaire was derived from an American population and may have not been adapted adequately for use in a UK population. Participants were not asked their degree of satiety at the beginning of the questionnaire, which if increased may have lowered ratings (Finlayson et al., 2008). Finally, a large number of components had eigenvalues greater than one that potentially loaded on very specific foods that could have major gene effects; future analyses aim to investigate specific food groups further.

Conclusions

We have found food preferences in our population tend to follow patterns based on taste and nutrient characteristics. Moreover, preferences for foods characterized by strong tastes, sweetness or high-carbohydrate content and meats are strongly determined by genetics. The metabolomics associations identified here suggest food liking may have an impact on intake of foods for which preferences are strongly determined by genetic factors, potentially as a function of taste responses. These findings may have implications for public health nutrition programs and nutritional epidemiology.

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Conflict of Interest

Robert P. Mohney is an employee of Metabolon, Inc. All other authors have no conflicting interests.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Supplementary Material

To view supplementary material for this article, please visit <http://dx.doi.org/10.1017/thg.2015.69>.

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