**TAS2R38 and Its Influence on Smoking Behavior and Glucose Homeostasis in the German Sorbs**

Maria Keller¹, Xuanshi Liu¹,², Tobias Wohland¹, Kerstin Rohde¹, Marie-Therese Gast³, Michael Stumvoll¹,³, Peter Kovacs¹, Anke Tönjes³, Yvonne Böttcher¹*

¹ IFB AdiposityDiseases, University of Leipzig, Leipzig, Germany, ² Bioinformatics Group, Department of Computer Science, University of Leipzig, Leipzig, Germany, ³ Department of Medicine, University of Leipzig, Leipzig, Germany

**Abstract**

**Background:** Genetic variants within the bitter taste receptor gene TAS2R38 are associated with sensitivity to bitter taste and are related to eating behavior in the Amish population. Sensitivity to bitter taste is further related to anthropometric traits in an genetically isolated Italian population. We tested whether the TAS2R38 variants (rs713598; rs1726866 and rs10246939) may be related to eating behavior, anthropometric parameters, metabolic traits and consumer goods intake in the German Sorbs.

**Materials and Methods:** The three SNPs were genotyped in a total cohort of 1007 individuals (male/female: 405/602). The German version of the three-factor eating questionnaire was completed by 548 individuals. Genetic association analyses for smoking behavior, alcohol and coffee intake, eating behavior factors (restrainment, disinhibition and hunger) and other metabolic traits were analyzed. Further, by combining the three SNPs we applied comparative haplotype analyses categorizing PAV (proline-alanine-valine) carriers (tasters) vs. homozygous AVI (alanin-valine-isoleucine) carriers (non-tasters).

**Results:** Significant associations of genetic variants within TAS2R38 were identified with percentage of body fat, which were driven by associations in women. In men, we observed significant associations with 30 min plasma glucose, and area under the curve for plasma glucose (0–120 min) (all adjusted \( P<0.05 \)). Further, we found that carriers of at least one PAV allele show significantly lower cigarette smoking per day (\( P=0.002 \)) as well as, albeit non-significant, lower alcohol intake. We did not confirm previously reported associations between genetic variants of TAS2R38 and eating behavior.

**Conclusion:** Our data suggest that genetic variation in TAS2R38 is related to individual body composition measures and may further influence consumer goods intake in the Sorbs possibly via individual sensitivity to bitter taste.

**Citation:** Keller M, Liu X, Wohland T, Rohde K, Gast M-T, et al. (2013) TAS2R38 and Its Influence on Smoking Behavior and Glucose Homeostasis in the German Sorbs. PLoS ONE 8(12): e80512. doi:10.1371/journal.pone.0080512

**Editor:** Maik Behrens, German Institute of Human Nutrition Potsdam-Rehbruecke, Germany

**Received** June 11, 2013; **Accepted** October 4, 2013; **Published** December 2, 2013

**Copyright:** © 2013 Keller et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Funding:** This work was supported by grants from the German Diabetes Association (to Y.B., A.T., P.K.) and from the DDS Foundation to (Y.B.). A.T. and Y.B. were supported by the Federal Ministry of Education and Research (BMBF), Germany, FKZ: 01EO1001. X.L. is financed by a research grant from the DFG (BO/3147-4 to Y.B.). This work was further supported by a Collaborative Research Center granted by the DFG (CRC 1052 “Obesity Mechanisms”); A01 (to M.S.); B03 (to P.K.) and C01 (to A.T.). K.R is funded by a research grant from the Boehringer Ingelheim Foundation. The publication was supported by a publication allowance from the Graduate Center LIFE Sciences of the Research Academy Leipzig at the University of Leipzig, Germany. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

**Competing Interests:** The authors have declared that no competing interests exist.

* E-mail: yvonne.boettcher@medizin.uni-leipzig.de

**Introduction**

The human gustatory sense is mainly mediated by different taste receptor cells (TRCs) clustered in taste buds predominantly located on the tongue [1]. Further, bitter taste receptors are also expressed in other parts of the gastrointestinal tract [2]. Water-soluble chemicals interact with the apical ends of TRCs resulting in activation of downstream signaling pathways and transmission of signals to the central nervous system [1,2]. The ability to taste bitterness significantly influences human eating behavior via the development of individual food preferences [2]. In humans, more than 30 different bitter taste receptors have been identified [3]. These G protein-coupled receptors of the TAS2R family are expressed in TRCs on the tongue and in cells of the gastrointestinal mucosa and are involved in energy and glucose metabolism [2,3]. Sensitivity to bitterness varies between individuals and is associated with genetic variants within genes encoding bitter taste receptors. One of these genes is the well characterized TAS2R38 [4]. Three single-nucleotide polymorphisms (SNPs) (rs713598; rs1726866 and rs10246939) within the TAS2R38 gene, resulting in three amino acid substitutions (A49P; A262V and V296I), are primarily responsible for individual variability in bitter taste perception in response to phenylthiocarbamide (PTC) and 6-n-propyl-2-thiouracil (PROP) [2,4]. Only two common haplotypes Ala-Val-Ile (AVI) and Pro-Ala-Val (PAV) are known outside sub-Saharan Africa [5,6]. Heterozygous and homozygous PAV haplotype carriers are more sensitive to PTC and PROP [6,7] compared to AVI/AVI-carriers. This allows one to classify
individuals as tasters or non-tasters based on their genotype [6,8]. It has been shown that SNPs within TAS2R38 (rs1726866) are nominally associated with the eating behavior phenotype disinhibition in Amish women [9]. Furthermore, in a genetically isolated Italian population it has been shown that among women with low dietary restraint, those classified as non-tasters tend to have higher body mass index (BMI) and waist circumference (WC) than tasters [4].

In addition to the roles outlined above, the family of TAS2R receptors may modulate digestive behavior and glucose homeostasis via signaling pathways e.g. of glucagon like peptide-1 (GLP-1) which is a modulator of insulin biosynthesis and secretion [9,10]. Dotson and colleagues have shown that genetic variation within several bitter taste receptors significantly influences glucose homeostasis [4,8].

Lastly, the sensitivity to bitter taste may influence alcohol intake [11] and smoking behavior [12]. As demonstrated by Duffy et al. 2004 [11] homozygous PAV carriers show lower alcohol intake compared to individuals homozygous for AVI. In line with this, Mangold et al. 2008 [13] observed a higher smoking quantity among non-tasters compared to tasters. Further, Cannon et al. 2005 [14] reported differential haplotypic associations and smoking behavior.

Here, we describe the analysis of three TAS2R38 variants and the corresponding haplotypes in a self-contained German population, the Sorbs, in regard to consumer goods consumption as well as eating behavior phenotypes. To shed further light on a potential role of TAS2R38 variants in glucose metabolism, we tested for genetic association with a wide range of metabolic phenotypes.

**Methods**

**Subjects**

The Sorbs cohort is a self-contained population from Eastern Germany which was extensively phenotyped for a wide range of anthropometric and metabolic phenotypes [15]. Phenotyping included standardized questionnaires for individual medical history, family histories and eating behavior factors (German version of three factor eating questionnaire, FEV) [16]. Weight, height, waist-to-hip-ratio (WHR), body impedance analysis and a 75 g oral glucose tolerance test (OGTT) after an overnight fast were also included. The main characteristics of the study subjects are summarized in Table 1.

Individuals with type 2 diabetes (T2D) were excluded when analyzing eating behavior factors and phenotypes of glucose metabolism. A total of 1007 subjects (male/female: 405/602) with mean age of 48±6.2 years and mean BMI 27.0±4.9 kg/m² were included. All subjects gave written informed consent and the study was approved by the ethics committee of the University of Leipzig.

**German Version of the Three-factor Eating Questionnaire**

Of the total cohort 548 sorbs completed the German version of the three-factor eating questionnaire (FEV) [16]. The questionnaire measures the factors (dietary restraint, disinhibition and hunger) influencing individual eating behavior, as described for the Sorbs elsewhere [17].

**Genotyping**

Genomic DNA was extracted using QIAmp DNA Blood Midi Kit (Qiagen Inc., Valencia, CA, USA) according to manufacturers instructions. Genotyping of rs1726866 was performed using TaqMan® SNP Genotyping Assay (Applied Biosystems by LifeTechnologies Carlsbad, CA, USA). Rs713598 and rs10246939 were genotyped using the KASPar genotyping system (KBioscience allele specific PCR Genotyping System; KBioscience, Teddington, Middlesex, UK). Fluorescence was detected by an ABI 7500 Real-Time PCR system.

**Quality Control**

All SNPs were in Hardy-Weinberg equilibrium (all \( P > 0.05 \)) To avoid genotyping errors, a random selection (~5%) of the sample was re-genotyped; all genotypes matched the initially designated genotypes. Water was used as a no template control (NTC). Of the NTCs, 100% were determined as empty samples.

**Statistics**

Non-normally distributed data were logarithmically transformed to approximate a normal distribution. Linear regression models adjusted for sex, age and lnBMI were employed to test for association of the three SNPs/haplotypes with eating behavior factors (restraint, disinhibition and hunger), anthropometric traits as well as glucose and insulin metabolism phenotypes. Moreover, sex stratified analyses were conducted. Linear regression models corrected for sex and age were applied to analyze consumer goods consumption (coffee, smoking and alcohol intake). Coffee consumption was defined as cups per day, smoking behavior as number of cigarettes per day and alcohol intake as number of glasses per week. Additive model of inheritance was tested. \( P \)-values <0.05 were regarded as providing nominal evidence for association. Given the directed “a priori hypotheses” of the study results were not corrected for multiple comparisons. Haplotypes were reconstructed for population genotype data using PHASE v2.1.1 [18] raised by rs713598 (A49P), rs1726866 (A262V) and rs10246939 (V296I). Three haplotypes were mainly detected: AVI

**Table 1. Main characteristics of the study cohort.**

|            | total | male | female | rs713598 | rs1726866 | rs10246939 |
|------------|-------|------|--------|----------|-----------|------------|
| N total    | 1007  | 405  | 602    | 155      | 509       | 333        |
| Age (yrs) | 48±16 | 48±16 | 48±15  | 48±15    | 47±16     | 49±17      |
| BMI (kg/m²)| 27.0±4.9 | 27.2±3.9 | 26.8±5.5 | 27.3±4.4 | 26.5±4.7 | 27.4±5.4 |
| WHR       | 0.87±0.1 | 0.95±0.1 | 0.83±0.1 | 0.88±0.1 | 0.87±0.1 | 0.88±0.1 |
| Body Fat (%)| 23.5±9.9 | 23.5±9.9 | 22.0±8.4 | 20.5±8.5 | 21.9±10.3 | 21.9±8.3 |

Data are presented as mean ± SD. Reference allele according to HapMap database, standardized to the reverse strand: rs713598 G; rs1726866 C; rs10246939 A. BMI: body mass index; WHR: waist-to-hip ratio.
Table 2. Association analysis of TAS2R38 SNPs with anthropometric measures and phenotypes of glucose and insulin homeostasis.

| Genotype | rs713598 | rs1726866 | rs10246939 |
|----------|----------|----------|-----------|
|          | CC (137) | CG (460) | GG (294)  |
| N male   | 54       | 185      | 116       |
| N female | 83       | 275      | 178       |
| BMI (kg/m²) |        |          |           |
| male     | 26.9 ± 3.3 | 26.5 ± 3.5 | 27.1 ± 3.6 |
| p-value  | 0.873*; 0.939* | 0.947*; 0.534* | 0.723*; 0.627* |
| female   | 26.7 ± 4.7 | 25.9 ± 5.2 | 26.7 ± 5.7 |
| p-value  | 0.023*; 0.909* | 0.013*; 0.680* | 0.012*; 0.832* |
| Body Fat (%) |        |          |           |
| male     | 17.4 ± 6.0 | 16.8 ± 5.8 | 17.2 ± 5.9 |
| p-value  | 0.93 ± 0.08 | 0.93 ± 0.08 | 0.93 ± 0.08 |
| female   | 23.8 ± 8.3 | 22.4 ± 9.2 | 23.2 ± 10.7 |
| p-value  | 0.938*; 0.368* | 0.670*; 0.993* | 0.852*; 0.963* |
| WHR      |          |          |           |
| male     | 5.4 ± 0.5 | 5.4 ± 0.5 | 5.4 ± 0.5 |
| p-value  | 0.517*; 0.448* | 0.478*; 0.668* | 0.757*; 0.979* |
| female   | 5.17 ± 0.5 | 5.13 ± 0.5 | 5.21 ± 0.6 |
| p-value  | 0.016*; 0.405* | 0.123*; 0.062* | 0.224*; 0.161* |
| Fasting Plasma Glucose (mmol/L) |          |          |           |
| male     | 9.1 ± 1.8 | 9.05 ± 1.6 | 8.71 ± 1.4 |
| p-value  | 0.083*; 0.070* | 0.82 ± 0.07 | 0.83 ± 0.07 |
| female   | 7.99 ± 1.5 | 8.00 ± 1.6 | 8.28 ± 1.7 |
| p-value  | 0.034*; 0.052* | 0.747*; 0.153* | 0.759*; 0.979* |
| Plasma Glucose 30 min (mmol/L) |          |          |           |
| male     | 5.39 ± 2.0 | 5.23 ± 1.8 | 5.00 ± 1.7 |
| p-value  | 0.836*; 0.052* | 0.747*; 0.153* | 0.759*; 0.979* |
| female   | 5.78 ± 1.7 | 5.44 ± 1.7 | 5.71 ± 1.6 |
| p-value  | 0.014*; 0.150* | 0.226*; 0.109* | 0.402*; 0.172* |
| Fasting Plasma Insulin (pmol/L) |          |          |           |
| male     | 40.07 ± 25.9 | 36.55 ± 22.8 | 36.36 ± 21.3 |
| p-value  | 0.314*; 0.150* | 0.226*; 0.109* | 0.402*; 0.172* |
| female   | 37.87 ± 18.7 | 38.26 ± 23.5 | 41.71 ± 25.0 |
| p-value  | 0.891*; 0.001* | 0.972*; 0.403* | 0.609*; 0.783* |
| Plasma Insulin 30 min (pmol/L) |          |          |           |
| male     | 273.8 ± 154.0 | 283.9 ± 168.1 | 294.3 ± 208.5 |
| p-value  | 0.089*; 0.910* | 0.972*; 0.403* | 0.609*; 0.783* |
| female   | 284.4 ± 141.5 | 300.7 ± 179.5 | 298.8 ± 197.1 |
| p-value  | 0.787*; 0.012* | 0.471*; 0.416* | 0.471*; 0.416* |
| 2 hr Plasma Insulin (pmol/L) |          |          |           |
| male     | 176.1 ± 225.8 | 144.4 ± 160.8 | 128.3 ± 141.7 |
| p-value  | 0.074*; 0.162* | 0.838*; 0.263* | 0.471*; 0.416* |
| female   | 197.7 ± 133.6 | 187.6 ± 147.6 | 195.4 ± 139.2 |
| p-value  | 0.140*; 0.012* | 0.013*; 0.013* | 0.032*; 0.032* |
| AUC Glucose 0–120 min (mmol/L) |          |          |           |
| male     | 14.53 ± 2.3 | 14.34 ± 2.5 | 13.82 ± 2.2 |
| p-value  | 0.026*; 0.003* | 0.191*; 0.013* | 0.291*; 0.032* |
| female   | 13.61 ± 2.6 | 13.36 ± 2.4 | 13.87 ± 2.6 |
| p-value  | 0.026*; 0.003* | 0.191*; 0.013* | 0.291*; 0.032* |
| AUC Insulin 0–120 min (pmol/L) |          |          |           |
| male     | 397.8 ± 274.2 | 401.5 ± 233.5 | 416.0 ± 289.1 |
| p-value  | 0.026*; 0.003* | 0.191*; 0.013* | 0.291*; 0.032* |
[alanine-valine-isoleucine (55.9%)], PAV [proline-alanine-valine (40.9%)] and AAV [alanine-alanine-valine (2.9%)]. SPSS statistics version 20.0.1 (SPSS, Inc.; Chicago, IL) was used for all statistical analyses.

Results

Association with Anthropometric Measures and Glucose Metabolism

Using linear regression analysis we identified significant associations between the three TAS2R38 genetic variants and percentage of body fat in non-diabetic women (all P-values < 0.05, Table 2). Minor allele carriers showed lower body fat content compared to homozygous major allele carriers (Table 2). No significant relationships to BMI and other anthropometric measures, such as WHR, were found. Furthermore, albeit non-significant, we observed slightly decreased BMI and body fat content in PAV haplotype carriers (PAV/PAV+PAV/AVI) compared to homozygous AVI haplotype carriers (Table 3).

Next, we tested whether TAS2R38 genetic variants influence phenotypes of glucose and insulin metabolism. In non-diabetic men, we found a relationship between genetic variants and 30 min plasma glucose levels as well as area under the curve (AUC) of plasma glucose (0–120 min). We observed increased AUC and glucose levels among minor allele carriers, applying additive model of inheritance (adjusted for sex, age and lnBMI, Table 2). Similar results were obtained when adjusting for age, sex and percentage of body fat. Moreover, we observed decreased 30 min plasma glucose levels and AUC values in PAV allele carriers (Table 3). No relationship was detected between TAS2R38 haplotypes and markers of insulin metabolism.

Table 3. TAS2R38 haplotypes: anthropometric measures and phenotypes of glucose and insulin homeostasis.

| Genotype (m/f) | N total | BMI (kg/m²) | Body fat (%) | WHR | Fasting plasma glucose (mmol/L) | Plasma glucose 30 min (mmol/L) | 2 hr plasma glucose (mmol/L) | AUC glucose (0–120 min) | P-value |
|---------------|--------|-----------|-------------|-----|--------------------------------|-----------------------------|---------------------------|--------------------------|---------|
| rs713598 AVI/AVI | 262 (111/151) | 26.7 ± 4.8 | 20.6 ± 9.3 | 0.87 ± 0.09 | 5.31 ± 0.58 | 8.59 ± 1.58 | 5.56 ± 1.75 | 14.10 ± 2.46 | 0.036 |
| rs1726866 AVI/AVI | 262 (111/151) | 26.7 ± 4.8 | 20.6 ± 9.3 | 0.87 ± 0.09 | 5.31 ± 0.58 | 8.59 ± 1.58 | 5.56 ± 1.75 | 14.10 ± 2.46 | 0.036 |
| rs10246939 AVI/AVI | 262 (111/151) | 26.7 ± 4.8 | 20.6 ± 9.3 | 0.87 ± 0.09 | 5.31 ± 0.58 | 8.59 ± 1.58 | 5.56 ± 1.75 | 14.10 ± 2.46 | 0.036 |

Data are presented as mean ± S.D. Type 2 diabetics were excluded. P-values were calculated using linear regression adjusted for age, sex and lnBMI (except for BMI). AVI = alanine-valine-isoleucine; PAV = proline-alanine-valine; BMI: body mass index; WHR: waist-to-hip ratio; AUC: area under the curve. Reference allele according to HapMap database, standardized to the reverse strand: rs713598 G; rs1726866 C; rs10246939 A. doi:10.1371/journal.pone.0080512.g001

TAS2R38 May Influence Smoking Behaviour, Alcohol and Coffee Consumption

We tested for associations between SNPs within TAS2R38 and smoking behaviour. No significant relationship was observed. However, carriers of at least one PAV haplotype showed significantly decreased cigarette smoking per day compared to homozygous AVI-carriers (Figure 1, Table 4).

We did not find effects of single genetic variants on alcohol consumption, however, categorizing individuals carrying at least one PAV haplotype vs. AVI/AVI homozygous carriers, we observed lower alcohol intake per week in the PAV group (Table 4). No associations were found for SNPs/haplotypes and coffee consumption.

Figure 1. TAS2R38 haplotypes and smoking. Data are presented as mean ± S.D. P-value was calculated using linear regression adjusted for age and sex. AVI = alanine-valine-isoleucine; PAV = proline-alanine-valine. doi:10.1371/journal.pone.0080512.g001
The main findings of the present study are: (i) a significant relationship of TAS2R38 genetic variation was found with percentage of body fat in women and further, an association with body composition measures observed (Table S1). However, we observed a non-significant trend for increased restraint scores in PAV allele carriers as well as decreased disinhibition values (Table S2).

**Table 4.** TAS2R38 haplotypes and consumer goods.

|                | AVI/AVI | PAV/AVI+PAV/PAV | P-value |
|----------------|---------|-----------------|---------|
| N              | 108     | 222             |         |
| smoking        | 12.5±10.1| 9.3±6.9         | 0.002   |
| N              | 306     | 665             |         |
| alcohol        | 2.87±1.28| 2.83±1.18       | 0.903   |
| N              | 250     | 558             |         |
| coffee         | 1.82±0.71| 1.82±0.78       | 0.994   |

Data are presented as mean± s.d. P-values were calculated using linear regression adjusted for age and sex. AVI = alanine-valine-isoleucine; PAV = proline-alanine-valine.

**TAS2R38 and Eating Behaviour**

Linear regression analyses for association of SNPs and haplotypes with the three different eating behaviour factors (restraint, disinhibition and hunger) did not show significant associations (Table S1). However, we observed a non-significant trend for increased restraint scores in PAV allele carriers as well as decreased disinhibition values (Table S2).

**Discussion**

The main findings of the present study are: (i) a significant relationship of TAS2R38 genetic variation was found with percentage of body fat in women and further, an association with body composition measures observed (Table S1). However, we observed a non-significant trend for increased restraint scores in PAV allele carriers as well as decreased disinhibition values (Table S2).

**Table 4.** TAS2R38 haplotypes and consumer goods.

|                | AVI/AVI | PAV/AVI+PAV/PAV | P-value |
|----------------|---------|-----------------|---------|
| N              | 108     | 222             |         |
| smoking        | 12.5±10.1| 9.3±6.9         | 0.002   |
| N              | 306     | 665             |         |
| alcohol        | 2.87±1.28| 2.83±1.18       | 0.903   |
| N              | 250     | 558             |         |
| coffee         | 1.82±0.71| 1.82±0.78       | 0.994   |

Data are presented as mean± s.d. P-values were calculated using linear regression adjusted for age and sex. AVI = alanine-valine-isoleucine; PAV = proline-alanine-valine.

The sample size of our cohort, especially the number of individuals with eating behavior data, is limited. Unfortunately, data were not available regarding phenotypic sensitivity to PROP or other bitter compounds, meaning a direct link between bitter tasting and consumer goods consumption cannot be made. Nonetheless, the data in regard to smoking and alcohol intake are in line with data previously reported [11,12,13].

In conclusion, our data suggest that, in Sorbs, genetic variation within TAS2R38 may be related to anthropometric measures and glucose homeostasis. Moreover, the ability to taste bitterness may influence the amount of alcohol and tobacco intake.

**Supporting Information**

**Table S1** TAS2R38 genetic variants and eating behavior factors. Data are presented as means ± SD. Type 2 diabetics were excluded. P-values were calculated using linear regression model adjusted for age, sex and lnBMI.

**Table S2** TAS2R38 haplotypes and eating behavior factors. Data are presented as means ± SD. Type 2 diabetics were excluded. P-values were calculated using linear regression model adjusted for age, sex and lnBMI. AVI = alanine-valine-isoleucine; PAV = proline-alanine-valine.
Acknowledgments

We thank all those who participated in the studies. We would like to acknowledge excellent technical assistance by Ines Müller.

Author Contributions

Conceived and designed the experiments: YB. Performed the experiments: MK TW. Analyzed the data: MK XL TB. Contributed reagents/materials/analysis tools: XL KR MTG MS AT. Wrote the paper: MK YB. Edited the manuscript: XL KR MS PK AT.

References

1. Sainz E, Cavenagh MM, Gutierrez J, Battey JF, Northup JK et al. (2007) Functional characterization of human bitter taste receptors. Biochem J 403: 537–543.
2. Bachmanov AA, Beauchamp GK (2007) Taste receptor genes. Annu Rev Nutr 27: 389–414.
3. Janssen S, Laermans J, Verhulst P, Thijs T, Tack J et al. (2011) Bitter taste receptors and -gustducin regulate the secretion of ghrelin with functional effects on food intake and gastric emptying. Proc Natl Acad Sci U S A 108: 2094–2099.
4. Tepper BJ, Koelliker Y, Zhao L, Ulrich NV, Lanzara C et al. (2008) Variation in the Bitter-taste Receptor Gene TAS2R38, and Adiposity in a Genetically Isolated Population in Southern Italy. Obesity 16: 2289–2295.
5. Wooding S, Kim U, Bamshad MJ, Larsen J, Jordé LB et al. (2004) Natural selection and molecular evolution in PTC, a bitter-taste receptor gene. Am J Hum Genet 74: 637–646.
6. Kim U, Jorgenson E, Coon H, Leppert M, Risch N et al. (2003) Positional cloning of the human quantitative trait locus underlying taste sensitivity to phenylthiocarbamide. Science 299: 1221–1225.
7. Bufe B, Breslin PAS, Kuhn C, Reed DR, Tharp CD et al. (2005) The molecular basis of individual differences in phenylthiocarbamide and propylthiouracil bitterness perception. Curr Biol 15: 322–327.
8. Dotson CD, Zhang L, Xu H, Shin Y, Vignes S et al. (2008) Bitter Taste Receptors Influence Glucose Homeostasis. PLoS ONE 3: e3974.
9. Stephens M, Donnelly P (2003) A comparison of bayesian methods for haplotype reconstruction from population genotype data. Am J Hum Genet: 73: 1162–1169.
10. Westenhoefer J (1989) Fragebogen zum Elberhalten (FEV). Handanweisung. Göttingen: Hogrefe.
11. Breitfeld J, Tonjes A, Gazal M, Schleinitz D, Bluher M et al. (2013) Role of vaspin in human eating behaviour. PLoS ONE 8: e54140.
12. Stunkard AJ, Messick S (1985) The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. J Psychosom Res 29: 71–83.
13. Veeramah KR, Tonjes A, Kovacs P, Gross A, Wegmann D et al. (2011) Genetic variation in the Sorbs of eastern Germany in the context of broader European genetic diversity. Eur J Hum Genet 19: 995–1001.
14. Veeramah KR, Tonjes A, Kovacs P, Gross A, Wegmann D et al. (2011) Genetic variation in the Sorbs of eastern Germany in the context of broader European genetic diversity. Eur J Hum Genet 19: 995–1001.
15. Pudel D, Westenhofer J (1989) Fragebogen zum Elberhalten (FEV). Handanweisung. Göttingen: Hogrefe.
16. Breitfeld J, Tonjes A, Gazal M, Schleinitz D, Bluher M et al. (2013) Role of vaspin in human eating behaviour. PLoS ONE 8: e54140.
17. Stunkard AJ, Messick S (1985) The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. J Psychosom Res 29: 71–83.
18. Westenhoefer J (1991) Dietary restraint and disinhibition: Is restraint a homogenous construct. Appetite 16: 45–55.
19. Stunkard AJ, Messick S (1985) The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. J Psychosom Res 29: 71–83.