NUTRITION IN THE HEALTHY CHILD

TASTE GENETICS, NUTRITION AND HEALTH: RELATION BETWEEN INHERITED FACTORS, FOOD BEHAVIOR AND FOOD-RELATED DISEASES

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Background

The relationship between innate behaviours and eating habits is particularly critical in children, where taste is a crucial determinant of food selection. Bitterness in food triggers an innate aversion that could be responsible for dietary restriction, whereas sweet and umami tastes bring craving for high-energy foods. To date, the most studied genotype-phenotype association related to taste is the sensitivity to bitterness, linked to common genetic variants in the bitter receptor TAS2R38. Three nonsynonymous substitutions at this locus give rise to functionally different isoforms associated to different phenotypes (Taster, Nontaster, Supertaster). Tasters are more sensitive to a variety of bitter substances and show greater dislike for bitter vegetables and fruits. Supertasters exhibit a great density of taste papillae and are more sensitive to other tastes and strong-tasting foods (sweets, capsaicin, alcohol and liquid fats). Therefore TAS2R38 phenotype is regarded as a general marker of taste sensitivity able to condition food choices. Recently taste receptors and effectors that mediate gustatory signals in the oral cavity have been found in gastrointestinal mucosa, suggesting a role in chemosensing that triggers the physiological responses to luminal content. So food perception is no longer confined to the field of nutrition and food preferences, but is rapidly expanding to gastrointestinal function and, possibly, dysfunction.

In this regard, it is likely that genetic variations in taste receptors could modify the interaction between food and body, leading to feeding disorders up to obesity and related metabolic dysfunctions. The characterization of taste receptors minor variants affecting the ability of initiating taste-specific signaling pathways raises the questions of if and how genetic polymorphisms in TAS receptors could be critical for the efficiency of the physiological processes of the gastrointestinal tract.

Main achievements

Assessment of relationship between genetic variants of the TAS2R38 receptor and dietary habits in healthy children and in the context of diet-related diseases, such as obesity

We investigated the food choices in healthy and in obese children to explore if genetic variations in taste sensitivity could affect adherence to healthy Mediterranean diet. Bitter sensitivity varies greatly among individuals and is associated with polymorphisms in the bitter receptor genes as well as with differences in fungiform papillae density. We explored the association of genetic variants in TAS2R38 receptor and in the taste bud growth factor gustin/CAVI with eating pattern of 705 healthy individuals (435 adults and 270 children) and 155 obese children. The feeding behaviour of children in relation to their mother's food preferences was also been investigated in 224 mother-child dyads, in order to stratify for familial environment and shared or unshared genomic profile. We observed that the genetic profile of the bitter-taste receptor TAS2R38 explains most of the variance in bitterness perception, but the related phenotype is strongly influenced by age, also in mother-child dyads that share the same genotype. Compared to adults, children are more sensitive and the greater sensitivity to bitter predicts lower preferences for vegetables. Instead, no correlation was found between CAVI polymorphisms and TAS2R38 phenotypes or food preferences. Thereafter we investigated the contribution of TAS2R38 variants to confer susceptibility to develop obesity, along with polymorphisms of the obesity-associated genes FTO, BDNF, Mc4R. We found a direct correlation between sensitivity to bitterness and BMI, in a model in which the variables that best discriminate obese children from healthy controls are the genetic variants in the BDNF and Mc4R along with the phenotype of bitter sensitivity.

Evaluation of TAS2R38 receptor polymorphisms as predictors or contributory cause of eating behaviour disorders

Food selectivity has been described in about a quarter of healthy infants up to 18 months or less, but it is regarded as a transient problem related to "neophobia" (the refuse of new unknown food by the age of weaning). In children with mental

disabilities, the rate of food selectivity lasting for over 24 months can be as high as 70-80% in children with autistic spectrum disorders (ASD) and is not associated with severity level of disease. ASD children refuse more frequently fruits and vegetables compared to typically developing (TD) kids, but it is unknown if these preferences depend on the taste identification abilities or other factors. We hypothesized that food refusal in ASD could be influenced by the TAS2R38 genotype. We explored the relationship between genetic variations in the TAS2R38 receptor and food refusal in ASD and in TD children with and without food selectivity. A statistically significant correlation between bitter sensitivity and food refusal was observed, with a prevalence of the TAS2R38-sensitive haplotype compared to the -insensitive one in ASD children with food selectivity. This result show that food refusal in ASD children is influenced by bitter sensitivity, thus suggesting the bitter taste test as a useful device to orientate tailored food proposals for the practical management of food selectivity in this condition.

Investigation of contribution of TAS2R38 receptor polymorphisms to susceptibility to functional gastrointestinal disorders (FGID)

The involvement of gut-expressed taste receptors in eliciting functional responses such as the control of food intake and glucose homeostasis has been documented in humans. We hypothesized that genetic variants of chemosensory receptors expressed in GI tract can contribute to susceptibility to FGID. We evaluated the association of gastrointestinal disorders with polymorphisms in TAS2R38 and TRPV1 receptors, the last implicated in visceral hypersensitivity. The contribution of polymorphisms in genes involved in gastrointestinal motility and inflammation, such as GNB3, IL-6 and TNF-α was also evaluated. The results of a first study on 92 children with FGID classified by the Rome IV criteria (Irritable Bowel Syndrome, Gastroesophageal reflux disease, Functional abdominal pain or functional constipation) and 83 age-matched unaffected controls suggest that the most significant variables associated to functional digestive disorders are polymorphisms in the IL6, TAS2R38 and TRPV1 genes. Regarding the variants in TAS2R38 receptor we observed a statistically significant difference in the distribution of both common and rare TAS2R38 diplotypes compared to the general population, with a double frequency of rare genotypes in the FGID cohort compared to controls. Future perspective in this field will be to outline susceptibility profiles linked to the combination of several polymorphisms as predictor of diagnosis of a functional gastrointestinal disorder and, in some instances, severity of bowel symptoms and poorer health-related quality of life.

Publications

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3. *Greco L e Negri R. Regolazione genetica ed ambientale del gusto. Nutrizione Umana Rivellese et al. Idelson Gnocchi eds Cap.19. 2017.*
4. *Riccio MP, Franco C, Negri R, Ferrentino RI, Maresca R, D'alterio E, Greco L, Bravaccio C. Is food refusal in autistic children related to TAS2R38 genotype? Autism Res. 2018; 11:531-538*