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Flavor and taste recognition impairments in people with type 1 diabetes

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BACKGROUND/OBJECTIVES: Adherence to dietary recommendations is a critical component in the management of type 1 diabetes (T1D). Taste and flavor significantly influence food choices. The aim of this study was to investigate taste sensitivity and flavor recognition ability in adults with T1D compared to healthy individuals.

SUBJECTS/METHODS: Seventy-two people with T1D and 72 matched healthy controls participated in the study. Participants underwent the gustometry test for sweet, sour, salty, and bitter tastes and the flavor test, which consisted of oral administration of aqueous aromatic solutions identifying 21 different compounds.

RESULTS: Participants with T1D had significantly lower flavor scores and gustometry scores than controls ($p < 0.0001$ and $p = 0.0063$, respectively). T1D individuals showed a lower perception of sour, bitter and salty tastes than controls, while the perception of sweet taste was similar. The sex differences and age-related decline in flavor perception observed in controls were not present in the participants with T1D. Neither BMI nor disease-related parameters such as fasting blood glucose on the day of the study, glycosylated hemoglobin, age at onset of diabetes, duration of diabetes, or type of insulin treatment (insulin pump or multiple daily injections) correlated with flavor and taste perception in the T1D participants.

CONCLUSIONS: Flavor and taste perception are impaired in adults with T1D, potentially affecting dietary adherence and food choices. This highlights the need for further research into the mechanisms underlying sensory changes in T1D and emphasizes the importance of targeted dietary interventions to improve health outcomes and quality of life in this population.

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INTRODUCTION

Type 1 diabetes (T1D) is an autoimmune disease that affects various systems of the body and leads to numerous complications. A targeted nutritional plan and adherence to dietary recommendations are fundamental to effectively managing the disease and reducing the risk of developing complications.

Dietary preferences are determined by physiological, social, psychological [1], and genetic factors [2], and the enjoyment of food is an important factor in such decisions. Taste and flavor, therefore, play a central role in shaping quality of life and daily activities and are also critical factors in detecting potential environmental hazards, such as spoiled food [3].

Deterioration in chemosensory functions such as taste and smell have been associated with various diseases [4], and dysgeusia [5–7], as well as olfactory dysfunctions [8] have also been described in people with diabetes. Often these symptoms have not been considered "per se" manifestations of T1D, but rather consequences of diabetic neuropathy, hyperglycemia, oral or dental disease, and medical treatments or medications commonly used in patients with diabetes [9, 10]. Despite the extensive research on taste function in people with diabetes, the results are still conflicting. Some studies showed no differences in taste perception between people with and without diabetes [5, 11, 12], while other studies indicated that people with diabetes have a lower ability to detect taste [13–15]. Impaired taste perception in T1D has been associated with disease duration and complications, particularly peripheral neuropathy [6]. More recently, Pugnaloni and colleagues [16] observed lower taste scores in individuals with type 2 diabetes than in healthy controls, and an age-related decline in taste function was found that was independent of sex, disease duration, and glycemic control. Changes in taste perception were not found in prediabetic individuals [17], while they have been described in people with abnormal glucose tolerance [18] and in young T1D patients [19–22].

The underlying mechanisms of taste disturbance in diabetes are still unknown. These could include a congenital or acquired defect in the taste receptor, poor glycemic control, micro- or macrovascular complications, neuropathy, or an abnormality of central taste perception in the brain [23], as well as the influence of various medications commonly used in people with diabetes [10]. Other factors contributing to taste disturbances in T1D may include inflammation of the oral mucosa and decreased salivary secretion [9, 24].

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Naka and colleagues reported a negative correlation between taste function and body mass index (BMI) [12], while Stolbová et al. suggested obesity as a possible cause of taste disturbance in people with type 1 and type 2 diabetes [25]. HbA1c, which reflects glycemic control over the previous three months, has been studied in relation to taste disturbances, with conflicting results [12, 23, 26–29]. The duration of diabetes may also play a role [6, 23]. In children with T1D, taste impairment has been associated with the early onset of the disease, which may be related to a greater number of autoimmune disorders, a smaller initial insulin reservoir, and higher insulin requirements [30, 31].

Flavor, rather than taste, is probably the most important neurosensory function influencing food choice and preference [32–34]. The perception of flavor is a multifaceted and complex sensory experience that is primarily influenced by the sense of smell, particularly the retro-nasal airflow triggered by volatile substances that are either chewed or dissolved in the oral cavity. Various stimuli in the mouth, such as the texture and viscosity of food and even the activation of nociceptors for static pressure and pain, play a role in conveying this information [35, 36]. The retronasal sense of smell likely plays an important role in the detection and enjoyment of flavors [37, 38] and thus contributes most to the hedonic response and "pleasantness" of food [39–41]. Ultimately, impaired flavor recognition can lead to problems in recognizing food, determining oral intake, and enjoying food [42]. A quantitative test to assess flavor recognition was developed and validated by our group [42]. The test was used to study flavor recognition in the general population [43], in individuals with overweight and obesity [44], and in patients with endocrine [42] and neurological disorders [45]. The test has also been modified to be suitable for home-isolated patients with Sars-COV-2 infection [46].

The aim of this study was to evaluate taste sensitivity and the ability to detect flavors in adults with T1D compared to healthy individuals, as this may have potential implications for adherence to dietary recommendations in people with type 1 diabetes.

SUBJECTS, MATERIALS, AND METHODS

Study Subjects

One hundred and seven adults (≥18 years) with type 1 diabetes mellitus were recruited for the study as part of their routine check-ups at the Diabetes Unit of the Federico II University Hospital. Healthy volunteers selected from a large database investigating the health status of the general population of the Campania region (http://www.campussalute.it) and matched with the patients for age, sex, BMI, and smoking habits were selected as controls.

After signing an informed consent form, participants were screened for the presence of smoking, alcohol abuse, and concomitant diseases such as endocrine, metabolic, and cerebrovascular disorders, seasonal allergies, rhinosinusitis, and medication. People with a BMI > 35 kg/m^2 or with current or chronic sinusitis, nasal polyps, or viral or seasonal rhinitis were not included in the study. Also excluded were people taking medication known to impair the sense of smell (e.g., antibiotics, griseofulvin, lithium, penicillamine, procarbazine, rifampicin, antipsychotics, antiepileptics, antidepressants, amiodarone, digoxin, and chemotherapeutic agents), inhaled medication or substances with addictive potential (e.g., cocaine).

The research was conducted in accordance with the Italian Bioethics Law and the Declaration of Helsinki. The flavor test was approved by the Ethics Committee of the Federico II University of Naples (IDs 253/13 and 93/19).

Flavor test

The flavor test was previously developed, validated, and patented (patent no. 0001426253, category A61B500 of the Italian Ministry of Economic Development) [42]. It consists of a series of 20 aromatic extracts corresponding to typical Italian flavors: Almond, Banana, Cheese, Chocolate, Coffee, Fish, Garlic, Mint, Hazelnut, Honey, Lemon, Licorice, Mushroom, Mustard, Onion, Peach, Roasted Beef, Smoked, Tea and Vanilla. The flavors were kindly provided by the manufacturer (Enrico Giotti Spa, Scandicci, Firenze, Italy). Each flavor was diluted as previously described [42] according to the manufacturer's instructions. An aliquot of 0.5 ml of each flavor was administered into the oral cavity and left for approximately 5 s. Before administering the next flavor, the mouth was rinsed twice with distilled water. At each administration, participants were asked to identify the flavor by making a choice from 5 suggested items. A total of 21 aromatics (including a blank, water) were administered. The flavor score (FS) was calculated as the sum of correctly identified flavors and ranged from 0 to 21 [42].

Gustometry

Gustometry was assessed as previously described [47]. In brief, four liquid taste solutions were used. Two concentrations of each tastant were prepared: (1) 0.1 and 0.2 g/ml sucrose for "sweet"; (2) 0.001 and 0.002 g/ml quinine hydrochloride for "bitter"; (3) 0.025 and 0.05 g/ml sodium chloride for "salty"; and (4) 0.1 and 0.2 g/ml citric acid for "sour".

These substances were dissolved in distilled water, and one drop of each solution (20 µL) was applied to the tongue surface. Before applying each taste solution, the mouth was rinsed twice with distilled water. After presentation of the stimulus, each subject was asked to choose one of the descriptors ("sweet", "sour", "salty", or "bitter"). The fifth basic taste "umami" was not considered in this study, as this taste is often underestimated or described as a different taste quality in the Italian population [48]. Each solution was applied twice in a pseudo-randomized order. The gustometry score (GS) was calculated as the sum of correctly identified tastes and ranged from 0 to 16.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics ver. 29.0.1.0. Results were expressed as means ± standard deviation (SD) for continuous variables or as frequencies for categorical variables.

The Kolmogorov–Smirnov test was used to test the hypothesis of normal distribution of the data. Most variables did not have a Gaussian distribution, so non-parametric tests were used for group comparisons (Kruskal–Wallis or Mann–Whitney tests). Correlations were calculated using Spearman's correlation analysis. Fisher's exact test was used to compare categorical data.

The main predictors of taste sensitivity and the ability to detect flavors were evaluated by multiple regression analysis with stepwise models having flavor and gustometry scores as dependent variables. For each dependent variable, the independent variables were the potential confounders (T1D diagnosis, age, BMI, and sex). Both T1D diagnosis and sex were included in the model as dummy variables.

For all statistical analyses, a p-value of <0.05 was considered significant.

RESULTS

Originally, 107 patients with type 1 diabetes mellitus (T1D) were recruited for the study. Of these, 35 were excluded due to the presence of previously diagnosed complications (neuropathy, nephropathy, or retinopathy) or BMI > 35 kg/m^2. The total population thus consisted of 72 patients with T1D and 72 control subjects (35 women and 37 men/group).

The characteristics of the subjects studied are listed in Table 1.

Flavor and taste perception

The flavor score (FS) determined in the subjects with type 1 diabetes was 13.6 ± 2.42, while it was 16.2 ± 1.94 in the control subjects ($p < 0.0001$) (Fig. 1A).

FS is determined by the ability to correctly identify the flavor from a range of possible options. Table 2 shows the percentage of correct responses for each flavor tested in the two groups of participants. The data analysis showed that the participants with T1D were significantly worse at recognizing the following flavors: Water, Mushroom, Lemon, Almond, Honey, Peach, and Fish compared to control subjects.

Gustometry also differed between people with T1D and control subjects and amounted to 14.00 ± 2.34 and 15.03 ± 1.47 ($p = 0.0063$), respectively (Fig. 1B). When the values obtained for the calculation of GS were broken down according to the four main tastes analyzed (sour, bitter, sweet and salty), participants with type 1 diabetes showed a lower perception of sour taste (3.49 ± 0.87 vs. 3.81 ± 0.43; $p = 0.0105$; Fig. 1C), bitter taste (3.40 ± 1.07 vs. 3.75 ± 0.71; $p = 0.0117$; Fig. 1D), and salty taste

Table 1. Characteristics of the population studied (T1D: people with type 1 diabetes mellitus).

	T1D	Controls	*p* Value
Female/male	37/35	37/35	1.000
Age ranges (years)	21–75	18–78	0.871
Body mass index (kg/m^2)	25.34 ± 4.12	24.10 ± 3.57	0.081
Glycated hemoglobin (%)	7.35 ± 0.79	–	
Duration of diabetes (years)	20.67 ± 10.27	–	
Insulin pump [n (%)]	55 (76.39)	–	
Multiple daily injections [n (%)]	17 (23.61)	–	

Table 2. Percentage of correct identification of each flavor in the participants with type 1 diabetes (T1D) and controls.

	T1D (%)	Controls (%)	*p* Value
Water	50.00	79.17	**<0.001**
Smoked	79.17	93.06	**0.028**
Garlic	50.00	55.56	0.617
Banana	90.28	88.89	1.000
Coffee	80.56	91.67	0.090
Roasted meat	83.33	91.67	0.207
Cocoa	13.89	25.00	0.140
Onion	81.94	86.11	0.650
Cheese	38.89	50.00	0.240
Mushroom	54.17	79.17	**<0.001**
Lemon	25.80	81.94	**<0.001**
Licorice	98.61	97.22	1.000
Almond	80.56	94.44	**0.021**
Mint	88.89	94.44	0.367
Honey	23.61	51.39	**0.001**
Hazelnut	77.78	77.78	1.000
Peach	66.67	94.44	**<0.001**
Fish	59.72	81.94	**0.006**
Mustard	37.50	38.89	1.000
Tea	80.56	87.50	0.363
Vanilla	68.06	77.78	0.260

Significance was determined using Fisher's exact test.
Significant *p*-values are indicated in bold.

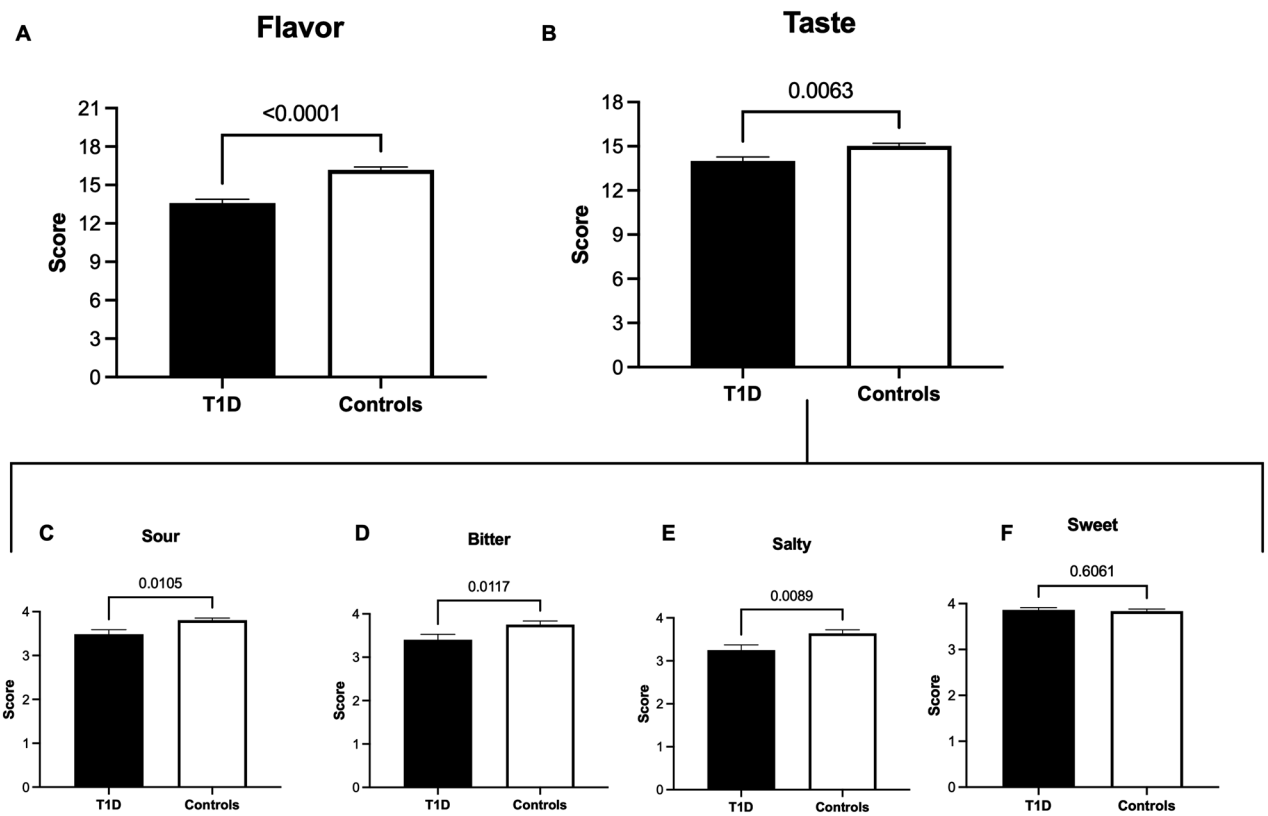

Fig. 1 Flavor (**A**) and taste (**B**) scores in participants with type 1 diabetes (T1D) and control subjects. In panel **C**–**F** the perception of the specific essential tastes are shown. The figure shows the mean ± SE of the values obtained. Exact *p*-values calculated with Mann–Whitney tests are indicated.

(3.25 ± 1.04 vs. 3.64 ± 0.70; $p = 0.0089$; Fig. 1E) compared to control subjects, while no significant differences were found in the perception of sweetness (Fig. 1F).

Sex and flavor and taste perception

Previous studies by our group have shown that women in the general population have a greater ability to correctly identify flavors, especially in older age groups [43]. For this reason, we decided to compare the ability to identify flavors and essential tastes in our study groups and differentiate them by sex. The data are shown in Fig. 2A, B. Males with T1D achieved a FS of 13.8 ± 2.6, while the FS of the male control group was 15.3 ± 2.0 ($p = 0.0148$). Women with T1D achieved an average FS of 13.4 ± 2.2, while the control subjects had an average FS of 17.1 ± 1.3 ($p < 0.0001$). While the perception of flavors was significantly lower in males than females among the controls ($p = 0.0020$), this difference disappeared in the T1D participants ($p = 0.8121$).

The differences in gustometry between T1D and control subjects, broken down by sex, did not reach significance.

Age, flavor, and taste perception

As previously reported, FS tends to decrease with increasing age [43], and these data are confirmed in our controls in this study ($R = 0.319$; $p = 0.06$). In contrast, in individuals with diabetes, scores remain constant with increasing age ($R = 0.058$; $p = 0.630$), although they are consistently reduced (Fig. 2C).

On the other hand, gustometry was not influenced by age in both patients and control subjects (T1D: $R = 0.083$; $p = 0.486$; Controls: $R = 0.055$; $p = 0.649$) (Fig. 2D).

Body mass index and flavor and taste perception

It has already been shown that an increase in BMI in the healthy population is associated with a reduction in flavor recognition [43]. This association was not observed in the participants with type 1 diabetes ($R = 0.012$; $p = 0.918$) and in the control subjects, in whom only a non-significant trend was observed ($R = 0.102$; $p = 0.393$) (Fig. 2E). Gustometry (Fig. 2F) did not correlate with BMI (T1D: $R = 0.153$; $p = 0.200$; Controls: $R = 0.062$; $p = 0.604$).

Combined effects of diabetes, sex, age, and BMI on flavor and gustometry scores

The overall model predicting the ability to recognize flavors explained 28.4% of the variance ($p < 0.001$). The best predictors were T1D ($\beta = -0.514$, $p < 0.001$) and age ($\beta = -0.155$, $p = 0.032$), both of which were significantly and inversely associated with flavor score, while sex and BMI did not contribute significantly to the model (Fig. 2G).

The overall model predicting the ability to recognize tastes (GS) explained 16.3% of the variance ($p < 0.001$). The best predictors were sex (female) ($\beta = 0.297$, $p < 0.001$), T1D ($\beta = -0.284$, $p < 0.001$), and BMI ($\beta = 0.176$, $p = 0.029$), all of which were significantly associated with GS. Age did not contribute significantly to the model (Fig. 2H).

Disease history and flavor and taste perception

To clarify whether the effects on flavor perception and gustometry are related to the clinical course of the disease, we examined the correlation between FS and GS with blood glucose on the day of the examination (Fig. 3A, B), glycosylated hemoglobin (Fig. 3C, D), age at diabetes onset (Fig. 3E, F) and diabetes duration (Fig. 3G, H), as well as the type of insulin treatment (insulin pump or multiple daily injections, Fig. 4A, B). None of the parameters examined showed a significant correlation with flavor or taste.

DISCUSSION

This study investigates the complex relationship between T1D and sensory perception, with a particular focus on taste and flavor.

The results of our study show that adults with T1D have a significantly lower gustometry score (GS) than comparable healthy controls. Among the T1D participants in our study, the reduction in GS was determined by a higher inability to recognize sour, bitter, and salty tastes, while no significant reduction was observed for sweet taste. This observation is in contrast to what was previously observed in adult T1D patients, where the most common impairment was a decreased perception of sweet taste [49]. In contrast, children and adolescents with T1D were significantly more likely to correctly recognize sweet taste compared to healthy children and adolescents [22]. This higher sensitivity to sweet taste was explained as a consequence of higher adherence to dietary recommendations that mainly focus on limiting the amount of easily digestible carbohydrates, i.e., sweet-tasting products. Children and adolescents who limit the daily amount of sugar in their diet may be more sensitive to this taste [22]. It is likely that the lack of a reduced ability to recognize sweetness in our participants can be explained in a similar way, as all of them are constantly monitored by expert dietitians.

Furthermore, we could not associate the reduced gustometry score observed in TD1 patients with any of the parameters studied, including age or BMI, blood glucose, HbA1c, age at onset and duration of disease, or type of insulin treatment. In this context, it should be noted that the relatively small sample size may have influenced the analysis of the subgroups.

Overall, a regression analysis was performed to evaluate the specific weight of the different factors influencing taste perception. This method allows us to quantify the individual contribution of each predictor variable, such as T1D, sex, age, and BMI, while controlling for the influence of the other variables. Using stepwise regression, the results underlined the significant influence of sex, T1D, and BMI on the ability to recognize tastes. Women were found to have higher GS compared to men, possibly due to inherent biological and hormonal differences that influence taste perception. The presence of T1D was significantly associated with lower GS, which is consistent with existing literature suggesting that metabolic changes in diabetes negatively affect sensory perception. Interestingly, BMI was found to be a positive predictor of GS, suggesting that individuals with a higher BMI may have better taste perception.

Flavor, rather than taste, is probably the most important neurosensory function influencing food choices. Studies on flavor perception are, therefore, more relevant and contribute more to the understanding of the multifaceted effects of T1D on individuals.

We have previously developed and validated a quantitative test to assess flavor perception [42], and here flavor perception was examined in people with T1D. The results show that T1D individuals exhibit a significant reduction in flavor scores. The reduction in the ability to detect flavors was applied to all 21 flavors tested and was significant for water, mushroom, almond, lemon, honey, peach, and fish. It is noteworthy that these flavors were diluted in different solutions (fish in absolute water; water, lemon, honey, and peach in 8% sucrose; mushroom in 3 g/l NaCl) [42]. This indicates that the inability of T1D participants to detect it was not related to the aqueous base of the solution, which probably influences the taste more than the flavor. Conversely, the flavors least often perceived by T1D patients were those diluted in a sweet solution, while the gustometry results suggest that sweet taste was not affected by the disease in our study participants.

When using the flavor test in the healthy general population, women achieved slightly but significantly higher FS values than men, especially in older individuals [43]. This effect was not present in the T1D participants in our study, where women and men showed no significant differences in FS. Similarly, previous observations reported a physiological age-related decrease in flavor recognition in healthy individuals [43, 44], which we were able to confirm in our healthy control cohort, but not in the participants with T1D, where age was a significant predictor of

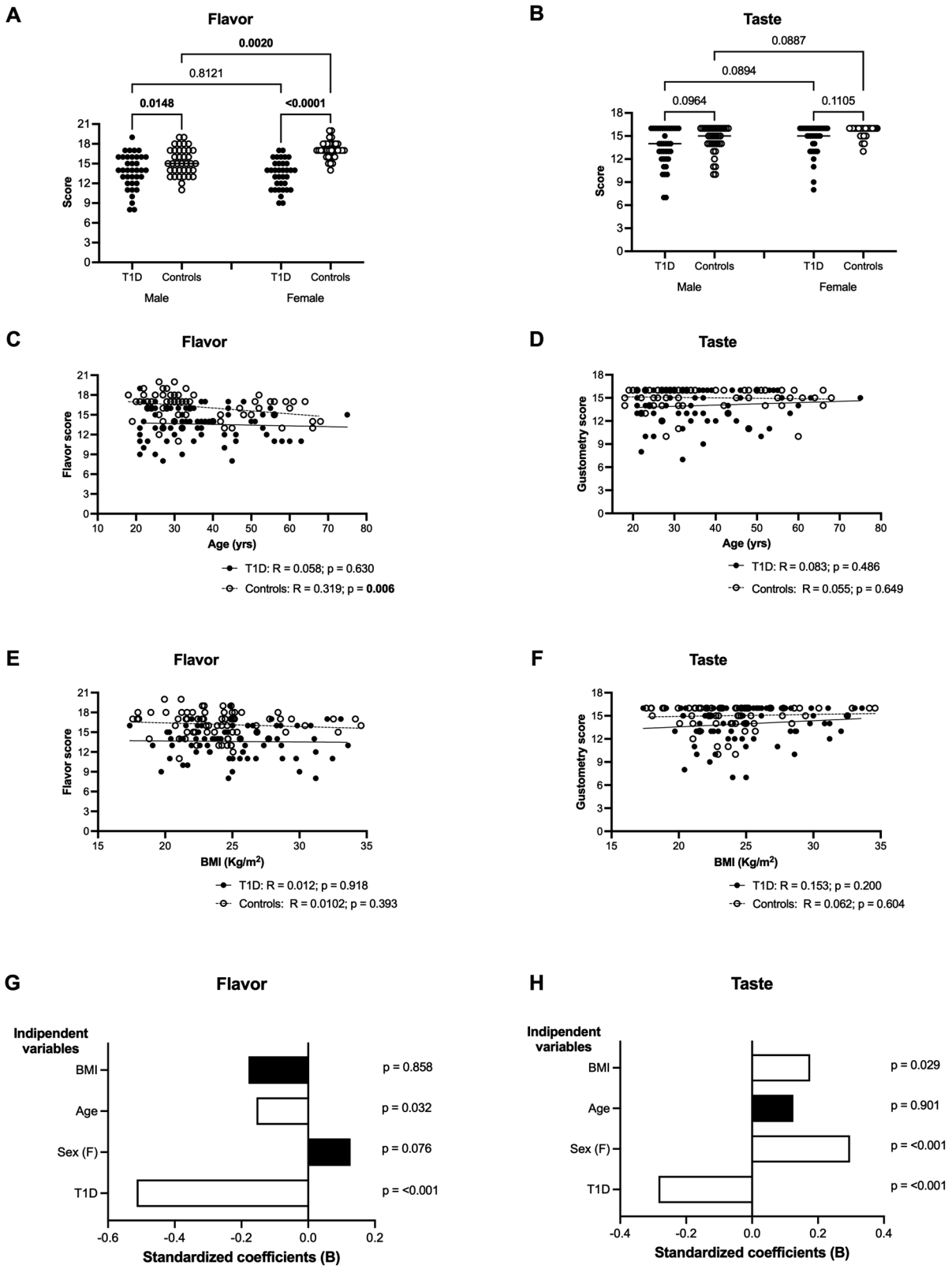

Fig. 2 Assessment of flavor (**A**, **C**, and **E**) and taste (**B**, **D**, and **F**) in the population studied, broken down by sex (**A** and **B**) and as a function of age (**C** and **D**) and BMI (**E** and **F**). The panels from **A** to **F** show the individual values and the mean values in different groups. A significant inverse correlation was only found between age and flavor scores in the control subjects ($p = 0.0063$). The standardized coefficients from the regression model are shown for flavor perception (panel **G**) and taste (panel **H**) for T1D, sex, age and BMI. Black bars represent non-significant predictors, while white bars represent significant predictors. The *p*-values are shown on the right-hand side of the bars.

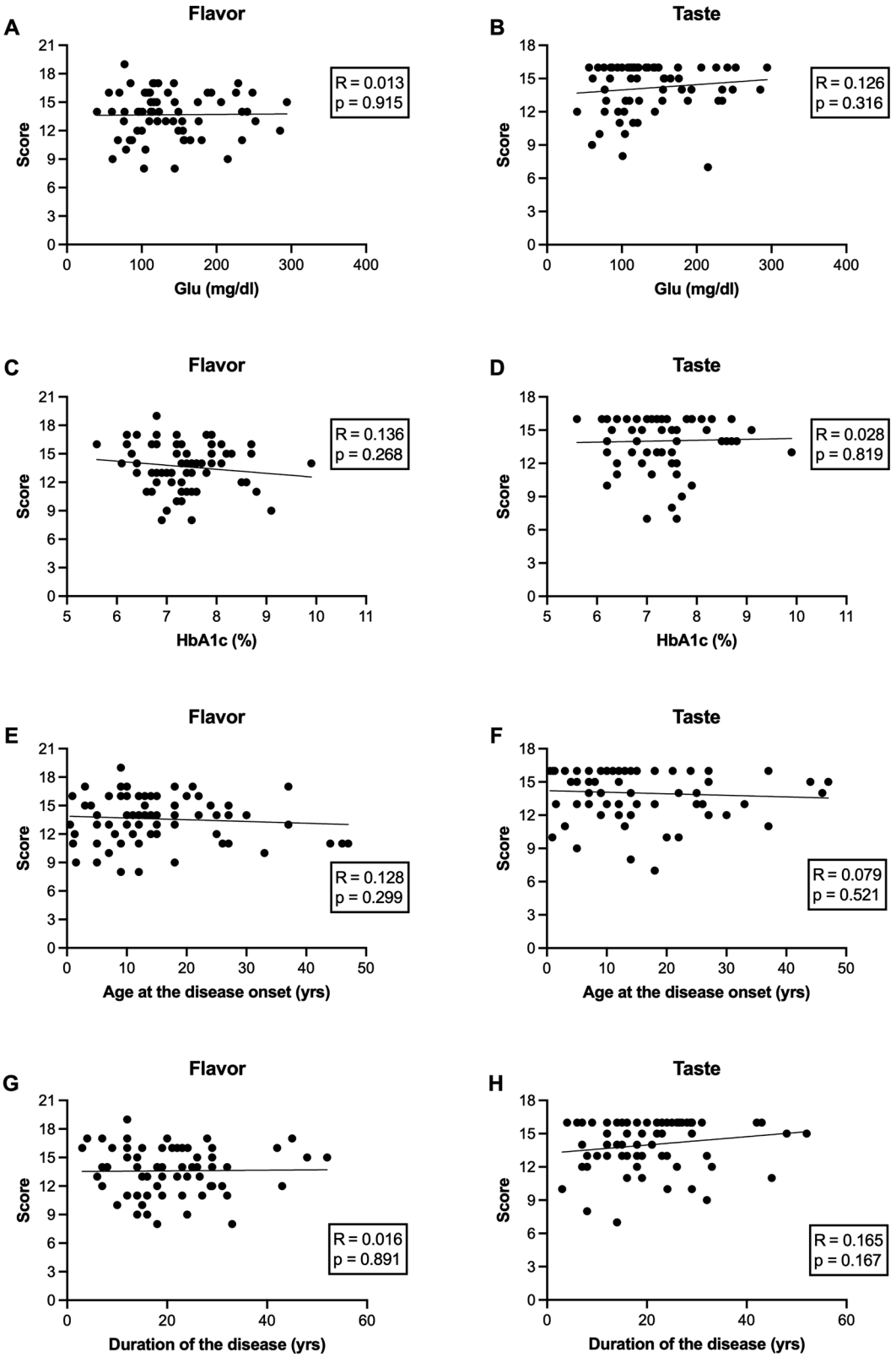

Fig. 3 Correlations between the evaluation of flavor (**A**, **C**, **E**, **G**) and taste (**B**, **D**, **F**, **H**) and clinical parameters (fasting blood glucose level on the day of the test [Glu], glycosylated hemoglobin [HbA1c], age at onset of diabetes, and duration of diabetes). None of the parameters examined showed a significant correlation with flavor or taste scores.

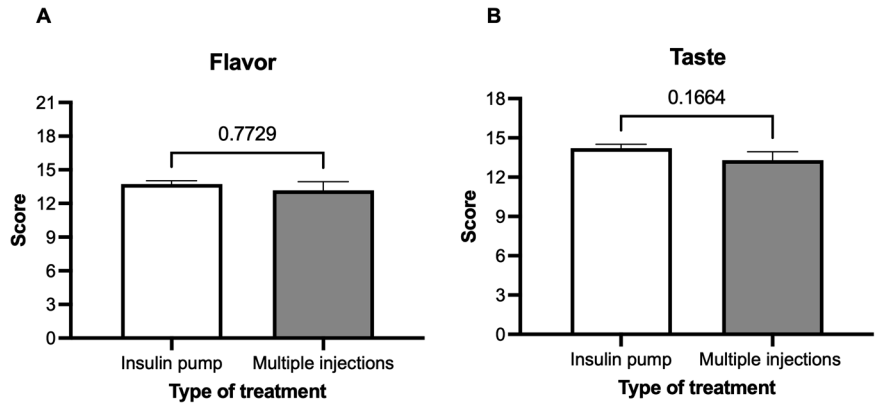

Fig. 4 Influence of type of insulin treatment in T1D participants on flavor (**A**) and taste (**B**) scores. The figure shows the mean ± SE of the values obtained. White bars represent scores in T1D participants treated with insulin pump, while gray bar are the scores in T1D participants receiving multiple daily insuline injections. The differences were not significant.

taste recognition ability in the multivariate regression analysis of the overall population.

Finally, a significant inverse correlation between flavor scores and BMI was previously reported in healthy subjects [44]. We did not observe this association in either the healthy controls or the T1D subjects. One possible explanation is the relatively narrow BMI range due to the exclusion of subjects with a BMI > 35 kg/m^2 in our study and the relatively small sample size. This could also explain why BMI was a significant predictor of taste sensitivity in the overall population, whereas it did not correlate significantly with taste sensitivity in the control group or the separate T1D cohort.

Overall, a regression analysis was performed to assess the specific weight of the different factors influencing flavor perception. The results suggest that both the presence of T1D and age are significant predictors of flavor recognition ability. The combination of these factors explained 28.4% of the variance in FS scores ($p < 0.001$).

Finally, we investigated whether the history of diabetes could be associated with the observed flavor recognition ability in our patients. Pretest blood glucose level, glycosylated hemoglobin, age at diabetes onset, duration of diabetes, and type of insulin treatment were not associated with FS, suggesting that sensory changes in T1D are influenced by factors beyond traditional clinical markers, likely through a complex interplay between metabolic factors, sensory perception, and diabetes-specific eating behaviors.

This study has some limitations and strengths that need to be emphasized. The first limitation of our study is the cross-sectional design and sample size, which may limit the generalizability of our findings to the broader T1D population, particularly to patients with advanced disease or complications. In addition, the exclusion of patients with diagnosed complications and the lack of measures for subclinical neuropathy mean that our results may not fully capture the spectrum of sensory changes in T1D.

Future research should address these limitations by conducting longitudinal studies with larger, more diverse patient populations. Such studies could track changes in taste and flavor perception over time, providing a more comprehensive understanding of the dynamic relationship between the disease and sensory function and potentially identifying critical periods of disease progression when interventions may be most effective. In addition, the inclusion of patients with a wider range of disease severity and complications would provide a more comprehensive understanding of sensory changes in T1D. In addition, assessment of objective measures of neuropathy and other potential confounders would help clarify the mechanisms underlying taste and flavor impairments in this population.

Despite these limitations, a key strength of the study is the use, for the first time, of flavor testing in people with T1D, which is a powerful tool for investigating this innovative aspect.

It opens up opportunities for targeted dietary interventions and highlights the potential challenges in adhering to dietary recommendations.

Herein, adults with T1D have been assessed for their ability to recognize tastes, and the results suggest a significant decline in this neurosensory function, mainly associated with an impairment of sour, bitter, and salty tastes. This is because people with impaired flavor perception tend to choose foods that are more palatable but often high in salt, sugar, or fat. This can lead to an increased consumption of processed and unhealthy foods. Similarly, impairment of these sensory functions can lead people to rely more on the texture of food to satisfy their senses, which can lead to a preference for crunchy, crispy, or creamy textures that are usually found in less healthy diets. Reduced flavor perception can have a negative impact on a person's overall quality of life, affecting their relationship with food and their enjoyment of eating.

In summary, this study shows sensory changes in people with T1D and forms the basis for further research into the underlying mechanisms. It could help to improve the quality of life and health outcomes of these people by highlighting potential pathways that could be useful for better adherence to dietary recommendations.

DATA AVAILABILITY

Materials described in the paper, including all relevant raw data, will be freely available to any researcher wishing to use them for non-commercial purposes upon specific request.

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AUTHOR CONTRIBUTIONS

ICN and GP were responsible for the flavor and gustometry testing and data analysis and contributed to the drafting of the article. PU was responsible for the critical analysis of the data and interpretation of the results and contributed to the preparation of the first draft and final version of the paper. GS, AC, MV, and AMR were responsible for patient follow-up and analysis of clinical data. RDV performed flavor and gustometry tests and prepared the first draft of the paper. GA and LB were responsible for the clinical evaluation of the patients. They supervised the tests, analyzed the results, and provided the scientific interpretation. AC developed and patented the flavor test. She supervised the projects and provided feedback on the final version of the paper. PEM designed the overall study, supervised the experiments, analyzed the results, and wrote the paper. All authors discussed the results and contributed to the paper.

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COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL

The research was performed in keeping with Italian Bioethics Law and the Declaration of Helsinki. The flavor test has been approved by the Ethical Committee of the Federico II University of Napoli (IDs 253/13 and 93/19). Before participating in this study, written informed consent was obtained from each participant, ensuring their voluntary and informed participation.

ADDITIONAL INFORMATION

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