Bitter taste receptor gene in patients with taste disorders

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ABSTRACT

Objective: The object of this study was to examine changes in the expression of taste receptor genes in patients who had loss of taste and those who had phantogeusia.
Methods and Materials: The subjects of this study consisted of 40 patients with loss of bitter taste and 43 patients with phantogeusia. Control group consisted of 24 subjects. We took specimens by scraping their foliate papillae. T2R family and TAS2R family gene expression was detected using RT-PCR and electrophoresis.
Results: The patients with loss of bitter taste showed a significant decrease in the frequency of expression of taste receptor genes T2R8 ($p<0.003$), 10 ($p<0.001$), 13 ($p=0.005$), 16 ($p<0.002$), TAS2R40 ($p<0.001$), and 48 ($p<0.02$) compared to the control group. The frequency of gene expression of TAS2R42 ($p=0.005$) and T2R3 ($p=0.026$) were significantly increased in patients with phantogeusia.
Conclusion: Expression of some genes was decreased in patients with loss of taste while expression of other genes was increased in patients with phantogeusia. It was suggested that conflicting changes in taste receptor gene expression were involved in the pathogenesis of the loss of taste and phantogeusia.

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INTRODUCTION

In the past decade, much has been learned concerning the physiology of taste, including the identification of taste receptor genes, signal transduction mechanisms, and neural transmission mechanisms. However, the pathophysiology and pathogenesis of taste disorders remain unclear.

Genes the taste receptor family, T2R, were identified in the region adjacent to the bitter taste-mediating genes in the human and mouse genome (1-2), and subsequent experiments using transgenic or knock-out mice have shown that the T2R taste receptors are important for bitter taste (3). T2R is a member of a large G-protein-coupled receptor (GPCR) multigene family with seven transmembrane domain receptors.

We have investigated the expression of taste receptor genes (T2R and TAS2R) in tongue tissue using RT-PCR method. The purpose of this study was to examine changes in the expression of taste receptor genes in patients who had loss of taste and those who had phantogeusia.

SUBJECTS

The subjects of this study consisted of 40 patients with loss of bitter taste and 43 patients with phantogeusia.

The patients with loss of bitter taste consisted of 18 males and 22 females, with an average age of 61 years (range, 25 to 86 years). The causative factors for hypogeusia were classified as follows: zinc deficiency (12 cases, 30%), drug-induced (7 cases, 18%), common cold (5 cases, 13%) and idiopathic factors for which no obvious underlying cause was known (16 cases, 40%). The phantogeusia patients consisted of 12 males and 31 females, with an average age of 66 years (range, 39 to 82 years). The phantogeusia patients consisted of 26 patients who complained of phantogeusia of bitter taste and 17 patients who complained of phantogeusia of an abnormal taste other than bitterness. A control group of healthy subjects consisted of 24 cases, 6 males and 18 females, with an average age of 68 years (range, 55 to 83 years) with no complaints of taste disorders.

METHODS

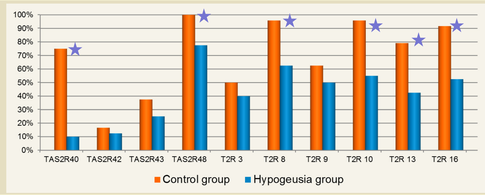
The tongue tissue was collected from the foliate papillae by a simple scraping method, and total RNA was extracted using TRIzol. The reverse transcription reaction was performed using SuperScript3 and PCR was performed using Ex Taq (Takara Bio, Inc.). The electrophoresis was done using an Agilent 2100 Bioanalyzer and the presence or absence of gene expression of T2R3, 8, 9, 10, 13, 16, TAS2R40, 42, 43 and 48 was examined. Statistical analysis was performed by using Fisher's exact probability test.

RESULTS

The patients with loss of bitter taste showed a significant decrease in the frequency of expression of taste receptor genes T2R8, 10, 13 , 16, TAS2R40 and 48 compared to the control group (Figure 1).

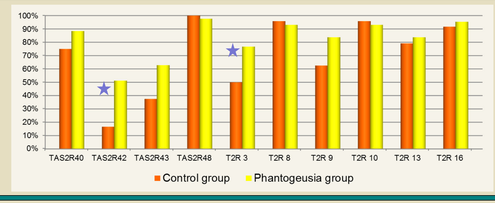
On the other hand, the frequency of gene expression of TAS2R42 and T2R3 were significantly increased in patients with phantogeusia (Figure 2). In patients with bitter taste phantogeusia (n = 26), three (TAS2R42, TAS2R43, and T2R3) of ten taste receptor genes examined showed significantly increased expression compared to healthy subjects (Figure 3).

From the viewpoint of the bitterness sensation, we compared hypogeusia patients to phantogeusia patients with bitter taste (Figure 4).



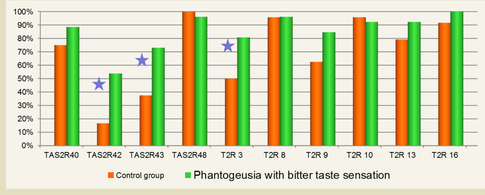
Gene	Control group 24 case (%)	Hypogeusia group 40 case (%)	P value
TAS2R40	18(75)	4 (10.0)	<0.001
TAS2R42	4(16.7)	5 (12.5)	ns
TAS2R43	9(37.5)	10 (25.0)	ns
TAS2R48	24(100)	31 (77.5)	<0.02
T2R 3	12(50)	16 (40.0)	ns
T2R 8	23(95.8)	25 (62.5)	<0.003
T2R 9	15(62.5)	20 (50.0)	ns
T2R 10	23(95.8)	22 (55.0)	<0.001
T2R 13	19(79.2)	17 (42.5)	<0.005
T2R 16	22(91.7)	21 (52.5)	<0.002

Figure 1.
Comparison of gene expression in control group and Hypogeuasia.



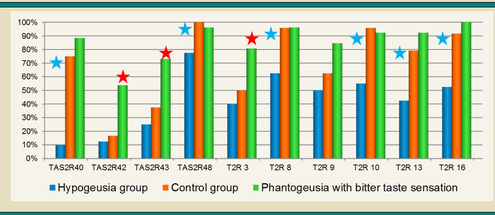
Gene	Control group 24 case (%)	Phantogeusia group 43 case (%)	P value
TAS2R40	18(75)	38(88.4)	ns
TAS2R42	4(16.7)	22(51.2)	0.005
TAS2R43	9(37.5)	27(62.8)	ns
TAS2R48	24(100)	42(97.7)	ns
T2R 3	12(50)	33(76.7)	0.026
T2R 8	23(95.8)	40(93)	ns
T2R 9	15(62.5)	36(83.7)	ns
T2R 10	23(95.8)	40(93)	ns
T2R 13	19(79.2)	36(83.7)	ns
T2R 16	22(91.7)	41(95.3)	ns

Figure 2.
Comparison of gene expression in control group and Phantogeusial.



Gene	Control group 24 case (%)	Phantogeusia with bitter taste sensation 26 case (%)	P value
TAS2R40	18(75)	23(88.5)	ns
TAS2R42	4(16.7)	14(53.8)	0.009
TAS2R43	9(37.5)	19(73.1)	0.022
TAS2R48	24(100)	25(96.2)	ns
T2R 3	12(50)	21(80.8)	0.036
T2R 8	23(95.8)	25(96.2)	ns
T2R 9	15(62.5)	22(84.6)	ns
T2R 10	23(95.8)	24(92.3)	ns
T2R 13	19(79.2)	24(92.3)	ns
T2R 16	22(91.7)	26(100)	ns

Figure 3.
Comparison of gene expression in control group and Phantogeusia with bitter taste.



Gene	Hypogeusia group 40 case (%)	Control group 24 case (%)	Phantogeusia with bitter taste sensation 26 case (%)
TAS2R40	4 (10.0) ★	18(75)	23(88.5)
TAS2R42	5 (12.5)	4(16.7)	14(53.8) ★
TAS2R43	10 (25.0)	9(37.5)	19(73.1) ★
TAS2R48	31 (77.5) ★	24(100)	25(96.2)
T2R 3	16 (40.0)	12(50)	21(80.8) ★
T2R 8	25 (62.5) ★	23(95.8)	25(96.2)
T2R 9	20 (50.0)	15(62.5)	22(84.6)
T2R 10	22 (55.0) ★	23(95.8)	24(92.3)
T2R 13	17 (42.5) ★	19(79.2)	24(92.3)
T2R 16	21 (52.5) ★	22(91.7)	26(100)

Figure 4.
Comparison of gene expression in hypogeusia and Phantogeusia with bitter taste.

DISCUSSION

In this study, the expression of 10 genes belonging to the T2R gene family were examined in patients who had loss of taste and those who had phantogeusia.

Phantogeusia is a unique taste disorder in which abnormal taste sensation occurs despite the absence of taste stimuli in the mouth. From the results obtained in this study, it was shown that the expression of three taste receptor genes significantly increased in the patients with phantogeusia compared to the healthy subjects. Also, these taste receptor genes, which showed significantly increased expression, were the three genes for which expression rates were relatively low in healthy subjects at 16.7-50%. In other words, it was shown that the expression of the taste receptor genes with usually low expression was increased in the patients with phantogeusia. This result suggests the possibility that increased expression of taste receptor genes is involved in the pathogenesis of phantogeusia and provides an important perspective for the elucidation of this disorder.

On the other hand, the expression of 6 genes (TAS2R40, TAS2R48, T2R8, T2R10, T2R13 and T2R16) was significantly decreased in patients with hypogeusia compared to healthy subjects, which showed a high expression of 75-100% in healthy subjects. Since a decrease in the expression was observed in accord with the clinical findings of hypogeusia, these 6 genes are likely involved in taste sensation in humans as taste receptor genes.

CONCLUSIONS

Among the 10 genes examined in this study, expression of some genes was decreased in patients with loss of taste while expression of other genes was increased in patients with phantogeusia, and conflicting changes in gene expression were observed. It was suggested that conflicting changes in taste receptor gene expression were involved in the pathogenesis of the loss of taste and phantogeusia. Further understanding of the pathogenesis of taste disorders will be possible with receptor level studies in the future.

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