Are stress and symptoms of depression associated with halitosis? A cross-sectional study

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Mood disorders such as stress and depression can promote alterations of several hormones. Aim: The present study aimed to evaluate if symptoms of depression and stress are associated with halitosis. The hypothesis is that halitosis is associated with stress and depression symptoms. Methods: All university students’ entrants in the Federal University of Pelotas (UFPel) were invited to participate. Self-reported halitosis was measured using a visual analog scale. Students were also asked about the presence of halitosis perceived by close individuals. The stress level was measured using a modified version of the Perceived Stress Scale and symptoms of depression were screened by Patient Health Questionnaire-2. Poisson Regression Models were performed. Results: Of a total of 2,058 students who participated in the study, only 16% of them have reported not having any degree of halitosis and 17.6% were informed of closed individuals having halitosis. After adjustments, stress and depression symptoms remained associated with halitosis self-reported. Individuals from the higher stressed quartile presented higher scores of halitosis (RR 1.37 CI95% [1.24–1.53]). Students who presented depressive symptoms showed higher scores of self-perceived halitosis (RR 1.20 CI95% [1.10–1.32]). When the association of stress and halitosis reported by close individuals was tested, symptoms of depression lost the association in the adjusted model, while individuals from the highest quartile from stress remained associated (PR 1.36 CI95% [1.02–1.81]). Conclusion: Halitosis was associated with stress even after control for oral health and socioeconomic variables.

Keywords: Halitosis. Depression. Stress. Psychological.
Introduction

Genuine halitosis is an oral malodor caused mainly due to volatile sulfur compounds produced by microorganisms present in the mouth affecting about 22% to 50% of individuals worldwide. A recent systematic review investigating the global prevalence observed that above 32% of individuals are affected by bad breath. The etiology of malodor can be originated from systemic or local factors. In most cases, inadequate oral hygiene practices are strongly associated with self-reported bad breath. In this way, poor oral hygiene causes oral health problems as carious lesions and periodontal disease, which in turn have also been attributed as the main reasons for malodor. Moreover, unhealthy habits such as alcohol use, smoking, and an unbalanced diet can be predisposing factors to its development. On the other hand, systemic diseases including gastrointestinal tract disorders, diabetes, renal and hepatic insufficiencies even as chronic sinusitis are some of the systemic factors correlated to self-report of halitosis.

The literature has also shown that psychological factors can play an important role in the prevalence of bad breath. Two different explanations have been addressed for this association. The use of medication for these disorders could alter the flow and composition of saliva leading to increased bacterial colonization and degradation of proteins present in the mouth, resulting in an elevation of the volatile sulfur-containing responsible for bad breath. Besides, individuals with mood disorders, such as depressive, stressed, and anxious people could present a decrease in self-care. These individuals are less motivated to maintain oral health, culminating in poor hygiene.

Halitosis can be measured through the objective (i.e. organoleptic test, volatile sulfur compounds -VSC) and subjective (self-report) parameters. Objective tests require trained and calibrated examiner even as specific equipment making these measurements more expensive and difficult to conduct in population-based studies. In this way, self-reported assessment can reduce the cost as well as the time to the examination being widely used in epidemiological studies. Self-reported halitosis cannot always be correlated with objective measurements (organoleptic test and VSC). In some cases, only the patient perceives the malodor, being this condition classified as pseudo-halitosis, which represents a minor part of the total diagnosed halitosis. Report of halitosis perceived by other persons, close to the individuals, could be an interesting measurement to complement the self-report measurement. Although different forms of measurement and classification of halitosis are used, self-perception is perhaps the most relevant measure, since it can reflect how an individual feel about his bad breath, which strongly affects not only the social life of the individual but also interpersonal contact, which could compromise the relationships, mainly when perceived by other individuals, impacting the quality of life.

Systemic disorders such as diabetes and renal/hepatic problems are less presented in young adults, so the development of halitosis in this population is more related to local and psychological factors. In this way, individuals in academic activities are more vulnerable to develop mood disorders. Few studies have evaluated factors associated with halitosis in young individuals, in representative samples. Thus,
the present study aimed to evaluate if symptoms of depression and stress are associated with self-reported halitosis and halitosis perceived by close individuals in university students in the south of Brazil. The study hypothesis was that stress and depressive symptoms are associated with both measurements of halitosis (self-related and perceived by other individuals) even after adjustments by socio-economic and oral health factors.

Materials and Methods

The present study was reported as recommended by the Strobe statement (Strengthening the Reporting of Observational Studies in Epidemiology) for cross-sectional studies. Compete methodology is available elsewhere11-13.

Setting and study design

Pelotas is a city in southern Brazil with approximately 400,000 inhabitants, considered one of the main educational poles of the state of Rio Grande do Sul. The city has five higher education institutions being only one public: Federal University of Pelotas (UFPel). Currently, this University has five Campi dispersed in the city. Approximately 13,000 undergraduate students are enrolled in this institution, where about 3,000 students enter each selection process that occurs once a year. In the first semester of 2016, a cross-sectional study was carried-out being applied to a self-reported questionnaire with entrants students of UFPel.

Sample size and power of the study

Considering the estimated number of entrants in the first half of 2015 (3000 students) and a prevalence of 50% (unknown) for the variables of interest, the margin of error of the study would be 1.8 percentage points within a 95% confidence interval. For analysis of association, this sample size is sufficient to detect a prevalence ratio of 1.4, considering a prevalence of exposure of 50%, prevalence of the outcome in exposed individuals of 5%, power of 80%, and α = 5%.

Participants

All regular entrants in the first semester of 2016 in UFPel were considered eligible for this study. The students were located by a list sent by their respective academic units. The questionnaire was applied in before lessons with the authorization of lecturers of each course. Students who were not able to complete the questionnaire and those who are studying subjects without regular enrollment with the institution were excluded. Students of courses out of Pelotas and from distance learning courses were also excluded from the sample.

Data collection

The fieldwork team was comprised of undergraduate and postgraduate students from UFPel Dental School. All team experienced a previous theoretical training of 4 hours with a presentation of the research instruments, logistics of the study with discussion and clarification of possible doubts. In order to test the applicability of the questionnaires, a pilot study was conducted with 100 university students (n = 100) of
the second semester (not eligible for the study). Five courses were randomly selected and the pilot test was performed. The questionnaire was adjusted to facilitate participants’ understanding, and the average time of 20 minutes for completing the instrument was estimated. Thus, in academic units, students received an explanation of the nature of the research, and students who agreed to participate signed a free and informed consent form. The questionnaire was self-administered with multiple-choice questions. This questionnaire was divided into 5 large blocks: block A- socio-economic, demographic, and social support data; block B- psychosocial variables; block C- self-perceived / subjective measures of oral health; block D- behavioral variables of oral health; block E - use of alcohol, tobacco, and other substances.

Outcomes
Self-reported halitosis was measured using a visual analog scale\(^7\) accompanied by the following question: “In the scale of zero to 10, being zero no odor and 10 extremely malodor, mark how do you rate your breath?”\(^4,7\). Responses from 0 to 10 were obtained and the variable was analyzed in discrete form. The students were also asked about the presence of bad breath referred by a close person through the following question: “Has any family member/friend/boyfriend ever reported that you have bad breath?” with the possible answers “yes” and “no”.

Independent variables
Demographic characteristics including sex and age (18 to 24; 25 to 34; and 35 or more) were collected. Family income was collected categorically in Brazilian Reals - BRL: (a) up to 500.00; b) 5,001.00 up to 1,000.00; c) 1,001.00 up to 2,500.00; d) 2,501.00 up to 5,000.00; e) 5,001.00 up to 10,000.00; and f) more than 10,001.00) and categorized in three categories: a) ≤ 1,000.00; b) 1,001.00 to 5,000.00 and c) ≥ 5,001.00. Oral health status was investigated using self-report measures. Gingival bleeding was estimated by the question: “Do your gums bleed when brushing your teeth?” (No; Sometimes; and Always). Experience of dental caries was verified using the question: “Do you actually have or have you ever had any tooth affected by tooth decay?” (Yes or No).

The use of alcohol and tobacco was collected in a separate questionnaire where only one numeric code linked the information of this questionnaire with the other information. In addition, the questionnaires were collected separately in an opaque box to increase the impersonality and consequently improve the reliability of the data collection. Thus, the students were asked about smoking habits and consumption of alcoholic beverages, as well as their frequency. Those who reported that “drink daily or almost daily” were considered as consumers of alcoholic beverages and those who reported “smoking at least weekly” were considered as smokers.

Stress’ level was measured using a modified version of the Perceived Stress Scale (PSS) validated for the Portuguese language. This questionnaire is comprised of ten questions related to the past month, which reflect events and situations, four questions positives, and six negatives. Each question presents five options in a Likert scale, ranging from 1 = never; 2 = almost never; 3 = sometimes; 4 = Less common; and 5 = very often. Scores of the positive questions are reverse-scored and negative scores are normally scored, thus all scales range from 0 to 40 points. A higher score
indicates greater stress. Thus, the variable was categorized in quartiles\textsuperscript{14}. Depression symptoms were investigated using Patient Health Questionnaire-2 (PHQ-2), an abbreviated version of Patient Health Questionnaire-9 (PHQ-9) for depression screening at the population level. The PHQ-2 represents the first two questions of PHQ-9: “Over the last 2 weeks, how often have you been bothered by any of the following problems? 1) “Little interest or pleasure in doing things” and 2) “feeling down, depressed, or hopeless” with possible responses “not at all”, “several days”, “more than half the days”, and “nearly every day”. The responses were scored respectively 0 to 3. The two questions can range from 0 to 6. Individuals that presented a score of 3 or higher were classified with symptoms of depression.

Statistical methods

Data were double entered in a spreadsheet of the software Excel 2013 (Microsoft Corporation). Statistical analyses were performed using Stata 12.0 software (Stata Corporation, College Station, TX, USA). The relative and absolute frequencies of the variables of interest were estimated. Multivariate Poisson Regression Models with robust variance were performed to analyze the associations between halitosis and stress and symptoms of depression. Self-reported halitosis was analyzed as a discrete outcome and halitosis perceived by other individuals was evaluated in a dichotomous way. Variables with P values of ≤0.250 in the crude analyses were included in the model fitting. A backward stepwise procedure was used to include or exclude explanatory variables in the model fitting. Variables included in the final adjusted model should present a p-value ≤ of 0.250. For the final model, the variables were considered significant if they had a p-value of ≤ 0.05 after adjustments. Prevalence Ratios were obtained for halitosis referred by close persons and Rate Ratios were obtained for self-reported halitosis. Both effect measures were estimated with 95% confidence intervals. Due to the high correlation between stress and symptom of depression (correlation coefficients = 0.422), the results for depression were not adjusted by stress.

Ethical issues

The institution (UFPel) and the Research Ethics Committee of the School of Medicine / UFPel approved this study under protocol 49449415.2.0000.5317.

Results

Of total eligible students identified (n=3,237), 63.6% (n= 2,058) signed the consent term and participated of the study, being 52.3% female (IC 95% 50.0 – 54.4). Refusals represented only 1.4% of the total sample. Around 66% of the sample were between 18 to 24 years old, with a family income ranging from 1,001.00 to 5,000.00 BRL (71.4%) (Table 1). Besides, about 16% of students presented symptoms of depression. Scores mean of stress was 16.3 (SD ± 6.8), of which 31.1% present more than 20 points in the score. Concerning oral health variables, almost 50% have reported no presence of gingival bleeding and nearly 33% have reported never presented dental caries. Only 16% of subjects have reported not having some degree of halitosis, while 61.3% reported a score between one and three VAS (Figure 1). Furthermore, 363 students (17.6%) were informed by closed individuals that they had halitosis.
Table 1. Description of the general characteristics of the sample.

| Variable/CATEGORY                | Total Sample | n (%) (CI 95%) |
|----------------------------------|--------------|----------------|
| Sex                              | 2080         |                |
| Female                           | 1,087 (52.2) | (50.0 – 54.4)  |
| Male                             | 993 (47.7)   | (45.6 – 49.9)  |
| Age (years)                      | 2080         |                |
| 16 to 17                         | 312 (15.0)   | (13.5 – 16.6)  |
| 18 to 24                         | 1,375 (66.1) | (64.0 – 68.1)  |
| 25 to 34                         | 215 (10.3)   | (09.6 – 11.7)  |
| 35 or more                       | 178 (8.6)    | (07.4 – 09.8)  |
| Family Income                    | 1717         |                |
| ≤ 1000                           | 280 (16.3)   | (14.6 – 18.1)  |
| 1001 to 5000                     | 1,057 (61.6) | (59.2 – 63.9)  |
| ≥ 5001                           | 380 (22.1)   | (20.2 – 24.2)  |
| Gingival bleeding                | 2,073        |                |
| No                               | 1,020 (49.2) | (47.0 – 51.4)  |
| Some times                       | 955 (46.1)   | (43.9 – 48.2)  |
| Always                           | 98 (4.7)     | (03.9 – 05.7)  |
| Dental caries experienced        | 2,077        |                |
| No                               | 684 (32.9)   | (30.09 – 35.0) |
| Yes                              | 1,393 (67.1) | (65.00 – 69.1) |
| Smoking                          | 2,025        |                |
| No                               | 1,812 (89.5) | (88.1 – 90.8)  |
| Yes                              | 213 (10.5)   | (09.2 – 11.9)  |
| Alcohol                          | 1,929        |                |
| No                               | 1,845 (95.7) | (94.6 – 96.5)  |
| Yes                              | 84 (4.3)     | (03.5 – 05.4)  |
| Depression symptoms              | 2,082        |                |
| No                               | 1,743 (83.7) | (82.06 – 85.3) |
| Yes                              | 339 (16.3)   | (14.72 – 17.9) |
| Stress (quartile)                | 2,089        |                |
| 1st (PSS scores 0 – 11)          | 550 (26.3)   | (24.5 – 28.3)  |
| 2nd (PSS scores 12 – 16)         | 571 (27.4)   | (25.4 – 29.3)  |
| 3rd (PSS scores 17 – 21)         | 489 (23.4)   | (24.6 – 25.3)  |
| 4th (PSS scores 22 – 40)         | 479 (22.9)   | (21.1 – 24.8)  |

Perceived Stress Scale (PSS)

Figure 1. Self-reported halitosis in analog visual scale (n=2054)
Table 2 shows the association between stress/symptoms of depression and self-perceived halitosis. In the crude model, individuals whom self-perceived halitosis showed to be associated with stress (p < 0.001). Individuals in the higher quartile of stress showed a rate ratio (RR) of halitosis 38% greater than individuals from the less stress quartile (RR 1.38 CI95% [1.25 – 1.52]). Individuals with depression symptoms too showed association with self-perceived halitosis (RR 1.23 CI95% [1.13 – 1.34]). After adjustments by sex, age, family income, and gingival bleeding (control variables that continued associated with self-perceived halitosis in the final model), both stresses even as depression symptoms remained associated with self-reported halitosis. Individuals from higher stressed quartile presented higher scores of halitosis (RR 1.37 CI95% [1.24 – 1.53]) as well as individuals form intermediates stressed quartiles - 3rd (RR 1.22 CI95% [1.09 – 1.35]) and 2nd (RR 1.14 CI95% [1.02 – 1.27]). Similarly, students who presented depressive symptoms showed higher scores of self-perceived halitosis (RR 1.20 CI95% [1.10 – 1.32]) in the final model.

Table 2. Crude (*) and adjusted (**) rate ratio (RR) of independent variables for halitosis self-perception in university students. Pelotas, RS, Brazil. Poisson Regression (n=1668).

| Variable/Category                  | RRc (CI95%) | p-Value | RRa (CI95%) | p-Value |
|------------------------------------|-------------|---------|-------------|---------|
| Sex (ref=Female)                   |             |         |             |         |
| Male                               | 1.04 (0.97 – 1.11) | 0.244   | 1.09 (1.01 – 1.17) | 0.029   |
| Age (yrs) (ref=16 to 18)           |             |         |             |         |
| 18 to 24                           | 1.07 (0.98 – 1.17) | 0.005   | 1.02 (0.92 – 1.11) | 0.002   |
| 25 to 34                           | 1.09 (0.95 – 1.24) |         | 1.06 (0.92 – 1.22) |         |
| 35 or more                         | 1.23 (1.07 – 1.40) |         | 1.25 (1.08 – 1.44) |         |
| Family income (ref= ≤ 1000)        |             |         |             |         |
| 1001 to 5000                       | 0.90 (0.81 – 0.99) |         | 0.92 (0.83 – 1.01) |         |
| ≥ 5001                             | 0.81 (0.71 – 0.91) | 0.001   | 0.86 (0.76 – 0.97) | 0.018   |
| Gingival bleeding (ref=No)         |             |         |             |         |
| Some times                         | 1.21 (1.13 – 1.31) |         | 1.19 (1.10 – 1.29) |         |
| Always                             | 1.54 (1.34 – 1.76) |         | 1.51 (1.30 – 1.74) |         |
| Dental caries experienced (ref=No) |             | 0.714   |             | -       |
| Yes                                | 1.01 (0.94 – 1.09) |         | -           |         |
| Smoking (ref=No)                   |             | 0.744   |             | -       |
| Yes                                | 1.02 (0.91 – 1.14) |         | -           |         |
| Alcohol (ref=No)                   |             | 0.431   |             | -       |
| Yes                                | 0.93 (0.79 – 1.11) |         | -           |         |
| Depression symptoms (ref=No) *     |             | < 0.001 |             | < 0.001 |
| Yes                                | 1.23 (1.13 – 1.34) | < 0.001 | 1.20 (1.10 – 1.32) | < 0.001 |
| Stress (quartile) (ref=1st - PSS scores 0 – 11) |             |         |             |         |
| 2nd (PSS scores 12 – 16)           | 1.14 (1.03 – 1.26) | < 0.001 | 1.14 (1.02 – 1.27) | < 0.001 |
| 3rd (PSS scores 17 – 21)           | 1.22 (1.10 – 1.34) |         | 1.22 (1.09 – 1.35) |         |
| 4th (PSS scores 22 – 40)           | 1.38 (1.25 – 1.52) |         | 1.37 (1.24 – 1.53) |         |

Perceived Stress Scale (PSS); * Depression was not adjusted by stress; The results displayed in final model are adjusted by stress.
When the association of stress and halitosis reported by close individuals was tested (Table 3), stress (p = 0.012) and symptoms of depression (p = 0.039) were associated with outcome in the bivariate analysis. Individuals that presented the greatest scores of stress have shown a prevalence of almost 50% higher than the individual with less stress. Similarly, students with symptoms of depression presented a prevalence of 27% higher than those individuals without depressive symptoms. On the other hand, after adjustments (by sex, family income, gingival bleeding, and dental caries), symptoms of depression lost the association, while individuals from the highest quartile from stress remained associated with halitosis reported by close individuals (PR 1.36 CI95% [1.02 – 1.81]).

Table 3. Crude (*) and adjusted (**) prevalence ratio (PR) of independent variables for halitosis reported by the closed person in university students. Pelotas, Brazil. Poisson Regression. (n=1686).

| Variable/Category                  | PRc (CI95%) | p-Value | PRa (CI95%) | p-Value |
|------------------------------------|-------------|---------|-------------|---------|
| Sex (ref=Female)                   |             |         |             |         |
| Male                               | 1.22 (1.01 – 1.47) | 0.039   | 1.31 (1.08 – 1.61) | 0.008   |
| Age (yrs) (ref=16 to 18)           |             |         |             |         |
| 18 to 24                           | 0.93 (0.71 – 1.21) | 0.335   |             | -       |
| 25 to 34                           | 0.84 (0.57 – 1.25) |         |             | -       |
| 35 or more                         | 1.27 (0.89 – 1.82) |         |             | -       |
| Family income (ref= ≤ 1000)        |             |         |             |         |
| 1001 to 5000                       | 0.82 (0.64 – 1.06) |         | 0.85 (0.66 – 1.09) |         |
| ≥ 5001                             | 0.65 (0.47 – 0.90) |         | 0.70 (0.51 – 0.98) |         |
| Gingival bleeding (ref=No)         | < 0.001     | < 0.001 |             |         |
| Some times                         | 1.82 (1.48 – 2.23) |         | 1.69 (1.35 – 2.11) |         |
| Always                             | 3.09 (2.26 – 4.20) |         | 2.87 (2.05 – 4.02) |         |
| Dental caries experienced (ref=No) |             |         |             |         |
| Yes                                | 1.24 (1.01 – 1.53) | 0.044   | 1.27 (1.01 – 1.59) | 0.037   |
| Smoking (ref=No)                   |             |         |             |         |
| Yes                                | 1.01 (0.74 – 1.37) |         |             | -       |
| Alcohol (ref=No)                   |             |         |             |         |
| Yes                                | 0.97 (0.59 – 1.57) |         |             | -       |
| Depression symptoms (ref=No)*      |             |         |             |         |
| Yes                                | 1.27 (1.01 – 1.60) | 0.039   | 1.27 (1.01 – 1.59) | 0.335   |
| Stress (quartile) (ref=1st - PSS scores 0 – 11) |             |         |             |         |
| 2nd (PSS scores 12 – 16)           | 1.23 (0.94 – 1.61) | 0.012   | 1.10 (0.82 – 1.46) | 0.061   |
| 3rd (PSS scores 17 – 21)           | 1.10 (0.82 – 1.46) |         | 1.03 (0.76 – 1.40) |         |
| 4th (PSS scores 22 – 40)           | 1.48 (1.14 – 1.93) |         | 1.36 (1.02 – 1.81) |         |
| -2 loglikelihood                   |             |         |             |         |
| Empty model = 1,988.8              |             |         | Final model = 1,610.9 |         |

Perceived Stress Scale (PSS); * Depression was not adjusted by stress; The results displayed in final model are adjusted by stress.
Discussion

The present study has evaluated the occurrence of halitosis from two points of view; self-reported and perceived by close individuals. From the total students investigated, 84% have reported some degree of halitosis and near 18% reported that they were informed they had halitosis by close individuals. Even after controlling by socioeconomic and gingival bleeding – the main local factor related to halitosis – more stressed individuals remained associated using both measures showing to be an important factor related to halitosis. On the other hand, students who showed depressive symptoms remained associated only with self-reported halitosis losing the association in the adjusted models from halitosis perceived by close individuals.

Genuine halitosis has been classified as the halitosis confirmed for organoleptic tests being objectively perceived while the pseudo-halitosis or halitophobia can occur even in cases when the bad breath is not detected by this test and for other individuals15. Although the organoleptic test has been considered the "gold standard" on halitosis evaluation, the use of a self-reported questionnaire has been used in the literature4,7. A recent study of meta-analysis comparing the prevalence obtained with clinical and self-reported measurements observed that the method adopted to evaluate halitosis did not influence the heterogeneity among studies1. To decrease this possible bias, we have asked students also if some close person had ever reported him/her about the presence of bad breath. This question was used to evaluate if the presence of halitosis perceived by other persons could also be associated with psychosocial variables and, thus, compare with results of self-perceived halitosis (pseudo-halitosis), promoting more robust evidence.

In this way, when self-perceived halitosis was investigated, a strong association with stress was observed. Even after adjustments, individuals with some degree of stress were related to higher scores of self-perceived halitosis. This can be explained due to the high correlation between self-reported measurements and pseudo-halitosis15 since that patient with some mood disorder could present a self-perception or self-judgment worse than other people due to psychological alterations that can change their perception of health5. On the other hand, in halitosis perceived by close individuals, the association was only observed in the students from the highest quartile of stress. These results corroborate with a study that has shown a strong relationship between halitosis and the levels of cortisol present in the saliva, mainly in pseudo-halitosis15. Moreover, another hypothesis is that it may due to the inclusion of only cases of genuine halitosis (perceived by other individuals) in the second halitosis question, which may show that only high levels of stress can act influencing genuine halitosis while the self-perception could be more easily influenced, although to confirm this hypothesis it is necessary an objective evaluation.

Despite stressed individuals presents an association with halitosis, we cannot establish a causal relationship between halitosis and stress, due to the design of the present study. Individuals with an elevated level of stress could present the tendency to answer more easily bad outcomes (bad breath) than individuals with a low level of stress. Also, stress can act leading to other conditions that cause halitosis (such as gastritis and reduced salivary flow). Besides, the presence of halitosis could conduct individuals to present with higher stress, since that bad breath impacts on quality of life9.
Stress and depression are comorbidities and normally can coexist as conditions related to mood disorders presenting elevate correlation\textsuperscript{16}. Similarly to the observed in the literature, we found a significant coefficient of correlation among these variables and, thus, we performed individual regression models to these variables. An explanation of this correlation is the act of mood disorders promotes the alteration of several hormones, stimulating biochemical modifications\textsuperscript{17,18}, i.e., the increase of levels of cortisol promoted by stress, that could significantly have altered the serotonin uptake, hence, influencing the depressive symptoms\textsuperscript{17,18}. This biochemical mechanism is attributed to the induction by the cortisol that promotes an increase in the expression of the gene that encodes the serotonin transponder, resulting in a drastic decrease of serotonin involved in brain synapses\textsuperscript{18}. However, not all individuals exposed to stress displaying depression and some genetic factors could influence this relationship\textsuperscript{19}. A longitudinal birth cohort tested the influence of stress in the polymorphism of gene 5-HTT displaying results that support this theory\textsuperscript{19}. This gene presents a short allele “s” in the region 5-HTTLPR (prevalence near 50% of Caucasian individuals with one “s” allele) that promotes less efficiency in the gene transcription, which could influence the response of serotonin to stressful events. A direct association of this gene and depression was not observed, but when the stressful events that occurred in the life course were considered in the analysis, the positive interaction of the investigated alleles and depression was observed\textsuperscript{19}.

These results highlight the associations of stress and depression and the possible mechanisms of correlation of these diseases. In the present study, while stress remained associated in both halitosis questions, this did not occur with depression, which lost the association in the adjusted model in the question of halitosis perceived by close individuals. Young individuals presented a less prevalence of depression compared to stress\textsuperscript{20} as well as stress prevailed over signs of depression or act as a trigger for depression\textsuperscript{21}. Thus, being a young population (mean of 23 years), it seems that stress was the variable that presented a key role related to halitosis. Besides, in the present study, we use an instrument for screening symptoms of depression and did not perform a clinical diagnostic. However, the use of PHQ-2 in screening depression symptoms is a useful and time-saving validated instrument. The evaluation of the occurrence of halitosis by two points of view promotes greater robustness to the outcome and helps to explain with more detail the effect of stress and depression in halitosis. Therefore, we observed that stress was the main psychological factor that remained associated in both halitosis measurements at the final model in the studied population. It is important to evidence that in both measurements of halitosis the socioeconomic and oral health variables were similarly associated, showing a consistent measurement among the outcome variables. Moreover, the combined use of both questions can provide major robustness of the results.

Universities’ students are a low investigated population, which presents a vulnerability to develop mood disorders\textsuperscript{10}. Our results showed an important part of the sample with symptoms of depression and with elevated levels of stress, corroborating with previous studies, an indication of the necessity of intervention programs to reduce these disorders\textsuperscript{16}. The use of cognitive and behavioral approaches was used to decrease bruxism associated with stress\textsuperscript{22} and can be recommended to decrease the stress
levels in this population and a more precise investigation of depressive symptoms is necessary\textsuperscript{16}. Besides, the investigation of the association between halitosis and stress/symptoms of depression in this population is very important, since that halitosis can impact the oral health-related quality of life\textsuperscript{9}.

However, some limitations have to be highlighted. Due to the sample of university students, individuals with low schooling were not included in the present study, which may have influenced our results by underestimating the prevalence. Therefore, extrapolation data should be performed with high caution. The present findings can be extrapolated to a population with high education levels and with elevated socioeconomic status. The losses were mainly caused by the impossibility of the location of individuals in their respective classrooms. However, similar questionnaire-based studies also showed this difficulty\textsuperscript{23}. Also, the oral health variables were investigated by self-report measurements. Although no oral health clinical examination has been performed, the self-reported oral health condition is a valid tool used. Besides, we observed that self-reported gingival bleeding (presents in the gingivitis and periodontitis) was a variable strongly associated in final models with both halitosis measurements. Although the most precise measure is the organoleptic test, self-referred measures are fundamental in epidemiological studies because they are simple, low-cost measures, besides being able to reduce the time of examination\textsuperscript{4,7}.

In conclusion, both halitosis measures (self-reported and reported by close individuals) were associated with stress even after control for oral health and socioeconomic variables. In contrast, symptoms of depression were associated only with self-reported halitosis.

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