

Tobacco Influence on Taste and Smell: Systematic Review of the Literature

Allessandra Fraga Da Ré¹ Léia Gonçalves Gurgel¹ Gabriela Buffon¹ Weluma Evelyn Rodrigues Moura¹
Deisi Cristina Gollo Marques Vidor² Márcia Angelica Peter Maahs¹

¹ Speech Therapy, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil

² Universidade Federal de Ciências da Saúde de Porto Alegre, Pró-reitoria de Extensão de Assuntos Comunitários, Porto Alegre, RS, Brazil

Address for correspondence Allessandra Fraga Da Ré, Universidade Federal de Ciências da Saúde de Porto Alegre, Fonoaudiologia, Rua Sarmento Leite, 245 Porto Alegre, Rio Grande do Sul 90050-170, Brazil (e-mail: alle.fraga@gmail.com).

Int Arch Otorhinolaryngol 2018;22:81–87.

Abstract

Introduction In Brazil, estimates show that 14.7% of the adult population smokes, and changes in smell and taste arising from tobacco consumption are largely present in this population, which is an aggravating factor to these dysfunctions.

Objectives The objective of this study is to systematically review the findings in the literature about the influence of smoking on smell and taste.

Data Synthesis Our research covered articles published from January 1980 to August 2014 in the following databases: MEDLINE (accessed through PubMed), LILACS, Cochrane Library, and SciELO. We conducted separate lines of research: one concerning smell and the other, taste. We analyzed all the articles that presented randomized controlled studies involving the relation between smoking and smell and taste. Articles that presented unclear methodologies and those whose main results did not target the smell or taste of the subjects were excluded. Titles and abstracts of the articles identified by the research strategy were evaluated by researchers. We included four studies, two of which were exclusively about smell: the first noted the relation between the perception of puff strength and nicotine content; the second did not find any differences in the thresholds and discriminative capacity between smokers and non-smokers. One article considered only taste and supports the relation between smoking and flavor, another considered both sensory modalities and observes positive results toward the relation immediately after smoking cessation.

Conclusion Three of the four studies presented positive results for the researched variables.

Keywords

- ▶ smoking
- ▶ olfaction disorders
- ▶ smell
- ▶ olfaction
- ▶ taste disorders

Introduction

The smell and taste are sensory systems that allow us, essentially, to perceive odors and flavors. However, these systems are complex and interconnected, being responsible not only for routine activities such as the perception of aromas and tastes as well as warning signs that prevent us from adverse situations, ensuring our survival.^{1,2}

To perform these functions, the two systems operate jointly, complementing the information received by the sense organs. This fact is reflected by, for example, the attenuation of taste perception in the presence of a change in the sense of smell, such as in nasal congestion caused by influenza.³ This is because the olfactory information is transmitted in two ways: the first related to olfactory neurons present in the nostrils, and the second to receptors present in the nasopharynx.

received
July 16, 2016
accepted
October 6, 2016
published online
February 13, 2017

DOI <https://doi.org/10.1055/s-0036-1597921>.
ISSN 1809-9777.

Copyright © 2018 by Thieme Revinter Publicações Ltda, Rio de Janeiro, Brazil

License terms



Therefore, during mastication, these neurons are activated, complementing the taste information with the sense of smell of what is being tasted. Thus, any change in smell also causes a change in taste, due to the lack of this information at the time of mastication.⁴

Another mechanism of interrelation between smell and taste occurs in the anticipatory phase of deglutition, when the olfactory stimulation helps the preparation of oral motor and digestive systems for the reception of food through the salivary secretion, increased gastric acid secretion, and time potential motor.⁵ The smell and taste disorders are common,⁶ having varied etiology and may be congenital or acquired. Among the acquired causes, the most cited in the literature are idiopathic, iatrogenic, aging, medications, vitamin deficiency, changes in the respiratory tract, neurological and psychiatric, trauma, neoplasia, total laryngectomy, and smoking.^{3,4,7,8}

In this context, today smoking is considered a public health problem because of its high prevalence and mortality resulting from tobacco-related diseases.⁹ In Brazil, estimates show that 14.7% of the adult population smokes,¹⁰ and changes in smell and taste arising from tobacco consumption are largely found in this population,¹¹⁻¹⁵ aggravating factor to these dysfunctions.¹⁶ Tobacco addiction exposes the smoker to ~4,720 toxic substances in tobacco smoke, 60 of which have carcinogenic potential, proven to be harmful to the health of the individual.⁹ When the olfactory and gustatory systems are exposed to these substances, they suffer injuries that might be reversible or permanent. The degree of the injury is related to the exposure time and the concentration and toxicity of tobacco.³

Cigarette smoke has an important impact in the respiratory tract, where inflammation and mutagenic and carcinogenic effects are the most common outcomes. Some of its components are damaging to the sensory systems, others exert toxic effects in the airway, possibly causing injury or death of cells. The substances contained in the smoke can cause a reduction in the cleaning ability of the airways and hyperplasia of mucus cells, resulting in increased mucus production.¹⁷ Physiologically, the changes caused in the olfactory neuroepithelium may be structural and / or functional. The exposure of the olfactory tissue generates the decrease of sensory cell production capacity, causing loss of sensibility to odors and olfactory recognition. The gustatory disturbance is a consequence of the change of form, quantity, and vascularization of the taste buds caused by tobacco consumption.¹⁸

Studies in the field of speech therapy, specifically, compared smokers and non-smokers regarding their alterations.^{5,19} These studies conclude that smoking is closely related to oral complications such as halitosis, apparent carious lesions and periodontal problems, which are risk factors for tooth loss and masticatory changes resulting from masticatory inefficiency.¹⁹ They also show that smokers have sensory recognition capability inferior to non-smokers and muscular compensation during swallowing.⁵ Finally, smoking has been associated with vocal related diseases as being a risk factor for maintaining adequate voice quality.²⁰

The speech therapist plays an important role in the studies and rehabilitation of tobacco use effects, since this affects the structures of the sensory-motor-oral system and interferes with functions such as breathing, phonation, chewing, and swallowing. Among the alterations caused by smoking habits are those of an anatomical nature, such as tooth loss and caries, and the development of oral and larynx cancer.²¹ Therefore, the speech therapist must be recognized as one of the health professionals able to warn about the risks that smoking imposes on human health, especially with regard to maintaining the quality of life of individuals and the expansion of the health promotion concept.²² Research involving the aforementioned changes are still scarce in the literature of the speech therapy area. In this context, the aim of this study is to review systematically the literature for the main findings about the influence of smoking in smell and taste.

Review Literature

The research covered articles published from January 1980 to August 2014 in the following databases: MEDLINE (accessed through PubMed), LILACS, Cochrane Library, and SciELO. We conducted two separate lines of research: one concerning smell and the other taste. The selected search terms related to smell were "Smoking," "Randomized Controlled Trial," "Olfaction Disorders," "Smell," "Modalities Sensory," "Olfaction," and their MeSH terms. The selected search terms related to taste were "Smoking," "Randomized Controlled Trial," "Taste Disorders," "Taste," "Dysgeusia," "Ageusia," and their MeSH terms. We did not include words related to the outcomes of interest to increase the sensitivity of this research. There was no restriction regarding the characteristics of the sample.

We included every randomized controlled trial involving the study of the relationship between the smell, taste, and smoking. In this study, the choice of randomized controlled trials is justified because they represent the most reliable scientific evidence. Systematic reviews, to be effective, must include only randomized controlled studies, which are high-quality evidence.²³ Exclusion criteria were: studies that did not show any clear methodological definition and those whose main outcome was not focused on the smell or taste of the subjects.

The investigators assessed titles and abstracts of all articles identified through the search strategy. All abstracts that did not provide sufficient information regarding the exclusion criteria were selected for evaluation of the full text. At the stage of the full text evaluation, two independent reviewers examined the full articles and made their selections according to the eligibility criteria, collecting data with regard to methodological characteristics, interventions, and outcomes of the studies using standardized forms. At all stages of the study, the disagreements were resolved through consensus. The main data collected were about the effects of smoking on smell and taste.

We conducted an analysis of the quality of the studies according to the confidentiality of the allocation list, intention to treat analysis, baseline comparability, blind assessment of outcomes, and description of losses and exclusions. The absence of a description of how the allocation list was generated was regarded as the absence allocation concealment. The

GRADE approach was used as recommended by the Cochrane Collaboration²⁴ for analysis of the quality of the tests. In each result, the quality of evidence was based on five items: (1) limitations of the methodology of the studies; (2) consistency of results; (3) subjectivity; (4) precision; and (5) potential for publication bias. The quality was reduced by one level for each factor not satisfied. The GRADE approach results in four quality levels of evidence: high, moderate, low, and very low.²⁵ The analysis of the data, in general, was descriptive and reported the methodological characteristics and the main evidence in accordance with the main objective of the research.

As a result of the initial search, 360 studies were identified in all databases, 58 were related to smell and 262 to taste. After a detailed analysis, four studies met the inclusion criteria and were considered relevant to the sample of this study. Articles excluded from this review had as reasons not to be included: the main result did not involve the studied senses or addressed the use of drugs. ►**Fig. 1** shows the flowchart of selection of the studies included in this review.

Of the four studies included, only one considered the two senses (smell and taste) simultaneously.¹⁵ Two studies^{13,24} considered only smell. One study¹⁴ considered only the change relative to taste. Particularly regarding smell, there is a positive outcome,¹⁵ as improvements were observed on the perception of smells after the cessation of tobacco consumption for at least seven days; another study¹³ indicated that the perception of strength of the cigarette puff is positively correlated with nicotine content, but it excludes smell as an important discriminative factor for the substance. Another study²⁴ reported no differences in thresholds and discriminative capacity between smokers and nonsmokers.

Regarding taste, both studies showed relation between the sensory perception and the smoking habit. In one of them,¹⁵ there was improvement in the perception of flavors after

cessation of smoking. Another study¹⁴ showed reduced sensitivity to certain substances in cigarette smokers, after cigarette consumption. In addition, this study showed sensitivity differences between sexes (women showed greater sensitivity reduction than men) in this condition, which was not observed among smokers in acute withdrawal. ►**Table 1** shows the main characteristics of the studies included in this review.

Regarding the analysis of the quality of the studies, all are considered to have moderate quality of evidence, considering the outcome “improved taste” and “improvement in smell.” Most articles had significant limitations related to the composition of the sample and study design. ►**Table 2** shows the main characteristics of the analysis of the outcomes found.

Regarding the methodological quality of the studies, the criterion related to the description of losses and exclusions appears to be what needs to be improved the most. The allocation concealment and blinding are also deficient in half of the studies evaluated. The main analytical characteristics are shown in ►**Table 3**.

Discussion

Two studies^{13,24} considered the effects of smoking on exclusively the sense of smell of the subjects. The first¹³ sought to determine whether the perception of puff strength correlates with the delivery of nicotine, and to evaluate the ability of nicotine discrimination by smell. The sample consisted of 15 male and female smokers with a mean age of 38.8 years and an average daily consumption of 6 cigarettes. This study showed that the nicotine content increased significantly with the perception of intensity in a linear pattern, with the perception of strength of the puff positively related to the nicotine content. The authors excluded smell as an important factor for the discriminability of nicotine, but highlighted the

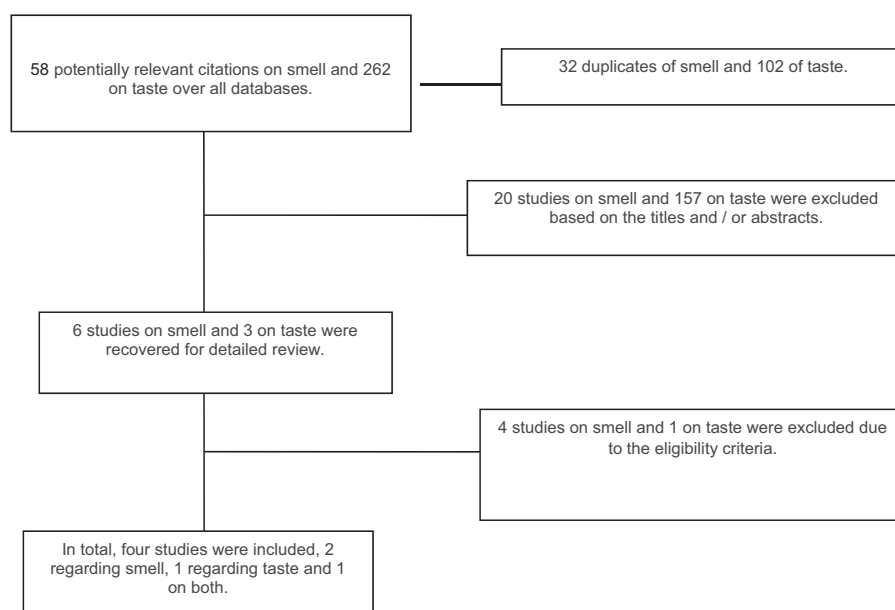


Fig. 1 Diagram of the selection process of articles.

Table 1 Characteristics of the studies included

Author (year)	Original language	Journal (IF)	n (age of sample)	Gender of the sample	Outcomes
Rose ¹³ (1984)	English	<i>Addictive Behaviors</i> (2.764)	15 smokers (age = 38,8; SD = 12,4)	Men and women. No ratio reported.	Found no differences in nicotine discrimination between the smoking group with sealed nose and those without sealing.
Thuerauf et al ²⁴ (2000)	English	<i>Journal of Clinical Psychopharmacology</i> (3.243)	30 volunteers (range = 22-43 years; average 29.9 years); 15 smokers and 15 nonsmokers	100% Men	Found no differences in thresholds and discriminative capacity between smokers and nonsmokers, indicating that the peripheral olfactory and trigeminal neurons binding sites are not affected by smoking history.
Mullings et al ¹⁴ (2009)	English	<i>J. Psychopharmacol</i> (2.386)	48 daily cigarette smokers (24 of each gender); (Mean = 27 years; SD = 9; range = 18-55)	50% men and 50% women	Higher pleasantness ratings given by non-abstinent smokers to sucrose compared the salt solutions, whereas for abstinent smokers there was no difference. Significant effect of the type of cigarette in women, causing a decrease in taste threshold.
Etter et al ¹⁵ (2013)	English	<i>Addiction</i> (4.738)	581 daily smokers (minimum 18 years of age)	NR	Improvements after cessation of the sense of smell, taste, and sore throat.

Abbreviations: IF, impact factor; n, sample size; NR, not reported.

Table 2 Analysis of outcomes

Outcome measure	Number of Studies	Limitations	Inconsistency	Subjectivity	Imprecision	Quality of Evidence	Author (year)
Taste improvements	2	moderate	low	low	moderate	moderate	Etter et al ¹⁵ (2013)
		moderate	low	low	low	moderate	Mullings et al ¹⁴ (2009)
Smell Improvements	3	moderate	low	low	moderate	moderate	Etter et al ¹⁵ (2013)
		moderate	low	low	low	moderate	Thuerauf et al ²⁴ (2000)
		low	low	low	moderate	moderate	Rose ¹³ (1984)

Table 3 Methodological quality of included studies

	Randomization	Allocation Concealment	Analysis by intention to treat	Baseline Compatibility	Blinding	Description of Losses and Exclusions
Etter et al (2013) ¹⁵	A	A	A	A	I	I
Rose (1984) ¹³	I	I	I	A	I	I
Thuerauf et al (2000) ²⁴	A	I	A	A	A	I
Mullings et al (2009) ¹⁴	A	A	A	A	A	A

Abbreviations: A, adequate; I, inadequate.

possibility that the responsiveness of the central nervous system to nicotine receptors is similar to the response of peripheral sensory organs.

Another study²⁶ also concludes that increasing the concentration of nicotine generates greater perception of puff strength by smokers, suggesting an association between nicotine content and perceived puff strength. Another conclusion of the article is the interaction between nicotine and the

reward and reinforcement areas of the central nervous system (CNS), corroborated by other research.²⁷ Studies²⁸ state that nicotine causes tolerance and dependence, due to acting in the dopaminergic pathways associated with the effects of pleasure and well-being. The data point to a probable relation between the dose of nicotine and the reinforcement of smoking due to the interactions of the substance, demonstrating an association between nicotine dose and smoker behavior.

The second study about smell²⁴ aimed to test its role and the trigeminal system in discriminating nicotine, differentiating smokers and nonsmokers. Thirty male volunteers with a mean age of 29.9 years participated. Of these, 15 were smoking at least 20 cigarettes a day for two years, and the others were non-smokers. During the study, the researchers applied 14 olfactory stimuli according to a list of random numbers. The subjects were instructed to group the stimuli into two categories (A and B). In addition, the subjects rated the pleasure of the 14 stimuli using a scale ranging from 0 (very unpleasant) to 100 (very pleasant). As a result, smokers considered nicotine less unpleasant than nonsmokers. The enantiomeric difference was statistically significant for non-smokers ($p < = 0.001$). They found no differences in thresholds and discriminative ability between the groups, indicating that the connection between peripheral olfactory neurons and the trigeminal nerve are not affected by smoking history.

Another study²⁹ could not find significant difference in identification performance and odor threshold between smokers and nonsmokers, although it has shown that smokers have a significant reduction in the volume of the olfactory bulb. This reduction occurs early on as a negative effect of smoking on the olfactory system. Other researches, however,²⁴ support the idea that smoking interferes with the olfactory sensation. The indices of the olfactory function in smokers were significantly lower than non-smokers regarding identification assessments, discrimination, and odor concentration content³⁰ and results showed that smokers have lower sensory recognition capability when compared with non-smokers,⁵ showing a positive correlation between decreased olfactory sensitivity and smoking and a negative correlation between olfactory sensitivity and amount smoked. Thus, the use of tobacco appears to have long-term negative effects on olfactory function due to changes in the olfactory epithelium and increased apoptosis of the olfactory neurons.

Studies related to smell included in the review showed gaps to be filled, because there is no consensus among authors over the association of smoking with changes in olfactory function, although there were differences between smokers and nonsmokers and among smoker groups with different characteristics. Despite this apparent paradox, other studies reinforce the findings of the selected articles.^{5,30}

Regarding taste, we only included one study¹⁴ in this review. The authors aimed to investigate the effects of short-term abstinence from smoking and acute administration of nicotine in smokers can change their taste perception, interfering with feeding behavior. The test included daily cigarette smokers of both sexes. Before the test, participants were randomly assigned to get 12 hours without smoking and move away from cigarette smoke. In the test session, participants completed subjective evaluations of humor³¹ and rated salt and sucrose solutions on intensity and pleasantness, followed by a measurement of the limit that such solutions could be detected.³² In the anxiety test, no significant effect was observed. A significant increase in the differences in taste perception was observed between the groups, according to the concentration and with the test substance.

Regarding pleasantness of taste, sucrose registered higher ratings in comparison with salt solutions. The withdrawal factor was also statistically significant, reflecting higher pleasantness ratings in non-abstinent. The data collected show the relation between smoking and flavor, which may contribute to the known effects of smoking on appetite and feeding behavior.

As for the influence of tobacco on appetite and feeding behavior suggested by the study,¹⁴ other studies attest to this relation. A study on weight gain after cessation of smoking³³ suggests that this may be related to greater efficiency in perceiving taste, leading to increased appetite. Another study³⁴ confirms this relation, noting the fact that anxiety can be an intervening factor in the feeding behavior of the ex-smoker.

Finally, the fourth and final study¹⁵ considered the effects of smoking on smell and taste. The authors aimed to test the reported abstinence symptoms by checking whether they are valid and trusted signals of cigarette withdrawal via a specific range. The sample consisted of 581 daily smokers randomly distributed. The authors divided them into two groups: continuous use of tobacco for two weeks and abstinent for at least seven days. The results of this study provide support for the verification of mood changes as tobacco withdrawal symptoms. The sense of smell, taste and sore throat also improved post-cessation. These positive effects of withdrawal occurred immediately after cessation, and this could be used to motivate smokers to give up the habit.

Previous studies also point to the relation between the olfactory and gustatory perceptions and use of tobacco. There is an improvement of perception when comparing smokers to non-smokers,^{15,35} or after smoking cessation, even if the withdrawal is short-term.³⁶ The results confirm the existence of impairment of sensations because of smoking, even if discreetly and reversibly, probably due to the continuous exposure of smokers to the substances in cigarette smoke inhaled during smoking.

Although the studies present in this review do not directly indicate that smoking has an effect on the smell and taste functions, the variables analyzed demonstrate the influence of smoking on the results found in the research, related to these sensory capabilities. It is noteworthy, though, that this association is dependent on several factors that are not uniformly controlled in these studies.

Regarding the articles, the sample composition appears to be relevant, depending on age and sex. Two of the articles included in this review^{14,24} reported these criteria as being important for the quality of the data. All studies seek to evaluate their outcomes, comparing smokers and non-smokers, where non-smokers might be in a condition of controlled abstinence, according to the research proposal. The establishment of a parameter for average consumption of cigarettes by participants as seen in three articles included,^{13,14,24} is important to compare studies. The lowest daily consumption was 6 cigarettes and the highest was 20.

Although it is not the main purpose of this review, the smoker's behavior is also influenced by the nicotine dose in cigarettes, corroborated by recent studies.^{26,28,37} Thus, the

higher the nicotine concentration, the greater the need for reinforcement of tobacco consumption. Due to smoking being a chronic disease and increasing the risk for the development of various pathologies, awareness of the subjects for the importance of smoking cessation and rehabilitation of the problems caused by it should be raised by health professionals in an interdisciplinary fashion, including speech therapists.

Final Comments

In short, this systematic review sought in literature findings on the relation between tobacco use and the changes in smell and taste, concluding that research in this field is still scarce. In addition, the joint analysis of the data is sometimes insufficient for making definitive conclusions. This occurs with some studies that show a positive association to the relation between tobacco use and olfactory and gustatory changes,^{14,15} and others report no relation between the variables.^{13,24} Among the limitations of included studies are small sample sizes, not mentioning the assessment protocols used by some studies, the inadequacy in describing the method employed, especially randomization,¹³ and the heterogeneity of types of sample between studies evaluated, making it more difficult to compare them.

For future studies, we would recommend the adoption of standardized methods applied continuously. Further research regarding the relations between tobacco use and changes in smell and taste are important, especially considering how long the subject has been smoking, the number of cigarettes smoked daily, and natural changes caused by aging, aggravated or not by the use tobacco.

References

- Starzewski AJúnior, Gregório T, Ribeiro AS, Guilherme A, Augusto LB. Distúrbios do olfato. *RBM ORL*. 2008;A3(3):78–84
- Santos DV, Reiter ER, DiNardo LJ, Costanzo RM. Hazardous events associated with impaired olfactory function. *Arch Otolaryngol Head Neck Surg* 2004;130(3):317–319
- Palheta Neto FX, Targino MN, Peixoto VS, et al. Sensorial abnormalities: smellandtaste. *Int Arch Otorhinolaryngol* 2011;15(3):350–358
- NIDCD. National Institute on Deafness and Other Communication Disorder [Internet]. Fact Sheet Smell Disorders; Available at: <https://www.nidcd.nih.gov/>. Accessed: December 21, 2015
- Santos KW, Echeveste SS, Vidor DC. Influence of gustatory and olfactory perception in the oral phase of swallowing in smokers. *CoDAS* 2014;26(1):68–75
- Vennemann MM, Hummel T, Berger K. The association between smoking and smell and taste impairment in the general population. *J Neurol* 2008;255(8):1121–1126
- Marchesan IQ, Marchesan IQ. Avaliação e terapia dos problemas da respiração. Fundamentos em fonoaudiologia: aspectos clínicos da motricidade oral. Rio de Janeiro: Guanabara Koogan; 1998:23–36
- Pellegrini G, Veleiro RVB, Gomes ICD. A percepção do gosto salgado em indivíduos com e sem obstrução nasal. *Revista CEFAC*. 2005;7(3):311–317
- Sociedade Brasileira de Pneumologia e Tisiologia, Sociedade Brasileira de Cardiologia. Tabagismo: parte 1. *Rev Assoc Med Bras* 2010;56(2):134–137
- INCA. Instituto Nacional de Câncer. [Internet]. Prevalência de Tabagismo Available at: <http://www2.inca.gov.br>. Accessed: December 21, 2015
- Jacob N, Golmard JL, Berlin I. Differential Perception of Caffeine Bitter Taste Depending on Smoking Status. *Chemosens Percept* 2014;7(2):47–55
- Churlaud G, Jacob N, Berlin I. Le tabagisme modifie la perception des saveurs et odeurs. *Alcool Addictol* 2009;31(2):145–148
- Rose JE. Discriminability of nicotine in tobacco smoke: implications for titration. *Addict Behav* 1984;9(2):189–193
- Mullings EL, Donaldson LF, Melichar JK, Munafò MR. Effects of acute abstinence and nicotine administration on taste perception in cigarette smokers. *J Psychopharmacol* 2010;24(11):1709–1715
- Etter JF, Ussher M, Hughes JR. A test of proposed new tobacco withdrawal symptoms. *Addiction* 2013;108(1):50–59
- Sugiyama K, Matsuda T, Kondo H, et al. Postoperative olfaction in chronic sinusitis: smokers versus nonsmokers. *Ann Otol Rhinol Laryngol* 2002;111(11):1054–1058
- Blancard ST, Godoy ID. Doenças Tabaco-relacionadas. In: Diretrizes para cessação do tabagismo. *Jornal brasileiro de pneumologia* 2004:19–29
- Deems DA, Doty RL, Settle RG, et al. Smell and taste disorders, a study of 750 patients from the University of Pennsylvania Smell and Taste Center. *Arch Otolaryngol Head Neck Surg* 1991;117(5):519–528
- Rech RS, Santos KWD, Maahs MAP, Vidor DCGM. Masticatory changes as a result of oral disorders in smokers. *Int Arch Otorhinolaryngol* 2014;18(4):369–375
- Santos KW, Vidor DCGM, Maahs MAP. Changes and vocal complaints: a comparative study between smokers and nonsmokers. *Int Arch Otorhinolaryngol* 2012;16(Suppl 1):106
- Goiato MC, Fernandes AÚR, Santos DMD, Conrado SN. Perfil de pacientes acometidos por câncer de laringe atendidos no centro de oncologia bucal-UNESP. *Rev Odonto Ciência – Fac. Odonto/PUCRS* 2006;21(51):3–8
- Botelho C, Castillo PL, Ayoub LTV. Tabagismo e saúde bucal. In: Diretrizes para cessação do tabagismo. *Jornal brasileiro de pneumologia* 2004:72–76
- Escosteguy CC. Methodological and statistical topics in randomized controlled clinical trials. *Arq Bras Cardiol* 1999;72(2):139–148
- Thuerauf N, Kaegler M, Renner B, Barocka A, Kobal G. Specific sensory detection, discrimination, and hedonic estimation of nicotine enantiomers in smokers and nonsmokers: are there limitations in replacing the sensory components of nicotine? *J Clin Psychopharmacol* 2000;20(4):472–478
- Guyatt GH, Oxman AD, Vist GE, et al; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ* 2008;336(7650):924–926
- Naqvi NH, Bechara A. The airway sensory impact of nicotine contributes to the conditioned reinforcing effects of individual puffs from cigarettes. *Pharmacol Biochem Behav* 2005;81(4):821–829
- Picciotto MR, Caldarone BJ, King SL, Zachariou V. Nicotinic receptors in the brain. Links between molecular biology and behavior. *Neuropsychopharmacology* 2000;22(5):451–465
- Balbani APS, Montovani JC. Métodos para abandono do tabagismo e tratamento da dependência da nicotina. *Rev Bras Otorrinolaryngol* 2005;71(6):820–827
- Schriever VA, Reither N, Gerber J, Iannilli E, Hummel T. Olfactory bulb volume in smokers. *Exp Brain Res* 2013;225(2):153–157
- Katotomichelakis M, Balatsouras D, Tripsianis G, et al. The effect of smoking on the olfactory function. *Rhinology* 2007;45(4):273–280

- 31 Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory (STAI) (Self Evaluation Questionnaire). Palo Alto, CA: Consulting Psychologists Press; 1983
- 32 Bartoshuk LM, Duffy VB, Green BG, et al. Valid across-group comparisons with labeled scales: the gLMS versus magnitude matching. *Physiol Behav* 2004;82(1):109–114
- 33 Gromysz-Kałkowska K, Wójcik K, Szubartowska E, Unkiewicz-Winiarczyk A. Taste perception of cigarette smokers. *Ann Univ Mariae Curie Sklodowska Med* 2002;57(2):143–154
- 34 Costa AA, Elabras Filho J, Araújo ML, Ferreira JES, Meirelles LR, Magalhães CK. Programa multiprofissional de controle do tabagismo: aspectos relacionados à abstinência de longo prazo. *RevSocerj*. 2006;19(5):397–403
- 35 Tamborindeguy CC, Moraes CB. Mudanças de peso e comportamento alimentar em ex-tabagistas. *DiscipSci*. 2009;10(1):107–114
- 36 Santos KW, Vidor DCGM, Maahs MAP. Preliminary studies comparing smokers and nonsmokers about the smell and taste perception. *Int Arch Otorhinolaryngol* 2012;16 (Suppl 1):106
- 37 Perkins KA. Discriminative stimulus effects of nicotine in humans. *Handb Exp Pharmacol* 2009;192(192):369–400