

Systematic Review

Revisão Sistemática

Sandro Júnior Henrique Lima¹
 Hildo Rocha Cirne de Azevedo Filho²
 Hilton Justino da Silva³

Keywords

Smell
 Subarachnoid Hemorrhage
 Intracranial Aneurysm
 Circle of Willis

Descritores

Olfato
 Hemorragia Subaracnóidea
 Aneurisma Intracraniano
 Círculo Arterial do Cérebro

Correspondence address:

Sandro Júnior Henrique Lima
 Programa de Pós-graduação em
 Neuropsiquiatria e Ciências do
 Comportamento, Universidade Federal
 de Pernambuco
 Rua Engenheiro Alves de Souza, 500,
 Jaguaribe, Escada (PE), Brasil, CEP:
 55500-000.
 E-mail: sandrofonho@hotmail.com

Received: 01/26/2015

Accepted: 06/08/2015

Methods of evaluation of smell in victims of subarachnoid hemorrhage patients: a systematic review

Métodos de avaliação do olfato em pacientes vítimas de hemorragia subaracnóidea: revisão sistemática

ABSTRACT

Purpose: To systematically review the methods for evaluation of smell in aneurysmal subarachnoid hemorrhage victims and to identify the changes found with the use of these methods. **Research strategy:** The literature search was performed in PubMed search platform and in the databases Web of Science, Scopus, PsycINFO, CINAHL, and ScienceDirect in August and September 2014. **Selection criteria:** Original articles published in any language, which addressed smell changes in aneurysmal subarachnoid hemorrhage and addressed to evaluate this function through specific methods were included. Review studies, case studies, book chapters, editorial, and studies that address the nonaneurysmal subarachnoid hemorrhage were excluded. **Data analysis:** The following variables were considered in data analysis: author/year, country, sample/age, treatment, method, the moment of smell evaluation, and results. **Results:** The search for articles resulted in 1,763 articles, of which, 9 original articles were selected for this review. It was observed that all articles were from European and Asian countries. Standardized and nonstandardized tests and questionnaires were used in olfactory assessment, and the goals ranged from assessing the smell before and/or after surgery in this population. **Conclusion:** Heterogeneity was observed in the methods used to evaluate the smell in aneurysmal subarachnoid hemorrhage and in the methods selected for application of evaluations. In addition, studies have demonstrated the existence of olfactory deficits in patients and the relationship between surgery and olfactory dysfunction.

RESUMO

Objetivos: Revisar de forma sistemática os métodos para avaliação do olfato em vítimas de hemorragia subaracnóidea aneurismática, e identificar as alterações encontradas com a utilização desses métodos. **Estratégia de pesquisa:** A pesquisa bibliográfica foi realizada na plataforma de busca PubMed e nas bases de dados Web of Science, Scopus, PsycINFO, CINAHL e ScienceDirect, tendo a busca de dados ocorrida em agosto e setembro de 2014. **Crerios de seleção:** Artigos originais publicados em qualquer língua que abordassem as alterações de olfato na hemorragia subaracnóidea aneurismática, com objetivo de avaliar essa função através de métodos específicos. Foram excluídos estudos de revisão; estudos de caso; capítulos de livro; editoriais e estudos que abordassem a hemorragia subaracnóidea não aneurismática. **Análise dos dados:** Foram consideradas como variáveis na análise dos dados: autor/ano, país, amostra/idade, tratamento, método utilizado, momento da avaliação do olfato e resultados. **Resultados:** A busca de artigos resultou em 1.763 artigos, desses, 9 artigos originais foram selecionados para esta revisão. Foi observado que todos os artigos foram desenvolvidos em países europeus e asiáticos e na avaliação do olfato utilizou-se desde testes padronizados e não padronizados a questionários, cujos objetivos variaram entre avaliar o olfato antes e/ou após o tratamento cirúrgico nessa população. **Conclusão:** Foi observada heterogeneidade nos métodos utilizados para avaliação do olfato na hemorragia subaracnóidea aneurismática, como também no momento selecionado para aplicação das avaliações. Além disso, os estudos evidenciaram a existência de déficit olfatório nos pacientes, e a relação entre o tratamento cirúrgico e a disfunção olfatória.

Study carried out at the Graduate Program in Neuropsychiatry and Behavioral Sciences, Universidade Federal de Pernambuco – UFPE – Recife (PE), Brazil.

(1) Graduate Program in Neuropsychiatry and Behavioral Sciences, Universidade Federal de Pernambuco – UFPE – Recife-PE, Brazil.

(2) Health Sciences Center, Graduate Program in Neuropsychiatry and Behavioral Sciences, Universidade Federal de Pernambuco – UFPE – Recife (PE), Brazil.

(3) Speech-Language Pathology and Hearing Department, Graduate Program in Neuropsychiatry and Behavioral Sciences, Universidade Federal de Pernambuco – UFPE – Recife (PE), Brazil.

Conflict of interests: nothing to declare.

INTRODUCTION

The aneurysmal subarachnoid hemorrhage (SAH) is characterized as the rupture and leakage of blood between the pia mater and arachnoid membrane⁽¹⁾. Its occurrence results in abrupt changes in the intracranial midst owing to associated factors, such as the presence of bruises, edema, cerebral vasospasm and hydrocephaly⁽²⁾, which makes the aneurysmal SAH a clinical even of great importance.

It has a high mortality rate, reaching out to 40% of the affected population, in addition to frequent occurrence of sequelae among survivor patients, of which about one-third ends up having some kind of disorder of motor, cognitive, or even behavioral nature⁽³⁻⁵⁾.

A change that may be triggered with the occurrence of blood leakage in the subarachnoid space is the olfactory dysfunction, possibly because of the anatomical closeness of the location of the hemorrhage to the olfactory system, being subject to factors associated to aneurysmal SAH, such as direct mechanical damage to the tissues, inflammatory processes, increased intracranial pressure, and local cortical ischemia⁽⁶⁻⁷⁾.

Besides that, owing to its characteristics, the surgical treatment for aneurysmal SAH may also influence the sense of smell; in this case, the alterations in this function may arise through the impact of the traction of brain tissues during exposure to the bleeding site⁽⁷⁾.

Considering this, many methods to evaluate smell are described in the literature, and they may be either qualitative or even quantitative in the evaluation of the olfactory system⁽⁸⁾. It is also described that, for the verification of the integrity of the system, the tests use means that evaluate the psychophysical, electrophysiological, and psychophysiological processes, related to the olfactory sense, and the analysis of image tests that define the situation of the structures connected to smell⁽⁹⁾.

However, there is little description of how the evaluation of smell is made in patients with aneurysmal SAH, and this knowledge is not only important in order to identify the characteristics of the olfactory alterations caused by this disease and its modifications by surgical treatment, but it can also help determine and disseminate the methods to be used in clinical practice for the evaluation of this function in neurological patients.

Thus, the objective of this study is to systematically review the methods for evaluation of smell in patients with aneurysmal SAH and to identify the alterations found with the use of such methods.

RESEARCH STRATEGY

The bibliographic research was carried out in the PubMed search platform and in Web of Science, Scopus, PsycINFO, CINAHL, and ScienceDirect databases, considering the data search happened in August and September 2014. In the research for articles, the following descriptors were used — Health Sciences descriptors (*descritores em ciências da saúde* [DeCS]) and medical subject headings (MESH) — for the recovery of subjects of scientific literature.

The following crossings in English, Portuguese, and Spanish languages were made: smell AND circle of Willis; smell AND subarachnoid hemorrhage; smell AND intracranial aneurysm; olfaction disorders AND circle of Willis; olfaction disorders AND subarachnoid hemorrhage; and olfaction disorders AND intracranial aneurysm.

The research was carried out by two researchers, independently and blindly. In the cases where there were disagreements, the third researcher was consulted, with the objective of reaching a consensus. The researchers followed a search protocol developed before the research.

SELECTION CRITERIA

The inclusion criteria for articles in the research were: articles originally published in any language, which would approach smell alterations in patients with aneurysmal SAH, with the objective of evaluating this function through specific tests.

Original articles with no reference in the title, in the abstract, or in the text with the subject addressed in this review, review studies, case studies, book chapters, editorials, and studies addressing the nonaneurysmal SAH were excluded.

DATA ANALYSIS

The data analysis followed a convergent selection method of three stages.

Initially, an identification of the articles was made from the crossing of descriptors, and then the first exclusion process was done from the reading of the titles, following the eligibility criteria.

Next, reading of the abstracts and subsequent exclusion of the articles that were unsuitable for the research was done. The remaining articles were fully read for the selection of studies for this review.

The methodological characteristics of the articles were analyzed according to the presence of randomization, inclusion and exclusion criteria, blinding, statistical analysis, and statistical comparison between groups in the selected studies. Such evaluation items were based on the Physiotherapy Evidence Database scale (PEDro) (Chart 1). It is described in the literature that this scale has moderate levels of reliability among evaluators, with an intraclass correlation coefficient (ICC) of 0.68 and confidence interval of 95% (95%CI) of 0.57–0.76⁽¹⁰⁾.

The results were presented according to the following variables of the selected articles: author/year, country, sample/age, treatment, method used (smell evaluation), moment of evaluation of smell, and results (Chart 2).

RESULTS

The search for data resulted in a total of 1,763 articles. In the PubMed platform, crossing the descriptors, 30 articles were found; in Web of Science, 17 articles were found; in the Scopus base, 66 articles were found; in PsycINFO, 1 article was found; in CINAHL, 8 articles were found; and in the ScienceDirect database, 1,641 articles were found.

Chart 1. Methodological classification of the articles selected

	Park et al., 2009 ⁽¹¹⁾	Bor et al., 2009 ⁽¹⁷⁾	Martin et al., 2009 ⁽¹²⁾	Moman et al., 2009 ⁽¹³⁾	Wermer et al., 2007 ⁽¹⁴⁾	Vries et al., 2007 ⁽¹⁵⁾	Aydin et al., 1996 ⁽²⁰⁾	Hiroaki et al., 1996 ⁽¹⁶⁾	Eriksen et al., 1990 ⁽¹⁸⁾
Specified inclusion criteria	Yes	No	Yes	Yes	Yes	Yes	No	No	No
Control group	No	No	Yes	No	No	No	No	No	No
Random allocation	No	No	No	No	No	No	No	No	No
Secrecy in the allocation	No	No	No	No	No	No	No	No	No
“Blind” subjects	No	No	No	No	No	No	No	No	No
“Blind” therapists	No	No	No	No	No	No	No	No	No
Statistical analysis	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Statistical comparison between groups	Yes	No	Yes	Yes	Yes	No	No	Yes	No

Chart 2. Results of the studies selected following the analyzed variables

Author/year	Country	Sample/age	Treatment	Method used (evaluation of smell)	Moment of evaluation of smell	Results
Park et al., 2009 ⁽¹¹⁾	South Korea	n=189 (120 women and 69 men); Group 1 (n=12); Group 2 (n=70); Group 3 (n=107); 25–76 years of age	Group 1: pterional contralateral approach Group 2: pterional approach for the anterior communicating artery Group 3: pterional ipsilateral approach	- Applying of a smell impairment questionnaire, at the clinic or by phone - Patients who reported alterations were submitted to the Sniffin' Sticks Test (Korean version)	12 to 38 months after surgery	- There was a significant correlation between the olfactory dysfunction, surgical technique used, and age - From the 189 patients, 21 of them presented olfactory dysfunction - The greater olfactory dysfunction findings were observed in group 1 (contralateral pterional approach), where 58% of the individuals showed alterations
Martin et al., 2009 ⁽¹²⁾	Spain	n=69; Group SAH in AcoA: 39 patients (24 men and 15 women); control group: 30 participants (17 men and 13 women); <60 years of age; mean of the SAH group: 49.2 years; mean of the control group: 49.5 years	43.5% of patients were submitted to surgery with pterional approach 53.8% received endovascular coil treatment, and one patient needed both techniques	- University of Pennsylvania Smell Identification Test (UPSIT) - Test with 40 microencapsulated odors and multiple choice answers - Subjective evaluation of smell and taste	Minimum of 6 months after the surgery	- SAH group showed worse performance in relation to the control group - 17 (43.6%) of 39 patients of group SAH versus 1 (3.3%) of the 30 control group showed olfactory alterations - There was a negative correlation between age and olfactory alterations
Moman et al., 2009 ⁽¹³⁾	Netherlands	n=90; Group of nonruptured aneurysms: 58 patients (43 women and 15 men); Group with SAH: 32 patients (22 women and 10 men); Group of nonruptured aneurysms: 35.7–79.8 years of age; Group with SAH: 28.2–88.6 years of age	32 patients showed clipped aneurysms and 26 embolized aneurysms	- Interview over the phone to investigate smell alterations - Sniffin' Sticks Test Battery (validated in Europe), with 12 odors - 20 participants of each group were elected to perform the smell test	Not informed	Interview: - From the patients treated for nonruptured aneurysm, 9 (28%) of the 32 patients treated surgically and none of the 26 patients treated by endovascular method (0%) reported having or having had olfactory loss - Of the 32 patients with SAH treated by endovascular method, 7 (22%) of them experienced olfactory loss Test: - Of the patients treated for nonruptured aneurysm, 13 (65%) patients treated surgically and 8 treated by endovascular method (42%) showed olfactory alterations - Of the patients with SAH treated by the endovascular method, 7 (35%) of them showed olfactory alterations

Continue...

Chart 2. Continuation

Author/year	Country	Sample/age	Treatment	Method used (evaluation of smell)	Moment of evaluation of smell	Results
Wermer et al., 2007 ⁽¹⁴⁾	Netherlands	n=315 (199 women and 116 men); 25–91 years of age (mean age of 60.3 years)	- 67 patients were treated by the endovascular method - 248 were treated surgically (clipping)	- Questionnaire for the olfactory alteration (by phone and at the clinic) - Visual analog scale of impact for olfactory loss was used	Mean period 7.5 years (1.2–20.4 years)	- 89 of the 315 patients (28%) reported olfactory loss after treatment of SAH, including 10 of the 67 patients treated by the endovascular method (15%) and 79 of the 248 patients treated surgically (32%)
De Vries et al., 2007 ⁽¹⁵⁾	Netherlands	n=13 (9 women and 4 men); 35–67 years of age (mean age of 49 years)	Frontobasal and frontotemporal neurosurgical procedures for clipping	- Subjective evaluation of smell - Sniffin' Sticks Test. Battery to verify the threshold, discrimination, and olfactory identification from pens with odors (butanol concentrations)	- 72 hours from SAH - Retake of the smell test 3 months after surgery	- Test after 72 hours from the SAH: olfactory alterations in 10 patients was identified: 3 anosmia and 7 hyposmia - Of these 10 patients, only 2 of them subjectly reported olfactory decrease - Test after 3 months from the surgery: 3 of the 10 patients showed anosmia, 4 of them hyposmia; and 3 of them normosmia
Hiroaki et al., 1996 ⁽¹⁶⁾	Japan	n=138; 33 patients with nonruptured aneurysm; 101 patients were examined; 49 patients submitted to surgery by AIA; 52 were submitted to surgery by BIA; 56 men and 45 women; Group AIA: 31–74 years of age (mean age of 56.5 years); Group BIA: 34–72 years of age (mean age of 53.9 years)	49 patients were treated surgically by anterior interhemispheric approach and 52 patients by basal interhemispheric approach	- Subjective evaluation through direct interview or by phone; - Bilateral application of the objective test of smell using vanilla extract	Not informed	- 15 patients (31%) revealed anosmia after surgery by the anterior interhemispheric approach, while only 1 patient (1.9%) showed anosmia after surgery by basal interhemispheric approach
Bor et al., 2009 ⁽¹⁷⁾	Netherlands	n=197 (129 women and 68 men); mean age (without aneurysm): 53 years; mean age (with aneurysm): 56 years	Endovascular embolization	- Semistructured questionnaire applied at the clinic or by phone - Visual analog scale of impact for olfactory loss was used	Minimum of 6 months after the SAH	- Olfactory loss was reported by 35 patients - 9 (26%) patients with olfactory loss did not report improvements in the function - 20 (57%) patients with olfactory loss presented full recovery of the function - 3 (8.5%) patients with olfactory loss presented partial improvements of the function - 3 patients did not know how to inform improvements in the function

Continue...

Chart 2. Continuation

Author/year	Country	Sample/age	Treatment	Method used (evaluation of smell)	Moment of evaluation of smell	Results
Aydin et al., 1996 ⁽²⁰⁾	Turkey	n=100 (54 women and 46 men); two patients without SAH.; 18–72 years of age	Right pterional craniotomy	- The vapor of saturated phenyl ethyl alcohol was used - Threshold olfactory test for butanol (two bottles, one with aqueous solution of butanol and another with water, for the identification of the odorant)	30 days after surgery	- Olfactory dysfunction in 15 patients (15% of the sample) was observed, considering 8 of them showed a decrease in smell and 7 of them, absence of it - 9 cases of olfactory dysfunction were in the ipsilateral side of the operation, 2 in the contralateral side, and 4 bilaterally - There was no relation of the olfactory alteration with the time of the surgery, treatment with mannitol and cerebral edema
Eriksen et al., 1990 ⁽¹⁸⁾	Denmark	n=25 (16 women and 9 men); 24 patients were diagnosed with SAH; 1 patient was diagnosed as not having SAH; 35–64 years of age (mean age of 49 years)	Frontotemporal surgery	- Mean observation period: 35.1 months - Subjective evaluation on olfactory alterations - Modified olfactometry using vapor of saturated phenyl ethyl alcohol - Sniff Test	Not informed	- In the subjective evaluation, 4 patients showed olfactory alterations - In the objective evaluation was revealed that 22 patients showed anosmia - In all cases, the anosmia was found in the operated side

Caption: SAH = subarachnoid hemorrhage; AcoA = anterior communicating artery; AIA = anterior inter-hemispheric approach; BIA = basal inter-hemispheric approach

Considering the inclusion and exclusion criteria adopted and after the withdrawal of repeated studies, only nine articles were included and analyzed in this systematic review (Figure 1).

In a preliminary analysis of the articles, it was possible to identify a methodological heterogeneity, which made it impossible to use statistical treatment (meta-analysis). Nevertheless, relevant conclusions could be extracted through this study.

It was observed that, from the studies analyzed, a part of the method were not presented: random allocation, secrecy in the allocation, and blinding of the research subjects; besides that, only part of them, equivalent to 55.5%, revealed pre-established selection criteria⁽¹¹⁻¹⁵⁾. It was also observed that most of them (77.7%) used statistical analysis of the data⁽¹¹⁻¹⁷⁾, and yet, owing to not being fully rigid as for the methodology used when developing the studies, there was difficulty in the use of integration statistical analysis of independent results.

On the basis of the period of publications, it was observed that few articles approached the theme in the 1990s⁽¹⁸⁻²⁰⁾, with the first study in the year of 1990⁽¹⁰⁾. From the studies analyzed, 66.6%^(11-15,17) were published from the year of 2007 onward, reflecting a period of 11 years without research. It was noticeable that the three first articles produced⁽¹⁸⁻²⁰⁾ investigated the alterations in smell after surgical intervention for the SAH and not ruptured aneurysms, showing greater concern with the repercussions in this function deriving from the microsurgery.

It is believed that such concerns was related to the evolution of surgical techniques, which initially happened in the 1960s to the 1970s with the description of pterional craniotomy⁽²¹⁾. Possibly, in this period, with the increase of surgeries directly involving the olfactory nerve, there were observed deficits in olfaction, which aroused interest from neurosurgeons.

Despite such evidence, it was observed that 77.7%^(11-13,17-20) of the studies selected were concerned about investigating the olfactory situation of patients after treatment, highlighting a much greater interest in the functional situation resulting from surgery.

According to the location of the studies, most of them were from European countries^(12-15,17,18) and two from Asia^(11,19). Besides that, Turkey, which is considered a Eurasian country, was the study site of one of the articles⁽²⁰⁾.

Four European articles were from Netherlands^(13-15,17); three of them^(14,15,17) were carried out in a school hospital in Utrecht, becoming one of the most concerned centers not only with the investigation of the association between smell and the surgical procedures used in the treatment of ruptured aneurysms but also with the repercussions resulting from this function by SAH itself, because it was in this center that the only studies evaluating the smell condition both pre and posttreatment were conducted^(14,15).

According to the results of the Global Burden of Disease, Injuries and Risk Factors (GBD), countries with low and medium

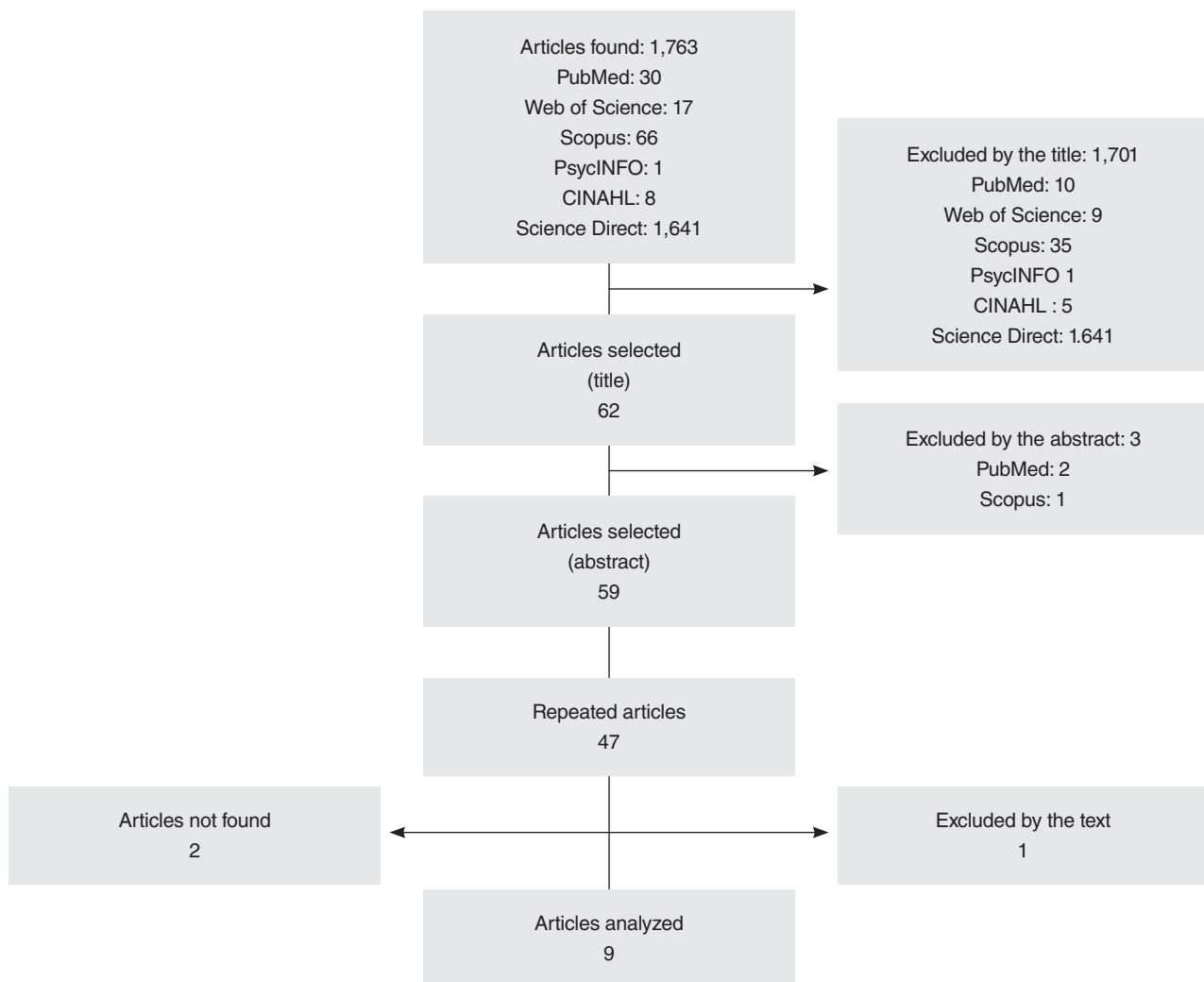


Figure 1. Flowchart of the number of articles found and selected after the applying of the inclusion and exclusion criteria

income showed, in 2010, more elevated rates of incidence and mortality connected to strokes, which included SAH⁽²²⁾.

Despite showing that the concern with the disease seems to be higher in these developing countries, possibly owing to more balanced health conditions in high-income countries, in addition to greater research resources, they end up developing more studies in the area, as observed in the articles found.

Another relevant factor in this review is that there were no studies from America, highlighting a greater interest by European and Asian countries in the development of studies evaluating the alterations in smell caused by aneurysmal SAH.

Considering information on the sample and the age range of the patients, it was verified that there was a great variation between articles, with a minimum of 13⁽¹⁵⁾ and maximum of 315 participants⁽¹⁴⁾. In addition, a variation in age of inclusion of the studies of at least 18 years of age⁽²⁰⁾ and a maximum of 91 years of age was observed⁽¹⁴⁾, showing heterogeneity in the conduction of the researches. It is believed that such variation is associated with the selection of the patients, motivated also by the demand for hospital admissions.

Another aspect pointing out to the definition of sampling of these studies is the incidence of aneurysmal SAH, which, though rare within the two first decades of life, it affects a broad age range, increasing the frequency up to 60 years of age⁽²³⁾.

It was also observed in the articles that the treatments used for aneurysmal SAH varied. These information show that the objectives set out in the studies were modified with the evolution of medical interventions, considering the period of publication, since that the first articles addressed the craniotomy^(11,14,15,18,19) and the most recent ones are set out to analyze smell also in embolization^(12-14,17), which is a more recent technique⁽²⁴⁾.

In the evaluation of smell, from standardized and nonstandardized tests to subjective questionnaires and an association of both were used. From the articles, two of them evaluated the olfactory function through questionnaires filled out in person or by phone, along with the impact scales of alteration in quality of life^(14,17).

Despite being able to rise important information on the functional perception of the patient in relation to smell, the questionnaires used in these studies have a subjective nature and this characteristics is strengthened by the way they

were applied. In addition to that, the translation of the results obtained in these instruments is made in a generic way, which makes it difficult to reproduce the findings.

However, the importance given to the quality of life, related to olfactory deficit, is a positive aspect of these studies, which highlights the effects caused by the functional decline of smell in this population.

Some articles used initial interviews in order to identify the patients with olfactory deficit, and later on, specific tests were performed^(11,13,15,19). This strategy appears to be negative, in that it may mask out the more subtle changes in olfactory function and not be revealed in the interviews.

Other studies used as means of investigation of the olfactory function the Sniffin' Sticks Test (Korean version)⁽¹¹⁾, University of Pennsylvania Smell Identification Test (UPSIT)⁽¹²⁾, Sniffin' Sticks Test (validated in Europe)⁽¹³⁾, Sniffin' Sticks Test battery⁽¹⁵⁾, modified olfactometry (using saturated phenyl ethyl alcohol vapor)⁽¹⁸⁾, and use of vanilla extract⁽¹⁹⁾ and butanol solutions⁽²⁰⁾.

It was possible to verify that 55.5% of the studies used standardized olfactory tests^(11-13,15,18), in some cases with regional validation, revealing that the standardization of the method is a criterion, which reinforced the choice of the kind of test of smell in the researches carried out.

The most often used test was the Sniffin' Sticks Test^(11,13,15), which consists of a standardized battery for the evaluation of smell, using felt pens with different odors. It is noteworthy that the results of this test are subject to regional influences. Thus, two articles used a regionally validated version of this test^(11,13), which suggests the higher accuracy in the results found in these studies.

In one of the articles analyzed, the UPSIT⁽¹²⁾ was used, which is a widely accepted smell test and considered the most often used one, specially owing to its accuracy and practicality in the application^(25,26). The UPSIT has four booklets, each containing ten microencapsulated olfactory stimuli, which are released when its surface is scratched. The marking of answers is made by four multiple choice alternatives, three of them represented by distractive odors and one alternative with the correct answer corresponding to the odor smelled.

Given the characteristics of this test, the answers may also experience the influence of the regions where it is carried out, which explains the several numbers of validations made for different countries. Nevertheless, in the study analyzed⁽¹²⁾, it was not informed whether or not there was adequacy in this sense.

On the basis of this, the increasing importance of regional adjustment to which the standardized tests should be submitted to in order to ensure the reliability of their results was observed, which was seen in only two studies in this review^(11,13).

The olfactometry was also described in one of the analyzed studies⁽¹⁸⁾, and owing to being able to provide qualitative results of olfaction, it appears as a relevant means, which needs greater investigation in order to better identify the effectiveness of its use in the evaluation of this function.

The moment of application of the smell evaluation varied considerably between articles, from 72 hours after hemorrhage⁽¹⁵⁾ up to 7.5 years on average after the surgery⁽¹⁴⁾. This period varied thus mainly because of the method used in the study, which had a marked heterogeneity. Two of the studies were

retrospective in nature^(11,14), another one was a cross-sectional observation⁽¹⁵⁾, while three of them did not inform for sure the time of application of the evaluation^(13,18,19).

A percentage of 44.4% of the studies evaluated patients through a longitudinal model of investigation^(11,12,15,17), which may reflect the need to observe lasting olfactory alterations resulting from hemorrhage and surgical intervention.

This fact is owing to the recovery of the olfactory nerve after a lesion, which may occur even 5 years after the trauma. It is believed that permanent alterations are those that present after 35 months or more^(18,20).

In relation to the results of the studies, in all of them, subjects with some kind of deficit in smell after SAH or after surgical treatment were observed. In the studies in which the treatment used in the participants was the craniotomy, through different accesses, there was an association between the olfactory dysfunction with the side of operation and the anatomical manipulation of adjacent regions to the olfactory nerve, for access to the hemorrhage site^(11,18-20).

It was suggested by the authors that the emerging of smell alterations in microsurgery is related to mechanical lesions caused to the olfactory nerve, during tissue retraction for the exposure of the ruptured artery^(19,20). It is also said that even the minimum pressure levels in the retraction of the frontal lobe may lead to temporary or permanent alterations in smell.

In the studies in which there were comparisons between the treatments by craniotomy and embolization, despite having been observed a greater incidence of olfactory alteration in patients treated by microsurgery, there was the presence of olfactory deficit even after endovascular embolization⁽¹²⁻¹⁴⁾, which was also seen in the study that aimed at evaluating this function only after embolization⁽¹⁷⁾.

On the basis of that, authors comment the existence of other factors that may trigger smell alteration, in addition to the direct mechanical damage to the olfactory nerve during surgery. These would be: contact between the extravasated blood, during hemorrhage, and the nerve; increased intracranial pressure at the moment of rupture of the aneurysm; ischemia in the cortical regions involved with the processing of olfactory information; and the occurrence of cerebral vasospasm, which may compromise the blood flow of the structures related to smell^(12,14).

The results also demonstrate the difference in tracking olfactory alterations in face of subjective evaluations and tests, in which greater number of cases of alterations during the performing of the tests, whether or not standardized^(13,15,18), was observed. This difference shows the importance of concern with the selection of method for the evaluation of the olfactory function, in which subjective alternatives must be used as a complement to the evaluation in order to avoid false-negative results.

Considering the results found in the studies analyzed, the need for researches that propose to evaluate the olfactory function both before and after surgical treatment of aneurysmal SAH was verified, in order to better clarify the influence of both the blood leakage and the surgical intervention in the onset of olfactory alterations. Besides, it is important to use resources of standardized investigation, so that the answers are safer and allow greater reproducibility of the findings.

CONCLUSION

From this review, it was possible to observe that, in the evaluation of smell in patients with SAH, the studies used from standardized and nonstandardized tests to subjective means for alteration tracking, bringing about possibly lower accuracy in the results obtained owing to methodological heterogeneity. Besides, the moment of evaluation varied considerably in the articles seen, which implies in difficulties in the comprehension of trigger factors for olfactory alterations found in this disease.

The studies showed evidence of deficit in the olfactory function of these patients and the relation between surgical treatment and the trigger for olfactory dysfunction. In spite of this, the results of the analyzed articles do not explain in detail the real damage of the hemorrhage and of surgical intervention in the genesis of the functional change.

**SJHL took part in the collection and analysis of the data and the writing of the manuscript; HRC and HJS performed the scientific guidance and took part in the review and writing of the manuscript.*

REFERENCES

- Pulsinelli WA. Doenças vasculares cerebrais - princípios. In: Goldman L, Bennett JC. Cecil: tratado de medicina interna. Rio de Janeiro: Guanabara Koogan; 2001. p. 2352-9.
- Clinchot DM, Kaplan P, Murray DM, Pease WS. Cerebral aneurysms and arteriovenous malformations: implications for rehabilitation. Arch Phys Med Rehabil. 1994;75(12):1342-51.
- Burgos RE, Diaz RC. Hemorragia subaracnoidea espontanea: diagnostico y tratamiento. Univ Med. 2002;43(4):260-5.
- Machado FS, Akamine N. Hemorragia subaracnoidea. In: Knobel E. Terapia intensiva: neurologia. São Paulo: Atheneu; 2002. p. 123-36.
- Mocco J, Komotar RJ, Lavine SD, Meyers PM, Connolly S, Solomon R. The natural history of unruptured intracranial aneurysms. Neurosurg Focus. 2004;17(5):E3.
- Crowley RW, Medel R, Kassell NF, Dumont AS. New insights into the causes and therapy of cerebral vasospasm following subarachnoid hemorrhage. Drug Discov Today. 2008;13(5-6):254-60.
- Griz MFL. Relação entre déficit da olfação e hemorragia subaracnoidea aneurismática antes e após tratamento [doutorado]. Recife: Universidade Federal de Pernambuco; 2014.
- Moura RGF, Cunha DA, Gomes ACLG, Silva HJ. Instrumentos quantitativos para avaliação do olfato na população infantil: artigo de revisão. CoDAS. 2014;26(1):96-101.
- Doty RL. Olfaction in Parkinson's disease and related disorders. Neurobiol Dis. 2012;46(3):527-52.
- Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003;83(8):713-21.
- Park J, Lee SH, Kang DH, Kim JS. Olfactory dysfunction after ipsilateral and contralateral pterional approaches for cerebral aneurysms. Neurosurgery. 2009;65(4):727-32.
- Martin GE, Junqué C, Juncadella M, Gabarrós A, de Miquel MA, Rubio F. Olfactory dysfunction after subarachnoid hemorrhage caused by ruptured aneurysms of the anterior communicating artery. Clinical article. J Neurosurg. 2009;111(5):958-62.
- Moman MR, Verweij BH, Buwalda J, Rinkel GJ. Anosmia after endovascular and open surgical treatment of intracranial aneurysms. J Neurosurg. 2009;110(3):482-6.
- Wermer MJ, Donswijk M, Greebe P, Verweij BH, Rinkel GJ. Anosmia after aneurysmal subarachnoid hemorrhage. Neurosurgery. 2007;61(5):918-22; discussion 922-3.
- De Vries J, Menovsky T, Ingels K. Evaluation of olfactory nerve function after aneurysmal subarachnoid hemorrhage and clip occlusion. J Neurosurg. 2007;107(6):1126-9.
- Hiroaki F, Nobuyuki Y, Edgar NV, Akifumi S. Anosmia after anterior communicating artery aneurysm surgery: comparison between the anterior interhemispheric and basal interhemispheric approaches. 1995;38(2):325-28.
- Bor AS, Niemannsburg SL, Wermer MJ, Rinkel GJ. Anosmia after coiling of ruptured aneurysms: prevalence, prognosis, and risk factors. Stroke. 2009;40(6):2226-8.
- Eriksen KD, Bøge-Rasmussen T, Kruse-Larsen C. Anosmia following operation for cerebral aneurysms in the anterior circulation. J Neurosurg. 1990;72(6):864-5.
- Fujiwara H, Yasui N, Nathal-Vera E, Suzuki A. Anosmia after anterior communicating artery aneurysm surgery: comparison between the anterior interhemispheric and basal interhemispheric approaches. Neurosurgery. 1996;38(2):325-8.
- Aydin IH, Kadioğlu HH, Tüzün Y, Kayaoğlu CR, Takçi E, Öztürk M. Postoperative anosmia after anterior communicating artery aneurysm surgery by the pterional approach. Minim Invasive Neurosurg. 1996;39(3):71-3.
- Yasargil MG, Fox JL, Ray MW. The operative approach to aneurysms of the anterior communicating artery. In: Krayenbühl H, editor. Advances and technical standards in neurosurgery. 2nd ed. Wien: Springer-Verlag; 1975. p. 114-70.
- Krishnamurthi RV, Moran AE, Forouzanfar MH, Bennett DA, Mensah GA, Lawes CM, et al. The global burden of hemorrhagic stroke: a summary of findings from the GBD 2010 study. Glob Heart. 2014;9(1):101-6.
- Inagawa T, Hirano A. Autopsy study of unruptured incidental intracranial aneurysms. Surg Neurol. 1990;34(6):361-5.
- Conrad MD, Pelissou-Guyotat I, Morel C, Madarassy G, Schonauer C, Deruty R. Estudo comparativo entre aneurismas rotos tratados por cirurgia e por via endovascular. Arq Neuro-Psiquiatr. 2002;60(1):96-100.
- Doty RL, Shaman P, Dann M. Development of the University of Pennsylvania Smell Identification Test: a standardized microencapsulated test of olfactory function. Physiol Behav. 1984;32(3):489-502.
- Doy RL, Newhouse MG, Azzalina JD. Internal consistency and short-term test-retest reliability of the University of Pennsylvania Identification Smell Test. Chem Senses. 1985;10(3):297-300.