ASSOCIATION BETWEEN SALIVARY HYPOFUNCTION AND FOOD CONSUMPTION IN THE ELDERLIES. A SYSTEMATIC LITERATURE REVIEW

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Abstract: *Objectives:* This systematic literature review aims to summarize the existing scientific evidence about the association between a reduced salivary function and food consumption in elderly people. *Methods:* A validated search strategy in two databases (PubMed and ISI Web of Knowledge) was carried out and retrieved papers together with their reference lists were screened by two independent reviewers. The quality of the included studies was critically appraised via the Quality Assessment Criteria for Evaluating Primary Research Papers. *Results:* From the originally identified studies (n=391), only 15 articles (all cross-sectional studies) met the pre-fixed inclusion/exclusion criteria. The methodological quality of the included studies was in general good, although only 3 from 15 obtained the maximum score. The control of confounding factors was the quality variable more poorly rated in the selected studies. Salivary hypofunction was associated with a decrease of the objective chewing and swallowing abilities and taste perception. Moreover, most of the selected studies showed a relationship between salivary hypofunction and food consumption (in terms of appetite loss, unbalanced dietary intake and malnutrition), although no causality could be established. *Conclusions:* This study highlights the fact that salivary hypofunction definition and measurements are different across the studies. Therefore, future research efforts should focus on establishing a gold standard to define and identify salivary hypofunction throughout life and on performing longitudinal studies controlling for confounding factors to establish causality. .

Key words: Hyposalivation, dietary intake, appetite, nutritional status, elderly.

Introduction

Saliva is a complex biological fluid composed by water, inorganic and organic molecules (1). Secreted by several salivary glands, saliva plays an important role in the preservation and maintenance of oral health and functions (2). First, saliva is known to be essential in fulfilling daily activities such as speaking. Second, it exerts a key role maintaining oral health under normal conditions: tooth and oral mucosa integrity, protection against dental caries, periodontal diseases, etc. (3; 4; 5). Third, as the first digestive fluid in contact with food, saliva is a key factor assisting the oral processing of food, whereby food is transformed into a bolus to be swallowed. During the mastication process, the lubrication function of saliva allows moistening of food and supports the creation of a bolus which in turn facilitates the ability to chew (6). Furthermore, some food components are released from the food matrix and dissolved in saliva, where they can be influenced by the presence of salivary components such as salivary enzymes that begin the process of food digestion (i.e. alpha-amylase) or metabolize flavor compounds (i.e. esterases, glycosidases) (7; 8).

In consequence, an alteration in the composition or amount of saliva released to the human mouth, produced as a consequence of a diminished salivary gland function, could have serious consequences. A reduced salivary output could induce a defect in lubrication, compromising the comfort while chewing and swallowing (3). These dysfunctions could be accompanied by an unbalanced flavor perception that could provoke an unpleasant sensory experience. Besides these effects, if the situation of dry mouth is maintained in the long term, the decline (or absence) of salivation per se may change the oral environment, which could cause infections, destruction of taste receptors (9) and formation of dental caries, which can derive in tooth losses (4), thus compromising even more the food oral processing. The sum of these events could therefore provoke a decline in food interest and a loss of appetite, resulting in a modification of people's dietary habits. The quantity, quality and variety of food consumed could be altered, thus contributing to a diminished nutritional status.

This cascade of reactions possibly induced by a reduced salivary output is of especial relevance for elderly people, the population group most affected by salivary disorders. Older people are more likely to take medications compared to other generations, which is a well-known factor of hyposalivation as a side effect (10). A recent meta-analysis has shown that the aging process is associated with reduced salivary flow per se in a salivary-gland-manner (11), and this reduction can not be fully explained on the basis of medications (11) or dental status (12). In the same time, this age group is frequently associated with poor appetite, weight loss and malnutrition (13; 14). However, the relationship between food consumption and salivary hypofunction in elderly population remains unclear. This could be due to the fact that very often the studies on this topic have measured the subjective sensation of dry mouth (xerostomia) instead of performing real measurements of saliva deficiencies (3, 15-19). Indeed, xerostomia and hyposalivation are two separate entities, which are not always correlated (20;

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21). Whereas xerostomia relates to a subjective evaluation of dry mouth, hyposalivation represents a decrease in the amount of saliva secreted to the oral cavity. Therefore the aim of this work was to systematically review the original articles studying the associations between salivary hypofunction measured objectively and alterations in food consumption in elderly population. In this review, food consumption has been addressed by the study of i) food oral processing, ii) food behavior (appetite and dietary intake) and iii) nutritional status. Out of scope of this article are external factors affecting food consumption such as food availability, cultural factors, etc.

Method

Search strategy

A review of the literature was conducted in September 2016 for all published articles containing information about the association between salivary hypofunction and i) food oral processing, ii) food behavior (appetite and dietary intake), and iii) nutritional status in the elderlies. The electronic databases PubMed and ISI Web of Knowledge were used to search for relevant articles (without date restriction). The search strategy consisted of a set of Medical Subject Headings (MeSH) terms and free text words subsequently combined. Following groups of key words were introduced:

1) food oral processing, mastication, chewing, swallowing, flavo(u)r, taste, aroma, texture, flavo(u)r perception, taste perception, aroma perception, texture perception, chemosensory perception, orosensory perception, food sensory perception, texture modification, aroma release, taste release, trigeminal sensation(s), food texture;

2) food consumption, food behavio(u)r, nutrition, appetite, food intake, malnutrition, undernutrition, malnourishment, eating, nutrient intake, eating capability, food liking, dietary pattern, meal frequency, eating frequency;

3) elderly, senior, ag(e)ing, old age, older adult(s), old(er) people, old(er) person(s);

4) saliva, hyposalivation, salivary flow, salivary composition, salivary protein(s), salivary secretion(s), salivary hypofunction, xerostomia, dry mouth, oral mucosa, mucosal wetness, mucosa dryness, oral dryness.

Selection criteria and study selection

Articles were included if they explored the association between an objective measure of salivary deficiencies and i) food oral processing (mastication, swallowing, orosensory perception), ii) food behavior (appetite and food intake) or iii) nutritional status. Only articles that defined salivary hypofunction were included in this systematic literature review (SLR). Therefore articles that did not explore populations with salivary disorders or that did not specify cut-off values of saliva deficiencies were not included in this SLR. Study design and settings were not defined as exclusion criteria because of the exploratory character of the review. Only articles written in English were included, no date limitation was performed.

Two reviewers (CMG and MVD) independently screened the titles and abstracts based on the selection criteria. If the abstract did not provide enough information to decide upon inclusion/exclusion, the full paper was retrieved for further screening. Disagreements about inclusion or exclusion were discussed between the reviewers until consensus was reached.

Data abstraction and synthesis

Two reviewers (CMG and MVD) independently extracted data from the included articles. The extracted data included study characteristics (author and year of publication, study design, sample size, settings (living condition), determinant, outcome, methods, main results and conclusions), and participant characteristics (age, gender, country/ethnicity, functional status). A synthesis of the data is reported in Table 1.

Quality assessment

The quality assessment of the review is based on "The quality assessment criteria for evaluating primary research papers from a variety of fields" (22). The used checklist contains the following items:

1. Is the objective of the study sufficiently described?
2. Is the study design evident and appropriate?
3. Is the method of subject selection described and appropriate?
4. Are subject characteristics sufficiently described (functional status, health, etc.)?
5. Are outcome measures well defined and robust to measurement?
6. Is the sample size appropriate?
7. Are analytic methods described, justified and appropriate?
8. Is some estimate of variance reported for main results?
9. Are they controlled for confounding?
10. Are the results reported in sufficient detail?
11. Are the conclusions supported by results?

Each question can be answered with 'yes', 'partial', 'no' and 'not applicable'. The summary score is the total sum ((number of 'yes' x 2) + (number of 'partial' x 1)) / total possible sum (28 – (number of 'not applicable' x 2). The associated scoring manual (22) was used to guide the scoring process. When the quality of a paper was debatable, a discussion between two independent reviewers was held until consensus was reached.

Results

Selected articles

Figure 1 shows the overview of the search strategy. A total of 391 articles were identified: PubMed (n=219), and ISI Web of Knowledge (n=172). Duplicate articles (n=102) were excluded. Additionally, 248 articles were excluded because the inclusion criteria (based on title and/or abstract) were not met. The full texts of 41 articles were reviewed in detail.

Table 1
Description of the 15 selected studies concerning salivary hypofunction and associated parameters related to food consumption

Reference	Study design*	Study population	Country	Functional status**	Parameter studied and method(s)	Results of the association between the parameter studied and salivary hypofunction
Dormenval et al., 1998	CS	sample size: 99 mean age ± SD (years) 82.5 ± 4.0 gender (% female): 70	Switzerland	H	Nutritional status: Anthropometric (BMI, triceps skinfold thickness and mid-arm circumference), and biological measurements (serum albumin concentration)	- BMI<21 (p<0.05) - triceps skinfold thickness: (p=0.01) - mid-arm circumference: (p<0.05) - serum albumin concentration: (p=0.01)
Dormenval et al., 1999	CS	sample size: 99 mean age ± SD (y/o): 82.5 ± 4.0 gender (% female): 70	Switzerland	H	Appetite: questionnaire	- Lack of appetite (p=0.05)
Samnieng et al., 2012	CS	sample size: 612 mean age ± SD (y/o): 68.8 ± 5.9 gender (% female): 74	Thailand	C	i) Oral function (tasting, speaking, swallowing, chewing): questionnaire ii) Nutritional status: MNA	- Oral function problems (p<0.05) - Low MNA score (p<0.05).
Syrjälä et al., 2013	CS	sample size: 157 mean age ± SD (y/o): 79.2± 3.6 gender (% female): 70	Finland	C	Nutritional status (risk of malnutrition): MNA-SF	- Risk of malnutrition (n.s)
Samnieng, 2014	CS	sample size: 612 mean age ± SD (y/o) : 68.8 ± 5.9 gender (% female): 74	Thailand	C	Appetite: questionnaire	- Appetite loss (p<0.05)
Iwasaki et al., 2016	CS	sample size: 352 mean age ± SD (y/o): 80.0 ± 0.0 gender (% female): 51	Japan	C	i)Dietary intake: validated food frequency questionnaire ii) Subjective capacities to eat and swallow: questionnaire	- Self-reported chewing difficulties (p<0.001) - Self-reported swallowing difficulties (p<0.036) -Total energy intake (n.s) - Low intake of n-3 polyunsaturated fatty acid, potassium, vitamin D, vitamin E, vitamin B6 and folate (p<0.05) - Low consumption of vegetable, fish and shellfish consumption (p<0.05)
Ikebe et al., 2006	CS	sample size: 328 mean age ± SD (y/o): 66.2 ± 4.1 gender (% female): 47	Japan	C	Masticatory performance: Gummy jellies test	- Masticatory ability: bivariate level (p=0.006) and multivariate level (p=0.046) - Masticatory performance: no support zone (p<0.003), 1 to 3 support zones (p=0.047), 4 support zones (n.s)

Table 1 (contined)

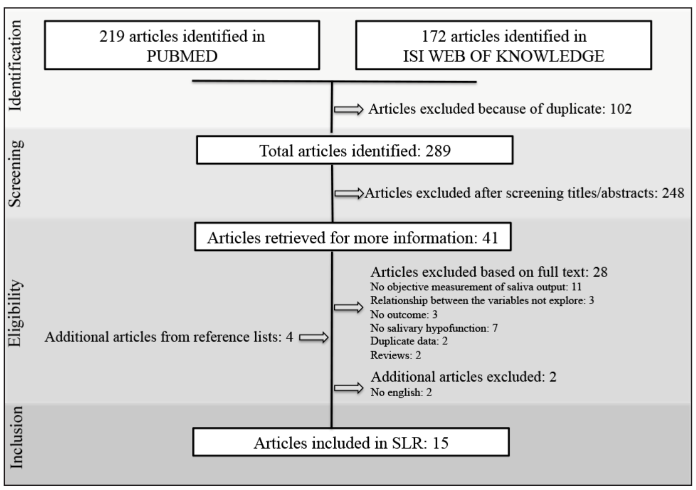
Reference	Study design*	Study population	Country	Functional status**	Parameter studied and method(s)	Results of the association between the parameter studied and salivary hypofunction
Mesas et al., 2010	CS	sample size: 267 mean age ± SD (y/o): 66.5 ± 4.1 gender (% female): 60	Brazil	C	Nutritional status: MNA	- Nutritional deficit (OR: 2.18, 95% CI: 1.06 – 4.50) (considering stimulated salivary flow <0.7 ml/min)
Poisson et al., 2014	CS	sample size: 159 mean age ± SD (y/o): 85.3 ± 5.7 gender (% female): 68	France	H	i) Dysphagia: swallowing abilities ii) Nutritional status: BMI, serum albumin concentration, MNA-SF iii) Dietary intake: 3-day records	-Dysphagia: univariate level (p<0.001) and multivariate level (n.s) - Malnutrition (n.s) - Protein and energy intake (n.s)
Soini et al., 2003	CS	sample size: 51 mean age ± SD (y/o): 83.7 ± 4.4 gender (% female): 78	Finland	C	Nutritional status (risk of malnutrition): MNA	- Risk of malnutrition (p = 0.049)
Solemdal et al., 2012	CS	sample size: 174 mean age ± SD (y/o): 83.5 ± 6.1 gender (% female): 68	Norway	H	Taste ability: taste strips method	- Total taste score (p=0.001), sweet sum score (p=0.007) and salty sum score (p=0.009) related to friction with mirror test - Total taste score (p=0.007), sweet sum score (p=0.001) and salty sum score (p=0.030) related to dry tongue - Salty sum score (p=0.023) related to salivary flow
Srinivasulu et al., 2014	CS	sample size: 81 mean age ± SD (y/o): 70.0 ± 7.1 gender (% female): 58	India	I	Nutritional status: MNA	- Nutritional status (p<0.001)
Ikebe et al., 2002	CS	sample size: 351 mean age ± SD (y/o): 66.7 ± 4.3 gender (% female): 46	Japan	C	Dissatisfaction with tasting; self-assessed chewing ability: questionnaire	- Dissatisfaction with tasting food (p<0.05) - Self-assessed chewing ability (p<0.01)
Shinkawa et al., 2009	CS	sample size: 502 mean age ± SD (y/o): 72.3 ± 6.7 gender (% female): 51	Japan	C	Satisfaction with chewing and swallowing abilities: questionnaire	- Subjective chewing ability (p=0.002) - Swallowing ability (n.s)

* CS: cross-sectional studies; ** C: community dwelling volunteers (independently living); I: Institutionalized volunteers; H: hospitalized patients

Twenty eight articles were excluded due to different reasons: not an objective measurement of the saliva flow but a subjective sensation of dry mouth (n=11), the relationship between the variables was not explored (n=3), cut-off value to determine salivary hypofunction not specified (n=7), the outcome measurements were not focused specifically on our research topic (n=3), redundant information due to a publication on the same data (n=2), or not original papers but reviews (n=2). The reference lists of all included articles were checked for additional articles. In consequence, four new papers were found to be of interest for this review but two of them (23, 24) were not written in English, so not included in the final list. The final group consisted of 15 articles. All of them were subjected to a methodological quality assessment.

Figure 1

Overview of the research strategy



Methodological quality

The methodological quality of the included studies was in general good: of the 15 selected articles the quality scores varied between 0.77 and 1 in a 0-to-1 rating scale (Table 2). Three articles (25-27) obtained the maximum score according to the above-mentioned manual scoring (22). On the contrary, the lowest score was attributed to the one (28) with the smallest sample size (n=51) (item n° 6). Moreover, in this work the study design (item n° 2), the analytical methods employed (item n° 7) and the results (item n° 10) were not sufficiently described. Furthermore, confounding factors (item n° 9) were partially taken into account.

In fact, the control of confounding factors (item n° 9) was the quality variable more poorly rated in the selected studies. This was due to the fact that most of the studies did not take into account all the factors established as confounding in this study: age, gender, drug intake, diseases, mental status, socio-economic status, dental status and place to live. Therefore this item was often rated as "partial".

Study characteristics

Table 1 gives an overview of the 15 selected articles. Publication year of the studies ranged from 1998 to 2016, showing that the interest on this topic is held and even increased over time (from 1998 to 2004: 4 studies; from 2005 to 2011: 4 studies; from 2012 to 2016: 7 studies). All the studies had a cross-sectional design. The studies were based on populations from all over the world (Brazil: 1, Finland: 2, Japan: 5, Norway: 1, Switzerland: 2, Thailand: 2; France:1; India:1), with exception of the African and Oceanic continent and north America. The sample size varied from 51 (28) to 640 (29) subjects. The gender distribution of subjects varied between 46% (30) and 78% (28) of females. Eighty per cent of the studies presented however, a higher percentage of women compared to men. The mean age was highly dispersed in the selected studies, ranging from 66 to 84 years old. The recruited populations were located either in institutions (5 studies) or in their own homes (10 studies). The subjects recruited in the selected studies were in good general health except for three studies: one study with hospitalized very sick volunteers (31), one study which included subjects receiving home care nurses visits (28) and one study (27) where the elderlies were living in their own homes prior to hospitalization for acute medical problems.

Analytical methods

Salivary hypofunction was determined differently across the selected studies (Table 3). Fourteen of the 15 studies measured the salivary flow rate either at rest, under stimulation by chewing a piece of paraffin-wax during saliva collection or both at rest and under stimulation. Most of these studies used the spitting method for the salivary collection but some preferred to measure the salivary flow using the draining method or the sterile compress method. The draining method consists in allowing saliva to drain out between parted lips into a test tube held near the mouth. The sterile compress method consists in placing a sterile compress under the tongue, then weighting the compress after a certain time to evaluate the amount of saliva incorporated. These studies have defined salivary hypofunction when the salivary flow was below a certain cut-off value. This reference value was 0.1 ml/min of saliva determined at rest in all the selected studies. However, the cut-off values employed to define salivary hypofunction under stimulation were not consensual and varied from 0.5 ml/min to 1.0 ml/min in the different studies. Very few studies have determined salivary hypofunction using alternative methods. Four over fifteen articles employed (besides the determination of salivary flow) additional measures to determine salivary hypofunction, such as the mirror test (that consists of measuring the stickiness of buccal mucosa when passing through it the back of a dental mirror) or the registration of dry tongue (presence of moisture or not). Only one study (32) did not use salivary flow to define hyposalivation. Authors measured the moisture of the buccal mucosa by using a device that evaluates the weight

Table 2
Quality assessment of the 15 selected studies

Reference	Question/ objective sufficiently described?	Study design evident and appropriate?	Method of subject selection is described and appropriate?	Subject characteristics are sufficiently described?	Outcome measures(s) well defined and robust to measurement/ misclassification bias? Means of assessment reported?	Sample size appropriate?	Analytic methods described/ justified and appropriate?	Some estimate of variance is reported for main results?	Controlled for confounding? (age, gender, drug intake, diseases, mental status, socio-economic status, dental status and place to live)	Results reported in sufficient detail?	Conclusions supported by results?	Sum Score
Dormenval et al., 1998	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Partial	Yes	0.91
Dormenval et al., 1999	Yes	Partial	Yes	Yes	Yes	Yes	Partial	Yes	Partial	Yes	Partial	0.82
Samnieng et al., 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Yes	0.95
Syrjälä et al., 2013	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Partial	Partial	0.86
Samnieng, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	0.95
Iwasaki et al., 2016	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1.00
Ikebe et al., 2006	Yes	Yes	Yes	Partial	Yes	Yes	Yes	Yes	Partial	Yes	Yes	0.91
Yoshinaka et al., 2007	Yes	Yes	Yes	Partial	Yes	Yes	Partial	Yes	Partial	Partial	Yes	0.82
Mesas et al., 2010	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1.00
Poisson et al., 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Partial	Yes	0.91
Soini et al., 2003	Yes	Partial	Yes	Yes	Yes	Partial	Partial	Yes	Partial	Partial	Yes	0.77
Solemdal et al., 2012	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	1.00
Srinivasulu et al 2014	Yes	Partial	Yes	Yes	Yes	Partial	Yes	Yes	No	Yes	Yes	0.82
Ikebe et al., 2002	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Partial	Yes	Yes	0.91
Shinkawa et al, 2009	Yes	Yes	Yes	Yes	Yes	Yes	Partial	Yes	Partial	Yes	Yes	0.91

Table 3
Objectives measurements to determine salivary hypofunction and corresponding cut-off values in the 15 selected studies

Article	Parameters measured	Methodology	Number of measures	Cut-off value to determine hyposalivation	References of the methodology
Articles that performed the measure of salivary flow to determine hyposalivation					
Dormenval et al., 1998	Unstimulated salivary flow rate, stimulated salivary flow rate	Measured during 6 min, spitting out each 2 min; collected between 9h and 11h	2	Unstimulated salivary flow rate < 0.1ml/min, Stimulated salivary flow rate < 0.5ml/min	(61)
Dormenval et al., 1999	Unstimulated salivary flow rate, stimulated salivary flow rate	Measured during 6 min, spitting out each 2 min; Collected between 9h and 11h	2	Unstimulated salivary flow rate < 0.1ml/min, Stimulated salivary flow rate < 0.5ml/min	(61)
Samnieng et al., 2012	Unstimulated salivary flow rate, stimulated salivary flow rate	Measured during 5 minutes	1	Unstimulated salivary flow rate < 0.1 ml/min Stimulated salivary flow rate < 0.5 ml/min	-
Syrjälä et al., 2013	Unstimulated salivary flow rate, stimulated salivary flow rate	Measured during 5 minutes (draining method)	1	Unstimulated salivary flow rate < 0.1ml/min, stimulated salivary flow rate < 1ml/min	(40, 62)
Samnieng, 2014	Unstimulated salivary flow rate	Measured during 5 minutes	1	Unstimulated salivary flow rate < 0.1 ml/min	
Iwasaki et al., 2016	Stimulated salivary flow rate	Measured during 3 minutes; Collected between 9h to 15h	1	Stimulated salivary flow rate < 0.5 ml/min	(58)
Ikebe et al., 2006	Stimulated salivary flow rate	Measured during 2 minutes at their own pace; collected between 10:00 am and 3:00 pm	1	Stimulated salivary flow rate < 0.5 ml/min	(30, 63)
Yoshinaka et al., 2007	Stimulated salivary flow rate	Measured during 2 minutes at their own pace	1	Stimulated salivary flow rate < 0.5 ml/min	(64)
Mesas et al., 2010	Stimulated salivary flow rate	No information provided	1	Stimulated salivary flow rate < 0.5 ml/min; Stimulated salivary flow rate < 0.7ml/min	(30, 36, 62, 66)
Poisson et al., 2014	flow under the tongue	Measured by placing a sterile compress under the tongue for 5 min	1	Salivary flow < 0.1 g/min	-
Articles that combined the measure of salivary flow rate with other measures of oral dryness					
Soini et al., 2003	Unstimulated salivary flow rate, stimulated salivary flow rate, Objective dry mouth	Measured during 5 min (Unstimulated salivary flow rate: let the saliva flow into the tube ; Stimulated salivary flow rate: spitting out each 1 min) ; collected between 9h and 11h	1	Unstimulated salivary flow rate < 0.1 ml/min, stimulated salivary flow rate < 0.8 ml/min Clinical dentist criteria	(67)
Solemdal et al., 2012	Stimulated salivary flow rate, mirror test, dry tongue	Measured during 3 minutes at their own pace	1	Stimulated salivary flow rate < 0.6 g/min Dental mirror sticked to the mucosa Tongue completely devoid of moisture	(68, 69)
Srinivasulu et al 2014	Stimulated salivary flow rate, Total protein content, calcium, pH, buffering capacity	Measured during 5 minutes at their own pace; collected early in the morning	1	Stimulated salivary flow rate < 0.5ml/min	(70)
Ikebe et al., 2002	Stimulated salivary flow rate, pH of saliva	Measured during 2 minutes at their own pace: Collected between 10:00 am and 3:00 pm	1	Stimulated salivary flow rate < 0.5 ml/min	(3, 20, 64, 71)
Articles that used other method to determine hyposalivation					
Shinkawa et al., 2009	Moisture of oral mucosa	Measured at the right buccal mucosa, during 2 sec	3	28.3% of the MCM value	(33)

percentage of water found in the mucosa, and determined salivary hypofunction when the moisture of oral mucosa was below 28.3% according to a previous study that validated the method (33).

Association between salivary hypofunction and food oral processing (8 studies)

The relationship between a diminished salivary function and food oral processing (mastication/chewing, swallowing, orosensory perception) has been examined in 8 articles (25, 27, 29-32, 34, 35). Only 3 studies measured objectively chewing, swallowing and taste abilities (27, 31, 34), while the others (n=5) employed questionnaires. The objective measurements consisted of the determination of masticatory performance, signs of dysphagia and taste ability. The evaluation of masticatory performance was achieved by measuring the amount of dissolved glucose after the mastication of test gummy jellies. The signs of dysphagia were reported using the water test during which the volunteers were asked to swallow four times an increasing volume of water to report any abnormal signs (coughing or voice modification). Finally, the taste ability test consisted in impregnating some strips with sweet, salty and bitter taste, then asking the volunteers to identify the tastes by putting the strips in the anterior region of the tongue.

Six of the eight studies investigated the association between salivary hypofunction and the chewing and/or swallowing abilities (25, 30-32, 34, 35). Ikebe and coworkers (2006) (34) found a significant association between lower values of masticatory performance and hyposalivation in independently living older adults. In another study with hospitalized very sick older patients, Poisson and collaborators (2014) (31) found a strong relationship at univariate level between individuals presenting a low salivary flow (<0.1 g/min) and dysphagia. However this effect was not observed at multivariate level, when considering other independent variables in the model. The rest of the studies evaluated chewing and/or swallowing abilities through questionnaires. Two works (25, 35) found a significant association between reduced saliva flow rate and perceived chewing and swallowing difficulties. Ikebe and collaborators (2002) (30) also found a relationship between hyposalivation and poor self-assessed chewing ability though it was not of statistical level. Finally, Shinkawa et al., (2009) (32) found a significant association between oral dryness (measured via the level of moisture of oral mucosa) and poor self-assessed chewing ability but no with swallowing.

The association between salivary gland hypofunction and orosensory perception was evaluated in four studies (27, 29, 30, 35). However, it is important to notice that all of them were only focused on one modality of flavor perception: taste. In these studies, taste ability was evaluated either objectively (taste detection through the filter-paper disc method) or by questionnaires considering taste as a marker for oral function (dissatisfaction with tasting). Only Solemdal et al., (2012) (27) studied the association of salivary hypofunction on the objective taste ability. These authors reported a significant and markedly reduced total taste score, particularly for sweet and salty taste, in patients with objective dry mouth (measured by the friction with mirror and dry tongue tests). Low sum score for salty taste was also related to low stimulated salivary flow rate. The rest of the studies evaluated taste ability through global questionnaires including self-assessed items on oral function, with contradictory results. Two studies (30, 35) found that hyposalivation was negatively and significantly correlated to self-assessed taste satisfaction, whilst Yoshinaka and coworkers (2007) (29) failed to find this correlation. In addition to the measure of salivary flow rate, Ikebe et al., (2002) (30) measured the pH of the stimulated saliva but no correlation between the pH and taste satisfaction could be established.

In summary, most of the studies on this topic have shown a relationship between a reduced salivary function and alterations in food oral processing (mastication, swallowing, orosensory perception). It should be noted that this relationship seems clearer when the outcomes were measured objectively rather than by questionnaires.

Association between salivary hypofunction and food behavior (4 studies)

Two studies (36, 37) examined the possible relationship between hyposalivation and appetite, and two others between hyposalivation and dietary intake (25, 31). For both categories, the outcomes were evaluated throughout the use of four different questionnaires: a questionnaire related to dietary intakes/nutrition and masticatory function (36), a single question-item on appetite (37); a 3-day record on food intake (31); a brief-type self-administered diet history questionnaire (25). The use of questionnaires could be justified by the fact that appetite is the subjective desire of eating foods. In 1999, Dormenval and coworkers (36) found that lack of appetite was associated with hyposalivation (stimulated salivary flow rate < 0.5 ml/min) in hospitalized Swiss patients. More recently, Samnieng (2014) (37) also found a positive correlation between lack of appetite and low resting salivary flow in independently living older Norwegians.

Regarding dietary intake, the two selected studies found no association between total energy intake and hyposalivation. However, when studying specific nutrient and food intake, Iwasaki and collaborators (2016) (25) found that the hyposalivation group had significantly lower intake of n-3 poly-unsaturated fatty acids, potassium, vit E, D, B6 and folate, which was in line with the observed reduction in the consumption of vegetables, fish and shellfish. Moreover, mean dietary intake of protein and vitamin B12 in the hyposalivation group tended to be lower than in the control group ($0.05 < P < 0.10$).

In summary, the scarce literature available on this topic showed an association between hyposalivation and appetite loss and unbalanced dietary intake in elderly people.

Association between salivary hypofunction and nutritional status (7 studies)

The association between salivary gland hypofunction and nutritional status has been evaluated in 7 studies. Five of them (26, 28, 35, 38, 39) evaluated the nutritional status using the Mini Nutritional Assessment (MNA). Meanwhile, Dormenval and coworkers, (1998) (40) assessed the nutritional status by quantifying biological malnutrition markers (BMI, level of serum albumin) and anthropometric measurements. Finally, Poisson et al., (2014) (31) employed both the MNA and the values of serum albumin concentration.

The results showed that hyposalivation was significantly associated with malnutrition in 4 studies (26, 35, 39, 40). Additionally, Syrjälä and co-workers (2013) (38) showed that subjects with low salivary flow (at rest or under stimulation) were slightly more at risk of malnutrition than subjects with normal salivary flow though their results were not statistically significant. Besides, Soini et al., (2003) (28) stated that no relation was found between hyposalivation and malnutrition. However, they found a significant association between the clinical dentist evaluation of dry mouth and the risk of malnutrition ($p=0.049$). On the contrary, Poisson and coauthors (2014) (31) did not find any relationship between hyposalivation (determined as salivary flow under the tongue <0.1 g/min) and MNA and/or biological malnutrition either at univariate or multivariate level. In addition to the measure of salivary flow rate, Srinivasulu et al., (2014) (39) measured the pH, the buffer capacity, the total protein and the total calcium of saliva samples. However, the authors did not highlight any significant correlation between the saliva composition and nutritional status.

In summary, five studies found a correlation between hyposalivation and malnutrition. Another study observed a relationship between the objective evaluation of dry mouth and the risk of malnutrition. Only one article did not find any association between the two variables. Therefore, and although most of the studies have shown some associations between salivary hypofunction and nutritional status, up to date this relationship is still controversial.

Discussion

Salivary hypofunction refers to alterations in the quality (composition) or quantity (salivary flow, residual saliva in the mouth) of saliva secreted into the human mouth (41). This situation could alter the orosensory perception while eating, which is one of the most recognized determinants for consumer's preferences and food consumption (7). As a result, the appetite, dietary intake and nutritional status of an individual could be compromised. This is of special relevance for elderly people, a population group frequently affected by both salivary and nutritional deficiencies. The aim of this work was to systematically review all the existing papers on this topic, in order to explore the relationships between a reduced salivary output and food consumption in the elderlies. In this paper only objective measurements of salivary hypofunction were considered, since the subjective complaint of dry mouth (xerostomia) is not always associated with an objective evidence of reduced salivary secretions (20; 42).

In total, 15 articles met the criteria for inclusion in this work (see Table 1). Eight of them studied the relationship of salivary hypofunction with food oral processing, 2 with appetite, 2 with dietary intake and 7 with nutritional status. In general, the selected studies clearly showed some associations between salivary hypofunction and the studied parameters. However, some controversial results have also been observed. It should also be noticed that the study characteristics are very different from one study to another, and the presence of not controlled confounding factors or methodological issues should be taken into account to interpret the results.

Discussion on the methods used to measure salivary hypofunction.

This review focuses on studies that objectively measured symptoms of salivary hypofunction. The prevalence of the population suffering these symptoms ranged from 14% (35) to around 50% (26; 28) in the selected articles. These differences were most likely dependent to the different characteristics of the studied populations (such as age, race, living place (community, institutions, and hospitals), functional status (healthy vs ill), drugs consumption, etc.) but also on the methods and cut-off values employed to determine salivary hypofunction.

For most of the selected studies (14 out of 15), the determination of the salivary flow below a cut-off value was the tool used to determine salivary hypofunction (see Table 3). However, a lack of consensus was observed regarding the type of saliva collected (at rest or under stimulation), the protocol employed to measure the salivary flow rate (spitting, draining method, cotton roll), and the cut-off value to determine hyposalivation. Of the 14 studies that measured saliva flow, five of them performed both resting and stimulated measurements (28; 35; 36; 38; 40), seven studies based their results on the measure of stimulated salivary flow (25; 26; 27; 29; 30; 34; 39), one study only measured the resting salivary flow rate (37) whilst one study performed the measure of salivary flow under the tongue (31). The use of resting or stimulated salivary flow rates provides different information since saliva is not delivered to the human mouth by the same salivary glands and in the same proportions under the two conditions. Therefore, whole saliva at rest, where the submandibular gland predominates, differs from that secreted during stimulation (more related to parotid gland function). Consequently, and in spite of the scarce literature on this topic, it is not surprising that the two measures are not always correlated (43).

Moreover, two studies used additional methods (dentist evaluation, mirror test and tongue moisture) to measure salivary hypofunction besides the determination of the salivary flow (27; 28). These methods could show a more advance phase of salivary hypofunction where the oral integrity (mucosa, tongue) has already been affected due to a prolonged hyposalivation situation held over time. In addition, only two studies (30; 39) reported, additionally to the measure of stimulated salivary flow, changes in saliva composition. This could be due to the fact that these analyses are time consuming and expensive, and therefore difficult to be performed to study big populations, as those employed in the selected articles.

Otherwise, one study (32) did not use the measure of salivary flow to determine salivary hypofunction but evaluated it by measuring the moisture of the buccal mucosa. The device used for this evaluation determined the weight percentage of water found in the mucosa. Originally developed to measure the moisture of the skin, the device was modified specifically for this study. As it is not a common method used to measure hyposalivation, it is not possible to compare the results of this study to the results of the other selected studies.

In addition to the different parameters employed to determine hyposalivation (salivary flow at rest or under stimulation, moisture of mucosa, etc), within the same parameter, the protocol was not always performed in the same way. Table 3 highlights the differences observed in collection times (from 1 to 6 minutes), hours of collection (respecting or not the circadian rhythms), collection protocols (free spitting vs controlled), etc., employed to measure salivary hypofunction. Moreover, only three articles (32, 36, 40) measured the selected parameters two or three times, whilst the other studies only performed the measures once. Therefore, no information about the accuracy of the methods could be obtained, that in the worst scenario could be traduced in a misclassification of people across the groups.

The cut-off value to determine salivary hypofunction was consensual across the studies for the saliva at rest. A value lower than 0.1 ml/min was considered hyposalivation. However for the salivary flow under stimulation a high dispersion on the cut-off values was encountered among studies. Indeed, there is no universally accepted reference value to determine hyposalivation using stimulated salivary flow rate. Most of the authors employed a cut-off value of 0.5 ml/min to define hyposalivation (25, 26, 29, 34, 35, 36, 40), whilst others employed values ranged from 0.5 to 1 ml/min (27, 38). The differences in the cut-off points could derive in an erroneous assignation of the participants to the groups and in a misinterpretation of the results, making difficult the comparison of the studies. This was displayed in the study of Mesas et al., (2010) (26). Authors employed two cut-off levels (stimulated salivary flow rate < 0.5 and stimulated salivary flow rate < 0.7 ml/min) to define hyposalivation, and they only found a significant association with nutritional status when using the value of 0.7 ml/min. For the other methods employed to define salivary hypofunction, like the "mirror test'' and dry tongue methods, the comparison across studies is difficult because they are less frequently employed and dependent on the dentist's criteria. The moisture of oral mucosa cannot be either compared since the method was only employed in one article.

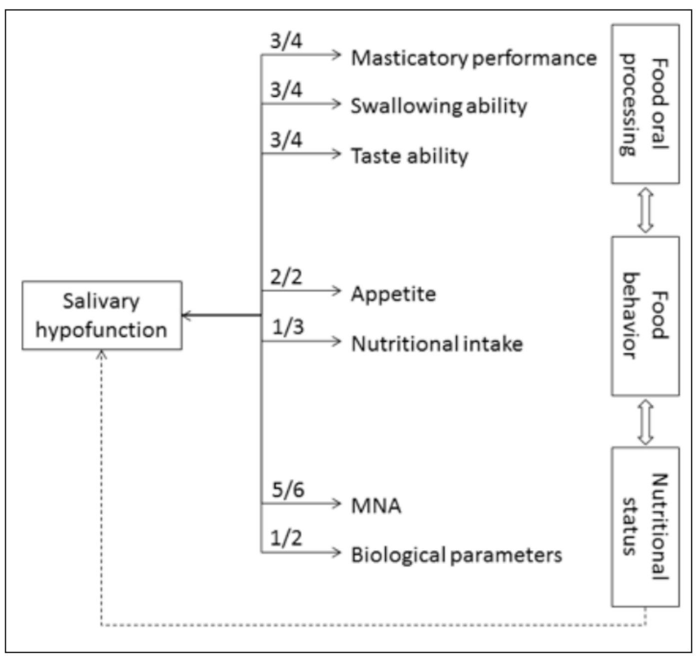
All these remarks highlight the idea that the diagnosis of salivary hypofunction is not consensual across the studies. Therefore, guidelines to measure salivary flow hypofunction with one or several complementary methods to evaluate the degree of dysfunction would be appropriate to allow an international standardization and a better comparison across the studies. Moreover longitudinal studies observing secretory function over time are required to establish causality. This would acknowledge setting up normal ranges or cut-off points to distinguish normal from abnormal salivary function. That amount is probably different across cultures (depending on gland sizes) (44).

Discussion on the relationship between salivary hypofunction with food oral processing, food behavior and nutritional status

Figure 2 represents schematically the associations between salivary hypofunction and food consumption found in the 15 selected articles. As a consequence of the cross-sectional design employed in the studies, no causal-effect relation can be established. Therefore, it cannot be concluded if salivary hypofunction is a cause or a consequence of the studied consumption parameters.

Figure 2

Schema resuming the main correlations found in this SLR between salivary hypofunction and the selected outcomes. The ratio (x/n) indicates the number of articles that highlighted a positive association between salivary hypofunction and the specific outcome (x) from the total number of articles that treated the topic (n)



As can be seen in Figure 2, salivary hypofunction was related to food oral processing, and in particular to mastication. It has been shown that elderly with hyposalivation had a reduced ability to break down foods into discrete portions by chewing to permit swallowing (34). This effect was more important in denture wearers with a lack of posterior occlusal contacts. Moreover, a relationship between hyposalivation and poor self-assessed chewing ability has been shown in four articles. Authors suggested that although presenting an altered masticatory performance is a multifactorial problem, salivary flow is a critical factor for masticatory function. However, the associations with dysphagia or swallowing have been less studied and results were controversial (31, 32).

In spite of chemosensory perception is a key factor for food enjoyment and one of the factors that motivate food consumption, its association with salivary gland hypofunction in the elderlies have received little attention. This could be due to the fact that food science has historically focused on the food and only in the later years some research groups have started to consider the interaction between food and human physiology to explain food perception. Moreover, to date most of the studies regarding the relation between the role of saliva on flavor release and perception have been conducted on healthy and young individuals (<65 y/o), while elderly population remains underexplored. Therefore only 4 articles met the inclusion criteria and they were all based on taste. While it has been found that salivary hypofunction is related to the objectively measured taste perception (27, 45), for the self-assessed taste ability results are controversial. However, most epidemiological studies do not include objective measurements of taste perception, probably because the evaluation through tests is more time-consuming than performing questionnaires.

To the author's knowledge the association between hyposalivation and texture or other modalities of orosensory perception (e.g aroma) in the elderlies has not been addressed by the scientific community yet. Some studies reported age-related loss of texture sensation (46, 47) and ultimately texture preference changes (48), but these studies have not investigated the role of a diminished saliva secretion in the observed results.

Assuming that a reduced salivary output produces an impaired food experience, the desire for food or drink known as appetite could be altered. This is in agreement with the findings of the two selected articles on this topic which shown a relationship between hyposalivation and loss of appetite (37, 40), even when the settings employed were very different in both of them. Consequently, this appetite loss could provoke a diminished food intake. However, the two studies on this topic found that the total energy intake was not impaired in elderly with hyposalivation. Nevertheless, when specific nutrients and/or group of foods were studied, the hyposalivator group presented a reduced consumption of vegetables, fish and seafood which was related to the lower intake of n-3 polyunsaturated fatty acids, potassium, vit C, E, B6 and folate after adjusting for confounders (number of teeth, denture use, sex, income, education, body mass index, smoking status, alcohol use, diabetes, medication, activities of daily living, depression and total calorie intake) (25). A reduced consumption of such specific nutriments/or groups of food, which are recognized for their health benefits (49-51), could have a negative impact on the health of this population.

Finally, an alteration of the dietary intake (quantitative or qualitative) could provoke an impairment of the nutritional status of the elderly population. Numerous studies have been conducted during the last decade to study the relationship between nutritional status and oral conditions in elderly, but to the authors' knowledge, only 7 studies have assessed the relationship between salivary hypofunction and nutritional status. However, some contradictory results have been found. While four articles found a significant correlation between MNA and hyposalivation, one did not. Although the method used to measure salivary flow was similar in the five studies, the cut-off values differed among them, which could explain the differences found in their results. On the other hand, the other two selected articles (28, 38) encountered only weak associations between nutritional status and hyposalivation or the dentist's estimation of dry mouth. Although other reasons (different cut-off levels, circadian rhythms not controlled, differences across populations) could explain these differences, it is interesting to observe that in these last two studies none of the subjects were malnourished but at risk of malnutrition. This is of importance since probably nutritional disturbances held over time can cause atrophy of salivary glands (39), producing a reduction of their function. If this is truth, alterations on saliva would be a consequence of an altered nutritional status. Unfortunately, as all the selected studies presented a cross sectional design no causality could be established and more studies are needed to validate this hypothesis.

Finally, the measure of the food consumption parameters was mostly performed by using subjective than objective methods. This could be due to the fact that the use of self-report questionnaires is less time consuming than performing objective determinations. However, as many studies have shown no correlation between the subjective feeling of dry mouth (xerostomia) and hyposalivation, there are no evidences of links between objective and subjective evaluations of the outcomes (29).

Limitations and strengths of the present SLR

The main strength of this work is that it is a solid literature search, with a complete overview of the relationship between an objective measurement of salivary hypofunction and the determinants of food consumption among the elderly population. Moreover, the selected studies represent the wide heterogeneity found in this population group (from healthy elderly individuals to chronically ill hospitalized old-people). The analysis of the quality of the selected articles let us to identify the most frequent risks across the studies and suggest new ideas for future works. For example, future studies on this topic should control better for confounding factors like gender, age, drug intake, diseases, mental status, socioeconomic status, dental status and place to live, because they are well-known factors that can alter salivary function (52-55) but also food consumption (56-59).

However, this study presents some limitations. Unfortunately, we were not able to perform a meta-analysis due to the obvious heterogeneity among the studies in relation to definitions and measurements as explained above. Also, we could not establish causality due to the cross-sectional nature of the selected studies. Therefore it cannot be concluded if hyposalivation is a cause or a consequence of the selected food consumption parameters.

Implication of this study

This study has revealed the urgent need to introduce and implement universal guidelines to assess salivary hypofunction. Moreover, cohort studies (with comparable groups following the same population for a longer period of time) and statistical control of the confounding factors are required to establish causality. Even if this review has pointed out some evidences about the relationship between salivary hypofunction and food consumption in the elderlies, the literature available on this topic is scarce. This is particularly obvious in some cases such as in the study of the relationship between hyposalivation and flavor perception. Therefore, there is a big opportunity for researchers, clinicians and food industry to better understand this association and if so, give nutritional recommendations and/or conceive products with sensory and nutritional properties adapted for people with salivary dysfunction.

Conclusions

The main findings of this review can be summarized in the following points: 1) to date, salivary hypofunction is mainly based on measures of salivary flow 2) definition and measures of hyposalivation are different across the studies; 3) salivary hypofunction has been related to a decrease of objective chewing and swallowing abilities and taste perception; very little is known about other modalities of chemosensory perception (e.g. aroma) 4) hyposalivation has been associated with appetite loss; 5) hyposalivation has been related to an unbalanced dietary intake but not with total intake; 6) it has been seen a relationship between saliva deficiencies and malnutrition, though some controversial results have also been shown. Although it is not possible to completely eliminate the potential effects of underlying methodological issues and in spite of the scarce number of publications on this topic it is suggested a relationship between salivary hypofunction and food consumption in the elderlies. Unfortunately, due to the cross-sectional nature of the articles, no causality could be established. Therefore longitudinal studies on this topic controlling for confounding factors are needed.

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