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Review Article

Sweet taste and obesity

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ABSTRACT

Keywords: Obesity Bariatric surgery Taste perception Psychophysics Reward-related feeding behavior

For more than 50 years, there has been evidence for greater consumption of sweet- foods in overweight humans and animals, relative to those that have a normal weight. Furthermore, it has long been suggested that energy deficit resulting from dieting, while moving the individual from a higher weight set point, would result in heightened susceptibility to palatable tastants, namely to sweet tastants. This was the motivation behind the first studies comparing sweet taste perception between individuals with obesity and those of a normal weight. These studies, using direct measures of taste, have been characterized by significant methodological heterogeneity, contributing towards variability in results and conclusions. Nevertheless, some of these findings have been used to support the theory that patients with obesity have decreased taste perception, particularly for sweet tastants. A similar hypothesis has been proposed regarding evidence for reduced brain dopamine receptors in obesity and, in both cases, it is proposed that increased food consumption, and associated weight gain, result from the need to increase sensory and brain stimulation. However, the available literature is not conclusive on the association between obesity and reduced sweet taste perception, with both negative and contradictory findings in comparisons between individuals with obesity and normal weight control subjects, as well as within-subject comparisons before and after bariatric surgery. Nevertheless, following either Roux-en-Y gastric bypass or sleeve gastrectomy, there is evidence of changes in taste perception, particularly for reward-related measures of sweet tastants, that should be further tested and confirmed in large samples, using consensual methodology.

1. Background

Obesity is associated with significant morbidity and mortality, and currently represents a global health challenge[1]. While it is associated with complex pathophysiology, increased availability of highly palatable foods and beverages, namely those rich in sugar or fat, is thought to be a major determinant of increasing rates of obesity worldwide[2]. Indeed, individuals with obesity have been shown to have altered sensitivity to food reward[3], which is thought to be related to changes in reward-related brain neurocircuitry, namely decreased striatal availability of dopamine D2 receptors (D2R)[3]. Sugar, through pleasant taste and postingestive value, triggers brain reward circuitries, stimulating consumption of foods that are rich in sugar[4-6]. Another important factor is that, while in non-obese subjects striatal D₂R availability is inversely associated with sweet preference, in subjects with obesity this association is lacking, through mechanisms that have not yet been clarified[7]. Beyond association between gustatory and

reward-related circuits in humans[8], there is also pre-clinical evidence in rodents [9] and fruit flies [10] that dietary sugar content influences sweet taste perception. For example, in *Drosophila melanogaster* a high sugar diet led to decreased response of 'sweet-taste sensing neurons', resulting in diminished behavioral responses to sweet tastants[10]. Importantly, reduction of sweet taste responses through neural manipulation resulted in overfeeding and obesity, further suggesting that sweet taste perception is a driver of obesity[10].

Evidence for association between taste, reward and morbid obesity has also been collected in the context of weight loss. Bariatric surgery is broadly accepted as the most efficient treatment for obesity, leading to significant weight loss and maintenance of weight, as well as improvement of obesity related comorbidities[11–13]. Several mechanisms have been proposed as determinants of changes in ingestive behavior following bariatric surgery, namely a global reduction of appetite, development of conditioned aversions and changes in reward-related feeding behavior[14], including modulation of taste-related reward

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[15]. Indeed, following Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG), currently the most commonly performed bariatric procedures, there is substantial evidence of self-reported decrease in consumption, cravings and preference for palatable sugar-rich and/or fat-rich foods (for review see Nance K., et al. [14]). Accordingly, patients report changes in taste perception of sweet foods after surgery [14].

However, across the several studies exploring taste perception in obesity[7,16–23], and its changes following bariatric surgery[24–30], there is a notable heterogeneity in methods and results. This has led to considerable difficulties in interpreting the available literature regarding the contribution of taste perception towards obesity. In this review, following an overview of taste physiology and psychophysical assessment of taste in humans, we will focus on studies that used direct measures of taste, using simple tastants rather than mixtures, to compare between patients with obesity and control subjects, as well as studies assessing the impact of bariatric surgery on taste perception.

2. Neurobiology of taste

Taste allows for identification and consumption of appetitive substances, like sucrose (sweet), and avoidance of potentially toxic and unpleasant compounds, such as quinine (bitter)[9]. In addition to informing feeding decisions, this system contributes to the physiological regulation of starch and fat digestion, initiated through salivary secretions[31], as well as to other elements of metabolic regulation through processes such as the cephalic phase of insulin secretion[9]. In common terms, taste is frequently used as an equivalent for flavor. However, flavor is better defined as the complex perception resulting from converging inputs from taste, texture and olfaction, induced by multisensory stimulation from foods during mastication and swallowing[32]. This review will focus primarily in taste, rather than flavor perception.

Taste buds, located in the epithelium of the tongue, palate and epiglottis, are the peripheral organs of gustation[33]. They are cell groups shaped similarly to a garlic-bulb, embedded in fungiform, foliate and circumvallate papillae, located on the anterior, lateral, and posterior regions of the tongue, respectively[9]. The taste receptor cells (TRCs) in taste buds respond to chemical stimuli dissolved in saliva, allowing for the detection of five distinct taste qualities: salt, sweet, bitter, sour (acid) and umami (savory taste of amino acids)[8,9,34]. TRCs within taste buds are classified, at least in part, according to their sensory function. In brief, Type II (receptor) cells have, in their apical surface, G-protein coupled receptors (GPCR) that are sensitive to bitter, sweet or umami tastants[34]. Type III (pre-synaptic) cells have ionotropic receptors to identify acidic stimuli (sour taste) and release GABA, serotonin and norepinephrine in synapses with neurons from cranial nerves[34]. Type I cells are glia-like [33,34] while type IV (basal) cells are undifferentiated cells located in the base of the taste bud[34]. Regarding salt taste, amiloride-sensitive epithelial sodium channels have been shown to be involved in rodents, although in humans, further research is needed[9]. Additional taste qualities have been proposed, such as that occurring via the fatty acid translocase cluster determinant 36 (CD36), that is thought to contribute, with texture perception via the somatosensory system, for identification of fat[8].

Activation of TRCs leads to neurotransmitter and peptide release onto afferent fiber terminals of cranial nerves VII, IX and X (facial, glossopharyngeal and vagus, respectively) that, in turn convey information to the central nervous system [35] specifically to the nucleus tractus solitarius, in the brainstem, that then relays neural information to the thalamus and insula[8]. The area of the insula receiving taste sensory information is the primary gustatory cortex, while areas of the orbitofrontal cortex responding to taste stimulation, as well as to other flavor-related sensory information (e.g., texture, temperature, and odor), are sometimes defined as the secondary gustatory cortex[8]. Neurons in the gustatory system also respond to the postingestive effects of food, as well as the homeostatic state[36] (for a review on peripheral and central gustatory processing see Oliveira-Maia AJ et al. 2011 [8]).

3. Psychophysical measures of taste

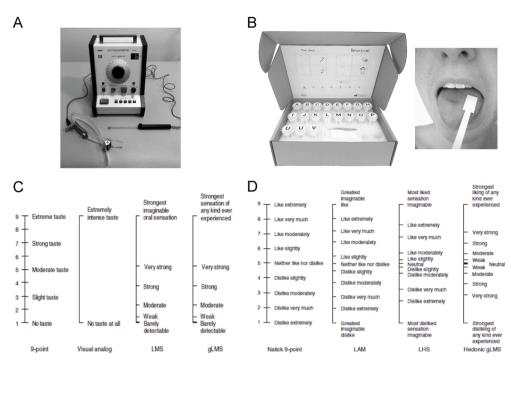
For interpretation of the literature involving taste perception in obesity, it is fundamental to understand the methods used for orosensory assessment. One of the main challenges of such assessment is to capture interindividual variability in perceptions of intensity (e.g., the perception of a soup being too salty or watered down [32]). There are two main complementary perspectives regarding intensity perception. One perspective treats intensity as a binary concept (i.e., the tastant is identified as absent or present) that is thus measured according to the threshold at which taste stimulation is identified. Both electrical (Fig. 1A) and chemical methods can be used to assess taste thresholds [32] (see Supplementary Table 1 for details). The other perspective assumes perceived intensity as a continuous construct^[32]. In this case, chemical tests (e.g. Fig. 1B) can be used with suprathreshold scaling, including the general labeled magnitude scale (gLMS) [37] which is, currently, the gold standard for this purpose (Fig. 1C; see Supplementary Table 1 for details). The general labeled hedonic scale (gLHS) [38], rather than assessing sensory-discriminative domains, assesses the degree of pleasantness, or unpleasantness, of the stimulus [14] (Fig. 1D). A full summary of methods commonly used for oral sensory assessment in humans is provided in Supplementary Table 1, highlighting their complexity and the need to consider methodological specificities in interpretation of the available data.

4. Studies of taste perception in individuals with obesity

In studies comparing taste perception between individuals with obesity and control subjects, using direct measures of taste, one of the most explored outcomes was detection and/or recognition thresholds. Distinct methods have been used, and overall, the results do not consistently support that individuals with obesity have altered taste sensitivity or require different concentrations of a specific tastant (e.g., sucrose) to detect taste (Table 1). Detailed inspection of the available data shows that 3 studies, using the constant stimuli method (see Supplementary Table 1 for details on this and other methods), did not find differences between individuals with obesity and normal weight control subjects in detection thresholds for sweet taste [18,19,26]. Another study, using the 3-stimulus drop method, found no differences relating to the presence of obesity for both detection and recognition thresholds for sweet, salt, bitter and sour tastants^[24]. Higher detection thresholds (i.e. lower taste sensitivity) in individuals with obesity relative to normal weight controls was reported for salt taste using a derivation of the method of limits among young adults[22], and for umami using the two-alternative forced-choice (2-AFC) staircase procedure in women [21]. These studies found no differences for several other tastants, including sucrose in both cases [21,22], and both quinine and citric acid in one of the studies [22]. Additionally, one of these studies revealed higher electrogustometry (EGM) thresholds in individuals with obesity, despite no correlations with chemical thresholds^[22]. While these studies provide limited evidence for higher detection thresholds for salt and umami, but not sweet, bitter or sour tastants, two other studies investigating recognition thresholds with an up-down staircase procedure found that these were lower, rather than higher, among individuals with obesity for sweet and salt, but not for bitter and sour tastants[20,23].

A study assessing acuity scores for supra-threshold concentrations of salt, bitter and sour tastants, using multiple-alternative forced-choice tests, found lower acuity among individuals with obesity[28]. This is consistent with higher detection thresholds for salt[22], but inconsistent with evidence for unchanged or lower thresholds for salt, bitter and sour, that have also been reported[20,22–24], as described above. On the other hand, and in accordance with findings of lower taste recognition thresholds for sweet and salt taste[20,23], the same studies described higher intensity ratings for these taste qualities in individuals with obesity when compared with subjects without obesity. In one of

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Fig. 1. Examples of methods used for assessment of oral sensations in humans.

A. Electrogustometer (Rion TR-06; Rion Co. Ltd., Tokyo, Japan). This equipment is commercially available for determination of electric taste thresholds. Stimulus can be applied at durations ranging from 0.5 to 2 s and current ranges from -6 dB to 34 dB, in 21 steps. The electric probe is connected to the left side of the equipment, while a neckband, that completes the circuit is connected to the other side. Reproduced from [41] with permission from Cambridge University Press, through PLSclear.

B. Taste strips test (Burghart Messtechnik GmbH, Wedel, Germany). This is a commercially available test comprising 16 containers with 4 concentrations of sweet, sour, salt and bitter as well as blank strips (image on the left, provided by Burghart Messtechnik GmbH). The strips are applied on the anterior third of the extended tongue (image on the right, reproduced from [42] with permission from Springer Nature, through RightsLink.

C. Examples of labeled scales used for intensity assessment. LMS – Labeled Magnitude Scale; gLMS – general Labeled Magnitude Scale. Adapted from [32] with permission from John Wiley & Sons, Inc, through RightsLink.

D. Examples of labeled hedonic scales. LHS – Labeled Hedonic Scale; gLMS- general Labeled Magnitude Scale. Adapted from [32] with permission from John Wiley & Sons, Inc, through RightsLink.

these studies this was shown using a 9-point scale in adolescents with early onset severe obesity[20], and in the other using a Visual Analogue Scale (VAS) in adults, where higher intensity ratings were also described for sour, but not bitter tastants[23]. However, another study also using a 9-point scale[16], as well as 3 studies using magnitude estimation [17–19] and two studies using the gLMS[7,21], did not find any differences for perceived intensity of sweet taste between weight category groups. One of the gLMS studies also did not find differences for intensity of umami taste[21].

While, for intensity assessment, studies already differ between reports of higher intensity in obesity relative to no weight-dependent differences, variability in findings for hedonic scaling is even greater, possibly due to higher sensitivity of this measure to heterogeneity of the scales used. In one study using a 9-point pleasantness scale, individuals with excess weight were shown to increase their pleasantness ratings as a factor of increasing concentrations of glucose, in contrast with normal weight individuals that found elevated concentrations of glucose increasingly less pleasant [16]. In another study using VAS, individuals with obesity reported higher pleasantness ratings for a 'relatively high' sucrose concentration (i.e. three concentration steps above their individual threshold), when compared to normal weight controls[23]. However, it has also been shown that individuals with obesity rate higher sucrose concentrations as less, rather than more, pleasant in a -4to 4 point scale [18], and several studies failed to find group differences using several distinct methods[7,17,19-21]. For other taste qualities, there are reports of lower pleasantness for salt[20], higher pleasantness for umami [21] and no weight-dependent differences for salt, sour or bitter[23].

5. Changes in taste perception following bariatric surgery

In studies conducted to test differences in taste perception following bariatric surgery, threshold estimation was also a common outcome, as shown in Table 2. Here, some[24–26,29], but not all studies[27,28,30],

revealed an improvement of taste sensitivity after bariatric surgery, but with inconsistent profiles across taste qualities. Specifically, following RYGB, there are reports of lower detection thresholds (i.e. increase in taste sensitivity) for sweet taste, using the constant stimuli method two months after surgery [26], and also for sweet taste, but not for bitter taste, up to 3 months after surgery, using an up-down/ staircase method [25]. The latter study also reported unaltered recognition thresholds for both sweet and bitter taste[25]. However, another study, using the 3-stimulus drop method, reported reduced detection and recognition thresholds up to 3 months after RYGB for sour and bitter tastants, but not for sweet or salt taste [24]. Furthermore, in two studies using the 2-AFC staircase method, and re-assessing patients after surgery at the point when approximately 20% of weight was lost, changes in detection threshold was not found for sweet, salt or umami taste after RYGB or Laparoscopic Adjustable Gastric Banding (LAGB)[27], nor for sweet or salt taste after RYGB or SG[30]. Finally, somewhat consistently with findings of reduced detection thresholds, taste acuity scores for sour, salt, sweet and bitter tastes improved 3 months after SG in one study [29], but remained unaltered 6 months following SG, LAGB or RYGB in another study [28].

Very few studies assessed suprathreshold intensity or hedonic assessments after bariatric surgery. Pepino et al. 2014 [27] showed that, in patients treated with RYGB or LAGB, following ~20% of surgically-induced weight-loss, there were no significant changes in suprathreshold intensity ratings (gLMS) for sweet, salt or umami tastants, while changes in preferences for sweet, but not umami, tastants did occur, as measured by a two-series, forced choice tracking procedure [27]. The authors also found that following RYGB, but not LAGB, the hedonic value of sucrose tasting, as measured by the gLHS, changed from pleasant to unpleasant[27]. The same group repeated this experiment in another bariatric group, following either RYGB or SG, confirming no postoperative change in suprathreshold intensity ratings (gLMS) for sweet, salt or umami taste, nor in preference for umami, but with reduction in preference and hedonic scores for sweet taste after

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Table 1

Studies that compared individuals with obesity with non-obese controls, using direct measures of taste.

Reference	Participants	N	Iethodology	Results	
		Outcome/Method	Taste stimuli/Method of application		
Rodin et al., 1976 [16]	Obese, n=16 Mildly overweight, n=16	Intensity (9-point scale) Pleasantness (9-point scale)	Glucose, 0.125-3 M Sip and taste without swallowing Glucose, 0.125–3 M	 No differences were found among weight category groups in intensity ratings. Individualswith obesity or who were mildly 	
	Normal weight, n=6 All women	Pleasantiless (9-point scale)	Sip and taste without swallowing	overweight rated higher concentrations of sweet more pleasantvs. normal weight participants.	
Thompson et al., 1977 [17]	Obese, n=14 Normal weight, n= 18	Intensity and pleasantness Magnitude estimation	Sucrose, 0.075-1.5 M Sip and taste without swallowing	- Individuals with obesity did not differ in response to sucrose vs. normal weight participants.	
	Age matched				
Grinker et al., 1978 [18]	Obese, n=39 Normal weight, n=13	Detection threshold Constant Stimuli	Sucrose, 0.175% (w/v) vs. water Sip and taste without swallowing	 Individuals with obesity did not differ in sucrose detection threshold vs. normal weight participants. 	
	Severely obese, n=39	Intensity Magnitude estimation	Sucrose, 1.95- 19.5% (w/v) Sip and taste without swallowing	- Individuals with obesity did not differ in intensity estimates vs. normal weight participants.	
	Mildly overweight, n=14 Normal weight,	Pleasantness (-4 to 4-point scale)	Sucrose, 1.95- 19.5% (w/v) Sip and taste without swallowing	- Individuals with obesity rated higher concentration of sucrose as less pleasant vs. normal weight.	
Frijters& Rasmussen-	n=13 Overweight, n=13	Detection threshold	Sucrose, 0.0006-0.02 M vs. water	- No differences between overweight vs. normal	
Conrad et al., 1982 [19]	Normal weight, n= 12	Constant stimuli Intensity	Sip and taste without swallowing Sucrose, 0.06-1.3 M	weight participants were found in any parameter.	
	All women	Magnitude estimation Liking (170 mm liking scale)	Sip and taste without swallowing Sucrose, 0.06–1.3 M		
Scruggs et al., 1994	Obese, n=6	Detection and recognition	Sip and taste without swallowing HCL, 0.5-500 mMvs. water	- Individuals with obesity did not differ in detection	
[24]	Normalweight,	thresholds	Urea, 90-5.000 mMvs. water	or recognition thresholds vs. normal weight	
	n=10	-stimulus drop	Sucrose, 6-5.8000 mMvs. water	participants.	
	All women		NaCl, 6-6.100 mM vs. water Calibrated drops placed on the tongue.		
Pasquet et al., 2007	Severe early onset	Recognition threshold	Sucrose and fructose, 2.0-1000 mM	- Adolescents with obesity had significantly lower	
[20]	obesity, n=39	Up-down/staircase	Citric acid, 0.40-25mM	recognition thresholds for sucrose and NaCl vs. no	
	Non-obese, n=48 Adolescents		NaCl, 1.77-1000 mM Quinine HCl, 0.4-400 mM PROP, 0.001-3.2 mM	obese participants.	
			Sip and taste without swallowing		
		Intensity (9-point scale)	Sucrose, 121- 970 mM NaCl, 32- 1000 mM Sip and taste without swallowing	 Adolescents with obesity rated sweet and salty tastants as more intense vs. non-obeseparticipants. 	
		Pleasantness (9-point scale)	Sucrose, 121- 970 mM NaCl, 32- 1000 mM	- Adolescents with obesity rated the lowest NaCl solution less pleasant, but not sucrose.	
Domine et al. 2010	Ohana n. 92	Detection threshold	Sip and taste without swallowing. Sucrose and MSG, 1 - 5.6×10^{-5} M vs.	Warran with chasity had significantly high or	
Pepino et al., 2010 [21]	Obese, n=23 Normal-weight, n=34	Detection threshold, 2-AFC staircase	water Sip and taste without swallowing	 Women with obesity had significantly higher detection thresholds for MSG,but not sucrose, whe compared to normal-weight participants. 	
	All women	Intensity (gLMS)	Sucrose, 0-1.05 M MSG, 0-0.18 M	- Women with obesity did not differ in intensity ratings given to MSG or sucrose vs. normal weight	
			Sip and taste without swallowing	participants.	
		Preferred concentration	Sucrose, 0.09-1.05 M	- Women with obesity preferred higher	
		Two series, forced choice tracking procedure	MSG, 0.005-0.064 M Sip and taste without swallowing	concentrations of MSG, but not sucrose, when compared to normal-weightparticipants.	
Bueter et al., 2011	Obese, n=9	Detection thresholds	Sucrose, 2.1-300 mM vs. water	- Individuals with obesity did not differed in sucro	
[26] Park et al., 2015	Normal weight, n=9 Obese, n=18	Constant Stimuli Detection thresholds	Sip and taste without swallowing Sucrose, 0.05-2.0 g/mL	detection threshold vs. normal weight participants - Individuals with obesity had significantly higher	
[22]	Normalweight,	Method of limits (derivation)	NaCl, 0.016-0.9 g/mL	detection thresholds for NaCl vs.normal weight	
	n=23 Voung adulta		Quinine HCl, 10 ⁻⁵ -0.03 g/mL Citric acid, 0.05-0.6 g/mL	participants.	
	Young adults				
	Toung aduits	Electrogustometry (EGM)	Cotton swab (whole mouth test) 22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and	- Individuals with obesity had significantly higher EGM thresholds on both sides of the posterior tong	
	-		22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally.	EGM thresholds on both sides of the posterior tongo vs. normal weight participants.	
Holinski et al., 2015 [28]	Obese, n=44: Non-obese, n=23	Taste acuity (multiple- alternative forced-choice	22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally. Sucrose, 0.05-0.4 g/mL Citric acid, 0.05-0.3 g/mL	EGM thresholds on both sides of the posterior tong	
	Obese, n=44:	Taste acuity (multiple- alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH,	22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally. Sucrose, 0.05-0.4 g/mL Citric acid, 0.05-0.3 g/mL NaCl, 0.016-0.25 g/mL Quinine HCl, 0.0004-0.006 g/mL Strips were applied to the midline of the	EGM thresholds on both sides of the posterior tongr vs. normal weight participants. - Individualswith obesity had lower overall taste	
	Obese, n=44: Non-obese, n=23	Taste acuity (multiple- alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH, Wedel, Germany	22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally. Sucrose, 0.05-0.4 g/mL Citric acid, 0.05-0.3 g/mL NaCl, 0.016-0.25 g/mL Quinine HCl, 0.0004-0.006 g/mL Strips were applied to the midline of the anterior third of the tongue.	EGM thresholds on both sides of the posterior tongo vs. normal weight participants. - Individualswith obesity had lower overall taste acuity scores vs. non-obese participants.	
	Obese, n=44:	Taste acuity (multiple- alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH,	22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally. Sucrose, 0.05-0.4 g/mL Citric acid, 0.05-0.3 g/mL NaCl, 0.016-0.25 g/mL Quinine HCl, 0.0004-0.006 g/mL Strips were applied to the midline of the	EGM thresholds on both sides of the posterior tongt vs. normal weight participants. - Individualswith obesity had lower overall taste	
[28] Pepino et al., 2016	Obese, n=44: Non-obese, n=23 Obese, n=24	Taste acuity (multiple- alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH, Wedel, Germany Intensity (gLMS) Preferred concentration Two series, forced choice	22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally. Sucrose, 0.05-0.4 g/mL Citric acid, 0.05-0.3 g/mL NaCl, 0.016-0.25 g/mL Quinine HCl, 0.0004-0.006 g/mL Strips were applied to the midline of the anterior third of the tongue. Sucrose, 0.00-1.05 M	EGM thresholds on both sides of the posterior tongo vs. normal weight participants. - Individualswith obesity had lower overall taste acuity scores vs. non-obese participants. - Individuals with obesity did not differ in any	
[28] Pepino et al., 2016	Obese, n=44: Non-obese, n=23 Obese, n=24	Taste acuity (multiple- alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH, Wedel, Germany Intensity (gLMS) Preferred concentration	22 possible EGM thresholds(8 dB to 34 dB)were measured on the anterior and posterior tongue, bilaterally. Sucrose, 0.05-0.4 g/mL Citric acid, 0.05-0.3 g/mL NaCl, 0.016-0.25 g/mL Quinine HCl, 0.0004-0.006 g/mL Strips were applied to the midline of the anterior third of the tongue. Sucrose, 0.00-1.05 M Sip and taste without swallowing Sucrose, 0.09-1.05 M	EGM thresholds on both sides of the posterior tongo vs. normal weight participants. - Individualswith obesity had lower overall taste acuity scores vs. non-obese participants. - Individuals with obesity did not differ in any	

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Table 1 (continued)

Reference	Participants	Methodology		Results	
		Outcome/Method	Taste stimuli/Method of application		
	Obese, n=23 Normalweight, n=31		Quinine HCL, 0.0001-0.025 g/100 mL Citric acid, 0.001-0.9 g/100 mL Spray dispenser (0.2 mL bolus of each tastant administered in the anterior part of the tongue).	- Individuals with obesity had significantly lower recognition thresholds for sucrose and NaCl vs. normal weight participants.	
		Intensity (VAS)	Sucrose, 0.01–20 g/100 mL NaCl, 0.01–5 g/100 mL Quinine HCL, 0.0001–0.025 g/100 mL Citric acid, 0.001–0.9 g/100 mL Spray dispenser (0.2 mL bolus of each tastant administered in the anterior part of the tongue).	- Individuals with obesity rated the lower concentrations of sucrose, NaCl and citric acid as more intense vs. normal weight participants.	
		Pleasantness (VAS)	Sucrose, 0.01–20 g/100 mL NaCl, 0.01–5 g/100 mL Quinine HCL, 0.0001–0.025 g/100 mL Citric acid, 0.001–0.9 g/100 mL Spray dispenser (0.2 mL bolus of each tastant administered in the anterior part of the tongue).	- Individuals with obesity rated one of the higher concentrations of sucrose as more pleasantvs. norma weight participants.	

Notes: Sucrose, glucose and fructose are tastants for sweet taste; sodium chloride (NaCl) for salty, citric acid and hydrochloric acid (HCl) for sour, quinine hydrochloride (HCl) and 6-n-propylthiouracil (PROP) for bitter and monosodium glutamate (MSG) for umami.

Abbreviations: 2-AFC staircase - Two-alternative forced-choice staircase procedure; gLMS - general labeled magnitude scale; VAS - Visual Analogue Scale.

both surgery types[30]. However, in work from another group, assessments of the 'just about right' concentration for sucrose, with ratings given on a VAS, did not reveal changes after RYGB[26]. Globally, the available literature does not support changes in the sensory-discriminative component of taste perception induced by bariatric surgery, but provides limited evidence in support of changes of reward-related and hedonic assessments, namely of sweet taste.

6. Discussion

In this review we provide perspective on the data available to support, or contradict, the general interpretation that individuals with obesity have reduced sweet taste perception, as is frequently proposed [9]. This interpretation has typically been framed jointly with the evidence for decreased availability of striatal D_2R in individuals with obesity, with both gustatory and dopaminergic factors proposed to contribute towards compensatory food consumption and weight gain [9]. In fact, in flies there is pre-clinical evidence that a high sugar diet results in diminished sweet perception, via decreased response of 'sweet-taste sensing neurons' [10]. Furthermore, in healthy human volunteers, reduction of sugar consumption has been shown to result in increased perception of sweet taste intensity, while pleasantness ratings remained unaltered[39]. Finally, a single nucleotide polymorphism, identified in humans, has been associated with higher perceived intensity of several sweet compounds, as well as with consumption of sweet foods[40], which may contribute towards interindividual differences in weight. As is shown here, however, the available studies directly assessing pure taste function of individuals with obesity, either comparing with normal weight control subjects, or assessing changes following bariatric surgery, do not clearly support the general interpretation regarding reduced sweet taste perception in obesity.

Studies comparing sweet taste detection thresholds between participants with and without obesity have found no differences[18,19,21,24, 26]. On the other hand, some[20,23], but not all studies[24], have described reduced recognition thresholds among individuals with obesity, that suggest enhanced, rather than reduced, sweet taste sensitivity. Inconsistently, after bariatric surgery there is limited evidence of reduced sweet taste detection thresholds[24–27,30], thus suggesting enhanced sweet taste sensitivity with weight loss, and no evidence of change in recognition thresholds[24,25]. Regarding suprathreshold sweet taste intensity assessments, while most studies find no obesity-dependent [7,16–19,21] or bariatric surgery-dependent [27,30] effects, reports of increased intensity ratings among individuals with obesity are available in two studies[20,23]. For other taste qualities, while there is less evidence that is mostly negative, some studies reveal increased detection thresholds[21,22], reduced recognition thresholds [20,23] or higher intensity ratings [20,23] in individuals with obesity, as well as reduced detection [24] or recognition [24] thresholds after bariatric surgery.

Regarding the hedonic dimension of taste, comparisons between individuals with obesity and normal-weight controls were mostly inconclusive, with no evidence of differences in sweet taste among participants with obesity in 4 studies[7,19–21], nor in salt, bitter or sour tastes in other studies[20,23]. Other studies, however, revealed increased[16,23], or reduced[18], hedonic ratings for sweet taste, reduced hedonic ratings for salt tastants [20] and increased preference for umami taste[21], among individuals with obesity. While studies after bariatric surgery are scarce, two of these studies support adjustments of sweet taste perception leading to lower preferences and hedonic scores[27,30]. However, confidence in the results of available research is limited, given methodological variability between studies, small sample sizes, and lack of adequate controls in longitudinal studies. More studies, with larger patient samples, are needed to address limitations of previous research.

In fact, we have very recently published results of a multicenter longitudinal cohort, recruiting more than 200 bariatric patients, and showing similar variation in suprathreshold intensity and pleasantness ratings of several tastants, including sweet, between those treated with bariatric surgery and a control group awaiting surgery. While our research is consistent with limited overall effects of bariatric surgery on taste, patients with higher sweet intensity ratings before surgery lost more weight, and reduction of sweet intensity ratings correlated with weight loss [43]. These findings, suggesting that associations between taste and bariatric surgery may be better interpreted at the individual, rather than the group level, are consistent with other recent work testing liking ratings for sucrose-sweetened mixtures containing fat, and showing that, in patients receiving RYGB, but not SG, higher preoperative preference for sucrose-sweetened mixtures, as well as activation of the ventral tegmental area by those mixtures, predicted greater weight loss[15]. Hypotheses considering interactions between sweet preferences and dopamine-related brain neural activity may thus be relevant for weight-loss induced by bariatric surgery, and should be further assessed in future research .

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Table 2

Studies that followed individuals with obesity before and after bariatric surgeryusing direct measures of taste.

Reference	Participants	Surgery/Follow-up	N	lethodology	Results
			Outcome/Method	Taste stimuli/Method of application	
Scruggs et al., 1994 [24]	Obese, n=6 All women	RYGB Pre, 1, 2 and 3 months postoperatively.	Detection/ Recognition thresholds 3-stimulus drop	HCL, 0.5-500 mMvs. water Urea, 90-5.000 mMvs. water Sucrose, 6-5.8000 mMvs. water NaCl, 6-6.100 mM vs. water Calibrated drops of the taste solutions/ water were placed on the tongue at identical locations.	- Following surgery there was a decrease in detection/recognition thresholds for HCL and urea, but not for sucrose or NaCl.
Burge et al., 1995 [25]	Obese, n=14	RYGB Pre, 1.5and 3monthspostoperatively.	Detection/ Recognition thresholds Up-down/staircase	Sucrose, 0.01-0.1 mol/L Urea, 0.01-0.5 mol/L Sip and taste without swallowing	- Following 1.5 months after surgery, detection thresholds for sucrose significantly decreased and remained so at 3 months.
Bueter et al., 2011 [26]	Obese, n=9 Normal weight, n=9 Obese, n=10 Normalweight, n=9	RYGB 1-week pre and 2 months postoperatively. Controls were tested at similar time points.	Detection thresholds Constant Stimuli 'Just about right' concentration (200 mm VAS)	Sucrose, 2.1-300 mM vs. water Sip and taste without swallowing Sucrose, 0-400 mM Sip and taste without swallowing	 Following surgery, patients had decreased detection thresholds for the lowest sucrose concentrations vs. controls. Following surgery there were no changes in the "just about right" concentration of sucrose vs. controls.
Pepino et al., Obese, 2014 [27] - RYGB, - LAGB,	Obese, n=27: - RYGB, n=17 - LAGB, n= 10	RYGB LAGB Before surgery and after ~20% surgically-induced weight loss	Detection thresholds 2-AFC staircase	Sucrose, MSG and NaCl All $1-10^{-4}$ M vs. water Sip and taste without swallowing	- Following surgery there were no changes in taste thresholdseither in RYGB or LAGB.
			Intensity (gLMS)	Sucrose, 0-1.05 M Glucose, 0-1.0 M NaCl, 0-0.56 M MSG, 0-0.18 M Sip and taste without swallowing	- Following surgery there were no changes in suprathreshold intensity ratings for any tastant.
			Preferred concentration Two series, forced choice tracking procedure	Sucrose, 0.09-1.05 M MSG, 0.018-0.180 M Sip and taste without swallowing	- Following surgery, both in RYGB and LAGB groups lower concentrations of sucrose were preferred.
	Obese, n=44:	LAGB	Sweet taste palatibility (gLHS and gLMS) Taste acuity	Sucrose 24% w/v Sip and taste without swallowing Sucrose, 0.05-0.4 g/ml	 Following RYGB, but not LAGB, the hedonic value of sucrose (gLHS) changed from pleasant to unpleasant. Six months after surgery, taste acuity was
et al., 2015 [28]	- Pre-SG, n=37 - Pre-LAGB, n=4 - Pre-RYGB, n=3 Non-obese, n=23	SG RYGB Pre, 0.5, 0.75 and 6 monthspostoperatively.	(multiple-alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH, Wedel, Germany	Citric acid, 0.05-0.3 g/ml NaCl, 0.016-0.25 g/ml Quinine HCl, 0.0004-0.006 g/ ml Strips were applied to the midline of the anterior third of the tongue.	not significantly different from controls.
Altun et al., 2016 [29]	Obese, n=52	SG Pre, 1 and 3 months postoperatively.	Taste acuity (multiple-alternative forced-choice paradigm) Taste strips Burghart Messtechnik GmbH, Wedel, Germany	Sucrose, 0.05-0.4 g/ml Citric acid, 0.05-0.3 g/ml NaCl, 0.016-0.25 g/ml Quinine HCl, 0.0004-0.006 g/ ml Strips were applied tothe anterior region of the tongue.	- Three months after surgery there was a significant increase in taste acuity for all tastants across the follow-up.
Nance et al., 2017 [30]	Obese, n=31: - Pre-RYGB, n=23 -Pre-SG, n=8	RYGB SG Before surgery and after ~20% surgically-induced weight loss	Detection thresholds 2-AFC staircase	Sucrose, glucose and NaCl, 1×10^{-4} -1M vs. water Sip and taste without swallowing	- There wasno changein detection thresholds after RYGB or SG.
			Intensity (gLMS)	Sucrose, 0.90-1050 mmol/L Glucose, 0.00-1000 mmol/L NaCl, 0.00-560 mmol/L MSG, 0.00-180 mmol/L Sip and taste without swallowing	- There were no changesin perceived intensities after RYGB or SG.
			Preferred concentration Two series, forced choice tracking procedure	Sucrose, 90-1005 mmol/L MSG, 18-180 mmol/L (warmed) Sip and taste without swallowing	 Following surgery, both in RYGB and SG groups lower concentrations of sucrose were preferred.
			Sweet taste palatibility (gLHS and gLMS)	Sucrose 24% w/v Sip and taste without swallowing	- Following both RYGB and SG, the hedonic of sucrose changed from pleasant to unpleasant.

Notes: Sucrose, and glucose are tastants for sweet taste; sodium chloride (NaCl) for salty, quinine hydrochloride and urea for bitter; citric acid and hydrochloric acid (HCl) for sour and monosodium glutamate (MSG) for umami.

Abbreviations: 2-AFC staircase - Two-alternative forced-choice staircase procedure; gLHS - general labeled hedonic scale; gLMS - general labeled magnitude scale; LAGB- Laparoscopic Adjustable Gastric Banding; RYGB - Roux-en-Y Gastric Bypass; SG - Sleeve Gastrectomy; VAS - Visual Analogue Scale.

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7. Conclusions

Available research suggests that changes of sweet taste with obesity and weight-loss may be more complex than simply considering decreased sweet taste perception. However, there are several indications that sweet taste may be related to weight and, importantly, that it may be a useful marker in the context of bariatric surgery, suggesting the need for further research with refined methods and large sample sizes.

Declaration of Competing Interest

Competing interests are not reported by Ribeiro. Oliveira-Maia is recipient of a grant from Schuhfried GmBH for norming and validation of cognitive tests, and national coordinator for Portugal of a Noninterventional Study (EDMS-ERI-143085581, 4.0) to characterize a Treatment-Resistant Depression Cohort in Europe, sponsored by Janssen-Cilag Ltd, and a of a trial of psilocybin therapy for treatmentresistant depression, sponsored by Compass Pathways, Ltd (EudraCT NUMBER: 2017–003288–36).

Authors Contributions

Ribeiro conducted the literature search. Ribeiro and Oliveira-Maia wrote the manuscript and approved the final version.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2021.01.023.

References

- Bray GA, Kim KK, Wilding JPH. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. Obes Rev 2017;18 (7):715–23. https://doi.org/10.1111/obr.12551.
- [2] Mullee A, Romaguera D, Pearson-Stuttard J, et al. Association between soft drink consumption and mortality in 10 european countries. JAMA Intern Med 2019: e192478. https://doi.org/10.1001/jamainternmed.2019.2478.
- [3] Stice E, Burger K. Neural vulnerability factors for obesity. Clin Psychol Rev 2019; 68:38–53. https://doi.org/10.1016/j.cpr.2018.12.002.
- [4] Tan H-E, Sisti AC, Jin H, et al. The gut-brain axis mediates sugar preference. Nature 2020;580(7804):511-6. https://doi.org/10.1038/s41586-020-2199-7.
- [5] Fernandes AB, Alves da Silva J, Almeida J, et al. Postingestive modulation of food seeking depends on vagus-mediated dopamine neuron activity. Neuron 2020;106 (5):778–88. https://doi.org/10.1016/j.neuron.2020.03.009. e6.
- [6] de Araujo IE, Oliveira-Maia AJ, Sotnikova TD, et al. Food reward in the absence of taste receptor signaling. Neuron 2008;57(6):930–41. https://doi.org/10.1016/j. neuron.2008.01.032.
- [7] Pepino MY, Eisenstein SA, Bischoff AN, et al. Sweet dopamine: sucrose preferences relate differentially to striatal D2 receptor binding and age in obesity. Diabetes 2016;65(9):2618–23. https://doi.org/10.2337/db16-0407.
- [8] Oliveira-Maia AJ, Roberts CD, Simon SA, Nicolelis MA. Gustatory and reward brain circuits in the control of food intake. Adv. Tech. Stand Neurosurg 2011:31–59. https://doi.org/10.1007/978-3-7091-0179-7_3.

- [9] Gutierrez R, Fonseca E, Simon SA. The neuroscience of sugars in taste, gut-reward, feeding circuits, and obesity. Cell Mol Life Sci 2020;77(18):3469–502. https://doi. org/10.1007/s00018-020-03458-2.
- [10] May CE, Vaziri A, Lin YQ, et al. High dietary sugar reshapes sweet taste to promote feeding behavior in drosophila melanogaster. Cell Rep 2019;27(6):1675–85. https://doi.org/10.1016/j.celrep.2019.04.027. e7.
- [11] Dicker D, Yahalom R, Comaneshter DS, Vinker S. Long-term outcomes of three types of bariatric surgery on obesity and type 2 diabetes control and remission. Obes Surg 2016;26(8):1814–20. https://doi.org/10.1007/s11695-015-2025-8. PMID: 26718983.
- [12] Cătoi AF, Pârvu A, Mureşan A, Busetto L. Metabolic mechanisms in obesity and type 2 diabetes: insights from bariatric/metabolic surgery. Obes Facts 2015;8(6): 350–63. https://doi.org/10.1159/000441259.
- [13] Sjostrom L., Narbro K., Sjostrom C.D., et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med.2007;357(8):741–52. doi: 10.1056/ NEJMoa066254.
- [14] Nance K, Acevedo MB, Pepino MY. Changes in taste function and ingestive behavior following bariatric surgery. Appetite 2020;146:104423. https://doi.org/ 10.1016/j.appet.2019.104423.
- [15] Smith KR, Papantoni A, Veldhuizen MG, et al. Taste-related reward is associated with weight loss following bariatric surgery. J Clin Invest 2020;130(8):4370–81. https://doi.org/10.1172/JCI137772.
- [16] Rodin J, Moskowitz HR, Bray GA. Relationship between obesity, weight loss, and taste responsiveness. Physiol Behav 1976;17(4):591–7. https://doi.org/10.1016/ 0031-9384(76)90157-8.
- Thompson DA, Moskowitz HR, Campbell RG. Taste and olfaction in human obesity. Physiol Behav 1977;19(2):335–7. https://doi.org/10.1016/0031-9384(77)90348-1
- [18] Grinker J. Obesity and sweet taste. Am J Clin Nutr 1978;31(6):1078–87. https:// doi.org/10.1093/ajcn/31.6.1078.
- [19] Frijters JE, Rasmussen-Conrad EL. Sensory discrimination, intensity perception, and affective judgment of sucrose-sweetness in the overweight. J Gen Psychol 1982;107(2d Half):233–47. https://doi.org/10.1080/00221309.1982.9709931.
- [20] Pasquet P, Frelut ML, Simmen B, Hladik CM, Monneuse MO. Taste perception in massively obese and in non-obese adolescents. Int J Pediatric Obes 2007;2(4): 242–8. https://doi.org/10.1080/17477160701440521.
- [21] Pepino MY, Finkbeiner S, Beauchamp GK, Mennella JA. Obese women have lower monosodium glutamate taste sensitivity and prefer higher concentrations than do normal-weight women. Obesity (Silver Spring, Md) 2010;18(5):959–65. https:// doi.org/10.1038/oby.2009.493.
- [22] Park DC, Yeo JH, Ryu IY, Kim SH, Jung J, Yeo SG. Differences in taste detection thresholds between normal-weight and obese young adults. Acta Otolaryngol 2015;135(5):478-83. https://doi.org/10.3109/00016489.2014.975370.
- [23] Hardikar S, Hochenberger R, Villringer A, Ohla K. Higher sensitivity to sweet and salty taste in obese compared to lean individuals. Appetite 2017;111:158–65. https://doi.org/10.1016/j.appet.2016.12.017.
- [24] Scruggs DM, Buffington C, Cowan GS. Taste acuity of the morbidly obese before and after gastric bypass surgery. Obes Surg 1994;4(1):24–8. https://doi.org/ 10.1381/096089294765558854.
- [25] Burge JC, Schaumburg JZ, Choban PS, DiSilvestro RA, Flancbaum L. Changes in patients' taste acuity after Roux-en-Y gastric bypass for clinically severe obesity. J Am Diet Assoc 1995;95(6):666–70. https://doi.org/10.1016/S0002-8223(95) 00182-4.
- [26] Bueter M, Miras A, Chichger H, et al. Alterations of sucrose preference after Rouxen-Y gastric bypass. Physiol Behav 2011;104(5):709–21. https://doi.org/10.1016/ j.physbeh.2011.07.025.
- [27] Pepino MY, Bradley D, Eagon JC, Sullivan S, Abumrad NA, Klein S. Changes in taste perception and eating behavior after bariatric surgery-induced weight loss in women. Obesity 2014;22(5):E13–20. https://doi.org/10.1002/oby.20649.
- [28] Holinski F, Menenakos C, Haber G, Olze H, Ordemann J. Olfactory and gustatory function after bariatric surgery. Obes Surg 2015;25(12):2314–20. https://doi.org/ 10.1007/s11695-015-1683-x.
- [29] Altun H, Hanci D, Altun H, et al. Improved gustatory sensitivity in morbidly obese patients after laparoscopic sleeve gastrectomy. Ann. Otol, Rhinol Laryngol 2016; 125(7):536–40. https://doi.org/10.1177/0003489416629162.
- [30] Nance K, Eagon JC, Klein S, Pepino MY. Effects of sleeve gastrectomy vs. Roux-en-Y gastric bypass on eating behavior and sweet taste perception in subjects with obesity. Nutrients 2017;10(1):18. https://doi.org/10.3390/nu10010018.
- [31] Matsuo R, Carpenter GH. The role of saliva in taste transduction. In: Doty LR, editor. Handbook of olfaction and gustation. 3rd ed. USA: John Wiley & Sons, Inc.; 2015. p. 625–36.
- [32] Snyder DJ, Sims CA, Bartoshuk LM. Psychophysical measures of human oral sensation. In: Doty LR, editor. Handbook of olfaction and gustation. 3rd ed. USA: John Wiley & Sons, Inc.; 2015. p. 751–73.
- [33] Roper SD, Chaudhari N. Taste buds: cells, signals and synapses. Nat Rev Neurosci 2017;18(8):485–97. https://doi.org/10.1038/nrn.2017.68.
- [34] Witt M, Reutter K. Anatomy of the tongue and taste buds. In: Doty LR, editor. Handbook of olfaction and gustation. 3rd ed. USA: Wiley & Sons, Inc.; 2015. p. 637–64.
- [35] Small DM, Faurion A. Mapping brain activity in response to taste stimulation. In: Doty LR, editor. Handbook of olfaction and gustation. 3rd ed. USA: John Wiley & Sons, Inc.; 2015. p. 775–94.
- [36] Vincis R, Fontanini A. Central taste anatomy and physiology. Handb Clin Neurol 2019;164:187–204. Elsevier.

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- [37] Green BG, Dalton P, Cowart B, Shaffer G, Rankin K, Higgins J. Evaluating the 'Labeled Magnitude Scale' for measuring sensations of taste and smell. Chem Senses 1996;21(3):323–34. https://doi.org/10.1093/chemse/21.3.323.
- [38] Lim J, Wood A, Green BG. Derivation and evaluation of a labeled hedonic scale. Chem Senses 2009;34(9):739–51. https://doi.org/10.1093/chemse/bjp054.
- [39] Wise PM, Nattress L, Flammer LJ, Beauchamp GK. Reduced dietary intake of simple sugars alters perceived sweet taste intensity but not perceived pleasantness. Am J Clin Nutr 2016;103(1):50–60. https://doi.org/10.3945/ajcn.115.112300.
- [40] Hwang LD, Lin C, Gharahkhani P, et al. New insight into human sweet taste: a genome-wide association study of the perception and intake of sweet substances. Am J Clin Nutr 2019;109(6):1724–37. https://doi.org/10.1093/ajcn/nqz043.

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- [41] Hawkes C, Doty R. Measurement of Gustation. Smell and Taste Disorders. Cambridge: Cambridge University Press; 2018. p. 138–81. https://doi.org/ 10.1017/9781139192446.005.
- [42] Landis BN, Welge-Luessen A, Brämerson A, Bende M, Mueller CA, Nordin S, et al. "Taste Strips" - a rapid, lateralized, gustatory bedside identification test based on impregnated filter papers. J Neurol 2009;256(2):242–8. https://doi.org/10.1007/ s00415-009-0088-y. 242 (2009).
- [43] Ribeiro G, Camacho M, Fernandes AB, Cotovio G, Torres S, Oliveira-Maia AJ, Food Reward in Bariatric Surgery Portuguese Study Group. Reward-related gustatory and psychometric predictors of weight loss following bariatric surgery: a multicenter cohort study. Am J Clin Nutr 2021:nqaa349. https://doi.org/10.1093/ ajcn/nqaa349. In press.