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Salivary gland biometry in female patients with eating disorders

Alessandro Bozzato · Pascal Burger ·
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Abstract High-resolution greyscale ultrasound is a generally accepted diagnostic tool for salivary gland enlargement, although no standard biometrical data for the sizes of unaffected parotid and submandibular glands exist. A lot of case reports describe non-inflammatory swelling of salivary glands as symptoms of eating disorders like anorexia nervosa or bulimia nervosa. They might be the only visible sign for the disease. With our prospective study we tried to quantify and compare biometrically the salivary gland in eating disordered patients, obese and normal-weight, healthy controls. A total of 70 females between 16 and 40 years of age were included of which 25 were healthy controls. All subjects underwent three-dimensional high resolution B-scan sonography of the parotid and submandibular gland. Gland volumes were calculated and a multiple regression analysis was done to investigate the

influence of an eating disorder on salivary gland size. A significant difference in the size of the parotid glands was seen between our three study groups of adipose and eating disordered patients and healthy, normal-weight controls. The parotid gland volumes were seen in the subgroup bulimia nervosa (BN), (parotid volume = 63,708 mm³) where the mean value was more than twice as high as in the control group (31,059 mm³). By using body mass index and group characteristic the parotid gland volume as the dependent variable could be estimated with an r^2 of 0.327 in multiple regression analysis. Only the parotid glands were significantly enlarged, while the submandibular glands show no signs of enlargement. Eating disorders influence size of parotid glands, still the factors and the pathogenesis leading to this enlargement seem to be different in adiposity on the one and different types of eating disorders on the other hand. Standard gland volumes could be established, comparable to former initial reports. Submandibular gland remains unaffected by these alterations. We could show that high-resolution ultrasound assessment of parotid gland volume adds a complementary quantitative parameter of organ affection in eating disorders (anorexia/bulimia nervosa).

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Introduction

Modern, high-resolution B-scan sonography has become an approved method in head and neck imaging. In the majority of clinically unclear cases of salivary gland enlargement depiction of topographic localisation and three-dimensional measurement of tumours and parenchyma can be achieved without difficulty. Although widely

used, no standard measurements for the sizes of parotid and submandibular glands in B-scan sonography exist. Even though there are some approximated values regarding length, width and depth volumetric assessment is problematic because of the irregular form of the glands, which cannot be estimated by the usage of a mathematical formula as commonly used for abdominal organs. Due to that, salivary gland enlargement is frequently approximated according to intuition and bilateral comparison.

A lot of case reports describe non-inflammatory swelling of the salivary glands—especially the parotid glands—as symptoms of eating disorders like anorexia nervosa or bulimia nervosa. These bilateral, painless, diffuse enlargements of the salivary glands are intermittent or persistent symptoms in up to 50% of the patients suffering from bulimia [1–7]. They might be the only visible sign for the disease.

As well as in eating disorders also in obesity body mass index (BMI) > 30 an enlargement particularly of the parotid glands was described [1, 8–10].

With our prospective cross sectional study our aim was to quantify biometrically the salivary gland size in three study groups—obese patients, eating disordered patients and normal-weight, healthy controls—and compared the results found with each other.

Subjects and methods

A total of 70 women between 16 and 40 years of age, before their menopauses, were included in the study. Smoking and contraception were allowed while pregnancy, lactation, hysterectomy were exclusion criteria. Our healthy controls needed to have a BMI between 18 and 25, no history of eating disorders in their past, no intake of corticoids or salivary gland disease stated in the case history. In the obese group women with a BMI > 30 before as well as after obesity surgery (gastric banding, gastric bypass) were included. In the eating disordered group the participants had to meet the DSM-IV guidelines for anorexia or bulimia nervosa and hand in a questionnaire (EDE-Q “Eating Disorder Examination Questionnaire” by Fairburn, 1994).

A total of 25 controls (age 22.6 ± 2.1 years; BMI 20.8 ± 1.5 kg/m²), 22 obese patients (age 32.3 ± 7.7 years; BMI 45.4 ± 9.4 kg/m²) and 23 women with an eating disorder—7 anorexia nervosa and 18 bulimia nervosa patients—(age 23.8 ± 6.2 years; BMI 19.1 ± 2.6 kg/m²) attended the study. This study had the approval of the local ethical committee. Personal data was collected by the usage of a questionnaire along with written informed consent from all participants. The questionnaire gathered information about the participant’s age, weight, height,

BMI, disease, patient history, medical history, smoking habits, medication, contraception and menstruation.

Ultrasound investigation of the salivary glands

A complete ultrasound B-scan investigation of the head and neck was done, using a modern ultrasound device (Acuson Antares, Siemens Medical Solutions USA, Inc.) with a multifrequency transducer. The parotid and submandibular glands were measured similar to the protocol by Dost [11] in length, width and depth (Figs. 1, 2 3).

Concerning the parotid gland the length was measured in a transversal, the width in a ramus-parallel plane. Its depth contained the superficial and the deep part of the gland. We chose a depth of penetration of 45–70 mm in order to estimate the deep parts of the gland sufficiently. The measurements of the submandibular gland were done in the paramandibular and the frontal plane. Distinctive features in the sonographic texture were also documented separately.

Measurement and statistic analysis

For this analysis the measurements for length, width and depth of each salivary gland, determined by B-scan sonography, were combined in order to get one single value

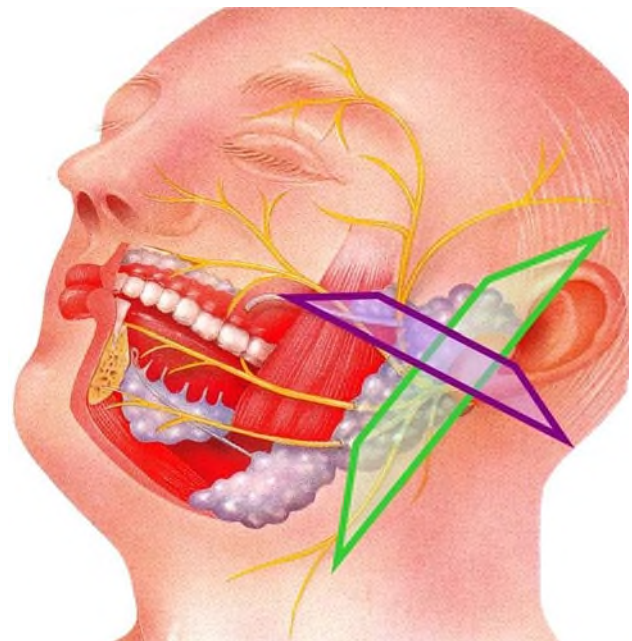


Fig. 1 Measurement of the parotid gland in two planes (modified after [12])

Fig. 2 Measurement of the parotid gland in B-scan sonography in transverse plane. *MSCM* sternocleidomastoid muscle, *VR* retromandibular vein, *GP* parotid gland, *UK* mandible, *MASS* masseter muscle

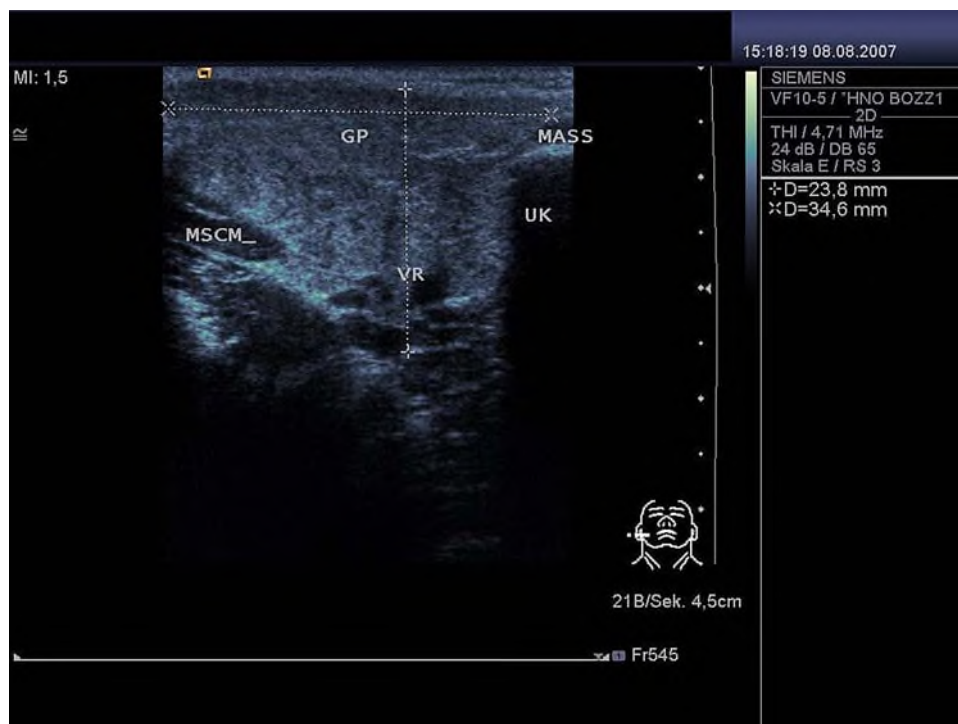


Fig. 3 Measurement of the submandibular gland in B-scan sonography in coronar plane. *T* tonsil, *ZU* tongue



for the gland. Following the irregular shape of the glands a single value cannot be found as easily as by using the Simpson's method (used for abdominal organs) [11]. For that we calculated a virtual value for the salivary gland's volumes in order to be able to compare the study groups to each other.

At first the values measured for length, width and depth for each gland were combined with each other to get a sterical value (mm^3). Then those gland-values for each side (left, right) were added. Because there were no significant differences described in studies between the values measured for left and right side and the parameter-value gland

enlargement is bilaterally equal we now divided the result of our addition by two. After this we had an average value for the volume of the respective gland. In order to incorporate the irregular, ellipsoid shape of the glands we multiplied our result by a correction factor of 0.8.

Formula: $\{[\text{left gland : length (mm)} \times \text{width (mm)} \times \text{depth (mm)}] + [\text{right gland : length (mm)} \times \text{width (mm)} \times \text{depth (mm)}]\} / 2 \times (0.8) = \text{gland volume } V.$

Metzger et al. [3] proposed in their study to calculate the salivary gland volume according to the spheric volume ($V = 4/3 \times r_1 \times r_2 \times r_3 \times \pi$). Only in order to compare our results to Metzger's we calculated the same way with our measurements. For all our other calculations we used our formula (as mentioned above) because the irregular and ellipsoid shape of the salivary glands could not be adequately reflected by the spheric volume.

The statistic analysis was done by the usage of SPSS 13.0 (SPSS Inc., USA) and JMP IN 5.01 (SAS Institute, USA) for Windows. Kruskal–Wallis test was used for testing significant differences between the groups; Mann–Whitney *U* test was used for the comparison of two groups or subgroups with each other. A *P* value of $P < 0.05$ was considered statistically significant. Furthermore correlation was estimated according to Spearman's correlation. A

multiple regression analysis finally completed the investigation of the influence of a combination of parameters evaluated on gland size.

Results

Descriptive statistics

There were 23 healthy, normal-weight women in our control group, 22 obese female patients in the adiposity and another 25 eating disordered females in psychosomatic group. The psychosomatic group consisted of 18 women suffering from bulimia nervosa and 7 suffering from anorexia nervosa. They formed the subgroups bulimia nervosa (BN) and anorexia nervosa (AN) which were distinguished most definitely by their average BMI: AN = 16.33, BN = 20.13.

The eating disordered patients as well as the obese ones had significantly larger parotid glands compared with the controls, according to the values calculated (Table 1).

The highest values were seen in the psychosomatic subgroup BN (parotid volume = 63,708 mm³) where the mean value was more than twice as high as in the control group (31,059 mm³) (Figs. 4, 5).

Table 1 Parotid gland volume in study population and subgroups

	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m ²)	Parotid volume (mm ³)
Controls, <i>n</i> = 23					
Mean	22.61	170.22	60.21	20.79	31,059
SD	2.13	7.57	5.44	1.48	9,499
Adipose group, <i>n</i> = 22					
Mean	32.27	169.18	129.17	45.36	52,352
Compared with controls				+118%	+69%
SD	7.59	8.40	27.09	9.42	18,911
Psychosomatic group, <i>n</i> = 25					
Mean	23.77	166.04	52.57	19.07	61,183
Compared with controls				−8%	+97%
SD	6.22	6.28	7.65	2.64	21,476
Psychosomatic subgroup					
AN, <i>n</i> = 7					
Mean	28.29	165.71	45.10	16.33	54,690
Compared with controls				−22%	+76%
SD	7.16	9.16	6.67	1.02	11,660
Psychosomatic subgroup					
BN, <i>n</i> = 18					
Mean	23.94	166.17	55.48	20.13	63,708
Compared with controls				−3%	+105%
SD	6.03	5.10	5.91	2.28	24,063

SD standard deviation, BMI body mass index, AN anorexia nervosa, BN bulimia nervosa

Fig. 4 Sonography of the parotid gland in anorectic patient with diffuse glandular enlargement in transverse plane. *MSCM* sternocleidomastoid muscle, *VR* retromandibular vein, *UK* mandible, *MASS* masseter muscle

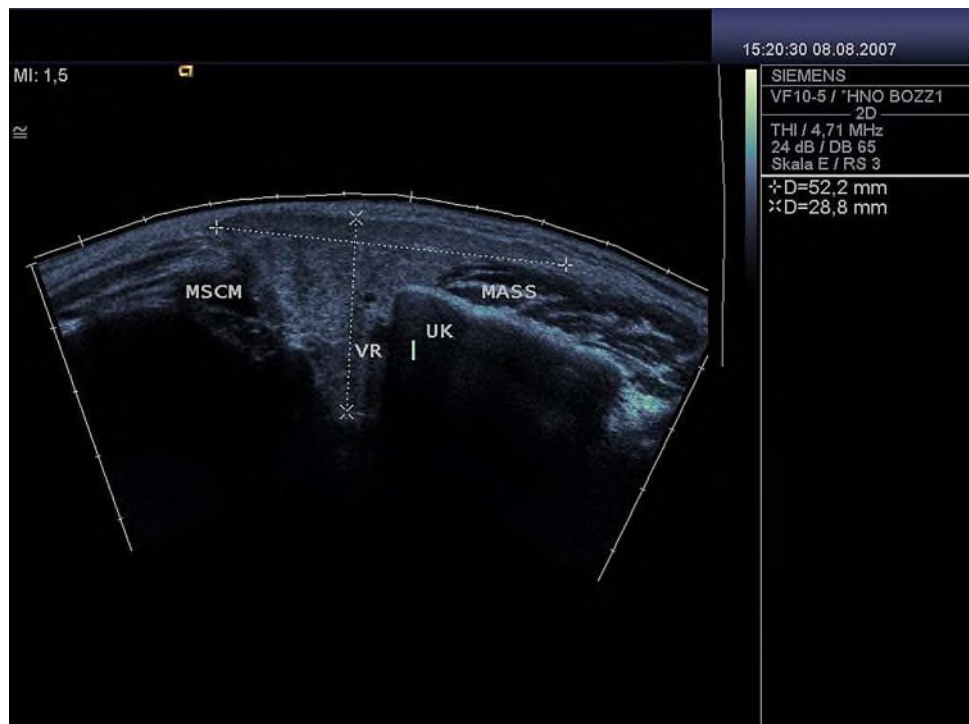
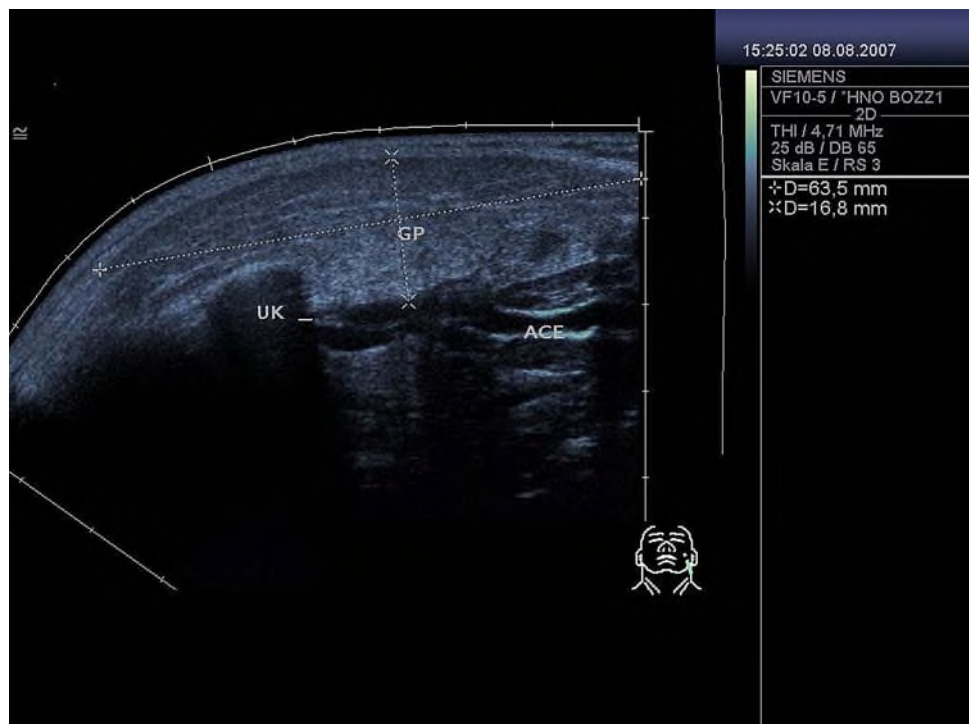


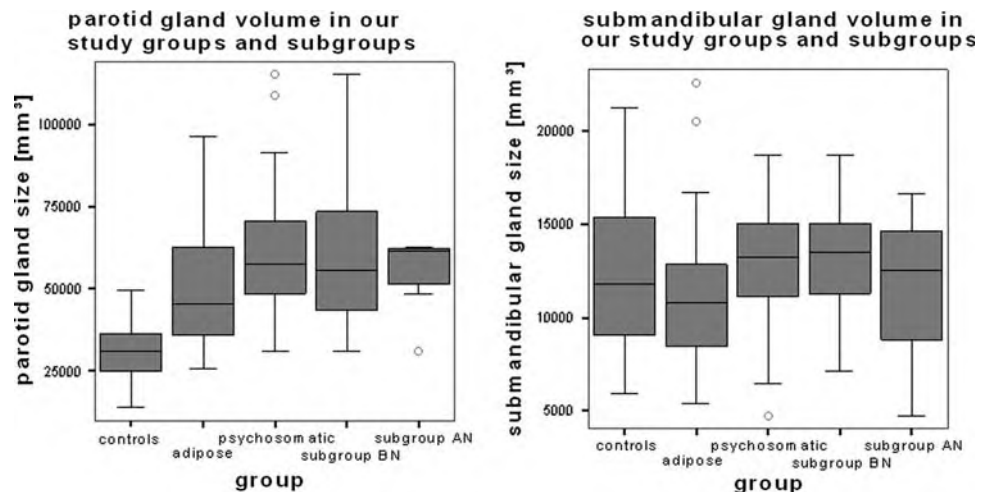
Fig. 5 The same parotid gland in coronar plane. *GP* parotid gland, *ACE* external carotid artery, *UK* mandible



Next were the whole psychosomatic group (all 25 patients, 61,183 mm³), then the psychosomatic subgroup AN (54,690 mm³) and the adipose group (52,352 mm³) which still had a 69% higher mean value compared with controls (Fig. 6).

No statistically significant difference between the values calculated for the submandibular gland volume could be seen in all groups and subgroups. Regarding the sonographic appearance of the echotexture no differences were observed in any of healthy controls and eating disordered groups.

Fig. 6 Three-dimensional volumes of parotid and submandibular gland in the three study groups Boxplots illustrating different gland volumes of the parotis gland in eating disordered. Regarding the submandibular gland no difference in volume could be observed between the subgroups



Significant differences between three study groups adipose-psychosomatic-control (Kruskal–Wallis test)

Significant differences between the three groups (adipose, psychosomatic, control) with $P < 0.01$ could be found for: body weight, BMI and parotid volume.

Significant differences between two study groups/subgroups (Mann–Whitney U test).

As we intended to see the differences between the groups affected by diseases and our controls we tested for differences by the Mann–Whitney U test by comparing healthy controls to each of the disordered groups separately. So the control group was matched with the adipose group, psychosomatic group, psychosomatic subgroup AN and psychosomatic subgroup BN separately. To see the differences between the two eating disorders we compared the psychosomatic subgroups AN and BN to each other. The comparison of obese patients with our controls showed significantly higher values ($P < 0.01$) concerning body weight, BMI and parotid volume. The psychosomatic group (AN- and BN-patients combined) showed similarly strong differences compared with our controls ($P < 0.01$ in each comparison). Still their body weight and BMI were significantly lower while the parotid volume was enlarged. Anorexics (psychosomatic subgroup AN) showed significantly lower body weight and BMI, significantly higher parotid gland size than controls. The patients suffering from bulimia nervosa (psychosomatic subgroup BN) showed lower weight and higher parotid gland size than controls ($P < 0.01$ in each comparison). Still there was no significant difference between bulimics and controls concerning the BMI.

The comparison of two psychosomatic subgroups revealed that the bulimics had significantly higher body weight and BMI than the anorexics ($P < 0.01$ in each comparison). There was no difference concerning the parotid gland size verifiable ($P = 0.65$).

Correlations (Spearman)

Regarding all 70 study participants there was a strong correlation between the group characteristic (adipose, psychosomatic, controls) and the body weight, as well as between the group characteristic and the parotid gland size ($P < 0.01$ in each correlation).

Further testings were done—as the tests for significant differences—with collectives consisting of two study groups.

In a collective of obese (adipose group) and normal weight (controls) patients there were significant correlations of the parotid gland size with group characteristic, BMI, body weight and age. Significant correlations of the parotid gland size with group characteristic, BMI and body weight were seen as well in a collective of eating disordered (psychosomatic group) and normal weight (controls) patients.

Correlations between the parotid gland size and body weight, group characteristic were detectable in a collective consisting of controls and psychosomatic subgroup AN. Regarding a collective of controls and psychosomatic subgroup BN there was only a correlation between the parotid gland size and the group characteristic. Within the psychosomatic group—a collective being composed of both psychosomatic subgroups—there were no significant correlations of the parotid gland size with any other parameter detectable.

Multiple regression analysis

In order to find out if the parotid gland size is affected by the interaction of several of the parameters investigated, a multiple regression analysis was included (Table 2).

With the parotid gland size as the dependent and the BMI and group characteristic (by the usage of two dummy

Table 2 Multiple regression analysis

Model	R	R^2	Adjusted R^2	SE of the estimate	
Model summary					
1	0.597 ^a	0.357	0.327	17,637.702	
Coefficients ^b					
Model	Unstandardized coefficients		Standardized coefficients	t	Significance
1	B	SE	Beta		
Constant factor	33,665.6	8,845.2		3.806	0.000
BMI	−125.406	386.985	−0.077	−0.324	0.747
Eating disordered	29,908.4	5,139.4	0.671	5.819	0.000
Obese	24,375.3	10,867.9	0.530	2.243	0.028

^a Predictors: (constant) dummy variables (obese, eating disordered), BMI

^b Dependent variable: parotid gland volume

variables) as two influential variables we could determine $r^2 = 0.327$.

Discussion

In our study, like in other publications before, a significant parotid gland enlargement in patients with adiposity or eating disorders in comparison to normal-weight, healthy participants could be confirmed.

In order to compare our results to other studies we initially want to draw attention to the values determined for length, width and depth of parotid and submandibular gland. The mean values for the parotid gland measured for the control group were altogether within the range of Dost's standard deviation. The volumes of the glands calculated with these mean values are almost equal as well: Dost: 31,585, our controls 31,059, a difference of 1.69% [11].

The obese and eating disordered patients in our study showed distinctively larger parotid glands than those two comparable groups of our healthy controls and the participants of Dost's studies. Compared with Dost our adipose group showed 66%, the psychosomatic group 94% larger parotid glands.

Concerning obese patients Heo found 2001 that the level of adiposity correlates in a significant, even a linear way with the size of the parotid glands [8]. Heo saw the increased storage of adipocytes in the parotid parenchyma as etiologic for this development—a theory which was already hypothesised by Du Plessis in 1956 [1]. Regarding our collective consisting of obese (adipose group) and normal-weight (control group) participants—a collective comparable to Heo's—a significant correlation between BMI and parotid gland size could be seen ($P < 0.01$). Still

this correlation cannot be found when testing only within either the control or the adipose group separately. Reasons for this might be differences within our and Heo's study population. Furthermore it seems quite unlikely that in cases of very severe obesity the linear correlation between BMI and parotid gland size is unsustainable.

Our study confirms the circumstance that the parotid glands are distinctively enlarged in cases of eating disorders (anorexia/bulimia nervosa). Psychosomatic subgroups, anorexics as well as bulimics had significantly enlarged parotid glands compared with our controls.

For his study in 1999, Metzger [3] investigated and measured the salivary glands in 17 females, bulimic patients and 21 healthy female controls—groups comparable to our 18 bulimics and 23 controls. Metzger found that the parotid glands in his bulimic participants were enlarged by 36%—a significant result which is comparable to our findings because his results were calculated with the spherical volume. The submandibular glands of Metzger's bulimic patients were enlarged by 27% compared with the controls—a result which did not reach statistic significance. When calculating the separate values for all our study groups and subgroups according to the spherical volume, as Metzger had done, the results differ by only 2.1–16.2% from the results of Metzger's control group for the submandibular gland size. We also could not find a significant enlargement of the submandibular glands in obesity or one of the eating disorders when comparing them to healthy controls. Consequently we could not back up the descriptions of parotid and submandibular gland swellings. As well the ones mentioned by Herrlinger [2] and Vavrina [13] in their case reports as the ones in Ogren's study [14] who investigated 49 bulimic patients and found parotid and submandibular swellings in 30% of the cases. The submandibular glands continuously produce, together with the

sublingual and the other small salivary gland in the oral cavity, the largest amount of the mucous part of saliva. In contrast to that the parotid glands produce a serous type of saliva which is secreted especially as a reaction to stress, excitation and irritation. If the patient's salivary glands find themselves in continuous situations of stress and irritation—for example through constant binge-eating and purging-behaviour, as in eating disorders—this circumstance appear to affect particularly the parotid glands. A structural change within those clinically flamboyant, ostentative parotid glands were also demonstrated histologically: changes within the parenchyma of the glands due to hypertrophy of the cells including an increased storage of zymogen granules and dislocation of the nuclei towards the basal parts were observed, as well as distinctively enlarged acini and compressed, intralobular excretory ducts [1, 13, 15]. There appears to be a difference concerning the pathogenesis of those parotid swellings in obesity and in eating disorders. In adipose patients an increased storage of adipose tissue in the parotid parenchyma seems to be the reason for the swelling.

Recapitulatory we found that a bilateral, painless parotid swelling can be found in obesity and, even more intelligibly, in eating disorders. The submandibular glands are not affected by this process. The gland volumes measured and calculated in this study—in obese, eating disordered and healthy participants—were similarly the ones measured in other studies before [3, 11], additionally no noticeable change of glandular echotexture could be observed. Due to the study design we could not observe the change of gland volume in course to activity of disease or influence by therapy, this should be the aim of a follow-up study, assessing gland size over a distinct period time.

In a multiple regression analysis we could demonstrate that suffering from an eating disorder in combination with an abnormal BMI has a very strong influence on the parotid gland size. Neurovegetative and hormonal processes, as well as the constant irritation of the salivary glands due to binge-eating and purging-behaviour (especially vomiting) with a potential concomitant electrolyte shift appear to be responsible for the parotid swellings in eating disorders.

High resolution B-scan ultrasound is therefore an adequately accurate and effective technique in measuring parotid gland size and depicting gland enlargement as manifestation of an eating disorder.

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