MRI signs of intracranial hypertension in morbidly obese and normal-weight individuals

MRT-Zeichen einer intrakraniellen Hypertension bei krankhaft adipösen und normalgewichtigen Personen

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ABSTRACT

Purpose Idiopathic intracranial hypertension (IIH) is associated with intracranial abnormalities, although not obligatory, which can be detected with cranial MRI. Obesity is an important risk factor for IIH and a pathogenetic link is suspected but the extent to which these MRI signs are already related to obesity has not yet been examined. We investigated whether IIH-MRI signs are present more often in obese individuals with a BMI > 30 kg/m² than in individuals of normal weight.

Materials and Methods Brain MRI of 32 obese and 53 normal-weight participants from the Food-Chain-Plus cohort were analyzed for three main signs of IIH: (I) stenosis of the transverse sinus, (II) increased width of the optic nerve sheath, and (III) reduction of pituitary height. In addition, a scoring system for the MRI signs was applied. Furthermore, tortuosity of the optic nerve and flattening of the posterior globe were considered as additional MRI signs.

Results Obese participants had a significantly higher MRI score ($p < 0.001$) than those in the normal-weight cohort, with significant differences in quantitative measurements of cerebral venous sinus stenosis ($p < 0.001$), widening of the optic nerve sheath ($p < 0.05$), and flattening of the pituitary gland ($p < 0.05$) also always being observed more frequently and in a more pronounced manner in the obese group. Furthermore, our findings correlated significantly with BMI and proportionately with hip and waist circumference.

Conclusion Obese individuals show a significantly higher prevalence of cerebral MRI signs related to IIH. This supports the hypothesis that obesity is a risk factor for possible intracranial hypertension and reinforces the suspicion that obesity is involved in the pathomechanism of IIH.

Key points:
- Obesity is associated with changes such as those seen in IIH.
- BMI, weight, and body measurements correlate with the expression of MRI signs of IIH.
- To prevent IIH symptoms in obesity, the pathomechanism must be further clarified.

ZUSAMENFASSUNG

Ziel Die idiopathische intrakranielle Hypertonie (IIH) wird mit zerebralen Anomalien in Verbindung gebracht, die in den meisten Fällen, jedoch nicht immer in der zerebralen MRT nachgewiesen werden können. Adipositas stellt hierbei ein wichtiger Risikofaktor für die IIH dar, zwischen denen ein pathogenetischer Zusammenhang vermutet wird. Inwieweit diese MRT-Zeichen jedoch unabhängig von einer entsprechenden Symptomatik mit einer Adipositas in Verbindung stehen, wurde bis dato nicht ergründet. Aus diesem Grund haben wir untersucht, ob die für eine IIH typischen MRT-Zeichen bei adipösen Personen mit einem BMI > 30 kg/m² häufiger vorhanden sind als bei normalgewichtigen Personen.

Material und Methoden Hierfür wurden Hirn-MRTs von 32 adipösen und 53 normalgewichtigen Personen aus der Food-Chain-Plus-Kohorte auf drei wesentliche Zeichen, welche üblicherweise bei einer IIH auftreten, untersucht: (I) Stenosen des Sinus transversus, (II) eine Erweiterung der Sehnervenscheide und (III) eine Verringerung der Hypophysenhöhe. Zusätzlich zu den quantitativen Messungen wurde ein Punktesystem für die MRT-Zeichen eingeführt. Auch eine Tortuosität der Sehnerven und die Abflachung des dorsalen Bulbi oculi wurden als zusätzliche MRT-Zeichen berücksichtigt.

Ergebnisse Adipöse Teilnehmer hatten einen signifikant höheren MRT-Score ($p = 0{,}0006$) als die normalgewichtigen Personen mit signifikanten Unterschieden in den quantitativen Messungen der Sinusstenose ($p < 0{,}0005$), der Erweiterung der Sehnervenscheiden ($p < 0{,}05$) und der Abflachung der Hypophyse ($p < 0{,}05$). Diese waren in der adipösen Gruppe sowohl häufiger als auch ausgeprägter zu beobachten. Zusätzlich hierzu korrelierten unsere Ergebnisse signifikant mit dem BMI sowie mit dem Hüft- und Taillenumfang.

Schlussfolgerung Adipöse Personen ohne Symptomatik einer IIH weisen eine signifikant höhere Prävalenz von zerebralen MRT-Zeichen auf, die mit einer IIH in Zusammenhang stehen. Dies unterstützt die Hypothese, dass Adipositas ein Risikofaktor für eine mögliche intrakranielle Hypertension ist, und erhärtet den Verdacht, dass Adipositas am Pathomechanismus der IIH beteiligt ist.

Kernaussagen:
- Eine Adipositas ist mit Veränderungen assoziiert, wie sie bei der IIH auftreten.
- BMI, Gewicht und Körpermaße korrelieren mit der Ausprägung der MRT-Zeichen einer IIH.
- Zur Prävention von IIH-Symptomen bei Adipositas muss der Pathomechanismus weiter abgeklärt werden.

Zitierweise
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ABBREVIATIONS

IIH	idiopathic intracranial hypertension
CSFP	cerebrospinal fluid pressure
ONS	optic nerve sheath
LONS	left optic nerve sheath
RONS	right optic nerve sheath
CVSS	cerebral venous sinus stenosis
BMI	body mass index
CSF	cerebrospinal fluid
ICC	intraclass correlation coefficient
11β-HSD 1	11-β-hydroxysteroid dehydrogenase type 1

Introduction

Idiopathic intracranial hypertension (IIH) refers to a syndrome comprising increased intracranial pressure without a reasonable underlying pathology and the absence of hydrocephalus [1]. Patients suffering from IIH are typically young women of childbearing age who present with various clinical symptoms, such as (pulsating) headache, visual deficit, tinnitus, and nausea [2]. In addition to medical history and a neurological/ophthalmological examination, the most important diagnostic methods include lumbar puncture, measurement of cerebrospinal fluid pressure (CSFP), and MRI of the brain to exclude an underlying primary pathology [3, 4]. However, MRI has evolved and improved in recent decades and several MRI signs were reported to be associated with the presence of IIH [5, 6]. These signs include, in particular, increased widening of the optic nerve sheath (ONS), stenosis of the transverse cerebral venous sinus (CVSS), reduction in pituitary height, optic nerve tortuosity, and flattening of the posterior optical globe [3, 7, 8]. Numerous studies have demonstrated the sensitivity and specificity of these signs in patients with IIH [5, 8, 9], and several of them are included in the diagnostic algorithm of IIH in adults and children.

Among reported risk factors, obesity is a common finding and might be present in up to 70–80 % of patients with IIH [10–12]. The underlying mechanism or cause is unknown and remains to be investigated, but several studies have suggested that there is a linear correlation between body mass index (BMI) and CSFP [13, 14]. The extent to which MRI signs for IIH are related to obesity and the extent to which they are generally common in an obese population independent of corresponding symptoms remain unclear and require further investigation.

Therefore, the data of a prospectively conducted study was analyzed to compare the prevalence of reported MRI signs of IIH between obese and normal-weight participants.

Materials and methods

Subjects

In a previous analysis of our study cohort, our results revealed the occurrence of inflammation, in the mediobasal hypothalamus of obese patients [15]. In this secondary analysis of the initial prospective study, brain MRI scans of 85 study participants of this Food-Chain-Plus cohort (FoCus) were analyzed for MRI signs of IIH. Initially, 1837 people were included in this former study. Of these, 111 received an MRI between August 2014 and June 2015. We had all the necessary sequences and information for 85 people. All participants gave written informed consent for MRI analysis and were fully informed about the purpose of the study. Here, 32 subjects were allocated to an obese group with BMI > 30 kg/m² and 53 to a sex- and age-matched control group with BMI < 30 kg/m². The characteristics of both groups are given in detail in ► **Table 1**.

MR Imaging

All MRI scans were performed on a 3 T MRI scanner (Ingenia CX, Philips Medical Systems) with a 32-channel head coil. Non-contrast-enhanced MRI of the brain was performed according

► **Table 1** Participant characteristics with number of participants per group, average age, and average body measurements with standard deviation. Furthermore, the number of participants per group with corresponding comorbidity. BMI: body mass index; art. hypertension: diagnosed arterial hypertension.

Patient characteristics			
	Normal weight	**Obesity**	**Significance**
Characteristics	**n or mean ± SD**	**n or mean ± SD**	**p**
Patients	53	32	
Women	48	31	
Men	5	1	
Age	50.75 ± 10.24	48.97 ± 10.28	0.4389
BMI (kg/m^2)	22.72 ± 1.98	43.41 ± 4.79	< 0.0001
Weight (kg)	66.94 ± 8.66	123.5 ± 13.92	< 0.0001
Hip cirmumference (cm)	100.9 ± 5.85	141.4 ± 9.59	< 0.0001
Waist circumference (cm)	79.39 ± 8.33	132.7 ± 11.20	< 0.0001
Art. hypertension	9	19	< 0.0001
Diabetes mellitus type II	4	6	0.1667

to a specific protocol that included the following sequences: 1) T1-MPR of the whole brain as planning sequence (TR = 8.2 ms, TE = 3.8 ms, FOV = 224 × 224 × 160 mm, voxel = 1 × 1 × 1 mm, matrix = 224 × 224 × 160 slices, scan time = 5:38 min); 2) coronal Short-Tau-Inversion-Recovery-Sequence (STIR), including the ONS and the pituitary gland (TR = 4770 ms, TE = 80 ms, FOV = 200 × 159 × 62 mm, voxel = 0,5 × 0,62 × 3 mm, matrix = 400 × 252 × 19 slices, scan time = 4:37 min); and 3) 3-dimensional phase-contrast magnetic resonance venography (MRV) of the cerebral sinus with secondary reconstructions (TR = 22 ms, TE = 6.6 ms, FOV = 230 × 183 × 160 mm, voxel = 0.9 × 1.17 × 1.6 mm, matrix = 258 × 156 × 200 slices, scan time = 7:42 min)

Imaging Signs and Scoring System

The MRI scans were evaluated for five different MRI signs common for IIH: (I) stenosis of the transverse cerebral venous sinus, (II) width of the ONS, (III) height of the pituitary gland, (IV) tortuosity of the optic nerve, and (V) flattening of the posterior globe. Here, (I) – (III) were considered as main signs and (IV) – (V) as additional signs. Each MRI scan was examined for these signs and then rated according to a scoring system based on accurate and objective measurement of the main signs. A detailed depiction of the scoring system is given in ► **Fig. 1**.

Stenoses of the transverse sinus (I) were measured at their narrowest point in relation to the normal width of the sinus prior to the stenosis. The width of the ONS (II) was measured 6 mm and 20 mm behind the bulbus in coronal sections on each side. These distances were chosen according to reports from the current literature, as they offered the highest specificity and sensitivity for dilatation [16]. The height of the pituitary gland (III) was measured in coronal sections while comparing this value with a sagittal T1-MPR to measure the middle of the pituitary gland. The value was correlated with the age-dependent normal value given in the literature [17]. According to our scoring system, a score between 0 and 3 points was given for (I) and (III) or 0 to 2 points for (II) (► **Fig. 1**). (IV) and (V) were evaluated solely for their presence (+) or absence (–).

The signs were rated by three blinded radiologists with different levels of neuroradiological experience (2 years, 3 years, and 5 years). Sinuses that were hypoplastic or aplastic and cases of narrowing due to prominent arachnoid granulation were not considered as stenosis and scored as 0. In 11 of 80 cases, a consensus reading of the venous sinus was performed due to differing results. For the evaluation of (II) and (III), mean values were used for analysis. For scoring of the CVSS and ONS, the highest score from both sides was taken and used for analysis.

Participant characteristics

All study participants completed a questionnaire about their disease history and clinical symptoms. BMI and hip and waist circumferences were measured prior to the MRI examination. All patient characteristics were compared to the MRI signs.

Statistics

The collected data were evaluated by using GraphPad Prism (GraphPad Prism 8, GraphPad Software), except for κ and ICC, which were analyzed with SPSS (Version 27, SPSS). For normal distribution, the Shapiro-Wilk test was applied. Data from obese and normal-weight participants were compared using the t-test and Mann-Whitney U test. The significance level was set to 0.05. The Spearman correlation coefficient test was used to investigate correlations between participant characteristics and MRI signs. Interobserver reliability was calculated using Fleiss-κ and ICC.

Reduction of pituitary gland height (age-correlated):

0 points:	inconspicuous up to 25 %
1 point:	reduction less than 50 % and > 25 %
2 points:	reduction by 50 % or more
3 points:	„empty sella“

Width of the optic nerve sheath:

0 points:	inconspicuous (6 mm: up to 5.8 mm; 20 mm: up to 4.8 mm)
1 point:	minor widening (6 mm: 5.9 – 6.4 mm; 20 mm: 4.9 – 5.2 mm)
2 points:	major widening (6 mm: > 6.4 mm; 20 mm: > 5.2 mm)

Stenosis of the transverse sinus:

0 points:	inconspicuous (< 25 % stenosis; hypoplasia or aplasia)
1 point:	minor stenosis (less than 50 % and > 25 %)
2 points:	major stenosis (50 % or more)
3 points:	flow interruption

0 – 8 points achievable

Prevalence of additional signs valued as present (+) or missing (-):

tortuosity of the optic nerve
flattening of the posterior globe

▶ **Fig. 1** Intracranial hypertension score. Main score with measured reduction of pituitary height, dilation of optic nerve sheath 6 mm and 20 mm behind the optic ocular globe, and extent of cerebral venous sinus stenosis at the transverse sinus with the respective classification in the scoring system. No signs of intracranial hypertension correspond to a score of 0. The maximum extent of the signs examined corresponds to a score of 8. In addition, the tortuous course of the optic nerve and the dorsal flattening of the bulb were examined for their presence and assessed apart from the score.

Results

Main findings

Significant differences ($p < 0.05$) were found for quantitative measurements of CVSS, dilatation of the ONS, and reduction in pituitary height, with the results being more severe for obese participants. The score was significantly higher for obesity referring to CVSS and the total score. Furthermore, significant correlations were found between scores and participant characteristics (▶ **Table 3**).

Stenoses of the transverse sinus

Two participants had to be excluded due to post-thrombotic abnormalities and a norm variant with an occipital sinus. Therefore, 30 obese participants and 53 normal-weight controls were analyzed. Compared to normal-weight participants, stenosis of the CVS was found more frequently and with a higher grade in obese participants at $p < 0.0005$ (▶ **Fig. 2**) (normal weight: mean score of 0.3396 ± 0.7056; obese: mean score of 1.1670 ± 1.1770). Fleiss-κ for interrater reliability was 0.606 on the right side and 0.640 on the left side upon comparison of all three raters prior to reaching a consensus (▶ **Table 2**).

Width of the optic nerve sheath

For each individual measurement position, the data for obese and normal-weight control subjects were compared. The mean ONS diameters in the control group were 4.53 ± 0.38 mm (right) and 4.42 ± 0.47 mm (left) 6 mm posterior to the globe and 3.92 ± 0.38 mm (right) and 3.84 ± 0.38 mm (left) 20 mm posterior to the globe. In obese participants, the mean values 6 mm posterior to the bulb were 4.73 ± 0.43 mm (right) and 4.69 ± 0.47 mm (left), and 20 mm posterior to the bulb were 4.27 ± 0.38 mm (right) and 4.19 ± 0.37 mm (left). This resulted in a significantly wider ONS in obese individuals 20 mm ($p < 0.0005$) and 6 mm ($p < 0.05$) behind the bulb on both sides.

The interobserver reliability was moderate to excellent, depending on the position, with an ICC of 0.781 (right) and 0.637 (left) 6 mm posterior to the bulb and 0.749 (right) and 0.859 (left) 20 mm posterior to the bulb (▶ **Table 2**). A comparison of the difference between groups did not reach statistical significance ($p = 0.0502$) but the score tended to be higher in the obese group (▶ **Fig. 2**).

Height of the pituitary gland

The height of the pituitary gland was correlated with the age-dependent normal value, resulting in percentages used for further investigations. The mean value was 84.34 ± 25.55 % in the control group and 77.42 ± 19.69 % in the obese group. Significant differences were found both in the absolute height ($p < 0.05$) and in the age-adjusted height of the pituitary gland ($p < 0.05$), showing a lower average height in obesity (▶ **Fig. 2**). The interobserver reliability was excellent, with an ICC of 0.890 (▶ **Table 2**). The difference for the score did not reach the level of significance ($p = 0.1716$) but the score tended to be higher in obese patients.

Secondary MRI signs

11 of 53 (21 %) normal-weight participants and 10 of 32 (31 %) overweight participants showed a tortuous course of the optic nerve ($p = 0.164$), with the incidence tending to be higher in the obese group. A flattening of the sclera was detected only in one normal-weight and two overweight participants.

Correlation of MRI signs with participant characteristics

None of the participants reported symptoms of IIH. Significant correlations between MRI signs and participant characteristics could be demonstrated in several constellations (▶ **Table 3**). Particularly noteworthy are the significant correlations of the total score, sinus score, and the ONS score with the BMI and absolute weight as well as with hip and waist circumference.

The incidence of optic nerve tortuosity tended to be higher in obese individuals ($p = 0.164$). No correlation was found with the diagnosis of migraine.

Total score

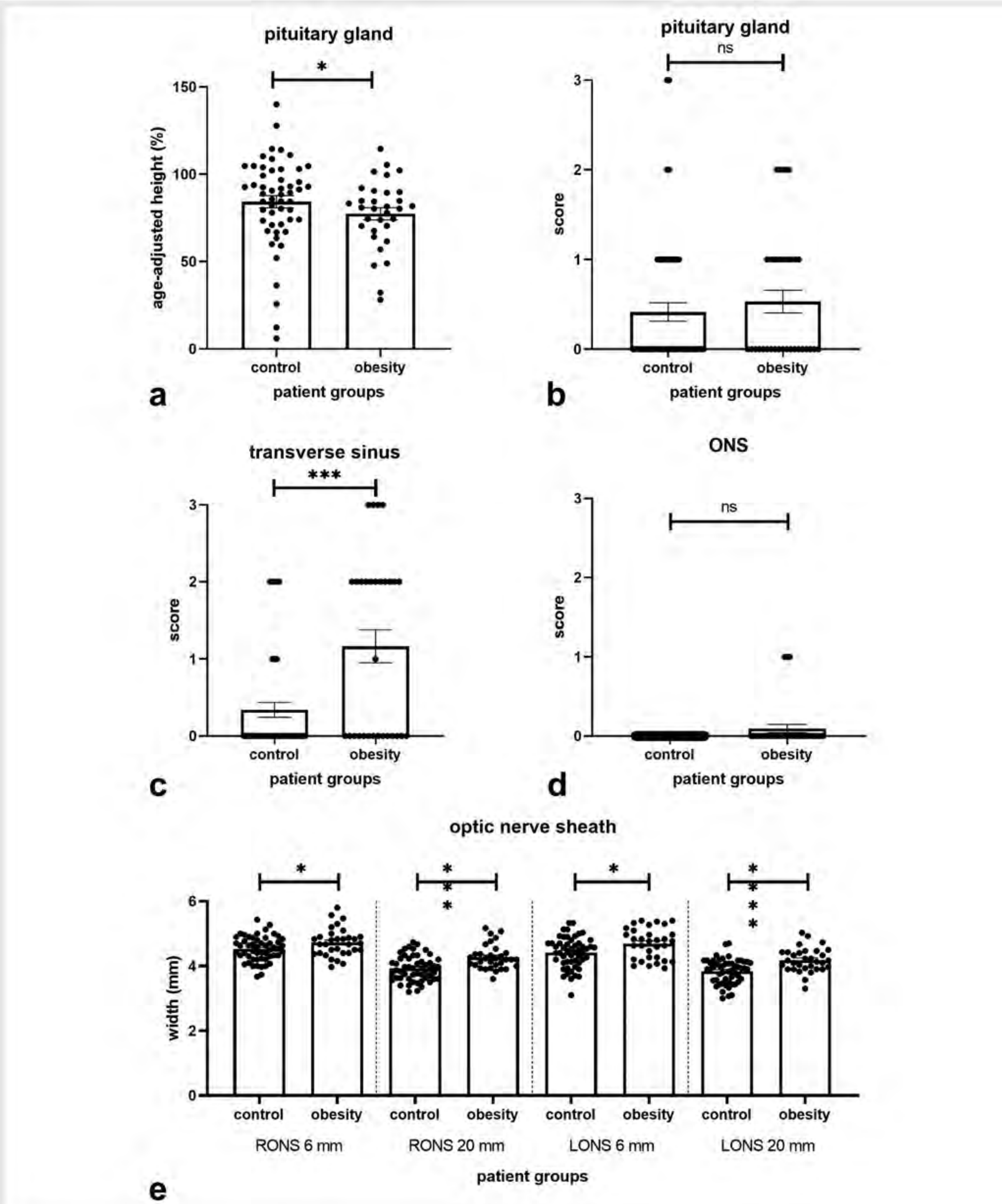
The combination of scores used in this study showed highly significant differences between the obese and normal-weight groups (▶ **Fig. 3**), with obesity being characterized by a markedly higher score ($p = 0.0006$). An exemplary comparison of the MRI signs and their respective scores is shown in ▶ **Fig. 4**.

▶ **Table 2** Interrater reliability. Listing of the interrater reliability for the specific parameters. ICC: intraclass correlation coefficient; r: right; l: left; RONS: right optic nerve sheath; LONS: left optic nerve sheath; ONS: optic nerve sheath.

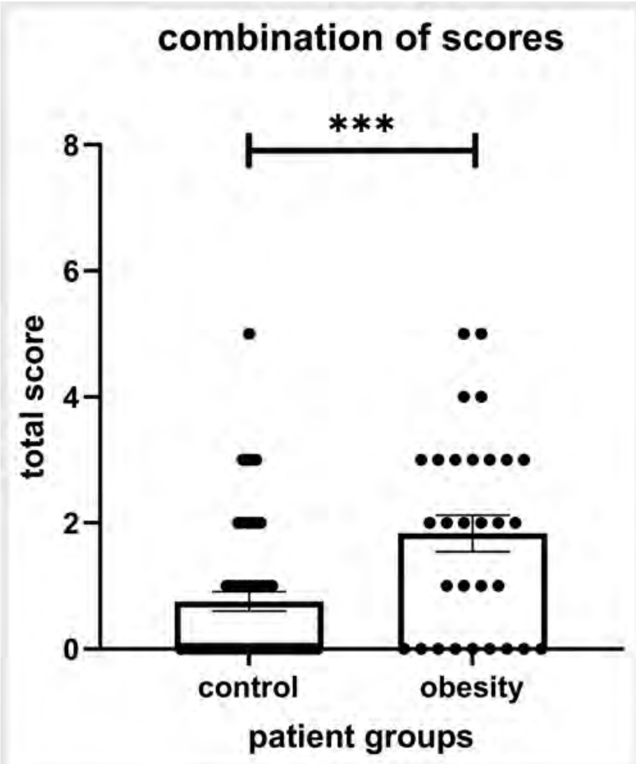
Interrater reliability	
	Fleiss-κ / ICC
Sinus score	0.631 (r)/0.641 (l)
RONS 1	0.781
RONS 2	0.749
LONS 1	0.637
LONS 2	0.859
ONS score	0.22
Pituitary gland height	0.89
Pituitary gland score	0.303

▶ **Table 3** Correlations. List of the respective Spearman correlation coefficients for corresponding comparisons of the parameters. Significant results are printed in bold. BMI: body mass index; RONS: right optic nerve sheath; LONS: left optic nerve sheath; ONS: optic nerve sheath; total score = pituitary score + score ONS + score sinus.

	BMI	**Weight**	**Hip circumference**	**Waist circumference**
Absolute pituitary height	**– 0.2615**	**– 0.2406**	– 0.1268	**– 0.2182**
Relative pituitary height	**– 0.2141**	– 0.1906	– 0.1136	– 0.1342
Score pituitary gland	0.1807	0.1349	0.0798	0.0868
RONS 1	**0.3236**	**0.3115**	**0.3221**	**0.3057**
RONS 2	**0.4167**	**0.4479**	**0.4709**	**0.4151**
LONS 1	**0.3298**	**0.3255**	**0.3467**	**0.3290**
LONS 2	**0.3348**	**0.3629**	**0.4339**	**0.3924**
Score ONS	**0.3014**	**0.2886**	**0.2928**	**0.2703**
Score sinus	**0.2954**	**0.3238**	**0.3349**	**0.2598**
BMI	1.0000	**0.9031**	**0.8271**	**0.8389**
Weight	**0.9031**	1.0000	**0.8989**	**0.8663**
Hip circumference	**0.8271**	**0.8989**	1.0000	**0.84**
Waist circumference	**0.8389**	**0.8663**	**0.8400**	1.0000
Total score	**0.3591**	**0.3404**	**0.3221**	**0.2914**



► **Fig. 2** Comparison of the various parameters in each case between groups of normal-weight (control) and obese subjects (obesity) with indication of the mean value and the standard error of the mean. The comparison of groups for the age-adjusted height of the pituitary gland (**a**), the pituitary score (**b**), the sinus score after consensus (**c**), the ONS score (**d**) as well as for the absolute values of the optic nerve sheaths at the four different positions (**e**) are shown. ONS: optic nerve sheath; RONS: right optic nerve sheath; LONS: left optic nerve sheath; SEM: standard error of the mean; ns: not significant; *: $p < 0.05$; **: $p < 0.005$; ***: $p < 0.0005$; ****: $p < 0.0001$



▶ **Fig. 3** Comparison of the total score between the group of normal-weight (control) and obese (obesity) subjects with indication of the mean value and the standard error of the mean. SEM: standard error of the mean; ***: $p < 0.0005$

Discussion

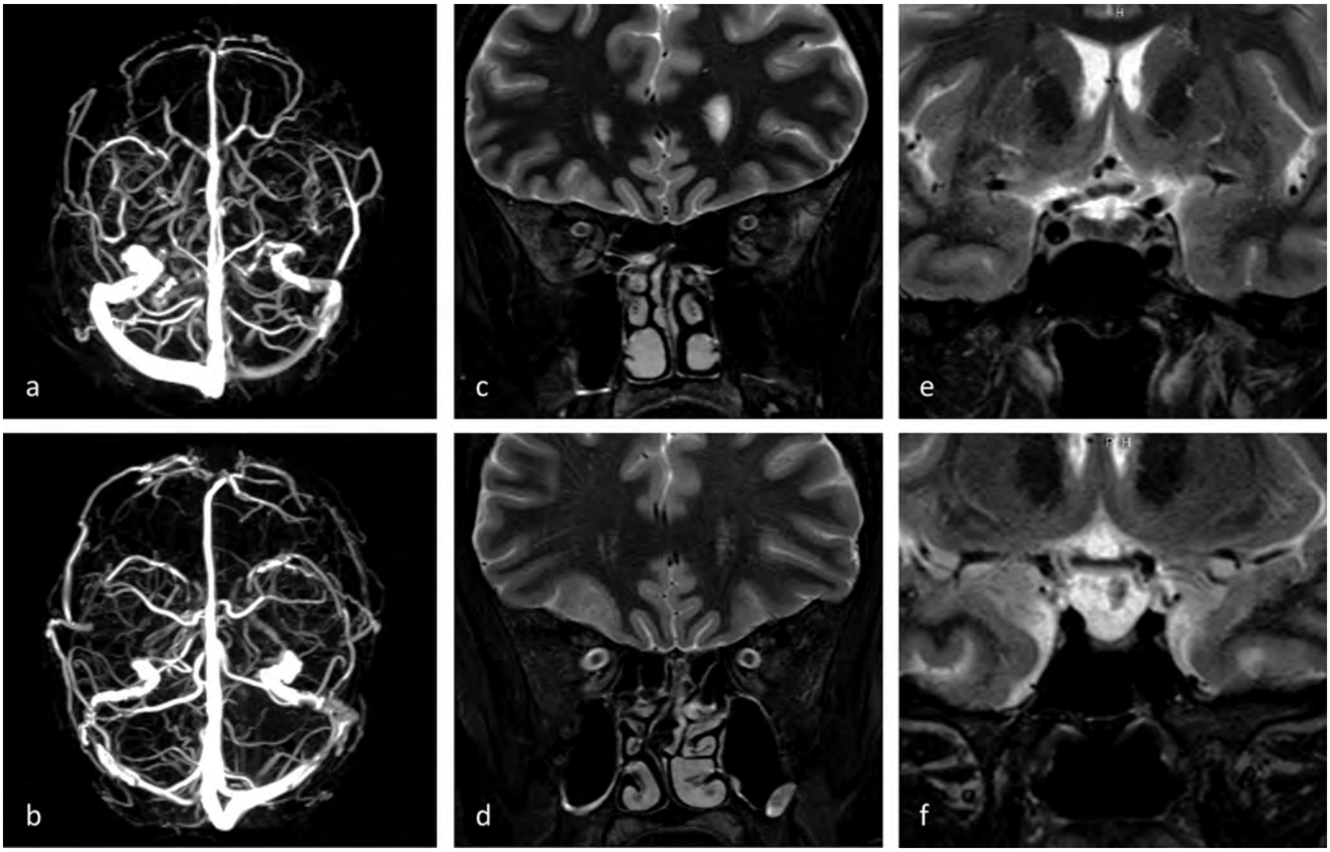
In this second evaluation of a prospective study, cerebral MRI examinations from 30 obese patients (BMI > 30) and 53 normal-weight controls (BMI < 30) were examined for the presence of cerebral MRI signs, as may occur in the setting of idiopathic intracranial hypertension. Regardless of the clinical diagnosis of IIH, we demonstrated that the associated MRI signs such as stenoses of the transverse sinus, widening of the ONS, and flattening of the pituitary gland occur significantly more frequently in obese patients than in normal-weight subjects.

It is known that obesity is a risk factor for the development of IIH and related increased intracranial pressure [10]. It is also known that the MRI signs investigated in this study correlate with the presence of IIH and can be used as an aid in clinical diagnosis. Data on an explicit correlation of MRI signs with CSFP are unfortunately not available, but their increased occurrence in IIH may suggest an association. Nevertheless, it has not been investigated to what extent these MRI signs generally appear in obesity and can be regarded as a consequence of obesity. Accordingly, the results of the present study show this relationship and allow the claim to be made that obesity could be involved in the pathophysiology of IIH. This hypothesis is additionally supported by positive correlations between BMI and the MRI signs measured here. A previously published report that an increase in venous pressure due to obesity may restrict venous outflow of the cerebral blood and increases CSFP [14] is further supported by our results, particularly by the positive correlations between hip and waist circumference and total score, ONS score, and sinus score. Thus, to correlate weight, CSFP, and venous pressure, it would be necessary to directly measure these parameters. However, such invasive measurements in asymptomatic obese individuals would be difficult to perform for ethical reasons.

Nevertheless, the strongest differences between groups according to our scoring system were observed for CVSS, suggesting that cerebral venous sinuses are most sensitive to a possible increase in CSFP, which is consistent with prior studies indicating that this is a highly sensitive sign in patients with IIH [18, 19]. Although the assessment of sinus stenoses provided very meaningful results, such assessments carry risks of being misinterpreted. In our study, we measured both sides and the higher stenosis was used to determine the score. However, Carvalho et al. in 2017 presented a possible approach for bilateral adjustment. That group used an index calculated by multiplying the stenosis scale of both transverse sinuses, thus taking both sides into consideration in their evaluation [19]. In our experience, venous sinuses are asymmetric in a large proportion of patients. To avoid bias and keep the score simple, we decided to use only the dominant side for scoring and not include unilateral aplasia or hypoplasia.

Another possible pitfall is the existence of arachnoid granulations, which may simulate a higher-grade sinus stenosis and inexperienced radiologists may make a false diagnosis. However, arachnoid granulations are typically characterized by a narrowing of the sinus that is usually short and rather roundish, while other cerebral sinuses appear unaffected. Additionally, arachnoid granulations are hyperintense on T2w images and a comparison with T1w sequences is often helpful, too. In contrast, sinus stenoses due to elevated intracranial pressure usually appear more elongated and tapered, while other venous sinuses are most often affected as well. The differing evaluations in such cases may account for the somewhat lower interrater reliability of the sinus score.

When comparing groups, the ONS score was not significantly different, in contrast to the sinus score. There may be several reasons for this difference: The ONS score in this study was adjusted for cut-off values and standard deviations of past studies that investigated differences between patients with IIH and healthy controls [20]. As the findings are not expected to be as severe in obese individuals as in patients diagnosed with IIH, the steps of the ONS score in this study might have had to be somewhat smaller or more than three scale levels should have been chosen. On the other hand, it is possible that the ONS does not react as sensitively to an increased CSFP and that, therefore, we were not able to detect sufficient differences between these groups according to that score. Nevertheless, a clear trend can already be seen in the ONS score, which only narrowly missed significance. Comparing the score with the absolute values of the ONS, these seem to be more sensitive. Significant differences were found in all four positions, especially in the posterior positions. Smaller differences were detected in positions 6 mm behind the bulb, which may be due to the sometimes difficult evaluation of the ONS as a result of motion artifacts. Overall, this shows that posterior positions are more accurate and less prone to error. This is also confirmed by



▶ **Fig. 4** MRI signs. Comparison of MRI signs between a normal-weight subject with a total score of 0 (BMI 18.62 kg/m²) and an obese subject with a total score of 5 (BMI 47.05 kg/m²). **a**. Axial MIP (maximum intensity projection) reconstruction of the 3 D MRV of the brain in a normal-weight subject without evidence of sinus stenosis, corresponding to a sinus score of 0. Hypoplasia of the left transverse sinus. **b**. Axial MIP reconstruction of the 3 D MRV of the brain in an overweight subject with sinus stenosis of the left transverse sinus, corresponding to a sinus score of 2. Hypoplasia of the right transverse sinus. **c**. Coronal STIR sequence over the optic nerve in a normal-weight subject 20 mm behind the optical bulb. Normal width of the ONS with an ONS score of 0. **d**. Coronal STIR sequence over the optic nerve in an overweight subject 20 mm behind the optic bulb. Significant dilatation of the ONS with an ONS score of 1 on both sides. **e**. Coronal STIR sequence at the level of the pituitary gland in a normal-weight subject. Normal height of the pituitary gland with a pituitary score of 0. **f**. Coronal STIR sequence at the level of the pituitary gland in an overweight subject. Significant reduction in height of the pituitary gland, corresponding to a pituitary score of 2.

the interrater reliability, which can be rated as good to excellent and suggests a reliability of the data for different levels of investigator experience.

The measurements of the ONS in all four positions showed positive correlations with the BMI as well as with absolute weight and hip and waist circumference. This suggests that obesity and increased CSFP are closely connected, which is further supported by the tendency of the optic nerve to take a more tortuous course with increased BMI.

Looking only at correlations to patient characteristics, the height of the pituitary gland was the least sensitive parameter, showing only a correlation with BMI. Nevertheless, the age-adjusted pituitary gland height demonstrates a significant flattening in obese individuals. At the same time, however, the experience of the rater has little influence on the evaluation of the pituitary height, as reflected by the excellent ICC between all raters.

Summarizing our results, obese individuals show a significantly higher prevalence of MRI signs, which can be associated with IIH. However, a major limitation of our study is that CSF pressure was not measured in this retrospective study cohort evaluation. The cause of this increased intracranial pressure in obesity, which has already been shown by directly measuring the opening pressure during lumbar puncture in non-imaging studies [13], remains unclear. Thus, various underlying pathomechanisms are still under discussion. For example, studies have shown that the intra-abdominal pressure increases due to increased BMI [11] and increased fat mass [21–23]. This, in turn, increases the intrathoracic pressure and central venous pressure, causing reduced venous outflow of the brain. This could decrease cerebrospinal fluid resorption and increase intracranial pressure accordingly. In this context, truncal obesity is of particular importance [22]. The significant correlations of the parameters we measured with waist circumference support this thesis.

Another cause could be the function of 11-β-hydroxysteroid dehydrogenase type 1 (11β-HSD 1). It has already been shown that both expression and activity of 11β-HSD 1 are dysregulated in obesity [22, 24]. 11β-HSD 1 is found in numerous organs but, above all, it has a significant effect on cortisol synthesis in the choroid plexus. Cortisol at this site leads to increased CSF production [10, 25] and consequently could increase intracranial pressure.

Furthermore, obesity represents a proinflammatory state in which the secretion of cytokines is increased [22, 25]. This condition favors an increased production of thrombophilic factors and, in turn, the development of microthromboses [24, 26]. If intracranial microthromboses develop, CSF reabsorption may be reduced, and intracranial pressure increased.

Another often discussed but still not fully understood pathomechanism is the production and effect of leptin. Studies have shown increased synthesis and chronically elevated serum concentrations of leptin, correlating positively with BMI [27]. Leptin, in turn, has a positive effect on CSF production within the choroid plexus, due to increased activity of Na+/K+-ATPase. Ultimately, this can also increase intracranial pressure [24].

In summary, numerous theories have attempted to explain how obesity affects the development of intracranial hypertension and to determine the underlying pathomechanism for this effect, but it is still not clear which mechanism is decisive. A combination of mechanisms is most likely, however, as not every obese patient develops IIH.

Finally, we have been able to show that obesity leads to cerebral morphological changes being presented as MRI signs known to be associated with IIH and related increased intracranial pressure. Consequently, when evaluating headaches or IIH, it should always be considered that, independent of corresponding symptoms, obese patients already tend to show MRI signs of IIH. In further studies, it would be important to compare these MRI signs with opening pressure of a lumbar puncture as well as with typical symptoms of IIH and to further investigate the possible pathomechanisms underlying the development of IIH. A special question here should also be to determine whether the increased intracranial pressure in obese individuals further promotes obesity. Such a study might also address the topic of hypothalamic leptin resistance.

CLINICAL RELEVANCE OF THE STUDY:

- Obese patients may already have severe MRI signs of idiopathic intracranial hypertension.
- MRI signs of idiopathic intracranial hypertension may not necessarily be related to symptoms of IIH in obese individuals.
- The role of obesity in the pathogenesis of intracranial hypertension needs to be clarified in detail in further studies to enable prevention of IIH symptoms in obesity.

Statements and Declarations

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Conflict of Interest

The authors declare that they have no conflict of interest.

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