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Quantitative study on whole brain volume in patients with obstructive sleep apnea based on synthetic magnetic resonance imaging

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Abstract

Objective To apply SyMRI to quantify whole brain volume changes in patients with varying degrees of obstructive sleep apnea (OSA).

Methods A total of 49 untreated adult patients diagnosed with OSA via polysomnography (PSG) at our hospital were included in this study. Among these patients, 21 were categorized into the mild-to-moderate OSA group, and 28 into the severe OSA group. Additionally, 31 healthy adults were recruited as the healthy control (HC) group. SyMRI post-processing software was used to obtain whole brain volume segmentation values.

Results In terms of the STOP-BANG questionnaire, the score of the severe OSA group was significantly higher than that of the mild-to-moderate OSA group ($P < 0.05$). Compared with the HC group, the mild-to-moderate OSA group and the severe OSA group exhibited a reduction in N3-stage sleep (both $P < 0.05$). Post-hoc multiple comparisons showed that compared with the HC group, the severe OSA group had increased GMV, BPV, and ICV, while the mild-to-moderate OSA group showed an increase in CSFV ($P < 0.05$). Additionally, compared with the HC group, the mild-to-moderate OSA group exhibited a decrease and the severe OSA group showed an increase in MYV ($P < 0.05$). Multiple comparisons of normalized volume fractions revealed that GMF, WMF, CSFF, MYF and BPVF were significantly different between the HC group and OSA groups (all $P < 0.05$).

Conclusion The brain volume parameters generated from SyMRI can quantify the degree of brain injury in patients with OSA.

Clinical trial number Not applicable.

Keywords Synthetic magnetic resonance imaging, Obstructive sleep apnea, Brain volume, Volume fraction

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Introduction

Obstructive sleep apnea (OSA) is a disorder characterized by repeated partial (hypopnea) or complete (apnea) obstruction of the upper airway during sleep [1]. These recurrent episodes of hypoxemia and hypercapnia negatively impact multiple organ systems throughout the body [2]. OSA is often considered an insidious health threat, as its subtle symptoms make it easy for patients to overlook, leading to delayed diagnosis and treatment. With the aging population, the prevalence of OSA keeps rising [3]. It is estimated that approximately 936 million people worldwide are currently affected by OSA [4]. Evidence has shown that OSA is a risk factor for anxiety/depression, cardio-cerebrovascular diseases, and cognitive impairment [5–7].

Research on OSA-related gray matter damage remains controversial. On one hand, previous studies using 3D-T1 structural imaging have confirmed OSA-induced gray matter damage, showing changes in gray matter volume (GMV) and cortical thickness. However, whether these changes represent an increase or decrease is debated, which may be associated with the choice of research methods, sample selection, and evaluation criteria [8–10]. On the other hand, the mechanisms underlying OSA-induced gray matter damage and whether this damage is reversible are also contentious. Many researchers suggest that patients with OSA experience extensive axonal and myelin damage [11, 12].

Synthetic magnetic resonance imaging (SyMRI) is an emerging quantitative magnetic resonance imaging (qMRI) technology that has gained attention in recent years. SyMRI enables brain volume segmentation based on intravoxel relaxation values, which are intrinsic properties of tissues. Since the segmentation relies on the physical attributes of tissues, it eliminates the influence of external factors such as imaging equipment, coil types, and post-processing techniques [13, 14]. Through a single scan, SyMRI not only generates various contrast-weighted images and quantitative maps but also provides measurements of GMV, white matter volume (WMV), cerebrospinal fluid volume (CSFV), and myelin volume (MYV). Previous studies have demonstrated that the automatic brain volume segmentation results from qMRI show high compatibility with manual segmentation results [15]. The volume segmentation results from SyMRI have been found to be consistent and reliable [16]. Myelin, which constitutes the primary component of white matter, plays a crucial role in research on brain development and neurodegeneration, and MYV cannot be measured by other MRI sequences. In this study, SyMRI-based volume segmentation was conducted to quantitatively measure GMV, WMV, and MYV in patients with OSA, thereby identifying neuroimaging biomarkers to explore the mechanism underlying brain injury in OSA.

Materials and methods

Study subjects

From March 2023 to March 2024, 49 patients diagnosed with OSA via polysomnography (PSG) were recruited from our center. Based on the apnea-hypopnea index (AHI), these patients were divided into a mild-to-moderate OSA group ($n = 21$, 5 events/hour ≤ AHI < 30 events/hour) and a severe OSA group ($n = 28$, AHI ≥ 30 events/hour). Additionally, 31 non-OSA volunteers were enrolled in the healthy control (HC) group through public advertisements. The inclusion criteria for the OSA group are as follows: (1) Untreated adults confirmed to have OSA via PSG (≥ 30 episodes of apnea during 7 h of sleep or AHI ≥ 5 events/hour). (2) The severity of OSA was classified according to the 2017 version of the Clinical Practice Guidelines for the Diagnostic Testing for Adult Obstructive Sleep Apnea issued by the American Academy of Sleep Medicine [17]: Mild-to-moderate OSA: 5 events/hour ≤ AHI < 30 events/hour; Severe OSA: AHI ≥ 30 events/hour. (3) Subjects were aged between 18 and 60 years, right-handed. For the HC group, healthy volunteers without OSA, matched by age and gender to the OSA group, with AHI < 5 events/hour, and right-handed were rendered eligible. Individuals meeting any of the following criteria were excluded from the study: (1) Presence of other sleep-related disorders; (2) Severe cardio-cerebrovascular diseases or neuropsychiatric disorders; (3) Significant intracranial structural abnormalities (such as severe white matter lesions, ischemic or hemorrhagic cerebrovascular diseases, marked brain atrophy, traumatic brain injury, or intracranial tumors); (4) Use of psychiatric medications or alcohol abuse; (5) Presence of metal implants in the body, claustrophobia, or inability to cooperate during the examination for other reasons. This study has been approved by the Ethics Committee of the Second Hospital of Hebei Medical University. Informed consent has been obtained from all participants.

MMSE and MoCA

The Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) are both screening tools used to assess cognitive function but with different focuses. MMSE evaluates global cognition, typically in the context of conditions like dementia, covering areas such as memory, orientation, attention, language, and visuospatial abilities, with a maximum score of 30 points. A score of 24 or below suggests cognitive impairment, while a score of 30 indicates no impairment. In contrast, MoCA is designed to be more sensitive in detecting mild cognitive impairment (MCI) and focuses more on executive function, memory, attention, and abstract thinking.

It also has a maximum score of 30, with a score of 26 or higher considered normal. Although both tests assess cognitive function, MoCA is often regarded as more sensitive, especially in detecting early cognitive decline or MCI.

PSG

PSG was conducted at least 7 h of sleep at night, continuously and synchronously recording more than 10 parameters, including electroencephalography (EEG), electrocardiography (ECG), electrooculography (EOG), chin electromyography (EMG), chest and abdominal movements, nasal and oral airflow, and fingertip oxygen saturation. On the day of monitoring, participants were prohibited from consuming stimulants such as coffee or alcohol and from taking any sleep-inducing medications.

Study equipment and sequences

All participants underwent cranial scanning using a GE SIGNA Architect 3.0T MRI scanner equipped with a specialized 48-channel head coil. The scanning sequences included a 3D T1 Bravo sequence and an SyMRI sequence. SyMRI axial scan parameters are as follows: Field of view (FOV) 24 cm × 24 cm, repetition time (TR) 4000 ms, time to echo (TE) 21.4/96.5 ms, matrix size 320 × 224, voxel size 0.75 × 0.75 × 5 mm, slice thickness 5 mm, inter-slice gap 1 mm (selected to balance scan time and partial volume effects), 22 slices in total, and a scan time of 4 min.

Image analysis

T1 and T2-weighted images for all participants showed no significant pathological changes in the brain. Post-processing of the images was performed using GE's SyMRI StandAlone 8.0.4. The software automatically generated brain volume segmentation values, including intracranial volume (ICV), brain parenchymal volume (BPV), GMV, WMV, CSFV, MYV, brain parenchymal volume fraction (BPVF), gray matter fraction (GMF), white matter fraction (WMF), cerebrospinal fluid fraction (CSFF), and myelin fraction (MYF).

Specifically, ICV is the sum of BPV and CSFV. BPV is the sum of GMV, WMV, and NoNV (non-gray matter/white matter/cerebrospinal fluid volume). BPVF is the ratio of BPV to ICV. GMF is the ratio of GMV to BPV. WMF is the ratio of WMV to BPV. CSFF is the ratio of CSFV to ICV. MYF is the ratio of MYV to BPV. A representative post-processed image is shown in Fig. 1.

Statistical methods

Statistical analysis was performed using SPSS 25.0 software. The Shapiro-Wilk test was used to assess the normality of the data. Continuous variables that followed a normal distribution were expressed as "mean ± standard deviation ($\bar{x} \pm s$)". Differences between the three groups were compared using one-way analysis of variance, with Bonferroni (for homogeneity of variance) and Welch tests (for heterogeneity of variance) used for post-hoc multiple comparisons. Continuous variables that did not follow a normal distribution were expressed as median (interquartile range) [M (P25, P75)], and the Kruskal-Wallis test was used to compare differences between the three groups, with post-hoc multiple comparisons adjusted using the Bonferroni correction. Categorical variables were expressed as frequencies (n), and differences between the three groups were analyzed using the chi-square (χ^2) test. A P-value of less than 0.05 was considered statistically significant.

Results

Between-group comparison of clinical data and sleep parameters

As shown in Table 1, there are statistically significant differences between the HC group, the mild-to-moderate OSA group, and the severe OSA group in BMI ($F = 9.003$, $P = 0.000$), neck circumference ($F = 18.438$, $P = 0.000$), AHI ($H = 69.730$, $P = 0.000$), mean oxygen saturation ($MSpO_2$) ($H = 49.678$, $P = 0.000$), lowest oxygen saturation ($LSpO_2$) ($H = 49.673$, $P = 0.000$), percentage of time in stage 1 of non-rapid eye movement (NREM) sleep (N1%) ($H = 15.992$, $P = 0.000$), percentage of time in stage 2 of NREM sleep (N2%) ($H = 23.750$, $P = 0.000$), percentage of time in stage 3 of NREM sleep (N3%) ($H = 37.600$, $P = 0.000$), and STOP-BANG score (The STOP-Bang acronym stands for: snoring history, tired during the day, observed stop of breathing while sleeping, high blood pressure, BMI > 35 kg/m² (or 30 kg/m²), age > 50 years, neck circumference > 40 cm and male gender) (H = -3.477, $P = 0.001$) (all $P < 0.05$).The results of multiple comparisons among the three groups are shown in Figs. 2. BMI and neck circumference in the severe OSA group are significantly higher than those in the HC group and the mild-to-moderate OSA group ($P < 0.05$ for both comparisons). Regarding the sleep parameters, both $MSpO_2$ and $LSpO_2$ in the severe OSA group are significantly lower than those in the HC and mild-to-moderate OSA groups, and $LSpO_2$ in the mild-to-moderate OSA group is lower than that in the HC group ($P < 0.05$ for both comparisons). Compared with the HC group, the severe OSA group shows an increase in N1 and N2 sleep and a significant reduction or absence of N3 sleep ($P < 0.05$). The mild-to-moderate OSA group exhibits an increase in N2 sleep and a decrease in N3 sleep compared with the HC group ($P < 0.05$). The STOP-BANG scores of the severe OSA group are higher than those of the mild-to-moderate OSA group ($P < 0.05$ for both comparisons).

There are no statistically significant differences between the HC group, the mild-to-moderate OSA group, and

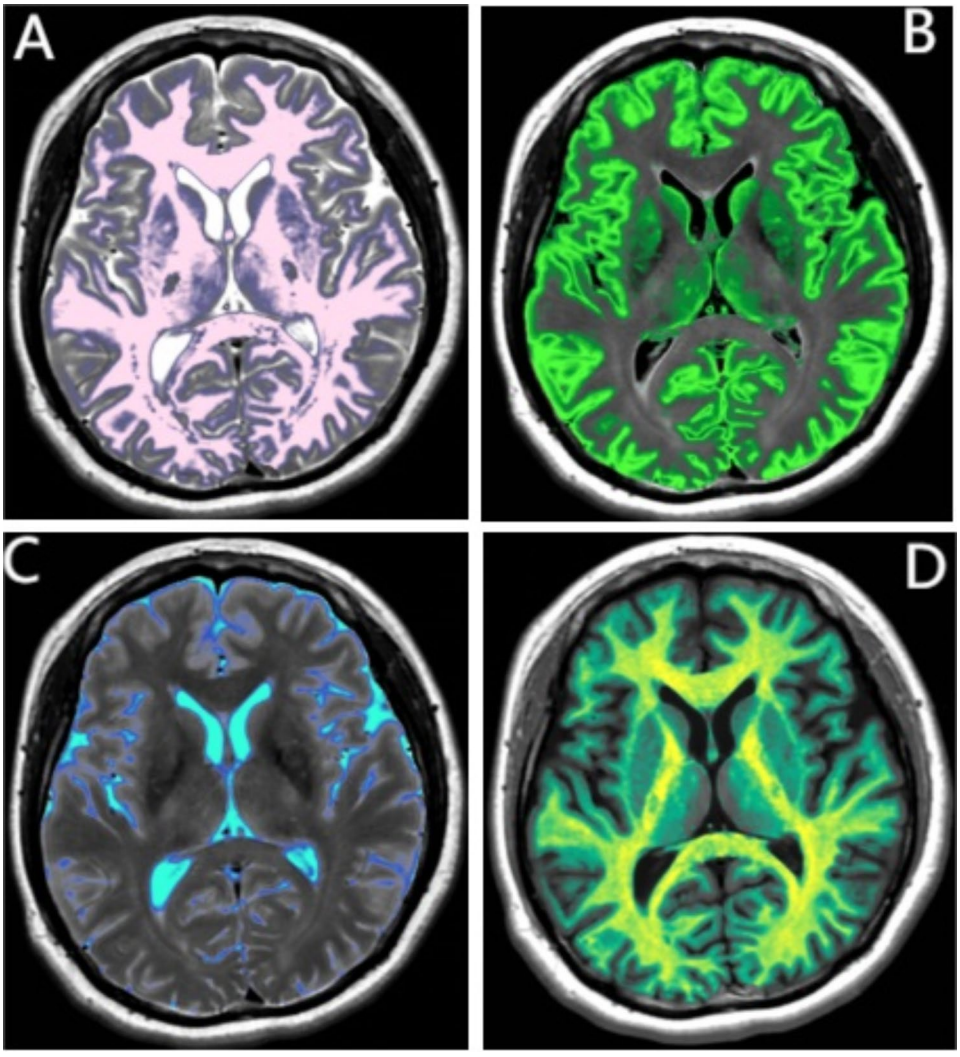

Fig. 1 SyMRI post-processing images. (**A**) White matter, with WMV in light pink color; (**B**) Gray matter, with GMV in green color; (**C**) Cerebrospinal fluid, with CSF in blue color; (**D**) Myelin, with MYV in yellow-green color (segmentation transparency overlays structural maps, with color intensity reflecting myelin content). It is visually reliable using SyMRI for brain volume segmentation

the severe OSA group in age ($F = 1.908$, $P = 0.155$), sex ($\chi^2 = 5.547$, $P = 0.062$), history of hyperglycemia ($\chi^2 = 1.334$, $P = 0.513$), hyperlipidemia ($\chi^2 = 1.479$, $P = 0.477$), hypertension ($\chi^2 = 5.513$, $P = 0.064$), total sleep time (TST) ($F = 2.280$, $P = 0.109$), sleep efficiency ($H = 0.597$, $P = 0.742$), percentage of rapid eye movement (REM) sleep (REM%) ($H = 5.007$, $P = 0.082$), score for the Mini-Mental State Examination (MMSE) ($H = 4.165$, $P = 0.125$), or score for the Montreal Cognitive Assessment (MoCA) ($H = 5.092$, $P = 0.078$). Additionally, there was no statistically significant difference between the mild-to-moderate and severe OSA groups in disease duration ($H = -0.712$, $P = 0.477$) or score for the Epworth Sleepiness Scale (ESS) ($H = -1.346$, $P = 0.185$).

Between-group comparison of whole-brain volume segmentation values

As shown in Table 2, there are statistically significant differences among the three groups in GMV ($H = 21.346$, $P = 0.000$), CSFV ($H = 7.449$, $P = 0.024$), MYV ($H = 10.148$, $P = 0.006$), BPV ($H = 15.894$, $P = 0.000$), ICV ($H = 13.747$, $P = 0.000$), GMF ($H = 17.721$, $P = 0.000$), WMF ($H = 16.916$, $P = 0.000$), CSFF ($H = 15.218$, $P = 0.000$), MYF ($H = 8.292$, $P = 0.000$), and BPVF ($H = 15.218$, $P = 0.000$), with all P-values being less than 0.05.

The multiple comparison results among the three groups are shown in Fig. 2. The severe OSA group exhibits significantly higher GMV, BPV, and ICV compared with the HC group, while the mild-to-moderate OSA group shows increased CSFV compared with the HC group ($P < 0.05$, respectively). In contrast, the mild-to-moderate OSA group has decreased MYV, while the

Table 1 Between-group comparison of clinical data and sleep parameters ($\bar{x}\pm s$ / M [P25, P75]/*n*)

Variable	HC (*n* = 31)	Mild-to-moderate OSA (*n* = 21)	Severe OSA (*n* = 28)	t/χ^2/H-value	*P*-value
Age (years)	46.2 ± 6.9	43.1 ± 10.7	42.1 ± 7.9	1.908	0.155
Sex (M/F)	23/8	14/7	26/2	5.547	0.062
BMI (kg/m^2)	26.6 ± 4.0●	26.8 ± 3.6▲	30.6 ± 4.1●▲	9.003	< 0.001*
Neck circumference (cm)	36.6 ± 4.0●	38.7 ± 3.2▲	42.3 ± 3.5●▲	18.438	< 0.001*
Past history (normal/abnormal)					
Hyperglycemia	26/5	16/5	20/8	1.334	0.513
Hyperlipidemia	25/6	14/7	22/6	1.479	0.477
Hypertension	26/5	13/8	16/12	5.513	0.064
Disease duration	-	8.0(5.0,14.0)	7.0(4.0,10.0)	− 0.712	0.477
TST	440.3 ± 70.8	400.7 ± 69.7	408.6 ± 76.9	2.280	0.109
Sleep efficiency (%)	95.4(91.5,97.7)	95.0(87.2,98.0)	97.0(86.5,98.2)	0.597	0.742
AHI (events/h)	0.7(0.0,2.0)●■	13.1(8.4,24.0)▲■	62.5(50.7,78.1)●▲	69.730	< 0.001*
$MSpO_2$ (%)	97.0(96.0,97.0)●	96.0(96.0,97.0)▲	91.0(88.3,94.0)●▲	49.678	< 0.001*
$LSpO_2$ (%)	87.0(86.0,90.0)●■	84.0(81.0,85.0)▲■	62.0(56.3,76.8)●▲	49.673	< 0.001*
N1%	2.6(1.7,6.0)●	5.0(3.6,10.0)	9.4(5.6,13.6)●	15.992	< 0.001*
N2%	64.3(58.7,69.2)●	67.9(60.6,72.6)▲	73.3(70.2,77.7)●▲	23.750	< 0.001*
N3%	12.2(8.1,16.7)●■	8.6(1.2,12.6)▲■	0.0(0.0,4.5)●▲	37.600	< 0.001*
REM%	18.6(15.2,21.8)	16.6(11.2,22.0)	14.3(11.4,19.5)	5.007	0.082
ESS score	-	9.8 ± 1.0	11.6 ± 1.0	-1.346	0.185
STOP-BANG score	-	5.0(4.0,5.0)●	6.0(5.0,6.0)●	-3.477	0.001*
MMSE score	30.0(30.0,30.0)	30.0(29.0,30.0)	30.0(29.0,30.0)	4.165	0.125
MoCA score	30.0(28.0,30.0)	30.0(28.0,30.0)	29.0(28.0,29.0)	5.092	0.078

Abbreviations: BMI - body mass index; AHI - apnea-hypopnea index; $LSaO_2$ - lowest oxygen saturation; $MSaO_2$ - mean oxygen saturation. N1%, N2%, N3%, and REM% represent the percentage of time spent in N1, N2, N3 sleep stages, and REM sleep, respectively. "*" indicates statistical significance ($P < 0.05$). "●" indicates a statistically significant difference compared with the mild-to-moderate OSA group. "▲" indicates a statistically significant difference compared with the HC group. "■" indicates a statistically significant difference compared with the severe OSA group

severe OSA group has increased MYV when compared with the HC group ($P < 0.05$, respectively). The results of standardized volume fraction analysis indicated that both the mild-to-moderate and severe OSA groups had increased GMF and decreased WMF compared with the HC group ($P < 0.05$, respectively). Additionally, the severe OSA group had lower CSFF compared with both the HC group and the mild-to-moderate OSA group ($P < 0.05$, respectively). The mild-to-moderate OSA group showed a decrease in MYF compared with the HC group, while the severe OSA group had a significantly higher BPVF compared with both the HC group and the mild-to-moderate OSA group ($P < 0.05$, respectively).

Discussion

Our study revealed that SyMRI-based brain volume quantification captures distinct patterns of GMV, MYV, and BPV changes in OSA severity. Specifically, severe OSA showed increased GMV, BPV, and ICV compared to HC, while mild-to-moderate OSA exhibited elevated CSFV. These findings align with the hypothesis of adaptive brain responses to hypoxia. OSA is recognized as a risk factor for various conditions such as anxiety/depression, cardio-cerebrovascular diseases, and cognitive impairment [18]. OSA-related cognitive, memory, and emotional changes may be associated with structural damage in the gray and white matter, such as gray matter atrophy or hypertrophy and disruptions in the integrity of white matter fiber tracts [8]. Previous studies on brain volume changes in patients with OSA have primarily relied on 3D T1-weighted imaging [19]. However, 3D T1-weighted images cannot measure MYV, a major component of white matter critical for studying white matter damage. To date, there is a research gap regarding the use of SyMRI for investigating brain volume changes in patients with OSA. Our study results showed that in the severe OSA group, GMV, MYV, BPV, and ICV exhibited an increasing trend, whereas these volume parameters did not show statistically significant differences between the mild-to-moderate OSA group and the HC group. Given the potential impact of individual brain volume differences among subjects on group comparisons, we standardized the absolute brain volume values for all participants to obtain normalized volume fractions. This adjustment allowed us to eliminate the influence of individual variability in brain volume during group comparisons. We observed that GMF and BPVF increased with OSA severity, while WMF and CSFF showed the opposite. Notably, MYF was only reduced in the mild-to-moderate OSA group compared with the HC group.

André C et al. [20] studied changes in sensitive brain regions among elderly patients with moderate-to-severe

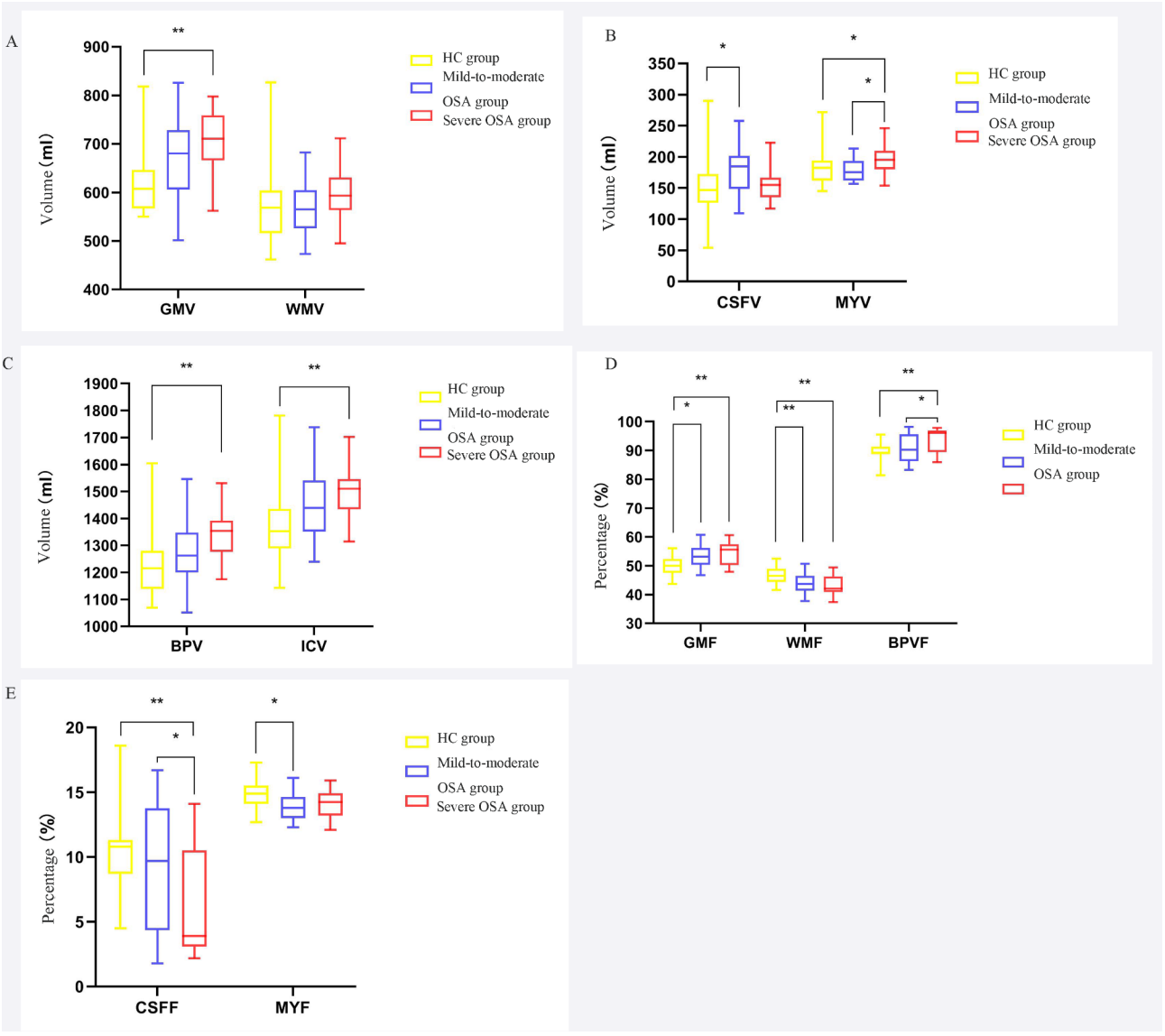

Fig. 2 Multiple comparisons of whole brain volume segmentation values. (**A**)–(**E**) represent the comparisons of GMV and WMV; CSFV and MYV; BPV and ICV; GMF, WMF, and BPVF; CSFF and MYF. Note: $^{*}P < 0.05$, $^{**}P < 0.01$

OSA who had normal cognitive function. They found hypertrophy in the precuneus and posterior cingulate gyrus in these patients, along with increased glucose metabolism, enhanced regional perfusion, and amyloid-β (Aβ) protein deposition. The increase in GMV may be attributed to amyloid deposition, representing an adaptive change during the pre-symptomatic stage of OSA [10]. Cross NE et al. [21] proposed a biphasic pattern in OSA neuroimaging, where more severe hypoxemia is associated with cortical thinning in some brain regions, while sleep fragmentation is linked to gray matter thickening or hypertrophy in multiple regions. Gray matter atrophy may underlie symptoms of somnolence or cognitive impairment, whereas individuals with mild or asymptomatic OSA often exhibit gray matter hypertrophy or no structural changes. Importantly, our whole-brain analysis complements prior regional studies [20, 21], suggesting that SyMRI captures global adaptive responses, while localized changes (e.g., precuneus hypertrophy) may require targeted subregional analyses. In this study, most of the patients with OSA were middle-aged men, and the cognitive scale scores showed that none of the participants had cognitive impairment. Therefore, the observed increase in GMV may represent an adaptive response to OSA in these patients.

Diffusion tensor imaging (DTI) is a non-invasive technique for imaging white matter fiber tracts. Kumar et al. [22] included newly diagnosed, untreated patients with OSA and used DTI to study white matter damage in the brain. The results showed acute brain damage in several

Table 2 Between-group comparison of quantitative values of brain volume segmentation (M [P25, P75])

Variable	HC ($n=31$)	Mild-to-moderate OSA ($n=21$)	Severe OSA ($n=28$)	H-value	*P*-value
GMV	607.2(567.6,646.1)●	680.1(606.3,728.4)	710.3(666.3,758.6)●	21.346	< 0.001**
WMV	568.9(516.4,603.8)	564.8(525.7,604.5)	593.3(563.7,630.8)	5.195	0.074
CSFV	146.5(126.1,172.3)■	184.4(148.4,201.9)■	155.2(135.3,166.4)	7.449	0.024*
MYV	182.1(161.6,193.8)●	175.0(162.1,193.3)▲	195.4(180.1,209.8)●▲	10.148	0.006**
BPV	1214.8(1138.6,1280.6)●	1262.9(1199.9,1347.1)	1354.3(1276.0,1392.1)●	15.894	< 0.001**
ICV	1352.2(1288.4,1434.8)●	1438.5(1350.7,1541.4)	1511.2(1433.4,1546.2)●	13.747	0.001**
GMF	50.0(47.6,52.3)●■	53.1(50.4,56.2)■	55.7(50.3,57.5)●	17.721	< 0.001**
WMF	46.5(44.4,49.0)●■	43.7(41.4,46.6)■	42.1(41.0,46.3)●	16.916	< 0.001**
CSFF	10.8(8.7,11.3)●	9.7(4.4,13.8)▲	3.9(3.1,10.5)●▲	15.218	< 0.001**
MYF	14.9(14.1,15.5)■	13.8(13.0,14.7)■	14.3(13.2,15.7)	8.292	0.016*
BPVF	89.20(88.70,91.30)●	90.30(86.25,95.65)▲	96.10(89.48, 96.90)●▲	15.218	< 0.001**

Abbreviations: GMV - gray matter volume; WMV - white matter volume; CSFV - cerebrospinal fluid volume; MYV - myelin volume; BPV - brain parenchymal volume; ICV - intracranial volume; GMF - gray matter fraction; WMF - white matter fraction; CSFF - cerebrospinal fluid fraction; MYF - myelin fraction; BPVF - brain parenchymal volume fraction. "*" indicates statistical significance ($P<0.05$). "●" indicates a statistically significant difference compared with the mild-to-moderate OSA group. "▲" indicates a statistically significant difference compared with the HC group. "■" indicates a statistically significant difference compared with the severe OSA group. *$P<0.05$, **$P<0.01$

regions of patients with OSA, involving areas crucial for cardiovascular and respiratory regulation, as well as cognitive and emotional regulation. Myelin damage was found to be more widespread and pronounced compared with axonal damage, potentially due to myelin's higher sensitivity to hypoxia and asymmetric perfusion injuries. Similarly, Lee MH et al. [11] used DTI in their study and discovered widespread white matter integrity disruption, even in mild OSA cases. Baril AA et al. [23] studied newly diagnosed, untreated patients with mild to severe OSA and found that a lower white matter diffusion coefficient was particularly evident in patients with mild OSA. However, in those with moderate to severe OSA, competing pathological processes of brain damage and brain compensation led to an apparent pseudo-normalization of diffusion metrics.

The brain, as a dynamic and self-regulating organ, initiates a repair process immediately upon myelin damage, inducing oligodendrocyte proliferation [24]. When the processes of myelin damage and regeneration reach a balance, WMV may exhibit pseudo-normalization. Thus, the absence of significant changes in WMV, GMV, or BPV does not necessarily indicate the absence of brain tissue damage. This could represent a transitional pathological stage, where the increase or decrease in GMV and white matter diffusivity coexist, with a deceptive appearance of normalcy arising from these contradictory patterns neutralizing each other. Notably, while whole-brain SyMRI quantifies the net effect of these processes, regional DTI analyses [11, 22] may disentangle localized damage from compensatory mechanisms.

In this study, we also found distinct trends in the changes of gray matter and white matter. As OSA worsened, both GMV and GMF exhibited an increasing trend, while WMV and WMF showed the opposite. Myelin, a crucial component of white matter, showed a slight decrease in its volume in mild cases, but a slight increase in severe cases. However, after BPV standardization, a reduction in MYF was observed only in patients with mild to moderate OSA. We speculate that OSA may affect different brain regions differently, and gray and white matter structures may have varying sensitivities to hypoxic damage. In some cases, the same brain region may initiate ischemic preconditioning in response to hypoxic injury, while in other cases, maladaptive responses may lead to brain damage [25]. However, whole-brain imaging techniques such as SyMRI quantify the combined effects of these patterns, whereas regional analyses (e.g., DTI or voxel-based morphometry) are required to resolve localized adaptations or injuries [21, 23]. Additionally, OSA is a highly heterogeneous disease, and the extent of brain damage may be influenced by individual variability, OSA clinical phenotypes, comorbidities, and demographic differences. Providing reliable imaging data to guide clinical treatment, SyMRI volumetric quantification holds significant value for assessing the severity and monitoring the progression of OSA and is particularly advantageous in detecting early myelin-specific changes, which may precede conventional MRI findings [11, 22].

This study has several limitations. First, we did not analyze mild OSA as a separate group because the number of mild OSA cases was relatively small. Second, the modest sample sizes of the HC, mild-to-moderate OSA, and severe OSA groups warrant larger, multi-center cohorts in future studies. Third, this study only analyzed whole-brain volumes of gray and white matter without performing subregional analyses of specific brain areas. Future studies integrating SyMRI with region-of-interest or voxel-wise approaches could clarify the spatial specificity of OSA-related brain changes. Lastly, as a cross-sectional study, it lacks the longitudinal data needed to observe

long-term changes, which should be addressed in future large-sample longitudinal studies.

Conclusion

The era of precision medicine in OSA has arrived, emphasizing personalized treatment plans tailored to individual patients. New OSA assessment indicators offer novel methods for clinical diagnosis and treatment, while also aiding in the monitoring of OSA-related target organ damage. SyMRI provides unique myelin-specific metrics and robust volumetric segmentation, offering a clinically feasible tool to quantify OSA-related brain adaptations. Our results highlight its potential for tracking neurodegeneration in OSA, particularly in early stages where conventional MRI may lack sensitivity. This technology promises to offer new insights into the relationships between the microstructure, function, and clinical phenotypes of the brain in patients with OSA and serves as a valuable supplement to neuroanatomical research.

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Author contributions
Li YP were responsible for the idea and initial manuscript of the article. Du XM and Lang XY collected and analyzed data. Geng ZJ helped draft the mansucript. All authors approved the final version of the manuscript.

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Data availability
All data generated or analyzed during this study are included in this published article.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of the Second Hospital of Hebei Medical University. Written informed consent was obtained from all participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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