· Clinical Research ·

Altered spontaneous brain activity patterns in hypertensive retinopathy using fractional amplitude of low-frequency fluctuations: a functional magnetic resonance imaging study

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Abstract
● **AIM:** To study functional brain abnormalities in patients with hypertensive retinopathy (HR) and to discuss the pathophysiological mechanisms of HR by fractional amplitude of low-frequency fluctuations (fALFFs) method.
● **METHODS:** Twenty HR patients and 20 healthy controls (HCs) were respectively recruited. The age, gender, and educational background characteristics of the two groups were similar. After functional magnetic resonance imaging (fMRI) scanning, the subjects' spontaneous brain activity was evaluated with the fALFF method. Receiver operating characteristic (ROC) curve analysis was used to classify the data. Further, we used Pearson's correlation analysis to explore the relationship between fALFF values in specific brain regions and clinical behaviors in patients with HR.
● **RESULTS:** The brain areas of the HR group with lower fALFF values than HCs were the right orbital part of the middle frontal gyrus (RO-MFG) and right lingual gyrus. In contrast, the values of fALFFs in the left middle temporal gyrus (MTG), left superior temporal pole (STP), left middle frontal gyrus (MFG), left superior marginal gyrus (SMG), left superior parietal lobule (SPL), and right supplementary motor area (SMA) were higher in the HR group. The results of a *t*-test showed that the average values of fALFFs were statistically significantly different in the HR group and HC group ($P<0.001$). The fALFF values of the left middle frontal gyrus in HR patients were positively correlated with anxiety scores ($r=0.9232$; $P<0.0001$) and depression scores ($r=0.9682$; $P<0.0001$).
● **CONCLUSION:** fALFF values in multiple brain regions of HR patients are abnormal, suggesting that these brain regions in HR patients may be dysfunctional, which may help to reveal the pathophysiological mechanisms of HR.
● **KEYWORDS:** hypertensive retinopathy; fractional amplitude of low-frequency fluctuation; brain region; magnetic resonance imaging
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INTRODUCTION
Hypertension is the most common chronic disease. It's reported that 9.4 million people worldwide die of hypertension every year[1]. According to a survey of hypertension in China from 2012 to 2015, 23.2% of the adult population over 18 years old (an estimated 244.5 million)

sufferred from high blood pressure[2]. Hypertension can cause a series of pathophysiological changes, affecting all systems of the body, typically as hypertensive retinopathy (HR)[3]. Of note, HR is the most common ocular manifestation and about 70% of hypertensive patients have fundus changes[4]. The manifestations of HR can be divided into two types: chronic HR and rapidly progressive HR. Hypertension can cause vasospasms and narrowing of retinal arteries, thickening of the vascular wall, and exudation, bleeding, and cotton wool spots in severe cases[4]. Long-term development of chronic HR or rapidly progressive HR may also lead to optic disc edema[4]. HR is one of the major causes of visual impairment in patients with hypertension, which not only has great influence on the daily life of patients, resulting in large inconvenient of patients, but also exerts a serious economic care burden to the society.

As is well known, the retina, as an extension of the diencephalon, has similar anatomical and physiological characteristics in their microcirculations due to the similar developmental patterns of their vascular systems[5]. Therefore, retinal microvascular abnormalities can often indicate vascular diseases in the brain or even the whole body[6-7]. Studies have shown that HR is a risk factor for death from cardiovascular disease[8] and is also associated with the risk of stroke[9-10]. Therefore, the public healthy crisis of HR cannot be ignored.

Functional magnetic resonance imaging (fMRI) is an imaging technique that reflects changes in the human brain neurometabolism, which can be applied to detect brain diseases and neurometabolic abnormalities[11]. The fMRI method can be divided into task fMRI and resting state fMRI (rs-fMRI). During brain scanning, task fMRI requires subjects to complete specific tasks to keep the brain active, while rs-fMRI requires the patient to do nothing so the brain is maintained in a resting state. Even in a resting state, the brain produces low-frequency fluctuations (0.01 to 0.08 Hz) in specific areas[12]. rs-fMRI studies mainly use the spontaneous low-frequency fluctuations of the resting brain to analyze brain connectivity and identify abnormalities of low-frequency fluctuations caused by pathological changes, which is conducive to diagnosis and prognosis of the disease[12]. This type of examination has been employed to the study of many diseases, such as Parkinson's disease[13-14], depression[15], Alzheimer's disease[16-17], obsessive-compulsive disorder[18-19], and hyperactivity[20] (Table 1)[13,15-16,18,20-25]. And the current accessible rs-fMRI analysis methods consisting of amplitude of low-frequency fluctuations (ALFF) and fractional amplitude of low-frequency fluctuations (fALFF) and others[21,26-27]. It's worthy noting that the amplitude of ALFFs is susceptible to physiological noise, such as respiration and heartbeats[28]. To address such drawback, with the introduction of the fALFF method obtained by dividing the low-frequency amplitude by the sum of all frequency amplitudes, effectively improving the ALFF method in terms of enhanced sensitivity and specificity of detecting local spontaneous brain activity[29]. Interestingly, this technology has also been used in the study of various ophthalmic diseases for their abnormal spontaneous brain activity, such as normal tension glaucoma[22], primary open angle glaucoma[23], neovascular glaucoma[24], optic neuritis[25], dry eye diseases[30] and so on. Similar to the aforementioned ophthalmic diseases, it's rationally to infer that HR might also accompany with abnormal spontaneous brain activity. However, there are few studies on the application of rs-fMRI-fALFF technology to HR. Although there have been similar studies on rs-MRI for HR, unlike their analysis methods[31-32] [degree centrality (DC) methods], we adopt fALFF method, which not only directly describes the intensity of brain activity but also has high sensitivity and specificity. We creatively introduced the rs-fMRI-fALFF technology to analyze the abnormal spontaneous low frequency fluctuations in the brain of HR patients and expect to uncover the pathophysiological mechanisms of HR (Figure 1).

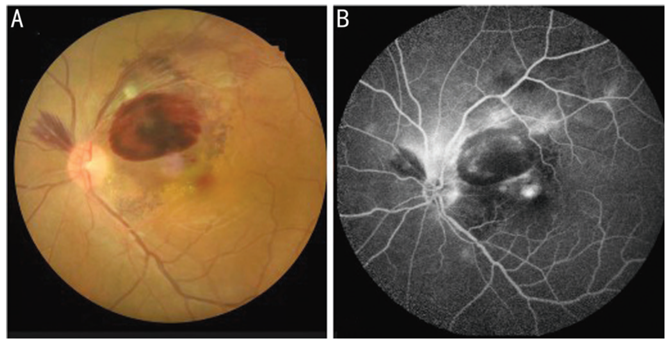

Figure 1 Typical examples of fundus camera (A) and fluorescence fundus angiography (B) in hypertensive retinopathy patients.

Table 1 rs-fMRI-fALFF method applied in neurogenic and ophthalmologic disease

Author	Year	Disease
Neurogenic disease		
Wang *et al*[13]	2018	Parkinson's disease
Hu *et al*[15]	2019	Depressive disorder
Zheng *et al*[16]	2018	Alzheimer disease
Bu *et al*[18]	2019	Obsessive-compulsive disorde
Zang *et al*[20]	2007	Attention deficit hyperactivity disorder
Ophthalmologic disease		
Li *et al*[22]	2021	Normal-tension glaucoma
Liu *et al*[23]	2014	Primary open angle glaucoma
Wu *et al*[21]	2019	Retinal vein occlusion
Zhang *et al*[24]	2021	Neovascular glaucoma
Yang *et al*[25]	2022	Optic neuritis

SUBJECTS AND METHODS

Ethical Approval The study methods and protocols were approved by the Medical Ethics Committee of the First

Affiliated Hospital of Nanchang University (Nanchang, China No.2021039) and followed the principles of the Declaration of Helsinki. All subjects were notified of the objectives and content of the study and latent risks, and then provided written informed consent to participate.

Subjects This study included 20 HR patients (10 men and 10 women) and 20 healthy controls (HCs; 10 men and 10 women). The diagnostic criteria for HR patients were: 1) a history of primary or secondary hypertension; 2) the presence of retinal changes (such as bleeding and exudation) caused by arterial diameter wall changes and abnormal vascular permeability as well as edema changes in the optic disc; 3) no other retinal or optic neuropathies, such as diabetic retinopathy, central retinal vein occlusion, optic disc vasculitis, anterior ischemic optic neuropathy, and papillary edema caused by increased intracranial pressure; 4) conscious and able to cooperate with relevant examinations. The exclusion criteria were: 1) patients withdiabetes mellitus or hyperlipidemia; 2) patients with life-threatening primary diseases or psychosis; 3) patients who were pregnant or lactating; 4) patients with severe eye diseases that affect vision such as keratitis, glaucoma, and macular degeneration; 5) individuals who were participating in clinical trials of pharmaceutical drugs; 6) those who were considered not suitable for clinical trials.

MRI Parameters A 3T MR scanner (Trio; Siemens AG, Berlin, Germany) was used for MRI scanning. Then, the functional data were obtained with a three-dimensional metamorphic gradient echo pulse sequence. Finally, 176 functional images (scanning parameters: repetition time=1900ms, echo time=2.26ms, turning angle=90°, layer thickness/gap=1.0/0.5 mm, field of view=250×250 mm, plane resolution=64×64, and 29 axial slices) were obtained.

fMRI Data Analysis Functional data were classified with MRIcro software (http://www.MRIcro.com). The functional data were preprocessed with Statistical Parametric Mapping software (SPM8; http://www.fil.ion.ucl.ac.uk/spm/) and the steps included: 1) slice timing, head-motion correction (subjects with x, y, or z maximum displacement greater than 1.5 mm or angular movement more than 1.5° were rejected); 2) all realigned data were then spatially homogenized into a standard Montreal Institute of Neurology (MNI) EPI template and resampled; 3) the regression image was smoothed using a full width at half maximum (FWHM) of 6 mm to weaken spatial noise; 4) covariates were used for regression analysis; 5) in order to reduce low-frequency drift and high-frequency noise, the time series of each voxel was band-pass filtered, and the band limit range was 0.01–0.10 Hz.

Statistical Analysis After controlling for the influence of age, the SPM8 toolkit (The MathWorks,Inc., Natick, MA, USA) was used to conduct independent two-sample *t*-test on the fALFF data of HR patients and HCs. Receiver operating characteristic (ROC) curves were used to determine the difference in the mean fALFF values between the two groups. This study used Pearson's correlation analysis to explore the relationship between fALFF values in specific brain regions and clinical behaviors in patients with HR.

Table 2 Demographics and clinical measurements of HR and HC groups mean±SD

Condition	HR	HCs	t	P^a
Male/female	10/10	10/10	N/A	>0.99
Age (y)	54.31±6.89	50.04±6.96	0.168	0.792
Weight (kg)	64.52±4.64	64.52±5.98	0.221	0.885
Handedness	20R	20R	N/A	>0.99
Duration of HR (y)	21.19±11.53	N/A	N/A	N/A
Best-corrected VA-left eye	0.54±0.16	1.12±0.22	-3.964	0.011
Best-corrected VA-right eye	0.55±0.27	1.10±0.15	-3.542	0.013
Confrontation VF	Full	Full	N/A	N/A
SBP (mm Hg)	162±21	124±16	2.942	0.024
DBP (mm Hg)	98±16	76±12	2.073	0.013
HR1 (beats per minute)	66±12	64±15	0.817	0.061

[a]$P<0.05$ independent *t*-tests comparing two groups. DBP: Diastolic blood pressure; HR: Hypertensive retinopathy; HR1: Heart rate; HCs: Normal controls; VA: Visual acuity; N/A: Not applicable; SBP: Systolic blood pressure; VF: Visual field.

RESULTS

Demographics The mean ages of HR patients and HCs were 54.31±6.89y and 50.04±6.96y, respectively. We found no significant difference in the gender distribution (P>0.99), age (P=0.792), and body weight (P=0.885) between HR patients and HCs (Table 2).

fALFF Differences The brain areas in the HR group with lower fALFF values than HCs were the right orbital part of the middle frontal gyrus (RO-MFG) and right lingual gyrus [Figure 2A and 2B (blue); Table 3]. In contrast, the fALFF values in the left middle temporal gyrus (MTG), left STP, left middle frontal gyrus (MFG), left superior marginal gyrus (SMG), left superior parietal lobule (SPL), and right supplementary motor area (SMA) were higher in the HR group [Figure 2A and 2B (red and yellow); Table 3]. The results of a two-sample *t*-test showed that the average fALFF values the HR group and HCs were statistically significantly different (P<0.001; Figure 2C).

Correlation Analyses The fALFF values in the left middle frontal gyrus of the HR patients were positively correlated with anxiety scores (r=0.9232; P<0.0001; Figure 3A) and depression scores (r=0.9682; P<0.0001; Figure 3B).

ROC Analysis ROC curve analysis was used to evaluate the average fALFF values of these areas. The AUCs of fALFF values were: RO-MFG (0.851), right lingual gyrus (0.854), left MTG (0.857), left STP (0.839), left MFG (0.860), left SMG (0.842), left SPL (0.839), and right SMA (0.845; Figure 4).

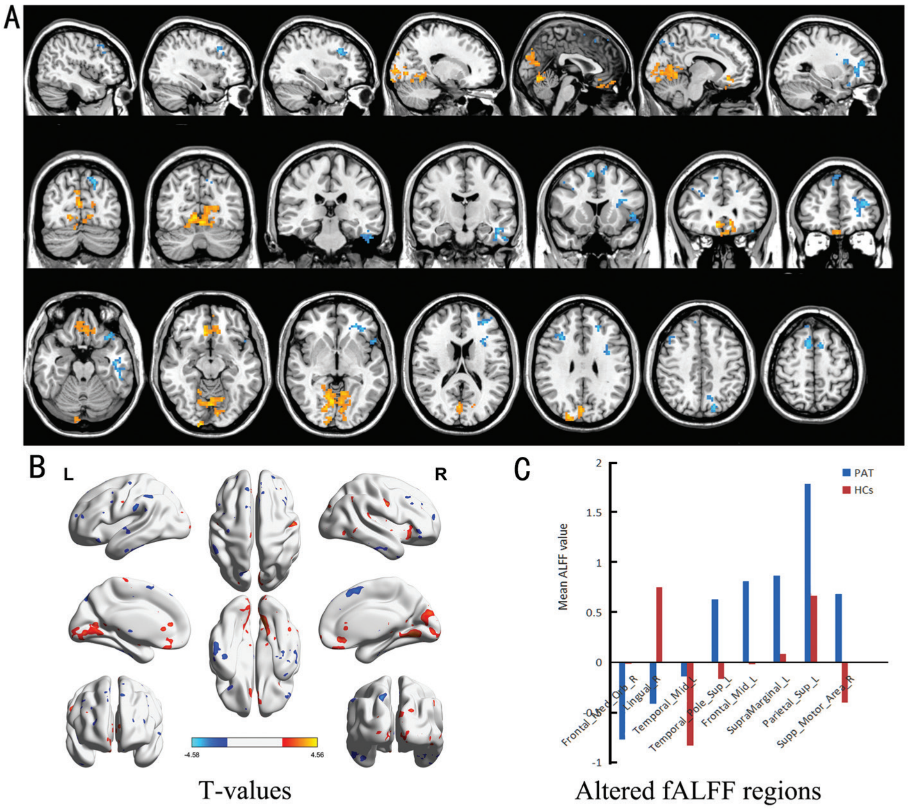

Figure 2 Spontaneous cerebral activity in HR patients and HCs A, B: Significant activity differences were observed in the Frontal_Med_Orb_R, Lingual_R, Temporal_Mid_L, Temporal_Pole_Sup_L, Frontal_Mid_L, SupraMarginal_L, Parietal_Sup_L and Supp_Motor_Area_R. The red or yellow denotes higher fALFF values, and the blue areas indicate lower fALFF values, respectively (P<0.01 for multiple comparisons using Gaussian-random field theory, z.2.3, P<0.01, cluster. 40 voxels, FDr corrected). C: The mean values of altered fALFF values between the HR and HC groups. fALFF: Fractional amplitude of low-frequency fluctuation; HR: Hypertensive retinopathy; HCs: Normal controls; Frontal_Med_Orb_R: Right orbital part of middle frontal gyrus; Lingual_R: Right lingual gyrus; Temporal_Mid_L: Left middle temporal gyrus; Temporal_Pole_Sup_L: Left superior temporal pole; Frontal_Mid_L: Left middle frontal gyrus; SupraMarginal_L: Left superior marginal gyrus; Parietal_Sup_L: Left superior parietal lobule; Supp_Motor_Area_R: Right supplementary motor area.

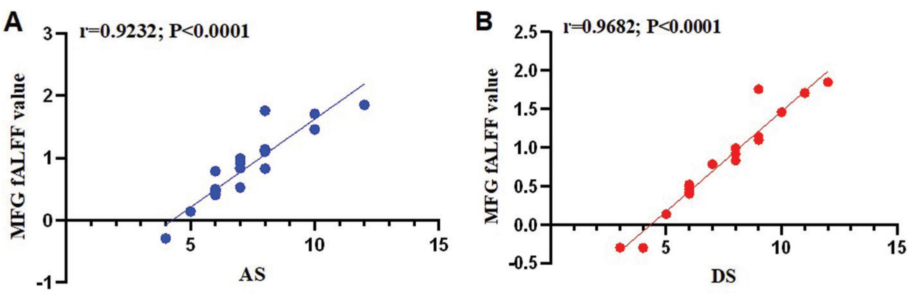

Figure 3 Correlations between the mean fALFF signal values of the MFG and score of anxiety scale and score of depression scale in HR patients A: AS in the HR group displayed a positively correlation with the fALFF value of the MFG (r=0.9232; P<0.0001); B: DS in the HRP group displayed a positively correlation with the fALFF value of the MFG (r=0.9682; P<0.0001). fALFF: Fractional amplitude of low-frequency fluctuation; HR: Hypertensive retinopathy; MFG: Middle frontal gyrus; AS: Anxiety scores; DS: Depression scores.

DISCUSSION

In clinical practice, doctors pay more attention to the ocular lesions and symptoms of patients with HR, but pay less attention to changes in brain activity and related functional changes in patients. Our study focuses on this neglected area, using the fALFF method to evaluate changes in resting brain activity in HR patients and reveal potential functional impairments and abnormalities. In order to detect early brain dysfunction in patients with hypertensive retinopathy and provide reference for clinical treatment and prevention. The fALFF approach has been used in the study of many ophthalmic diseases and it plays an important role in explorations of the relationship between eye diseases and spontaneous low frequency fluctuations of the brain[23-27] (Table 4). To our knowledge, this study is the first to use the fALFF method to assess changes in resting brain activity in HR

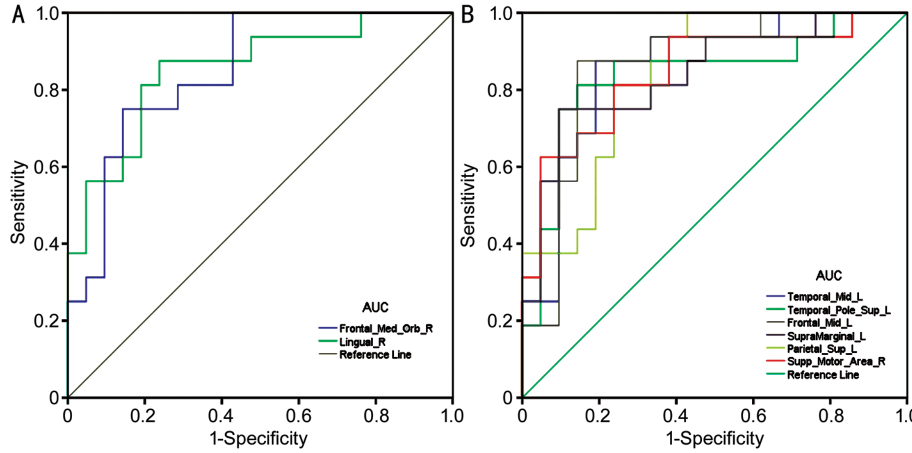

Figure 4 ROC curve analysis of the fALFF values for altered brain regions The AUCs of fALFF values were as follows: A: Frontal_Med_Orb_R (0.851), Lingual_R (0.854); B: Temporal_Mid_L (0.857), Temporal_Pole_Sup_L (0.839), Frontal_Mid_L (0.860), SupraMarginal_L (0.842), Parietal_Sup_L (0.839), Supp_Motor_Area_R (0.845). ROC: Receiver operating characteristic; AUC: Area under the curve; fALFF: Fractional amplitude of low-frequency fluctuation; HCs: Normal controls; Frontal_Med_Orb_R: Right orbital part of middle frontal gyrus; Lingual_R: Right lingual gyrus; Temporal_Mid_L: Left middle temporal gyrus; Temporal_Pole_Sup_L: Left superior temporal pole; Frontal_Mid_L: Left middle frontal gyrus; SupraMarginal_L: Left superior marginal gyrus; Parietal_Sup_L: Left superior parietal lobule; Supp_Motor_Area_R: Right supplementary motor area.

Table 3 Brain areas with significantly different fALFF values between groups

Brain areas	MNI coordinates			BA	Peak voxels	T value
	X	Y	Z			
HC>HR						
Frontal_Med_Orb_R	9	30	-12	11	155	4.07
Lingual_R	9	-66	-3		549	4.12
HC<HR						
Temporal_Mid_L	-45	-12	-21	20	141	-4.26
Temporal_Pole_Sup_L	-36	24	-21	47	72	-3.75
Frontal_Mid_L	-33	45	18	10	162	-4.1
SupraMarginal_L	-60	-27	30	40	50	-3.78
Parietal_Sup_L	-18	-75	45	7	57	-4.04
Supp_Motor_Area_R	9	15	57	6	119	-3.83

P<0.05 was significantly different for multiple comparisons using Gaussian random field theory (z.2.3, *P*<0.01, cluster.40 voxels, Alphasim corrected). fALFF: Fractional amplitude of low-frequency fluctuation; HR: Hypertensive retinopathy; HC: Normal control; Frontal_Med_Orb_R: Right orbital part of middle frontal gyrus; Lingual_R: Right lingual gyrus; Temporal_Mid_L: Left middle temporal gyrus; Temporal_Pole_Sup_L: Left superior temporal pole; Frontal_Mid_L: Left middle frontal gyrus; SupraMarginal_L: Left superior marginal gyrus; Parietal_Sup_L: Left superior parietal lobule; Supp_Motor_Area_R: Right supplementary motor area.

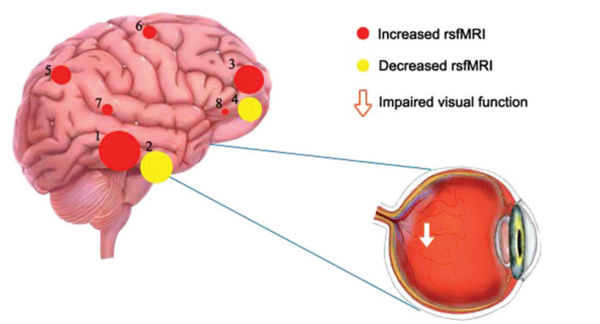

Figure 5 The mean fALFF values of altered brain regions The red denotes higher fALFF values, and the yellow areas indicate lower fALFF values, respectively. The size of red and yellow dots is a rough indication of how much value has fallen. fALFF: Fractional amplitude of low-frequency fluctuation.

patients. The fALFF values in the RO-MFG and right lingual gyrus in the HR group were lower than in the HC group. In the left MTG, left STP, left MFG, left SMG, left SPL, and right SMA, the fALFF values in HR group were higher than in the HC group (Figure 5).

The orbitofrontal cortex includes the secondary taste cortex and the secondary and tertiary olfactory cortices. It also receives information about object vision from the visual area of the temporal lobe[33]. This brain region participates in the recognition of facial emotional expression and is related to the behavioral extinction and reversal learning of animals and humans[34]. Taken together, the orbitofrontal cortex can receive taste and touch information and connect it with vision. Additionally, it can control and correct emotion-related behaviors by identifying emotional expressions[33]. A study on rsfMRI-fALFF in patients with anxious depression (AD) showed that fALFF values of the RO-MFG were decreased in the AD group, indicating the emotion-related behaviors regulatory function of RO-MFG[35]. Our results displayed that the fALFF values in the RO-MFG of HR patients were lower than that of HCs, suggesting that HR patients may have

Table 4 Brain regions alternation and its potential impact

Brain regions	Experimental result	Brain function	Anticipated result
Orbitofrontal cortex	HRs<HCs	Facial emotion perception, social functioning	Anxious depression
Lingual gyrus	HRs<HCs	Visual memory, facial emotion perception, color processing	Visual memory impairment
Middle temporal gyrus	HRs>HCs	Semantic processing and memory, auditory processing, social cognition	Social cognitive impairment
Superior temporal pole	HRs>HCs	Semantic processing, emotional processing, social behavior	Mood processing disorders
Middle frontal gyrus	HRs>HCs	Visual and selective attention tasks, object working memory, Chinese character conversion	Depressive disorder
Supramarginal gyrus	HRs>HCs	Verbal working memory, upright sensation, and gestural production	Apractoagnosic syndrome
Superior parietal gyrus	HRs>HCs	Visual attention shifting function	Optic ataxia
Supplementary motor area	HRs>HCs	Motor control and execution, verbal expression and fluency, visuospatial conversion and music processing	Movement disorder, speech delay

HR: Hypertensive retinopathy; HCs: Healthy controls.

impaired facial expression recognition and impaired normal social behaviors.

The lingual gyrus is responsible for visual memory[36], facial expression recognition[37], and color processing[38]. In one case report, a patient sufferred from visual memory dysfunction after lingual gyrus involvement[39]. It has been reported that the fALFF values in the bilateral lingual gyrus of patients with retinitis pigmentosa were significantly lower than that of HCs[40]. In our study, the fALFF values in the right lingual gyrus of HR patients were lower than that of HCs, implying that HR may cause visual memory, facial expression recognition, and color processing disorders.

The MTG is located at the junction of the auditory and visual cortices and it receives and integrates auditory and visual information[41-43]. In addition, studies have shown that MTG is also related to semantic processing and memory[44-46]. Another study revealed that the left MTG is closely related to social cognition (theory of mind)[43,47]. Our result illustrated that, the fALFF values of the left MTG in HR patients was higher in comparsion with HCs. We speculate that patients with HR may have functional disorders such as disorders of semantic processing and semantic memory, auditory processing, and social cognition.

The concept of a temporal pole (TP) has only been proposed recently, and this brain region only exists in non-human primates, apes, and humans[48]. Because it is located on the outside of the amygdala, behind the preorbital cortex, and is closely connected with the edge and parietal areas, it is considered to be part of the extended limbic system[49]. People often suggest the brain regions related to social emotional processing are the amygdala and orbitofrontal cortex, but the TP, which is located between the two regions and receives and sends connecting information, is often ignored[50]. The main function of the right STP is to participate in emotional processing, social behavior, and personal and situational memory by using visual and auditory information, while the left STP is mainly responsible for semantic processing[51-52]. The results showed that the fALFF values for left STP in HR patients were higher than that of HCs, suggesting that the activity of this brain region was abnormal. Therefore, we suspect that there are disorders in semantic processing, emotional processing, and social behaviors of patients with HR.

The MFG is located between the suprafrontal sulcus and the inferior frontal sulcus. It has been found that the MFG plays a significant role in attention[53], memory[54], advanced execution, and decision-making[55]. Compared with the right MFG, the left MFG is mainly responsible for visual and selective attention tasks in terms of attention[53], and is mainly related to object working memory[54]. In addition, it also has the function of dealing with emotional stimulation and emotional regulation[54]. A study on Chinese orthography, phonology, and semantic processing found that the left MFG was involved in the conversion of orthography to phonemes and the semantics of Chinese characters[56]. Our study confirmed that the fALFF values of the left MFG in HR patients were higher than that of HCs, suggesting that HR patients may have functional disorders such as problems with visual and selective attention tasks, object working memory, and Chinese character conversion.

The SMG is arched around the end of the posterior branch of the lateral sulcus and is situated at the front of the inferior parietal lobule (IPL)[57]. As part of the IPL, the SMG is involved in a variety of cognitive functions, including verbal working memory[58], auditory short-term memory[59], and upright sensation[60]. In addition, SMG also has the function of gesture generation, including the use of tools, and related knowledge such as how to use gestures[61-63]. In a fMRI study of the brain and gestures, it was found that activation of the SMG had a left hemispheric bias, which had nothing to do with the subjects' handedness[61]. In some ways, the functions of the left and right sides of the margin are not exactly the same. For example, in terms of tone memory and rhythm memory, the functions of the left and right SMG are separated; that is, the left SMG is mainly related to tone memory, while the right SMG seems to be related to rhythm memory[64]. In this study, it was found that the fALFF values of the left SMG in HR patients were higher, suggesting that HR may be associated with the functions of verbal working memory, upright sensations, and gesture generation.

Both the SPL and the SMG belong to the parietal lobe; the part above the parietal sulcus is the SPL and the SMG is located below the parietal sulcus. It's known that patients with SPL damage will develop visual ataxia, eye movement disorders, difficulty with looking continuously at an object, which is characterized by the inability to follow movement of the object and divert attention[65-66]. This performance is consistent with the results of most studies on the function of the SPL, which have shown that when subjects look at an object, the SPL is activated, indicating that the superior parietal lobule is related to the transfer of visual attention[67-69]. In our study, the fALFF values in the left SPL of HR patients were higher, so the visual attention transfer function of HR patients may be impaired.

The SMA is located in the superior frontal gyrus. In terms of anatomy and function, the SMA can be divided into three subregions: anterior auxiliary motor area, auxiliary eye movement area, and the auxiliary motor area itself[70]. Unilateral SMA resection can cause the auxiliary motor area syndrome, which is mainly characterized by transient contralateral generalized dyskinesia and a language disorder[71]. The SMA is mainly involved in movement control and execution, language expression and fluency, visual space conversion, music processing, and other functions[72-75]. In this study, the fALFF values in the right SMA were higher in HR patients, it's rationally inferred that the above functions may be impaired in these patients.

Long-term visual impairment in HR patients often leads to mental and psychological disorders. Although anxiety and depression are not the main symptoms of HR patients compared to blurred vision, they are very common and challenging accompanying symptoms. The fALFF values of the MFG in HR patients in this study were positively correlated with the anxiety and depression scale results. Therefore, we speculate that anxiety and depression in HR patients may be related to an increase in fALFF values of MFG (Figure 6).

In conclusion, this study has the limitation of having a small sample size. We will expand the sample size in future in-depth research to exclude the influence of geographical and other environmental factors on the experimental results, in order to obtain more accurate data. In conclusion, the fALFF values of multiple brain regions in patients with HR were abnormal in this study, suggesting that multiple brain regions in HR patients may be dysfunctional. These results will provide a reference for further study of the pathophysiological mechanisms of HR (Figure 7). In addition, the results of this study will provide new ideas for clinical diagnosis and treatment.

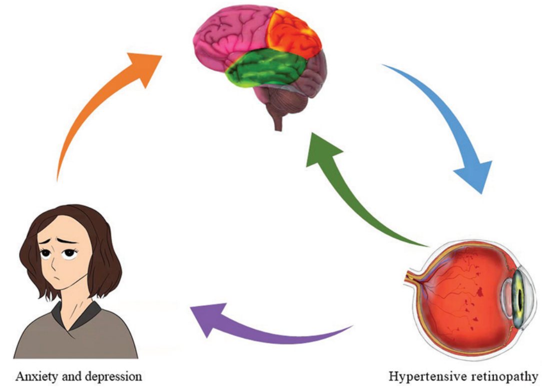

Figure 6 Relationship between magnetic resonance imaging and HR Once HR occurs, it may affect the function of vision and lead to abnormal nerve activity in areas of the brain that are related to emotional processing. HR: Hypertensive retinopathy.

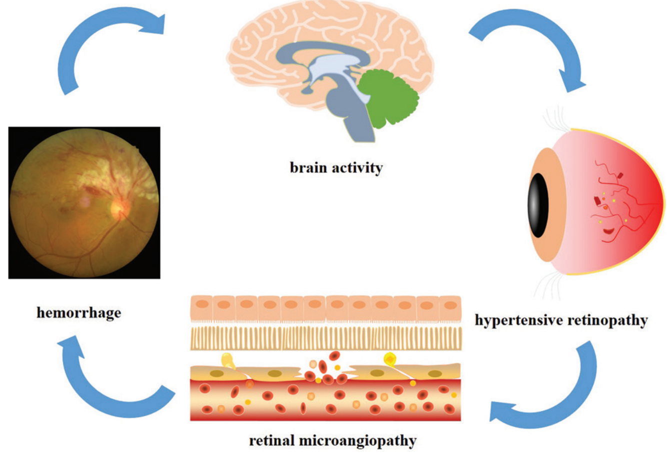

Figure 7 Relationship between hypertensive retinopathy and clinical manifestation Retinal under the condition of hypertension promoted arterial vasospasm and narrowing, which leads to retinal exudation, bleeding and changes in brain activity.

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