• Clinical Research •

Detecting altered spontaneous activities of different brain areas in diabetic vitreous hemorrhage patients: a magnetic resonance imaging study

Kai Yan[1], Jing Yu[2], Yan-Mei Zeng[3], Cheng Chen[3], Lei Zhong[4], Jin-Yu Hu[3], Liang-Qi He[3], Xiao-Yu Wang[3], Qian Ling[3], Xu Chen[5], Yi Shao[4], Yao Yu[6,7]

[1]Department of Radiology, Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medical University, Hangzhou 310007, Zhejiang Province, China
[2]Department of Acupuncture and Moxibustion, Hangzhou TCM Hospital Affiliated to Zhejiang Chinese Medical University, Hangzhou 310007, Zhejiang Province, China
[3]Department of Ophthalmology, the First Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi Province, China
[4]Department of Ophthalmology, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, National Clinical Research Center for Eye Diseases, Shanghai Key Laboratory of Ocular Fundus Diseases, Shanghai Engineering Center for Visual Science and Photomedicine, Shanghai Engineering Center for Precise Diagnosis and Treatment of Eye Diseases, Shanghai 200080, China
[5]Department of Ophthalmology and Visual Sciences, Maastricht University, Maastricht 6200MA, Limburg Province, The Netherlands
[6]Department of Endocrinology and Metabolism, The First Affiliated Hospital of Nanchang University, Jiangxi Clinical Research Center for Endocrine and Metabolic Disease, Jiangxi Branch of National Clinical Research Center for Metabolic Disease, Nanchang 330006, Jiangxi Province, China
[7]Department of Endocrinology and Metabolism, Gaoxin Hospital of the First Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi Province, China
Correspondence to: Yao Yu. Department of Endocrinology and Metabolism, Gaoxin Hospital of the First Affiliated Hospital of Nanchang University, Nanchang 330006, Jiangxi Province, China. 375135747@qq.com
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Abstract

● **AIM:** To compare spontaneous brain regional activities between diabetic vitreous hemorrhage patients (DVHs) and healthy controls (HCs).

● **METHODS:** Thirty-two DVHs and 32 HCs were enrolled in this study. Baseline demographic and vision data were compared between groups using an independent sample *t*-test. Resting-state functional magnetic resonance imaging (rs-fMRI) was used in all participants. fMRI data was obtained and analyzed using MRIcro and SPM8 software. Fractional amplitude of low-frequency fluctuation (fALFF) technology was used to measure regional spontaneous brain activity, and sensitivity was tested using receiver operating characteristic curves (ROCs). The fALFF values were analyzed using REST software and two-sample *t*-tests were used to compare values between groups. Hospital anxiety and depression scale (HADS) score was assessed in DVHs and Pearson's correlation was used to test relationships between mean fALFF value and both HADS score and duration of DVH.

● **RESULTS:** Except for the best-corrected visual acuity (BCVA) in both eyes, which showed a statistically significant difference ($P<0.05$), there were no statistically significant differences in the other indicators ($P>0.05$) between the HCs and DVHs group. Compared with controls, fALFF value was higher in DVH in cerebellum posterior lobe (CPL) and lower in right anterior cingulate cortex (ACC) and right medial orbitofrontal cortex (OFC). In DVH patients, mean fALFF value of CPL was positively correlated with HADS score and duration of diabetes. However, no such correlation was found, for right ACC or right medial OFC. DVH may lead to abnormal activities in certain brain regions related to visual control and mood.

● **CONCLUSION:** Visual impairment caused by DVH may lead to adjustment in regional visual brain activities and may be related to depression or reward system processing in some brain regions.

● **KEYWORDS:** diabetic vitreous hemorrhage; functional magnetic resonance; fractional amplitude of low-frequency fluctuation; cerebellum posterior lobe; right anterior cingulate cortex; right medial orbitofrontal cortex; clinical trials

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INTRODUCTION

Vitreous hemorrhage (VH) in diabetes, also called diabetic vitreous hemorrhage (DVH), is a serious and universal complication of diabetic retinopathy (DR) that can cause blindness in patients[1]. DR leads to abnormal growth and leakage of small blood vessels, causing complications including VH[2]. In DR, the retina develops lesions including microaneurysms, hemorrhages and hard exudates[3], which lead to retinal ischemia. As the disease progresses, retinal neovascularization may occur, with the formation of leaky new vessels. These abnormal vessels penetrate the vitreous and lead to VH[4] in which blood is found in the vitreous body. It is often secondary to trauma, Terson syndrome and proliferative diabetic retinopathy (PDR)[1]. The latter is the most frequent reason cause of VH in adults. VH is associated with decreased visual acuity (VA), posterior vitreous detachment, retinal detachment, retinal tears and blindness[1]. The hemorrhage occurs rapidly and is often painless. According to previous studies, there are about 7 cases of spontaneous VH among every 100 000 people in one year[5]. Thus, VH is a disease of high prevalence clinically.

Research has increased understanding of brain activity in eye disease. In the visual system, the optic nerve is formed by axons of retinal ganglion cells and transmits signals relating to external visual stimuli to the lateral geniculate nucleus, which then sends them on to the visual cortex. Dysfunction of the visual system may also affect related brain neural activities which may become significantly different from normal. Research has shown altered brain activity in visual dysfunction. Wang *et al*[6] found regional changes in spontaneous brain activities in patients with DR and nephropathy. However, while VH is a common disease relating to visual loss in adults, its effects on brain activities are poorly understood.

Brain scanning techniques such as magnetic resonance imaging (MRI) have been put into use frequently in assessing changes in microstructure, white matter integrity, metabolic alterations, and other functional and structural changes in brains of patients with DR to help reveal the mechanism of vision loss in this disease[7]. As a widely used tool in neuroimaging, functional magnetic resonance imaging (fMRI) detects variations in brain region activity. These variations are often localized to one region and time-varying[8]. The technique is noninvasive and sensitive to alterations in perfusion and oxygenation of blood in the area of interest, related to neuronal activity in the brain. Resting-state functional magnetic resonance imaging (rs-fMRI) is the measurement of regional brain activity when the brain is in a resting situation with no task to undertake. rs-fMRI has been used to investigate brain activity in visual diseases. Liang *et al*[9] used the rs-fMRI to observe brain activities in patients with unilateral blindness. The technique has also been used to observe brain changes in DR and nephropathy[10-11]. Structural MRI presents anatomical structures and cannot reflect brain function. Fractional amplitude of low-frequency fluctuation (fALFF) is based on fMRI data and can capture low-frequency oscillatory signals of spontaneous neural activity in the brain, directly demonstrating brain functional activity. Moreover, it is sensitive to micro functional changes and can detect intrinsic changes in neural activity when the brain structure does not show significant changes in the early stages of the disease, which is beneficial for early diagnosis and intervention. Positron emission tomography (PET) focuses on metabolic activity and has a weak response to neural activity. fALFF focuses on low-frequency fluctuations in fMRI signals, which are associated with many important brain functions. It can specifically measure amplitude changes and accurately reflect functional patterns. Electroencephalogram (EEG) and magnetoencephalography (MEG) have high temporal resolution, but low spatial resolution, making it difficult to accurately locate. fALFF is based on high spatial resolution of fMRI and can accurately target various local brain regions. In addition, many imaging functions require specific tasks and are susceptible to interference from multiple factors. fALFF can be measured in a resting state, avoiding task interference, and can naturally and comprehensively reflect the intrinsic functions of the brain, making it more friendly to special groups of subjects. Amplitude of low-frequency fluctuation (ALFF) is used as a measuring tool in rs-fMRI for regional intensity of low-frequency fluctuation (LFF) measurement. It is believed that LFFs of blood oxygen-level-dependent (BOLD) fMRI signals can reflect spontaneous neuronal activities in the brain and may be detected synchronously in bilateral parts of the brain such as visual regions. ALFF has been a useful and reliable tool in detecting alterations in brain activities in many common diseases including schizophrenia[12] early Parkinson's disease[13], Leukoaraiosis[14] and others. Also this technique was applied in eye diseases including unilateral blindness[15], and retinal detachment[16]. fALFF is used in the same way as ALFF but is calculated differently. Recently, this method has been used more often in a range of diseases including post stroke depression[17], and some eye diseases such as retinal vein occlusion[18] and normal tension glaucoma[19].

rs-MRI was used in the present study to detect and measure ALFF in DR patients with VH and in sighted healthy controls (HCs), and thus to reveal alterations in regional brain activity

between these two groups.

PARTICIPANTS 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) 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.

Participants Thirty-two patients with DVH and 32 HCs were enrolled. Patients meeting the following criteria were eligible for inclusion in the DVH group: 1) no eye disease other than DR; 2) no diagnosis of severe disease influencing brain activities, such as cerebral concussion or Alzheimer's disease.

HCs were matched to DVH patients according to gender and age. Individuals meeting the following criteria were eligible for inclusion in the control group: 1) diabetes without DVH; 2) no medical history of eye diseases.

Including criteria for both groups are as follows: 1) no brain disease affecting the right anterior cingulate cortex (ACC) and/or cerebellum posterior lobe (CPL); 2) no mental health disorders; 3) no contraindication to MRI examination. Best-corrected visual acuity (BCVA) was measured in both groups. rs-fMRI was used in both groups. Exclusion criteria: 1) stroke; 2) epilepsy; 3) schizophrenia; 4) history of serious mental illnesses such as bipolar disorder.

MRI Parameters During this research, the same MRI scanner (3-Telsa; Trio; Siemens, Munich, Germany) was used to scan all participants in both groups. Scan parameters were as follows: repeat time=2000ms, echo time=40ms, layer thickness=4.0/1 mm, field of view=240×240 mm, inversion angle=90° and plane resolution=64×64. Thirty axial slices covering the brain were recorded, and functional images were acquired. Participants were scanned in the supine position and the entire procedure duration was approximately 8min.

fMRI Data Acquisition and Analysis MRIcro (http://www.MRIcro.com) software was used to obtain data significance and to clean incomplete fMRI data. fMRI images were created using Statistical Parametric Mapping software (SPM8, http://www.fil.ion.ucl. ac.uk/spm/).

fALFF Data Analysis Calculation and analysis of fALFF value was conducted using REST software (REST, http://www.restfmri.net). To exclude noise signals, a band-pass filter of 0.01-0.08 Hz was also used.

HADS Score Acquisition HADS score of DVHs was collected by a questionnaire. The questionnaire used was the Chinese translation of hospital anxiety and depression scale (HADS) designed by Zigmond and Snaith[20]. The higher the score is, the higher level of depression.

Table 1 Basic information of participants in the study

Condition	DVHs	HCs	*t*	*P*
Male/female	16/16	16/16	N/A	>0.99
Age (y)	52.43±9.51	50.92±9.65	0.243	0.846
Weight (kg)	69.92±10.26	67.83±11.87	0.167	0.904
Handedness	32R	32R	N/A	>0.99
Duration of DVH (d)	42.16±12.65	N/A	N/A	N/A
BCVA-left eye	0.45±0.12	1.04±0.16	-3.653	0.011
BCVA-right eye	0.44±0.15	1.06±0.14	-3.321	0.012
Duration of DM (y)	15.68±5.79		N/A	N/A
HbA1c (%)	5.64±0.51	4.42±0.62	0.107	0.826

Independent *t*-test compared between two groups (P<0.05). HCs: Healthy controls; N/A: Not applicable; DM: Diabetic mellitus; DVH: Diabetic vitreous hemorrhage; BCVA: Best-corrected visual acuity.

Statistical Analysis GraphPad prism 8 (Graph Pad Software Inc., San Diego, CA, United States) software was used for data analysis. Between-group differences in mean fALFF values were analyzed using a two-sample *t*-test. Receiver operating characteristic curves (ROCs) were used to analyze the sensitivity of fALFF and test whether fALFF can be a marker for altered brain activities. Pearson's correlation was used to assess relationships between mean fALFF values of DVH patients and two different indices, the HADS score and duration of DVH. Note that higher HADS scores indicate higher levels of depression and anxiety. Statistical significance was indicated by P<0.05. Comparison of mean fALFF value between DVH patients and HCs was analyzed using Gaussian random field (GRF) theory (MATLAB R2020b, MathWorks, United States, URL: https://www.mathworks.com/products/matlab.html; SPM 8, Wellcome Centre for Human Neuroimaging, United Kingdom, URL: https://www.fil.ion.ucl.ac.uk/spm/). Statistical threshold at voxel level was set at 0.005. Statistical threshold at cluster-level was set at the level of 0.05 and the cluster value was set at 57. This approach was chosen as it is a commonly used method in fMRI studies to control the family-wise error rate. Bonferroni correction is a more conservative approach that might overly inflate the risk of type II errors in fMRI studies with a large number of voxels. GRF theory, on the other hand, takes into account the spatial smoothness of the data and provides a more balanced correction method.

RESULTS

No significant differences in age (P=0.846) or weight (P=0.904) were found between the two groups. However, differences were found in BCVA of DVHs and HCs. *t* value of BCVA-left between DVHs and HCs was -3.653 and *t* value of BCVA-right between DVHs and HCs was -3.321 (Table 1). It can be seen that in CPL fALFF value was higher in DVHs compared with HCs, while it was lower in DVHs than HCs in the right ACC or the right medial orbitofrontal cortex

Table 2 fALFF values of different brain regions comparing between HCs and DVHs

Brain area	MNI coordinates			BA	Number of voxels	*P*
	X	Y	Z			
HC<DVH						
CPL	-6	-21	-24	-	235	-4.8198
HC>DVH						
Cingulum_Ant_R/Frontal_Med_Orb_R	6	39	6	32	127	4.4805

Multiple comparison corrects using GRF theory (P<0.05). Statistical threshold of voxel level: 0.05. Statistical threshold of cluster-level: 0.05. Cluster value: 57. GRF: Gaussian random field; fALFF: Fractional amplitude of low-frequency fluctuation; HCs: Healthy controls; DVHs: Diabetic vitreous hemorrhage patients; BA: Brodmann area; CPL: Cerebellum posterior lobe; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right medial orbitofrontal cortex.

Table 3 Two sample *t*-test between HCs and DVHs groups in mean fALFF value difference comparison

Brain area	HC (mean±SD)	DVH (mean±SD)	*t*	*P*
CPL	0.8083±0.04678	0.9216±0.0844	5.951	<0.0001
Cingulum_Ant_R/Frontal_Med_Orb_R	1.188±0.07367	1.034±0.06668	8.621	<0.0001

Two sample *t*-test compared between HCs and DVHs (P<0.05). fALFF: Fractional amplitude of low-frequency fluctuation; HCs: Healthy controls; DVHs: Diabetic vitreous hemorrhage patients; SD: Standard deviation; CPL: Cerebellum posterior lobe; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right medial orbitofrontal cortex.

Table 4 Other diseases used fALFF as a method in resting state fMRI

Author	Year	Disease	Brain areas	
			Increased fALFF	Decreased fALFF
Egorova *et al*[17]	2017	Post stroke depression	DLPFC, right precentral gyrus and left insula	N/A
Tong *et al*[18]	2020	Retinal vein occlusion	Left cerebellum, right cerebellum, right brainstem, left insula	Right alcarinesalcus, right thalamus, left lingual gyrus
Li *et al*[19]	2021	Normal tension glaucoma	N/A	Right angular gyrus, precuneus
Ding *et al*[15]	2022	Congenital monocular blindness	Right middle and inferior temporal gyri, middle and superior frontal gyri, left superior frontal, and angular gyrus	Left inferior occipital and temporal gyri, superior temporal gyrus, inferior parietal lobe and post-central gyrus

fALFF: Fractional amplitude low-frequency of fluctuation; N/A: Not applicable; DLPFC: Dorsolateral prefrontal cortex; fMRI: Functional magnetic resonance imaging.

(OFC; Figure 1, Table 2). These differences were significant (P<0.0001; Table 3).

Receiver Operating Characteristic Curve In this research, fALFF values were considered as a marker for brain changes in patients with DVH compared with HCs. Analysis of the sensitivity of fALFF values in different brain regions was conducted using ROCs. Area under the curves (AUC) for fALFF at the cerebellar posterior lobe was 0.958 (P<0.0001; Figure 2A) and at the right ACC or right medial OFC was 0.952 (P<0.0001; Figure 2B).

Correlation Analysis Mean fALFF value at CPL was positively correlated with the HADS score (r=0.7739, P<0.0001) and duration of DVH (r=0.7003, P<0.0001; Figure 3). Mean fALFF value at the right ACC and right medial OFC were not significantly correlated with either HADS (P>0.05) or duration of DVH (P>0.05; Figure 4).

DISCUSSION

Fractional ALFF of resting state fMRI is a useful and widely used tool in brain scanning. Research has shown links between eye disease and brain function, and accordingly fALFF of resting state fMRI has become increasingly common in observing brain dysfunctions related to eye diseases (Table 4). fALFF is highly sensitive and more accurate than ALFF in detecting neural diseases in the brain, consistent with the findings of the present study (Figure 2). Mean fALFF differences between DVHs and HCs varied between brain regions (Tables 2 and 3). Values were higher in DVH than controls in the CPL but were lower in DVH than controls in the right ACC and right medial OFC (Figures 1 and 5). In DVH, mean fALFF value was positively correlated with HADS score and duration of DVH in CPL region (Figures 3 and 4).

As one of three main regions in the cerebellum, the CPL lies below the primary fissure. It occupies an important position in motor coordination, including eye movement[21]. Dysfunction in this region may lead to visual problems and visual diseases may also cause abnormal activities in this region. Consistent with the present findings, previous research has found abnormal fMRI measures of brain activity in the CPL in patients with eye disease including corneal ulcer, comitant strabismus and DVH[22-24].

CPL may also be involved in cognitive and emotional control[25]. It may receive inputs from brainstem and cerebral cortex, whose activation is related to happiness[26] and minor damage to CPL can lead to emotional dysfunction including

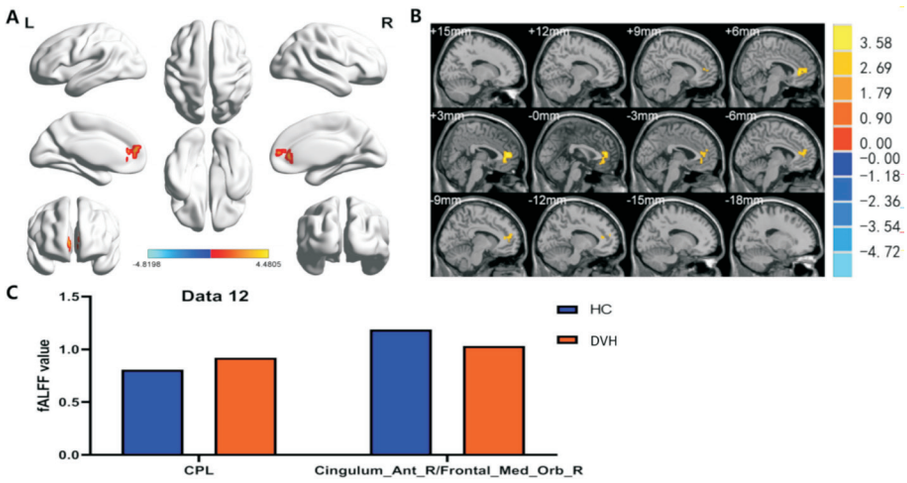

Figure 1 fMRI images and fALFF data analysis in two groups A, B: Different brain activities in CPL, right anterior cingulate cortex and right medial orbitofrontal cortex. The red means increasing fALFF value. The blue part means decreasing fALFF value. C: Data analysis of fALFF values in CPL, right anterior cingulate cortex and right medial orbitofrontal cortex. L: Left; R: Right; HC: Healthy control; DVH: Diabetic vitreous hemorrhage; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right medial orbitofrontal cortex. fALFF: Fractional amplitude of low-frequency fluctuation; CPL: Cerebellum posterior lobe; fMRI: Functional magnetic resonance imaging.

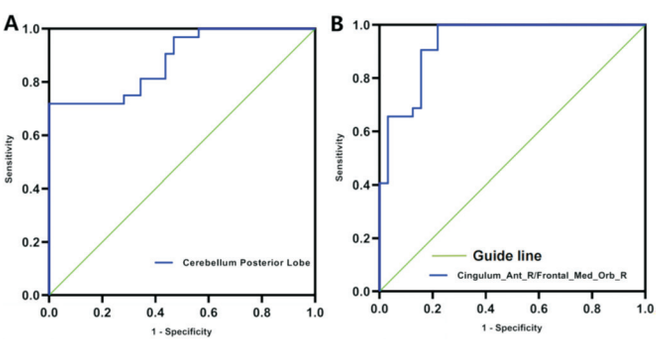

Figure 2 ROC curve of mean fALFF values of altered brain areas A: Area under the ROC curve were 0.8818 (P<0.0001; 95%CI: 0.8007-0.9630) for CPL; B: Area under the ROC curve were 0.9336 (P<0.0001; 95%CI: 0.8751-0.9921) for Cingulum_Ant_R/Frontal_Med_Orb_R. ROC: Receiver operating characteristic; fALFF: Fractional amplitude of low-frequency fluctuation; CI: Confidence interval; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right orbitofrontal medial cortex.

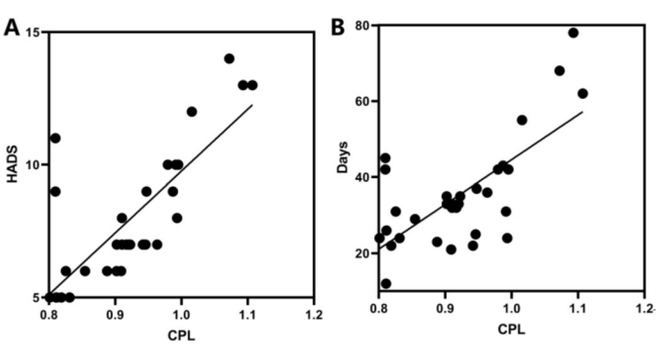

Figure 3 Correlation of mean fALFF value of CPL in DVHs A: Positive correlation in mean fALFF value and HADS (r=0.7739, P<0.0001, 95%CI: 0.5824-0.8840); B: Positive correlation in mean fALFF value and duration of DVH (r=0.7003, P<0.0001, 95%CI: 0.4652-0.8431). fALFF: Fractional amplitude of low-frequency of fluctuation; CPL: Cerebellum posterior lobe; DVHs: Diabetic vitreous hemorrhage patients; HADS: Hospital anxiety and depression scale; CI: Confidence Interval.

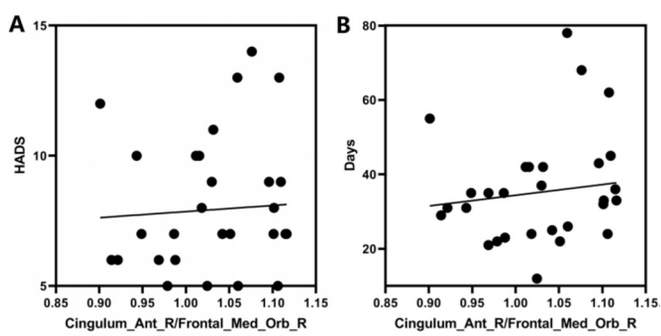

Figure 4 Correlation of mean fALFF value of right ACC/medial OFC in DVHs A: Correlation in mean fALFF value and HADS; B: Correlation in mean fALFF value and duration of DVH. fALFF: Fractional amplitude of low-frequency fluctuation; ACC: Anterior cingulate cortex; OFC: Orbitofrontal cortex; DVHs: Diabetic vitreous hemorrhage patients; HADS: Hospital anxiety and depression scale; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right orbitofrontal medial cortex.

depression. In one study on depressive patients, fMRI measures of voxel-wise degree centrality values in CPL were reduced[27]. In addition, negative correlation has been found between voxel-wise degree centrality value and HADS scores in exophthalmos patients[28], suggesting a link between visual anomaly, depression and abnormal activity in the CPL.

In the present research, HADS scores were collected in patients with DVH and were positively correlated with mean fALFF value of the CPL, which may suggest a link between DVH and depression. Depression level may in turn be related to abnormal activities in CPL (Figure 6). Duration of disease is often considered a factor in its severity. In this study, mean fALFF value of CPL in DVH was positively correlated with duration of the disease, suggesting an association between DVH dysfunction in CPL, the latter perhaps related to depression level in patients (Table 5).

Table 5 Results and related diseases of brain areas alterations

Brain area	Results	Function	Possible diseases
CPL	HC<DVH	Motor coordination Happiness activation	Depression
Cingulum_Ant_R/Frontal_Med_Orb_R	HC>DVH	Reward system processing	Reflect reward system dysfunction

CPL: Cerebellum posterior lobe; HC: Healthy control; DVH: Diabetic vitreous hemorrhage; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right medial orbitofrontal cortex.

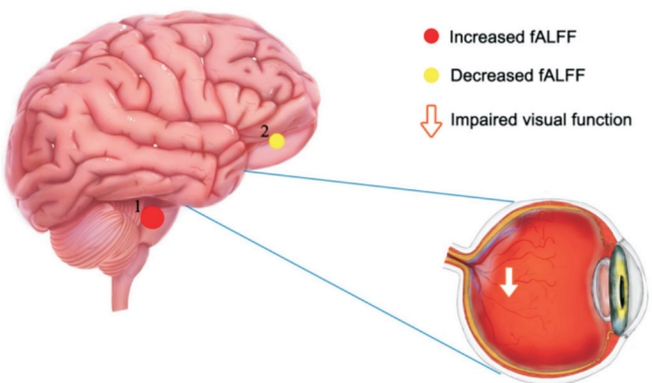

Figure 5 Altered fALFF values existed in different brain areas in DVH patients In DVHs, increased mean fALFF value existed in CPL while decreased mean ALFF value existed in Cingulum_Ant_R and Frontal_Med_Orb_R. fALFF: Fractional amplitude of low-frequency fluctuation; DVHs: Diabetic vitreous hemorrhage patients; CPL: Cerebellum posterior lobe; Cingulum_Ant_R: Right anterior cingulate cortex; Frontal_Med_Orb_R: Right medial orbitofrontal cortex.

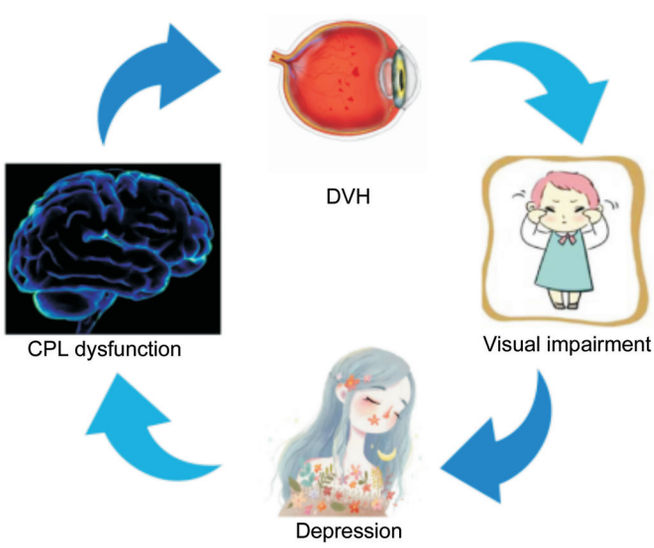

Figure 6 Possible relation between CPL fMRI result and depression result in DVHs DVH leads to visual impairment, which may lead to abnormal depression level in patients. This may cause the abnormal activities in CPL. DVH: Diabetic vitreous hemorrhage; CPL: Cerebellum posterior lobe; fMRI: Functional magnetic resonance imaging.

The ACC is the anterior third of the cingulate cortex, which surrounds the corpus callosum and is involved in many neural processes including emotion processing (its major function)[29], memory[30] and action. ACC is a part of the limbic system and receives input mainly from the OFC and amygdala, both of which have important roles in emotion processing. Therefore, ACC dysfunction is related to many mood disorders. Decreased ACC activities have been found in bipolar disorder[31], depression[27], and schizophrenia[32]. Recent research has found abnormal activity in the ACC in some visual diseases. In congenital comitant strabismus, ALFF in the ACC was decreased and was negatively correlated with HADS score and duration of the disease[33]. In unilateral blindness, Liao *et al*[10] reported that mean fALFF value in the left ACC was reduced and negatively correlated with a depression scale score, suggesting depression and ACC dysfunction in this condition.

In the present research, decreased mean fALFF value was found in the right ACC and right medial OFC regions in DVH, in agreement with previous studies (Tables 2 and 3). However, mean fALFF values in these two regions in DVH were not correlated with either HADS score or disease duration, in contrast with previous research (Figure 4). This may suggest that DVH is not linked with the neural pathways in ACC and OFC related to depression, although it is linked with dysfunction in these two regions. Perhaps this dysfunction leads to anomalies in reward systems, since part of the ACC is highly functionally linked with the medial OFC (Table 5).

The ROC curve in our study indicates that fALFF values have high sensitivity in distinguishing DVH patients from HCs. At the technical level, fALFF measurement relies on mature fMRI technology, and many large hospitals have equipped it with equipment. At the same time, computer technology and medical image processing software have matured and can accurately calculate and analyze fALFF values, making the technology feasible. In terms of clinical application, studies have shown that patients with depression have significantly abnormal fALFF values in the prefrontal limbic system, which can assist in the diagnosis of early and atypical patients. During treatment, changes in fALFF values can reflect the condition and treatment effectiveness, providing personalized treatment assistance and complementing traditional diagnosis and other auxiliary examinations. From an economic perspective, increasing the cost of fALFF measurement is not high for hospitals with fMRI equipment; The cost of equipment procurement is also decreasing for hospitals that are not equipped. Through medical insurance coverage and cost regulation, patients are expected to bear the cost of examinations, which can also reduce indirect costs from a

societal perspective. In terms of ethics, fMRI examination is non-invasive, radiation free, and poses no risk of violating patient privacy and dignity. Fully informing patients of relevant information and obtaining informed consent before the examination is in compliance with ethical principles, therefore the feasibility of this examination is relatively high. However, we also need to acknowledge these limitations. The current research is conducted in a research environment and needs to be further validated in clinical practice. Previously, we have conducted fMRI studies on changes in intrinsic functional connectivity in the primary visual cortex of young patients with concomitant exotropia[34], abnormal local spontaneous neural activity in the visual pathway of patients with retinal detachment[35], and functional connectivity between the hemisphere of the dorsal visual pathway in patients with unilateral acute open eye injury[36]. All of these studies have achieved good results, further demonstrating the value of MRI in clinical research and diagnosis.

There are limitations in this research. The sample was small, thus the results may lack universality. Scanning areas were limited, restricting the exploration of brain regions. Our study only shows correlational relationships between DVH, altered brain activity, and depression. While we found significant correlations between the fALFF values in certain brain regions (such as CPL) and depression scores (HADS) as well as DVH duration, this does not necessarily imply causation. The visual impairment caused by DVH may lead to changes in visual pathways and related brain neural activity, which in turn may be related to emotional changes. However, further longitudinal or intervention studies are needed to establish causal relationships. In the future, we will track DVH patients over time and observe changes in brain activity and depressive symptoms before and after DVH treatment. The control group in our study includes people with diabetes but no DVH. In future studies, we will add such a control group to deepen our understanding of the pathophysiological mechanisms involved. Finally, although the CPL and right ACC both have roles in ocular position adjustment, the present research did not investigate this factor. Therefore, this aspect of the research would benefit from further study.

In conclusion, significantly different fALFF values in certain brain regions in DVH compared with HCs suggests that visual impairment caused by DVH may affect activity in brain regions related to vision. Together with the HADS score results, these findings also suggest a link between depression, visual deterioration and dysfunction of related brain regions in patients with DVH. Further research is needed to reveal the mechanisms underpinning these findings.

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