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Research Article

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Analysis of interhemispheric functional connectivity with the congenital blindness: interactions between blindness and emotional regulation

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Abstract

Purpose Negative emotions, as an important risk factor, promote the development of many diseases. The study is designed to discuss alterations of interhemispheric functional connectivity (FC) with congenital blindness (CB) subjects by adopting voxel-mirrored homotopic connectivity (VMHC). Based on the alterations in FC, we assessed whether there was an interaction between blindness and emotional regulation.

Method VMHC values were collected from 24(males/females = 9/15) subjects with congenital blindness and 24(males/females = 9/15) healthy controls. The gender, age and other information of the healthy controls were closely matched with the disease group. The VMHC values were applied to assess alterations in hemispheric FC between the two groups. Receiver Operating Characteristic (ROC) were applied so as to classify the mean VMHC values of the CB and HC subjects. In addition, an evaluation, which was applied the Pearson Correlation analysis, was employed to compare the correlation between VMHC values of specific brain areas and clinical features of CB subjects.

Result The area under curve (AUC) was 0.8750 ($P < 0.0001$) for bilateral fusiform gyrus (FFG), 0.9670 ($P < 0.0001$) for bilateral superior occipital gyrus (SOG), 0.9653 ($P < 0.0001$) for bilateral thalamus (THA) and 0.9462 ($P < 0.0001$) for bilateral paracentral lobule (PCL). Furthermore, anxiety scores (AS) and depression scores (DS) displayed a positive correlation with the VMHC values of bilateral thalamus ($r = -0.943$; $P < 0.001$ and $r = 0.869$; $P < 0.001$) in CB group.

Conclusion In the CB group, aberrant interhemispheric FC was observed in specific cerebral regions. These altered VMHC values in the cerebral areas might be potential diagnostic markers of emotional disorders and aberrant brain activities in the CB patients. Humanistic care and necessary psychological treatment for blind patients may be one of the measures to prevent vision from persistent loss in the future. At the same time, the changes of brain function may also provide new ideas for individualized treatment of patients with anxiety, depression and other emotional disorders.

Keywords Congenital blindness, Interhemispheric functional connectivity, Anxiety and depression, Voxel-mirrored homotopic connectivity (VMHC), Predictive

preventive personalised medicine (3P/PPPM)

Introduction

Blindness is one of the most severe consequences of eye diseases. It estimated that 43.3 million people will be blind in 2020[1]. Furthermore, it predicted that this number will grow to about 61 million by 2050[1]. Effective treatments against blindness, especially congenital blindness, are still missing.

Blindness, which is associated with eye dysfunction, is also related to aberrant visual cortex function. Studies have indicated that the maturation process of the visual cortex is indispensable from the assistance of typical visual experience[2-4]. A prominent reduction, which displayed in the early visual cortex, in the volumes of grey matter exhibited with the early blindness patients[5]. An enhancement of regional homogeneity was observed in the occipital region of early blindness patients [6]. In addition, the two sides of the cerebrum need to develop in parallel so that matches of information processing between brain hemispheres can be ensured. Synchronization between hemispheres of the cerebrum also operated on visual processing. A study of VMHC analysis revealed that in the primary visual cortex, and in the visual association cortex, there is a noticeable reduction of interhemispheric functional connectivity[7]. X. Huang et al. demonstrated that interhemispheric functional connectivity became abnormal in late blindness patients [8]. Foubert L et al. stated that despite aberrant postnatal visual experience, the synchronicity of neural activity, showing in the adult visual cortex, was likely to remain[9]. Another research displayed synchrony between brain hemispheres closely connected with visual experience [10].

In order to assess changes in cerebral structure and function, we could use resting-state functional magnetic resonance imaging (rs-fMRI), a non-invasive neuroimaging technology[11]. The VMHC, a method included in rs-fMRI technology, could be applied to investigate the interhemispheric FC [12]. A number of investigates of ophthalmic diseases has been assessed by the VMHC method, such as monocular blindness, primary open-angle glaucoma, unilateral retinal detachment, strabismus, amblyopia and so on [13-17] (Table 3).

The loss of vision can be extreme damage to individual physical and mental health simultaneously. Almost all of our daily activities are visually based. The loss of vision contributes to various emotional changes. The anxiety and depression of blind patients are easily caused by worries about their future living conditions, discrimination and excessive sympathy from all parts of society. An MRI-based study revealed a prominent diminution in the volume of the left amygdala in the primary open-angle glaucoma patients [18]. The amygdala, as is known, is an important part of the emotional regulatory pathways. In other words, eye diseases, especially those that affect vision, may interact with emotional regulation. To provide more evidence for this hypothesis, AS and DS of CB patients were also collected in this study to evaluate whether there is an interaction between blindness and emotional regulation.

At present the medical field is going through a big revolution. The way of medical service is changing from "treat existing diseases" to "diagnose probable diseases" and "prevent diseases" [19, 20], which is also known as "PPPM" (predictive, preventive, and personalized medicine) [21]. Investigating the relation between blindness and emotional regulation may provide crucial evidence for predicting and preventing emotional disorders in blind patients. In addition, it may offer new ideas for individualized treatment of patients with anxiety disorder, depressive disorder and other emotional disorders because of confirmation of the interaction between blindness, alternations of interhemispheric FC and emotional regulation.

Therefore, the VMHC method was adopted to discuss alterations of cerebral hemispheric FC in CB. We also tried to assess whether there was an interaction between blindness and emotional regulation.

Materials and Methods

Participants

Twenty-three participants with CB (males/females = 9/15) were recruited on the basis of the inclusion standards from 2015.06.13 to 2015.07.05: 1) Blindness occurred at birth or shortly after birth; 2) best-corrected visual acuity of oculus uterque < 0.05. The exclusion criteria were: 1) brain disease and cardiovascular disease, 2) conditions

of psychiatric disorders, 3) metabolic and immune system disease. 23 health controls (males/females = 9/15) were enlisted in the research, who are of a similar age range. Requirements were listed below: 1) with the visual acuity (VA)≥ 1.0 and without any Ophthalmic disease; 2) without metabolic and immune system disease; 3) without Psychiatric disorders; 4) without malformations in the cerebral parenchyma; 5) accessible to the rs-MRI examination.

MRI parameters

The 3-Tesla MRI scanner (Germany, Siemens, Munich) was applied to collect information of participants. Subjects lie relaxed and flat, keeping their head unmovable simultaneously, when they are be scanning. They also need to close their eyes and remain awake, avoiding active thinking. Firstly, we obtained T1 and T2 sequence information by the scanner. The details were: gap = 0.5 mm; thickness = 1.0 mm; echo time = 2.26 ms; repetition time = 1,900 ms; field of view = 250×250 mm; acquisition matrix =256×256; flip angle = 9°. The functional image data, which comprised 240 consecutive time points, were obtained by scanning the whole brain. The details were: gap = 1.2 mm; thickness =4.0 mm; echo time = 30 ms; repetition time = 2,000 ms; field of view = 220×220 mm; acquisition matrix = 64×64; flip angle = 90°.

MRI data processing

In order to standardize the obtained functional MRI images, the software of DPARSFA (http://rfmri.org/DPARSF) and toolkit of SPM8(http://www.fil.ion.ucl.ac.uk/spm) were applied. Image data from the initial ten time points of each subject is eliminated because of unstable machine signals and the maladjustment of participants. Then, we screened the remaining images and excluded some subjects who didn't meet the requirements. Details of the requirements are as follows: angular rotation≤1.5° and head movement in the x, y or, z direction≤1.5 mm. At the same time, we also standardized the time difference in the scanning process. In order to reduce the inaccuracy of MRI data in spatial structure, MRI data were normalized into average MRI images. These images were then segmented by the Dartel toolkit. For purpose of making the fMRI images meet the spatial criteria of Montreal

Neurological Institute (MNI), the standard echoplanar image template was employed. After that, all voxels were re-sampled according to the 3mm×3mm×3mm resolution standard. The influence of high-frequency noise on data is reduced by low-frequency filtering (0.01-0.08 Hz). Moreover, the influence of other signals, such as cerebrospinal fluid signals and head movement, were decreased by multiple regression method.

Statistical analysis for VMHC

The VMHC maps were normalized with Fisher's z transformation in the REST (http://resting-fmri.sourceforge.net). The voxel-wise difference between the HC and CB groups was examined by performing two-sample t-tests($P<0.05$). Multiple comparisons were examined by performing Gaussian Random Field theory (the voxel level $P< 0.05$; cluster size>50 voxels; FDR corrected).

Statistical analysis

The demographic information was analyzed by SPSS ver.26,0 (IBM Corp, USA). In other words，the independent sample T-test was adopted for the analysis of age ($P < 0.01$). Sex and handedness were analyzed by Chi-square test ($P < 0.01$). Two-sample t-tests ($P< 0.05$; cluster > 50 voxels; FWE corrected) were adopted to inspect the mean VMHC values. The relation between specific cerebral areas and emotional performance was assessed by Pearson correlation. It regarded that $P<0.01$ shows a statistically significant difference. The average VMHC values in specific cerebral areas of CB and HC subjects were distinguished with Receiver Operating Characteristic (ROC) curve.

Brain-behavior correlation analysis

Cerebral regions, which identified as the areas of interest in the CB individuals, were analyzed by REST instruments. The associations between VMHC values of specific cerebral areas in the CB subjects and clinical characteristics were evaluated in accordance with association analysis, and $P < 0.01$ identified as the statistically significant difference.

Result

Demographics and optical measurements

23 patients with congenital blindness (9 males, 15 females) and 23 healthy controls

(9 males, 15 females) involved in this study. No remarkable diversities in gender (P > 0.99) and age (P = 0.867) between the HC and the CB subjects. In CB group, the best-corrected visual acuity of oculus uterque was no light perception or anophthalmia. It in HC group was 1.0. Details described in Table1.

Table 1 Demographic and clinical information of CB and HC groups

	CB	HC	t-value	P value
Male/female	9 / 15	9 / 15	N / A	> 0.99
Age (years)	14.5±3.5	14.29±3.46	0.169	0.867
Handedness	23R	23R	N / A	> 0.99
Duration of Congenital blindness (months)	166±46	N / A	N / A	N / A
Best-corrected VA-OU	nLP	1.0	N / A	N / A

Two groups were compared by independent t-tests (P<0.01 referred to statistically significant diversities).
HC, healthy controls; CB, Congenital blindness; VA, visual acuity; N/A, not applicable; OU, oculus uterque; nLP, no light perception.

VMHC differences

Compared with HC, VMHC in the CB group significantly decreased in two regions: bilateral fusiform gyrus(t=-5.82) and bilateral superior occipital gyrus (t=-7.92) (Fig. 1, Table 2). The VMHC values of bilateral thalamus(t=7.93) and bilateral paracentral lobule(t=7.89) in CB patients remarkably increased than those of HC (Fig. 1, Table 2). A histogram (Fig. 1c) represents the difference of average VMHC values in the CB and HC groups.

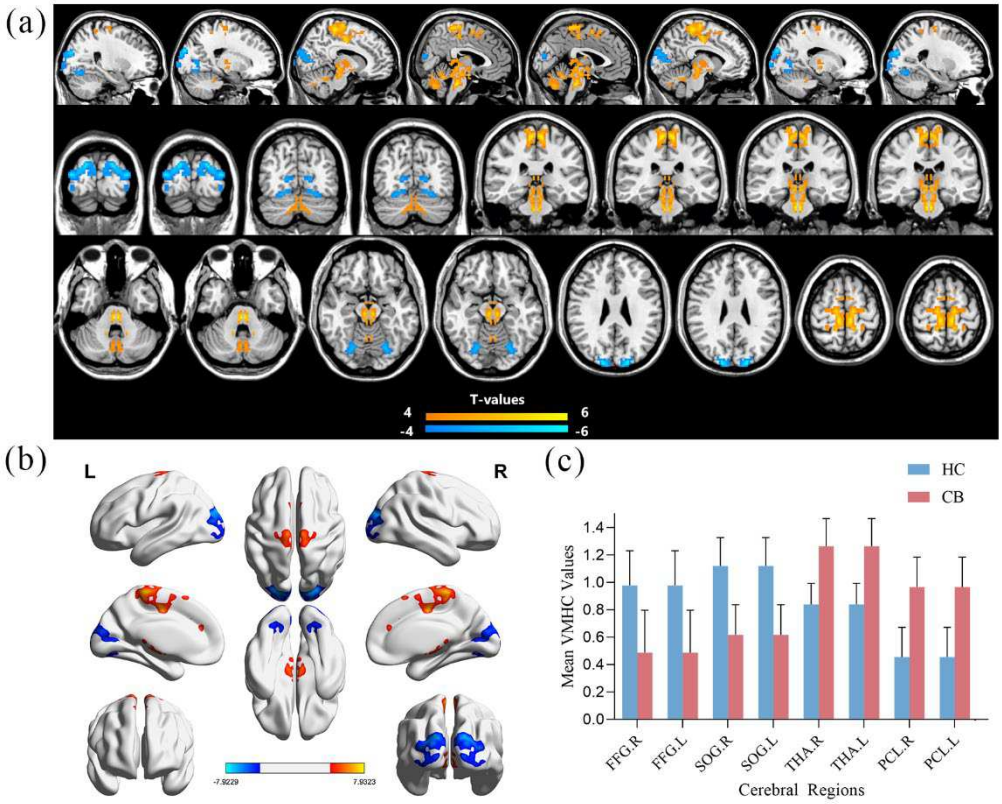

Fig. 1. Alterations of interhemispheric FC in the CB and HC. Obvious diversities were showed in the FFG, SOG, THA and PCL. The higher VMHC values was represented by orange regions and the lower VMHC values was displayed by blue regions. Multiple comparisons were examined by performing GRF theory (the voxel level P< 0.05; cluster size>50 voxels; FDR corrected). (a) and (b) The average value of altered VMHC values in the CB and HC groups. (c): The diversities of the interhemispheric FC were great in the FFG, SOG, THA and PCL.

FC, functional connectivity; CB, Congenital blindness; HC, healthy controls; FFG, Fusiform gyrus; SOG, Superior occipital gyrus; THA, Thalamus; PCL, Paracentral lobule; GRF, Gaussian random field; VMHC, voxel-mirrored homotopic connectivity.

Table 2 Encephalic regions with prominent variation VMHC values

Encephalic regions	BA	MNI coordinates			Peak voxels	T-value	ROI order
		X	Y	Z			
CB<HC							
Fusiform Gyrus R	37	24	-72	-15	76	-5.82	Cluster 3
Fusiform Gyrus L	37	-24	-72	-15	76	-5.82	Cluster 4
Superior Occipital Gyrus R	18	18	-90	27	524	-7.92	Cluster 5
Superior Occipital Gyrus L	18	-18	-90	27	524	-7.92	Cluster 6
CB>HC							
Thalamus R		3	-27	-33	494	7.93	Cluster 1
Thalamus L		-3	-27	-33	494	7.93	Cluster 2
Paracentral Lobule R	6	9	-30	63	477	7.89	Cluster 7
Paracentral Lobule L	6	-9	-30	63	477	7.89	Cluster 8

Multiple comparisons were examined by performing GRF theory (the voxel level P< 0.05; cluster size>50 voxels; FDR corrected).
BA, brodmann area; VMHC, voxel-mirrored homotopic connectivity; MNI, Montreal Neurological Institute; ROI, region of interest; CB, Congenital blindness; HC, healthy controls; GRF, Gaussian random field; L, left; R, right.

Receiver operating characteristic (ROC) curve

For verifying the diversities in VMHC might turn into necessary diagnostic biomarkers, the ROC curve analysis was regarded as statistical evidence to differentiate illness from health controls. The area under curve (AUC) of every specific cerebral region were shown below: bilateral fusiform gyrus (0.8750; P< 0.001; 95%CI,0.8045-0.9455,) (Fig. 2a); bilateral superior occipital gyrus (0.9670; P<0.001; 95% CI,0.9331-1.000) (Fig. 2a); bilateral thalamus (0.9653; P<0.001; 95% CI,0.9363-0.9943) (Fig. 2b); bilateral paracentral lobule (0.9462; P<0.001; 95% CI, 0.9060-0.9864) (Fig. 2b).

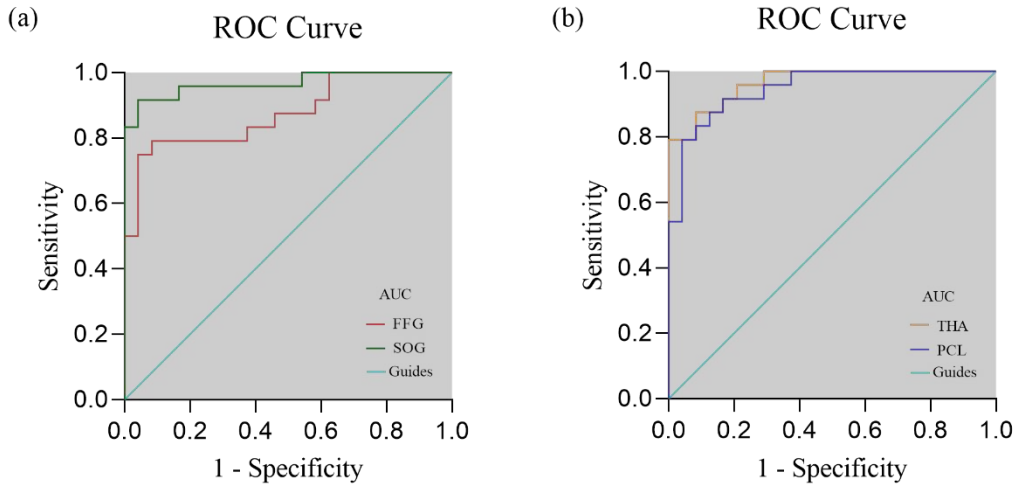

Fig. 2: ROC curve analysis for the average value of altered VMHC. The quality of the classification model was measured with the AUC. It was identified as a superb accuracy when the AUC value is over 0.8. (a) The AUC was 0.8750 (95% CI 0.8045-0.9455, p < 0.0001) for FFG, and 0.9670 (95% CI 0.9331-1.000, p <0.0001) for SOG. (b) The AUC was 0.9653 (95% CI 0.9363-0.9943, p <0.0001) for THA, and 0.9462 (95% CI 0.9060-0.9864, p<0.0001) for PCL.

VMHC, voxel-mirrored homotopic connectivity; ROC, receiver operating characteristic; CI, confidence interval; AUC, area under curve; FFG, Fusiform gyrus; SOG, Superior occipital gyrus; THA, Thalamus; PCL, Paracentral lobule.

Correlation analysis

In CB group, the AS and DS displayed a positive correlation with the VMHC values of bilateral thalamus (r =− 0.9432; P< 0.0001 and r = 0.8694; P< 0.0001) (Fig. 3).

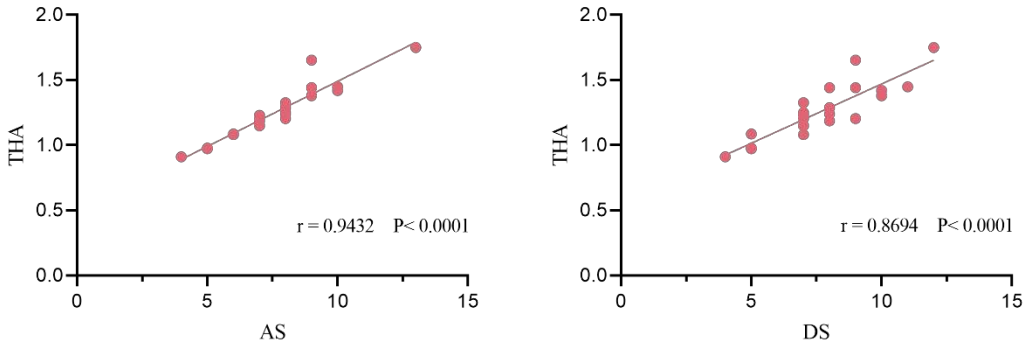

Fig. 3 Correlation between the emotional characteristics and VMHC values of the bilateral thalamus. In the thalamus, positive correlations were displayed between the altered VMHC values and (a) AS (r =− 0.9432; P< 0.0001) / (b) DS (r = 0.8694; P< 0.0001).

VMHC, voxel-mirrored homotopic connectivity; AS, anxiety scores; DS, depression scores.

Discussion

The VMHC method could regarded as statistical evidence to indicate alterations in interhemispheric FC. Past researches have adopted the method in other ophthalmological diseases (Table 3). Based on previous research, our research took the lead to dig the interhemispheric FC taking part in CB individuals. Compared with HC, VMHC in the CB group significantly decreased in two regions: bilateral fusiform gyrus(t=-5.82) and bilateral superior occipital gyrus (t=-7.92). The VMHC values of bilateral thalamus(t=7.93) and bilateral paracentral lobule(t=7.89) in CB patients remarkably increased than those of HC (Fig. 1; Table 2; Fig. 4).

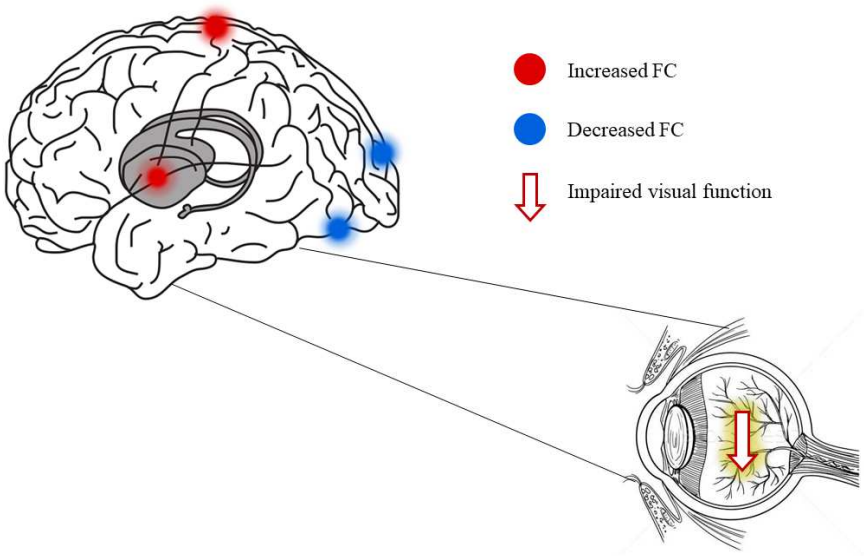

Fig. 4 Summary of the altered VMHC values in the CB group. VMHC in CB group significantly decreased in two regions: bilateral fusiform gyrus(t=-5.82) and bilateral suprerior occipital gyrus(t=-7.92), and increased remarkably in two regions: bilateral thalamus(t=7.93) and bilateral paracentral lobule(t=7.89). The degree of alterations is indicated by the size of the spot.
VMHC, voxel-mirrored homotopic connectivity; CB, congenital blindness.

Table 3 Ophthalmological diseases assessed by VMHC method

References	Year	Diseases	Brain Areas	
			OD > HC	OD < HC
Liang, M. Xie, B, et al. [22]	2017	Anisometropic and Strabismic Amblyopia	LGG/FFG	
Shao, Y. Bao, J, et al. [13]	2018	Monocular Blindness		LGG/CAL/CUN
Wang, Q. Chen, W, et al. [14]	2018	Primary Open-Angle Glaucoma		V1/V2/V3/V4/V5
Ye, L. Wei, R, et al. [23]	2018	Unilateral Acute Open Globe Injury		CUN/LGG/MOG/ CAL
Qing, Y. Kang, H. H, et al. [15]	2018	Unilateral Retinal Detachment		STG/OL/CUN
Dong, Z. Z. Zhu, F. Y, et al. [24]	2019	Acute Eye Pain		CAL/LGG/Pre-CG/Pos-CG/MFG
Shi, W. Q. Liu, J. X, et al. [25]	2019	Corneal Ulcer		CAL/LGG/Pre-CG/Pos-CG/MFG
Peng, J. Yao, F, et al. [16]	2021	Strabismus And Amblyopia		CE/FSO/TI/FS
Zhang, S. Gao, G. P, et al. [17]	2021	Strabismic Amblyopia	CA/CAU/HIP/CC1	

VMHC, voxel-mirrored homotopic connectivity; OD, ophthalmological diseases; LGG, lingual gyrus; FFG, fusiform gyrus; CAL, Calcarine; CUN, cuneus; V1, Primary visual cortex; V2, Secondary visual cortex; V3/V4/V5, Associative visual cortex; MOG, middle occipital gyrus; STG, superior temporal gyrus; OL, occipital lobe; Pre-CG, precentral gyrus; Pos-CG, postcentral gyrus; MFG, medial frontal gyrus; CE, Cerebellum; FSO, bilateral frontal superior orbital; TI, temporal inferior; FS, frontal superior; CA, cingulum ant; CAU, caudate; HIP, hippocampus; CC1, cerebellum crus 1; HC, healthy control.

The ROC curve analysis could be used as statistical evidence to differentiate illness from healthy controls. The quality of the classification model was measured with the area under ROC curve (AUC), a standard. It was identified as a superb accuracy when the AUC value is over 0.8. In our research, great AUC values, discovered in all regions of interest, were observed by the ROC curve analysis. It indicated that the VMHC method might be capable diagnostic indicator of detecting dysfunctional brain activity and mood disorder in CB patients (Fig. 2).

Recognition-related functional zone

The fusiform gyrus is contained in the occipital lobe and temporal lobe, also named the lateral occipitotemporal gyrus [26]. It considered that the fusiform gyrus is specific to hominoids [27]. Although functions of the fusiform gyrus were not defined, it has been shown to take part in higher processing of visual information (Table 4). Some research have shown that the fusiform gyrus is directly related to facial recognition [28-30] (Table 4). Based on a fMRI study of patients with congenital blindness, in the fusiform gyrus, visual experience was proved to be a nonsignificant factor affecting the formation of face-selectivity[31]. Besides, the left occipitotemporal region, especially the fusiform gyrus, make a difference in the process of reading [32]. Cohen's team has conducted extensive researches in this area and discovered that the fusiform gyrus regulated and controlled the process of word recognition through visual functions [33-35]. Therefore, the region was also termed as "visual word form area" [34-36]. According to functional neuroimaging, a study based on patients with pure alexia and hemiopsia also demonstrated the left fusiform gyrus took part in the regulation of visual word-recognition[37]. In this research, the CB group indicated decreased VMHC in the fusiform gyrus (Fig. 1; Table 2; Fig. 4), which may be associated with the deficiency of visual signals processing in CB. Because of the deficiency of necessary visual experience, the recognition to word based on vision may impaired in patients with congenital blindness.

Table 4 The alternations of FC in specific cerebral regions and its possible influences

Cerebral Regions	Laboratory Findings	Brain Function	Possible Influences
Fusiform Gyrus	CB < HC	Management of higher visual information; Facial recognition; Word recognition	Visual dysfunction; Prosopagnosia; Dyslexia
Superior Occipital Gyrus	CB < HC	Object recognition; Spatial analysis; Episodic memory	Visual dysfunction; Spatial disturbance; Memory dysfunction
Thalamus	CB > HC	Transduction of sensory and motor signals; Regulation of sleep, consciousness, alertness, emotion and memory	Sensory deficits; Permanent coma; Episodic event memory deficits; Emotional processes dysfunction
Paracentral Lobule	CBs > HC	Motor and Sensory innervations; Regulation of defecation and micturition; Regulation of emotion	muscle weakness; Urinary incontinence; Emotional processes dysfunction

HC, healthy controls; CB, Congenital blindness

The occipital gyrus is charge of object recognition [38]. The superior occipital gyrus was revealed that it related to spatial ability[39, 40] (Table 4). In a meta-analysis of brain regions, which related to spatial ability, connections were displayed between the left superior occipital gyrus and large-scale spatial ability, while activation of the right superior occipital gyrus took part in regulation of large-scale and small-scale spatial ability[40]. Multiple sensory functions are involved in the normal process of spatial recognition. A study, based on early blind people, has revealed that the middle occipital gyrus was highly activated during spatial recognition involving auditory and tactile[41]. And our research discovered that in the bilateral superior occipital gyrus, CB patients displayed reduced VMHC values (Fig. 1; Table 2; Fig. 4), which suggest the aberrant FC in the superior occipital gyrus. Hence, it hypothesized the superior occipital gyrus is more involved in vision-related spatial recognition.

Functional zone of motor and sensuous innervation

The thalamus generally regarded to be a relay station between different subcortical regions and the cerebral cortex [42]. Thalamus includes several thalamic nuclei, sensory signals of vision, audio, touch and so on can be processed and transmitted to the cerebral cortex through their own thalamic nucleus (Table 4). The region associated with visual signals transmission is the lateral geniculate nucleus [43]. The medial geniculate nucleus serves as a relay station for auditory signals to the primary auditory cortex [43]. Touch and proprioceptive signals also delivered to the corresponding cortical regions through the thalamic nucleus [43]. A number of studies have exhibited that the blindness showed better auditory sense[44-46], as well as higher tactile sensitivity in their fingertips[47-49]. Our results showed CB had increased VHMC values in the bilateral thalamus (Fig. 1; Table 2; Fig. 4). The increase of VMHC values might connected with the enhancement of auditory and tactile sensitivity. But we don't know which part of the thalamus in CB subjects was changed. We should zone the thalamus into more detailed areas so that the function' changes in CB patients of the thalamus will be understood in future studies.

The paracentral lobule is charge of motor and sensuous innervation in the contralateral lower extremity[50, 51] (Table 4). A study of patients with superior parietal lobule injury displayed that integration of sensorimotor connected with paracentral lobule[52]. It also controls defecation and urination[53, 54] (Table 4). In the research, CB group displayed an obvious increase of VHMC in the Paracentral lobule (Fig. 1; Table 2; Fig. 4), which may be a reflection of improved control of lower extremity.

Emotion-related functional zone

The thalamus, a mass of gray matter, is on the dorsal side of the diencephalon [55]. Some of its features include delivery of sensory signals, regulation of sleep, consciousness, alertness, emotion, and function of memory [56-60] (Table 4). Damage to the thalamus can lead to various serious consequences, such as sensory deficits, permanent coma, episodic event memory deficits and so on [57, 58, 60] (Table 4). Moreover, recent studies indicated that the thalamus exerted essential effects on

emotional visual information processing by the colliculi- pulvinar-cortical pathway and/or the colliculi- pulvinar-amygdalar pathways [61, 62]. In this study, in CB patients, the VMHC values increased in the bilateral thalamus and those in the bilateral occipital lobe decreased (Fig. 1; Table 2; Fig. 4). It seemed to indicate abnormalities in the emotional processing associated with the colliculi- pulvinar pathway. An experiment with a mouse model of depression has revealed the thalamus mediated allodynia, which based on a depression-like state, was associated with the anterior cingulate cortex [59]. Moreover, patients in the CB group expressed more anxiety and with higher AS and DS than the control group. AS and DS were positively related to VMHC values of the thalamus (Fig. 3). It is likely that the abnormal interhemispheric functional connectivity is also associated with impairment of the impaired emotional processes with CB. The visual dysfunction subjectively aggravated the subjects' anxiety and depression. Meanwhile, visual deprivation may further affect emotional regulation by altering FC between brain hemispheres, creating a blind - anxiety vicious circle. It is possible that negative emotions can in turn affect brain function and even be a major risk of blindness. Examples of sudden blindness due to serious psychic accidents are sometimes reported in the social news. These may also be hints that Unhealthy emotion and visual dysfunction may be reciprocal causation (Fig. 5).

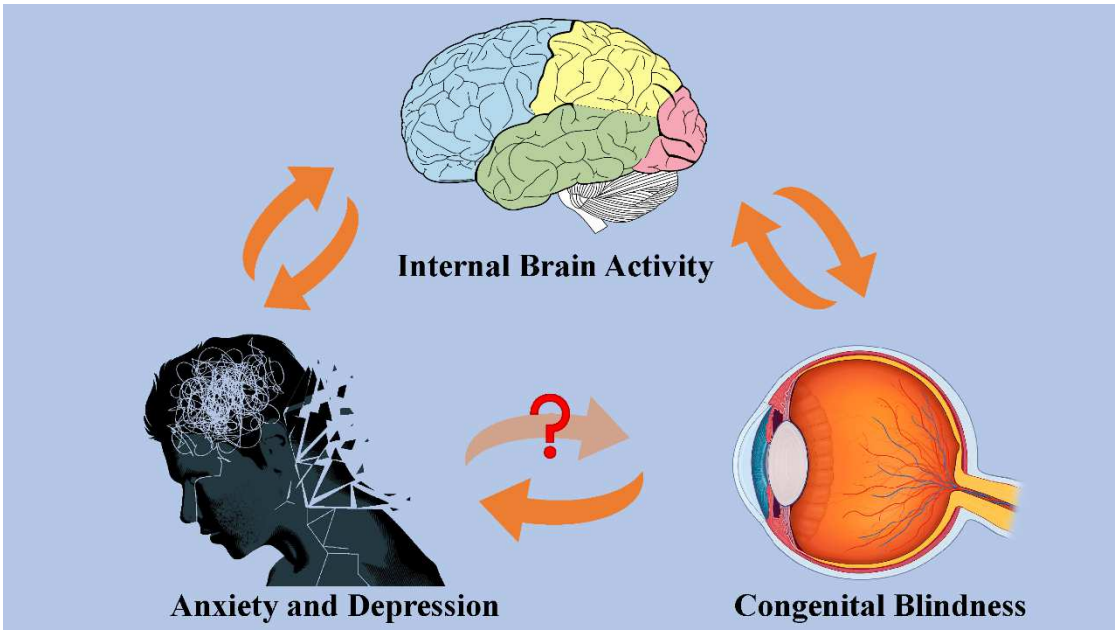

Fig. 5 Potential interactions between visual dysfunction, brain functions and emotion regulation. Patients in the CB group expressed higher AS and DS than the control group. They also had visual impairment and altered function in specific brain regions. The evidence suggested potential interactions between visual dysfunction, brain functions and emotion regulation.
CB, congenital blindness; AS, anxiety scores; DS, depression scores.

The paracentral lobule, which continues from the precentral and postcentral gyri [63]. A study by Daniel M. Wolpert has revealed that in the right paracentral lobule, significant decrease of cortical thickness was displayed in the at-risk mental state subjects[64]. A recent study has revealed that increased FC in the bilateral paracentral lobule-right amygdala was shown in the suicidal behavior group [65] (Table 4). The results suggested that the paracentral lobule might exert an effect on the regulation of mood disorder and suicidal behavior. That is to say, in this study, the increased VHMC in the paracentral lobule might involve in mood processing. However, insignificant linear relationship was displayed between AS and DS and VMHC values in this study. The effect of the paracentral lobule on emotional function will need more evidence to attest.

However, some limitations in the research should be taken into account. The small sample size of our research may adversely affect the statistical results. What's more, the CB participants with different duration of blindness may have an adverse influence on the VMHC values in the CB. Third, CB subjects, caused by multiple reasons, were

implicated, which would be classified so that the modifications of the brain will be probed more accurately. Finally, we assessed the emotional state of patients in the CB group only by AS and DS. A more comprehensive and systematic assessment of psychological status should be carried out.

Conclusions and expert recommendations

To sum up, in specific cerebral areas, aberrant cerebral interhemispheric functional connectivity was displayed in the CB group. AS and DS displayed a positive correlation with the VMHC values of bilateral thalamus in the CB group. The abnormal FC between the cerebral hemispheres associated with emotional processing suggested that there may be an interaction between emotional regulation and visual dysfunction.

Early predicted method for emotional disorders

The ROC curve analysis could be used as statistical evidence to differentiate illness from healthy controls. In our research, great AUC values, discovered in all regions of interest, were observed by the ROC curve analysis. That is to say, these altered VMHC values in the cerebral areas might be potential diagnostic markers of mood disorder and aberrant brain activity in the CB patients. The VMHC values may be an early predicted sign for emotional disorders such as anxiety and depression in blind patients. In clinical practice, we may be able to apply the VMHC method, a quantitative technique, to better evaluate the emotional state of patients with visual impairment. It may suggest that patient is at high risk of suffering from anxiety, depression and other mental diseases because of the functional abnormalities in the brain areas related to emotional regulation. Early prediction allows us to adopt measures in time to prevent extreme consequences.

Prevention and individualized treatment of emotional diseases in patients with congenital blindness

Previous studies have revealed that visual impairment seems to be one of the risk factors for infantile autism[66]. Moreover, people with congenital blindness have an increased risk of schizophrenia [67, 68]. A study has displayed that glaucoma may be not only an eye disease, but also a complex neural disease [18]. Our study also revealed

abnormal brain function in patients with congenital blindness. That is a problem we need to explore in the future that whether abnormal brain activity and emotional regulation will also affect visual function. Based on the potential role of mental state in various diseases, humanistic care and necessary psychological treatment for blind patients may be one of the measures to prevent vision from persistent loss in the future. At the same time, the changes of brain function may also provide new ideas for individualized treatment of patients with anxiety, depression and other emotional disorders. Through various treatment to improve the damaged brain function, the negative emotions such as anxiety and depression may be able to be alleviated. We could customize the individualized treatment for the patients according to the changes of VMHC values and FC.

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Author contribution JK, YP and MK took charge of the process of data collection and analysis, who also wrote the manuscript. HS, XL, TS and LT were responsible for the recruitment of volunteers and the collection of data. The data were statistically analyzed and the first draft was revised by LZ, SX and JW. YS put forward the idea, preliminarily designed the study and supported it. All authors accepted the final draft.

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Data availability From the corresponding author, you can available the datasets which were applied and analyzed in this study.

Declarations

Ethical approval and consent to participate The Medical Ethics Committee of the First Affiliated Hospital of Nanchang University (Nanchang, China) approved this research. The steps were subject to the theories of the Declaration of Helsinki. All participants and their parents cooperated by their own volition and signed informed

consent forms after acknowledging the research goals and hidden risks.

Patient consent for publication Not applicable.

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