Article

Study on the Relationship between Cerebral Blood Perfusion, Neuronal Cytokines and Cognitive Function in Patients with Alzheimer's Disease

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Abstract

Background: Alzheimer's disease (AD) is a common neurodegenerative disorder characterized by the progressive emergence of multiple cognitive deficits. Early diagnosis is of great significance for the intervention and treatment of AD. The objective of this study is to explore the relationship between cerebral blood perfusion, neuronal cytokines and cognitive function in patients with AD.

Methods: AD patients admitted to the 903 Hospital of the People's Liberation Army Joint Logistics Support Force from June 2020 to January 2023 were retrospectively selected as the study objects, and 65 healthy people who underwent physical examination during the same period were included in the control group. Subjects in both groups underwent 3.0 T magnetic resonance imaging (MRI) to observe their cerebral blood perfusion parameters. The level of cognitive function in both groups was assessed using the Montreal Cognitive Assessment (MoCA). Venous blood was collected from both groups, and the serum levels of brain-derived neuronal factor (BDNF) and glial cell-derived neurotrophic factor (GDNF) were measured by enzyme-linked immunosorbent assay (ELISA). The correlation of serum BDNF and GDNF levels with cerebral blood perfusion parameters and MoCA score in the AD group was analyzed using Spearman analysis.

Results: The cerebral blood flow signal intensity of the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe of the observation group was significantly lower than that of the control group ($p < 0.001$). The visuospatial, executive functions, naming, attention, language function, abstract generalization ability, memory ability, orientation, and total MoCA scale scores were significantly lower than those of the control group ($p < 0.001$). The serum levels of BDNF and GDNF in the observation group were significantly lower than those in the control group ($p < 0.001$). The results of Spearman analysis showed that cerebral blood perfusion parameters of the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe were positively correlated with cognitive function scores in AD patients, serum BDNF and GDNF levels were positively correlated with cognitive function scores in AD patients, and the correlation was statistically significant ($p < 0.05$).

Conclusion: In AD patients, blood perfusion parameters and serum BDNF and GDNF levels were significantly lower than those of healthy people. Cerebral blood perfusion parameters of the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe, and BDNF and GDNF levels were positively correlated with cognitive function scores in AD patients.

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Keywords

Alzheimer's disease; neuronal cytokines; cerebral blood perfusion; cognitive function; correlation

Introduction

Alzheimer's disease (AD) accounts for about 80% of dementia diagnoses [1]. AD is characterized by the progressive emergence of multiple cognitive deficits and is associated with persistent cognitive decline [2]. It is a slowly progressing neurodegenerative disease that begins with mild memory loss and eventually leads to extensive executive and cognitive function being severely impaired [3]. With the rapid growth of the global population and the continuous extension of average life expectancy, especially the severe population aging trend in China, elderly people with cognitive impairment are becoming gradually common [4]. There are about 50 million cases of dementia worldwide, and the number of patients is expected to triple by 2050 due to an aging population [5]. The main clinical symptoms of AD are cognitive impairment, memory loss, and other symptoms, and even changes in behavior and personality [6]. These changes seriously affect the work ability and quality of life of patients and their caregivers [7]. If AD patients are not treated in time, with the disease progressing, they will lose their ability to live daily, which threatens their life and health [8].

The pathogenesis of AD is still unclear. In addition to the classic β-amyloid plaque (Aβ) theory and Tau theory, some studies have shown that changes in cerebral blood flow play a key role in the entire development of AD [9,10]. Therefore, cerebral perfusion changes are closely related to disease progression. The early diagnosis of AD plays a crucial role in the implementation of interventions and treatment for the condition, and neuropsychological examinations commonly used in clinical practice have certain limitations. Magnetic resonance imaging (MRI) has high spatial resolution, high detection sensitivity, and diversity of detection sequences, and is increasingly applied in AD [11,12]. The types and causes of cognitive dysfunction are highly complex, including chronic underlying diseases such as hypertension and reactive neuropathy [13]. In addition, numerous research investigations have demonstrated a correlation between abnormally reduced levels of brain-derived neuronal factor (BDNF) and increased risk of cognitive impairment [14–16]. Glial cell-derived neurotrophic factor (GDNF) belongs to the family of neurotrophic factors. Reduced GDNF levels increase the likelihood of AD, which has attracted widespread attention in recent years [17]. Both GDNF and BDNF play crucial roles in the progression and development of cognitive dysfunction in AD, and they hold potential as novel biomarkers. Based on previous studies, this study examined the cerebral blood perfusion parameters, changes in neuronal cytokines [BDNF, GDNF], and cognitive function levels in AD patients. The aim of the study is to explore the correlation with cognitive function and actively seek the influencing factors of cognitive function, early diagnosis, prevention, and treatment of AD patients.

Materials and Methods

Research Subjects

AD patients hospitalized in 903 Hospital of the People's Liberation Army Joint Logistics Support Force from June 2020 to January 2023 were retrospectively selected as the study objects, and their clinical information was analyzed. AD patients were selected as the observation group (n = 65), and healthy subjects with complete data were selected as the control group (n = 65). This study was approved by the Medical Ethics Committee of 903 Hospital of the People's Liberation Army Joint Logistics Support Force (202404241101002), and the informed consent was signed by the patients or their families throughout the experiment.

Inclusion criteria for subjects included in this study were as follows: ① Meet the diagnostic criteria of Alzheimer's disease in the "China Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Impairment (2): Guidelines for the Diagnosis and Treatment of Alzheimer's Disease (2018)" [18]. ② Exclude other conditions that may cause cognitive dysfunction based on the patient's clinical onset, objective cognitive impairment assessment results, and biomarkers. ③ Right-handed. ④ There are no contraindications to Magnetic Resonance (MR) scanning. ⑤ Mini-Mental State Examination Scale score <24 points. ⑥ All patients participated in this study voluntarily and signed informed consent.

Subjects were not included in this study based on these exclusion criteria: ① Patients with a history of serious physical or neurological disease or head trauma. ② Those with incomplete imaging data. ③ Combined with diseases such as thyroid dysfunction, severe anemia, or severe infection. ④ A history of drug, alcohol, or other psychoactive substance abuse or dependence. ⑤ Individuals with visual impairments (including color blindness) or hearing disorders.

Data Collection

Prior to the study, the researchers underwent training, the extensive literature on AD was reviewed, and a general information questionnaire was compiled. General data such as age, medical history, and body mass index (BMI) were collected.

Experienced neurology specialists collected the clinical data of all subjects to obtain a complete clinical history, physical examination, and corresponding laboratory tests. All scales were collected by the same experienced neurologist. The neurologist completes the measurement at one time in the same independent, quiet environment and then records the basic conditions of the subject based on the comprehensive results of medical history, physical examination, laboratory examination, Mini-Mental State Examination (MMSE) scale, etc., then comparing them with the diagnostic standards. This study used the GE Discovery 750 3.0T MR instrument (GE Discovery MR 750 3.0T, GE Healthcare, Milwaukee, WI, USA) to collect images from all subjects. All subjects were informed of precautions in detail before scanning. To ensure image quality, each subject was required to lie quietly on the examination bed, and the subject's head was fixed using a plastic cushion matched with the MR instrument to keep the head centered and still. To avoid artifacts from patient activity, subjects wore disposable earplugs to reduce noise. During the image acquisition process, the subjects were instructed to close their eyes, keep their bodies relaxed and as still as possible, not to think deliberately, and to avoid falling asleep until the end of the scan.

Image Data Parameter Settings

Subjects were given a headband and instructed to lie down with relaxed sagittal positioning, and T2WI was used. The matrix is 256 × 256, the pixel size is 0.7 × 0.7 × 3.0, TE 97 ms, layer thickness 3.0 mm, and TR 7000 ms, 2 collections. According to the T1WI scan, the pixel size is 1.0 × 1.0 × 1.0, TE 3.16 ms, layer thickness 1.0 mm, TR 1900 ms, and one acquisition is performed. Finally, the partial volume-corrected 3D-ASL image was quantified into a cerebral blood flow map through a single-chamber model to obtain a cerebral perfusion map. Semiquantitative measurements of cerebral blood flow and signal intensity were obtained. Assessment of the quality of the perfusion map, including removing images with heavy artifacts and motion artifacts at the skull base, and evaluation of whether there are locations of reduced perfusion in the cerebral blood flow map were conducted. The measurement locations of each patient include bilateral temporal lobes, frontal lobes, occipital lobes, and parietal cortices. Analysis software is then used to measure all the locations mentioned above. Regions of interest (ROIs) are detected three times for each location to ensure their sizes are consistent and the specific average is recorded. The cerebral sulci, venous sinuses, and ventricles were avoided during measurement to reduce errors. The blood flow signal intensity of the two groups of research subjects' bilateral occipital, parietal, temporal, and frontal lobes was detected and recorded.

Cognitive Function Assessment

To assess the overall cognitive status of both the observation and control groups, the Montreal Cognitive Assessment (MoCA) was employed. The MoCA scale is a comprehensive tool to assess cognitive function. It covers seven aspects: visuospatial and executive functions, naming, attention, language functions, abstraction, memory ability (including instant and near memory), and orientation—a comprehensive evaluation of cognitive function. With a total of 12 questions and 30 items, the scale has a maximum score of 30 points. A lower score on each factor indicates a greater degree of cognitive dysfunction. One point is added to the final score for individuals with less than 12 years of education. Currently, the MoCA scale is the most commonly used screening method to assess the degree of cognitive impairment in both clinical and research fields.

Neurofactor Level Detection

5 mL of fasting peripheral venous blood was collected from all subjects and placed in a centrifuge (Allegra X-30R, BECKMAN, Brea, CA, USA) with a centrifuge speed of 3000 r/min and a centrifuge radius of 10 cm for 15 min. Serum was taken and stored for detection. Serum samples must be diluted at least 20-fold with the calibrator diluent before measurement. Add BDNF/GDNF to the pre-enzyme-labeled wells for incubation. The enzyme-labeled wells were coated with human brain-derived neurotrophic factor (ab108319, Abcam, Cambridge, MA, USA)/human glial cell-derived neurotrophic factor monoclonal antibodies (ab176564, Abcam, Cambridge, MA, USA). Then, wash, add horseradish peroxidase-labeled (P8375, Sigma-Aldrich, St Louis, MO, USA) BDNF/GDNF antibody, and then incubate and wash to remove unbound enzyme. Substrates A and B were then added to produce blue, which the acid transformed into the final yellow color. Each plate was washed three times, and the concentration of the standard curve was obtained. The absorbance (A) value was measured at 450 nm, and the corresponding content of the measured factor was found on the standard curve according to the sample A value.

Table 1. Comparison of general information of the two groups of subjects [$\bar{x} \pm s$, n (%)].

Items		Control group (n = 65)	Observation group (n = 65)	χ^2/t-value	p-value
Gender	Male	35 (53.85)	37 (56.92)	0.125	0.724
	Female	30 (46.15)	28 (43.08)		
Age (years)		64.55 ± 5.54	65.41 ± 5.17	0.915	0.362
BMI (kg/m^2)		24.15 ± 2.08	24.38 ± 2.16	0.618	0.537
Years of education (years)		10.24 ± 2.53	10.44 ± 2.61	0.444	0.658

Note: BMI, body mass index.

Table 2. Comparison of cerebral blood perfusion parameters between the two groups of subjects ($\bar{x} \pm s$).

Groups	Left frontal lobe	Right frontal lobe	Left temporal lobe	Right temporal lobe	Left parietal lobe	Right parietal lobe	Left occipital lobe	Right occipital lobe
Control group	41.34 ± 2.47	40.42 ± 2.71	43.67 ± 2.04	43.82 ± 2.41	44.79 ± 2.33	45.15 ± 2.45	45.28 ± 2.91	45.86 ± 2.45
Observation group	37.42 ± 2.14	38.37 ± 2.02	37.08 ± 1.96	36.83 ± 2.35	40.43 ± 2.29	39.48 ± 2.16	40.57 ± 2.54	41.19 ± 2.24
t-value	9.670	4.890	18.781	16.742	10.760	13.996	9.831	11.342
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Statistical Analysis

Statistical data analysis was conducted using SPSS23.0 software (IBM, Amenk, NY, USA). Measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$). Independent sample t-test was used to compare the data, and repeated measurements were used to analyze the comparison at multiple time points. Count data were represented by [n (%)], and the χ^2 test was used for data comparison. Spearman analysis was used for correlation analysis. $p < 0.05$ was considered statistically significant.

Results

Comparison of General Information of the Two Groups of Subjects

There was no significant difference in gender, age, BMI, years of education, and other general data between the two groups ($p > 0.05$), indicating comparability (Table 1).

Comparison of Cerebral Blood Perfusion Parameters between the Two Groups of Subjects

The results showed that the cerebral blood perfusion parameters of the two groups of subjects were compared. The blood flow signal intensity of the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe in the observation group was significantly lower than that of the control group ($p < 0.001$) (Table 2 and Fig. 1).

Comparison of Cognitive Function Scores between the Two Groups of Subjects

The results showed that comparing the MoCA scale scores of the two groups of subjects, the observation group's visuospatial and executive functions, naming, attention, language function, abstract generalization ability, memory ability, orientation, and total MoCA scale scores were all significantly lower than the control group ($p < 0.001$) (Table 3).

Comparison of Neuronal Cytokine Levels

The results indicated that the serum levels of both BDNF and GDNF in the observation group were significantly lower than those in the control group ($p < 0.001$) (Table 4).

Correlation between Cerebral Blood Perfusion Parameters, Neuronal Cytokines, and Cognitive Function

Spearman analysis showed that cerebral blood perfusion parameters of the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe were positively correlated with cognitive function scores in AD patients. Serum BDNF and GDNF levels in AD patients were positively correlated with cognitive function scores ($p < 0.05$) (Table 5).

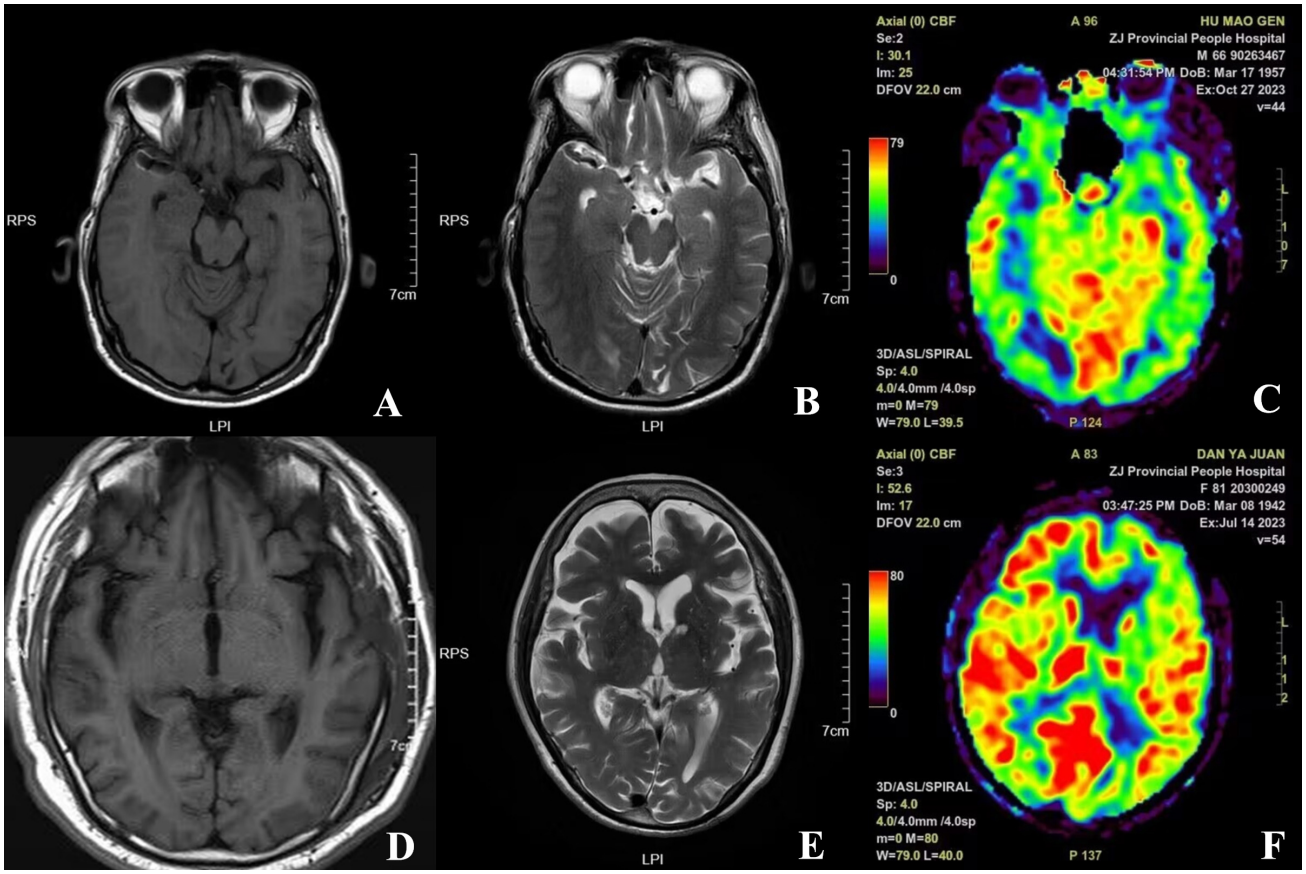

Fig. 1. Comparison of magnetic resonance and cranial blood flow perfusion imaging between the control and observation groups. (A–C) Subjects in the control group, male, 66 years old, without dementia. The Montreal Cognitive Assessment (MoCA) score was 27 points, and there was no abnormality in cognitive function. (D–F) Subjects in the observation group, male, 81 years old, with mild dementia. The MoCA score was 19 points, indicating abnormal cognitive function. No apparent widening of sulci and fissures was found in the patient's conventional scan sequence images, and no definite signs of atrophy of the hippocampal structure were found. However, the patient's cerebral blood perfusion was in the temporal lobe and bilateral anterior and posterior cingulate regions. Perfusion values were significantly lower than control subjects.

Discussion

AD is a neurodegenerative disease that mainly damages cognitive function. The decline of cognitive function is closely related to age and neuropathology. Pathological investigations have revealed that AD is primarily characterized by the accumulation of β-amyloid plaque (Aβ) and neurofibrillary tangles formation resulting from abnormal Tau protein phosphorylation [19]. Additional pathological alterations associated with AD include synaptic and mitochondrial dysfunction, impaired insulin signaling, vascular damage, inflammatory response, cell cycle abnormalities, and cholesterol metabolism defects [20]. Other risk factors for AD include diet, vascular factors, exposure to infectious sources, etc. Internal and external risk factors affect oxygen-free radical generation and gene regulation. These processes will accelerate aging and ultimately lead to AD [21]. Because there is still a lack of specific therapeutic drugs and treatment plans for late-stage dementia in clinical research. Therefore, targeting the pathogenic mechanism of AD and early intervention are still the top priorities in clinical work.

Numerous studies have demonstrated that there is obvious brain structural damage during the course of AD. However, changes in brain function usually precede the loss of gray matter volume and can help evaluate the condition earlier [22–24]. Blood perfusion is one of the important indicators for evaluating neural activity. During neuronal activity, sufficient energy (glucose) and oxygen are continuously delivered to the brain to maintain the normal physiological metabolism of brain neurons [25]. Therefore, it is consistent with the activity trajectory of neurons and is considered one of the most sensitive indicators. In addi-

Table 3. Comparison of MoCA scale scores between the two groups of subjects ($\bar{x} \pm s$, score).

Groups	Executive function	Name	Attention	Language function	Abstract ability	Memory capacity	Orientation	Total score
Control group	3.55 ± 0.41	2.78 ± 0.34	5.67 ± 2.04	3.62 ± 0.41	2.79 ± 0.33	3.85 ± 0.45	6.28 ± 0.41	26.16 ± 2.45
Observation group	3.16 ± 0.66	2.24 ± 0.25	4.08 ± 1.96	2.43 ± 0.35	2.43 ± 0.29	3.48 ± 0.36	5.17 ± 0.54	23.19 ± 2.24
t-value	4.047	10.316	4.531	17.797	6.607	5.176	13.199	7.213
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Note: MoCA, Montreal Cognitive Assessment.

Table 4. Comparison of serum levels of neural cytokines in the two groups of subjects ($\bar{x} \pm s$).

Groups	Patients	BDNF (ng/mL)	GDNF (pg/mL)
Control group	65	12.82 ± 1.38	482.35 ± 31.22
Observation group	65	9.40 ± 1.04	336.46 ± 29.16
t-value		15.957	27.533
p-value		<0.001	<0.001

Note: BDNF, brain-derived neuronal factor; GDNF, glial cell-derived neurotrophic factor.

Table 5. Correlation between cerebral blood perfusion parameters, neural cytokines, and cognitive function scores.

Items	*r*-value	*p*-value
Left frontal lobe	0.511	<0.05
Right frontal lobe	0.487	<0.05
Left temporal lobe	0.571	<0.05
Right temporal lobe	0.511	<0.05
Left parietal lobe	0.429	<0.05
Right parietal lobe	0.358	<0.05
Left occipital lobe	0.531	<0.05
Right occipital lobe	0.542	<0.05
BDNF	0.382	<0.05
GDNF	0.415	<0.05

tion, cerebral blood perfusion can be detected in the early stages of AD and is implemented throughout AD onset [26]. Understanding the relationship between cerebral blood perfusion and cognitive function is important.

This study included a total of 65 patients diagnosed with AD from our hospital. The research objectives focused on examining differences in cerebral blood perfusion and alterations in levels of nerve factors, detailed changes in various aspects of cognitive function compared with healthy subjects and analyzing their relationship with cognition functional relationship. The findings revealed that in comparison to the control group, the observation group exhibited significantly reduced cerebral blood perfusion in various regions of the brain, including the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe. These results indicate that individuals with AD manifest alterations in blood flow, leading to decreased perfusion in different brain regions, especially in the bilateral temporal lobes, bilateral parietal lobes, and other busy areas. The reduction in blood flow perfusion is more obvious than that of healthy people. This may be due to the common cerebral blood flow lesions in AD patients. Cerebral vascular amyloid deposition, lacunar infarction, gliosis, arteriolar sclerosis, and other conditions can cause capillary contraction and reduce cerebral blood perfusion [27]. Study has shown that carriers of AD risk factors have relatively low blood perfusion in brain areas such as the medial temporal lobe and hippocampus, revealing that normal elderly people carrying AD risk factors are more likely to develop perfusion abnormalities [28]. According to research reports, the earliest brain areas affected by AD are mainly the hippocampus and parahippocampal gyrus, and then gradually involve the posterior cingulate gyrus, precuneus, frontoparietal lobes, etc. Local and sustained decreases in blood perfusion in the brain can lead to cerebral cortical atrophy [29]. In addition, our observations revealed notable declines in visuospatial and executive functions, naming, attention, language function, abstract generalization ability, memory ability, orientation, and total MoCA scale scores within the observation group compared to the control group. These findings suggest varying degrees of cognitive decline among AD patients regarding language and perception. The observation group exhibited notably lower cognitive function scores in the language dimension compared to the control group (Table 2), which is parallel to the trend of decreased cerebral blood perfusion in the bilateral parietal lobes.

Previous study on neural localization believe that the parietal lobe is the central part of the contralateral somatosensory cortex [30]. Its main function is integrating, organizing, comparing, and analyzing somatosensory information to form a complete perceptual concept. AD patients have certain attention disorders. Attention is closely related to various cognitive functions, and these performances are related to disorders of the parietal lobe functional area [31]. The temporal lobe is related to hearing, language, and memory. Changes in blood flow perfusion in the temporal lobe region of AD patients predict functional changes,

and are related to early memory loss, speech function, and visual function loss in AD patients [32]. The course of AD can be roughly divided into three stages: preclinical, mild cognitive impairment (MCI), and dementia. Changes in cerebral blood flow can reflect both neurodegeneration and vascular pathologic burden. Correlation with pathological markers major pathological changes in AD include brain tissue-specific Aβ and tau protein deposits detected by cerebrospinal fluid and PET [33]. The decrease of cerebral blood flow is related to the occurrence and development of vascular pathological burden, which provides supporting evidence for AD complicated with cerebral small vascular disease and reminds the clinic to strengthen the early control of vascular risk factors in AD. This study selected the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe to analyze the correlation between cerebral blood flow signal intensity and cognitive function scores. Spearman analysis results showed that the cerebral blood flow signal intensity of AD patients in the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right parietal lobe, left occipital lobe, and right occipital lobe was positively correlated with cognitive function scores. The frontal association area is associated with higher cognitive functions of attention and memory [34]. Combining with the previous studies and the conclusions of this study, it is speculated that the temporal and parietal lobes and some frontal and occipital lobe areas are jointly involved in the pathogenesis of AD. The cerebral blood flow signal in the right parietal lobe is significantly related to the intensity of the cerebral blood flow signal in the frontal lobe of AD patients with cognitive dysfunction. The level of cognitive function in AD patients can be predicted and evaluated according to the detection results of cerebral blood flow signals in different regions in clinical practice.

BDNF and GDNF are essential for the survival and homeostasis of central neurons [35]. Reduced levels of BDNF in the entorhinal cortex, or forebrain, are associated with poor memory [36]. BDNF also has neuroprotective effects in ischemic models. The lack of endogenous BDNF makes the brain more susceptible to ischemic damage. Endodermal BDNF activates endothelial tyrosine kinase receptor-B (TrkB) receptors to induce the release of vascular relaxation factors. By extension, cerebral blood flow depends on endothelial BDNF/TrkB signaling [37]. We found that serum levels of both BDNF and GDNF were significantly lower in the study group compared to the control group, suggesting a reduction in the synthesis or release of these neurotrophic factors in AD patients. However, the mechanism of this change is still unclear; whether it signifies a pathological process or a compensatory response requires further investigation. Spearman analysis revealed a positive correlation between serum BDNF and GDNF levels and MoCA scores within the observation group. This suggests that reduced levels of BDNF and GDNF lead to a sustained decline in cognitive function in AD patients as well. BDNF, a member of the neurotrophic factor family, is widely distributed throughout the central nervous system. It can protect neural function, improve brain tissue's hypoxia state, and promote neuronal function recovery [38,39]. BDNF can improve I/R-induced brain injury by blocking the activation of Caspase-3 [40] and support the survival of cholinergic neurons, inhibit brain injury caused by cerebral ischemia and hypoxia, and improve spatial learning and memory disorders [41]. BDNF can also reduce the infarct size after cerebral ischemia and improve the neurological prognosis through exogenous supply [42].

GDNF, belonging to the transforming growth factor (TGF-β) superfamily, is a potent neurotrophic factor promoting neuronal survival, neural progenitor cell differentiation, and synaptic formation, playing an important neuroprotective role in neurodegenerative diseases. Loss of GDNF can seriously affect the maintenance, proliferation, and differentiation of both central and peripheral nervous system cell populations. GDNF is associated with neurodevelopmental changes and is a potentially related gene for AD [43]. High levels of BDNF and GDNF can reduce neuronal apoptosis and ischemic brain tissue injury [44]. Analysis of possible reasons is that reduced cerebral blood perfusion can increase neuronal metabolic disorders, tissue ischemia, and hypoxia can also increase nerve cell apoptosis. BDNF and GDNF show a decreasing trend, and the fixation effect of nerve cells on information is reduced, affecting the formation and stabilization of patients' memories, decreasing their cognitive functions and promoting the progression of AD [45,46]. However, this study has limitations, such as a limited sample size and a single hospital included, and it did not monitor the dynamic changes of neural factors. In future studies, the sample size can be expanded, and multicenter studies can be carried out to deeply and comprehensively explore hippocampal cerebral blood perfusion and its correlation with cognitive function in AD patients.

Conclusion

To sum up, cerebral blood perfusion parameters in each brain area of AD patients were significantly lower than those of healthy people, and serum BDNF and GDNF levels were significantly reduced. Cerebral blood perfusion parameters of the left frontal lobe, right frontal lobe, left temporal lobe, right temporal lobe, left parietal lobe, right

parietal lobe, left occipital lobe, and right occipital lobe, and BDNF and GDNF levels were positively correlated with cognitive function scores in the AD patients. The findings could help assess and diagnose AD, enhancing the scientific accuracy of clinical diagnoses and treatments.

Availability of Data and Materials

The data used to support the findings of this study are included within the article, and during the present study are available from the corresponding author on reasonable request.

Author Contributions

HJL and YW designed the research study. YF and XC performed the research. WDZ analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of 903 Hospital of the People's Liberation Army Joint Logistics Support Force (202404241101002). The entire experimental procedure was explained to the patient or their family, and all patients signed informed consent. The study was carried out in compliance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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