Correlation between the degree of cognitive impairment and emotional state in patients with Alzheimer's disease.

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Abstract. This study aimed to investigate the correlation between cognitive dysfunction and emotional state in patients with Alzheimer's disease and then propose intervention strategies. One hundred twenty-five patients with Alzheimer's disease from June 2019 to May 2022 were selected as the study subjects and divided into two groups based on the degree of cognitive impairment, both receiving routine drug treatment and cognitive rehabilitation intervention. The Montreal Cognitive Assessment (MoCA) and the Positive and Negative Affect Scale (PANAS) were used to evaluate the cognitive function and emotional status of two groups of patients before the intervention and four and eight weeks of intervention and to analyze the correlations between the two. The results showed statistically significant differences between the two groups MoCA and PANAS scores ($P<0.05$). Before the intervention, the patient's MoCA score was positively correlated with the PANAS positive emotion score and negatively correlated with the PANAS negative emotion score ($P<0.05$). After four and eight weeks of intervention, the patient's MoCA score was positively correlated with the PANAS positive emotion score ($P<0.05$) and negatively correlated with the PANAS negative emotion score ($P<0.05$).

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Correlación entre disfunción cognitiva y estado emocional en pacientes con enfermedad de Alzheimer y su intervención.

Resumen. El objetivo de este estudio fue explorar la correlaciónón entre la disfunciónón cognitiva y el estado emocional en pacientes con enfermedad de Alzheimer. Se seleccionaron 125 pacientes diagnosticados con enfermedad de Alzheimer entre junio de 2019 y mayo de 2022 como sujetos de investigaciónón, divididos en dos grupos según el grado de disfunción cognitiva, y ambos recibieron tratamiento farmacológico convencional e intervenciónón de rehabilitaciónón cognitiva. La función cognitiva y el estado emocional de los pacientes antes de la intervención, a las 4 semanas de intervención y a las 8 semanas de intervención se evaluaron utilizando la escala de evaluación de la función cognitiva de Montreal (MoCA) y la escala de emociones positivas y negativas (PANAS), respectivamente. Los resultados del análisis de la prueba repetida ANOVA mostraron diferencias estadísticas significativas en la puntuación de la dimensión emocional PANAS entre los dos grupos de pacientes (p<0,05). Los resultados del análisis de correlación de Pearson mostraron que después de 4 y 8 semanas de intervencion, la puntuación MoCA del paciente se relacionó positivamente con el estado de ánimo positivo de PANAS (p<0,05) y negativamente con el estado de ánimo negativo de PANAS (p>0,05). En conclusión, el grado de disfunción cognitiva en pacientes con enfermedad de Alzheimer está estrechamente relacionado con el estado emocional. Una intervención cognitiva razonable ayuda a eliminar las emociones negativas de los pacientes y tiene un impacto positivo en la aceleración de la progresión del tratamiento y la mejora de la calidad de vida.

INTRODUCTION

Alzheimer's disease is a progressive degenerative neurological disease with memory impairment, aphasia, and agnosia as typical manifestations. According to statistics, by the end of 2019 [1], China had more than 6 million cases of Alzheimer's disease, and with the prolongation of age, the prevalence rate gradually grew. The disease has become one of the major diseases threatening the health and life quality of the elderly population. Clinical studies have shown that the disease triggers motor symptoms such as static tremor, motor retardation and abnormal gait, as well as non-motor symptoms such as cognitive dysfunction, memory loss and complicated social interaction [1]. In most patients are usually accompanied by abnormal emotional states, who show emotional depression and occasional irritation at the initial stage of the disease, but will evolve into impatience and restlessness as the disease progresses, hindering the treatment

of the disease. Other studies have shown [2] that patients with Alzheimer's disease develop both cognitive dysfunction and abnormal emotional states, which may exist independently or interact with each other, but the specific association between the two is not yet clear. Hence, in order to further explore the relationship between the two, this study conducted research and analysis on the correlation between cognitive dysfunction degree and emotional state in patients with Alzheimer's disease. Relevant intervention strategies were formulated accordingly, which are now reported below.

Patients and methods

General data: One hundred twenty-five patients with Alzheimer's were selected as the study subjects from June 2019 to May 2022. Inclusion criteria: (1) With symptoms such as memory loss, decreased judgment ability, and abnormal emotional changes, the results of neuropsychological tests, thin layer CT scans, and positron scans comply with the diagnostic criteria for Alzheimer's disease according to the 2018 Chinese Guidelines for the Diagnosis and Treatment of Dementia and Cognitive Disorders: Guidelines for the Diagnosis and Treatment of Alzheimer's Disease [3]; (2) MoCA scale score <26 points; (3) Age ≤ 75 years old; (4) The condition was stable. Furthermore, the family members knew the research content, voluntarily participated and signed a consent form. Exclusion criteria: (1) Alcoholic dementia and vascular dementia, with Hachinski Ischemia Index Scale score >4 points [4]; (2) Management of drug-resistant epilepsy; (3) Complicated with severe heart, liver, kidney, or lung dysfunction diseases; (4) Concomitant severe anxiety disorder, depression, schizophrenia and other mental and psychological disorders; (5) Weight <40kg, blood pressure <90/60mmHg or >160/100mmHg, blood pressure fluctuation >30mmHg; (6) Combined with other central nervous system disease; (7) Clinical data missing >10%.

METHODS

Intervention Methods

After enrollment, both groups of patients received routine medication treatment and underwent cognitive function intervention under the guidance of rehabilitation therapists and specialized nurses. The intervention included: (1) Aerobic exercise: Before exercise, the patient's heart rate at maximum exercise load was determined through cardiopulmonary exercise test evaluation and maximal exercise test using an improved Bruce scheme. The aerobic exercise intensity was set at 70% of the maximum exercise load heart rate. The training items could include aerobic exercise, cycling, treadmill exercise, etc. Aerobic exercise was conducted for one hour after breakfast and two hours after dinner, with each exercise time controlled between 60 to 90 minutes. During the exercise, the patient could rest for 5 to 10 minutes, 3-5 times per week, performing continuous aerobic exercise for eight weeks. (2) Targeted cognitive training: Targeted cognitive training usually consisted of five parts: orientation and reality training, memory, computation and language function training. *Directional training* mainly involves repeatedly asking the patient about the season, date, time, city, etc., every three minutes, six times a day; *memory function training* mainly involved informing the patient of the name of a particular item, immediately asking the patient the name of the item, and then asking once every three minutes, six times a day; *computation function training* mainly involved designing simple addition, subtraction, multiplication, and division test questions for patients, guiding them to calculate test questions based on specific daily life events; *language function training* mainly aims to extend the communication time between family members and patients as much as possible, focusing on familiar things in daily life, and allowing patients to execute some simple commands with the assistance of family members; *real-*

ity training requires patients to plan their daily activities and gradually develop a good lifestyle pattern day after day.

Survey tool: (1) <u>Cognitive function</u>. The MoCA scale was used to evaluate patients' cognitive function. The scale consists of eight cognitive domains: visual space and executive function (5 points), naming (3 points), memory/delayed recall (5 points), attention (3 points), calculation (3 points), language (3 points), abstract thinking (2 points), and directional ability (6 points). The total score is 30 points, and a score <26 indicated the patient had cognitive impairment. The lower the score, the more severe the cognitive impairment. The Cronbach scale coefficient α was 0.818 [5]. (2) <u>Emotional state</u>. The PANAS scale is used to evaluate the emotional state of patients. The scale consists of two emotional dimensions: positive and negative emotions, each containing ten emotional adjectives. After each emotional adjective, five options are set, ranging from "almost no" to "extremely many", and each is assigned a score of 1-5 points. The total score for a single domain is 10-50 points. The higher the score, the more positive/negative the patient emotions. The scale Cronbach coefficient α ranged from 0.800 to 0.820.

Survey method: Before the patient intervention, at four weeks and eight weeks of intervention, two nurses with uniform professional training were instructed to fill out the MoCA scale (completed within 10 minutes) and PANAS scale in a quiet room with the same guidance language. Once completed, they were immediately collected.

Statistical method: SPSS 27.0 software was used to process and analyze the data, with the mean value ± standard deviation (X±SD) representing the measurement data (t-test) and the percentage representing counting data (χ^2test); Pearson correlation analysis was performed on the correlation between the degree of cognitive impairment and emotional state of patients; GraphPad Prism 9 software was used to draw line chart and heat map. *P*<0.05 was considered statistically significant.

RESULTS

Comparison of general information of patients

Out of 125 patients included in this study, two withdrew from the study midway, three had missing clinical data >10%, and one had poor intervention compliance and did not receive effective improvement through psychological support, all of which were excluded. Finally, 119 valid data were ultimately collected, with a questionnaire response effectiveness rate of 95.20%. According to the patient's MoCA score, they were divided into two groups, with 73 cases in the mild disorder group and 46 cases in the moderate to severe disorder group. There was no statistically significant difference in gender, family genetic history, and presence or absence of hearing loss between the two groups of patients (*p*>0.05). There was a statistically significant difference in age, course of disease, and head CT between the two groups of patients (*p*<0.05). Please refer to Table 1 for details.

Comparison of patient cognitive function

The overall analysis found that there were statistically significant differences in MoCA scores and total scores between the two groups of patients (*p*<0.05), and only memory/delayed recall and attention interaction differences between the two groups of patients were statistically significant (*p*<0.05). Compared within the group, the MoCA cognitive domain scores and total scores of the two groups of patients at four weeks and eight weeks of intervention were higher than before intervention (*p*<0.05), while the MoCA cognitive domain scores and total scores of the two groups of patients at eight weeks of intervention were higher than those at four weeks of intervention (*p*<0.05). Compared between groups, the MoCA cognitive domain scores and total scores of patients in the mild disorder group before intervention, four weeks of interven-

Table 1
Comparison of general information between the two groups of patients.

Items		Mild impairment group (n=73)	Moderate to severe disorder group (n=46)	χ2/t/Z	p
Gender	Female	30(41.10)	18(39.13)	0.045	0.831
	Male	43(58.90)	28(60.87)		
Age		61.19±8.47	68.65±6.86	-5.023	<0.001
Course of disease Years (mean±SD)		4.01±1.35	8.24±2.17	13.103	<0.001
Family genetic history	No	61(83.56)	38(82.61)	0.018	0.892
	Yes	12(16.44)	8(17.39)		
Hearing loss	No	67(91.78)	42(91.30)	0.000	1.000
	Yes	6(8.22)	4(8.70)		
Head CT	Normal	9(12.33)	3(6.52)	-4.961	<0.001
	Mild atrophy	45(61.64)	9(19.57)		
	Moderate atrophy	14(19.18)	17(36.96)		
	Severe atrophy	5(6.85)	17(36.96)		

Values are expressed as n (%).

tion, and eight weeks of intervention were higher than those in the moderate to severe disorder group (P<0.05). Please refer to Table 2 for details.

Comparison of patient emotional states

The overall analysis found that there were statistically significant differences in the scores of various emotional dimensions of PANAS between the two groups of patients (p<0.05), and the interactive differences in PANAS negative emotional scores between the two groups of patients were statistically significant (p<0.05). Compared within the group, the positive emotional scores of the two groups of patients at eight weeks and four weeks of intervention were higher than before intervention, while the negative emotional scores were lower than before intervention (p<0.05). The positive emotional scores of both groups of patients after eight weeks of intervention were higher than those after four weeks of intervention, while the negative emotional scores were lower than those after four weeks of intervention (p<0.05). Comparing the groups, the posi-

tive emotional scores of patients in the mild disorder group before intervention, four weeks of intervention, and eight weeks of intervention were higher than those in the moderate to severe disorder group. In contrast, the negative emotional scores were lower than those in the moderate to severe disorder group (p<0.05). Please refer to Table 3 and Fig. 1 for details.

Correlation between the degree of cognitive impairment and emotional state of patients

The Pearson correlation analysis results showed that before intervention, except for the calculation dimension, the scores of each cognitive domain dimension of the patient's MoCA were positively correlated with the PANAS positive emotion score (p<0.05), while the scores of each cognitive domain dimension of the patient's MoCA were negatively correlated with the PANAS negative emotion score (p<0.05). After four weeks of intervention and eight weeks of intervention, the MoCA scores of patients showed a positive

Table 2
Comparison of MoCA Cognitive Domain Scores and Total Scores between two groups of patients.

Cognitive domain	Time	Mild impairment group (n=73)	Moderate to severe disorder group (n=46)	t	p
Visual space and executive function	Before intervention	3.32±0.47	1.46±0.50	20.489	<0.001
	Intervention for four weeks	3.67±0.47	1.78±0.42	22.181	<0.001
	Intervention for eight weeks	4.00±0.37	2.07±0.33	28.893	<0.001
Name	Before intervention	1.97±0.23	1.76±0.43	3.467	0.001
	Intervention for four weeks	2.05±0.23	1.89±0.31	3.273	0.001
	Intervention for eight weeks	2.11±0.31	1.98±0.26	2.374	0.019
Memory/delayed recall	Before intervention	3.22±0.45	1.78±0.42	17.472	<0.001
	Intervention for four weeks	3.73±0.48	2.00±0.21	23.045	<0.001
	Intervention for eight weeks	4.04±0.31	2.37±0.49	22.898	<0.001
Attention	Before intervention	1.97±0.16	1.22±0.42	13.882	<0.001
	Intervention for four weeks	2.08±0.28	1.67±0.47	5.937	<0.001
	Intervention for eight weeks	2.19±0.40	1.89±0.31	4.347	<0.001
Calculation	Before intervention	1.96±0.31	1.83±0.38	2.078	0.040
	Intervention for four weeks	2.15±0.36	1.89±0.31	4.012	<0.001
	Intervention for eight weeks	2.32±0.47	2.15±0.36	2.010	0.047
Language	Before intervention	2.00±0.24	1.80±0.40	3.353	0.001
	Intervention for four weeks	2.04±0.20	1.91±0.28	2.880	0.005
	Intervention for eight weeks	2.19±0.40	2.00±0.30	2.816	0.006
Abstraction	Before intervention	0.93±0.25	0.74±0.44	3.005	0.003
	Intervention for four weeks	1.03±0.16	0.85±0.36	3.676	<0.001
	Intervention for eight weeks	1.11±0.31	0.98±0.33	2.169	0.032
Directive force	Before intervention	2.89±0.36	1.85±0.42	14.505	<0.001
	Intervention for four weeks	2.97±0.16	1.91±0.55	15.416	<0.001
	Intervention for eight weeks	3.10±0.93	2.13±0.54	6.382	<0.001
Total score	Before intervention	18.26±0.50	12.43±2.83	17.231	<0.001
	Intervention for four weeks	19.73±1.53	13.91±2.38	16.218	<0.001
	Intervention for eight weeks	21.05±2.71	15.57±2.21	11.540	<0.001

Values are expressed as mean ± SD, points.

Table 2
Continuation

Visual space and executive function: $F_{group}/F_{time}/F_{interaction}$=1201.342/59.948/0.230, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.795;

Naming: $F_{group}/F_{time}/F_{interaction}$=15.880/11.213/0.577, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.563;

Memory/delayed recall:$F_{group}/F_{time}/F_{interaction}$=764.494/1321.194/6.301, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.002;

Attention:$F_{group}/F_{time}/F_{interaction}$=105.003/58.112/16.016, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/<0.001;

Calculation:$F_{group}/F_{time}/F_{interaction}$=15.172/21.538/1.893, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.155;

Language: $F_{group}/F_{time}/F_{interaction}$=16.137/10.940/1.326, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.269; **Abstract thinking**: $F_{group}/F_{time}/F_{interaction}$=13.946/14.957/0.407, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.667;

Directional force: $F_{group}/F_{time}/F_{interaction}$=190.214/5.893/0.238, $P_{group}/P_{time}/P_{interaction}$=<0.001/0.004/0.788; Total score: $F_{group}/F_{time}/F_{interaction}$=274.967/96.583/0.604, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.548.

Table 3
Comparison of PANAS Emotional Dimension scores between two groups of patients.

Dimension	Time	Mild impairment group (n=73)	Moderate to severe disorder group (n=46)	t	p
Positive emotions	Before intervention	29.90±3.32	23.80±2.40	10.808	<0.001
	Intervention for 4 weeks	31.56±3.40	25.26±2.20	11.179	<0.001
	Intervention for 8 weeks	32.86±3.46	26.80±2.70	10.084	<0.001
Negative emotions	Before intervention	30.00±3.32	35.74±3.14	-9.377	<0.001
	Intervention for 4 weeks	28.52±3.67	34.02±2.47	-8.965	<0.001
	Intervention for 8 weeks	26.95±3.63	32.96±3.31	-9.103	<0.001

Values are expressed as $\bar{x}$ ± SD, Points.

Positive mood: $F_{group}/F_{time}/F_{interaction}$=116.369/706.314/1.955, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.146; Negative emotions:$F_{group}/F_{time}/F_{interaction}$=85.093/799.196/6.094, $P_{group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.003.

correlation with PANAS positive emotions ($p<0.05$) and a negative correlation with PANAS negative emotions ($p<0.05$). Please refer to Table 4 for details.

DISCUSSION

Cognitive impairment is one of the typical clinical manifestations of Alzheimer's disease patients, and the severity of this symptom is closely related to the patient's age. Among 119 Alzheimer's disease patients included in this study, approximately 61.34% had mild cognitive impairment, which was higher than previous studies [6]. This might be due to the fact that the overall age of patients with Alzheimer's disease included in this study was lower than in previous studies, and most of them were in the early stages of disease development. The older patients were, the more severe their cognitive impairment was. This view was also drawn through statistical analysis of the age of patients with mild and moderate to severe cognitive impairment. At present, although the pathogenesis of Alzheimer's disease is not yet known, previous studies have pointed out that neuroinflammation is a crucial factor in the spread of misfolded proteins in the body's brain, leading to cognitive dysfunction in Alzheimer's patients. Cognitive impairment not only led to progressive memory impairment, language impairment, and impaired visuospatial function in patients

Table 4
Correlation between the degree of cognitive impairment and emotional state of patients.
(*r* value)

MoCA	Before intervention		Intervention for four weeks		Intervention for eight weeks	
	Positive emotions	Negative emotions	Positive emotions	Negative emotions	Positive emotions	Negative emotions
Visual space and executive function	0.676**	-0.661**	0.835**	-0.791**	0.812**	-0.768**
Name	0.320**	-0.392**	0.524**	-0.534**	0.575**	-0.551**
Memory/delayed recall	0.877**	-0.853**	0.867**	-0.818**	0.836**	-0.796**
Attention	0.750**	-0.751**	0.696**	-0.694**	0.665**	-0.666**
Calculation	0.134	-0.199*	0.657**	-0.677**	0.623**	-0.673**
Language	0.273**	-0.325**	0.375**	-0.383**	0.585**	-0.587**
Abstraction	0.493**	-0.553**	0.512**	-0.506**	0.581**	-0.568**
Directive force	0.740**	-0.724**	0.776**	-0.732**	0.809**	-0.825**
Total score	0.790**	-0.802**	0.896**	-0.864**	0.935**	-0.921**

*$P<0.05$，**$P<0.01$.
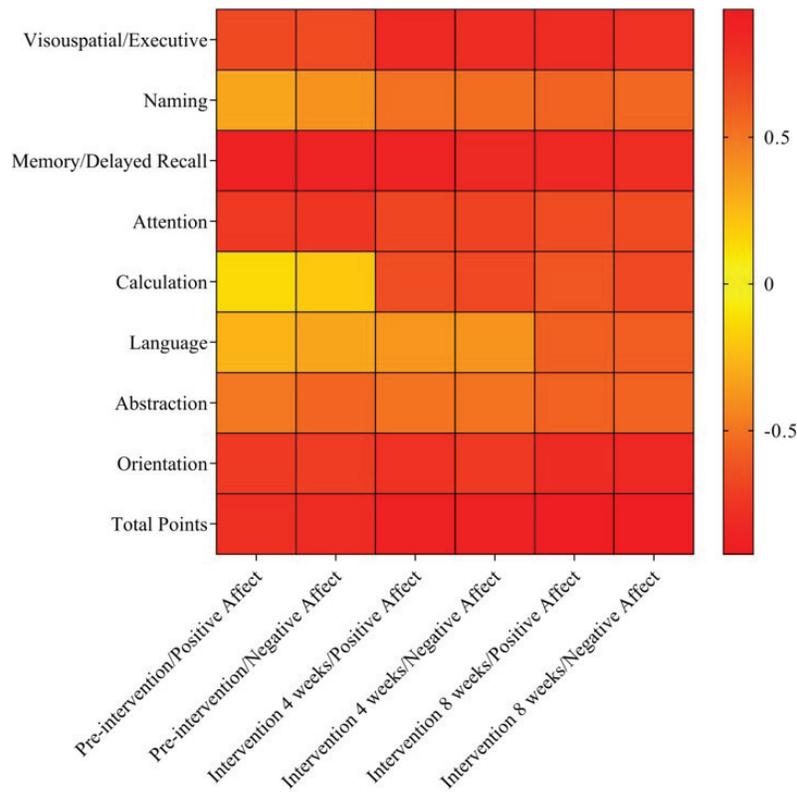
Fig. 1. Heat Map of the correlation between the degree of Cognitive Impairment and Emotional State in patients.

but also led to facial recognition and computational impairment, seriously affecting the quality of life of patients and causing a severe burden on their families [7]. Therefore, actively guiding patients to undergo cognitive rehabilitation interventions positively improved their cognitive function and quality of life. Based on conventional drug therapy, this study guided all enrolled patients to undergo aerobic exercise, pathway electrical stimulation and targeted cognitive training. The results showed that after an eight-week rehabilitation intervention, the MoCA scores in each cognitive domain of the two groups of patients were effectively improved compared to before the intervention, consistent with the research results of Costanzo et al. [8], Cheng et al. [9], Li et al. [10], and others. This result fully demonstrated that suitable cognitive rehabilitation interventions could often effectively improve the cognitive function level of Alzheimer's disease patients.

Regarding the relationship between the degree of cognitive impairment and emotional state in Alzheimer's disease patients, the Pearson correlation analysis results of this study showed that the MoCA scores and total scores of various cognitive domains in Alzheimer's disease patients were positively correlated with PANAS-positive emotions, and negatively correlated with PANAS-negative emotions. This suggested that the more severe the cognitive impairment in Alzheimer's disease patients, the less positive emotional expression they had, and the more negative emotional expression they had, which was consistent with Boutoleau-Bretonnière C et al. [11]. The research results of Moon et al. [12] and Craft et al. [13] were consistent. In addition, this study also found through cognitive rehabilitation interventions for patients that during the eight-week intervention, not only did the MoCA scores and total scores of each cognitive domain show a continuous upward trend, but their PANAS positive emotional score also showed a corresponding upward trend. In contrast, their PANAS negative emotional score showed a downward trend,

indirectly reflecting that the emotional state of Alzheimer's disease patients would gradually improve with the improvement of cognitive function. This study suggested that this result might be related to cognitive decline and decreased ability to live in Alzheimer's disease patients, leading to physiological and psychological balance disorders. Other studies suggested that after cognitive dysfunction in Alzheimer's disease patients, central neurotransmitters such as serotonin (5-HT) and norepinephrine (NE) were insufficient, leading to emotional disorders. Yoon et al.[14] believed that cognitive impairment might be related to damage to the frontal and temporal lobes, which could lead to decreased memory and execution abilities, intellectual decline, delayed thinking and behavior, and thus exacerbated negative emotions in patients. There was interaction and integration between cognition and emotion, a deep integration process of the brain. Cognition and emotion interacted with each other, such as some people being calm in times of trouble. Happiness and anger did not manifest in appearance, which belonged to the influence of cognition on emotions. When a person was emotional, such as happiness, they often agreed to things that were usually difficult to promise, which was the impact of emotion on cognition. However, Guo [15] study found that the probability of anxiety and depression symptoms only increased in the early stages of cognitive decline in Alzheimer's disease patients and decreased with further decline in cognitive function. This indicated that there was a specific correlation between the emotional state of Alzheimer's disease patients and the degree of cognitive dysfunction, but this relationship would gradually dissolve as the cognitive dysfunction continued to worsen.

In summary, the degree of cognitive impairment in Alzheimer's disease patients is negatively and positively correlated with their positive and negative emotions, respectively. Implementing intervention measures to enhance patients' cognitive abilities can

help improve their emotional state, promote disease recovery, and improve quality of life. In addition, this study only explored the impact of cognitive function on emotional state in Alzheimer's disease patients. Therefore, future research needs to improve patients' emotional states through a series of means to explore the impact of emotional states on cognitive function in Alzheimer's disease patients. Whether the correlation between the two will decrease with the continuous worsening of cognitive dysfunction in patients remains to be verified.

Conflict of interest

The authors declare that they have no conflict of interest.

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Authors contribution

ZQ put forward the research experiment and proposed intervention strategies. JC analyzed the data, and FX helped with the constructive discussion. ZQ, JC and FX made significant contributions to manuscript preparation.

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