

Original Article

Effect of cognitive behavioral intervention on anxiety, depression, and quality of life in patients with epilepsy

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Received April 12, 2022; Accepted June 22, 2022; Epub July 15, 2022; Published July 30, 2022

Abstract: Objective: This study aimed to investigate the effect of cognitive behavioral therapy (CBT) on quality of life, anxiety, and depression in patients with epilepsy. Methods: Each study subject was randomly assigned to a CBT (n=46) or control (n=49) group (1:1 ratio), and the first group underwent an 8-week CBT treatment. Anxiety, depression, and quality of life (QOLIE-31) were assessed at both baseline and endpoint using the Self-Rating Anxiety Scale (SAS), Hamilton Depression Scale (HDMA) and quality of life in Epilepsy-31 (QOLIE-31) scales. The statistical analyses included between-and within-group comparisons of the effects of CBT on these measures and associations with demographic and clinical variables. Results: No differences were found between variables at baseline ($P>0.05$). The repeated-measures analyses found that CBT group had greater improvement in depression score compared to the control group ($P<0.05$). The analysis of anxiety score showed that compared to the control group, CBT intervention had no statistical significance in the total anxiety population. However, the CBT intervention decreased anxiety in women and Combined-drug group ($P<0.05$). The CBT group had greater improvement in overall score, medication effect, and seizure worry score than the control group ($P<0.05$). Stratified analysis found total and medication effects score of CBT intervention group for the combined-drug group were higher than those of the single drug group ($P<0.05$). Conclusion: Increases in overall scores, seizure worry, cognitive functioning, and medication effect were better in the CBT group. CBT can improve anxiety, depression, and quality of life in patients with epilepsy. Women and combined-drug patients with epilepsy benefit most from CBT.

Keywords: Epilepsy, anxiety, depression, quality of life, cognitive behavioral intervention

Introduction

Epilepsy is the most common chronic neurological disease, affecting 50 million people worldwide [1, 2]. Mood disorder is the most common complication of epilepsy [3-6]. The most common mood disorders are depression [7-9], anxiety [10, 11], attention problems [12], learning disabilities [13], aggression [14] and autism [15]. These complications are not the clinical manifestations of epilepsy, but they often affect the quality of life, sometimes more than the seizure itself [16]. The emotional problems of epilepsy are significantly related to the risk of suicide in sick adolescents [17, 18]. Concerned about the adverse drug interaction between antidepressants and antiepileptic

drugs, doctors are reluctant to use antidepressants for patients with epilepsy. This concern is the main obstacle to the treatment of depression in patients with epilepsy [19]. Therefore, psychotherapy may be an effective method for treating these patients.

Cognitive behavior therapy (CBT) is a psychotherapy method that achieves a therapeutic effect to change patients' thinking and behavior. It had beneficial effects on the mood and quality of life of patients with mental diseases and chronic physical diseases [20]. In this study, patients with epilepsy were selected as research subjects. They were treated using CBT, and effects on anxiety, depression and quality of life were examined.

Material and methods

Subjects

Ninety-five patients with epilepsy in the outpatient department or ward of the Department of Neurology of Suzhou Hospital Affiliated to Nanjing Medical University were selected for the study. These patients had disease that met the 2017 epilepsy diagnostic criteria issued by the international Anti-Epilepsy Alliance. All subjects completed the evaluation and intervention between October 2020 to April 2021. The inclusion criteria were: (1) 18-43 years of age. (2) Simple Intelligence Scale score >27 points. (3) Informed consent of patients. The exclusion criteria were: (1) Diseases with severe cardiopulmonary, liver and kidney dysfunction. (2) Patients with poor compliance and uncoordinated treatment. The study was approved by the ethics committee of Suzhou Hospital Affiliated to Nanjing Medical University (K-2022-050-K01). All subjects understood the purpose and evaluation and intervention process of this study and provided written informed consent.

Research methods

This 8-week randomized controlled study used a computer-generated random grouping method. Each subject was randomly assigned into the CBT group and control group (1:1) group ratio. A professionally trained psychotherapist was responsible for the 8-week CBT intervention. Two senior attending physicians completed the baseline and 8-week assessment of the two groups of patients.

Assessment tools and indicators

The general demographic data include age, gender, education, income level, marriage, family history, total course of disease, seizure type, seizure frequency, and taking antiepileptic drugs.

The Self-Rating Anxiety Scale consisted of 20 items. The statistical index was a rough score, which was then multiplied by 1.25 to obtain an integer, which was the standard score. A higher score indicated more anxiety. The Hamilton Depression Scale included 24 items. A score >20 points indicated the presence of depression; a higher the score indicated a more severe degree of depression.

The quality of life in Epilepsy-31 scale consisted of 31 items. This tool is used to evaluate quality of life and represents the overall health status of individuals with epilepsy. It included seven categories (seizure worry, Emotional well-being, energy/fatigue, Cognitive functioning, social functioning, Medication effects, and Overall quality of life). One Overall score that ranged from 0 to 100 was also calculated. The Score for each category = sum of scores of each question divided by the number of questions. Finally, the score is multiplied by different weight scores to obtain each score, and the Overall score was obtained by adding each sub item. The higher the total score, the better the quality of life.

CBT intervention method

Forty-six patients were included for CBT intervention. All admitted patients were trained by qualified specialists for 8 weeks. Group sessions were once a week, one hour per session. Each group consisted of 6 to 8 people. The content of the sessions is presented in **Table 1**.

Statistical analysis

The data for each patients were analyzed according to randomization group. Results for categorical variables were presented as frequencies and percentages and were analyzed using two-tailed chi-square tests. If continuous data met the assumption of a normally distributed, the results were presented as means and standard deviation values. The results were presented as a median and interquartile range values if the data did not have a normal distribution. T test was used to compare two groups for analysis of continuous data, if the data were normally distributed. For qualitative evaluation of intervention effect (the score for Depression/Anxiety/quality of life for epileptics-31 and its dimension) and comparisons between the CBT and control groups, we performed repeated measurement ANOVA. We performed post hoc analyses using a generalized estimation model to assess score results for the different scales for the CBT group. The formula used for the model was $Y = \alpha + \beta_1 * \text{group} + \beta_2 * \text{group} + \beta_3 * \text{group} * \text{time}$. The results were expressed as the difference between the effect in the intervention group and the effect in the control group. At the same time, we used a generalized estimation model to analyse differences between subgroups (male/female, Com-

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Table 1. The content of CBT intervention

Time (week)	Content
First	Introduces the principles and objectives of CBT General information about epilepsy and related psychological aspects
Second	Carry out health education on epilepsy related knowledge, so that patients can understand their own cognitive and behavioral patterns, and how thinking affects emotional, physical and behavioral responses
Third-Fourth	Understand the causes of individual depression, learn to monitor the patients' negative thinking and cognition, and record the emotion log
Fifth-Sixth	The importance of taking medicine. Patients discuss their own use of epilepsy drugs and their mechanisms and methods. Therapists explain the use of drugs in detail and answer patients' questions, emphasizing the standardized use of drugs
Seventh	Clear the negative emotions of patients; Reduce seizures, inform patients to maintain a stable state of mind and avoid emotional fluctuations
Eighth	Setting goals Encourage patients to apply the benefits of treatment to their lives Manage epilepsy seizures and emotions

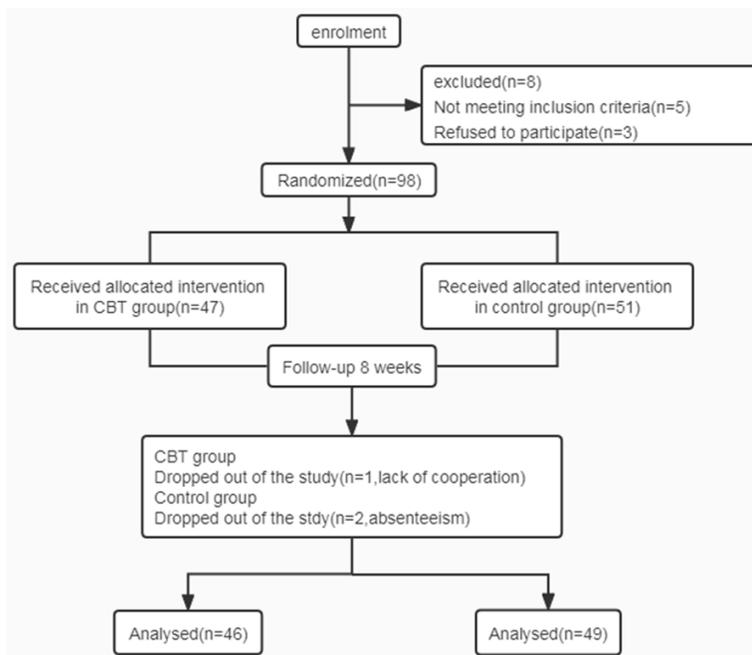


Figure 1. Flow chart for patients screen in the study.

bin-drug group/single-drug group). The differences were reported using 95% confidence intervals. There were no missing data in the treatment groups. All analyses were performed using SPSS version 21.0 (SPSS Inc, Chicago, IL, USA). P value <0.05 in a two-sided test was considered a significant result.

Results

Three of the 98 enrolled patients dropped out of the study, including 1 in the cognitive-behavior

intervention group (lack of cooperation). 2 patients were in the control group (absenteeism). Ninety-five patients completed the 8-week intervention and evaluation, including 46 cases in the cognitive-behavior intervention group and 49 cases in the control group. A flow chart is presented in **Figure 1**.

Comparison of baseline characteristic between the CBT group and control group

No significant differences were found between the two groups for age, gender, years of education, income, marriage, family history, course of disease, seizure type, seizure frequency, use of antiepileptic drugs, the Self-Rating Anxiety Scale and Hamilton Depression Scale ($P>0.05$) **Table 2**.

Comparison of anxiety and depression scores between the two groups, before and after intervention

The results for the Intra-group analysis indicated there were significant differences in anxiety score and depression score between the two groups, before and after intervention ($P<0.05$). Compared to the control group, the value of

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Table 2. Comparison of baseline characteristics between CBT group and control group

	CBT group (n=46)	Control group (n=49)	T/x ² value	P-value
Age (years, x±s)	30.56±5.57	31.16±6.32	-0.487	0.627
Male:female	21/25	20/29	0.226	0.634
Education level (years, x±s)	14.63±2.52	14.34±2.53	0.546	0.583
Income level [n (%), RMB]			0.599	0.741
3000-5000	8 (17.4)	6 (12.2)		
5000-8000	26 (56.5)	28 (57.1)		
10000	12 (26.1)	15 (30.7)		
Marital status [n (%)]			0.258	0.879
Married	29 (63.0)	31 (63.3)		
Unmarried	13 (28.3)	15 (30.6)		
Divorced	4 (8.7)	3 (6.1)		
Family history	2/44	3/46	1.000	0.530
Total course of disease (years)	5.00±3.60	6.26±3.85	-1.650	0.102
Seizure type			0.450	0.503
Focal seizures	26 (56.5)	31 (63.3)		
Generalized seizures	20 (43.5)	18 (36.7)		
Seizure frequency (month)			0.028	0.867
≤1 time	28 (60.9)	29 (59.2)		
≥1 time	18 (39.1)	20 (40.8)		
Antiepileptic drugs			0.536	0.464
Combined drug group	35 (76.1)	34 (69.4)		
Single group	11 (23.9)	15 (30.6)		
SAS	29.30±4.60	28.89±5.15	0.404	0.687
HDMA	17.32±4.64	17.02±4.44	0.328	0.744
Leukocyte count (10*9/L)	6.69±1.60	6.86±1.92	-0.451	0.653
Absolute value of neutrophils (10*9/L)	4.53±1.54	4.90±1.91	-1.007	0.316
Fasting blood glucose (mmol/L)	5.54±0.66	5.33±0.68	1.568	0.120
Urea (mmol/L)	5.30±1.72	5.11±1.32	0.617	0.538
Creatinine (umol/L)	64.86±8.26	63.32±8.32	0.907	0.367
aspartate aminotransferase (U/L)	23.10±7.35	21.45±8.90	0.984	0.328
alanine aminotransf (U/L)	34.40±6.23	33.60±7.63	0.559	0.578

Note: Self-Rating Anxiety (SAS), Hamilton Depression (HDMA).

the depression score in the CBT group decreased after intervention, and the difference was significant. There was no significant difference in anxiety score before versus after intervention ($P>0.05$). At the end of 8 weeks, there were no significant difference in anxiety and depression scores between the two groups (**Table 3; Figure 2A, 2B**).

Comparison of changes in quality of life scores between the two groups, before and after intervention

Intra-group analysis found there were significant differences in Emotional well-being, energy/fatigue, cognitive function, social function,

medication effects, overall quality of life, seizure worry and overall score between the two groups, before and after intervention ($P<0.05$). The changes in overall quality of life, seizure worry and overall score in the CBT group before and after intervention were higher than those in the control group ($P>0.05$). At the end of 8 weeks, there were no significant difference in emotional well-being, overall quality of life, or seizure worry ($P<0.05$) (**Table 3; Figure 2C-J**).

Analysis of the effect of intervention on anxiety and depression, based on a generalized estimation model

The analysis of anxiety score found that compared to the control group, the CBT intervention

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Table 3. Anxiety, depression, and quality of life scores between CBT group and control group

	CBT group (n=46)		Control group (n=49)		F1 (P) value	F2 (P) value	F3 (P) value
	Intervention pre	Intervention post	Intervention pre	Intervention post			
Anxiety	29.30±4.60	22.41±5.26	28.89±5.15	23.36±5.88	70.59 (<0.01)	1.19 (0.28)	0.01 (0.92)
Depression	17.32±4.64	12.10±2.85	17.02±4.44	13.91±3.27	112.56 (<0.01)	6.21 (0.01)	2.32 (0.13)
Quality of life							
Emotional well-being	50.39±3.89	55.15±5.42	48.85±3.78	51.15±4.96	37.42 (<0.01)	3.50 (0.68)	11.11 (<0.01)
Energy/fatigue	50.58±4.70	55.41±5.33	51.67±4.98	54.36±4.52	112.57 (<0.01)	0.91 (0.34)	0.46 (0.49)
Cognitive functioning	55.36±5.23	59.17±6.00	54.59±5.36	58.75±5.51	28.69 (<0.01)	0.12 (0.72)	0.22 (0.63)
Social functioning	45.56±4.52	48.54±6.46	44.55±4.00	47.63±4.45	26.45 (<0.01)	0.02 (0.89)	2.16 (0.15)
Medication effects	53.00±5.08	63.43±7.60	54.79±4.66	58.12±7.45	46.16 (<0.01)	12.29 (0.01)	3.88 (0.05)
Overall quality of life	55.76±4.88	65.13±5.64	54.63±3.93	61.02±6.45	86.55 (<0.01)	3.99 (0.05)	8.18 (<0.01)
Seizure worry	40.32±3.38	53.34±6.07	39.65±3.11	49.02±6.13	248.27 (<0.01)	5.74 (0.02)	10.18 (<0.01)
Overall score	57.26±7.60	66.58±5.72	59.91±7.78	62.06±5.65	51.15 (<0.01)	8.90 (<0.01)	0.51 (0.47)

Note: F1 value is intra group comparison, which refers to the analysis of variance of all subjects before and after intervention; F2 value is the intra group comparison, which refers to the analysis of variance of the difference in the degree of improvement between the two groups, which is the intervention*Time interaction; F3 value is the comparison between groups, which refers to the analysis of variance of the intervention end points of the two groups.

group effect was not statistical significance for anxiety in the total population, However, in the CBT intervention group, anxiety decreased in women and in the combined-drug group {3.16 (-5.01-1.31), -3.01 (-4.91-1.12), $P<0.05$ }. There was no significant difference for the single-group ($P=0.898$). The analysis of depression score found CBT intervention had a statistically significant effect on depression in the total population (**Table 4**).

Generalized estimation model analysis of the effect of intervention on quality of life scores and dimensions

The analysis revealed that, compared with the control group, CBT intervention increased by 7.18 (3.23-11.14), 3.65 (0.93-6.38), 3.80 (1.84-5.77) and 7.21 (3.36-11.06) in the dimensions of overall score, seizure worry, cognitive functioning and medication effects, respectively. A stratified analysis found the total score and medication effects score of the CBT intervention group in the combined-drug group was higher than that in the single-drug group, and the difference was significant (**Table 5; Figure 3A-J**).

Discussion

Epilepsy is a chronic disease of the central nervous system; it has many causes. According to epidemiological studies the prevalence of epilepsy is 5-11.2% [2, 21, 22] and the prevalence in China is as high as 7%. At present, there are more than 9 million patients with epilepsy in

China, and 450,000 patients are newly diagnosed with epilepsy every year. About 70% of patients with epilepsy can control the disease using standardized drug treatment, but 30% have a poor drug treatment response and eventually develop intractable epilepsy [23]. Research results in populations in China and other countries indicate recurrent seizures, long-term use of antiepileptic drugs, and extensive social discrimination make patients suffer great physical, psychologic, and social trauma, significantly reduce quality of life - [24, 25], and significantly increase social and family burdens.

Some patients find epilepsy is often complicated by anxiety and depression due to concerns about seizures and adverse drug reactions. Research findings indicate the number of suicides in patients with epilepsy combined with anxiety and depression is 32 times higher than that in the general population [17, 18, 22, 26]. Anxiety and depression affect the decline in patients' quality of life. Therefore, during clinical diagnosis and treatment, we should find and treat anxiety and depression to improve their quality of life.

Treatment of epilepsy with anxiety and depression mainly includes drug treatment and psychotherapy. Due to the increased risks of seizure frequency and interaction with antiepileptic drugs, clinical use of selective serotonin reuptake inhibitors (SSRIs) is limited [27-29]. CBT and SSRIs have the same effect on patients with epilepsy with anxiety and depres-

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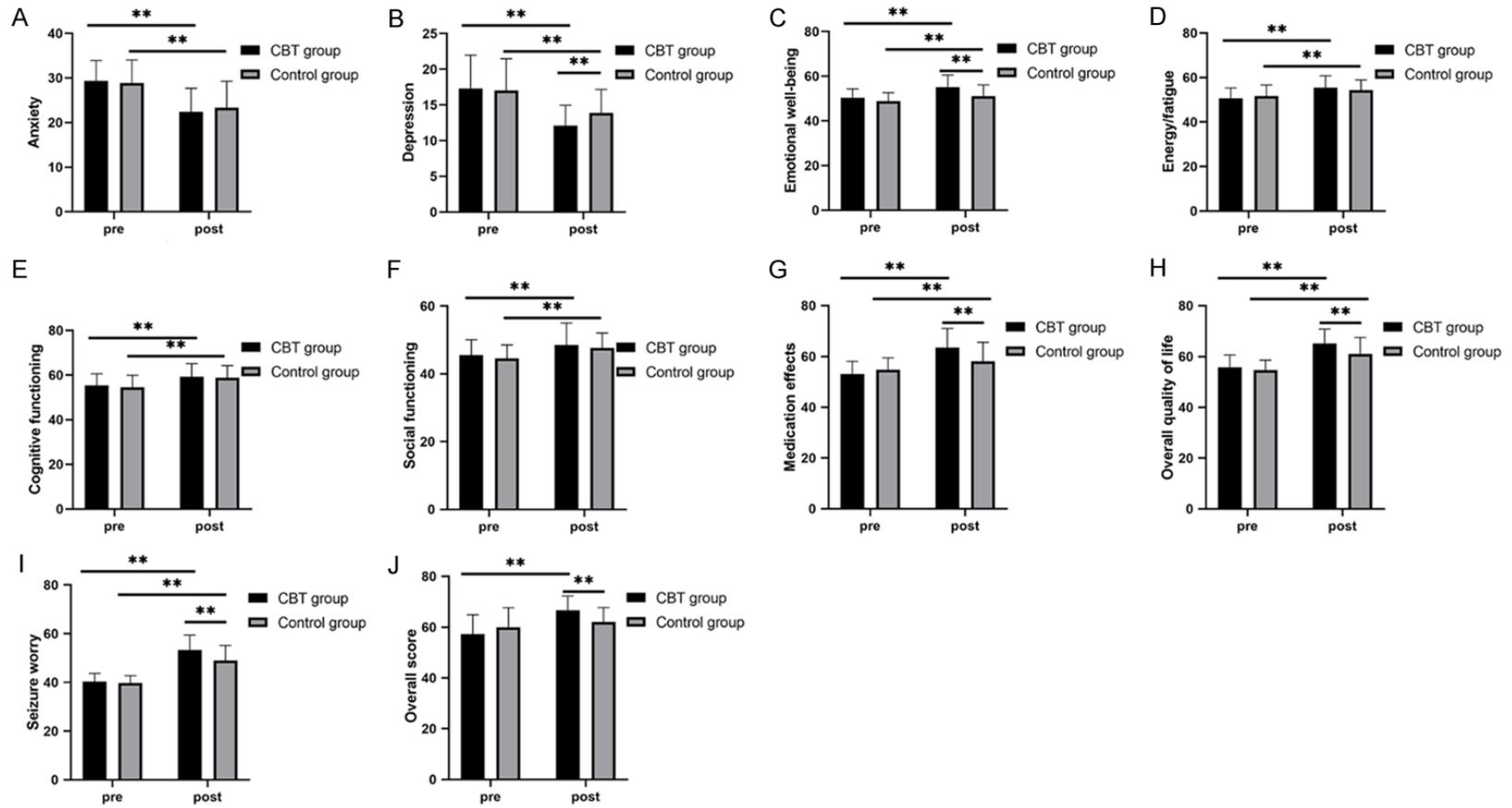


Figure 2. A-J. Anxiety, Depression, quality of life scores between CBT and control group.

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Table 4. Analysis of the effect of intervention based on a generalized estimation model on anxiety and depression

	Depression		Anxiety	
	β (95% CI)	P Value	β (95% CI)	P Value
Time	-3.10 (-4.45–1.75)	<0.001	-5.53 (-7.53–3.53)	<0.001
Group	0.31 (-1.50-2.12)	0.741	0.41 (-1.54-2.35)	<0.001
Group * time	-2.12 (-3.70–0.53)	0.009	-1.37 (-4.09-1.37)	0.681
Male (N=41)				
Time	-5.85 (-8.94–2.76)	<0.001	-4.00 (-6.49–1.51)	0.002
Group	0.64 (-2.18-3.45)	0.657	-1.62 (-4.53-1.29)	0.275
Group * time	-0.53 (-4.53-3.47)	0.795	-0.71 (-3.48-2.05)	0.612
Female (N=54)				
Time	-5.31 (-7.93–2.69)	<0.001	-2.48 (-3.94–1.02)	0.001
Group	0.26 (-2.40-2.91)	0.850	1.77 (-0.52-4.07)	0.129
Group * time	-2.01 (-5.74-1.72)	0.291	-3.16 (-5.01–1.31)	<0.001
Combined drug group (N=69)				
Time	28.35 (26.69-30.02)	<0.001	-2.47 (-4.06–0.89)	0.002
Group	-5.00 (-7.31–2.69)	0.215	1.36 (-0.76-3.48)	0.210
Group * time	1.39 (-0.81-3.59)	0.160	-3.01 (-4.91–1.12)	0.002
Single group (N=26)				
Time	-6.73 (-10.59–2.88)	<0.001	-4.53 (-6.94–2.12)	<0.001
Group	-2.22 (-6.17-1.73)	0.270	-2.61 (-5.87-0.65)	0.116
Group * time	0.92 (-4.61-6.44)	0.745	0.17 (-2.42-2.76)	0.898

sion [30-32]. CBT is an evidence-based psychotherapy method. It can cause cognitive changes (correcting patients' thoughts and belief systems) through various methods and bring lasting changes in emotion and behaviors [33]. As the most commonly used psychotherapy method, CBT can effectively improve mental and chronic physical diseases [34-36].

CBT can improve depression and anxiety symptoms and quality of life in patients with epilepsy [37-40]. The results of this study indicate patients who underwent CBT experienced improvements in anxiety, depression, and quality of life. However, we further analyzed the anxiety scores and found CBT intervention was more effective in women and in subgroups of patients prescribed combined medications. Female patients with epilepsy worry more about the sudden onset of disease and social discrimination, which easily results in anxiety. CBT can reduce anxiety in patients by correcting their thoughts and beliefs. CBT may be more effective for combined medication users because most of this population experience multiple forms of seizure or intractable epilepsy, and thus more anxiety.

CBT improves the quality of life of patients with epilepsy by improving their mental state [38, 41]. The results of this study indicated both the CBT group and control group improved in all dimensions of quality of life, but the CBT group had significant improvements in drug effect and seizure worry. Results from comparisons with the control group suggested, CBT had a positive effect on drug effect and seizure worry in patients with epilepsy. The total scores of the CBT intervention group were higher than those in the single-drug group, and the drug effect score of CBT intervention group was higher than that of the single-drug group. Patients prescribed combined medication may be more affected by emotional disorders and worry about adverse drug reactions. CBT can help patients identify negative cognition, correct harmful psychology and behavior, and enhance interpersonal skills and psychological adaptability. Therefore, controlling epilepsy can also improve social function and quality of life of patients.

In conclusion, CBT intervention can improve the psychological state of patients, reduce the

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Table 5. Analysis of the effect of intervention based on a generalized estimation model on Quality of life score and dimensions analysis

	β (95% CI)		
	Time	Group	Group * time
Overall score	2.14 (-0.65-4.93)	-2.66 (-5.72-0.40)	7.18 (3.23-11.14)*
Combined drug group (N=69)	1.74 (-1.45-4.92)	-3.59 (-7.18-0.00)*	8.52 (3.88-13.17)*
Single group (N=26)	3.07 (-2.49-8.63)	-0.43 (-5.83-4.97)	3.30 (-3.62-10.21)*
Male (N=41)	-1.2 (-5.91-3.51)	-2.56 (-6.85-1.72)	7.91 (1.38-14.44)*
Female (N=54)	4.45 (1.28-7.61)*	-3.18 (-7.03-0.68)	7.07 (2.55-11.59)*
Seizure worry	9.37 (7.48-11.25)*	0.67 (-0.62-1.97)	3.65 (0.93-6.38)*
Combined drug group (N=69)	10.29 (8.05-12.54)*	0.83 (-0.61-2.23)	1.59 (-1.57-4.75)
Single group (N=26)	7.27 (4.04-10.49)*	0.32 (-2.48-3.11)	9.37 (4.69-14.05)*
Male (N=41)	9.95 (6.90-13.00)*	1.58 (-0.38-3.54)	2.15 (-2.50-6.79)
Female (N=54)	8.97 (6.58-11.34)*	-0.12 (-1.73-1.48)	4.8345 (1.69-7.98)*
Emotional well-being	2.65 (1.24-4.07)*	1.53 (0.01-3.06)*	2.11 (-0.11-4.33)
Combined drug group (N=69)	2.21 (0.67-3.74)*	1.18 (-0.58-2.95)	2.08 (-0.41-4.57)
Single group (N=26)	3.67 (0.69-6.64)*	1.96 (-0.80-4.71)	2.61 (-1.91-7.12)
Male (N=41)	3.45 (1.08-5.82)*	2.01 (-0.44-4.47)	1.31 (-2.24-4.86)
Female (N=54)	2.10 (0.39-3.82)*	1.00 (-0.81-2.82)	2.66 (-0.16-5.48)
Energy/fatigue	2.70 (0.95-4.43)*	-1.08 (-3.01-0.84)	2.13 (-0.59-4.86)
Combined drug group (N=69)	2.82 (0.77-4.87)*	-1.52 (-3.91-0.87)	2.41 (-0.82-5.63)
Single group (N=26)	2.40 (-0.87-5.67)	-0.19 (-3.28-2.89)	1.15 (-3.76-6.05)
Male (N=41)	2.55 (-0.46-5.56)	-2.33 (-5.60-0.94)	0.35 (-3.98-4.70)
Female (N=54)	2.79 (0.71-4.87)*	-0.23 (-2.52-2.05)	3.65 (0.27-7.03)*
Cognitive functioning	0.00 (0.00-0.00)	0.78 (-1.33-2.89)*	3.80 (1.84-5.77)*
Combined drug group (N=69)	0.00 (0.00-0.00)	0.63 (-1.80-3.06)	3.46 (1.10-5.81)*
Single group (N=26)	0.00 (0.00-0.00)	0.98 (-3.24-5.19)	4.91 (1.62-8.19)*
Male (N=41)	0.00 (0.00-0.00)	2.16 (-1.21-5.54)	4.71 (1.65-7.78)*
Female (N=54)	0.00 (0.00-0.00)	-0.38 (-2.99-2.22)	3.04 (0.54-5.54)*
Social functioning	3.08 (1.38-4.78)*	1.01 (-0.69-2.72)	-0.10 (-2.20-2.00)
Combined drug group (N=69)	2.08 (-0.06-4.25)	0.23 (-1.80-2.25)	0.77 (-1.83-3.37)
Single group (N=26)	5.33 (3.11-7.56)	3.01 (-0.11-6.12)	-1.97 (-5.20-1.26)
Male (N=41)	3.30 (0.30-6.30)*	0.59 (-1.96-3.14)	-0.30 (-3.71-3.11)
Female (N=54)	2.93 (0.94-4.92)*	1.21 (-1.03-3.44)	0.03 (-2.67-2.73)
Medication effects	3.22 (0.62-5.83)*	-1.80 (-3.74-0.15)	7.21 (3.36-11.06)*
Combined drug group (N=69)	2.76 (-0.70-6.23)	-2.49 (-4.76-0.24)*	7.92 (3.28-12.56)*
Single group (N=26)	4.27 (1.07-7.46)*	-0.13 (-3.92-3.67)	5.37 (-2.00-12.74)
Male (N=41)	4.70 (0.70-8.70)*	-0.99 (-3.89-1.92)	4.49 (-1.43-10.41)
Female (N=54)	2.21 (-1.17-5.59)	-2.46 (-5.02-0.09)	9.27 (4.29-14.26)*
Overall quality of life	6.37 (4.09-8.65)*	1.11 (-0.82-3.04)	3.00 (-0.01-6.01)
Combined drug group (N=69)	6.21 (3.35-9.06)*	0.54 (-1.81-2.89)	3.45 (-0.21-7.11)
Single group (N=26)	6.73 (3.05-10.41)*	2.61 (-0.88-6.10)	1.72 (-3.54-6.99)
Male (N=41)	6.30 (2.74-9.86)*	1.92 (-0.89-4.72)	1.84 (-2.44-6.13)
Female (N=54)	6.41 (3.45-9.38)*	0.269 (-2.23-2.77)	3.99 (-0.20-8.17)

Note: *P<0.05.

occurrence of negative emotions, and have significant effects on improvement in anxiety, depression and quality of life of patients with epi-

lepsy. This treatment method also has the advantages of low operation difficulty and medical cost savings. It can be used as an auxiliary

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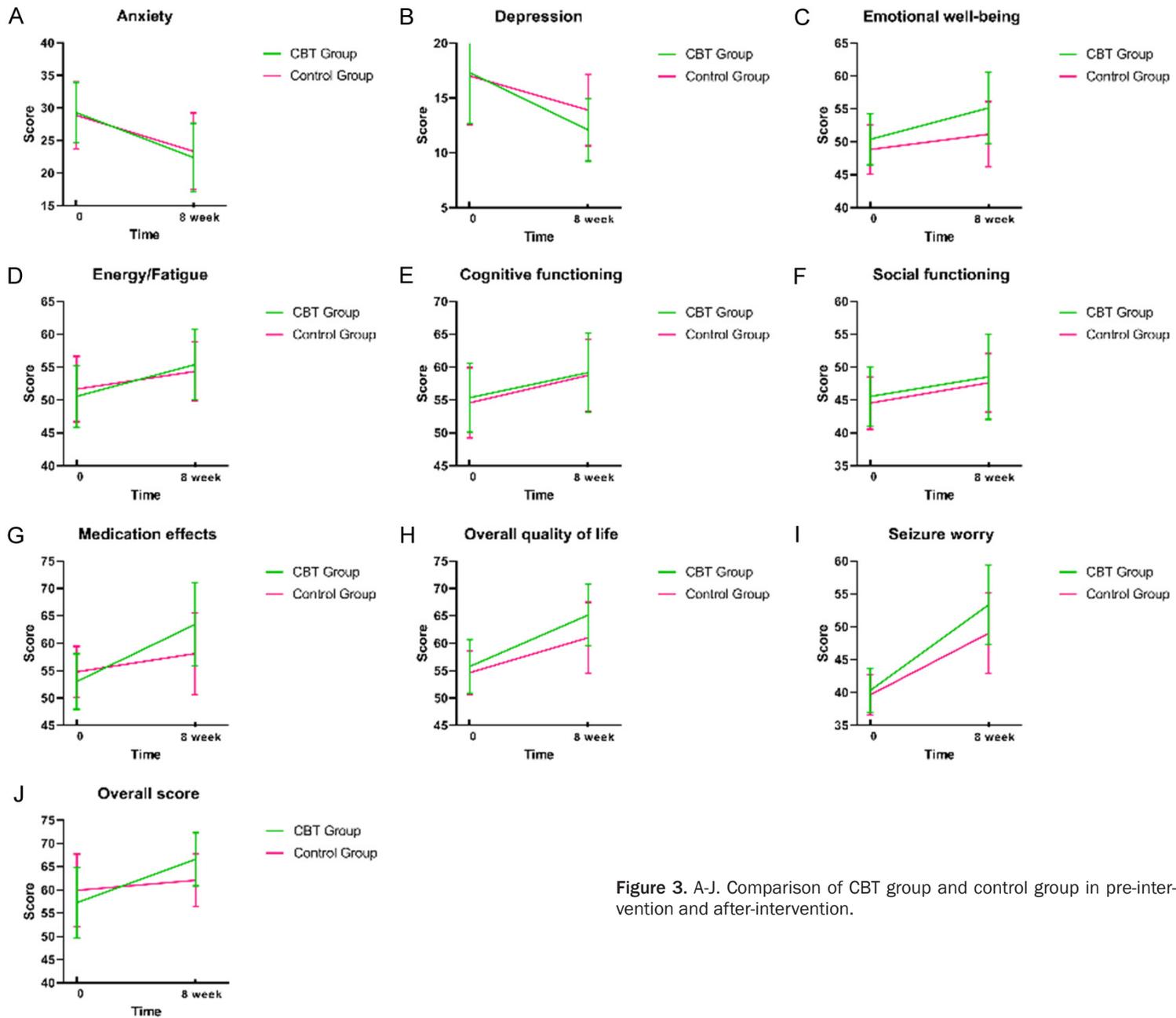


Figure 3. A-J. Comparison of CBT group and control group in pre-intervention and after-intervention.

means for the treatment of epilepsy in the clinic.

Acknowledgements

We are grateful for support from all participants. This work was supported by CAAE Epilepsy Research fund-UCB (No. 2020004B), The Suzhou Science and Technology Prosperity Youth Science and Technology Project (No. KJXW2019029), and Suzhou science and technology development plan project (skjyd2021-223).

Disclosure of conflict of interest

None.

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References

- [1] Liu C, Wen XW, Ge Y, Chen N, Hu WH, Zhang T, Zhang JG and Meng FG. Responsive neurostimulation for the treatment of medically intractable epilepsy. *Brain Res Bull* 2013; 97: 39-47.
- [2] Song P, Liu Y, Yu X, Wu J, Poon AN, Demaio A, Wang W, Rudan I and Chan KY. Prevalence of epilepsy in China between 1990 and 2015: a systematic review and meta-analysis. *J Glob Health* 2017; 7: 020706.
- [3] Kanner AM. Management of psychiatric and neurological comorbidities in epilepsy. *Nat Rev Neurol* 2016; 12: 106-116.
- [4] Beattie JF, Koch SA, Bolden LB and Thompson MD. Neuropsychological consequences of sleep disturbance in children with epilepsy. *Epilepsy Behav* 2016; 57: 118-123.
- [5] Stavrinides P, Constantinidou F, Anastassiou I, Malikides A and Papacostas S. Psychosocial adjustment of epilepsy patients in Cyprus. *Epilepsy Behav* 2012; 25: 98-104.
- [6] Kanner AM. Epilepsy and mood disorders. *Epilepsia* 2007; 48 Suppl 9: 20-22.
- [7] Alhashimi R, Thoota S, Ashok T, Palyam V, Azam AT, Odeyinka O and Sange I. Comorbidity of epilepsy and depression: associated pathophysiology and management. *Cureus* 2022; 14: e21527.
- [8] Butler T, Harvey P, Cardozo L, Zhu YS, Mosa A, Tanzi E and Pervez F. Epilepsy, depression, and growth hormone. *Epilepsy Behav* 2019; 94: 297-300.
- [9] Elger CE, Johnston SA and Hoppe C. Diagnosing and treating depression in epilepsy. *Seizure* 2017; 44: 184-193.
- [10] Zhu XR, Zhu ZR, Wang LX, Zhao T and Han X. Prevalence and risk factors for depression and anxiety in adult patients with epilepsy: caregivers' anxiety and place of residence do matter. *Epilepsy Behav* 2022; 129: 108628.
- [11] Roth-Rawald J, Friedrich J, Straub HB and Weck F. Anxiety about health of patients suffering from epilepsy. *Psychother Psychosom Med Psychol* 2022; 72: 243-249.
- [12] Brissart H, Forthoffer N and Maillard L. Attention disorders in adults with epilepsy. Determinants and therapeutic strategies. *Rev Neurol (Paris)* 2019; 175: 135-140.
- [13] Pavlou E and Gkampeta A. Learning disorders in children with epilepsy. *Childs Nerv Syst* 2011; 27: 373-379.
- [14] Gyimesi J. Epilepsy, violence, and crime. A historical analysis. *J Hist Behav Sci* 2022; 58: 42-58.
- [15] Francis A, Msall M, Obringer E and Kelley K. Children with autism spectrum disorder and epilepsy. *Pediatr Ann* 2013; 42: 255-260.
- [16] Kobau R, Cui W, Kadima N, Zack MM, Sajatovic M, Kaiboriboon K and Jobst B. Tracking psychosocial health in adults with epilepsy—estimates from the 2010 National Health Interview Survey. *Epilepsy Behav* 2014; 41: 66-73.
- [17] Hesdorffer DC, Ishihara L, Webb DJ, Mynepalli L, Galwey NW and Hauser WA. Occurrence and recurrence of attempted suicide among people with epilepsy. *JAMA Psychiatry* 2016; 73: 80-86.
- [18] Harnod T, Lin CL and Kao CH. Evaluating clinical risk factors for suicide attempts in patients with epilepsy. *J Affect Disord* 2018; 229: 79-84.
- [19] Noe KH, Locke DE and Sirven JI. Treatment of depression in patients with epilepsy. *Curr Treat Options Neurol* 2011; 13: 371-379.
- [20] Gandy M, Sharpe L and Perry KN. Cognitive behavior therapy for depression in people with epilepsy: a systematic review. *Epilepsia* 2013; 54: 1725-1734.
- [21] Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshe SL, Pelton J, Roulet Perez E, Scheffer IE and Zuberi SM. Operational classification of seizure types by the international league against epilepsy: position paper of the ILAE commission for clas-

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- sification and terminology. *Epilepsia* 2017; 58: 522-530.
- [22] Falcone T, Dagar A, Castilla-Puentes RC, Anand A, Brethenoux C, Valleta LG, Furey P, Timmons-Mitchell J and Pestana-Knight E. Digital conversations about suicide among teenagers and adults with epilepsy: a big-data, machine learning analysis. *Epilepsia* 2020; 61: 951-958.
- [23] Bonnett LJ, Tudur Smith C, Donegan S and Marson AG. Treatment outcome after failure of a first antiepileptic drug. *Neurology* 2014; 83: 552-560.
- [24] Akosile CO, Anomneze JU, Okoye EC, Adegoke BOA, Uwakwe R and Okeke E. Quality of life, fatigue and seizure severity in people living with epilepsy in a selected Nigerian population. *Seizure* 2021; 84: 1-5.
- [25] Siarava E, Hyphantis T, Katsanos AH, Pelidou SH, Kyritsis AP and Markoula S. Depression and quality of life in patients with epilepsy in Northwest Greece. *Seizure* 2019; 66: 93-98.
- [26] Christensen J, Vestergaard M, Mortensen PB, Sidenius P and Agerbo E. Epilepsy and risk of suicide: a population-based case-control study. *The Lancet Neurology* 2007; 6: 693-698.
- [27] Gilliam FG, Barry JJ, Hermann BP, Meador KJ, Vahle V and Kanner AM. Rapid detection of major depression in epilepsy: a multicentre study. *Lancet Neurol* 2006; 5: 399-405.
- [28] Hill T, Coupland C, Morriss R, Arthur A, Moore M and Hippisley-Cox J. Antidepressant use and risk of epilepsy and seizures in people aged 20 to 64 years: cohort study using a primary care database. *BMC Psychiatry* 2015; 15: 315.
- [29] Maguire MJ, Weston J, Singh J and Marson AG. Antidepressants for people with epilepsy and depression. *Cochrane Database Syst Rev* 2014: CD010682.
- [30] Gilliam FG, Black KJ, Carter J, Freedland KE, Sheline YI, Tsai WY and Lustman PJ. A trial of sertraline or cognitive behavior therapy for depression in epilepsy. *Ann Neurol* 2019; 86: 552-560.
- [31] DeRubeis RJ, Siegle GJ and Hollon SD. Cognitive therapy versus medication for depression: treatment outcomes and neural mechanisms. *Nat Rev Neurosci* 2008; 9: 788-796.
- [32] Dunlop BW, Rajendra JK, Craighead WE, Kelley ME, McGrath CL, Choi KS, Kinkead B, Nemeroff CB and Mayberg HS. Functional connectivity of the subcallosal cingulate cortex and differential outcomes to treatment with cognitive-behavioral therapy or antidepressant medication for major depressive disorder. *Am J Psychiatry* 2017; 174: 533-545.
- [33] Mondin TC, Cardoso Tde A, Jansen K, Silva Gdel G, Souza LD and Silva RA. Long-term effects of cognitive therapy on biological rhythms and depressive symptoms: a randomized clinical trial. *J Affect Disord* 2015; 187: 1-9.
- [34] Ost LG, Havnen A, Hansen B and Kvale G. Cognitive behavioral treatments of obsessive-compulsive disorder. A systematic review and meta-analysis of studies published 1993-2014. *Clin Psychol Rev* 2015; 40: 156-169.
- [35] Lunkenheimer F, Domhardt M, Geirhos A, Kilian R, Mueller-Stierlin AS, Holl RW, Meissner T, Minden K, Moshagen M, Ranz R, Sachser C, Staab D, Warschburger P, Baumeister H and consortium C. Effectiveness and cost-effectiveness of guided internet- and mobile-based CBT for adolescents and young adults with chronic somatic conditions and comorbid depression and anxiety symptoms (youthCOACHCD): study protocol for a multicentre randomized controlled trial. *Trials* 2020; 21: 253.
- [36] Macfarlane GJ, Beasley M, Prescott G, McNamee P, Keeley P, Artus M, McBeth J, Hannaford P, Jones GT, Basu N, Norrie J and Lovell K. The maintaining musculoskeletal health (MAMMOTH) study: protocol for a randomised trial of cognitive behavioural therapy versus usual care for the prevention of chronic widespread pain. *BMC Musculoskelet Disord* 2016; 17: 179.
- [37] Tuvesson H, Eriksen S and Fagerstrom C. mHealth and engagement concerning persons with chronic somatic health conditions: integrative literature review. *JMIR Mhealth Uhealth* 2020; 8: e14315.
- [38] Macrodimitris S, Wershler J, Hatfield M, Hamilton K, Backs-Dermott B, Mothersill K, Baxter C and Wiebe S. Group cognitive-behavioral therapy for patients with epilepsy and comorbid depression and anxiety. *Epilepsy Behav* 2011; 20: 83-88.
- [39] Gandy M, Karin E, Fogliati VJ, McDonald S, Titov N and Dear BF. A feasibility trial of an internet-delivered and transdiagnostic cognitive behavioral therapy treatment program for anxiety, depression, and disability among adults with epilepsy. *Epilepsia* 2016; 57: 1887-1896.
- [40] de Barros ACS, Furlan AER, Marques LHN and de Araujo Filho GM. Effects of a psychotherapeutic group intervention in patients with refractory mesial temporal lobe epilepsy and comorbid psychogenic nonepileptic seizures: a nonrandomized controlled study. *Seizure* 2018; 58: 22-28.
- [41] Leeman-Markowski BA and Schachter SC. Cognitive and behavioral interventions in epilepsy. *Curr Neurol Neurosci Rep* 2017; 17: 42.