RESEARCH ARTICLE

Changes in brain-derived neurotrophic factors in schizophrenic patients with spiritual psychoreligious therapy

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Abstract

Objective: To examine the effect of Spiritual Quranic Emotional Freedom Technique therapy on the level of brain-derived neurotrophic factor in schizophrenic patients.

Method: The quasi-experimental study was conducted from August to December 2021 at the Polytechnic of Health, Kendari, Indonesia, and comprised patients of either gender aged >20 years who had been diagnosed with schizophrenia by psychiatrists using the text-revised version of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders, had Brief Psychiatric Rating Scale score 50-60, and were part of the treatment programme at the polyclinic. They were divided into experimental group A and control group B. Patients in group A were given 30 days of Spiritual Quranic Emotional Freedom Technique therapy, while those in group B received only education about the spiritual therapy with the recommendation to listen to the Quran verses. A set of healthy controls memorizing the Quran was enrolled from the Islamic Boarding School, Kendari, and placed in group C. They were given education about the need to keep reading and learning the Quran. The intervention was done 2 times per week for 4 weeks. Serum brain-derived neurotrophic factor level for all groups and the Brief Psychiatric Rating Scale score for groups A and B were assessed at baseline and post-intervention. Data was analysed using SPSS 22.

Results: Of the 30 subjects, 16(53.3%) were females and 14(46.7%) were males. There were 11(36.7%) subjects aged 31-40 years. Each of the 3 groups had 10(33.3%) subjects. There was a significant decrease in Brief Psychiatric Rating Scale scores in groups A and B post-intervention ($p<0.000$). There was a significant increase in serum brain-derived neurotrophic factor levels post-therapy in groups A and C ($p<0.001$), while in group B it was not significant ($p=0.500$).

Conclusion: Spiritual Quranic Emotional Freedom Technique therapy could enhance clinical improvement and brain function in schizophrenic patients.

Keywords: Spiritual, The Quran, Psychoreligious, Schizophrenic. (JPMA 74: 1458; 2024)

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Introduction

About 1% global population suffers from schizophrenia, a severe chronic mental condition that impairs perception, cognition and social interaction.[1] Schizophrenia patients have a protracted healing process involving medicine and therapy, and have a shortened life expectancy.[2] The number of schizophrenia patients in Indonesia reaches 450,000 with insufficient access to mental health care and services.[3] Symptoms of schizophrenia are usually divided into positive and negative categories due to their effects and treatment. The positive symptoms include hallucinations, delusions, suspicion, and conceptual disorganisation, while the negative symptoms include social withdrawal, direct affect and emotional withdrawal. Neuropsychiatric symptoms enhance the effect of negative symptoms on the quality of life (QOL) of schizophrenic patients.[4]

Brain-derived neurotrophic factor (BDNF) is a key molecule involved in plastic changes related to learning and memory. It is a neurotrophic factor produced by the brain that plays a key role in synaptic plasticity, neuron growth, survival, differentiation and repair during neurodevelopment.[5] BDNF is widely distributed in the central nervous system (CNS) and is involved in the energy metabolism and pathophysiology of schizophrenic patients. Several previous investigations found that peripheral BDNF levels were very low in chronic schizophrenia patients. In schizophrenic patients, BDNF is also linked to learning and memory, as well as a variety of cognitive impairments, such as learning, memory, executive function, and attention.[6]

Antipsychotic medications, psychological therapies for patients and families, and a biopsychosocial paradigm form the foundation of schizophrenia treatment. Religion is a form of coping that helps individuals to deal with a wide variety of difficult life situations. Spirituality and therapy based on religion are crucial in the lives of patients with

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schizophrenia, and are the key success factor in better wellness management.[7]

Approaches to religion are multidimensional and are used when a person experiences stress, crisis, life burdens, problem-solving situations, as it prevents and reduces negative emotions.[8] Moreover, the presence of spirituality in nursing and healthcare is growing. The holistic nursing perspective helps the nurses understand each patient as a biopsychosocial and spiritual individual. Spiritual healing is one of the therapeutic techniques for schizophrenia patients.[9] For Muslims, the Quran treatment is a therapeutic therapy and a cure for bodily, spiritual and social illnesses.[10] Listening to and reading the Quran has been scientifically proven to have a calming effect, promote relaxation, and eliminate harmful physical and mental disorders as it stimulates the release of endorphins in the brain, which improve mood and memory, improves the ability to focus on positive thoughts and experiences, diverts negative thoughts, and reduces stress, anxiety and depression. It is a non-pharmacological treatment that works in conjunction with other treatments.[11,12]

Spiritual Quranic Emotional Freedom Technique (SQEFT) therapy is an intervention that combines the Quran therapy and the emotional freedom technique (EFT), and is expected to be an intervention for mental health practitioners as well as the patients' families and communities in improving the physical, functional, social, psychological, and spiritual QOL of schizophrenic patients.[13,14]

The current study was planned to examine the effect of SQEFT on the level of BDNF in schizophrenic patients.

Patients and Methods

The quasi-experimental study was conducted from August to December 2021 at the Polytechnic of Health, Kendari, Indonesia. After approval form the institutional ethics review board, the sample size was calculated using the resource equation method.[15] The sample was raised using stratified random sampling technique. Those included were patients of either gender aged >20 years who had been diagnosed with schizophrenia by psychiatrists using the text-revised version of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR)[16] had Brief Psychiatric Rating Scale (BPRS)[17] score 50-60, and were part of the treatment programme at the polyclinic. They were divided into experimental group A and control group B. A set of healthy age-matched controls was enrolled from the Islamic Boarding School, Kendari, who cleared the Mini International Neuropsychiatric Interview (MINI),[18] diligently reading the Quran and were living in the boarding school. They were placed in group C.

The exclusion criteria for groups A and B comprised residence outside Kendari, consumption of alcohol, addiction to psychotropics and other substances, active immunomodulatory therapy status, infectious and chronic diseases, uncooperative, not willing to be a respondent. The exclusion criteria for group C comprised sickness, age <20 years, inability to read the Quran. Informed consent was taken from all the subjects.

Patients in group A were given 30 days of SQEFT, while those in group B received only education about the spiritual therapy with the recommendation to listen to the Quran verses. Those in group C were given education about the need to keep reading and learning the Quran. The intervention was done 2 times per week for 4 weeks.

BPRS is a short scale to often used to assess the patient's actual clinical picture (severity of psychopathology) during the treatment process. It is an 18-item tool that is score on a Likert-type scale into seven categories; none, very light, light, medium, medium-heavy, heavy, and very heavy. Each class is assigned a grade of 1-7 with an overall score range of 18-126. BPRS score <60 indicates that the patient's condition is better and cooperative. BPRS is used to detect positive symptoms, negative symptoms, affective symptoms, depression, mania and motor skills. BPRS was measured in group A and B at baseline and post-therapy. Serum BDNF level was assessed for all the subjects in the 3 groups at baseline and post-therapy. Venous blood that was collected and put in a tightly closed tube/bottle and was further sealed to prevent leakage. It was then stored in a special bag prepared by the Universitas Hasanuddin (UNHAS) laboratory in Makassar, Indonesia, which also designed all the tools used for testing and enzyme linked immunosorbent assay (ELISA).

The blood samples were brought to Makassar by air and the researchers themselves took the samples directly to the UNHAS laboratory for testing with BDNF ELISA kit type LS-F2402 made lifespan Bioscience, inc in Nort America. are: is a 96-well ELISA for the Quantitative detection of Human BDNF in samples of Cell Culture Supernatants, Cell Lysates, Plasma, Serum and Tissue Homogenates. It is based upon a Sandwich assay principle and can be used to detect levels of BDNF as low as 15 picograms per milliliter. Serum samples were diluted 1:50 for standard procedure. The standard maximum concentration was set to 2000 pg/mL and the standard minimum concentration was 62.5 pg/mL. All standard concentrations were measured in duplicates; samples and blanks were measured in two to eight replicates, depending on the assay layout. The calculation of protein concentrations from measured was performed automatically by a Fluorescence facilitating a serial dilution standard curve.[19]

Data was analysed using SPSS 22. Data was expressed as frequencies and percentages or as mean +/- standard deviation. Kolmogorov-Smirnov test, paired samples t-test, t-test, Wilcoxon signed ranks test were used as appropriate. P<0.05 was considered statistically significant.

Results

Of the 30 subjects, 16(53.3%) were females and 14(46.7%) were males. There were 11(36.7%) subjects aged 31-40 years. Each of the 3 groups had 10(33.3%) subjects (Table 1).

There was a significant decrease in BPRS scores in groups A and B post-intervention (p<0.001). There was a significant increase in serum BDNF levels post-therapy in groups A and C (p<0.001), while in group B it was not significant (p=0.500) (Table 2, Figure).

Table-1: Characteristics of the participants.

Respondent characteristics	Group A n=10 (%)	Group B n=10 (%)	Group C n=10 (%)
Gender			
Male	4 (40)	5 (50)	5 (50)
Female	6 (60)	5 (50)	5 (50)
Age (years)			
21-30	3 (30)	3 (30)	4 (40)
31-40	4 (40)	3 (30)	4 (40)
41-50	3 (30)	4 (40)	2 (20)
Education			
Primary school	4 (40)	3 (30)	0 (0)
Junior high school	2 (20)	5 (50)	0 (0)
Senior High School	4 (40)	2 (20)	3 (30)
College	0 (0)	0 (0)	7 (70)
Work			
Work	2 (20)	1 (10)	7 (70)
Not working	8 (80)	9 (90)	3 (30)
Marital status			
Married	5 (50)	4 (40)	7 (70)
Single	5 (50)	6 (60)	3 (30)
Ethnic group			
Muna	2 (20)	2 (20)	2 (20)
Buton	4 (40)	0 (0)	1 (10)
Bugis	1 (10)	3 (30)	2 (20)
Tolaki	1 (10)	1 (10)	4 (40)
Jawa	1 (10)	0 (0)	1 (10)
Makassar	1 (10)	4 (40)	0 (0)
Length of illness			
1-5 years	6 (60)	5 (50)	
6-10 Years	3 (30)	3 (30)	
11-15 years	1 (10)	2 (20)	
Illness Relapse			
1 time	3 (30)	2 (20)	
2 time	3 (30)	3 (30)	
3 time	2 (20)	3 (30)	
4 time	2 (20)	2 (20)	

Table-2: BDNF levels and BPRS values of the subjects.

Variable		Pre test Mean±SD	Post test Mean±SD	p-value
BDNF				
Group A	SQEFT	103.77±34,07	196.79±49,46	0.000
Group B	Education	106.03±32,45	104.85±34,82	0.500
Group C	Normal_Health	166.62±18.68	206.19±24,38	0.000
BPRS				
Group A	SQEFT	50.60±3.13	41.50±2.54	0,000
Group B	Education	59.00±1.15	55.80±2.48	0,001`

BDNF: Brain-derived neutrophin factor, BPRS: Brief psychiatric rating scale, SQEFT: Spiritual Quranic Emotional Freedom Technique.

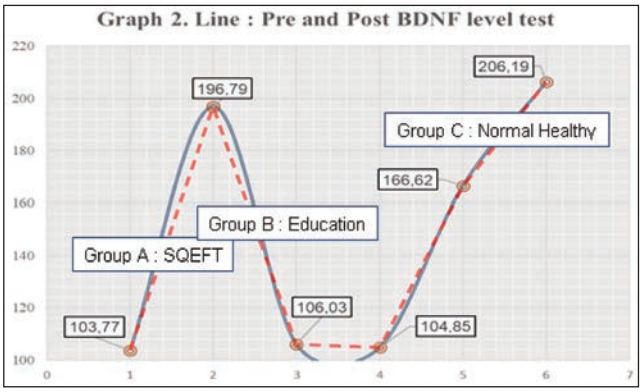

Figure-1: Pre and post intervention Brain derived neutrophin factor (BDNF) levels.

Discussion

To our knowledge, the current study is the first to report the effect of SQEFT on BDNF changes, especially in schizophrenia patients. The most common duration of illness was 1-5 years, and the greatest frequency of relapses was 1-3 times. Risk factors associated with relapse have been identified as medication adherence, occupational status, ability of daily living and payment method of medical costs, with medication adherence being the most powerful predictor of relapse.[20]

SQEFT psychospiritual therapy had an impact on decreasing BPRS value in the current study. A decrease in clinical symptoms of sentiments, like anxiety, guilt, despair and somatics, is indicated by a lower BPRS value. The positive signs that are felt include thought content, conceptual disorganisation, hallucinatory behaviour, aggrandisation, and negative symptoms, such as flat affect, emotional withdrawal, motor retardation, resistance and activation. BPRS has a validity value against symptoms of schizophrenia, which can be continually used and adjusted with changes and treatments over time.[13,14]

BDNF is a neurotrophic factor in the synthesis, metabolism, and the release of neurotransmitters is critical, which is linked to neurodevelopmental abnormalities and nervous system modifications in schizophrenia. Meta analyses have revealed that BDNF gene mutations may be a risk factor for

schizophrenia. The BDNF gene mutation causes a reduction in hippocampal grey matter volume and an increase in the work of specific grey matter types, such as the dorsolateral frontal area. Several BDNF gene variants have been linked to volume disparities in the frontal lobe caudate nucleus, putamen, and grey matter in schizophrenic individuals.[5,21,22]

BDNF is known as a regulator of dopamine gamma-aminobutyric acid (GABA) and serotonin receptors, which act through the tropomyosin receptor kinase B (TrK B) and has an important role in the survival and function of neurons. So it may have relevance in the pathophysiology of central nervous system (CNS) disorders, such as schizophrenia. Several conducted studies have shown conflicting results.[23] In the current study, BDNF serum levels of schizophrenic patients in the SQEFT group before treatment and the non-SQEFT group remained low. There was a decrease in BDNF serum levels in perfluorinated compound (PFC) in schizophrenic patients than healthy patients with the same age range, and there was a decrease in serum BDNF in patients with early episodes of schizophrenia treatment, which was lower than in healthy controls.[24] A decrease in BDNF can occur over 20 years in response to neurodegenerative processes in patients with chronic schizophrenia.[25] There was a decrease in BDNF serum levels in schizophrenia patients during 40 days of treatment than healthy controls.[26] The significantly decreased BDNF level in schizophrenic patients correlates with impaired cognitive function.[27]

In a study of schizophrenic patients and healthy controls aged 20-80 years, serum BDNF and PFC grey matter levels were significantly lower at older age in both schizophrenic and healthy controls, while BDNF in white matter did not decrease with age in either group.[24]

A study on chronic schizophrenia patients and healthy controls revealed that BDNF levels in schizophrenic patients were considerably lower than the controls (p=0.001), implying that BDNF has a role in the pathophysiology of schizophrenia and its related cognitive deficits, particularly memory problems.[28]

EFT is a psychological version of acupuncture therapy that does not use needles, but aligns its energy system to the body's meridian points by tapping with fingertips. EFT is the most well-known form of "energy psychology" combining cognitive and exposure techniques with the stimulation of selected acupuncture points (acupoints) by tapping on them.[29] EFT is used as a clinical intervention in nursing care, training and research, and is an effective method to improve a variety of physical and emotional problems of the patients. Frequently referred to as "tapping", this technique combines the cognitive reprocessing benefits of exposure and acceptance therapy with the energetic disturbance releases associated with acupuncture and other energy therapies.[30]

The Quran therapy will add to this therapy's perfection because it is adequate for the heart and soul's cleanliness. According to religious teachings, praying and doing zikr, and listening to the holy verses of the Quran are spiritual interventions that can be applied in psychiatric services.[13,14,31]

The SQEFT therapy is part of a spiritual intervention that is the primary concern of professional nursing. Health workers should apply spiritual research in patients' treatment and care.[13] Spiritual care is needed to improve the patients' QOL. Spiritual needs will prepare oneself to face any difficulties experienced during illness.[32,33]

The SQEFT intervention's efficacy was sustained from the first to the fourth week of training. Changes in negative symptoms, positive symptoms, affect, activity, mania, higher cognition, psychological improvement, morale, motivation, and better and cooperative communication skills were seen in all patients who received therapy in the current study. Besides increasing the spiritual level of the patients, schizoprenia patients prayed more often, and in the third week of the therapy, the patients could carry out independent therapy in pairs, indicating that SQEFT therapy was effective.[13,34]

The religious practice of reading the Quran and praying is a stress-reducing therapy most often used by Muslims.[32,34,35] The findings indicate that Quran recitation can be used as a non-pharmacological treatment to complement existing therapies.[11]

Physiological and psychological roles of the Quran therapy have been the subject of several investigations. Listening to the Quran for 20 minutes three times a week for one month lowered depression symptoms in Muslim haemodialysis patients. Listening to the Quran was particularly successful in Iran at bringing calm and relaxation, as well as focussing the mind on pleasant events and removing negative thoughts. The Quran aided in the reduction of stress and sadness. It was found to be a straightforward, easy-to-apply and cost-effective therapy for haemodialysis patients feeling severe distress and depression, as well as a diminished QOL.[11,35,36]

A 2013 study stated that the sound of the Quran verses can change the brain's physiological function, which results in an effect based on the sound of a particular passage of the Quran that affects the human heart and soul, causing brain neurotransmitters to release hormones.[34] Listening to the

holy verses of the Quran produced an alpha wave on electroencephalogram (EEG) that was higher than the size of the wave in resting conditions or when listening to music.[37]

The healing power of the Quran is a fundamental part of the belief that it is a book of healing from psychological illnesses. Patients also believe that recovery with the Quran is definite, including prayer as a solution for psychological health.[38]

Future longitudinal, large-scale studies comprising psychiatric patients with various diagnoses are needed to provide better insight and to validate the current findings.

Conclusion

The BPRS value decreased post-therapy, while serum BDNF level increased post-therapy. Differences in the neurocognitive function of group A patients were more significant than group B. Better cognitive performance showed that SQEFT therapy could be used by families and health professionals to help cure schizophrenic patients.

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Author Contribution:

AOV: Concept, design, writing, reviewing, literature, final approval.
AA: Concept, design, data analysis, final approval.
HK: Concept, design, evaluated the statistically, final approval.
HE: Concept, design, data analysis and interpretation, final approval.