

# Changes in serum BDNF levels after treatment of panic disorder patients

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## Abstract

**Aim:** Panic disorder is a significant psychiatric disorder that more frequently occurs in women, with daily attacks such as fear of death, limiting the patient's daily life. It is often associated with agoraphobia. The aim of this study was to investigate the relationship between BDNF levels and the clinical features of panic disorder.

**Material and Methods:** The study was carried out between January 2015 and July 2015 with 42 female patients and 38 healthy females who were admitted to Psychiatry Outpatient Clinic. The patients who were diagnosed with panic disorder without agoraphobia included in the study. The Panic Disorder Severity Scale (PDSS) was applied to the patients. Serum BDNF was measured by sandwich ELISA.

**Results:** The mean age of the 38 female patients was  $35.1 \pm 11.5$  years. The mean age of the control group of 38 healthy women was  $34.9 \pm 9.82$  years. Serum BDNF levels measured before treatment were significantly lower than BDNF levels measured after treatment ( $p < 0.001$ ). Serum BDNF levels measured before treatment were significantly lower than BDNF levels of the control group ( $p < 0.001$ ). While there was a statistically significant negative correlation between BDNF levels and PDSS scores before treatment.

**Conclusion:** Serum BDNF levels were significantly increased after treatment. The PDSS scores also decreased significantly after treatment. These results inform us about the effectiveness of the treatment. BDNF levels may also be considered as an indicator of the clinical follow-up of the panic disorder without agoraphobia.

**Keywords:** Panic disorder; brain-derived neurotrophic factor; agoraphobia.

## INTRODUCTION

Panic disorder (PD) is an anxiety disorder characterized by sudden panic attacks that reduce daily functioning (1). During panic attack, patients frequently resort to clinics other than psychiatry due to dizziness, feeling of fainting, palpitations, tremor, nausea, and chest pain. Panic attacks block daily activities due to symptoms such as loss of control and fear of death. Panic disorder is seen more frequently in female gender (2). Agoraphobia is defined as fear of not being able to survive alone and may be associated with panic disorder (3).

Psychodynamic and biological factors are investigated in the studies to determine the etiology of panic disorder (4). In studies investigating the neurobiology of panic disorder, neurotransmitter systems that regulate brain functions, genetic factors and neuroanatomical formations are emphasized (5). There are also studies suggesting that

neurobiological factors associated with the disease may be effective (6,7,8).

Biological markers, which can be used to monitor the efficacy of treatment in panic disorder patients were also investigated (9,10,11). In a study, it was found that plasma 3-methoxy-4-hydroxyphenylglycol (MHPG) levels were significantly lower in patients responding to drug treatment in panic disorder compared to the non-responding group (9). In another study, it was reported that serum ghrelin and total cholesterol levels were significantly lower after drug treatment of patients with panic disorder with agoraphobia (12). In another study, serum BDNF levels of patients with good response to cognitive behavioral therapy (CBT) in panic disorder with agoraphobia were found to be higher than patients with poor response to treatment (10). Studies on this subject are generally on groups with panic disorder with agoraphobia (9,10,11). Biological markers have not yet been established in order

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to determine the response of the disease to treatment.

One of the factors involved in the pathogenesis of panic disorder is brain-derived neurotrophic factor (BDNF) (13,14,15). BDNF provides neuronal development, differentiation and neuronal plasticity (16). BDNF, which is shown to cross the blood brain barrier, can be measured in serum to obtain information about the level of brain tissue (17). It has been reported that low serum BDNF levels play a role in the etiopathogenesis of anxiety, depression, anorexia nervosa and bulimia nervosa (18,19,20,21). In a study, serum BDNF levels were significantly lower in depressive patients before treatment (19). Studies have shown that estrogen regulates BDNF expression and significant changes in serum BDNF levels were found only in women (22,23). Depressive behavior was found to be increased in postmenopausal women (24).

In our literature review, we did not find any studies on serum BDNF levels in patients with panic disorder without agoraphobia. The aim of our study is to find out whether the serum BDNF levels can be a suitable biomarker in the diagnosis, treatment and follow-up period of panic disorder without agoraphobia in women patients.

## MATERIAL and METHODS

The study was carried out between January 2015 and July 2015 with 42 female patients and 38 healthy females who were admitted to Psychiatry Outpatient Clinic. The patients who were diagnosed with panic disorder without agoraphobia according to DSM-IV (25) diagnostic criteria, included in the study. The research project was approved by the Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki. The participants were informed on the procedures to be performed. Consent form was obtained from the participants. The presence of comorbid psychiatric disorders such as depression, obsessive-compulsive disorder, schizophrenia, bipolar disorder and delusional disorder, neurological diseases, history of mental retardation, history of alcohol, smoking and substance abuse, a history of drug treatment within the last three months and history of pregnancy were determined as exclusion criteria. The control group was selected from healthy individuals who were age and sex matched and did not have any physical or psychological illness, and a personal or family history of psychiatric disorder.

Paroxetine, a selective serotonin reuptake inhibitor (SSRI), was initiated in patients diagnosed with panic disorder without agoraphobia (20 mg / day). The Panic Disorder Severity Scale (PDSS) was applied at the beginning and 12 weeks of the study. PDSS is a 7-item, semi-structured and a self-report scale. PDSS provides information about panic incidence, anticipation anxiety, avoidance of physical sensations, level of occupational and social functioning (26,27). Each item is rated 0 to 4 by the patient. The total score range is 0-28. Scale's validity, reliability and standardization studies have been made in Turkey (28).

After the fasting period of at least 12 hours, 8-10 ml

blood was taken from the patient and control group. Blood samples were centrifuged at 4000 rpm for 10 minutes to separate the serum. Serums stored at -80° C were measured by immunoassay sandwich ELISA kit (Yh-Biosearch BDNF, China). The serum BDNF levels of the female patients diagnosed with panic disorder without agoraphobia was compared to the healthy control group.

## Statistical Analyses

Data were analyzed using the SPSS version 15.0 (SPSS/IBM, Chicago, IL, USA) statistical analysis package. The results are presented as mean  $\pm$  standard deviation in normally distributed groups, or otherwise as medians. In conditions in which parametric test assumptions were not met, non-parametric test alternatives as the Mann-Whitney U-test and the Kruskal-Wallis tests were employed. In conditions that met the parametric test assumptions, the Student's test was used to analyze the differences between the means of the two independent groups, and differences among more than two groups were investigated using an analysis of variance. Correlations between continuous variables were analyzed using Pearson's and Spearman's correlation coefficients. Categorical data were analyzed with the chi-square test for significance or Fisher's exact test. P values of <0.05 were accepted as significant.

## RESULTS

The mean age of the 38 female patients with panic disorder without agoraphobia was  $35.1 \pm 11.5$  years. The mean age of the control group of 38 healthy women was  $34.90 \pm 9.82$  years.

There was no significant difference between the patient and control groups in terms of age, gender, marital status or educational level ( $p > 0.05$ ) (Table 1).

**Table 1. The comparison of PD group and control group in terms of socio-demographic data**

	Patient Group (n=38)	Control Group (n=38)	P
Age (years)	35.1 $\pm$ 11.5	34.90 $\pm$ 9.82	n.s
Age of PD Onset	24 $\pm$ 5.2		n.s
The Duration of illness (years)	5 $\pm$ 3.1		
Marital Status (n,%)			
Married	25 (66%)	29 (76%)	n.s
Single	13 (34%)	9 (24%)	n.s
Education Level (n,%)			
Primary school	12 (32%)	14 (37%)	n.s
High school and above	26 (68%)	24 (63%)	n.s
Economic Status (n,%)			
Low/Middle	31 (82%)	33 (87%)	n.s
High	7 (18%)	5 (13%)	n.s

**n.s : non-significant, PD: Panic Disorder**

Serum BDNF levels measured before treatment were significantly lower than BDNF levels measured after treatment ( $p < 0.001$ ). Serum BDNF levels measured before treatment were significantly lower than BDNF levels in the control group ( $p < 0.001$ ). There was no statistically significant difference between post-treatment BDNF levels and control group BDNF levels ( $p = 0.204$ ), (Table 2).

Table 2. BDNF and PDSS score levels before and after treatment and relationship between them

	Pre-treatment Patient Group (n=38)	Post-treatment Patient Group (n=38)	Control Group (n=38)	p
BDNF (meanSD) (ng/ml)	4.32 ± 1.67	5.88 ± 1.73	6.19 ± 1.51	0.001 <sup>a,b*</sup> 0.204 <sup>c</sup>
PDSS score (meanSD)	16 ± 5	7 ± 3		0.001*

\*: Statistically significant  
a : The relationship between pre-treatment group and post-treatment group  
b: The relationship between pre-treatment group and control group  
c: The relationship between post-treatment group and control group  
BDNF: Brain-derived Neurotrophic Factor  
PDSS: Panic Disorder Severity Scale

While there was a statistically significant negative correlation between BDNF levels and PDSS scores before treatment, there was no significant relationship between BDNF levels and PDSS scores after treatment.

## DISCUSSION

According to the results of our study; Serum BDNF levels measured before treatment were significantly lower than the levels after treatment and compared to the control group. In addition, there was a significant negative correlation between pre-treatment BDNF levels and PDSS scores. There was no significant relationship between BDNF levels and PDSS scores after treatment. The significant increase in BDNF levels in our study was consistent with other studies in the literature.

Serum BDNF levels may vary depending on stress in many psychiatric disorders. Therefore, BDNF is thought to be an important biomarker for anxiety disorders, depression, posttraumatic stress disorder and schizophrenia (29). In a meta-analysis, it was stated that, selective serotonin reuptake inhibitors, successfully suppressed panic attacks via upregulating BDNF expression in the rat cerebral cortex (30). Kobayashi et al., (2005) found that BDNF levels of 26 patients who responded well to treatment with 10 consecutive psychiatric interviews for 1 hour per week were significantly higher than 16 patients with poor response to treatment (10). Kobayashi et al. suggest that serum BDNF levels may be important in evaluating response to treatment. Strohle et al., (2010) reported that patients with panic disorder had significantly increased serum BDNF levels after 30 minutes of exercise compared to the control group (31).

In a study (Gul et al., 2015) of 14 patients with PD with agoraphobia and 9 patients with PD without agoraphobia, ghrelin, triglyceride (TRG), total cholesterol (Total-C), low density lipoproteins (LDL-C) and very low density lipoproteins (VLDL-C) levels were higher in the group of PD with agoraphobia than in PD without agoraphobia (12). After the drug treatment, serum Ghrelin and Total-C levels were found to be significantly decreased compared to pretreatment values. In this study, it is stated that GHR and lipid profiles may show a pathophysiological relationship especially in patients with PD with agoraphobia. As in the present study, biomarker studies were performed more frequently in patients with PD with agoraphobia. In our study, serum BDNF levels were significantly increased in PD patients without agoraphobia.

Panic disorder is more common in female sex. Kobayashi et al., (2005) in the study of the relationship between BDNF levels and cognitive behavioral therapy in panic disorder, the patient group consisted of 33 women and 9 men (10). In a study by Strohle et al., which evaluated serum BDNF levels in patients with panic disorder in 2010, the patient group consisted of 9 women and 3 men. They found that serum BDNF levels increased with exercise (31). Molendijk et al., (2012) evaluated serum BDNF levels in 393 anxiety disorder patients, who did not receive drug treatment, and 382 healthy controls (32). There was no statistically significant difference in BDNF levels between the patient and control groups. However, in this study, lower BDNF levels were found in female patients than that of female controls and male patients. We believe that the fact that patient and control group were selected from women only, increased the significance of our study. Limitations of our study are the small sample size of patients and control groups and including only patients with panic disorder without agoraphobia.

## CONCLUSION

The serum BDNF levels can inform about anxiety levels in patients with PD without agoraphobia and can show the effectiveness of the treatment to the clinicians. In the future, BDNF levels may also be used as an indicator of the clinical follow-up of PD. However, in order to understand whether BDNF can be a marker in this sense, we think that more extensive studies are needed.

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