The impact of antidepressant treatment on brain-derived neurotrophic factor level: An evidence-based approach through systematic review and meta-analysis

Vijayakumar Arumugam, Vini Susan John, Nisha Augustine, Taniya Jacob, Sagar Maliakkal Joy, Suchandra Sen, Tuhinadri Sen

Abstract:
OBJECTIVES: Antidepressant treatment alters brain-derived neurotrophic factor (BDNF) levels, but it is not well established whether BDNF can be used as a marker to prove the efficacy of antidepressant treatment. The present systematic review and meta-analysis aim at assessing the influence of antidepressant treatment on BDNF level and the Hamilton Depression Rating Scale (HDRS) score, thereby to establish the rationale of utilizing BDNF as a predictive biomarker and HDRS score as an indicator for antidepressant treatment efficacy.

MATERIALS AND METHODS: Search was conducted in PubMed, Science Direct, and Cochrane databases using the key words “BDNF” and “Depression” and “Antidepressants.” On the basis of the inclusion and exclusion criteria, studies were filtered and finally 6 randomized controlled trials were shortlisted.

RESULTS: Comparison of serum BDNF level before and after antidepressant treatment was performed and the result showed that antidepressant treatment does not significantly affect the BDNF levels (confidence interval [CI]: −0.483 to 0.959; standard mean difference [SMD]: 0.238, \( P = 0.518 \)). Egger’s regression test (\( P = 0.455 \)) and heterogeneity test (\( I^2 = 88.909\% \)) were done. Similarly, comparison of HDRS scores before and after antidepressant treatment indicated improvement in HDRS score suggesting positive outcome (CI: 1.719 to 3.707; SMD: 2.713, \( P < 0.001 \)). Egger’s regression test (\( P = 0.1417 \)) and heterogeneity test (\( I^2 = 89.843\% \)) were performed. Publication bias was observed by funnel plot.

CONCLUSION: Changes in BDNF levels do not occur uniformly for all the antidepressants. Hence, to use BDNF as a biomarker, it needs to be seen whether the same is true for all antidepressants.

Keywords: Antidepressants, brain-derived neurotrophic factor, depression, Hamilton rating scale for depression, meta-analysis

Introduction

Affective disorders have been on the rise worldwide. Current estimates state that around one in ten individuals suffer from depression at least once in a life time, which would require medical treatment.[1] Major depressive disorder (MDD) is a mental disorder characterized by a pervasive and persistent low mood that is accompanied by low self-esteem coupled with a loss of interest or pleasure in normally enjoyable

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MDD has a significant socioeconomic impact and is associated with a deterioration in the quality of life which raises the susceptibility to several other complex disorders. Depression has a familial disposition and may be aggravated on exposure to severe stressors.

The diagnosis of MDD differs from other complex disorders in that it depends on the verbal communication and other subjective measures. Hence, a biological marker would be greatly desired to confirm the diagnosis of MDD. A biomarker can be used as an indicator that can be measured and assessed to predict normal biological, pathogenic processes, or a pharmacological response to a therapeutic intervention. Biomarkers can be used for predicting treatment course. They may also assist discovery of new antidepressant drugs. MDD treatment is long and very often fails to meet up to the remission criteria. Assessment of cure with the help of a biomarker could reduce ambiguity and give therapy a definite direction and lead to personalized treatment.

The biomarkers which could be used for denoting antidepressant treatment response are shown in Figure 1.

Brain-derived neurotrophic factor (BDNF) has been extensively studied with regard to antidepressant response prediction. BDNF is a key regulator of synaptic plasticity and plays an important role in cognitive functions. It is a secretory protein and a member of the neurotrophin family of growth factors, which acts in both central and peripheral nervous system. It helps in the survival of existing neurons, and in the growth and differentiation of new neurons and synapses. The neurotrophin hypothesis of depression is associated with reduced brain BDNF levels in depressive states which are alleviated with antidepressant therapy and increase in the BDNF levels. Several studies have reported an association between BDNF and antidepressant response whereas certain others have obtained conflicting results.

Brunoni et al. performed a systematic review and meta-analysis which dealt with the association of major depression and BDNF levels. The meta-analysis was performed to study the correlation between BDNF and depression (prognosis of antidepressant therapy). The results showed that BDNF levels were associated with clinical changes in depression. The study suggested that BDNF could be used together with the depression rating scales to address the efficacy of antidepressant therapy.

The Hamilton Depression Rating Scale (HDRS) is a clinician administered depression assessment scale. It has proven useful for many years as a way of determining

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**Figure 1:** Overview: Biomarkers of antidepressant treatment response. CRH = corticotropin-releasing hormone; CYP = Cytochrome P450, Dex = Dexamethasone, FKBP5 = FK506-binding protein 5, IGF-1 = Insulin-like growth factor 1, QEEG = Quantitative electroencephalographic, rACC = Rostral anterior cingulate cortex, REM = Rapid eye movement, VEGF = Vascular endothelial growth factor.
a patient’s level of depression before, during, and after treatment. In clinical studies of antidepressants, HDRS total score is used for establishing and comparing the treatment efficacy.

Our study is an attempt to identify the association of antidepressants with BDNF levels so as to analyze the use of BDNF as a predictive biomarker for assessing the efficacy of antidepressant therapy. The HDRS was taken as an indicator for antidepressant treatment outcome.

**Materials and Methods**

The aim of the study was to analyze the use of BDNF as a predictive biomarker which would be indicative of antidepressant treatment outcome in MDD patients. Hence, we fixed the hypothesis that there is no significant variation in BDNF before and after antidepressant treatment.

**Selection criteria**

Randomized controlled trials (RCTs) analyzing the pre and post treatment BDNF levels and HDRS score in MDD patients, regardless of age, gender, sample size, and ethnic background were selected. We included only the studies published in English. Plasma or serum BDNF concentration was expressed in picogram/ml. Studies published during 2000–2014 were selected. Review articles and studies assessing BDNF polymorphism, BDNF m-RNA levels, and postmortem studies were excluded from the study.

**Search strategy for identification of studies**

The study has been done in accordance to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. The authors independently conducted the literature search in PubMed, Science Direct, and Cochrane using the key words “BDNF” and “Depression” and “Antidepressants.” Data were extracted independently by six authors (S.S, A.V, V.S,J, N.A, T.J, and S.M.J) and the discrepancies were resolved by consultation with the seventh author (T.S). From the initial search, a total of 566 results were obtained. These results were further screened and segregated on the basis of human studies, year of publication (2000/01/01-2014/12/31), abstracts available, and clinical trials. With these criteria we obtained a total of 285, 281, 258, and 41 studies, respectively. The reference lists of the articles were cross-checked to identify other significant studies. Titles and abstracts of the relevant articles identified were screened for eligibility, and any abstract which was potentially relevant was reviewed in full text. Finally, 6 RCTs that met the criteria were included based on (FAST and PICO) methods. PICO model is a tool which helps organizing and focusing the foreground research question. PICO denotes patient/population, intervention/exposure, comparison and outcome, respectively [Table 1]. Four simple questions can be used to identify if the study is worth reading and using and is called the FAST method. FAST method signifies finding, appraisal, synthesis, and transferability of results. The literature search and trial selection process has been shown in Figure 2. All the 6 RCT’s addressed the pre and post treatment BDNF levels in MDD patients treated with antidepressants. All the RCT’s included in the study were assessed using the Jadad score, which independently assesses the methodological quality of a clinical trial [Table 2].

**Data extraction and analysis**

Details extracted from each trial revealed information about the year of publication, sample size, treatment given, duration of treatment, age, gender, mean and standard deviation (SD) of BDNF level, and HDRS score in pre- and post-treatment patient. The summary of the six RCT’s shortlisted for the study has been included in Table 2.

All the analyses were performed using the software “Comprehensive Meta-Analysis”. In all of the selected studies, BDNF levels and HDRS scores were
There is no increase in the serum level of BDNF. For venlafaxine-treated patients, a significant increase in BDNF levels was observed after 6 weeks of treatment. HDRS score was considerably reduced with venlafaxine group. A decrease in HDRS score was significant whereas change in BDNF level was not significant with venlafaxine group. A decrease in HDRS score was observed after 6 weeks of treatment.

For paroxetine-treated patients, a significant increase in BDNF level was observed after 6 weeks of treatment. HDRS score was considerably reduced with paroxetine group. A decrease in HDRS score was significant whereas change in BDNF level was not significant with paroxetine group. A decrease in HDRS score was observed after 6 weeks of treatment.

An increment of BDNF in the fluoxetine group was almost significant whereas change in BDNF level was not significant with venlafaxine group. A decrease in HDRS score was observed after 6 weeks of treatment.

There is no increase in the serum level of BDNF. There was significant change in HDRS score.

Plasma BDNF levels significantly increased after 6 weeks of treatment. HDRS score was considerably reduced with fluoxetine group. A decrease in HDRS score was significant whereas change in BDNF level was not significant with fluoxetine group. A decrease in HDRS score was observed after 6 weeks of treatment.

For paroxetine-treated patients, a significant increase in BDNF level was observed after 6 weeks and 6 months. Serum BDNF levels were significantly decreased by 8 weeks after paroxetine or milnacipran treatment.

For sertraline-treated patients, a significant increase in BDNF level was observed after 6 weeks of treatment. HDRS score was considerably reduced with sertraline group. A decrease in HDRS score was significant whereas change in BDNF level was not significant with sertraline group. A decrease in HDRS score was observed after 6 weeks of treatment.

For escitalopram-treated patients, a significant increase in BDNF level was observed after 6 weeks of treatment. HDRS score was considerably reduced with escitalopram group. A decrease in HDRS score was significant whereas change in BDNF level was not significant with escitalopram group. A decrease in HDRS score was observed after 6 weeks of treatment.

Serum BDNF levels in responders to both drugs at 8 weeks were higher than those in nonresponders. The HDRS scores had significantly decreased by 4 weeks after paroxetine or milnacipran treatment.

A total of 154 subjects with MDD were considered in all the studies.

Among the studies, two trials were conducted in Turkey, and remaining studies were conducted in Italy, Japan, Korea, and Germany. Duration of intervention for all the studies was between 5 and 12 weeks. All the selected articles followed the DSM-IV criteria for the diagnosis of MDD. Immunoassay was used to assess the levels of BDNF in all the studies. There were no particular age limits for the patients. Both females and males participated in the studies. Different classes of antidepressants in different doses were used in the selected studies. In all the studies, the changes in BDNF levels and HDRS score (before and after antidepressant treatment) were measured. Among the 6 articles selected for the meta-analysis, 3 of them[21,22,23] reported a decline of BDNF by 12% in paroxetine-treated patients.

For venlafaxine-treated patients, a significant increase in BDNF levels was observed after long-term treatment but not for 5 weeks. No significant increase in BDNF levels was noticed in patients treated with escitalopram-treated groups. An Italian study conducted by Aydemir et al.[24] and another study by Aydemir et al.[25] suggested a correlation between antidepressant treatment and BDNF concentration where the same was found to be increased. An Italian study conducted by Matrisciano et al.[26] reported that different antidepressant drugs have variable effects on serum BDNF levels. A study on Turkish population conducted by Başterzi et al.[23] did not reveal any significant change, whereas a similar study in Germany by Hellweg et al.[23] indicated a decline of BDNF by 12% in paroxetine-treated patients.

Impact of antidepressant treatment on brain-derived neurotrophic factor level

The data extracted from the articles with regard to BDNF before and after antidepressant treatment is summarized in Table 3. Using the random effects model, comparison of serum BDNF levels (before and after antidepressant therapy) was performed, and from these results, it could be suggested that antidepressant therapy is associated with a change in BDNF level, but did not produce any significant impact on it [Figure 3]. (CI: -0.483–0.959; SMD: 0.238, P = 0.518). The effect size was similar in most of these studies. To identify bias, the funnel plot was utilized and possibilities of bias were observed. Further, Egger’s regression analysis was performed which indicated the absence of publication bias (P = 0.455).

Table 2: Design and characteristics of studies included in meta-analysis

| Author               | Year | Treatment given | Follow-up | Intervention                                                                 | Jadad score |
|----------------------|------|-----------------|-----------|------------------------------------------------------------------------------|-------------|
| Aydemir et al.       | 2005 | Venlafaxine     | 12 weeks  | The increase in serum BDNF level and decrease in HDRS score were statistically significant | 1           |
| Basterzi et al.      | 2009 | Fluoxetine and venlafaxine | 6 weeks | An increment of BDNF in the fluoxetine group was almost significant whereas change in BDNF level was not significant with venlafaxine group. A decrease in HDRS score was observed after 6 weeks of treatment | 2           |
| Hellweg et al.       | 2007 | Paroxetine      | 5 weeks   | There is no increase in the serum level of BDNF. There was significant change in HDRS score | 3           |
| Lee et al.           | 2008 | Paroxetine, citalopram, and venlafaxine | 6 weeks | Plasma BDNF levels significantly increased after 6 weeks of treatment. HDRS score was considerably reduced | 1           |
| Matrisciano et al.   | 2009 | Sertraline, escitalopram, and venlafaxine | 24 weeks | For sertraline-treated patients, a significant increase in BDNF level was observed after 5 weeks and 6 months. For venlafaxine-treated patients, a significant increase in levels was observed after long-term treatment but not for 5 weeks. No significant increase in BDNF levels was noticed in patients treated with escitalopram-treated groups | 1           |
| Yoshimura et al.     | 2007 | Paroxetine and milnacipran | 8 weeks | Serum BDNF levels in responders to both drugs at 8 weeks were higher than those in nonresponders. The HDRS scores had significantly decreased by 4 weeks after paroxetine or milnacipran treatment | 1           |

BDNF=Brain-derived neurotrophic factor, HDRS=Hamilton Depression Rating Scale

reported (mean ± SD). From these values, standard mean difference (SMD) with 95% confidence intervals (CI) for individual studies was computed using random effect analyses model. Further, funnel plot was computed and heterogeneity test was also carried out. Tests were considered statistically significant when the P value was found to be <0.05.

Results

Search results

A total of 566 studies were identified, among which 5 studies were selected based on the criteria mentioned earlier. Among the six articles that were chosen from cross references, only one article met our conditions for inclusion criteria while the remaining five were excluded from the study. Finally, six randomized control trials that met the criteria were included in the systematic review and meta-analysis. A total of 154 subjects with MDD were considered in all the studies.

Among the studies, two trials were conducted in Turkey, and remaining studies were conducted in Italy, Japan, Korea, and Germany. Duration of intervention for all the studies was between 5 and 12 weeks. All the selected articles followed the DSM-IV criteria for the diagnosis of MDD. Immunoassay was used to assess the levels of BDNF in all the studies. There were no particular age limits for the patients. Both females and males participated in the studies. Different classes of antidepressants in different doses were used in the selected studies. In all the studies, the changes in BDNF levels and HDRS score (before and after antidepressant treatment) were measured. Among the 6 articles selected for the meta-analysis, 3 of them[21,22,23] clearly classified the patients as responders and nonresponders based on the HDRS score and one[24] of them classified the patient group into responders and nonresponders based on both HDRS score as well as BDNF levels. The remaining article[21,22] did not divide the group based on the response, but they evaluated the change in BDNF levels as well as HDRS scores. Two of the Asian studies by Lee and Kim[24] and Yoshimura et al.[26] and another study by Aydemir et al.[25] suggested a correlation between antidepressant treatment and BDNF concentration where the same was found to be increased. An Italian study conducted by Matrisciano et al.[26] reported that different antidepressant drugs have variable effects on serum BDNF levels. A study on Turkish population conducted by Başterzi et al.[23] did not reveal any significant change, whereas a similar study in Germany by Hellweg et al.[23] indicated a decline of BDNF by 12% in paroxetine-treated patients.

Impact of antidepressant treatment on brain-derived neurotrophic factor level

The data extracted from the articles with regard to BDNF before and after antidepressant treatment is summarized in Table 3. Using the random effects model, comparison of serum BDNF levels (before and after antidepressant therapy) was performed, and from these results, it could be suggested that antidepressant therapy is associated with a change in BDNF level, but did not produce any significant impact on it [Figure 3]. (CI: -0.483–0.959; SMD: 0.238, P = 0.518). The effect size was similar in most of these studies. To identify bias, the funnel plot was utilized and possibilities of bias were observed. Further, Egger’s regression analysis was performed which indicated the absence of publication bias (P = 0.455).
The imputed funnel plot was then computed to identify heterogeneity. This was further confirmed using the heterogeneity test when $I^2$, $Q$, and $P$ values were found to be 88.909%, 45.081, and 0.001 respectively, thus indicating considerable heterogeneity [Table 4].

Impact of antidepressant treatment on Hamilton Depression Rating Scale score
Data extracted from articles with regard to HDRS score before and after antidepressant treatment is given in Table 5. HDRS score before and after antidepressant treatment was also compared using random effect model and the results indicate that the score improves after antidepressant therapy; hence, the HDRS score signifies a positive antidepressant treatment outcome [Figure 4]. (CI: −1.719–3.707; SMD: 2.713, $P < 0.001$). The effect size was similar in most of these studies. The funnel plot was computed to identify probabilities of any kind of bias. This was further evaluated by Egger’s regression analysis which confirmed the absence of publication bias ($P = 0.1417$) and the asymmetry in the funnel plot may be due to other bias. The imputed funnel plot was obtained to detect heterogeneity. It was further confirmed using the heterogeneity test which gave an $I^2$ value of 89.843%, $Q$ value of 49.228, and ($P < 0.001$) indicating considerable heterogeneity [Table 4].

Table 3: Data extracted from articles with regard to brain-derived neurotrophic factor before and after antidepressant treatment

| Study name            | Sample size | BDNF levels before treatment (pg/ml) | BDNF level after treatment (pg/ml) |
|-----------------------|-------------|-------------------------------------|-----------------------------------|
|                       |             | Mean  | SD     | Mean | SD     |
| Aydemir et al.        | 10          | 17900 | 9100   | 34600| 7100   |
| Basterzi et al.       | 29          | 42005 | 12630  | 47775| 12973  |
| Hellweg et al.        | 20          | 13.250| 5.112  | 12.016| 4.846  |
| Lee et al.            | 32          | 698.1 | 537.7  | 1028.9| 744.5  |
| Matrisciano et al.    | 21          | 35370 | 14340  | 49600| 13000  |
| Yoshimura et al.      | 42          | 9550  | 7770   | 16850| 7850   |

Table 4: Results of heterogeneity study

| Study variable | Heterogeneity | |
|----------------|---------------|
|                | $I^2$ (%)     | $Q$  | $P$  |
| BDNF           | 88.909        | 45.081 | 0.001 |
| HDRS           | 89.843        | 49.228 | <0.001 |

BDNF=Brain-derived neurotrophic factor, SD=Standard deviation

Discussion
Several articles have been published which deal with the association of BDNF levels in MDD patients. Studies have suggested that BDNF can be used as a diagnostic marker in depressive patients as the level of BDNF is low in depressive patients and antidepressants increase the BDNF level in accordance to the neurotrophin hypothesis. Inspite of such suggestions from several studies, it is still not applied to clinical practice, as many contradictions exist on this topic. Moreover, none of the studies have proven the usefulness of BDNF as a biomarker to predict the antidepressant treatment efficacy. A previous meta-analysis\textsuperscript{[18]} has reported an...
Table 5: Data extracted from articles with regard to Hamilton Depression Rating Scale score before and after antidepressant treatment

| Study name            | Sample size | HDRS levels before treatment | HDRS level after treatment |
|-----------------------|-------------|------------------------------|---------------------------|
|                       |             | Mean            | SD     | Mean  | SD  |                  |                          |
| Aydemir et al.        | 10          | 23.2            | 4.6   | 8.2   | 3.9 |                  |                           |
| Basterzi et al.       | 29          | 26.1            | 4.2   | 11.56 | 8.1 |                  |                           |
| Hellweg et al.        | 20          | 22.6            | 3.9   | 11.7  | 8.4 |                  |                           |
| Lee et al.            | 32          | 28.6            | 8.4   | 8.8   | 8.0 |                  |                           |
| Matrisciano et al.    | 21          | 17.57           | 5.24  | 9.4   | 5.6 |                  |                           |
| Yoshimura et al.      | 42          | 24              | 2     | 11    | 3  |                  |                           |

HDRS=Hamilton Depression Rating Scale, SD=Standard deviation

The present meta-analysis was an initiative to identify whether antidepressant therapy is associated with changes in BDNF and if the same can be used as a predictive biomarker with regard to antidepressant treatment efficacy. The change in HDRS score in regard to antidepressant therapy was taken as an indicator for antidepressant treatment outcome. While studying the association between antidepressants and BDNF level, the pooled "P" value (P > 0.05) with 95% CI suggested that the antidepressant treatment does not have a significant impact on BDNF level. The HDRS data analysis indicates a decrease in the severity of depression (P < 0.001). Hence, BDNF levels may not reflect antidepressant therapy outcome, and therefore, this restricts its use as a biomarker.

Certain limitations must be considered while interpreting the results of our studies. The sample size included in the meta-analysis is considerably small. Antidepressant classes, dosage regimen, duration of treatment, and ethnicity of the patient population are varied among the studies. The outcome definitions are also different among the studies.

MDD is a heterogeneous illness for which there is no effective method to assess the treatment response. BDNF regulates synaptic plasticity in neuronal networks involved in depressive behaviors.[27] Even though antidepressants play a vital role in the regulation of BDNF, further information is required regarding the role of specific classes of antidepressants on BDNF concentrations.

**Conclusion**

Changes in BDNF levels do not occur uniformly for all the antidepressants. Hence, to use BDNF as a biomarker, it needs to be seen whether the same is true for all antidepressants.

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Conflicts of interest
There are no conflicts of interest.

References
1. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. Arch Gen Psychiatry 2005;62:593-602.
2. Barlow D, Durand Y. Abnormal Psychology. 1st ed. Belmont, CA: Wadsworth/Thomson Learning; 2007. p. 292-5.
3. Pyne JM, Patterson TL, Kaplan RM, Ho S, Gillin JC, Golshan S, et al. Preliminary longitudinal assessment of quality of life in patients with major depression. Psychopharmacol Bull 1997;33:23-9.
4. Biomarkers Definitions Working Group. Biomarkers and pharmacogenetics. Future Med 2008;9:1353-8.
5. Rush AJ, Trivedi MH, Nierenberg AA, Wisniewski SR, Stewart JW, et al. Effects of chronic antidepressant treatment on serum brain-derived neurotrophic factor levels in depressed patients: A preliminary study. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:261-5.
6. Başterzi AD, Yazıcı K, Aslan E, Delialioğlu N, Taşdelen B, et al. Results of a long-term open-label study with mirtazapine in patients with major depressive disorder. Spectr 2012;17:155-63.
7. Aydemir O, Deveci A, Taneli F. The effect of chronic antidepressant treatment on serum brain-derived neurotrophic factor levels in depressed patients: A preliminary study. Prog Neuropsychopharmacol Biol Psychiatry 2005;29:261-5.
8. Faries D, Herrera J, DeBrota D, Demitrack M, Fisher WA, et al. The responsiveness of the Hamilton Depression Rating Scale. J Psychiatr Res 2000;34:3-10.
9. Taylor WD, McQuoid DR, Ashley-Koch A, MacFall JR, Bridges J, Krishnan RR, et al. BDNF val66Met genotype and 6-month remission rates in late-life depression. Pharmacogenomics J 2011;11:146-54.
10. Chi MH, Chang HH, Lee SY, Lee IH, Gean PW, Yang YK, et al. Brain derived neurotrophic factor gene polymorphism (Val66Met) and the early response to antidepressant in Chinese Han population. Psychiatr Genet 2012;22:214-5.
11. Zou YF, Wang Y, Liu P, Feng XL, Wang BY, Zang TH, et al. Association of brain-derived neurotrophic factor genetic val66Met polymorphism with severity of depression, efficacy of fluoxetine and its side effects in Chinese major depressive patients. Neuropsychobiology 2010;61:71-8.
12. Ikenouchi-Sugita A, et al. Serum levels of brain-derived neurotrophic factor (BDNF), BDNF gene Val66Met polymorphism, or plasma catecholamine metabolites, and response to mirtazapine in Japanese patients with major depressive disorder (MDD). CNS Spectr 2012;17:155-63.
13. Yoshimura R, Kishi T, Suzuki A, Umene-Nakano W. Ikenouchi-Sugita A, et al. Serum levels of brain-derived neurotrophic factor (BDNF), BDNF gene Val66Met polymorphism, or plasma catecholamine metabolites, and response to mirtazapine in Japanese patients with major depressive disorder (MDD). CNS Spectr 2012;17:155-63.
14. Yoshimura R, Kishi T, Suzuki A, Umene-Nakano W. Ikenouchi-Sugita A, et al. Serum levels of brain-derived neurotrophic factor (BDNF), BDNF gene Val66Met polymorphism, or plasma catecholamine metabolites, and response to mirtazapine in Japanese patients with major depressive disorder (MDD). CNS Spectr 2012;17:155-63.
15. Yoshimura R, Kishi T, Suzuki A, Umene-Nakano W. Ikenouchi-Sugita A, et al. Serum levels of brain-derived neurotrophic factor (BDNF), BDNF gene Val66Met polymorphism, or plasma catecholamine metabolites, and response to mirtazapine in Japanese patients with major depressive disorder (MDD). CNS Spectr 2012;17:155-63.
16. Yoshimura R, Kishi T, Suzuki A, Umene-Nakano W. Ikenouchi-Sugita A, et al. Serum levels of brain-derived neurotrophic factor (BDNF), BDNF gene Val66Met polymorphism, or plasma catecholamine metabolites, and response to mirtazapine in Japanese patients with major depressive disorder (MDD). CNS Spectr 2012;17:155-63.