Low serum brain derived neurotrophic factor in non-suicidal out-patients with depression: Relation to depression scores

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ABSTRACT

Context: Low brain-derived neurotrophic factor (BDNF) has been implicated in the pathophysiology of depression. The relation between BDNF and severity of depression has been investigated.

Aims: In this study, we aimed to measured serum BDNF levels in never-treated non-suicidal out-patients with depression and relate this to the severity of depression.

Settings and Design: This study was conducted in an out-patient setting in a tertiary care psychiatric hospital on consenting depressed patients.

Materials and Methods: Forty three (19 females) antidepressant-naive out-patients with depression, aged between 18 and 55 years and 24 (13 females) age-matched healthy volunteers gave consent for the study. Serum BDNF levels were assayed by using the sandwich enzyme-linked immunosorbent assay method on morning serum samples before starting treatment. These were compared between patients and controls using independent sample t-test. Pearson’s correlation coefficient was used to assess the association between baseline BDNF and Hamilton depression rating scale (HDRS).

Results: Serum BDNF was significantly lower in patients with depression (mean±standard deviation (SD)=18.59±4.9 ng/ml) than in healthy volunteers (mean±SD=23.6±5.6 ng/ml; \( P = 0.001 \)). There was a significant negative correlation between the HDRS total scores and BDNF levels (\( P = 0.04 \)), indicating that more severely depressed patients had lower BDNF scores.

Conclusions: Serum BDNF level is lower in non-suicidal out-patients with depression. The inverse correlation between ratings of depression and BDNF levels suggests possible relationship between depression, (role of illness on) BDNF levels and neuroplasticity thereof.

Key words: Brain derived neurotrophic factor, depression, hamilton depression rating scale

INTRODUCTION

Decreased neuroplasticity in hippocampus is pathophysiologically linked to depression.[1] This can help us understand the link between stress and depression.[2] Brain derived neurotrophic factor (BDNF) is a modulator of neuroplasticity in the brain (neuronal survival, synaptic signaling and synaptic consolidation) and is implicated in the pathophysiology of depression,[3,4] through the stress pathway.[5]

Decreased serum BDNF levels in drug free patients with depression in comparison with healthy controls has been reported.[6] BDNF levels have been shown to increase with antidepressant treatment.[7,9] Some studies have shown an
association between the severity of depression and low BDNF levels.\textsuperscript{10} Given this relationship, it is understandable that non-suicidal (perhaps milder) depressive patients did not have as low BDNF levels as their suicidal counterparts.\textsuperscript{11} In this study, we investigated if serum BDNF in never-treated non-suicidal patients with depressive disorder is lower than matched healthy comparison controls, and the relation of serum BDNF to depression scores.

**MATERIALS AND METHODS**

**Subjects**

Consecutive never treated patients with depression were recruited ($n=43$, females=19) from the out-patient psychiatry clinic of a research and clinical care hospital. They were aged between 18 and 55 years and had a score of 11 or more on the 17 item Hamilton depression rating scale (HDRS).\textsuperscript{12} Diagnosis of major depressive disorder according to Diagnostic and Statistical Manual of Mental Disorders-IV,\textsuperscript{13} was confirmed by a psychiatrist using Mini International Neuropsychiatric Interview.\textsuperscript{14} Only patients who had a score of $\leq 2$ on the suicide item of Hamilton rating scale for depression (HDRS) were included. This status too was confirmed by the psychiatrist who made a diagnosis of depression. Patients with mental retardation, substance abuse disorders (except nicotine and caffeine), organic disorders such as dementia, epilepsy or cerebrovascular accidents, history suggestive of psychosis or bipolar disorder or catatonia were excluded. Age and education-matched healthy consenting volunteers were recruited ($n=24$, 13 females). The same exclusion criteria were used as for the patients. Consent was obtained from all subjects. The Institutional Ethics Committee of the National Institute of Mental Health and Neurosciences approved the study.

**Assessment of BDNF**

A total volume of 5 ml venous blood was collected from patients (before starting any medication) and healthy controls in anticoagulant-free tubes between 9 and 11 am and serum was separated after 30 min by centrifugation (2900 rpm for 15 min). Coded serum sample was stored at $-80^\circ\text{C}$. Serum BDNF levels were measured by using the enzyme-linked immuno sorbent assay by using commercial reagents (Aquin Technologies Private Limited) according to the manufacturer’s instructions. The laboratory staff was unaware of clinical details. The intra- and inter-assay coefficient of variations was 1.34% and 4.34%, respectively.

**Statistical analysis**

Independent sample $t$-test was used to compare patients and healthy volunteers in terms of age, education and baseline serum BDNF levels. Pearson’s correlation coefficient was computed between baseline BDNF and HDRS scores as well as duration of illness.

**RESULTS**

There was no difference between patients with depression and healthy controls with regards to age, sex and education [Table 1]. Mean age of onset of illness was 32.2 years (SD: 8.9), mean duration of illness was 11.7 months (SD: 14.6) and mean HDRS score was 18.5 (SD: 4.6). Serum BDNF was significantly lower in patients with depression in comparison with healthy volunteers and the effect size of the difference was 1.0 [Table 1]. There was significant negative correlation between serum BDNF levels and depression scores on the 17-item HDRS (Spearman’s $r=-0.32$, $P=0.040$). Serum BDNF levels did not correlate with duration of illness. Serum BDNF was not different between sexes either within patients or controls.

**DISCUSSION**

The present study shows that serum BDNF levels were lower in never-treated, non-suicidal patients with depression in comparison with the healthy controls. This is consistent with previous reports. Serum BDNF values were in a range comparable to previous studies. Brunoni \textit{et al.} (2008),\textsuperscript{13} reviewing 20 studies on 1504 patients found a value of 19.59 ng/ml for patients and 25.78 ng/ml for controls with an effect size of 0.91. Bocchio-Chiavetto \textit{et al.},\textsuperscript{16} in a meta-analysis of 15 studies found an average value of 20 ng/ml in patients compared with 32 ng/ml in controls. This consistent finding indicates that decreased BDNF levels may be an important factor in the pathophysiology of depression.

Severity of depression was negatively correlated with BDNF level in our study. This was despite most patients (75%) having a HDRS score $<22$ (perhaps as only non-suicidal patients were included). This is similar to previous studies that have showed a negative correlation between severity of depression and BDNF levels.\textsuperscript{17-20} The effect size found in this study was 1.0, similar to that reported in earlier studies.\textsuperscript{13} BDNF is present in both the central and peripheral nervous system.\textsuperscript{21} Pan \textit{et al.}\textsuperscript{22} have reported that BDNF crosses the blood brain barrier, so that serum BDNF concentrations may reliably reflect BDNF brain concentrations.

In summary, out-patients with major depression have low levels of serum BDNF. The BDNF levels were negatively correlated with depression scores suggesting a pathophysiological role in the illness.

**Table 1: Demographic and clinical details of the subjects**

| Group Variables | Depression N=43 | Controls N=24 |
|-----------------|-----------------|--------------|
| Age in years    | 33.0 (8.5)      | 31.9 (9.8)   |
| No. of females* (%) | 19 (44)      | 13 (54)      |
| Education in years | 10.8 (5.1)    | 10.6 (5.5)   |
| Serum BDNF** ng/ml | 18.59±4.9    | 23.6 (5.6)   |

Values are mean (SD) and *numbers (%) of subjects; **Significant difference between groups ($t=3.8; P<0.001$); BDNF – Brain-derived neurotrophic factor.
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