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Journal of Affective Disorders 105 (2008) 279–283

JOURNAL OF AFFECTIVE DISORDERS

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Brief report

Plasma and serum brain-derived neurotrophic factor (BDNF) in depressed patients during 1 year of antidepressant treatments

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Received 12 March 2007; received in revised form 7 May 2007; accepted 7 May 2007
Available online 5 June 2007

Abstract

Background: Brain-derived neurotrophic factor (BDNF) has been hypothesized to be involved in the neurobiology of major depression. The aim of this study was to assess the possible relationships between depressive symptoms and serum and/or plasma BDNF levels during 1 year of antidepressant treatment.
Methods: Plasma and serum BDNF levels were assayed in 15 drug-free depressed patients and in 15 healthy control subjects at baseline and the 1st, 3rd, 6th and 12th month of antidepressant treatment.
Results: At baseline, patients' serum and plasma BDNF levels were significantly lower ($p<.001$ and $p=.004$, respectively) than those found in healthy control subjects. However, while from the 1st month of treatment patients' plasma BDNF levels did not differ significantly from those observed in healthy control subjects, serum BDNF levels in patients remained significantly lower at all times.
Limitations: The main limitations of the current study are represented by the small sample size and the high discontinuation rate.
Conclusions: Untreated depressed patients showed reduced baseline serum and plasma BDNF levels, as compared with control subjects. The clinical improvement paralleled the normalization of plasma BDNF after 1 month of treatment, while, at every assessment time, patients' serum BDNF levels were lower than those of control subjects. This would suggest that serum BDNF might represent a non-specific trait marker of depression.

Keywords: Brain-derived neurotrophic factor (BDNF); Plasma BDNF; Serum BDNF; Major depression; Antidepressant treatment

1. Introduction

Brain-derived neurotrophic factor (BDNF), a member of the neurotrophin family, present in both the central and the peripheral nervous system (Lindsay et al., 1994), has

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doi:10.1016/j.jad.2007.05.005

been implicated in the pathophysiology of depression (Duman and Monteggia, 2006), a disorder which seems to be associated to atrophy of hippocampus, amygdala and prefrontal cortex (Carroll, 2004). According to this model, the lower BDNF activity would contribute to both the atrophy of the limbic structures and to mood disorders (Hashimoto et al., 2004). Interestingly, all the morphological changes in the brain reported in depressed patients seem to be reverted by the long-term administration of antidepressants which would induce an upregulation of BDNF (Coppel et al., 2003; Malberg and Duman, 2003; Santarelli et al., 2003; De Foubert et al., 2004).

Peripheral BDNF is mainly stored in human platelets and circulates in plasma at levels 100-fold lower than those of serum (Yamamoto and Gurney, 1990). Although its regulation in peripheral blood is still poorly understood (Radka et al., 1996; Lommatzsch et al., 2005), positive correlations between cortical and serum BDNF levels has been reported in rodents (Karege et al., 2002a). Drug-free depressed patients (Karege et al., 2002b) and healthy subjects with depressive personality traits (Lang et al., 2004) show decreased serum BDNF levels which would increase after antidepressant treatment (Gonul et al., 2003; Shimizu et al., 2003; Gervasoni et al., 2005; Aydemir et al., 2005).

In the present study, we aimed to examine the effect of 1 year of treatment with different antidepressants on plasma and serum BDNF levels of depressed patients.

2. Methods

2.1. Subjects

Fifteen outpatients, drug-free for at least 15 days and recruited at the Department of Psychiatry, University of Pisa, were consecutively enrolled in the study. All patients were suffering from a current major depressive episode, single episode or recurrent, diagnosed according to Diagnostic and Statistical Manual for Mental Disorders (DSM-IV-TR, American Psychiatric Association, 2000) using the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998). Fifteen healthy subjects with no history of past or current chronic physical or mental diseases and not taking regular medications were recruited as the control group. Severity of depression was assessed using the Hamilton Rating Scale for Depression (HDRS; Hamilton, 1960) and the Montgomery–Åsberg Depression Rating Scale (MADRS; Montgomery and Åsberg, 1979). Antidepressant drugs administered were citalopram (20–40 mg/die; $n=8$), sertraline (50–100 mg/die; $n=5$), paroxetine (20–40 mg/die; $n=2$), amitriptyline (25–50 mg/die; $n=2$), imipramine (25–100 mg/die; $n=1$), trimipramine (25–50 mg/die; $n=2$), and desipramine (25–100 mg/die; $n=1$).

Table 1
Demographic and clinical characteristics of depressed patients and control subjects at baseline

	Depressed patients ($n=15$)	Control subjects ($n=15$)	p value
Sex (F/M)	13/2	12/3	ns
Age (years)	47.0±10.8	36.9±9.2	<.01
HRSD	22.8±5.3	2±0	<.001
MADRS	29.6±5.6	3±0	<.001

HRSD, Hamilton Depression Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale.
Age, HRSD and MADRS scores are shown in mean±SD.

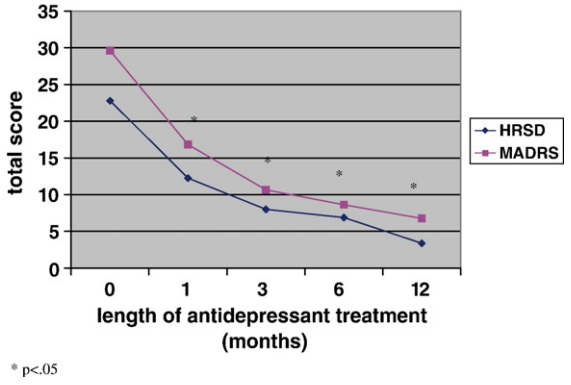

Fig. 1. HRSD and MADRS total score of the patients at baseline and after 12 months of antidepressant treatment. *$p<.05$. HRSD, Hamilton Depression Rating Scale; MADRS, Montgomery–Åsberg Depression Rating Scale.

After the baseline evaluation, clinical assessments and recollection of blood were conducted at the 1st, 3rd, 6th and 12th month of treatment. A written informed consent was obtained from each patient to participate in the study that was approved by the Ethics Committee of the University of Pisa.

2.2. Measurement of plasma and serum BDNF

Blood was taken from the antecubital vein of fasting patients and normal control subjects between 9 and 10 a.m. (Lommatzsch et al., 2005). Plasma and serum were refrigerated at −20 °C before assaying BDNF content with an enzyme-linked immunosorbent assay Kit (Promega, Wallisellen, Switzerland). Briefly, 96-well plates were coated with anti-BDNF monoclonal antibody and incubated at 4 °C for 18 h (Karege, 2005). Plates were incubated in a blocking buffer for 1 h at room temperature, then samples were added. Samples and BDNF standards were maintained at room temperature under shaking for