BDNF as a biomarker of clinical response in bipolar disorder: 16 week follow-up study

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Introduction

An association of serum Brain-Derived Neurotrophic Factor (BDNF) levels with acute mood episodes has been described in bipolar disorder (BD)[1]. Mainly, a low BDNF levels are related to episodes of mania and depression[2,3]. Then, we hypothesized that the normalization of BDNF levels may be associated with clinical stabilization.

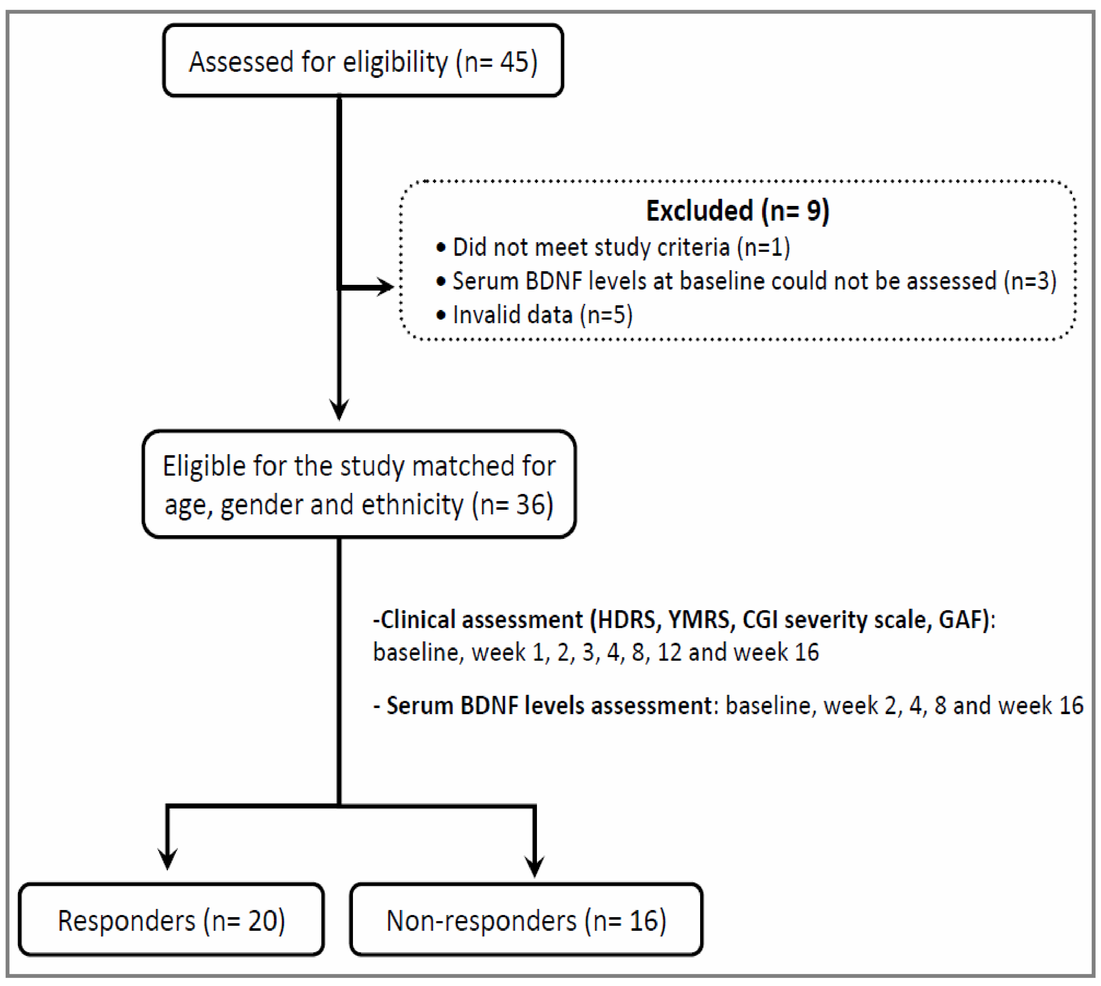
Objectives

The aim of this study was to prospectively investigate the effect of treatment on serum BDNF levels in patients with BD.

Methods

This is a naturalistic, open-label longitudinal trial performed in the BD Program of Hospital de Clínicas in Porto Alegre, Brazil including drug-free patients with BD during an acute mood episode compared to healthy controls matched for age, gender and ethnicity.

Flow diagram to depict stages of the study



- **Inclusion criteria**
  - ✓*Patients:* ≥18 years old with BD diagnosis, currently in manic, mixed or depressive episode, be off medication ≥2 weeks and diagnosis confirmed according to the SCID-I by trained certified psychiatrists.
  - ✓*Controls:* ≥18 years old, never diagnosed with a psychiatric disorder (SCID/NP).
- **Exclusion criteria:** history of neurodegenerative disorders, mental retardation, current cancer, chronic or acute infection and glucocorticoid treatment.

Study was approved by the Ethical and Research Committee and patients provided a written informed consent.

- **Biochemical analysis:** A blood sample of 10 mL were withdrawn from each subject [5 mL were introduced into a free-anticoagulant vacuum tube for serum BDNF level determination and 5 mL were placed into an ethylene diamine tetraacetic acid (EDTA) vacuum tube for DNA analysis]. BDNF levels were measured with sandwich-ELISA, using a commercial kit (Millipore, Temecula, USA). Genomic DNA was extracted using standard procedures. The genotyping of the *BDNF* val66met SNP polymorphism was performed using 5'nuclease TaqMan allelic discrimination assay on the ABI 7500 Sequence Detection System (Applied Biosystems, Carlsbad, USA).
- **Statistical analysis:** Dichotomous variables were compared with Chi-squared tests. Before-and-after scale scores were compared with the Wilcoxon signed-rank test. A multivariate approach to repeated-measures ANOVA and the last observation carried forward (LOCF) as imputation method for missing data.

Results

Sociodemographic features in patients with bipolar disorder and controls

	Patients (n= 36)	Controls (n= 36)	*p*-value
Age (years)[a]	37.8 (11.8)	38.4 (11.5)	0.807
Gender (female)[b]	25 (69.4)	25 (69.4)	1.0
Ethnicity (caucasian)[b]	31 (88.6)	33 (91.7)	0.710
Serum BDNF levels (ng/mL)[a]	49.8 (13.1)	43.9 (14.6)	0.075

[a]: values are indicated as mean (standard deviation), assessed by *t*-test.
[b]: values are indicated as n (%) assessed by Fisher's exact test.

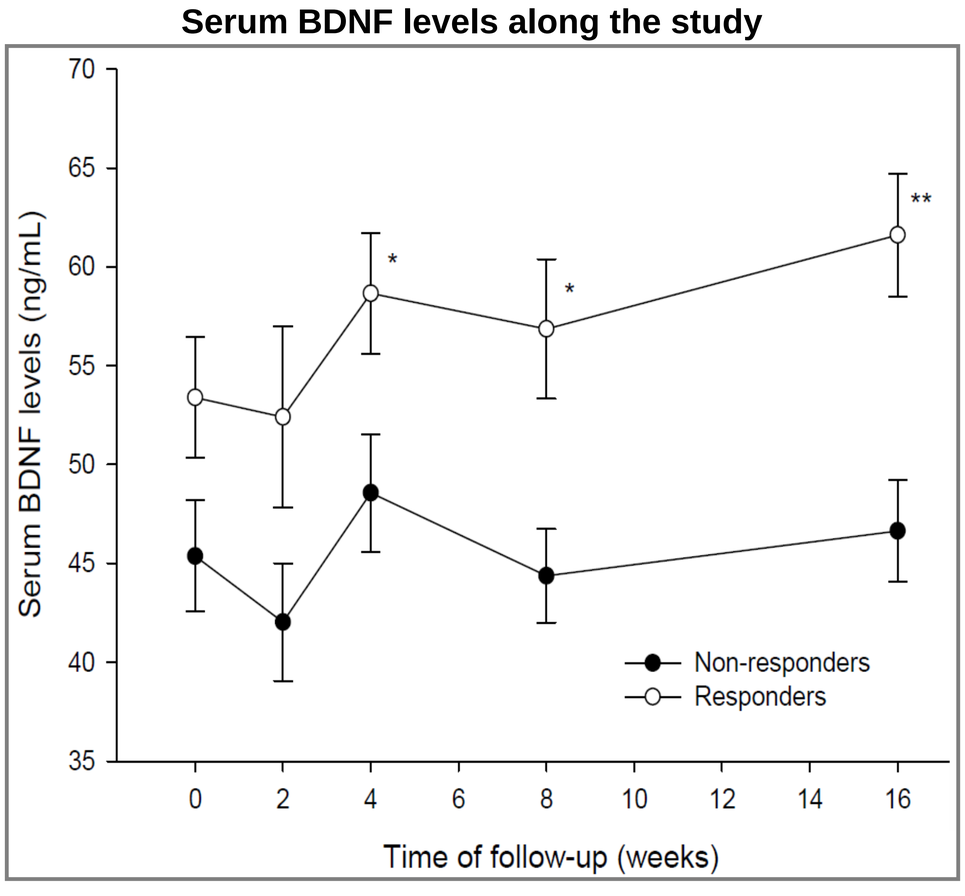
Baseline features of BD patients

	Patients (n= 36)	
Bipolar disorders type [a]		
I	24	(66.7)
II	11	(30.6)
not specified	1	(2.8)
Polarity of the episode [a]		
Depressive	22	(61.1)
Manic	4	(11.1)
Mixed	10	(27.8)
Family history of psychiatric disorder [a]	21	(60.0)
Total No. of previous episodes [b]		
No. of depressive episodes	7.8	(9.6)
No. of manic episodes	5.1	(6.1)
Time since first episode (years)[b]	4.9	(6.4)
No. of attempted suicides [b]	0.7	(1.3)
Comorbid psychiatric disorder [a]	15	(41.7)
Treatment [a]		
Lithium	5	(13.9)
Divalproex	4	(11.1)
Lamotrigine	1	(2.8)
Quetiapine	24	(66.7)
Risperidone	2	(5.6)
Haloperidol	4	(11.1)
Clonazepam	8	(22.2)

[a]: values are indicated as n (%)
[b]: values are indicated as mean (SD)
No.: number

- Using clinical severity scales, a significant improvement was observed [(CGI ($p<0.001$), HDRS ($p<0.001$) and YMRS ($p=0.011$) from baseline after treatment as well as a functional improvement [GAF ($p=0.003$)].
- No changes were detected in BDNF levels along the follow-up even when *val66met* gene polymorphism was considered.
- Significantly higher BDNF levels were found in responders at weeks 4, 8 and 16 ($p<0.05$), with trends already present at baseline.

Serum BDNF levels along the study



Conclusions

BDNF levels during the acute mood episode could be associated with treatment response in bipolar disorder.

Bibliography

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Disclosures

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