ORIGINAL ARTICLE

Serum concentrations of brain-derived neurotrophic factor and mental disorders in imprisoned women

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Objective: Mental disorders and early trauma are highly prevalent in female inmates. Brain-derived neurotrophic factor (BDNF) plays an important role in learning, memory processes, and mood regulation. The aim of this study was to evaluate the relationship between serum BDNF levels and mental disorders among imprisoned women as compared with age- and education-matched controls.
Methods: A consecutively recruited sample of 18 female prisoners with mental disorders was assessed for sociodemographic, criminal, and clinical variables using standardized instruments, the Mini International Neuropsychiatric Interview Plus (MINI Plus), and serum BDNF levels.
Results: High rates of childhood sexual abuse and posttraumatic stress disorder (PTSD) were found in the group of forensic patients. Serum BDNF levels in the forensic group did not differ from those of healthy controls, and were significantly higher when compared with those of women with mental disorders hospitalized in a general hospital.
Conclusion: Elevated serum BDNF levels were found in imprisoned women. The results of this study may suggest neurobiological mechanisms similar to those seen in previous clinical and preclinical studies showing the involvement of BDNF in the pathophysiology of PTSD.

Keywords: Posttraumatic stress disorder; prisons; women; violence; aggression; biological markers

Introduction

Neurotrophic factors, or neurotrophins, play an important role in regulating several cellular activities, including gene expression and growth, differentiation and survival of cells in the central nervous system (CNS), and response to external stimuli, including stress. The brain-derived neurotrophic factor (BDNF) is one of the most abundant and widely distributed neurotrophins in the CNS, is highly expressed in the prefrontal cortex and hippocampus,[1,2] and plays an important role in neuroplasticity and neuroprotection.[3]

In recent decades, studies have shown the involvement of BDNF in the pathogenesis of several neuropsychiatric disorders – including major depressive disorder, bipolar disorder, and schizophrenia[4,5] – and in posttraumatic stress disorder (PTSD).[6,7] Decreased BDNF levels have been reported in patients with bipolar disorder during both manic and depressive episodes as compared with patients in remission (euthymic) and with healthy controls,[8-10] and are known to occur in subjects with longstanding dis-

ease.[11] In traumatic symptomatology, data regarding changes in peripheral BDNF levels in patients with PTSD are still contradictory. Low BDNF levels in PTSD patients have been reported in three studies.[12-14] In another study,[15] no association was found between changes in BDNF and PTSD, yet among the different traumatic events surveyed, sexual abuse had the strongest effect on reducing BDNF levels. Conversely, Hauck et al.[16] and Matsuoka et al.[17] showed that patients with recent trauma and PTSD had higher concentrations of BDNF. These authors, supported by research findings in animal models, argue for the hypothesis that an increase in serum BDNF levels in the early stages of trauma acts as a compensatory mechanism.[18]

Clinical studies indicate that early-life stress predisposes to the development of psychopathology in adulthood. Early traumatic events and childhood sexual and physical abuse are highly prevalent in forensic samples.[19] Furthermore, studies have shown a high degree of comorbid psychopathologies, namely substance dependence[20,21] and PTSD.[22] Moreover, research has shown that over 80% of imprisoned women have had at least one DSM-IV-TR psychiatric diagnosis in their lifetime and that 70% have met criteria for a disorder in the last 6 months.[20] The set of mental disorders found in female inmates is remarkably similar to those reported in the

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literature regarding early abuse[23] and predisposition to the development of psychopathology in adulthood, especially depressive and anxiety disorders.

A systematic review and meta-analysis of 62 surveys and 23,000 prisoners found a pooled prevalence of about 4% for psychosis, 12% for major depression, and 21% for antisocial personality disorder (ASPD) in women.[24] Another systematic review reported an estimated prevalence of 10-21% for PTSD in the female prison population.[22] The estimated prevalence of these same disorders in the general female population is 1% for psychosis,[24] 5-7% for major depression,[24] 0.5-1% for personality disorder,[24] and 3% for PTSD.[22] In a recent study including 109 samples totaling 33,588 prisoners in 24 countries, Fazel & Seewald[25] found high levels of psychiatric morbidity among prisoners in several countries. However, they did not identify whether these rates have increased over time or whether prevalence varies between low- and middle-income countries compared to high-income countries. Their study[25] found a 3.9% prevalence of psychosis (95%CI 2.7-5.0) in female inmates and 3.6% (95%CI 3.1-4.2) in male inmates, with a higher prevalence of psychosis in low-income countries (95%CI 4.2-6.8). The prevalence of major depression was 14.1% (95%CI 10.2-18.1) in female prisoners and 10.2% (95%CI 8.8-11.7) in male prisoners. Drug and alcohol problems are also common among female criminals. A review of 13 studies with a total of 7,563 prisoners assessed on reception into custody[26] showed that 10-24% of women and 17-30% of men were diagnosed with alcohol abuse or dependence. In this study, estimates regarding the prevalence of drug abuse and dependence ranged from 30-60% in imprisoned women and 10-48% in imprisoned men. Another study based on routine clinical assessment of 801 imprisoned women on admission into prison demonstrated that 70% were dependent on at least one substance and 7.9% met criteria for substance abuse.[21]

These studies indicate that the prevalence of psychiatric illness in prisoners is significantly elevated, with rates higher than those found in the community for most mental disorders.[24-27] It is believed, however, that the mental health problems found cannot be attributed to the stress of imprisonment alone. It is more likely that pre-existing disorders are exacerbated within the prison environment.[23] It could be argued that higher rates of abuse and neglect among imprisoned female populations contribute to higher rates of mental disorders in these samples. The high prevalence of mental disorders and exposure to early stressors in female inmates reinforce data from international organizations that identify high rates of PTSD, substance use disorder, and suicide among this population, in addition to the experience of victimization, including sexual and physical abuse, neglect, and domestic violence, as well as little prior contact with public policies.

This study sought to elucidate the interaction between the environmental and neurobiological mechanisms involved in mediating the risk of mental illness in a subgroup of female prisoners. To the best of our knowledge, this is the first study to assess serum BDNF levels in forensic samples of women requiring psychiatric treatment for a mental disorder during the period of imprisonment. In this study, serum BDNF levels were analyzed in three groups: mentally disordered patients admitted to a forensic hospital, mentally disordered patients in a general hospital, and healthy subjects (without criminal behavior or mental illness).

Methods

Participants

We conducted a controlled cross-sectional study of a consecutive sample of 18 mentally disordered women who were hospitalized in a forensic hospital, 18 women hospitalized in the psychiatric unit of a general hospital, and 18 healthy women. The participants were individually matched for age and education (± 3 years). Axis I psychiatric diagnoses were defined in patients who met the DSM-IV-TR criteria by using the Mini International Neuropsychiatric Interview Plus (MINI Plus).[28] The MINI Plus is a standardized diagnostic interview which is consistent with the DSM-IV-TR criteria. The diagnosis of ASPD was established using the criteria found in the antisocial personality module of the MINI Plus.[28] Childhood sexual abuse was assessed through the Childhood Trauma Questionnaire (CTQ).[29] Individuals who obtained a raw score of at least six on the CTQ item responses were classified as sexually abused. Childhood sexual abuse was defined by the authors as "sexual contact or conduct between a child younger than 18 years of age and an adult or older person." Bernstein & Fink report mean internal consistency estimates of 0.92 for the sexual abuse subscale, and test-retest reliability has been reported as 0.81 for sexual abuse throughout a 1.6- to 5.6-month time period.[30] Clinicians experienced in assessing mental disorders using DSM-IV criteria administered a semi-structured diagnostic interview (MINI Plus) to the patients and to the control group, as well as standard protocols for collection of sociodemographic data, current and previous history of mental disorder, of childhood sexual abuse, of psychotropic medication use, and information on criminal history. The healthy controls were selected among caregivers of outpatients from the gynecology and pediatrics departments of the general hospital who presented no axis I mental disorders, no diagnosis of ASPD, and no criminal history. Subjects who exhibited moderate or severe mental retardation or inability to communicate verbally were excluded. Specifically for the healthy control group, anyone using medication for the treatment of psychiatric disorders, having a self-reported psychiatric illness and/or having been diagnosed as such by the MINI Plus, or having self-reported neurological diseases was excluded from the sample.

This study was approved by the Research Ethics Committee of Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Brazil (protocol 1110/10) and was conducted in accordance with the ethical standards of the Declaration of Helsinki. All participants gave their informed consent.

Blood samples

Four milliliters of blood were drawn from each subject by venipuncture into an anticoagulant-free vacuum tube. All samples were collected in the morning. The blood was centrifuged at 4,000 g for 10 min and serum collected and stored at -80°C for up to 6 months. Serum BDNF levels were measured by sandwich ELISA using a commercial kit in accordance with the manufacturer's instructions (Millipore, USA). Briefly, microtiter plates (96-well flat-bottom) were coated for 24 h at 4°C with the samples diluted 1:100 in sample diluent and a standard curve ranging from 7.8 to 500 pg/mL of BDNF. Plates were then washed four times with wash buffer followed by the addition of biotinylated mouse anti-human BDNF monoclonal antibody (diluted 1:1,000 in sample diluent), which was incubated for 3 h at room temperature. After washing, a second incubation was carried out with streptavidin-horseradish peroxidase conjugate solution (diluted 1:1,000) for 1 h at room temperature. After addition of substrate and stop solution, the amount of BDNF was determined (absorbance set at 450 nm). Tests were not performed in duplicate. The standard curve demonstrates a direct relationship between optical density and BDNF concentration.

Statistical analysis

Continuous variables were described as mean and standard deviation when their distribution was normal, and as median (interquartile range) when not normally distributed. Categorical variables were presented as absolute (n) and relative (%) frequencies. Normality was tested using the Shapiro-Wilk test and homogeneity of variances was tested via the Levene test. Means were compared between groups by one-way ANOVA, followed by a post-hoc Tukey test when statistical significance was reached. The *t* test was used for comparison of means between groups. Medians were compared between groups using the Mann-Whitney *U* and Kruskal-Wallis tests, followed by the Tamhane test when statistical significance was achieved. Categorical variables were analyzed by Pearson's chi-square test or Fisher's exact test, followed by testing of adjusted residuals when statistical significance was reached. To control for confounding factors, variables with a p-value < 0.25 on bivariate analysis were included in a multivariate linear regression model using the backward extraction method. The level of significance was set at 5%. All analyses were carried out in SPSS version 21.0.

Results

Table 1 shows the sociodemographic and clinical variables of the samples. The three groups did not differ significantly in age, educational attainment, or marital status. Regarding clinical history, the group of forensic patients showed no differences when compared to patients from the general hospital for the following variables: age at onset, age of first hospitalization,

number of previous hospitalizations, number of suicide attempts, and number of comorbidities. Axis I comorbidities were highly prevalent in the forensic and community patients (77.78 vs. 88.89%, p = 0.658), and the most prevalent are described in Table 1. The group of forensic patients and the group of women admitted to the general hospital proved very similar in relation to history of mental illness, prevalence of mental disorders, and treatment with psychotropic medications (Table 1), except for the use of mood stabilizers, which was more frequent in the forensic group (p = 0.041).

Table 2 presents the results regarding history of trauma and criminal history. The groups differed significantly as to history of childhood sexual abuse (p = 0.025), presence of PTSD (p = 0.026), and criminal history (p < 0.001), which were significantly more frequent in patients from the forensic hospital. As could be expected, family history of crime perpetration was more prevalent (p = 0.036) in the forensic group.

BDNF levels were assessed using parametric tests, because their distribution was symmetrical. ANOVA data indicated that serum BDNF levels were significantly higher in patients from the forensic sample (58.12±16.67 ng/mL) as compared with patients admitted to the general hospital (43.15±18.34 ng/mL, p = 0.015). We found no significant difference in serum BDNF levels between the group of forensic patients and the group of healthy female controls (63.19±18.59 ng/mL), as shown in Figure 1.

Multivariate analyses were used to further clarify factors that were independently associated with BDNF levels, whereas variables with p < 0.25 (age, number of years of education, PTSD, single marital status, OCD, study group, age of first psychiatric hospitalization, and number of psychotropic medications and mood stabilizers) on bivariate analysis were deemed covariates for BDNF. For this analysis, we excluded the control group of healthy women. As shown in Table 3, the multivariate analysis (n=36) found positive associations between serum BDNF and the variables number of years of education (β = 0.364; p = 0.020) and being in the forensic group (β = 0.425; p = 0.006). An inverse association was observed among individuals with PTSD, which indicates that PTSD is independently associated with lower serum BDNF levels (β = -0.413; p = 0.028). Likewise, single women who had never had a stable relationship had significantly lower BDNF levels than did those who were in a relationship at the time or had had previous companions (β = -0.440; p = 0.005). This model explained 42.3% of variability in BDNF levels. Despite the significant frequency of childhood sexual abuse in the group of forensic patients (p = 0.04), our study did not find any association between childhood sexual abuse and serum BDNF levels. These findings persisted even when controlling for the use of psychotropic medication, risk and number of suicide attempts, mood state, childhood sexual abuse, body mass index (BMI), menstrual cycle, comorbidities (axis I and III), and ASPD. The significant increase in BDNF in the forensic group cannot be explained by a difference between these groups regarding substance use disorders. The results suggest that the

Table 1 Sociodemographic and clinical characteristics of the study sample

	Forensic hospital (n=18)	General hospital (n=18)	Healthy controls (n=18)	p-value
Age (years)	34.39±11.72	35.56±11.39	35.22±11.32	0.952*
Weight (kg)	67.5±14.14	68±13.97	71.29±15.56	0.721*
Duration of imprisonment/hospitalization (months)	4.5 (2-21)	0.65 (0.18-0.78)	N/A	< 0.001[†§]
Age of first hospitalization (years)	31.24±13.65	28,31±8.93	N/A	0.475*
Age at symptom onset (years)	24.13±12.35	22.59±10.09	N/A	0.697*
Number of suicide attempts	3.45±2.58	2.44±1.81	N/A	0.336*
Number of years of education[‡]	4 (3-9.5)	5 (3.75-8)	4 (3-9.5)	0.876[§]
Number of comorbidities (axis I)	2 (1.5-4)	4 (2-6)	N/A	0.184[§]
Number of previous hospitalizations	1 (0-2.5)	1 (0-3.25)	N/A	0.707[§]
Marital status, n (%)				
Married/with partner	8 (44.4)	7 (38.89)	12 (66.67)	0.458[‖]
Separated	5 (27.78)	4 (22.22)	3 (16.67)	
Single	5 (27.78)	7 (38.89)	3 (16.67)	
Clinical history, n (%)				
History of mental illness (past)	17 (94.44)	17 (94.44)	N/A	0.999[‖]
Previous suicide attempts (present)	11 (61.11)	9 (50.00)	N/A	0.502[‖]
Risk of suicide (current/present)	13 (72.22)	8 (44.44)	N/A	0.091[‖]
Axis III medical conditions (present)	4 (22.22)	4 (22.22)	3 (16.67)	0.999[‖]
Antisocial personality disorder	4 (22.22)	1 (5.56)	N/A	0.177[‖]
Axis I comorbidities, n (%)				
Psychotic mood disorder (current)	4 (22.22)	5 (27.78)	N/A	0.546[‖]
Affective disorder type I (current)	3 (16.76)	4 (22.22)	N/A	0.483[‖]
Schizophrenia (current)	4 (22.22)	3 (16.76)	N/A	0.999[‖]
Obsessive compulsive disorder (current)	0 (0)	6 (33.33)	N/A	0.019[‖]
Specific phobia (current)	4 (22.22)	6 (33.33)	N/A	0.457[‖]
Substance abuse/dependence (current)	9 (50)	7 (38.89)	N/A	0.737[‖]
Psychotic episode (current)	11 (61.11)	12 (66.67)	N/A	1.000[‖]
Depressive episode (current)	7 (38.89)	6 (33.33)	N/A	1.000[‖]
Manic episode (current)	1 (5.56)	6 (33.33)	N/A	0.088[‖]
Psychotropic medications, n (%)				
SSRIs	3 (16.76)	5 (27.78)	N/A	0.691[‖]
Tricyclics	4 (22.22)	1 (5.56)	N/A	0.338[‖]
Atypical antipsychotics	4 (22.22)	5 (27.78)	N/A	0.999[‖]
Typical antipsychotics	13 (72.22)	9 (50.0)	N/A	0.171[‖]
Mood stabilizers	7 (38.89)	1 (5.56)	N/A	0.041[†‖]
Lithium	4 (22.22)	5 (27.78)	N/A	0.999[‖]
Benzodiazepines	5 (27.78)	3 (16.67)	N/A	0.691[‖]
Use of psychotropic medication (current)	16 (88.89)	16 (88.89)	N/A	0.999[‖]
Two or more psychotropic drugs in use (current)	13 (72.22)	9 (50.00)	N/A	0.252[‖]

Data presented as mean ± standard deviation or median (interquartile range [IQR]), unless otherwise stated.
N/A = not applicable; SSRIs = selective serotonin reuptake inhibitors.
* One-way ANOVA; [†] $p < 0.05$; [‡] 1 to 4 years of education = primary school, 5 to 8 years of education = middle school; [§] Mann-Whitney U and Kruskal-Wallis tests; [‖] chi-square test.

interference of different variables connected to the specific characteristics of each of the groups analyzed might be mediating the BDNF variability found in the group of forensic patients, as discussed below.

Discussion

To the best of our knowledge, this was the first study to examine serum BDNF levels in female inmates. The results showed a significant increase in serum BDNF levels in a sample of forensic patients as compared with mentally ill patients in the general population. No significant difference was found between BDNF levels in the forensic sample and those in the healthy control group. In this study, changes in BDNF levels could not be attributed to differences in the prevalence of alcohol or drug use disorders, axis I, axis II (ASPD), or axis III comorbidities,

exposure to sexual abuse in childhood, use of psychotropics, or mood state. Furthermore, our results demonstrated a high prevalence of childhood sexual abuse, risk of suicide, and PTSD in the forensic sample, thereby corroborating the findings of countless previous studies. Nevertheless, no association was observed between PTSD and childhood sexual abuse. Therefore, in our study, PTSD may have been mediated by other forms of interpersonal violence, including involvement in extreme traumatic situations such as sudden death, injury, or threat to the physical integrity of a close person, as shown in a recent prevalence study in Brazil that investigated the relationship between traumatic events and mental disorder.[31] Moreover, we did not identify exposure to childhood sexual abuse as a factor associated with changes in BDNF levels as reported previously.[15]

According to the literature, decreased BDNF levels are associated with several psychiatric disorders. Our results

Table 2 History of sexual abuse, PTSD, and criminal activity of the study sample

	Forensic hospital (n=18)	General hospital (n=18)	Healthy controls (n=18)	p-value*
Trauma				
Childhood sexual abuse (present)	10 (55.56)	4 (22.22)	3 (16.67)	0.025
PTSD (present)	8 (44.44)	2 (11.11)	N/A	0.026
Lifelong violence (PTSD or sexual abuse) (present)	15 (83.33)	6 (33.33)	3 (16.67)	< 0.001
Criminal history				
Family history of crime perpetration (present)	8 (53.33)	2 (11.76)	5 (27.78)	0.036
Personal history of crime perpetration (present)	18 (100.00)	3 (16.67)	0 (0)	< 0.001
Type of crime				
Robbery	5 (27.78)	1 (33.33)	N/A	
Trafficking	1 (5.56)	2 (66.67)	N/A	
Theft	1 (5.56)	0 (0)	N/A	
Attempted homicide, aggression, and/or assault	4 (22.22)	0 (0)	N/A	
Homicide	5 (27.78)	0 (0)	N/A	
Filicide	1 (5.56)	0 (0)	N/A	
Multiple serious crimes	1 (5.56)	0 (0)	N/A	

Data presented as n (%).
N/A = not applicable; PTSD = posttraumatic stress disorder.
* Chi-square test.

support this hypothesis, since we found significantly lower BDNF levels in the community sample of mentally ill patients who were hospitalized in a general hospital. However, although we expected to find decreased BDNF levels in forensic patients, because they were also mentally disordered women, this result was surprisingly not confirmed. This would indicate that other variables might be mediating the increase in BDNF levels in the forensic sample. Given that the mechanisms involving BDNF are complex and influenced by various factors[15] and that response to environmental factors seems to affect its expression, we must also mention the effects
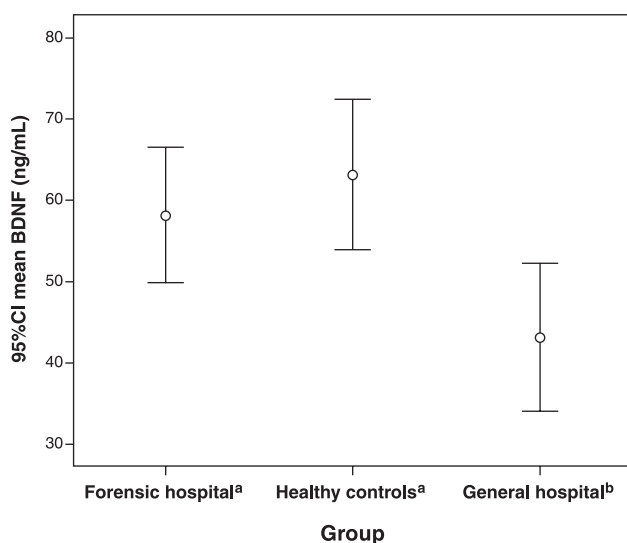

Figure 1 Serum levels of brain-derived neurotrophic factor (BDNF) in female forensic patients, female patients hospitalized in the psychiatric unit of a general hospital, and healthy controls. [ab] Descriptors followed by the same superscript letter do not differ significantly (p = 0.004). 95%CI = 95% confidence interval; BDNF = brain-derived neurotrophic factor.

resulting from prison-related stress – triggered by isolation, detachment from motherhood and family ties, and deprivation of social relationships – as well as stress stemming from institutional violence and from the precarious conditions of prison spaces.

Previous studies have shown a high prevalence of anxiety and depressive disorders in prison, in addition to symptoms such as having problems sleeping, suicidal ideation, and suicide attempts. In the present study, we found a high risk of suicide and a high prevalence of PTSD in the forensic sample. Therefore, the exacerbation of emotional state in prison and increased vulnerability due to the lasting effects of histories of violence and abuse probably indicate that many female prisoners present a clinical state of stress. Moreover, the similarity between the characteristics described above and the emotional and cognitive alterations observed in PTSD or acute stress disorder (ASD) are quite evident. One must bear in mind that, in PTSD, there is excessive consolidation of traumatic memories, which may be intrusive to the point of interrupting sleep and thoughts.

Given the above and the characteristics of the forensic sample in relation to the prevalence of childhood sexual abuse and exposure to other forms of interpersonal violence, our discussion could support the findings of recent research into the neurobiology of PTSD, which has been gaining ground in recent years. Hauck et al.[16] found that patients with PTSD and ASD caused by recent trauma (occurring in the year of assessment) had higher levels of BDNF, yet this difference was not significant in patients with long-term PTSD (i.e., lasting over 4 years). Preclinical studies based on a model of early-life stress due to maternal separation showed an increase in neurotrophins in the dorsal and ventral hippocampus when re-exposed to stress in adulthood.[18] Another study concerning the effects of maternal separation (without additional stress) on neurotrophin levels also identified an increase in neurotrophins in specific regions of the CNS.[32] Moreover, acute immobilization stress and chronic

Table 3 Multivariate linear regression using the backward method to assess factors independently associated with BDNF levels (n=36)

	B (95%CI)	β	p-value
Number of years of education	1.64 (0.28 to 3.01)	0.364	0.020
PTSD	-17.16 (-32.36 to -1.96)	-0.413	0.028
Single	-17.37 (-29.12 to -5.62)	-0.440	0.005
Forensic group	15.83 (4.87 to 26.78)	0.425	0.006

95%CI = confidence interval; B = regression coefficient; β = standardized regression coefficient; BDNF = brain-derived neurotrophic factor; PTSD = posttraumatic stress disorder.

restraint stress in rats were associated with a significant increase in plasma BDNF levels.[33,34] As mentioned above, the literature suggests that BDNF is involved in the neurobiology of PTSD and points towards different mechanisms of action or compensatory responses that cause changes in BDNF levels in different areas of the CNS in response to recent or chronic trauma, seeking to differentiate the mechanisms involved in long-term PTSD.

The possible interference of exposure to recent traumatic events and of the diagnosis of PTSD and ASD with changes in serum BDNF levels requires further investigation in longitudinal studies with larger samples. To date, only six studies with different designs were published on the association between PTSD and BDNF levels in clinical samples, showing contradictory results. Only one prospective cohort study, of 103 patients severely injured in motor vehicle accidents,[17] found significantly higher BDNF levels over a 6-month follow-up period in the PTSD group after controlling for age and sex. The authors concluded that elevated serum BDNF levels could be a biomarker of PTSD after a traumatic event.[17] Another recent study did not find any difference in BDNF levels between a partial PTSD group and a healthy control group. However, decreased BDNF levels were found in subjects with full PTSD, which suggests that the increase in BDNF levels in partial PTSD patients may be acting as a mechanism of neuroprotection against full PTSD.[14]

On the other hand, reduced serum BDNF levels were found in a group of patients exposed to trauma who developed PTSD as compared to trauma-exposed individuals who did not develop PTSD.[13] In agreement with these findings, one hypothesis is that the elevation of BDNF found in the sample of forensic patients as compared with patients admitted to the general hospital was mediated by a clinical state of stress, which, in turn, may be exacerbated by the stress of prison. This characteristic is specific to the sample analyzed and is probably related to the alterations in peripheral BDNF levels found in our study. Taken together, these data might suggest a greater neurotrophic response to repeated exposure to stress events, which possibly indicates that some individuals develop a compensatory and neuroprotective response, as previously suggested by Stratta et al.[14] and Faure et al.[18]

Therefore, it is probable that, in our study, patients diagnosed with PTSD are no longer able to develop these neurobiological compensatory resources; thus, the association between PTSD and decreased BDNF levels in incarcerated women may be associated with a response

to long-term cumulative effects of stress on the body. This mechanism is similar to that observed in the progression of bipolar disorder[35] and was observed by Hauck et al. in patients with long-term PTSD.[36] Clearly, additional studies with prospective longitudinal designs are necessary to test these hypotheses and to outline the mechanisms involved in the neurobiology of trauma exposure.

As expected, we found reduced serum BDNF levels in the sample of patients with mental disorders hospitalized in the general hospital. We believe that this change may be mediated by a between-group difference as to other variables associated with the course and progression of the disease, including its severity and the response to drug treatment. The participants of this group can be characterized clinically as community patients referred by the mental health network for inpatient treatment of acute manifestations of mental illness. In this sense, the recent literature on the relationship between acute mood episodes and systemic toxicity has suggested that there is an association between repeated exposure to mood episodes and the progressive effects of the illness.[37,38] Especially with regard to response to drug treatment, Grande et al.[39] found a lower response to treatment with quetiapine and decreased BDNF concentrations in manic/mixed states, and increased BDNF levels in depressive states. This finding should be considered in the analysis of our results, since manic episodes were more present in the group of community mentally disordered patients. However, due to our small sample size, these differences may have not been identified through statistical tests.

Finally, results from multivariate analysis show two sociodemographic variables independently associated with serum BDNF levels: single marital status and number of years of education. We were unable to determine whether being single, i.e., never having had a marital relationship, is associated with more severe mental disease. Our study design did not allow establishment of which factor came first (reverse causality), but single women did exhibit lower BDNF levels. On the other hand, the number of years of education correlated positively with higher serum BDNF levels, which may confirm the role of education as a long-term protective factor and the involvement of BDNF levels in cognition, memory, and learning – findings that are in line with previous studies.

This study indicated that psychiatric disorders and traumatic events are very common among incarcerated women and represent a major public health problem. Our results suggest that identification and treatment of the problems related to traumatic events and victimization

during incarceration may buffer and prevent the negative impacts of violence on women's mental health.

It is important to emphasize that this was an exploratory study conducted with a small sample and can be considered preliminary. Limitations that may have influenced our results include the heterogeneity of psychiatric diagnoses and comorbidities in this sample as well as the different classes of psychotropic drugs used by the patients. Furthermore, BDNF levels were assessed peripherally, yet it remains unknown to what extent peripheral BDNF levels correspond to CNS levels. However, BDNF has been shown to cross the blood-brain barrier, and preclinical studies demonstrated a high positive correlation (r = 0.81) between serum and cortical BDNF levels.[40] Additionally, the results of this study are based on retrospective cross-sectional evaluations that preclude determination of causal pathways and recall bias, which may be considered an important limiting factor. Finally, the high rates of childhood sexual abuse and violence identified in the group of forensic patients may influence other personality characteristics that we did not assess through a specific instrument.

To the best of our knowledge, this is the first report of elevated serum BDNF levels in female forensic samples. These results may have indicated neurobiological mechanisms similar to those found in clinical and preclinical studies on the role of BDNF in the pathophysiology of PTSD. Given the high prevalence of substance abuse, depression, and PTSD, and the lasting effects of histories of violence and childhood sexual abuse, it is paramount that due importance be given to the challenge of improving mental health and investing in research programs in forensic environments. Finally, it is likely that the neurobiological mechanisms involved in individuals who are in a situation of social vulnerability, exposed to violence, mental illness, and criminal history are even more complex.

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Disclosure

The authors report no conflicts of interest.

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