



## ORIGINAL ARTICLE

# Childhood trauma and dimensions of depression: a specific association with the cognitive domain

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**Objective:** To investigate associations between a history of childhood trauma and dimensions of depression in a sample of clinically depressed patients.

**Methods:** A sample of 217 patients from a mood-disorder outpatient unit was investigated with the Beck Depression Inventory, the Hamilton Depression Rating Scale, the CORE Assessment of Psychomotor Change, and the Childhood Trauma Questionnaire. A previous latent model identifying six depressive dimensions was used for analysis. Path analysis and Multiple Indicators Multiple Causes (MIMIC) models were used to investigate associations between general childhood trauma and childhood maltreatment modalities (emotional, sexual, and physical abuse; emotional and physical neglect) with dimensions of depression (sexual, cognition, insomnia, appetite, non-interactiveness/retardation, and agitation).

**Results:** The overall childhood trauma index was uniquely associated with cognitive aspects of depression, but not with any other depressive dimension. An investigation of childhood maltreatment modalities revealed that emotional abuse was consistently associated with depression severity in the cognitive dimension.

**Conclusion:** Childhood trauma, and specifically emotional abuse, could be significant risk factors for the subsequent development of cognitive symptoms of major depression. These influences might be specific to this depressive dimension and not found in any other dimension, which might have conceptual and therapeutic implications for clinicians and researchers alike.

**Keywords:** Depression; dimensions; childhood trauma; emotional abuse; cognition

## Introduction

Major depressive disorder (MDD) is multifactorial.<sup>1</sup> Both genetic and environmental risk factors have been linked to depressive symptomatology.<sup>2</sup> Among the latter, childhood trauma is one of the most consistently replicated factors that influence subsequent risk for major depression, and the relationship has been shown to be causal.<sup>3</sup>

Some studies have found an association between lifetime trauma and atypical depression.<sup>4</sup> Others have found an association between history of physical or sexual abuse (SA) in childhood and MDD with reversed neurovegetative signs.<sup>5,6</sup> Physical or SA has also been linked to MDD with psychotic features (as opposed to MDD without psychotic features).<sup>7</sup> Nevertheless, it is not clear whether childhood trauma is linked more broadly and nonspecifically to depressive symptomatology, or if it is associated with more specific features of this heterogeneous disorder.

In a recent work, we used exploratory and confirmatory factor analysis (EFA and CFA, respectively) to identify six dimensions of depression that could be graded on a continuum of severity in the following ascending order: sexual, cognitive, insomnia, appetite, non-interactiveness/motor retardation, and agitation.<sup>8</sup>

The objective of the present study was to investigate the associations between a history of childhood trauma and dimensions of depression in a sample of clinically depressed adult patients. This issue was addressed by measuring the association between childhood trauma (general trauma and different modalities of childhood maltreatment: SA, physical abuse [PA], emotional abuse [EA], physical neglect [PN], and emotional neglect [EN]) and different dimensions of depression: sexual, cognitive, insomnia, appetite, non-interactiveness/motor retardation, and agitation.

## Materials and methods

### Sample selection

Consecutive patients from the outpatient depression unit of a tertiary general hospital were asked to participate in the study. The inclusion criteria were adulthood and a

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primary diagnosis of MDD, as described in the DSM-IV and ICD-10 and evaluated by the Brazilian version of the Mini International Neuropsychiatric Interview. Only patients in a current major depressive episode were included; patients in remission were ineligible. The exclusion criteria were a history of manic or hypomanic episodes, any neurological disorder that could hinder assessment of psychomotor disturbance, and inaptitude in responding to the presented instruments. The research protocol was approved by the Ethics Committee of Hospital de Clínicas de Porto Alegre (HCPA), state of Rio Grande do Sul, Brazil. All patients provided written informed consent for participation using a form which had been previously approved by the HCPA Ethics Committee.

### *Measurement instruments*

Beck Depression Inventory (BDI), Brazilian Portuguese version<sup>9</sup>

The BDI is a 21-item, self-reported, patient-rated scale designed to assess symptoms of depression. BDI is among the most widely used self-rated instruments in clinical and research settings, and has been translated into many languages. The Brazilian Portuguese version shows psychometric properties equivalent to the English version, with Cronbach's alpha coefficients of 0.88 for depressed patients and 0.81 for controls.<sup>9</sup> The 21 items are each scored from 0 to 3, and assess the following issues: 1) sadness; 2) future pessimism; 3) lack of enjoyment; 5) guilt; 6) feelings of being punished; 7) disappointment with oneself; 8) self-blame; 9) suicidal thoughts; 10) crying; 11) irritability; 12) interest in people; 13) making decisions; 14) appearance; 15) work; 16) sleep; 17) tiredness; 18) appetite; 19) weight loss; 20) health anxiety; and 21) interest in sex.

Hamilton Depression Rating Scale (HDRS)<sup>10</sup>

The HDRS is a 17-item clinician-rated scale that assesses symptoms and signs of depression, and is one of the instruments most extensively used to evaluate the severity of depression. The HDRS was developed in the late 1950s with the aim of assessing the effectiveness of antidepressant treatment. Its 17 items assess the following issues (score range in parentheses): 1) depressed mood (0-4); 2) feelings of guilt (0-4); 3) suicide (0-4); 4) early insomnia (0-2); 5) middle insomnia (0-2); 6) late insomnia (0-2); 7) work and activities (0-4); 8) psychomotor retardation (0-4); 9) agitation (0-4); 10) psychological anxiety (0-4); 11) somatic anxiety (0-4); 12) gastrointestinal somatic symptoms (0-2); 13) general somatic symptoms (0-2); 14) genital symptoms (0-2); 15) hypochondriasis (0-4); 16) weight loss (0-2); and 17) insight (0-2). Ratings cover the 1-week period preceding the interview.

The CORE Assessment of Psychomotor Change (CORE)<sup>11</sup>

The CORE is an 18-item clinician-rated instrument that assesses psychomotor signs of depression. The version used in the present study was culturally adapted and translated to Brazilian Portuguese by our group following International Society for Pharmacoeconomics and Outcomes

Research guidelines. The CORE is meant to be used when there is already a primary diagnosis of major depression and to distinguish between melancholic and non-melancholic categories.

Ratings are mainly behavioral and based on how subjects are observed to conduct themselves during the interview instead of on subjective feelings. Since the instrument rates finely observed behavioral nuances, clinical experience with depressive and other psychiatric and medical patients is required. Signs should first be appraised as categorically present or absent (quality), and, if present, are then ranked regarding severity (quantity). A score of 0 indicates the sign is absent or trivial, while scores of 1 to 3 indicate definite presence with increasing severity. This goes along with the author's conceptualization of melancholic depression as a categorical-dimensional disorder.

It is assumed that there is a main factor underpinning the CORE (non-interactiveness), which splits into retardation and agitation factors. The instrument comprises 18 items, each scored from 0 to 3 and separated into three subscales for the three aforementioned factors. The non-interactiveness items are: 1) non-interactiveness (item 1); 2) non-reactivity (item 4); 3) inattentiveness (item 8); 4) poverty of associations (item 12); 5) impaired spontaneity of speaking (item 16); and 6) length of verbal responses (item 7). The retardation items are: 1) slowed movement (item 13); 2) facial immobility (item 2); 3) body immobility (item 10); 4) postural slumping (item 3); 5) delay in motor activity (item 15); 6) delay in responding verbally (item 6); and 7) slowing of speech rate (item 17). The agitation items are: 1) facial apprehension (item 5); 2) facial agitation (item 9); 3) motor agitation (item 11); 4) stereotyped movement (item 18); and 5) verbal stereotypy (item 14).

### *Dimensional assessment*

The dimensions of depression explored in the present study were based on six latent factors, developed using EFA carried out on the items belonging to the three above-mentioned instruments, in a sample of 399 patients, in the following ascending order of severity: sexual, cognitive, insomnia, appetite, non-interactiveness/motor retardation, and agitation.<sup>8</sup> After selection of the most adequate model, a CFA was performed to investigate the adjustment of the model to our sample, along with model-based item factor loadings and thresholds. The CFA model was fitted to polychoric correlations using the robust weighted least squares means and variance adjusted (WLSMV) estimator, which provided the following goodness-of-fit indices: chi-square of 1,480.451, comparative fit index (CFI) of 0.909, Tucker-Lewis index (TLI) of 0.903, root mean square error of approximation (RMSEA) of 0.041, and weighted root mean square residual (WRMR) of 1.260. These parameters relate to the previous total sample of 399 patients, not the current sample of 217 patients. We also found that these dimensions are better captured by the integration of instruments that target different facets of the depressive syndrome, evaluating symptoms and signs from both clinicians' and

patients' perspectives, and by using psychometric instruments with diverse conceptual backgrounds.

### *Assessment of trauma*

Childhood Trauma Questionnaire (CTQ), Brazilian Portuguese version<sup>12</sup>

The CTQ is a 28-item self-reported patient rating scale intended to recognize occurrences of childhood abuse and neglect in adults and adolescents. The CTQ appears to be more trustworthy in assessing childhood maltreatment in comparison to other methods, such as personnel observations and parental accounts.<sup>13</sup> It is accepted in various countries as a crucial instrument for the assessment of traumatic childhood occurrences.<sup>12</sup> The 28-item version used herein assesses EA, PA, SA, EN, and PN. EA refers to verbal offenses to a child's sense of worth or well-being, or any embarrassing, degrading, or menacing behavior directed against a child by an older person. PA refers to bodily offenses to a child by an older person that constitute a risk or occurrence of physical harm. SA refers to any kind of sexual conduct or contact between a child and an older person. EN refers to a caretakers not providing for basic emotional and psychological needs, such as love, support, acceptance, and encouragement. PN refers to caretakers not providing basic physical needs, including food, shelter, and safety. Each of the 28 items is scored in the following range of responses: never true, rarely true, sometimes true, often true, and very often true. For data analysis, we used an alternative model proposed by Grassi-Oliveira et al.<sup>14</sup> The major differences between the original and the alternative solutions are related to the definition of child neglect, with item numbers 2 and 26 loading on the EN subscale instead of the proposed original PN subscale, which is in agreement with previously reported studies in other societies.<sup>14</sup> The proposed alternative five-factor solution yielded improvement in the model parameters, and all fit indices were within the expected range.<sup>14</sup>

Given that the Brazilian Portuguese version of the CTQ structure was not previously tested in a sample of depressive patients, we investigated a high-order model with one high-order factor and five low-order factors, which showed a good fit in the sample of depressive patients ( $n=217$ , number of free parameters = 131, chi-square = 364.931,  $df = 270$ ,  $p < 0.0001$ , RMSEA = 0.04, 90% confidence interval [90%CI] RMSEA = 0.029-0.050, CFI = 0.990, TLI = 0.989, WRMR = 0.838). A supplemental table containing factor loadings and the significance of each of the CTQ items is available from the authors upon request.

### *Diagnostic procedures*

Three psychiatrists (EAV, MAC, and LS) with experience in the assessment and treatment of depression performed the clinical evaluations. All psychiatrists had at least 3 years of psychiatric training, with a minimum of 6 months of training with the assessment instruments. The psychiatrists also watched an instructional video before using the CORE. With

the objective of increasing inter-rater reliability, the three psychiatrists together performed the first 6 months of assessments. Medical students delivered the self-reported questionnaires, and when patients were unable to complete them by themselves, the medical students were instructed to read them aloud and explain any misunderstood item (assisted application).

### *Statistical analysis*

Associations between trauma and dimensions of depression were performed using Multiple Indicators Multiple Causes (MIMIC) and path analysis on structural equation models. For fitting of MIMIC and path analysis models, the CORE14 item (verbal stereotypy) was excluded from the model because there was more than one zero cell in bivariate tables with several items. The models were fitted to polychoric correlations using the WLSMV estimator, as we were dealing with categorical variables. The following goodness-of-fit indices were used: chi-square, CFI, TLI, RMSEA, and WRMR. To demonstrate good fit to the data, research suggests that an estimated model should have WRMR values near or below 0.9, RMSEA values close to 0.06 or below, and CFI and TLI values close to 0.95 or greater. All statistical analyses were implemented with Mplus 7.0.

## **Results**

The final sample consisted of 217 patients with unipolar depression. The sociodemographic and clinical profile of the final sample is presented in Table 1. Prevalence of childhood maltreatment modalities is presented in Table 2.

Path analysis was used to investigate the association between the high-order trauma factor and the six depression dimensions. The analysis revealed that a history of childhood trauma was uniquely associated with cognitive aspects of depression, but not with any other depressive dimensions. These results are presented in Table 3.

A second model investigated the associations between lower-order trauma factors and the six depression dimensions. Again, no associations emerged from the other depressive dimensions, and the lower-order factor EA was consistently associated with depression severity in the cognitive dimension. EN reached trend-level significance, whereas other traumatic lower-order factors did not seem to contribute to severity in the cognitive factor. These results are presented in Table 4.

## **Discussion**

We found evidence that a history of childhood trauma is uniquely associated with cognitive aspects of depression, but not with other depression dimensions, such as sexual, insomnia, appetite, non-interactiveness/retardation, and agitation. In addition, the lower-order trauma factor EA was associated with depression severity in the cognitive domain. For the sake of clarity, we will split our discussion between psychological and biological implications, which

**Table 1** Sociodemographic and clinical characteristics of the sample

	Depressive patients (n=217)
Age (years)	50.61 ± 10.55
Female gender	187 (86.2)
Marital status	
Married	122 (56.2)
Single	19 (8.8)
Separated	53 (24.4)
Widowed	23 (10.6)
Education (years)*	7.37 ± 3.63
Ethnicity*	
White	160 (73.7)
Other	54 (24.9)
Employment status	
Employed	33 (15.2)
Unemployed	57 (26.3)
Retired	50 (23.0)
On disability benefits	48 (22.1)
Unwaged domestic work	21 (9.7)
Others	8 (3.7)
Socioeconomic level†	
Class A	2 (0.9)
Class B	55 (25.3)
Class C	111 (51.2)
Class D	46 (21.2)
Class E	3 (1.4)
BDI	34.13 ± 9.95
HDRS	20.96 ± 5.34
CORE	5.47 ± 5.44
CTQ total	21.99 ± 19.10
Emotional abuse*	5.75 ± 5.21
Physical abuse*	3.64 ± 4.49
Sexual abuse*	1.89 ± 4.09
Emotional neglect*	8.85 ± 7.75
Physical neglect	1.76 ± 2.48

Data presented as n (%) or mean ± standard deviation.

BDI = 21-item Beck Depression Inventory; CORE = CORE Assessment of Psychomotor Change; CTQ = 28-item Childhood Trauma Questionnaire; HDRS = 17-item Hamilton Depression Rating Scale.

\* Variables with missing values.

† Gross household income per month in US\$ (socioeconomic level): A = 4,550.00; B = 2,275.00 to 4,549.99; C = 910.00 to 2,274.99; D = 455.00 to 909.99; E = up to 454.99.

are obviously not independent epistemic perspectives and are actually frequently interconnected.

### Psychological implications

The cognitive model, as conceptualized by Beck, proposes that certain types of negative interpretations of experience (depressive cognitions) can engender symptoms of depression.<sup>15</sup> Stress-diathesis models of depression argue that depressogenic cognitive structures are dormant until set in motion by stressful events, and, once activated, they start a pattern of negative self-referenced information processing that results in depression.<sup>16</sup> In keeping with these theories, there is evidence that depressive patients undergoing severe pre-onset life

**Table 2** Prevalence of childhood maltreatment modalities in the sample (n=217)

Prevalence	n (%)	Missing
Physical neglect	25 (11.5)	0
Emotional neglect	122 (56.2)	3
Sexual abuse	32 (14.7)	2
Physical abuse	46 (21.2)	3
Emotional abuse	50 (23.0)	2
General childhood trauma	123 (56.7)	7

events exhibit more cognitive than somatic symptoms than those who have not, and experience differential treatment outcomes.<sup>17</sup>

As noted by Ingram & Ritter,<sup>16</sup> several theories with relatively diverse conceptual backgrounds indicate that interactions with early caretakers provide the basis for negative information processing structures. A central conceptual subject that occurs across these proposals, despite their differences in theoretical details, is that disruptions in the basic bonding processes between children and their caretakers produce vulnerability structures that may form the core of depressive episodes that occur later in life. Their results support the idea that cognitive variables form a pathway between troublesome parent-child/adolescent interactions and depression.<sup>16</sup>

Our findings indicate that adults who had suffered more specific emotional forms of abuse as children were at heightened risk of developing cognitive symptoms of depression when becoming depressed later in life. In our understanding, these results are in accordance with the aforementioned cognitive model of depression.

In a large community sample, Dias et al.<sup>18</sup> found that EA was the strongest predictor for psychological symptoms compared to any other form of childhood maltreatment. EA predicted all forms of psychological symptoms, with larger effect sizes for interpersonal sensitivity, depression, and paranoid ideation,<sup>18</sup> possibly by impairing the development of cognitive structures for social interactions and providing a basis for the occurrence of symptoms displaying interpersonal components.<sup>19</sup> Experiencing verbal abuse throughout childhood was frequently self-reported, and was significantly associated with adult psychological distress.<sup>18</sup> In another recent study with a sample involving distinct psychiatric disorders, Martins et al.<sup>20</sup> found that EA, among different types of early life stresses, was positively associated with psychopathology in adulthood, especially with mood disorders. Patients with a history of EA had higher severity scores for all symptoms, such as depression, hopelessness, suicidal ideation, anxiety, and impulsivity.

### Biological implications

Over-reactivity of the hypothalamic-pituitary-adrenal (HPA) axis is one of the most consistent psychoneuroendocrinological findings in major depression.<sup>21</sup> The HPA axis is the most prominent neuroendocrine stress response system that serves to adapt an organism to change in demand, thus preserving stability and health.<sup>21</sup> Therefore, it would be a tenable hypothesis that HPA axis changes could mediate the manifestation of depressive symptoms as a

**Table 3** Standardized path analysis model estimates investigating the association between the high-order trauma factor and the six depression dimensions\*

	Estimates <sup>†</sup>	SE	Est/SE	p-value
Insomnia	-0.008	0.062	-0.136	0.892
Motor retardation/non-interactiveness	-0.024	0.049	-0.486	0.627
Agitation	0.118	0.075	1.58	0.114
Cognitive	<b>0.157</b>	<b>0.049</b>	<b>3.217</b>	<b>0.001</b>
Appetite	0.043	0.064	0.666	0.505
Sexual	0.124	0.068	1.827	0.068

CFI = comparative fit index; Est/SE = test statistic (z value); SE = standardized error; RMSEA = root mean square error of approximation; TLI = Tucker-Lewis index.

\* Model fit indices: RMSEA = 0.024 (90% confidence interval = 0.021-0.027); CFI = 0.964; TLI = 0.963.

<sup>†</sup> Estimates = unstandardized parameter estimate.

response to childhood trauma. In an influential work, Heim et al.<sup>21</sup> found evidence supporting this hypothesis.

Allostasis and allostatic load are useful concepts for comprehension of the psychoneuroendocrinological consequences of stress,<sup>22</sup> as well as of the consequences

of childhood trauma in the present context. Allostasis involves the active processes by which the body responds to daily events and maintains stability (i.e., homeostasis). The term means “achieving stability through change.”<sup>23</sup> The concept of allostatic load was proposed as a means

**Table 4** Standardized regression estimates from the Multiple Indicators Multiple Causes (MIMIC) model investigating the association between lower-order trauma factors and the six depression dimensions\*

	Estimates <sup>†</sup>	SE	Est/SE	p-value
Insomnia				
Physical neglect	0.15	0.269	0.558	0.577
Emotional neglect	-0.268	0.571	-0.47	0.639
Sexual abuse	-0.007	0.104	-0.071	0.944
Physical abuse	0.163	0.366	0.445	0.656
Emotional abuse	-0.572	0.694	-0.824	0.41
Motor retardation/non-interactiveness				
Physical neglect	-0.361	0.289	-1.246	0.213
Emotional neglect	-0.408	0.551	-0.741	0.458
Sexual abuse	-0.132	0.092	-1.423	0.155
Physical abuse	0.247	0.315	0.786	0.432
Emotional abuse	-0.201	0.607	-0.33	0.741
Agitation				
Physical neglect	0.189	0.307	0.614	0.539
Emotional neglect	-0.017	0.692	-0.025	0.98
Sexual abuse	-0.008	0.113	-0.071	0.943
Physical abuse	0.369	0.35	1.055	0.291
Emotional abuse	-0.411	0.762	-0.539	0.59
Cognitive				
Physical neglect	0.061	0.231	0.265	0.791
Emotional neglect	0.853	0.447	1.909	0.056
Sexual abuse	0.065	0.094	0.689	0.491
Physical abuse	-0.453	0.284	-1.595	0.111
Emotional abuse	<b>1.392</b>	<b>0.559</b>	<b>2.491</b>	<b>0.013</b>
Appetite				
Physical neglect	0.457	0.301	1.519	0.129
Emotional neglect	0.238	0.601	0.395	0.693
Sexual abuse	0.033	0.106	0.309	0.757
Physical abuse	0.058	0.37	0.157	0.875
Emotional abuse	-0.252	0.693	-0.364	0.716
Sexual				
Physical neglect	-0.026	0.349	-0.076	0.94
Emotional neglect	0.694	0.62	1.12	0.263
Sexual abuse	0.175	0.133	1.313	0.189
Physical abuse	-0.438	0.409	-1.072	0.284
Emotional abuse	1.157	0.74	1.563	0.118

SE = standardized error; Est/SE = test statistic (z value); RMSEA = root mean square error of approximation; CFI = comparative fit index; TLI = Tucker-Lewis index.

\* Model fit indices: RMSEA = 0.025 (90% confidence interval = 0.022-0.028); CFI = 0.961; TLI = 0.959.

<sup>†</sup> Estimates = unstandardized parameter estimate.

of referring to the physiological degradation of an organism as a result of repeated cycles of allostasis, which have cumulative effects that could manifest as structural and functional deterioration.<sup>22</sup> A child constantly exposed to episodes of EA would be subjected to repeated bouts of allostasis. The body responds to almost any event or challenge by releasing chemical mediators that help to cope with the situation. However, chronic elevation of the same mediators may produce unwanted and harmful physiological effects.<sup>24</sup> A vast array of chemical and inflammatory mediators are involved in responses to stress challenges such as childhood trauma, including (but not limited to) release of catecholamines (norepinephrine, dopamine),<sup>23</sup> HPA axis and corticotropin-releasing hormone (CRH) system activation,<sup>21</sup> release of pro-inflammatory cytokines,<sup>25</sup> and immune system activation.

Ultimately, the brain is the organ that “decides” what is stressful and what is not, which, in turn, determines the behavioral and physiological responses of the organism. One of the ways that stress hormones may regulate function within the brain is by changing the structure of neurons.<sup>23</sup> The hippocampus is one of the most sensitive and plastic areas of the brain and plays a vital role cognitive function, making it an especially vulnerable structure and a frequent target for a variety of chemical mediators. In animal models, allostatic overload as a consequence of chronic stress causes atrophy of neurons in the hippocampus and prefrontal cortex, which are brain areas involved in memory, selective attention, and executive function, along with hypertrophy of neurons in the amygdala, a brain area involved in fear, anxiety, and aggression.<sup>23</sup> This is in line with our finding of an association between childhood trauma and the cognitive dimension of depression, as many of the cognitive symptoms of depression could be putatively attributed to hippocampal and prefrontal cortex dysfunctions.

The hippocampus plays a central role in the acquisition (encoding) and consolidation (storing) of episodic-declarative memory.<sup>26,27</sup> This form of memory is closely related to experiences of EA, which are characterized by verbal offenses to a child's sense of worth or well-being. Furthermore, mounting evidence suggests that the hippocampus promotes the convergence of contrasting cortical representations of items or actions and their spatiotemporal context into a coherent representation by sparse conjunctive neural coding.<sup>28</sup> This association of item and context then leads to the phenomenological experience of recollection, which is a mental faculty pertaining to the cognitive sphere of brain functioning. Glucocorticoid receptors are richly expressed in the hippocampus,<sup>29</sup> and hippocampal volume loss is well documented in chronic stress,<sup>30</sup> in animal models of exogenous glucocorticoid administration,<sup>31</sup> and in patients with Cushing syndrome.<sup>32</sup> Adrenal glucocorticoids usually display adaptive effects in the short run, but contribute to pathophysiology in the presence either of repeated stress or of HPA axis deregulation (allostatic overload).<sup>33</sup>

As noted by Lucassen et al., a lasting decrease in neurogenesis following severe or chronic stress exposure, either in adulthood or early in life, may denote impaired

hippocampal plasticity and could contribute to the cognitive symptoms of depression. However, by itself, it would be unlikely to produce the full syndrome of MDD.<sup>26</sup> In addition, altered hippocampal function may influence the activity of neural circuitry in the prefrontal cortex, amygdala, and nucleus accumbens, which receive inputs from the hippocampus and are associated with emotionality.<sup>27</sup> Interestingly, altered brain monoamine levels resulting from antidepressant treatment demonstrate a consistent reinforcing effect on adult hippocampal neurogenesis.<sup>34</sup> Consistent with this hypothesis, Samplin et al.<sup>35</sup> found that males from a community sample with a history of EA had smaller hippocampal volumes. Childhood trauma was assessed by the same 28-item CTQ. In our study, only the lower-order trauma factor, EA, was associated with depression severity in the cognitive domain.

Looking at the whole picture suggests the following line of reasoning: 1) HPA axis hyperactivity mediates the consequences of childhood trauma in adult depression; 2) HPA hyperactivity adversely impacts hippocampal neurogenesis; 3) altered hippocampal function contributes to the cognitive symptoms of depression; and 4) more specific forms of childhood trauma (EA) present a stronger association with cognitive aspects of depression. Therefore, we propose that specific effects of stress on the hippocampus might be responsible for mediating the consequences of childhood EA on the cognitive dimension of adult depression.

### *Limitations*

The most significant limitation of this study is that all data collection was cross-sectional. Therefore, although our findings demonstrate an association between childhood trauma and cognition, this association cannot be taken as directly causal. Memory biases should be taken into account, especially in the context of depressed mood and affect. As an example, one alternative possibility could be that depressed patients with particularly pronounced cognitive symptoms could present a memory bias for early traumatic experiences. However, there is evidence attesting to the stability of self-reported data on childhood trauma over time,<sup>36</sup> with another study finding that the influences of mood state and life experience appear to have little effect on the stability of the perception of parenting over time.<sup>37</sup> Both forms of assessment elevated the risk of psychopathology to a similar degree in a recent study investigating the associations of psychopathology with prospective vs. retrospective childhood maltreatment ascertainment in a large and representative sample in New Zealand.<sup>38</sup> Nevertheless, prospective study designs are warranted to elucidate this and other questions.

### *Strengths*

This study has some important strengths: it investigates a history of childhood trauma in a fairly large sample of patients with MDD, the statistical treatment makes use of sophisticated methods, and the findings may be relevant for treatment and research. There are important clinical differences between depressive disorders with

and without childhood maltreatment.<sup>39</sup> Maltreated individuals experience depressive symptoms at an earlier age and have a more continuous course; have more severe mood, neurovegetative, and so-called endogenous symptoms of depression; have more comorbidities, particularly substance abuse; and more commonly present with psychotic features, suicide attempts, and deliberate self-harm.<sup>39</sup> As compared with previous studies, our work advances the current understanding of the specificity of such an important risk factor to the phenotypic expression of major depression. Furthermore, by showing that EA could be a specific risk factor for symptoms pertaining to the cognitive dimension of depression, it may help with treatment planning. As an example, in a previous study, childhood maltreatment was associated with better response to cognitive therapy or medication than to interpersonal therapy in adult patients with MDD.<sup>40</sup> In this other landmark study, 681 chronically depressed patients were treated with either pharmacotherapy (nefazodone), psychotherapy (Cognitive Behavioral System of Psychotherapy, CBASP), or a combination thereof.<sup>41</sup> Overall, patients responded more favorably to the treatment combination than to either treatment in isolation. However, in the subset of patients with a history of childhood trauma, psychotherapy was clearly superior to antidepressant monotherapy, and the combination provided little added benefit. As there is also evidence that some profiles of depressive symptoms may show differential responses to antidepressant treatments,<sup>42</sup> combining specific information concerning the patient's history (EA) with specific clusters of depressive symptoms (cognitive symptoms) could be a way of further refining treatment choices.

### *Practical implications*

EA usually does not leave easily perceptible marks, whether during childhood and adolescence or later in life. Therefore, the accumulating knowledge of the potential harmful effects of EA should be made a priority in child and adolescent psychiatry, as well as in general mental health. Glaser<sup>43</sup> proposed a framework for understanding, detecting, and intervening in situations of EA and neglect. According to his standpoint, the probability of detecting EA and neglect could be raised by sorting information in the appropriate levels of concern: 1) social and environmental factors, 2) caregiver risk factors, 3) caregiver-child interactions, and 4) child functioning. Thus, opportunities for intervention are set not only in the patient or in the family, but also in the community, integrating knowledge regarding risk and protective factors for both caregivers and children. Still, whenever prevention and intervention measures fail in the course of childhood and adolescence, mental health care systems may develop initiatives aiming to decrease the impact of EA on physical and mental health later in life as well.

The results of the present study also suggest the possibility of opening new avenues of research, such as investigating the neurobiological pathways that lead individuals who have experienced emotional traumatic

experiences as children to develop specific cognitive symptoms of depression in adulthood.

Childhood trauma in general, and EA in particular, could be significant risk factors for the subsequent development of cognitive symptoms of MDD. These influences might be specific to this depressive dimension and not found in any other dimensions, which might have conceptual and therapeutic implications for both researchers and clinicians. This finding reinforces the current idea that some dimensions present in current psychiatric categories could have pathophysiological specificities.

### **Disclosure**

The authors report no conflicts of interest.

### **References**

- 1 Klein DN, Glenn CR, Kosty DB, Seeley JR, Rohde P, Lewinsohn PM. Predictors of first lifetime onset of major depressive disorder in young adulthood. *J Abnorm Psychol.* 2013;122:1-6.
- 2 Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington H, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science.* 2003;301:386-9.
- 3 Kendler KS, Aggen SH. Clarifying the causal relationship in women between childhood sexual abuse and lifetime major depression. *Psychol Med.* 2014;44:1213-21.
- 4 Withers AC, Tarasoff JM, Stewart JW. Is depression with atypical features associated with trauma history? *J Clin Psychiatry.* 2013;74:500-6.
- 5 Levitan RD, Parikh SV, Lesage AD, Hegadoren KM, Adams M, Kennedy SH, et al. Major depression in individuals with a history of childhood physical or sexual abuse: relationship to neurovegetative features, mania, and gender. *Am J Psychiatry.* 1998;155:1746-52.
- 6 Matza LS, Revicki DA, Davidson JR, Stewart JW. Depression with atypical features in the National Comorbidity Survey: classification, description, and consequences. *Arch Gen Psychiatry.* 2003;60:817-26.
- 7 Gaudiano BA, Zimmerman M. The relationship between childhood trauma history and the psychotic subtype of major depression. *Acta Psychiatr Scand.* 2010;121:462-70.
- 8 Vares EA, Salum GA, Spanemberg L, Caldieraro MA, Fleck MP. Depression dimensions: integrating clinical signs and symptoms from the perspectives of clinicians and patients. *PLoS One.* 2015;10:e0136037-e0136037.
- 9 Gorenstein C, Andrade L. Validation of a Portuguese version of the Beck Depression Inventory and the State-Trait Anxiety Inventory in Brazilian subjects. *Braz J Med Biol Res.* 1996;29:453-7.
- 10 Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry.* 1960;23:56-62.
- 11 Parker G, Hadzi-Pavlovic D. *Melancholia: a disorder of movement and mood. A phenomenological and neurobiological review.* New York: Cambridge University; 1996.
- 12 Grassi-Oliveira R, Stein LM, Pezzi JC. [Translation and content validation of the Childhood Trauma Questionnaire into Portuguese language]. *Rev Saude Publica.* 2006;40:249-55.
- 13 Polanczyk G, Caspi A, Williams B, Price TS, Danese A, Sugden K, et al. Protective effect of CRHR1 gene variants on the development of adult depression following childhood maltreatment: replication and extension. *Arch Gen Psychiatry.* 2009;66:978-85.
- 14 Grassi-Oliveira R, Cogo-Moreira H, Salum GA, Brietzke E, Viola TW, Manfro GG, et al. Childhood Trauma Questionnaire (CTQ) in Brazilian samples of different age groups: findings from confirmatory factor analysis. *PLoS One.* 2014;9:e87118.
- 15 Teasdale JD. Change in cognition during depression-psycho-pathological implications: discussion paper. *J R Soc Med.* 1983;76:1038-44.
- 16 Ingram RE, Ritter J. Vulnerability to depression: cognitive reactivity and parental bonding in high-risk individuals. *J Abnorm Psychol.* 2000;109:588-96.

- 17 Keers R, Uher R, Gupta B, Rietschel M, Schulze TG, Hauser J, et al. Stressful life events, cognitive symptoms of depression and response to antidepressants in GENDEP. *J Affect Disord.* 2010;127:337-42.
- 18 Dias A, Sales L, Hessen DJ, Kleber RJ. Child maltreatment and psychological symptoms in a Portuguese adult community sample: the harmful effects of emotional abuse. *Eur Child Adolesc Psychiatry.* 2015;24:767-78.
- 19 Wright MO, Crawford E, Del Castillo D. Childhood emotional maltreatment and later psychological distress among college students: the mediating role of maladaptive schemas. *Child Abuse Negl.* 2009;33:59-68.
- 20 Martins CM, Von Werne Baes C, Tofoli SM, Jurueña MF. Emotional abuse in childhood is a differential factor for the development of depression in adults. *J Nerv Ment Dis.* 2014;202:774-82.
- 21 Heim C, Newport DJ, Mletzko T, Miller AH, Nemeroff CB. The link between childhood trauma and depression: insights from HPA axis studies in humans. *Psychoneuroendocrinology.* 2008;33:693-710.
- 22 Mello MF, Faria AA, Mello AF, Carpenter LL, Tyrka AR, Price LH. [Childhood maltreatment and adult psychopathology: pathways to hypothalamic-pituitary-adrenal axis dysfunction]. *Rev Bras Psiquiatr.* 2009;31:S41-8.
- 23 McEwen BS. Protective and damaging effects of stress mediators: central role of the brain. *Dialogues Clin Neurosci.* 2006;8:367-81.
- 24 McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med.* 1998;338:171-9.
- 25 Felger JC, Lotrich FE. Inflammatory cytokines in depression: neurobiological mechanisms and therapeutic implications. *Neuroscience.* 2013;246:199-229.
- 26 Lucassen PJ, Meerlo P, Naylor AS, van Dam AM, Dayer AG, Fuchs E, et al. Regulation of adult neurogenesis by stress, sleep disruption, exercise and inflammation: implications for depression and antidepressant action. *Eur Neuropsychopharmacol.* 2010;20:1-17.
- 27 Sahay A, Hen R. Adult hippocampal neurogenesis in depression. *Nat Neurosci.* 2007;10:1110-5.
- 28 Opitz B. Memory function and the hippocampus. *Front Neurol Neurosci.* 2014;34:51-9.
- 29 De Kloet R, Wallach G, McEwen BS. Differences in corticosterone and dexamethasone binding to rat brain and pituitary. *Endocrinology.* 1975;96:598-609.
- 30 Joels M, Karst H, Krugers HJ, Lucassen PJ. Chronic stress: implications for neuronal morphology, function and neurogenesis. *Front Neuroendocrinol.* 2007;28:72-96.
- 31 Sapolsky RM, Uno H, Rebert CS, Finch CE. Hippocampal damage associated with prolonged glucocorticoid exposure in primates. *J Neurosci.* 1990;10:2897-902.
- 32 Starkman MN, Gebarski SS, Berent S, Scheingart DE. Hippocampal formation volume, memory dysfunction, and cortisol levels in patients with Cushing's syndrome. *Biol Psychiatry.* 1992;32:756-65.
- 33 McEwen BS. Plasticity of the hippocampus: adaptation to chronic stress and allostatic load. *Ann N Y Acad Sci.* 2001;933:265-77.
- 34 Lee MM, Reif A, Schmitt AG. Major depression: a role for hippocampal neurogenesis? *Curr Top Behav Neurosci.* 2013;14:153-79.
- 35 Samplin E, Ikuta T, Malhotra AK, Szeszko PR, Derosse P. Sex differences in resilience to childhood maltreatment: effects of trauma history on hippocampal volume, general cognition and subclinical psychosis in healthy adults. *J Psychiatr Res.* 2013;47:1174-9.
- 36 da Silva SS, da Costa Maia A. The stability of self-reported adverse experiences in childhood: a longitudinal study on obesity. *J Interpers Violence.* 2013;28:1989-2004.
- 37 Wilhelm K, Niven H, Parker G, Hadzi-Pavlovic D. The stability of the Parental Bonding Instrument over a 20-year period. *Psychol Med.* 2005;35:387-93.
- 38 Scott KM, McLaughlin KA, Smith DA, Ellis PM. Childhood maltreatment and DSM-IV adult mental disorders: comparison of prospective and retrospective findings. *Br J Psychiatry.* 2012;200:469-75.
- 39 Teicher MH, Samson JA. Childhood maltreatment and psychopathology: a case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. *Am J Psychiatry.* 2013;170:1114-33.
- 40 Harkness KL, Bagby RM, Kennedy SH. Childhood maltreatment and differential treatment response and recurrence in adult major depressive disorder. *J Consult Clin Psychol.* 2012;80:342-53.
- 41 Nemeroff CB, Heim CM, Thase ME, Klein DN, Rush AJ, Schatzberg AF, et al. Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma. *Proc Natl Acad Sci U S A.* 2003;100:14293-6.
- 42 Uher R, Maier W, Hauser J, Marusic A, Schmael C, Mors O, et al. Differential efficacy of escitalopram and nortriptyline on dimensional measures of depression. *Br J Psychiatry.* 2009;194:252-9.
- 43 Glaser D. How to deal with emotional abuse and neglect: further development of a conceptual framework (FRAMEA). *Child Abuse Negl.* 2011;35:866-75.