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Childhood Trauma and Treatment Implications in Major Depressive Disorder in South Korea: Comparison with Medical Outpatients and Two-Year Follow-Up

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Background: Little is known about the specific types of childhood trauma and their relationship to treatment-related issues in major depressive disorder (MDD). This study examined trauma experiences and treatment-related variables in outpatients with MDD at a psychiatric department of a university hospital in Korea.
Methods: First, 75 outpatients with MDD were compared to medical outpatients without MDD matched by age, sex, income, and educational qualifications. Both groups completed the Life Stressor Checklist-Revised, which assesses comprehensive life events. Second, treatment-related variables and medication compliance measured by the Compliance Rating Scale were investigated for the two-year period after the initial assessment.
Results: The MDD group had experienced a significantly higher number of lifetime traumas than the control group ($p=0.003$), including more frequent witnessing of family violence ($p<0.001$), adulthood physical assault by a family member ($p<0.001$), and childhood emotional abuse (CEA) ($p<0.001$). CEA was associated with early onset of the first depressive episode and premature termination of pharmacotherapy; childhood physical neglect was associated with premature termination and less time in therapy.
Conclusion: Our findings support the important influence of childhood emotional trauma and its relationship to treatment retention.

Keywords Major depressive disorder; Child abuse; Child neglect; Treatment adherence and compliance; Patient dropouts

INTRODUCTION

There is a growing body of literature proposing an etiological association between experiences of previous trauma, particularly ones of an early interpersonal nature, and later development of major depressive disorder (MDD) [1]. Numerous cross-sectional retrospective studies have supported this view [2-4]. For example, increased risks of MDD episodes were reported from an adverse childhood experiences (ACE) study examining retrospective cohort of more than 9,000 primary care patients [3]. In this study, virtually all childhood adversities (i.e., emotional, physical and sexual abuse; physical violence against mother; household substance abuse; living with a criminal family member; and parental separation or divorce) increased the odd ratios of both lifetime and recent depressive episodes. Furthermore, strong dose-dependent relationships were observed between the number of trauma types experienced and the risk of MDD in the ACE study and elsewhere [3,4].

Prospective longitudinal studies also suggested the causal relationship between childhood trauma and de-

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pression. A prospective study of a large population cohort reported that childhood abuse and separation before the age of 16 increased the risk of a mood disorder by 1.9 times, which was found when subjects were re-evaluated after 3 years at the age of 19 [5]. Another longitudinal study had followed children with reported childhood abuse or neglect for 20 years and showed that both child physical abuse and multiple abuse elevated the risk of lifetime MDD by 1.6 and 1.8 times, respectively, while neglect raised the risk of MDD by 1.6 times [4].

Additionally, it has been established through research that childhood trauma has a negative impact on the course of a depressive illness: in particular, multiple studies have consistently reported an early onset, increased severity of symptoms, longer and frequent episodes, and a poor response to treatment, which explains the chronic and morbid clinical course of MDD compared to those without any childhood trauma [2]. Treatment implications of childhood trauma and depression are particularly noteworthy. In a meta-analysis of 10 clinical trials with pharmacotherapy or combined pharmacotherapy and psychotherapy, childhood abuse was associated with a lack of remission in 9 studies suggesting that child maltreatment in general seems to be a negative outcome factor or at least mediator [2]. However, the type of childhood trauma that is more related to a poor outcome is unknown at present, although emotional abuse was suggested in one study [6].

Researchers have often focused exclusively on sexual and physical abuse but have reported inconsistent results regarding their influences on the manifestation and course of depression [4,7]. However, there exist strong correlations within the types of abuse, especially between emotional abuse and other types of abuse [8]; studies which did not include emotional abuse or neglect may yield inflated correlations between physical or sexual abuse and variables studied. Likewise, a large health maintenance organization study found that when an emotionally abusive family environment was controlled, associations between physical or sexual abuse and mental health scores were substantially decreased [8]. One study on primary care patients showed that only childhood emotional abuse (CEA) and neglect significantly predicted depressive symptoms even after controlling physical and sexual abuse [9]. Another study compared adults with MDD with healthy subjects and found that childhood emotional trauma and physical abuse were more common in the MDD group but not sexual abuse and physical neglect [6]. At present, emotional abuse and neglect seem the most crucial in regard with the risk of depression [3,8] and its effect on treatment outcome [6,10].

That said, to be able to label emotional trauma as a major and distinct childhood adversity that affects depression, we need to have data indicating that emotional abuse is particularly more common in individuals with depression compared to the general population and individuals with other psychiatric illnesses. Bernet and Stein [6] compared adults with MDD with healthy subjects and found that childhood emotional trauma and physical abuse were more common in the MDD group, but sexual abuse and physical neglect were not. However, this finding is insubstantial because the demographic variables of the control group were not matched up with the MDD.

Additionally, to our knowledge, only one recent study has examined the relationship between childhood trauma and the medication adherence in individuals with major depression [11]. In the study, it was reported that CEA was more common in the suboptimally adherent group (49.2% vs. 36.5%). This paucity of literature focusing on treatment adherence is disappointing given that premature medication discontinuation is substantially high and closely related to relapse/recurrence and increased health costs of MDD. In an observational study with 4,312 health plan users with new onset depression, it was found that 49% discontinued antidepressant medication within one month, and 62% within 1 to 3 months [12]. A systemic review on adherence and outcome studies with MDD demonstrated that non-adherent patients had increased risks of relapse/recurrence, emergency department visits, and hospitalizations [13].

Therefore, in this study, we first aimed to determine whether childhood emotional trauma is a distinct type that differentiates those with MDD from matched non-psychiatric control. Second, we examined the effect of childhood trauma, particularly the effect of emotional abuse on treatment retention and adherence to medication among patients with MDD who received antidepressant medications. For two years after the initial assessment, outpatients with MDD at a psychiatric unit in South Korea were retrospectively followed-up for course and treatment-related variables.

MATERIALS AND METHODS

1. Subjects and procedures

During the 2-year study period, consecutive series of new outpatients with MDD were recruited from Hanyang University Guri Hospital, Gyeonggi Province, South Korea. To meet the inclusion criteria, participants had to be aged between 16 and 70 years and have a current diagnosis of MDD. The diagnosis of MDD was made using the Structured Clinical Interview for diagnostic and statistical manual (DSM)-IV Axis I Disorders-Clinician Version [14]. Patients with a severe medical condition, neurological disease, organic mental disorder, intellectual disability, or inability to read or write the Korean language were excluded. All participants provided informed consent to participate in the research, and approval was obtained from the Institutional Review Board of the Hanyang University Guri Hospital (IRB No. 2015-05-013). The total number of eligible patients was 98, but 23 (23.5%) refused to participate, yielding a final sample size of 75. The patients were followed up for 2 years to determine natural course of illness, considering treatment retention, medication compliance, status of remission, and hospitalization.

To develop a matched control series, we used previously surveyed data of outpatients from the medical departments of the same hospital, who had no history of psychiatric disorders including depression [15], and we established a list of 75 control participants matched to the MDD patients by age, sex, education level, and annual income status. We did not find significant differences in other sociodemographic variables including marital status, employment, or religiosity between the two groups (Table 1).

2. Measures

1) Life Stressor Checklist-Revised

The Life Stressor Checklist-Revised (LSC-R) is a self-

Table 1. Baseline characteristics of outpatients with MDD vs. matched controls

Variable	MDD (n=75)	Control (n=75)	t or χ^2	p-value
Age (y)	41.69±15.78	41.51±15.73	0.07	0.940
Sex			0.00	1.000
Male	24 (32.0)	24 (32.0)		
Female	51 (68.0)	51 (68.0)		
Marital status			2.43	0.300
Married	37 (50.0)	45 (60.0)		
Divorced/widowed	14 (18.9)	8 (10.7)		
Never married	23 (31.1)	22 (29.3)		
Employment			4.73	0.090
Employed	23 (31.9)	23 (30.7)		
Unemployed	19 (26.4)	10 (13.3)		
Student/housewife	30 (41.7)	42 (56.0)		
Education			0.70	0.710
Less than high school	19 (26.0)	15 (20.0)		
High school graduate	25 (34.2)	36 (48.0)		
Beyond college	29 (39.7)	24 (32.0)		
Annual income[a]			0.36	0.840
<20,000	30 (43.5)	29 (38.7)		
20,000-39,999	25 (36.2)	30 (40.0)		
>40,000	14 (20.3)	16 (21.3)		
Religion			0.36	0.550
Religious	46 (64.8)	45 (60.0)		
Nonreligious	25 (35.2)	30 (40.0)		

Values are presented as mean±standard deviation or number (%). Total sum of cases may not be 75 due to missing data.
MDD, major depressive disorder.
[a]In US dollars.

reported checklist that includes questions about lifetime exposure to traumatic and stressful experiences [16]. The LSC-R assesses traumatic events that meet DSM-IV definition and other minor traumas or stressors such as divorce, abortion, and emotional abuse not covered by the DSM criteria [17]. This scale was chosen because it accommodates our research goal due to its broad coverage of lifetime traumatic and adverse events and also because its sound psychometric properties are in the Korean, as well as the original English version [18,19].

Some items in LSC-R assess lifetime experience without differentiating whether the event during childhood or adulthood. Thus, for the purpose of our research, these particular items were recoded to dissociate childhood and adulthood events depending whether they occurred before or after the age of 16. Examples of these were items 11 (emotional abuse) and 12 (witnessing family violence). This dissociation was possible because each item of the LSC-R has sub-items asking the respondent when the incident happened and how long it lasted.

2) Symptom Checklist-90-Revised

The Symptom Checklist-90-Revised (SCL-90-R) was used to measure general symptoms of distress. The SCL-90-R is a 90-item multidimensional self-report inventory that covers a broad range of psychological symptoms. This questionnaire comprises of nine clinical sub-scales and three global indices and we used scores of the Depression subscale and Global Severity Index as indicators for depressive symptoms and general severity of symptoms [20].

3) Compliance Rating Scale

The Compliance Rating Scale is a simple Likert-type clinician-rating instrument developed to measure adherence to medication [21]. The score ranges from 1 to 7 (higher score represent better adherence): 1) complete refusal, 2) partial refusal (e.g. refused depot) or only accepts minimum doses, 3) accepts only because it is compulsory or is very reluctant and requires persuasion or often questions the need for it, 4) occasional reluctance (e.g. questions need for medication once a week), 5) passive acceptance, 6) moderate participation with some knowledge and interest in medication and thus no prompting required, and 7) active participation (i.e., readily accepts), and shows some responsibility for regimen. The psychiatrist in charge assessed the overall adherence during the specific treatment period by evaluating reports from patients and their care-givers, attitudes or behaviors observed in response to medication, and any inconsistency between length of prescription and hospital visits. Patients with a score less than 4 were considered as non-adherent [22].

3. Definitions of terms

Remission of a depressive episode was defined according to a recommendation presented by the MacArthur Foundation Research Network on the Psychobiology of Depression: complete remission (score=2) was defined as no diagnostic fulfillment of a major depressive episode but without minimal symptoms; partial remission (score=1) was defined as no diagnosis with minimal symptoms; no remission for diagnosis of the episode even after treatment (score=0). Dropout, the premature termination of treatment, was considered to be when the subject received less than 12 weeks of antidepressant medication.

4. Analysis

The independent t-test and χ^2 test were used to compare sociodemographic data and traumatic events of MDD patients and medical outpatients. For correlational analyses, we conducted either Pearson or Spearman's rank or Kendall's tau b analyses. To control the effect of third variables, further partial correlation was performed. All statistical calculations were performed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Co., Armonk, NY, USA) and the alpha level was set at 0.05 bidirectionally.

RESULTS

1. Characteristics of the sample

From the 75 outpatients with MDD who were compared to medical patients, 8 (10.7%) were excluded because they had either no prescribed medication or insufficient clinical data leaving a final sample of 67 for further analyses. Two-thirds of participants were female (n=44, 65.7%), about a half were married (n=33, 49.3%), and more than one-third had college education (n=25, 36.3%). The median duration of depressive illness of these patients was 2.3 years (range, 0.1-18.7 years) and

the median age of onset was 35.7 years (range, 12.7-76.5 years). About two-thirds (n=44, 65.7%) of cases were the first depressive episodes. A median time of 3.7 months (range, 0-112 months) was needed before seeking treatment. About a half (n=34, 50.7%) prematurely terminated treatment within 12 weeks of medication and one-third (n=23, 34.3%) complied with the medication regimen. About two-thirds (65.7%, n=44) were defined as non-adherent or non-compliant to treatment. During the course of therapy, complete remission was achieved in only 23.9% of patients (n=16), partial remission in 44.8% (n=30), and no remission in 7.5% (n=5). Within the 24 months of follow-up period, the median length of time they continued treatment for was 2.8 months (range, 0-24 months).

The non-interpersonal traumas in 67 depressed patients were as follows: witnessing a serious accident (n=21, 31.3%), involved in a serious accident (n=16, 23.9%), and involved in a disaster (n=15, 23.9%). The interpersonal traumas were witnessing family violence during childhood (n=31, 46.3%), experiencing physical assault by family or intimate partner in adulthood (n=25, 25.4%), parental divorce or separation in childhood (n=12, 17.9%), childhood physical abuse (n=11, 16.4%), childhood emotional abuse (n=11, 16.4%), childhood sexual abuse (CSA) (n=6, 9.0%), death of loved one during childhood (n=7, 10.4%), and childhood physical neglect (n=4, 6.0%).

2. Comparison of traumatic events

The MDD group experienced a significantly higher number of traumatic events (mean=5.3, standard deviation [SD]=3.5) compared to the control group (mean=3.5, SD=3.9) (t=3.0, df=148, p=0.003). More specifically, the following individual events were significantly more common in the MDD group: 1) witnessing family violence (p<0.001), 2) CEA (p<0.001), 3) physical assault by family during adulthood (p=0.001), and 4) being robbed, mugged, or physically attacked (p=0.042) (Table 2).

3. Childhood trauma and treatment variables

CEA was significantly related to early onset of depressive illness (ρ=0.298, p=0.014) and dropout (b=0.275, p=0.025). The correlation with time remained in treat-

Table 2. Prevalence of life-time trauma in outpatients with MDD vs. matched control

Items of Life Stressor Checklist-Revised	MDD (n=75)	Control (n=75)	χ^2	p-value
Serious disaster	17 (22.7)	18 (24.0)	0.04	0.850
Serious accident	21 (28.0)	23 (30.7)	0.13	0.720
Witnessing a serious accident	19 (25.3)	15 (20.0)	0.61	0.440
Parental separation or divorce[a]	13 (17.3)	6 (8.0)	2.95	0.086
Childhood emotional abuse	13 (17.3)	1 (1.3)	11.35	<0.001
Childhood physical neglect	5 (6.7)	1 (1.3)	4.11	0.120[b]
Sudden death of someone close[a]	7 (9.3)	2 (2.7)	2.96	0.166[b]
Death of someone close to you[a]	6 (8.0)	6 (8.0)	0.00	1.000
Witnessing family violence[a]	37 (49.3)	10 (13.3)	22.59	<0.001
Witnessing a robbery, mugging, or attack	7 (9.3)	4 (5.3)	0.88	0.347
Being robbed, mugged, or attacked	10 (13.3)	3 (4.0)	4.13	0.042
Childhood physical abuse	13 (17.3)	6 (8.0)	2.95	0.086
Adult physical assault	20 (26.7)	5 (6.7)	10.80	0.001
Sexual harassment	5 (6.7)	8 (10.7)	0.76	0.384
Forced genital touching before age 16	6 (8.0)	2 (2.7)	2.11	0.276[b]
Forced genital touching after age 16	1 (1.3)	2 (2.7)	0.34	0.999[b]
Forced intercourse before age 16	0 (0.0)	1 (1.3)	1.01	0.999[b]
Forced intercourse after age 16	2 (2.7)	2 (2.7)	0.00	0.999[b]

Values are presented as number (%).
MDD, major depressive disorder.
Some of items with insignificant findings are not shown.
[a]Happening before age 16, [b]By Fisher's exact test.

Table 3. Correlation among childhood or adult trauma and clinical variables in outpatients with depression (n=67)

Variable	Age of onset	Duration	Time to therapy	Compliance[a]	Dropout[b]	Remission	Time in therapy
Childhood emotional abuse	−0.30*	0.08	−0.21	−0.18	0.28*	−0.21	−0.22
Childhood physical neglect	0.02	−0.16	−0.03	−0.17	0.25*	−0.22	−0.25*
Witnessing family violence	−0.04	0.16	0.13	0.12	0.02	−0.07	−0.01
Childhood physical abuse	−0.24	0.17	0.05	−0.01	0.03	−0.16	0.06
Adult physical violence	−0.13	0.15	−0.07	0.05	0.03	0.03	−0.11
Childhood sexual abuse	−0.14	0.01	0.01	−0.15	−0.01	−0.09	0.03
Adult sexual abuse	−0.15	0.09	0.12	−0.08	−0.13	−0.06	−0.07

Values are Spearman's rho except correlations with dropout (Kendall's tau-b).
[a]Measured with the Compliance Rating Scale. [b]Premature termination before 12 weeks of medication.
*p<0.05.

ment was near statistical significance (ρ=−0.218, p=0.076). Further, childhood physical neglect (CPN) was associated with dropout (τb=0.248, p=0.044) as well as less time in therapy (ρ=−0.254, p=0.038) (Table 3). We did not find any association between the experience of trauma and duration of illness, delayed time before seeking treatment, compliance rating and remission status.

As the level of education was significantly correlated with both CEA and CPN and symptom severity was correlated with CEA, we controlled their effect on these correlations to find that significant relations no longer remained except between CEA and dropout (p<0.05).

DISCUSSION

With regard to the first aim of this study, as expected, patients with MDD who were compared to matched medical outpatients reported a significantly higher number of lifetime traumatic events, particularly those events of interpersonal nature both in child and adulthood. This finding is in line with previous literature and thus supports the fact that there is more experience of interpersonal trauma among depressive patients [6,15]. It is particularly noteworthy that CEA or CPN were the experiences that discriminated depressive patients from control [6]. One study noted and supported our finding in that CEA was by far the strongest ACE that discriminate the depressed patients from non-psychiatric control group [23]. Likewise, only a history of CEA not physical and sexual abuse mediated a relationship between adult life stress and depressive symptoms [24]. In addition, Hankin found that only CEA not physical and sexual abuse predicted later changes in depressive symptoms and that this was mediated by attachment style, negative life events and cognitive styles [25].

However, the impact of emotional abuse may not be specific to depression; a recent study using large epidemiological data showed that CEA was associated with a broad spectrum of mental disorders including mood disorders, anxiety disorders, substance use disorders, and personality disorders [26]. Thus, rather than it being specific to depression per se, CEA seems to be a universal childhood risk factor for adult mental health problems. On the other hand, the term CEA encompasses a variety of offensive actions, which range from belittling to terrorizing the child; therefore, the negative impact of CEA will be of varying degrees, and thus its long-term effects may be less specific to certain disorders. To support this view, emotional neglect, which has a narrower definition and is homogeneous in meaning, in fact, impacted certain disorders (i.e., depression and social phobia) in a more specific way [26].

Furthermore, our finding indicates that a general pattern of 'cumulative abuse' throughout one's lifetime, in which there was CEA and CPN/witnessing family violence, lead to subsequent adult experiences of intimate partner violence (IPV) and psychopathology [27]. Likewise, a general population study has noted that cumulative interpersonal trauma predicts post-traumatic stress disorder (PTSD) [28]. It is likely that adults raised in a violent family environment may adopt violence-tolerant roles in their relationship with their partners [29], further increasing the risk of developing a depressive illness.

The majority of studies did not investigate the wit-

nessing of family violence as an independent variable of childhood trauma; however, the ACE study indicates that the emphasis should be on broader areas of negative childhood experiences in addition to abuse and neglect [30]. Moreover, emotional abuse and witnessing domestic violence often co-exist [31], and the impact of emotional abuse may be inflated due to the potential overlap with witnessing violence that was not included in the investigation. In a similar vein, in their logistic regression model, Russell et al. [32] demonstrated that having witnessed domestic violence predicted an increased risk of depressive symptoms in young adults independent of other types of family violence. Given the finding that witnessing alone (not with other child abuse) did not predict development of adult PTSD in a community sample of female [33], further studies are needed to disentangle the interaction of these two adverse events in the development of adult psychiatric illnesses.

In our study, sexual trauma did not show a significant difference between the depressive patients and control. Although, a number of previous studies have proclaimed the association of depression with CSA [34,35], other reports, however, have reported contradictory negative findings [6,36]. A relative low endorsement rate of both childhood and adult sexual violence in the present study may play a role for the negative finding.

Concerning the second research question of this study, we have found that only CEA and CPN were associated with treatment variables: either premature termination or less time remained in therapy. This is in line with the only study that examined medication adherence and childhood trauma amongst depressive patients; childhood emotional neglect (CEN) was significantly more common in patients with suboptimal adherence and CPN approached the statistical significance [11]. However, when the childhood emotional trauma was entered with other variables such as severity of depression in a multivariate analysis, the significance disappeared unlike our finding in which CEN remained significant after controlling depressive symptoms. It should be addressed that our study did not measure depression with a more comprehensive depression inventory.

That being said, several studies examined other forms of treatments in other diagnostic groups. For example, dropout from inpatient treatment for anorexia nervosa was associated with CSA in the bulimic subtype but this association was not found within the restrictive type, but this study examined CSA only [37]. Another study found that dropout from psychotherapy for bulimia has been dose-dependently associated with childhood trauma but did not find specificity to certain types of trauma [38]. Steuwe et al. [24] have reported that CEA was associated with dropout from dialectical behavior therapy among inpatients with borderline personality, whereas CPN was protective against dropout. This study is in line with our finding that only CEA stood out in terms of dropout from treatment, but it contradicted our report on the association of CPN was associated with less time stayed in therapy. To discover the reason for this contradictory finding, a different population and type of treatment should be considered first; in addition, a psychometric issue concerning CPN in the childhood trauma questionnaire (CTQ) that is used for the study should be mentioned. It has often been suggested that CPN subscale in CTQ had poor construct validity from factor analyses while other subscales of the CTQ displayed sound psychometric properties [25,39].

Among those in PTSD therapy, history of CSA did not predict either treatment adherence or therapeutic alliance [40]. However, non-adherence to medication was associated with childhood physical abuse and low service engagement with witnessing family violence during childhood in individuals with early psychosis [41]. Furthermore, the aforementioned study demonstrated that poor alliance also contributed significantly to non-adherence along with childhood trauma that leads to a lack of trust and a dysfunctional attachment style in the interpersonal relations of childhood trauma sufferers who as a result may withhold from treatment offered by health care professionals.

Another explanation would be the poor responses to medication among childhood trauma survivors, which may cause these patients to prematurely withdraw from treatment. For example, from the MDD patients who received either psychotherapy or antidepressant, those with childhood emotional or physical abuse went through longer days of remission (median 89 vs. 67 days) [42]. A poor treatment response, resulting in patients being dissatisfied with treatment, is considered one of the most important factors in discontinuing antidepressant treatment [43].

In conjunction with premature termination, patients with a history of CEA had the first depressive episode at an earlier age; this finding is in concordance with those of previous studies [6,44]. This underscores the negative impact of CEA on the severity and chronicity of depres-

sion.

Our study has some limitations. First, research participants were treatment-seeking outpatients at a psychiatric department of a university-affiliated hospital; therefore, patients with less severe depression may have been overrepresented in our sample. Second, the control group selected to match the MDD group was heterogeneous with regard to the nature of physical diseases. Third, this study is a retrospective study based on participant recall and self-reporting of life events. Fourth, we did not measure duration and severity of each traumatic event, which should have shed more insight on the dose-dependent relationship among our participants. Furthermore, treatment variables were rather simple and many mediators were not examined such as the existence of trusting relationships, attachment patterns, insight and motivation for treatment, and side effects of medication. Finally, we did not control the clinical variables including severity and number of depressive episodes that can mediate link between childhood trauma and treatment retention.

Clinicians should screen for diverse types of childhood and adult interpersonal trauma in treatment-seeking depressive patients, especially CEA and develop a strategy for management and treatment. For example, it was reported that depressive patients with childhood trauma respond better to psychotherapy than to pharmacological treatment [45]. A recent neuroimaging study showed that a subgroup of depressive patients with a distinct neuronal connectivity and high scores of childhood trauma did not respond to conventional antidepressant treatment [46]. Further research is needed to confirm our findings in a larger clinical population. In addition, the effects of different traumas on the presentation and course of depressive illness should be explored.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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REFERENCES

1. Mandelli L, Petrelli C, Serretti A. The role of specific early trauma in adult depression: a meta-analysis of published literature. Childhood trauma and adult depression. Childhood trauma and adult depression. Eur Psychiatry 2015;30:665-80.
2. Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. Am J Psychiatry 2012;169:141-51.
3. Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF. Adverse childhood experiences and the risk of depressive disorders in adulthood. J Affect Disord 2004;82:217-25.
4. Widom CS, DuMont K, Czaja SJ. A prospective investigation of major depressive disorder and comorbidity in abused and neglected children grown up. Arch Gen Psychiatry 2007;64:49-56.
5. Jonker I, Rosmalen JGM, Schoevers RA. Childhood life events, immune activation and the development of mood and anxiety disorders: the TRAILS study. Transl Psychiatry 2017;7:e1112.
6. Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. Depress Anxiety 1999;9:169-74.
7. Gladstone G, Parker G, Wilhelm K, Mitchell P, Austin MP. Characteristics of depressed patients who report childhood sexual abuse. Am J Psychiatry 1999;156:431-7.
8. Edwards VJ, Holden GW, Felitti VJ, Anda RF. Relationship between multiple forms of childhood maltreatment and adult mental health in community respondents: results from the adverse childhood experiences study. Am J Psychiatry 2003;160:1453-60.
9. Spertus IL, Yehuda R, Wong CM, Halligan S, Seremetis SV. Childhood emotional abuse and neglect as predictors of

psychological and physical symptoms in women presenting to a primary care practice. Child Abuse Negl 2003;27:1247-58.
10. Kaplan MJ, Klinetob NA. Childhood emotional trauma and chronic posttraumatic stress disorder in adult outpatients with treatment-resistant depression. J Nerv Ment Dis 2000;188:596-601.
11. Baeza-Velasco C, Olié E, Béziat S, Guillaume S, Courtet P. Determinants of suboptimal medication adherence in patients with a major depressive episode. Depress Anxiety 2019;36:244-51.
12. Akincigil A, Bowblis JR, Levin C, Walkup JT, Jan S, Crystal S. Adherence to antidepressant treatment among privately insured patients diagnosed with depression. Med Care 2007;45:363-9.
13. Ho SC, Chong HY, Chaiyakunapruk N, Tangiisuran B, Jacob SA. Clinical and economic impact of non-adherence to antidepressants in major depressive disorder: a systematic review. J Affect Disord 2016;193:1-10.
14. First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical interview for DSM-IV axis I disorders: clinician version (SCID-CV). Washington, DC: American Psychiatric Press; 1997.
15. Park SC, Kim D, Jang EY. Prevalence and symptomatic correlates of interpersonal trauma in South Korean outpatients with major depressive disorder. Compr Psychiatry 2016;66:46-52.
16. Wolfe G, Kimmerling R. Gender issues in the assessment of PTSD. In: Wilson JP, Keane TM, eds. Assessing psychological trauma and PTSD. New York; 1997. p. 192-238.
17. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Psychiatric Association; 1994.
18. Choi KR, Seng JS, Briggs EC, Munro-Kramer ML, Graham-Bermann SA, Lee RC, et al. The dissociative subtype of posttraumatic stress disorder (PTSD) among adolescents: co-occurring PTSD, depersonalization/derealization, and other dissociation symptoms. J Am Acad Child Adolesc Psychiatry 2017;56:1062-72.
19. Xie H, McHugo GJ, Fox MB, Drake RE. Substance abuse relapse in a ten-year prospective follow-up of clients with mental and substance use disorders. Psychiatr Serv 2005;56:1282-7.
20. Derogatis LR, Rickels K, Rock AF. The SCL-90 and the MMPI: a step in the validation of a new self-report scale. Br J Psychiatry 1976;128:280-9.
21. Choi KR, Briggs EC, Seng JS, Graham-Bermann SA, Munro-Kramer ML, Ford JD. Service usage typologies in a clinical sample of trauma-exposed adolescents: a latent class analysis. Psychol Trauma 2018;10:652-61.
22. Choi KR, Kim D, Jang EY, Bae H, Kim SH. Reliability and validity of the Korean version of the lifetime stressor checklist-revised in psychiatric outpatients with anxiety or depressive disorders. Yonsei Med J 2017;58:226-33.
23. Hung CT, Taylor RB, Paterson N. The analysis of tricyclic antidepressant drugs at therapeutic blood levels by reversed-phase high-performance liquid chromatography using pairing and organic counter-ions. J Pharm Biomed Anal 1983;1:73-82.
24. Steuwe C, Berg M, Driessen M, Beblo T. Impact of therapist change after initial contact and traumatic burden on dropout in a naturalistic sample of inpatients with borderline pathology receiving dialectical behavior therapy. Borderline Personal Disord Emot Dysregul 2017;4:14.
25. Kim D, Park SC, Yang H, Oh DH. Reliability and validity of the Korean version of the childhood trauma questionnaire-short form for psychiatric outpatients. Psychiatry Investig 2011;8:305-11.
26. Taillieu TL, Brownridge DA, Sareen J, Afifi TO. Childhood emotional maltreatment and mental disorders: results from a nationally representative adult sample from the United States. Child Abuse Negl 2016;59:1-12.
27. Scott-Storey K. Cumulative abuse: do things add up? An evaluation of the conceptualization, operationalization, and methodological approaches in the study of the phenomenon of cumulative abuse. Trauma Violence Abuse 2011;12:135-50.
28. Briere J, Agee E, Dietrich A. Cumulative trauma and current posttraumatic stress disorder status in general population and inmate samples. Psychol Trauma 2016;8:439-46.
29. Widom CS, Frank H. The intergenerational transmission of violence. New York: Harry Frank Guggenheim Foundation; 1989.
30. Finkelhor D, Shattuck A, Turner H, Hamby S. A revised inventory of Adverse Childhood Experiences. Child Abuse Negl 2015;48:13-21.
31. Dong M, Anda RF, Felitti VJ, Dube SR, Williamson DF, Thompson TJ, et al. The interrelatedness of multiple forms of childhood abuse, neglect, and household dysfunction. Child Abuse Negl 2004;28:771-84.
32. Russell D, Springer KW, Greenfield EA. Witnessing domestic abuse in childhood as an independent risk factor for depressive symptoms in young adulthood. Child Abuse Negl 2010;34:448-53.
33. Kulkarni MR, Graham-Bermann S, Rauch SA, Seng J. Witnessing versus experiencing direct violence in childhood as correlates of adulthood PTSD. J Interpers Violence 2011;26:1264-81.
34. Kounou KB, Bui E, Dassa KS, Hinton D, Fischer L, Djassoa G, et al. Childhood trauma, personality disorders symptoms and current major depressive disorder in Togo. Soc Psychiatry Psychiatr Epidemiol 2013;48:1095-103.
35. Wise LA, Zierler S, Krieger N, Harlow BL. Adult onset of major depressive disorder in relation to early life violent victimisation: a case-control study. Lancet 2001;358:881-7.
36. Hovens JG, Giltay EJ, Wiersma JE, Spinhoven P, Penninx BW, Zitman FG. Impact of childhood life events and trauma on the course of depressive and anxiety disorders. Acta Psychiatr Scand 2012;126:198-207.
37. Carter JC, Bewell C, Blackmore E, Woodside DB. The im-

pact of childhood sexual abuse in anorexia nervosa. Child Abuse Negl 2006;30:257-69.
38. Mahon J, Bradley SN, Harvey PK, Winston AP, Palmer RL. Childhood trauma has dose-effect relationship with dropping out from psychotherapeutic treatment for bulimia nervosa: a replication. Int J Eat Disord 2001;30:138-48.
39. Gerdner A, Allgulander C. Psychometric properties of the Swedish version of the Childhood Trauma Questionnaire-Short Form (CTQ-SF). Nord J Psychiatry 2009;63:160-70.
40. Keller SM, Zoellner LA, Feeny NC. Understanding factors associated with early therapeutic alliance in PTSD treatment: adherence, childhood sexual abuse history, and social support. J Consult Clin Psychol 2010;78:974-9.
41. Lecomte T, Spidel A, Leclerc C, MacEwan GW, Greaves C, Bentall RP. Predictors and profiles of treatment non-adherence and engagement in services problems in early psychosis. Schizophr Res 2008;102:295-302.
42. Miniati M, Rucci P, Benvenuti A, Frank E, Buttenfield J, Giorgi G, et al. Clinical characteristics and treatment outcome of depression in patients with and without a history of emotional and physical abuse. J Psychiatr Res 2010;44:302-9.
43. Hung CI. Factors predicting adherence to antidepressant treatment. Curr Opin Psychiatry 2014;27:344-9.
44. Klein DN, Arnow BA, Barkin JL, Dowling F, Kocsis JH, Leon AC, et al. Early adversity in chronic depression: clinical correlates and response to pharmacotherapy. Depress Anxiety 2009;26:701-10.
45. 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.
46. Tokuda T, Yoshimoto J, Shimizu Y, Okada G, Takamura M, Okamoto Y, et al. Identification of depression subtypes and relevant brain regions using a data-driven approach. Sci Rep 2018;8:14082.