Childhood Trauma and Depressive Symptoms in Type 1 Diabetes

Alec Roy, MD; Monique Roy, MD; and David Goldman, MD

Background: To examine the relationship of childhood trauma to depressive symptoms in type 1 diabetes, a chronic disease in which the frequency of depression is increased.

Method: One hundred fifty African American patients with type 1 diabetes seen between August 1993 and January 1998 completed the Beck Depression Inventory and Childhood Trauma Questionnaire. They were also genotyped for a functional serotonin transporter promoter polymorphism (*5-HTTLPR*) that modulates resiliency. Patients who had Beck Depression Inventory scores above and below 14 were compared.

Results: Diabetic patients who had Beck Depression Inventory scores ≥ 14 had experienced significantly more different types of childhood trauma than those with Beck Depression Inventory scores < 14 ($P < .001$), independent of potential interaction with *5-HTTLPR* genotype.

Conclusions: Childhood trauma appears to be a determinant of depressive symptoms in type 1 diabetes, independently of genotype of a functional locus modulating resiliency.

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Corresponding author: *Alec Roy, MD, Psychiatry Service (116A), Department of Veterans Affairs, NJHCS, 385 Tremont Ave, East Orange, NJ 07018 (Alec.Roy@va.gov).*

Depression is a common and important problem among persons with type 1 diabetes.[1–4] For example, Lustman et al[4] reported that 23.6% of a group of type 1 diabetic patients met *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition (*DSM-III*) criteria for major depression. Similarly, Popkin et al[5,6] found that 25% and 24% of early onset type 1 diabetic inpatients and long-standing type 1 diabetics met *DSM-III* criteria for major depression. Depression in diabetics is important not only because it is frequent and because of the suffering it causes but also because it is a risk factor for poor glycemic control and retinopathy.[4]

The etiology of depression is multifactorial. In recent years, the developmental effect of childhood trauma has been well established as a risk factor for depression. For example, MacMillan et al[7] in a community study in Ontario reported that women who had experienced childhood physical or sexual abuse had significantly higher rates of depression. Other epidemiologic and clinical studies have similarly shown that childhood trauma is associated with the development of depression.[8] In their study, Bernet and Stein[8] administered the Childhood Trauma Questionnaire (CTQ) to 47 depressed patients and 41 healthy controls and reported that the depressed patients had significantly higher CTQ scores for emotional abuse, emotional neglect, and physical abuse. Interestingly, for the issue of comorbid depression in diabetics, Levitan et al[9] reported a marked association of childhood trauma with comorbid depression and anxiety.

Interaction between a functional serotonin transporter promoter polymorphism (*5-HTTLPR*) and stressful life events has been reported in depression. This appears to represent an effect of this locus on emotional response and resiliency, as has been shown via neuroimaging studies revealing altered amygdala fMRI response to emotional probes[10] and altered connectivity between the amygdala and brain regions that modulate amygdala response,[11,12] with that connectivity predicting depressive symptoms.[12] Caspi et al[13] found that individuals who had the *5-HTTLPR* S allele and had also experienced childhood trauma or stressful life events after 21 years of age had an increase in depressive symptoms, whereas the l/l homozygotes did not. Since that publication, additional replications and extensions of this finding have been published as well as studies that have failed to confirm these findings.[14–22] A recent meta-analysis[23] found no significant association between *5-HTTLPR* genotype and depression and no interaction between genotype and recent stressful life events and depression.

There has been a dearth of studies of depression among African Americans with diabetes.[24] Therefore, as we had access to a medical clinic for African Americans with type 1 diabetes, it was decided to further examine depression, and the relationship of childhood trauma to depression in African American diabetics. In order to do this, we administered the CTQ and Beck Depression Inventory (BDI) to 150 African American type 1 diabetics who were also genotyped for *5-HTTLPR*. The hypothesis tested was that childhood trauma would be associated with depressive symptoms in African American type 1 diabetic patients, despite the fact that all type 1 diabetes patients can be considered as having had a significant stress exposure in the form of this chronic disease.

METHOD

Subjects were a consecutive series of 150 type 1 diabetic African Americans seen between August 1993 and January 1998 in a medical clinic at New Jersey Medical School, Newark. All patients had been diagnosed with diabetes and treated with insulin before 30 years of age, were currently on insulin, were African American, and were aged more than 18 years. Excluded were patients with type 2 diabetes; those diagnosed after age 30 years, whether on insulin or not; and patients with maturity-onset diabetes of youth. As it was considered inappropriate to administer the CTQ to minors, those under 18 years of age were excluded. All

Table 1. Characteristics of the 150 African Americans With Type 1 Diabetes[a]

Characteristic	
Age, mean (SD), y	29.5 (10.1)
Duration of diabetes mellitus, mean (SD), y	11.1 (8.9)
Sex	
Male	64 (42.4)
Female	86 (57.0)
Socioeconomic status	
Middle-high	60 (40.0)
Low	90 (60.0)
Beck Depression Inventory score ≥ 14	35 (23.3)
No. of types of childhood trauma	
None	42 (27.8)
1	42 (27.8)
2	26 (17.2)
3	24 (15.9)
4–5	17 (11.3)
5-HT promoter	
L_AL_A	42 (28.0)
L_AL_G	38 (25.2)
L_GL_G	15 (9.9)
L_AS	28 (18.5)
L_GS	18 (11.9)
SS	9 (6.0)

[a]Data shown as n (%) unless otherwise noted.

Table 2. Relationship Between Childhood Trauma and Depressive Symptoms[a]

No. of Types of Childhood Trauma	Beck Depression Inventory Score < 14 (n = 115), n (%)	Beck Depression Inventory Score ≥ 14 (n = 35), n (%)
0	40 (34.8)	2 (5.7)
1	36 (31.3)	6 (17.1)
2	16 (13.9)	9 (25.8)
3	13 (11.3)	11 (31.4)
4–5	10 (8.7)	7 (20.0)

[a]Depressed patients had experienced significantly more types of trauma ($P < .001$).

Table 3. Relationship Between *5-HTTLPR* Genotypes and Depressive Symptoms[a]

Triallelic Genotype	Beck Depression Inventory Score < 14 (n = 115), n (%)	Beck Depression Inventory Score ≥ 14 (n = 35), n (%)
SS	8 (7.0)	1 (2.9)
L_GS	12 (10.4)	6 (17.1)
L_AS	24 (20.9)	4 (11.4)
L_GL_G	13 (11.3)	2 (5.7)
L_AL_G	29 (25.2)	8 (22.9)
L_AL_A	29 (25.2)	14 (40.0)

[a]No significant differences were found.

subjects signed informed consent statements, and the study was approved by the institutional review board at the New Jersey Medical School.

Structured Interview

A structured clinical interview was conducted by a physician to determine the patients' sociodemographic and medical history. The information from the patients was supplemented by collateral information from medical records and from previous treating professionals. Patients' socioeconomic statuses were classified from the Goldthorpe and Hope[25] classification of occupations into middle-high (level 1–22) and lower (level 23–36) class, using the occupations of the heads of the households.

The patients completed the CTQ and BDI.[26–30] The CTQ 24-item version yields scores for 5 traumas experienced in childhood: physical abuse, physical neglect, emotional abuse, emotional neglect, and sexual abuse. Reliability and validity of the CTQ have been demonstrated, including in African Americans.[31] Childhood Trauma Questionnaire scores for each of the 5 traumas range from 5 to 25. The BDI is a 21-item inventory measuring depressive symptoms. Patients who scored 14 or above on the BDI were classified as depressed. We had used this cutoff previously to differentiate depressed and nondepressed diabetics, and this cutoff has been found to have high predictive value for screening depressive disorder in diabetics.[32,33]

Patients were also genotyped for *5-HTTLPR*. Genomic DNA was extracted from blood drawn at the examination. In addition to the L and S functional alleles, which differ by 2 copies of an imperfect 20–23 bp repeat sequence, a third functional *5-HTTLPR* allele formed by an A>G SNP that almost always occurs within the L allele is relatively common in European Americans (0.09–0.15) and still more abundant in African American populations (0.24). This L_G allele is associated with a low rate of HTT transcription, such that this L_G allele is functionally similar to the S allele.[34] Genotyping of *5-HTTLPR* for S, L_G, and L_A alleles was performed using a 2-stage 5′ exonuclease assay, as described by Hu et al.[34] The high expressing L allele is L_A. The 2 functionally equivalent low expressing alleles are L_G and S. Population stratification was examined with 186 ancestry informative markers.

In the statistical analyses, the number of types of childhood trauma reaching criteria on the CTQ and six *5-HTTLPR* genotypes, based on function, were examined in relation to BDI scores above or below 14 by the χ^2 test. Because of power considerations, we also compared 2 groups—a low expression group defined as SS or SL_G, and high expression group composed of all the other 4 genotypes. Finally, the main effects and interaction of CTQ scores and the 2-category genotype grouping on depression were evaluated by logistic regression.

RESULTS

The socioeconomic, clinical, CTQ, and *5-HTTLPR* data of the 150 type 1 African American diabetics are shown in Table 1. Thirty-five of the 150 patients (23.3%) had a BDI score ≥ 14.

On the CTQ, the depressed diabetic patients (n = 35) had experienced significantly more types of childhood trauma than the nondepressed diabetics (n = 115; $P < .001$; Table 2).

There was no significant difference in the distribution of the 6 triallelic *5-HTTLPR* genotypes between the depressed and nondepressed diabetics (Table 3). Similarly, there was no significant difference between the depressed and nondepressed diabetics for the low expression (20% vs 17.4%) or high

expression (80% vs 82.6%) *5-HTTLPR* genotypes. Logistic regression revealed no significant interaction between total CTQ scores and *5-HTTLPR* genotype in relation to BDI scores (odds ratio = 1.13; 95% CI, 0.09–13.54; $P = .92$).

DISCUSSION

The first finding in the present study was that 35 of the 150 (23.3%) type 1 diabetic patients had a BDI score of 14 or greater. This high percentage of patients with meaningful depression scores on the BDI is very similar to the approximately one-quarter of type 1 diabetics reported to have depressive symptoms in previous studies and reflects that type 1 diabetes is a disorder associated with a raised risk of having depressive symptoms.[3,6,33] The second and novel finding of the present study is that childhood trauma, but not *5-HTTLPR* genotype, was significantly associated with depressive symptoms in the diabetics. In fact, 20% of the diabetics with BDI scores ≥ 14 had experienced 4 or 5 types of childhood trauma compared with 8.7% of the diabetics with BDI scores below 14.

The significant association of childhood trauma with BDI scores ≥ 14 in the type 1 diabetics is in accordance with the large literature showing that childhood trauma plays a role in the etiology of depression.[8] Furthermore, a dose-response relationship between childhood adversities and depression was reported among health maintenance organization attendees in the Adverse Childhood Experiences study.[35,36] The adjusted prevalence of depression was increased 2 to 3 times among health maintenance organization attendees who reported having experienced 4 or more types of adverse childhood experience when compared with patients who had experienced none. Similarly, in the present study, there was a marked difference in the percentage of diabetics with BDI scores ≥ 14 found among those who had experienced 4 or more types of childhood trauma compared to those who had experienced none (41.2% vs 4.8%). Our findings suggest the possibility that ascertainment of history of childhood trauma may be useful in evaluating the risk for diabetics to develop depressive symptoms and thus have a raised risk of poor medication adherence and complications.[37]

Childhood trauma may play a role in the development of depressive symptoms in diabetics in several ways. First, childhood trauma may play a role in the development of other Axis I and II psychiatric disorders, disorders that are often comorbidly associated with depression and frequently found in diabetics.[8,38] Second, childhood trauma may have an enduring impact on neurobiological systems that are involved in the pathophysiology of depression; for example, dysregulation of the hypothalamic-pituitary-adrenal axis, which is found in diabetics.[39–44] Third, childhood trauma may impact brain structures that may moderate response to life events, and depressed diabetics have been shown to have focal subcortical biophysical abnormalities in the head of the caudate nucleus and high prefrontal glutamate levels.[45–49] Fourth, childhood trauma may play a role in the development of neuroticism and hostility—personality dimensions known to be predisposing to depression.[38,50] Fifth, having experienced childhood trauma has been shown to impact an individual's coping strategies and ability to manage stress, and depressed diabetics have often experienced an excess of adverse life events.[51] Sixth, childhood trauma may interact with genes to amplify the risk of depression.[52] However, no significant interaction was found between CTQ scores and *5-HTTLPR* genotype, and there was no main effect of genotype. The study was underpowered, and other 5-HTT polymorphisms were not examined, but the negative findings are in accordance with a meta-analysis that found no evidence that the serotonin transporter alone, or in interaction with stressful life events, is associated with depression.[23,53,54]

Strengths of the present study include that a homogeneous sample of only type 1 diabetic patients was studied; that depressive symptoms were studied, as they are associated with poor medication adherence and complications in type 1 diabetes; and that all the subjects studied were African Americans, a high-risk group known to have a higher prevalence of poor glycemic control and diabetic complications.[37] Limitations include that this was a sample of convenience, that the self-report BDI measurement of depressive symptoms was used rather than a structured psychiatric interview. However, the BDI has been used extensively to measure symptoms of depression in diabetes and other medical disorders.[32] The BDI cutoff score of 14 used here has been found to have high predictive value as a screening instrument for depressive disorders in both the general population and in diabetics.[32,55] Other limitations were that we had no measure of hypothalamic-pituitary-adrenal axis function and that the childhood trauma data were derived from a self-report questionnaire. However, the CTQ has been shown to have high reliability and validity.[26–29,31,56] Furthermore, both Bifulco et al[57] and Goodman et al[58] observed good reliability in the reporting of childhood trauma. Also, Fergusson et al[59] reported an almost uniform absence of association between reports of childhood abuse and psychiatric measures, consistent with previous studies showing that the reporting of childhood trauma in not influenced by psychiatric state at the time of reporting. Population stratification was examined with 186 ancestry informative markers and found not to be a significant factor.[60]

In summary, as far as we are aware, this is the first study reporting a relationship between childhood trauma and depressive symptoms in type 1 diabetic patients. This finding is of interest as data from the US National Comorbidity Survey Replication[61] show that the estimated attributable fractions for psychiatric disorders attributed to having experienced any adverse childhood event ranged from 22% to 32% among women and 20%–24% among men. The authors conclusion that prevention efforts to reduce exposure to adverse childhood events could substantially reduce the prevalence of psychopathology in the general population might well also apply to diabetics and patients with other medical disorders.

Author affiliations: Psychiatry Service, New Jersey Veterans Affairs Health Care System, East Orange (Dr A. Roy); Department of Ophthalmology, University of Medicine and Dentistry of New Jersey Medical School, Newark (Dr M. Roy); and Laboratory of Neurogenetics, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Rockville, Maryland (Dr Goldman).
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REFERENCES

1. Carney C. Diabetes mellitus and major depressive disorder: an overview of prevalence, complications, and treatment. *Depress Anxiety.* 1998;7(4):149–157.
2. Lustman PJ, Anderson RJ, Freedland KE, et al. Depression and poor glycemic control: a meta-analytic review of the literature. *Diabetes Care.* 2000;23(7):934–942.
3. Musselman DL, Betan E, Larsen H, et al. Relationship of depression to diabetes types 1 and 2: epidemiology, biology, and treatment. *Biol Psychiatry.* 2003;54(3):317–329.
4. Lustman PJ, Griffith LS, Clouse RE, et al. Psychiatric illness in diabetes mellitus. Relationship to symptoms and glucose control. *J Nerv Ment Dis.* 1986;174(12):736–742.
5. Popkin MK, Callies AL, Lentz RD, et al. Prevalence of major depression, simple phobia, and other psychiatric disorders in patients with long-standing type I diabetes mellitus. *Arch Gen Psychiatry.* 1988;45(1):64–68.
6. Popkin MK, Callies AL. Psychiatric consultation to inpatients with 'early-onset' type I diabetes mellitus in a university hospital. *Arch Gen Psychiatry.* 1987;44(2):169–171.
7. MacMillan HL, Fleming JE, Streiner DL, et al. Childhood abuse and lifetime psychopathology in a community sample. *Am J Psychiatry.* 2001;158(11):1878–1883.
8. Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. *Depress Anxiety.* 1999;9(4):169–174.
9. Levitan RD, Rector NA, Sheldon T, et al. Childhood adversities associated with major depression and/or anxiety disorders in a community sample of Ontario: issues of co-morbidity and specificity. *Depress Anxiety.* 2003;17(1):34–42.
10. Hariri AR, Mattay VS, Tessitore A, et al. Serotonin transporter genetic variation and the response of the human amygdala. *Science.* 2002;297(5580):400–403.
11. Heinz A, Jones DW, Mazzanti C, et al. A relationship between serotonin transporter genotype and in vivo protein expression and alcohol neurotoxicity. *Biol Psychiatry.* 2000;47(7):643–649.
12. Pezawas L, Meyer-Lindenberg A, Drabant EM, et al. 5-HTTLPR polymorphism impacts human cingulate-amygdala interactions: a genetic susceptibility mechanism for depression. *Nat Neurosci.* 2005;8(6):828–834.
13. Caspi A, Sugden K, Moffitt TE, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science.* 2003;301(5631):386–389.
14. Eley TC, Sugden K, Corsico A, et al. Gene-environment interaction analysis of serotonin system markers with adolescent depression. *Mol Psychiatry.* 2004;9(10):908–915.
15. Kendler KS, Kuhn JW, Vittum J, et al. The interaction of stressful life events and a serotonin transporter polymorphism in the prediction of episodes of major depression: a replication. *Arch Gen Psychiatry.* 2005;62(5):529–535.
16. Kaufman J, Yang B-Z, Douglas-Palumberi H, et al. Social supports and serotonin transporter gene moderate depression in maltreated children. *Proc Natl Acad Sci U S A.* 2004;101(49):17316–17321.
17. Kaufman J, Yang BZ, Douglas-Palumberi H, et al. Brain-derived neurotrophic factor-5-HTTLPR gene interactions and environmental modifiers of depression in children. *Biol Psychiatry.* 2006;59(8):673–680.
18. Gillespie NA, Whitfield JB, Williams B, et al. The relationship between stressful life events, the serotonin transporter (5-HTTLPR) genotype and major depression. *Psychol Med.* 2005;35(1):101–111.
19. Wilhelm K, Mitchell PB, Niven H, et al. Life events, first depression onset and the serotonin transporter gene. *Br J Psychiatry.* 2006;188(3):210–215.
20. Zalsman G, Huang YY, Oquendo MA, et al. Association of a triallelic serotonin transporter gene promoter region (5-HTTLPR) polymorphism with stressful life events and severity of depression. *Am J Psychiatry.* 2006;163(9):1588–1593.
21. Surtees PG, Wainwright NW, Willis-Owen SA, et al. Social adversity, the serotonin transporter (5-HTTLPR) polymorphism and major depressive disorder. *Biol Psychiatry.* 2006;59(3):224–229.
22. Cervilla JA, Molina E, Rivera M, et al; PREDICT Study Core Group. The risk for depression conferred by stressful life events is modified by variation at the serotonin transporter 5HTTLPR genotype: evidence from the Spanish PREDICT-Gene cohort. *Mol Psychiatry.* 2007;12(8):748–755.
23. Risch N, Herrell R, Lehner T, et al. Interaction between the serotonin transporter gene (5-HTTLPR), stressful life events, and risk of depression: a meta-analysis. *JAMA.* 2009;301(23):2462–2471.
24. de Groot M, Lustman PJ. Depression among African-Americans with diabetes: a dearth of studies. *Diabetes Care.* 2001;24(2):407–408.
25. Goldthorpe J, Hope K. *The Social Grading of Occupations: A New Approach and Scale*. New York, NY: Oxford University Press; 1974:134–143.
26. Bernstein DP, Ahluvalia T, Pogge D, et al. Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population. *J Am Acad Child Adolesc Psychiatry.* 1997;36(3):340–348.
27. Bernstein DP, Fink L, Handelsman L, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *Am J Psychiatry.* 1994;151(8):1132–1136.
28. Bernstein D, Fink L. *Childhood Trauma Questionnaire: A Retrospective Self-Report Manual*. San Antonio, TX: The Psychological Corporation; 1998.
29. Bernstein DP, Stein JA, Newcomb MD, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl.* 2003;27(2):169–190.
30. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. *Arch Gen Psychiatry.* 1961;4:561–571.
31. Scher CD, Stein MB, Asmundson GJ, et al. The childhood trauma questionnaire in a community sample: psychometric properties and normative data. *J Trauma Stress.* 2001;14(4):843–857.
32. Lustman PJ, Clouse RE, Griffith LS, et al. Screening for depression in diabetes using the Beck Depression Inventory. *Psychosom Med.* 1997;59(1):24–31.
33. Roy A, Roy M. Depressive symptoms in African-American type 1 diabetics. *Depress Anxiety.* 2001;13(1):28–31.
34. Hu XZ, Lipsky RH, Zhu G, et al. Serotonin transporter promoter gain-of-function genotypes are linked to obsessive-compulsive disorder. *Am J Hum Genet.* 2006;78(5):815–826.
35. Anda RF, Felitti VJ, Bremner JD, et al. The enduring effects of abuse and related adverse experiences in childhood: a convergence of evidence from neurobiology and epidemiology. *Eur Arch Psychiatry Clin Neurosci.* 2006;256(3):174–186.
36. Chapman DP, Whitfield CL, Felitti VJ, et al. Adverse childhood experiences and the risk of depressive disorders in adulthood. *J Affect Disord.* 2004;82(2):217–225.
37. Roy MS, Roy A, Affouf M. Depression is a risk factor for poor glycemic control and retinopathy in African-Americans with type 1 diabetes. *Psychosom Med.* 2007;69(6):537–542.
38. Johnson JG, Cohen P, Brown J, et al. Childhood maltreatment increases risk for personality disorders during early adulthood. *Arch Gen Psychiatry.* 1999;56(7):600–606.
39. Heim C, Plotsky PM, Nemeroff CB. Importance of studying the contributions of early adverse experience to neurobiological findings in depression. *Neuropsychopharmacology.* 2004;29(4):641–648.
40. Roy M, Collier B, Roy A. Hypothalamic-pituitary-adrenal axis dysregulation among diabetic outpatients. *Psychiatry Res.* 1990;31(1):31–37.
41. Roy MS, Roy A, Gallucci WT, et al. The ovine corticotropin-releasing hormone-stimulation test in type I diabetic patients and controls: suggestion of mild chronic hypercortisolism. *Metabolism.* 1993;42(6):696–700.
42. Roy MS, Roy A, Brown S. Increased urinary-free cortisol outputs in diabetic patients. *J Diabetes Complications.* 1998;12(1):24–27.
43. Nemeroff C. Neurobiological consequences of childhood trauma. *J Clin Psychiatry*. 2004;65(suppl 1):18–28.
44. Gotlib IH, Joormann J, Minor KL, et al. HPA axis reactivity: a mechanism underlying the associations among 5-HTTLPR, stress, and depression. *Biol Psychiatry.* 2008;63(9):847–851.
45. Bremner JD. Long-term effects of childhood abuse on brain and neurobiology. *Child Adolesc Psychiatr Clin N Am.* 2003;12(2):271–292.
46. Bennett AJ, Lesch KP, Heils A, et al. Early experience and serotonin transporter gene variation interact to influence primate CNS function. *Mol Psychiatry.* 2002;7(1):118–122.
47. Spinelli S, Chefer S, Suomi SJ, et al. Early-life stress induces long-term morphologic changes in primate brain. *Arch Gen Psychiatry.* 2009;66(6):658–665.
48. Kumar A, Gupta R, Thomas A, et al. Focal subcortical biophysical abnormalities in patients diagnosed with type 2 diabetes and depression.

Arch Gen Psychiatry. 2009;66(3):324–330.
49. Lyoo IK, Yoon SJ, Musen G, et al. Altered prefrontal glutamate-glutamine-gamma-aminobutyric acid levels and relation to low cognitive performance and depressive symptoms in type 1 diabetes mellitus. *Arch Gen Psychiatry.* 2009;66(8):878–887.
50. Roy A. Childhood trauma and neuroticism as an adult: possible implication for the development of the common psychiatric disorders and suicidal behaviour. *Psychol Med.* 2002;32(8):1471–1474.
51. Roy M, Collier B, Roy A. Excess of depressive symptoms and life events among diabetics. *Compr Psychiatry.* 1994;35(2):129–131.
52. Wichers M, Kenis G, Jacobs N, et al. The BDNF Val(66) Met × 5-HTTLPR × child adversity interaction and depressive symptoms: an attempt at replication. *Am J Med Genet B Neuropsychiatr Genet.* 2008;147B(1):120–123.
53. Lazary J, Lazary A, Gonda X, et al. New evidence for the association of the serotonin transporter gene (SLC6A4) haplotypes, threatening life events, and depressive phenotype. *Biol Psychiatry.* 2008;64(6):498–504.
54. Munafò MR, Durrant C, Lewis G, et al. Gene X environment interactions at the serotonin transporter locus. *Biol Psychiatry.* 2009;65(3):211–219.
55. Lasa L, Ayuso-Mateos JL, Vázquez-Barquero JL, et al. The use of the Beck Depression Inventory to screen for depression in the general population: a preliminary analysis. *J Affect Disord.* 2000;57(1–3):261–265.
56. Thombs BD, Lewis C, Bernstein DP, et al. An evaluation of the measurement equivalence of the Childhood Trauma Questionnaire—Short Form across gender and race in a sample of drug-abusing adults. *J Psychosom Res.* 2007;63(4):391–398.
57. Bifulco A, Brown GW, Lillie A, et al. Memories of childhood neglect and abuse: corroboration in a series of sisters. *J Child Psychol Psychiatry.* 1997;38(3):365–374.
58. Goodman LA, Thompson KM, Weinfurt K, et al. Reliability of reports of violent victimization and posttraumatic stress disorder among men and women with serious mental illness. *J Trauma Stress.* 1999;12(4):587–599.
59. Fergusson DM, Horwood LJ, Woodward LJ. The stability of child abuse reports: a longitudinal study of the reporting behaviour of young adults. *Psychol Med.* 2000;30(3):529–544.
60. Roy A, Hu XZ, Janal MN, et al. Interaction between childhood trauma and serotonin transporter gene variation in suicide. *Neuropsychopharmacology.* 2007;32(9):2046–2052.
61. Afifi TO, Enns MW, Cox BJ, et al. Population attributable fractions of psychiatric disorders and suicide ideation and attempts associated with adverse childhood experiences. *Am J Public Health.* 2008;98(5):946–952.