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Retrospective chart review-based assessment scale for adverse childhood events and experiences

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Abstract

Aim: Adverse childhood experiences (ACEs) are highly prevalent in the general population, and their lifelong impact on physical and mental health is profound. In assessing ACEs, it is vital to consider the pathways and modalities by which an individual internalizes events as an adverse experience and its effects on their biological, psychological, and social function. However, conventional assessments of ACEs are inadequate in that they do not comprehensively assess the source of the adverse event and the pathway and mode of its impact on the individual.

Methods: This study developed an original scale for ACEs that classifies the source of the event and the pathway and mode of its impact on the individual from a retrospective review of medical charts. We also used this scale to investigate the ACEs in 536 patients with psychiatric disorders (depression, bipolar disorder, and schizophrenia).

Results: This scale consisted of 28 items, and its reliability and validity were sufficient. We also found that 45.9% of the patients studied had at least one ACE, ranging from 43.5% to 51.5% for all disorders. Psychological trauma (bullying) from peers was the most common cause at 27.2%.

Conclusion: We developed a retrospective chart review-based assessment tool for ACEs which enables the examination of the source of the events of ACEs and the pathways and modalities of their impact on the individual. The frequency of ACEs is high

regardless of the type of psychiatric disorder, and horizontal trauma (bullying victimization) is as frequent as vertical trauma (parental maltreatment).

KEYWORDS
adverse childhood experiences, assessment scale, bullying victimization, maltreatment, retrospective chart review

INTRODUCTION

Adverse childhood experiences (ACEs) are traumatic events experienced under the age of 18 years. Examples include violence, abuse, neglect, witnessing domestic or community violence, and a family member's suicide. The functional aspects of the environment and the home where a child lives are also included in ACEs and can include substance abuse, mental health issues, separation from one's parents, and familial incarceration.[1]

Several studies have demonstrated that ACEs increase the risk of developing mental illness and symptom formation, increase the prevalence of physical illness, lead to premature death, have a significant impact on an individual's long-term life, and reportedly affect the development of the next generation.[2–8] A WHO study reported that more than one-third of the population experience ACEs.[9] In a survey conducted in the United States between 2015 and 2017, 60.9% of those surveyed experienced at least one type of ACE[10] and were associated with major depressive disorder,[11,12] bipolar disorder,[13–15] or schizophrenia.[16] A study of 229 patients with depression, 102 patients with bipolar disorder, 216 patients with schizophrenia, and 132 healthy individuals found that 55.5% of patients with depression, 61.8% of patients with bipolar disorder, 47.2% of patients with schizophrenia, and 20.5% of healthy individuals experienced at least one type of ACE. The most-reported ACE types in the patient group were physical neglect and emotional neglect, and the least reported were sexual and physical abuse.[17] In a study of 83 individuals with major depressive disorder, 74 with bipolar disorder, 91 with schizophrenia spectrum disorders, and 85 healthy individuals, the absence, loss, and financial difficulties of young mothers were more prevalent among the group with bipolar disorder, whereas abuse of cannabis, psychological abuse, physical abuse, and loneliness were more common in the schizophrenia spectrum disorder group.[18]

In Japan, a study using the World Mental Health Japan Survey showed that the risk of depression and anxiety disorder increases with ACEs. Unlike the United States, the predictive influence of ACEs in Japan was found only among childhood-onset mental disorders but not among those with adulthood onset.[19] Moreover, the effects of ACEs extend into older age.[20,21]

ACEs affect mental health predicaments such as risk factors for mental illness and modifiers of pathological conditions, and a wide range of human health outcomes. Counteracting ACEs and prevention are essential international health concern. Individual traumatic experiences are a result of a combination of events and situations. These are experienced as physically or emotionally harmful (sometimes life-threatening) and are defined as having a long-term negative effect on an individual's functional, mental, physical, social, emotional, and spiritual welfare.[22] To formulate effective countermeasures against ACEs, it is crucial to consider the kind of event that occurred when evaluating them and how the individual perceived that event.

The effects of psychological stress on mental function were first noticed as “shell shock” and post-traumatic stress disorder (PTSD) in war veterans. As a result, the definition of traumatic events was limited to fatal trauma or witnessing death, therefore the objectiveness of the event was thought to be essential. Following this, a trailblazing study called the Adverse Childhood Experiences Study (ACE study), conducted from 1995 to 1997 by the Centers for Disease Control and Prevention and Kaiser Permanente, re-focused attention toward ACEs themselves.[23] This study examined the relationship between the presence or absence of ACEs experienced before the age of 18 and physical and mental health and social adaptation in adulthood. A questionnaire (Adverse Childhood Experiences Score, ACE Score) that classifies ACEs into 10 items was used; if an ACE was present, 1 point was given (maximum 10 points). In addition to the content of individual ACEs, the study focused on cumulative ACEs, meaning the effect of having multiple ACEs. More than half of the respondents chose at least two ACEs. This indicated that ACEs were not exceptional events but a familiar problem that could occur in any household. The ACE Score has been translated into multiple languages; a Japanese version was created by Tsuboi in 2014, and its validity and reliability have been demonstrated.[24]

The question items of the ACE Score are separated into psychological, physical, sexual, and familial dysfunction (mental illness, witnessing violence against one's mother, criminal acts in the house, etc.). The questionnaire assesses whether events of various types occur in an individual's life. However, it does not go as far as to determine how they were experienced. Furthermore, the World Health Organization (WHO) has developed the Adverse Childhood Experiences International Questionnaire (ACE-IQ), which contains questions on inappropriate or inadequate care and familial dysfunction during childhood and questions on extrafamilial violence.[25] Surveys using this questionnaire have been conducted[26]; however, the ACE-IQ fails to assess how individuals experienced the ACEs that they reported.

Existing questionnaires such as the ACE Score and ACE-IQ do not signify whether the source of ACE is interpersonal. Furthermore, within interpersonal relationships, they fail to determine whether the source involved the individual's parents (vertical relationship), peers (horizontal relationship), or a third party. However, from a clinical and neuroscientific standpoint, its subjective/objective significance, the source of the ACE, how it was experienced by the individual, and its impact on them are all critical considerations. In the development of the human brain and mind, bonding and attachment based on the

parent–child relationship are particularly important during childhood, and maltreatment, such as abuse, as the opposite, influences the onset of mental disorders in adulthood.[27,28] Social relationships during adolescence, such as bullying victimization and social exclusion, also increase the risk of developing mental disorders.[28] Therefore, it is important to assess the vertical and horizontal relationships of ACEs in an integrated manner.

Other instruments used to assess the ACEs include the Childhood Trauma Questionnaire (CTQ),[29] a 70-item questionnaire on physical, sexual, and emotional abuse and neglect, and its short form (CTQ-SF; 28 items),[30] and the Early Trauma Inventory (ETI), a clinician-administered, 56-item scale[31] and its self-report (ETI-SR) (62 items) and short-form (ETI-SR-SF; 27 items) versions.[32] On the other hand, no questionnaire has been developed with the intention of investigating ACEs in a retrospective survey of medical records. While questionnaires such as the ACE Score and ACE-IQ are reliable because the individual reads the questions and responds to them on his/her own, there is concern that some individuals who have experienced ACEs may recall the circumstances of the trauma against their will when asked questions that remind them of the trauma, especially in the case of those with mental disorders. As physicians/healthcare providers ask patients about their life history and the course of their illness to date, episodes that are told spontaneously are also highly reliable, and we felt that creating a tool to investigate ACEs from these medical records in a retrospective manner would be important in studying the importance of ACEs in mental disorders.

In this study, we performed the following investigations. First, we developed a scale that allows for categorizing ACEs through retrospective examination of medical records and how they were experienced by an individual. We examined the scale's reliability and validity using data collected from mental illness patients. Second, we examined the similarities and differences between ACEs in depression, bipolar disorder, and schizophrenia. In previous studies, the influence of ACEs in major depression has been the focus of early attention, followed by schizophrenia, where more emphasis has been placed on the involvement of biological factors. However, the importance of ACEs in bipolar disorder, which is also an endogenous psychiatric disorder, has not been well studied. In this study, we wanted to obtain evidence of the importance of ACEs particularly in bipolar disorder. This study aimed for the scale to serve as the beginning of an effort to establish a neurobehavioral understanding of the effects of ACEs on human psychology and behavior, and thereby on life quality, personal recovery, and growth following psychological trauma.

METHODS

Subjects

Individuals were selected to participate in the 4-day inpatient program for psychiatric diagnosis conducted by the Department of Neuropsychiatry at the University of Tokyo Hospital, between September 1, 2009 and March 31, 2019. The program targeted patients with depressive symptoms and was a hospitalization program focused on the intensive implementation of various tests that are difficult to administer during routine outpatient visits and detailed interview-based collection of medical history, and so on.

The medical conditions that fit the eligibility criteria were as follows: depressive disorder, unspecified depressive disorder, bipolar I disorder, bipolar II disorder, unspecified bipolar disorder, or schizophrenia via a psychiatric diagnostic interview (Structured Clinical Interview for DSM-IV, SCID).[33] However, a clinically experienced psychiatrist who served as attending physician during hospitalization provided diagnoses following the International Statistical Classification of Diseases and Related Health Problems (ICD-10)[34] for individuals for whom the use of SCID was problematic, those who did not receive a SCID, or those for whom the SCID did not produce a precise diagnosis.

In the present study, informed consent was obtained from 602 patients out of the total of 649 that participated in the 4-day inpatient program for psychiatric diagnosis between September 1, 2009 and March 31, 2019. Of these, 536 individuals met the eligibility criteria (Table 1). There were 356 individuals in the depression group (336 with major depressive disorder by SCID, 15 with unspecified depressive disorder by SCID, 5 with F32-33 by ICD-10), 147 in the bipolar disorder group (52 with bipolar I disorder by SCID, 80 with bipolar type II disorder by SCID, four with unspecified bipolar disorder by SCID, and 11 with F31 by ICD-10), and 33 in the schizophrenia group (25 with schizophrenia by SCID and eight with F20-29 by ICD-10) (Table 2). The remaining 66 patients were excluded because they did not meet the eligibility criteria for diagnosis.

Clinical assessments

Evaluation of intellectual function

The Japanese Adult Reading Test (JART)[35] was used to estimate premorbid intellectual function. The JART involves reading aloud 50 two- to three-character words and efficiently allows for the easy estimation of an intelligence quotient (IQ). In this study, a self-administered, shortened version of the test, consisting of 25 items, was used[36] and regression was used to estimate the premorbid IQ.

For measurement of the present intellectual function, the Wechsler Adult Intelligence Scale (WAIS) was used. The WAIS has been revised multiple times since the first publication of a Japanese version in 1950, and in this study, given the time at which study participants were tested, the WAIS-R,[37] III,[38] and IV[39] versions were used to measure the present IQ.

Depressive symptoms, manic symptoms, quality of life, and evaluation of social function

To evaluate depressive symptoms, we used a self-evaluation for depression (depressive state) (The Center for Epidemiologic Studies

TABLE 1 Demographic information of the study subjects

	All (*N* = 536)				ACEs (+) (*N* = 246)				ACEs (−) (*N* = 290)				ACEs (+) versus (−)			
	Mean	SD	Min	Max	Mean	SD	Min	Max	Mean	SD	Min	Max	*t*	d.f.	*p*	Effect size
Age (years)	38.9	12.3	16	84	37.1	11.1	17	80	40.3	13.0	16	84	3.06	534	0.002[a]	0.13
Gender (male/female)	273/263 (50.9%:49.1%)				105/141 (42.7%:57.3%)				168/122 (57.9%:42.1%)				12.38	1	0.000[b]	0.15
Years of education	14.6	2.2	9	21	14.3	2.2	9	20	15.0	2.2	9	21	3.72	534	0.000[a]	0.16
Estimated age at onset	29.6	11.9	7	78	27.9	11.2	10	78	31.0	12.2	7	78	2.79	430	0.006[a]	0.13

Abbreviations: ACEs, adverse childhood experiences; d.f., degrees of freedom; SD, standard deviation.

[a]Independent *t*-test.

[b]χ^2 test.

TABLE 2 Prevalence of ACEs across diagnostic groups

	N	ACEs (+)	ACEs (−)
Depressive disorder	356	155 (43.5%)	201 (56.5%)
Bipolar disorder	147	74 (50.3%)	73 (49.7%)
Schizophrenia	33	17 (51.5%)	16 (48.5%)
Total	536	246 (45.9%)	290 (54.1%)

Note: χ^2 test. $\chi^2 = 2.39$, d.f. = 2, $p < 0.30$.

Abbreviation: ACEs, adverse childhood experiences.

Depression Scale [CES-D],[40] the Beck Depression Inventory-Second Edition [BDI-II],[41] and the 17-item Hamilton Depression Rating Scale [HAMD17]).[42] The CES-D is a self-administered evaluation scale in which respondents answer questions about the frequency of depressive symptoms in the past week. Scores range from 0 to 60, with higher scores indicating more substantial depressive symptoms. The BDI-II is also a self-administered evaluation scale that evaluates the severity of depressive symptoms over the last 2 weeks. Scores range from 0 to 63, with higher scores indicating more substantial depressive symptoms. Self-assessment of depressive symptoms was performed using the CES-D and BDI-II following the examination time. The total BDI-II score was converted to a CES-D score using a regression equation as the estimated CES-D value (see Supporting Information S1). The HAMD17 scale evaluates the degree and frequency of depressive symptoms over the past week; scores range from 0 to 52, with higher scores indicating more substantial depressive symptoms.

To evaluate manic symptoms, we used the Young Mania Rating Scale (YMRS).[43] The YMRS is a scale for evaluating the degree and frequency of mania and was evaluated in this study for the last week. YRMS scores range from 0 to 60, with higher scores indicating more substantial mania.

To evaluate the quality of life, we used the World Health Organization Quality of Life 26 (WHO QOL-26) scale.[44] The WHO QOL-26 scale evaluates quality of life over the last 2 weeks. It consists of four domains (physical, psychological, social, and environmental) and one domain that evaluates the overall quality of life. Each domain is scored 0–5, with higher scores indicating higher quality of life.

To evaluate social functioning, we used the Global Assessment of Functioning (GAF) scale.[45] The GAF scale measures psychological, social, and occupational functioning along a virtual continuum of mental health and illness over the last week, with scores ranging from 0 to 100. The higher the score, the higher the function.

Development of an original retrospective chart review-based assessment scale for adverse childhood events and experiences, and verification of its reliability and validity

Development of an original retrospective chart review-based assessment scale for adverse childhood events and experiences

After referencing existing questionnaires, including the ACE score[23,24] and the ACE-IQ,[25] a total of four individuals—two clinically experienced psychiatrists, one clinical psychologist, and one psychiatric social worker—investigated external factors and causes of ACEs and how they were internalized.

Regarding external targets and causes of ACEs, parents (caregivers) have the most significant external influence on an individual's childhood. The influence of siblings living in the same house or area on the target individual is also substantial. As children grow older, they may be influenced by the friends and peers they spend time with at school and by adults other than family members (e.g., through regional conflicts, wars, etc.). Furthermore, regarding the effects of the social system, even medical and welfare services provided to protect the individual may act as ACEs (e.g., physical restraint practiced in the medical field or temporary protection provided at a child guidance center). Finally, regarding environmental impact, natural disasters and financial hardships may drastically alter children's lives. After considering these myriad factors, we divided the external influences and causes of ACEs into six categories. In

addition, following repeated investigations and examinations, we surmised 10 ways in which the ACEs were internalized.

Of the 60 possible combinations of the six categories of external ACE factors and the 10 routes of internalization, we created an original scale containing 28 questions corresponding to the 28 combinations we surmised might occur in the real world (Supporting Information: Appendix A [English translated version]; Supporting Information: Appendix B [original Japanese version]). The original Japanese version was used for data collection in this study. The English translated version is presented for international readers' reference, but was not tested for reliability or validity under an English-speaking environment.

Reliability of the original scale

We retrospectively investigated whether events corresponding to items in the original scale were described in patients' medical records, and if so, which items were applicable. Subsequently, to verify the inter-rater reliability of our original scale, two clinical psychologists independently investigated discharge summaries contained in the medical record information of 20 randomly selected patients, and the total concordance rate between the ratings given by two raters was examined. Furthermore, to check intra-rater reproducibility, one clinical psychologist conducted the assessment again after a month for the 20 patients.

Validity of the original scale

To verify the validity of our original scale, a clinical psychologist surveyed all 536 cases using both the ACE Score[23,24] and the original scale on independent occasions. Pearson's correlation coefficient was calculated between scores on the ACE Score and those in our original scale. Furthermore, the Japanese version of the self-administered scale, The Child Abuse and Trauma Scale (CATS[46]) (Japanese version, version 5.1.J, developed by Dr. H. Tanabe, 2006), was administered to 27 newly admitted patients (December 2019–June 2022), and Spearman's rank correlations were calculated between scores on the CATS and those on our ACEs scale. SPSS version 21 for Windows was used for statistical analyses (IBM Japan Ltd.).

Efficacy of the original scale

Prevalence of ACEs in the diagnostic groups

To verify the efficacy of our original scale, we calculated the prevalence of ACEs separately for the three diagnostic groups and performed a χ^2 test to compare the proportion of subjects with ACE(s) in each group. Furthermore, sources of events and routes of internalization of ACEs were investigated.

Comparison of each clinical variable between the group with ACE(s) and the non-ACE(s) group

We performed an independent t-test (χ^2 test for gender) between the group with one or more ACEs (group) and the non-ACEs group for differences in clinical variables. The significance level was set at $p < 0.004$ (0.05/12 multiple comparisons; Bonferroni's correction).

RESULTS

Reliability of our scale

To verify the inter-rater reliability of our original ACEs scale, two clinical psychologists independently and retrospectively investigated discharge summaries in the medical records of 20 randomly selected patients; the total concordance rate for the ratings was 80%. For intra-rater reproducibility, one clinical psychologist conducted another survey after a month or more; the test–retest concordance rate was 88%.

Validity of our scale

To verify the validity of our original ACEs scale, all cases were investigated using the ACE score, and a positive correlation was found between the original ACEs scale and the ACE Score ($r = 0.609$, $p < 0.001$). Furthermore, Spearman's rank correlations showed a significant positive association between scores on the CATS and those on our ACEs scale ($\rho = 0.563$, $p = 0.002$).

Efficacy of our scale

We conducted a retrospective survey of patients' medical records using our original scale for ACEs and found that 246 of 536 patients surveyed (45.9%) had at least one ACE. The number of individuals with at least one ACE in each group was 155 (43.5%) for the depression group, 74 (50.3%) for bipolar disorder, and 17 (51.5%) for schizophrenia. There was no significant difference in the proportion of subjects with at least one ACE between the three groups ($\chi^2 = 2.39$, d.f. = 2, $p < 0.30$) (Table 2).

Regarding sources of events and manner of internalization across all illness groups, the proportion of (horizontal-psychological [invasion]) ACEs was highest, with 146 individuals (59.3% of the 246 individuals in the ACEs group) having experiences applicable to this category. The following most common categories were as follows: 62 individuals with vertical-psychological separation (19 separations by death, 43 separations), 32 individuals with vertical-physical (violence), 28 individuals with vertical-familial (illness or imprisonment), and 27 individuals with vertical-psychological (invasion) (Table 3).

While 246 individuals had at least one relevant ACE experience, on examining how many questions each individual's experiences

applied to, we found that 150 individuals had one applicable experience, 60 individuals had two, 19 individuals had three, nine individuals had four, and eight had five.

We performed an independent *t*-test (gender was used as χ^2 test) between one or more ACE (groups) and the non-ACEs group; the average age of the ACEs group was 37.1 years and for the non-ACEs group it was 40.3 years, which is a significant difference ($t = 3.06$, d.f. = 534, $P < 0.01$, effect size 0.13). Regarding gender, the ACEs group comprised 105 males (42.7%) and 141 females (57.3%), whereas the non-ACEs group had 168 males (57.9%) and 122 females (42.1%); this was a significant difference ($\chi^2 = 12.38$, d.f. = 1, $p < 0.001$, effect size 0.15). The average number of years of education was 14.3 years for the ACEs group and 15.0 years for the nonapplicable group, again showing a significant difference ($t = 3.72$, d.f. = 534, $p < 0.01$, effect size 0.16) (Table 1).

A significant difference was observed in the WAIS-FIQ scores ($t = 3.06$, $p < 0.002$, effect size 0.13). While they did not meet the expected significance threshold of $p < 0.004$, differences were observed for CES-D scores ($t = -2.18$, $p < 0.030$, effect size 0.09), WHO QOL-26 mean ($t = 2.58$, $p < 0.010$, effect size 0.11), WHO QOL-26 physical scores ($t = 1.97$, $p < 0.049$, effect size 0.09), WHO QOL-26 social scores ($t = 2.53$, $p < 0.012$, effect size 0.11), and

TABLE 3 Prevalence of each item of ACEs across diagnostic groups

Item #	Source of the adverse event	Pathway and mode of impact on the individual	Total *N*	%	Diagnostic groups		
					Depressive disorder	Bipolar disorder	Schizophrenia
1	Vertical	Psychological (attachment)	11	2.1	8	3	0
2	Vertical	Psychological (separation)	62	11.6	42	17	3
3	Vertical	Psychological (invasion)	27	5.0	19	6	2
4	Vertical	Psychological (witness)	17	3.2	9	8	0
5	Vertical	Physical (violence)	32	6.0	16	12	4
6	Vertical	Physical (behavioral restriction)	4	0.7	2	2	0
7	Vertical	Physical (sexual)	6	1.1	2	4	0
8	Vertical	Family	28	5.2	19	9	0
9	Vertical	Environmental	3	0.6	3	0	0
10	Horizontal	Psychological (separation)	4	0.7	4	0	0
11	Horizontal	Psychological (invasion)	146	27.2	86	46	14
12	Horizontal	Psychological (witness)	1	0.2	1	0	0
13	Horizontal	Physical (violence)	21	3.9	12	6	3
14	Horizontal	Physical (sexual)	3	0.6	1	2	0
15	Third-party	Psychological (invasion)	13	2.4	11	2	0
16	Third-party	Psychological (witness)	1	0.2	1	0	0
17	Third-party	Physical (violence)	8	1.5	4	3	1
18	Third-party	Physical (behavioral restriction)	1	0.2	1	0	0
19	Third-party	Physical (sexual)	4	0.7	3	1	0
20	Third-party	Family	0	0.0	0	0	0
21	Third-party	Environmental	1	0.2	1	0	0
22	Group	Environmental	3	0.6	2	1	0
23	System	Psychological (separation)	0	0.0	0	0	0
24	System	Psychological (invasion)	3	0.6	2	1	0
25	System	Physical (violence)	3	0.6	2	1	0
26	System	Physical (behavioral restriction)	1	0.2	0	1	0
27	Environment	Environmental	0	0.0	0	0	0
28	Environment	Group	0	0.0	0	0	0

Abbreviation: ACEs, adverse childhood experiences.

WHO QOL-26 environmental scores ($t = 2.71$, $p < 0.008$, effect size 0.12) (Table 4).

DISCUSSION

After referencing tools such as the ACE score scale and the ACE-IQ, we created an original scale capable of categorizing ACEs by their source (interpersonal or not) and the type of interpersonal relationship (parental [vertical], peer [horizontal], or third-party [some other relationship]). The results of our analyses indicate the scale is reliable and valid.

By examining the ACEs and non-ACE groups using our original ACEs scale, we determined that individuals in the ACE group that developed a disorder at a younger age were more likely to be female and had fewer years of education. The results obtained in this study, using the original ACEs scale, were similar to those in other studies.

While it is known that ACEs increase an individual's risk of developing mental illness, most previous research on ACEs focused on events that occurred in the context of vertical (parent–child) relationships. However, the results of this study indicate that ACEs in horizontal (peer) relationships are the most common type across illnesses. It is already known that horizontal relationships pose risks for depression[47] and schizophrenia,[48] and evidence along these lines is emerging for bipolar disorder[49] or psychotic symptoms in bipolar disorder.[50] The results of our original scale align with these findings. While surveys of ACEs that include those occurring in horizontal relationships (bullying victimization) have been conducted, no study has investigated both vertical and horizontal relationships by the manner of internalization. The review article by Zovetti et al.[49] examined previous literature that investigated brain regions associated with childhood trauma in bipolar patients, and found hippocampus, amygdala, thalamus, and frontal lobe as relevant regions. It is possible that childhood traumatic experiences, either directly or in interaction with genetic factors, may form a vulnerability of brain regions as an intermediate phenotype and increase the risk of bipolar disorder. On the other hand, Acosta et al.[50] found an association between being bullied as childhood trauma and psychotic symptoms in bipolar disorder. Thus, it remains unclear whether a specific type of trauma is specifically involved in bipolar disorder itself, or whether it nonspecifically causes changes in brain functions such as the limbic system, frontal lobe, and hypothalamic-pituitary-adrenal axis that increase risk for mood and psychotic symptoms, thereby increasing vulnerability to various psychiatric disorders. Therefore, we believe that this study investigation is of great significance and warrants future investigations to answer the question more precisely.

On examining the association between our original ACEs scale results and an evaluation of intellectual function, we found that the WAIS-FIQ of individuals in the ACEs group was significantly lower than that for individuals in the non-ACEs group. The reason for the significant difference in the WAIS-FSIQ is unknown, although the effect size was not large (0.13). Various interpretations are possible,

TABLE 4 Comparison of clinical variables between ACEs (+) versus (−) individuals

	All ($N = 536$)		ACEs (+) ($N = 246$)		ACEs (−) ($N = 290$)		ACEs (+) versus (−)			
	Mean	SD	Mean	SD	Mean	SD	t	d.f.	p[a]	Effect size
JART IQ	106.8	9.5	106.5	9.7	107.0	9.3	0.66	527	0.512	0.03
WAIS IQ[c]	99.3	14.8	97.1	14.4	101.1	14.9	3.06	527	0.002[b]	0.13
CES-D[d]	27.4	11.7	28.6	11.8	26.4	11.6	−2.18	529	0.030	0.09
HAMD17	11.4	6.7	11.6	6.7	11.2	6.7	−0.72	527	0.472	0.03
YMRS	1.8	3.6	1.9	3.6	1.6	3.7	−0.77	500	0.441	0.03
WHO QOL-26 average	2.60	0.55	2.53	0.56	2.66	0.54	2.58	531	0.010	0.11
WHO QOL-26 physical	2.35	0.69	2.29	0.67	2.41	0.70	1.97	531	0.049	0.09
WHO QOL-26 psychological	2.35	0.68	2.30	0.70	2.39	0.66	1.47	531	0.143	0.06
WHO QOL-26 social	2.82	0.80	2.72	0.83	2.90	0.76	2.53	531	0.012	0.11
WHO QOL-26 environmental	3.06	0.62	2.98	0.66	3.13	0.58	2.71	531	0.008	0.12
WHO QOL-26 total	2.03	0.77	1.98	0.77	2.08	0.76	1.52	531	0.130	0.07
GAF	44.3	12.0	43.4	11.5	45.0	12.3	1.53	532	0.127	0.07

Abbreviations: CES-D, The Center for Epidemiologic Studies Depression Scale; GAF, Global Assessment of Functioning; HAMD17, 17-item Hamilton Depression Rating Scale; JART, Japanese Adult Reading Test; WAIS, Wechsler Adult Intelligence Scale; WHO QOL-26, World Health Organization Quality of Life 26; YMRS, Young Mania Rating Scale.

[a]Independent t-test (gender is χ^2 test).

[b]Bonferroni corrected $p < 0.05$.

[c]WAIS-R, $N = 75$; WAIS-III, $N = 442$, WAIS-IV, $N = 12$.

[d]CES-D, $N = 446$; BDI-II (Beck Depression Inventory-Second Edition), $N = 85$. The total BDI score was converted to a CES-D score using a regression equation and used as the estimated CES-D value.

such as whether intellectually compromised people are more likely to be exposed to ACEs events, or whether the experience has a greater impact on them. Furthermore, while not statistically significant with Bonferroni correction, the ACE group had severe subjective depression and poorer quality of life. Although we cannot determine whether these results stem from genetic or socio-environmental factors, public health policies to prevent ACEs and environmental factors are of considerable importance.

This study has some limitations. First, we used the ACE Score for validity testing, which is a self-administered questionnaire, but the investigators used a retrospective chart review to perform the scoring. Since this is not the original method of answering the ACE Score, the results must be considered with caution.

This study examined the relationships between ACEs, cognitive function, and clinical symptoms in depression, bipolar disorder, and schizophrenia groups using a sufficiently large sample of 536 individuals. The depression group consisted of 356 individuals, while the bipolar disorder group had 147 and the schizophrenia group had 33. These differences between the number of individuals in each illness group indicate that the intergroup analyses may be considered incomplete. Further studies should evaluate whether the characteristics of each disease can be seen by increasing the number of research participants in the bipolar disorder and schizophrenia groups.

The subjects of this study were patients who participated in the inpatient program with detailed clinical assessment through interviews and psychological testing. Patients who participated in the program may have prolonged depressive symptoms or limited clinical response from previous treatment in other clinics or hospitals. To verify the generalizability of the results of this study, further research is required across a wide range of patient populations, including patients with shorter duration of illness and those who had a favorable treatment response. However, since this inpatient program was designed to make a differential diagnosis of depressive symptoms through intensive brain imaging and other tests, and the medical history interview was conducted by a ward physician not directly involved in the study, we believe that there is no specific bias in the content of the interview.

It is stressful for patients to recall their ACEs, and patients may be reluctant to speak entirely about their experiences if they do not have sufficient rapport with their medical care provider. However, we can safely assume that most patients in the program participated out of a proactive desire to understand and improve their symptoms. The details of patient medical histories were collected and medical interviews were conducted to allow enough time for rapport building. We therefore consider it unlikely that the information given by patients in this study was less extensive than the information available in regular outpatient visits or via prospective epidemiological surveys.

We considered that the method of retrospectively investigating ACEs might result in recall bias. A previous meta-analysis of 16 studies that included data on the degree of agreement between prospective and retrospective ACE scales showed a low degree of agreement between the two. However, the degree of agreement was high when retrospective ACEs were based on interviews rather than questionnaires and studies with small sample size.[51] Furthermore, it must be noted that if the interviews about ACEs were performed in an unstructured way under the clinical settings, the "not applicable" response on the scale would include things that were really experienced but not mentioned (Supporting Information: Appendix A). In fact, the participants of this study were those in the 4-day inpatient program for psychiatric diagnosis. During the hospitalization period, the attending physicians and healthcare providers took the time to carefully interview the patients about their life and current medical history. However, it is possible that this interview method may have bias in the results because even if there were ACEs, if the patient did not talk about them, the score would result in "no ACEs." It should also be noted that it is difficult to cover all ACEs in our method, and that even if the patient had experienced ACEs, it may not be mentioned if the patient believes it is not an ACE. Consequently, we must consider the possibility of recall bias when interpreting the results of studies that involve a retrospective survey of ACEs. In contrast, however, experiences that would objectively be classified as negative may over time be reinterpreted during an individual's life and eventually be recognized as a positive experience in an individual's life story. In the future, we must combine prospective and retrospective assessments to study the long-term effects of ACEs on an individual's life. This will help us to explore the mechanisms for the prolonged negative effects of traumatization following adverse events and the prevention of exposure to traumatic events themselves.

CONCLUSION

While questionnaires and scales designed to evaluate ACE-related events have previously been created, none have classified the source of the event and the pathway and mode of its impact on the individual. We developed an original ACEs assessment scale and verified its validity and reliability. The results of our original scale indicate that approximately half of our subjects underwent ACEs and that the most common ACE type was being bullied by peers. Furthermore, in addition to patients with depression and schizophrenia, ACEs were common among patients with bipolar disorder. The ACEs scale in this study has the advantage of allowing psychiatric institutions and clinics to quantify ACEs from medical record data in the usual clinical setting. In professional educational institutions, it will be useful to raise awareness of ACEs by increasing the resolution of their pathways and mode of their impact on the individual.

AUTHOR CONTRIBUTIONS

Mika Yamagishi, Yoshihiro Satomura, Hanako Sakurada, Akiko Kanehara, Eisuke Sakakibara, Naohiro Okada, Sho Yagishita, Masato Fukuda, and Kiyoto Kasai conceptualized and designed the study. Mika Yamagishi, Yoshihiro Satomura, Hanako Sakurada, Akiko Kanehara, and Kiyoto Kasai acquired the data. Mika Yamagishi and

Kiyoto Kasai analyzed the data and drafted the manuscript. All authors participated in result interpretation; moreover, they reviewed and approved the final version of the manuscript.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data from this study cannot be made publicly available due to Ethics Committee regulations. However, it may be made available upon reasonable request from the researcher and with the approval of the Ethics Committee.

ETHICS APPROVAL STATEMENT

The study was approved by the Ethics Committee of the University of Tokyo, Graduate School of Medicine (Ethics Committee of Graduate School of Medicine approval numbers 0630 and 3202). The calculation of the BDI-II to CES-D conversion equation from the anonymous data was approved by the Research Ethics Committee, Department of Arts and Sciences, The University of Tokyo (approval #487).

PATIENT CONSENT STATEMENT

The purpose of the research was fully explained to all collaborators, and their consent was obtained in writing (Ethics Committee of Graduate School of Medicine approval numbers 0630 and 3202). In addition, the opt-out method was applied to the retrospective extraction and analysis of ACEs from the chart information (Ethics Committee of Graduate School of Medicine approval #3349).

CLINICAL TRIAL REGISTRATION

N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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