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Original Article

The Effects of Adverse Childhood Experiences on Japanese Substance Use Disorder Patients: Verification of the Model Mediated by Distrustfulness, Sense of Rejection, and Sense of Coherence

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Abstract

Adverse childhood experiences (ACEs) have been demonstrated to be a risk factor for substance use disorder (SUD). We hypothesized that distrustfulness due to the accumulation of ACEs is the key psychological factor that drives those at risk to rely on substances of abuse, instead of healthy interpersonal relationships, to cope with negative emotions. To examine this hypothesis that addiction develops from distrustfulness created by ACEs, we carried out covariance structure analysis to clarify the mediating factors that link ACEs with the severity of SUD.

Subjects: SUD patients who first visited the Kanagawa Psychiatric Center Addiction Clinic (Japan) between May 2015 and November 2016 were asked to complete a series of self-administered questionnaires, including 17 items concerning ACEs, the sense of trust scale, sense of rejection scale, sense of coherence (SOC) scale, Alcohol Use Disorders Identification Test (AUDIT), and Drug Abuse Screening Test (DAST-20). In total, 437 SUD patients were subject to our analysis, among whom 217 had alcohol use disorder (AUD) and 220 had drug use disorder (DUD); the mean age on admission was 48.2±10.5 years and 37.3±10.1 years, respectively.

Method: Covariance structure analysis was performed to investigate the hypothetical

model that the accumulation of ACEs increases distrustfulness and the sense of rejection in SUD patients, which in turn reduces the SOC.

Results: In AUD patients, the sense of rejection was directly associated with the AUDIT score, whereas in DUD patients, the SOC scale was directly associated with the DAST score.

The mediation analysis confirmed that in AUD patients, the positive association between ACEs and AUDIT score, and negative association between ACEs and SOC scale was partly mediated by distrustfulness and sense of rejection. In DUD patients, the positive association between ACEs and DAST score was partly mediated by distrustfulness, sense of rejection, and SOC.

A high goodness of fit was obtained for each path model (AUD: goodness of fit index [GFI]=0.993, adjusted GFI[AGFI]=0.967, comparative fit index[CFI]=0.998, root mean square error of approximation [RMSEA] =0.029, DUD: GFI=0.993, AGFI=0.966, CFI=0.998, RMSEA=0.033).

Conclusion: The present path model revealed that, in both AUD and DUD patients, the total number of ACEs was directly and positively associated with the degree of distrustfulness, sense of rejection, and AUDIT and DAST scores, whereas the SOC scale was not. The association between ACEs and the SOC scale was mediated by distrustfulness and the sense of rejection. The resulting psychological isolation may cause SUD patients to rely more on substances of abuse to cope with negative emotions, as reflected by the increased AUDIT and DAST scores. For AUD patients, the sense of rejection is a significant trigger for drinking behavior, whereas for DUD patients, the subjective feeling of incompetence in dealing with stresses may be a stronger trigger for drug use. The present analysis underscores the significance of childhood adverse experiences in the severity of SUD, and highlights the importance of supporting children and adolescents at risk as a substance abuse prevention strategy.

Keywords: substance use disorders, adverse childhood experiences, distrustfulness, sense of rejection, sense of coherence

Introduction.

The etiology of substance use disorders has been debated from various perspectives. On the psychosocial side, many studies have already reported the association between adverse childhood

experiences, such as being the victim of abuse, separation from parents, and parental substance abuse, and the risk of substance abuse and the development of substance use disorders.10)12)32)40)50)53) The Adverse Childhood Experience (ACE) Study15), an epidemiological study of childhood adversity, examined the association between the accumulation of adversity experiences and later health risks and behavioral problems. In terms of problems related to substance use disorders, a previous study reported that a group with four or more adverse childhood experiences was 4.7 times more likely to use illicit drugs, 7.4 times more likely to be addicted to alcohol, and 10.3 times more likely to inject drugs than a group with no adverse childhood experiences. There is a link between interpersonal distrust and dependence on alcohol and drugs and chronic traumatic experiences early in life.16) The self-medication hypothesis reported by Khantzian hypothesized that patients with substance use disorders were more likely to replace pain caused by interpersonal relationships with drugs due to feelings of isolation and distrust caused by harsh experiences during their upbringing.24)

In the field of mental health, sense of trust is an important concept, and maintaining a balance in which trust exceeds distrust is essential for the development of a healthy personality.4)14) Beard reported that distrust due to interpersonal trust deficits was a source of stress and was associated with mental and physical illness, and that the level of trust and stressful life events had implications for preventive psychiatry.7) In the treatment of substance use disorders, trust in oneself and rebuilding healthy relationships with others are emphasized.18) In particular, substance abusers with traumatic experiences of abuse are rarely able to share a sense of trust and safety from the beginning of treatment due to excessive vigilance based on their traumatic experiences; thus, it is necessary to maintain a safe therapeutic environment and take time to gain a sense of trust.17) Furthermore, it has been reported that alcohol and drug addicts and victims of abuse have a higher sense of loneliness and alienation than people who have never abused drugs or been abused.8)27)35) There are some studies using the sense of coherence scale (SOC)5), which is an indicator of stress-coping skills that was proposed by Antonovsky. These studies suggest that low stress-coping skills are associated with alcohol dependence and a tendency to develop alcohol consumption-related problems44), and that SOC and addiction severity are correlated with post-traumatic stress

symptoms.6)

Kobayashi explained the lack of interpersonal trust of patients with substance use disorders from the perspective of the "distrustfulness hypothesis " of addiction, which was based on the self-medication hypothesis.25) Patients with substance use disorders are unable to trust others or themselves due to difficulties in life caused by various adversity experiences during their development, they are unable to recognize their own negative emotions, such as loneliness, and have difficulty seeking help from others. It is hypothesized that substance use disorders are the results of trying to survive psychological isolation, and that the only way to cope with the inability to regulate one's own emotions and cope with stress is to use alcohol and drugs. Adverse childhood experiences include not only obvious abusive experiences but also experiences, such as chronic tensions in the family, that are difficult for outsiders to see. In order to test the distrustfulness hypothesis, Kobayashi hypothesized that inadequate coping with stress due to an impaired sense of trust mediated the relationship between the cumulation of adverse childhood experiences and the severity of substance use disorder. Kobayashi conducted a survey using self-administered scales to measure adversity experiences during the subjects' upbringing, severity of alcohol or drug use disorders, and sense of trust.26) The results showed that those who abused stimulants and other drugs had more explicit adversity experiences, such as abuse, while those who abused other drugs (e.g., psychotropic drugs) and alcohol had unexplicit adversity experiences such as excessive expectations and continuous harsh discipline. In addition, the severity of substance use disorder was significantly correlated with higher levels of distrust. In a multicenter study of patients with alcohol use disorders in 10 locations in Japan, Cho and colleagues conducted multiple regression analysis using the Alcohol Use Disorders Identification Test (AUDIT)19) as the objective variable, and the cumulative frequency of adverse childhood experiences, the SOC scale, and the trust scale as explanatory variables. The results showed that the strongest influence on AUDIT was found in the subscale "distrust" of the trust scale, followed by "sense of acceptance," "sense of rejection," "trust for self (low)," "trust for others (low)," and "SOC score (low)," which partially supported the distrustfulness hypothesis.9)

Research studies showing that the severity of substance use disorders is related to adverse childhood experiences, distrustfulness as a result of impaired trust, sense of rejection by

others, and insufficient stress-coping skills are increasing. However, to the best of our knowledge, there are no empirical studies that have shown which variable and how each variable mediates the process of developing severe substance use disorder. Previous studies suggest that patients with a genetic predisposition for impulsivity and hyperactivity have lower stress-coping skills and confidence as a result of developing a substance use disorder. We expanded on the research of Kobayashi26) by increasing the number of patients with alcohol and drug use disorders enrolled in the study; furthermore, we attempted to present the distrustfulness hypothesis as a process. We developed a model of the distrustfulness hypothesis in patients with substance use disorders, which states that "the cumulation of adverse childhood experiences strengthens the sense of interpersonal distrust and sense of rejection, and as a result, the ability to rely on others and cope with stress decreases, and substance abuse becomes more severe." The purpose of this study was to examine the validity of the model using a covariance structure analysis based on a self-administered psychological scale. The model was administered to patients at the outpatient clinic for addiction at the Kanagawa Psychiatric Center (hereafter referred to as "our hospital").

I. Methods

1.Participants

Of the 788 first-visit outpatients with dependence at our hospital between May 2015 and November 2016, 582 patients, excluding 23 patients who refused to consent to the survey and 183 patients who had medical conditions that interfered with their ability to answer the questionnaire or were incapable of giving consent, were surveyed orally and in writing by the staff in charge of the preliminary examination. After obtaining verbal and written consent to participate in the survey, the staff in charge of the preliminary examination administered a self-administered questionnaire to the subjects before the medical examination, asking for information on basic attributes such as sex, age at first medical examination, years of education, age at first use of addictive substances, and age at habituation. A self-administered questionnaire was administered before the medical examination. We excluded a further 76 patients who did not complete the questionnaire and 69 patients whose primary diagnosis was other than substance use disorder, and 437 patients were finally included in the analysis. Of these, 217 (169 males and 48 females) were diagnosed with alcohol use disorders based on the Diagnostic

and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (the "alcohol group"), and 220 (162 males and 58 females) were diagnosed with other substance use disorders (the "drug group"). In this study, coexisting cases of alcohol and drugs were categorized into the drug group as they were diagnosed as "other drug use disorders" and considered to have multidrug dependence.

2. Measurements

1) Adverse childhood experiences (ACEs)

The cumulative frequencies of the 17 ACEs were calculated using a yes-no questionnaire where "yes" was converted to "1". The minimum value was 0 and the maximum value was 17. The main questionnaire that measures ACEs is the ACE Study questionnaire, which was developed by the Kaiser Permanente Medical Care Program and the Centers for Disease Control and Prevention (CDC) using data from 17,737 insured individuals with Kaiser Permanente health insurance. The questionnaire includes three categories of abuse (including psychological abuse) and five categories of household dysfunction (mother treated them violently, household member was alcoholic or drug user, household member with mental illness, parents divorced or separated, household member was imprisoned). There were eight items in total. The higher the number of ACE categories, the more likely a person is to have multiple and serious health risk factors.11)15) In Japan, the ACE questionnaire was developed based on the eight ACE items described above, and Matsuura et al. added one item based on a survey on childhood adversity experiences in juvenile training schools.30)31) Masuda et al. developed the Japanese version of the intra-familial adverse childhood experiences questionnaire (eight items) and extra-familial adverse childhood experiences (five items).28) In order to investigate the childhood adversity experiences of patients with alcohol use disorder, Cho, referring to these previous studies, selected and added items to the experiences that are often reported in the life histories of patients with substance use disorder through consultation with doctors specializing in addiction medicine, and the final 17 items were used as childhood adverse childhood experiences items, which included experiences of abuse and ambiguous experiences.9) The 17 items consisted of: chronic physical illness, academic failure, bullying, long-term school absenteeism, history of correctional guidance, harsh discipline from caregivers, excessive expectations, chronic illness in the family, mental illness in the family, substance abuse in

the family, poverty, child neglect, physical abuse, psychological abuse, sexual abuse, separation from parents, and suicide in the family. The cumulative frequency of these 17 items was calculated by asking the respondents whether they had experienced them before they were 15 years old.

2) Sense of distrust

The eight items of "distrust," a subscale of the adult version of the Trust Scale, were used.2) The Trust Scale was developed by Amagai to measure interpersonal trust multidimensionally. It defined trust as "the feeling of being able to trust and rely on others and oneself." The scale consists of three subscales: "trust for self" for the intrapersonal aspect, "trust for others" for the interpersonal aspect, and "distrust" for the negative aspect. In this study, we used the subscale "distrust," which measures the negative aspect of trust: "I cannot trust people." Distrust is a four-point scale consisting of eight items, such as "I feel that I may be betrayed someday even by people I can rely on now," and "I feel that I will be destroyed if I do not protect myself well." The higher the total score of the eight items, the higher the level of distrust.1)3) The reliability of this scale has been reported to be sufficient with a Cronbach's alpha coefficient of 0.81.3) The validity of the scale has been verified in relation to the Locus of Control scale22) and the Self-Esteem Scale.37) As for the standard values, Amagai reported the mean and standard deviation of each item by age group and sex, and the mean and standard deviation of the scale scores for the eight items were calculated as 17.2 ± 2.4 for men in their 30s and 17.5 ± 2.3 for women, and 17.3 ± 2.5 for men in their 40s and 17.6 ± 2.7 for women.4)

3) Sense of rejection

The eight items of the Sense-of-Rejection scale, which was developed by Sugiyama and Sakamoto, were used.42) Sugiyama and Sakamoto conceptualized "sense of acceptance," which is the perception and emotion that "I am valued by others," and "sense of rejection," which is the perception and emotion that "I am neglected or ignored by others."41) The Sense-of-Rejection scale used in this study is a five-point scale consisting of eight items, including "I tend to be thought badly of," "I am often neglected by others," and "if things go wrong, I will be abandoned." The higher the total score of the eight items, the higher the perceived rejection. The reliability was reported to be sufficient ($\alpha = 0.85$), and the validity was verified by correlation coefficient as consistent with the hypothesis of the Attachment Style Scale.45) The mean values used for the standard values were 17.37 ± 5.13 for males and 16.33 ±

5.40 for females.42)

4) Stress-coping skills

In this study, we used the SOC scale5), which is a concept of stress-coping ability proposed by Antonovsky from the standpoint of salutogenesis, as a common health factor that exists in the core of a group of people who maintain physical and mental health and successfully cope with stress.5) Based on this concept, the SOC scale was developed as a scale to measure the sense of being able to cope with stress by believing in consistency and stability in the world and asking for help from others. In this study, we used the Japanese version of the 13-item 7-point SOC scale.51) The questionnaire consisted of 13 items, including the following questionnaire statements: "Do you have the feeling that you are in an unfamiliar situation and don't know what to do?", "Do you have the feeling that you don't really care about what goes on around you?", "How often do you have feelings that you're not sure you can keep under control?". The scores were distributed between 13 and 91. The higher the score, the better the ability to cope with stress and the healthier the mental and physical state. In terms of reliability, Togari et al. reported a sufficient value of α = 0.84 in their research47), and in terms of validity, Endo et al. supported the criterion-correlation validity with the Self-rating Depression Scale.13,54) Togari et al. calculated the criterion values for the Japanese version using survey data from a nationally representative sample, and an overall mean score of 59.0 ± 12.2 was reported.47)

5) Substance use disorder severity

The AUDIT, which is used to screen for alcohol use disorder, was administered to patients whose primary substance of dependence was alcohol.19) The Drug Abuse Screening Test-20 (DAST-20)39) was administered to patients whose primary substance of dependence was other drugs to measure the severity of drug abuse and dependence. The reliability of the Japanese version of AUDIT was reported by Hiro and Shima to be good (α = 0.81)19), and to have high validity in screening problem drinkers and alcoholics by comparing it with the Japanese version of the Cut down, Annoyed by criticism, Guilty feeling, Eye-opener alcoholism screening scale.23) On this scale, a score of 12 or higher is the cutoff point for problem drinking, and a score of 15 or higher is the cutoff point for alcoholism.20) The DAST-20 is a 20-item questionnaire uses a "yes" or "no" response to measuring the severity of drug abuse and dependence. Shimane et al. reported that the reliability of the questionnaire was high with α = 0.95, and the coefficient of reliability by the

retest method was 0.86. The validity of the questionnaire was satisfactory with a correlation coefficient of 0.85 using the Severity of Dependence Scale-J36), and 0.41 using AUDIT.39) A score of 0 indicates "no problem," 1-5 indicates "low level," 6-10 indicates "moderate level," 11-15 indicates "substantial level," and 16-20 indicates "severe level."

3. Statistical analysis

First, the mean values of age at first diagnosis, mean years of education, age of first use, age of habituation, and each scale score were calculated for the alcohol and drug groups. The two groups were compared by Mann-Whitney U test. Next, the hypothesized model of causal influence of ACEs cumulative frequency, distrust, sense of rejection, and SOC as explanatory variables with AUDIT for the alcohol group and DAST for the drug group as objective variables were developed, and tested using analysis of covariance structure. The analysis of covariance structure is an analysis method in which the analyst formulates and tests hypotheses about the causal relationships among variables.34) First, the causal chain of ACEs → distrust → sense of rejection → SOC → AUDIT/DAST was drawn as a path diagram, and the standardized path coefficients representing the strength of the relationship between each item were calculated. Next, the model was modified by deleting non-significant paths if any, and the goodness of fit of the model was examined. We used the $\chi 2$ value, Goodness of Fit Index (GFI), Adjusted Goodness of Fit Index (AGFI), Comparative Fit Index (CFI), and Root Mean Square of Approximation (RMSEA) as measures of goodness of fit. The GFI and AGFI take values from 0 to 1, with a value closer to 1 being considered a more explanatory model and a value greater than 0.90 being considered a good fit. The smaller the RMSEA, the more desirable it is; generally, 0.05 or less is good, and 0.10 or less is acceptable.

In this study, the cumulative frequency of ACEs was used as an exogenous variable, and the "distrust" of the trust scale, the sense of rejection scale, the SOC scale measuring stress-coping ability, and AUDIT or DAST were used as endogenous variables. When the indirect effects of distrust, sense of rejection, and SOC were considered in the effects of childhood adversity on the severity of substance use disorder, 95% confidence intervals were calculated using the bootstrap method (resampling frequency 2,000), and the significance of the indirect effects was examined by mediation analysis. The significance of the indirect effect was examined by mediation analysis. The bootstrap

method is one of the methods to estimate the characteristics of the population by repeated resampling from the sample population, and the indirect effect is considered significant when the value range of the confidence interval does not include zero. Statistical analyses were conducted using SPSS Statistics version 25 and Amos Graphics version 25.

4. Ethical consideration

This study was conducted with the approval of the Ethics Committee of the Kanagawa Prefectural Psychiatric Center. The protocol was explained orally and in writing, and consent for publication was obtained, and the research was conducted with consideration for the protection of personal information.

II. Results

1. Characteristics of participants in each group

Mann-Whitney's U test results for the basic attributes and the scale scores of the questionnaire for the alcohol and drug groups are shown in Table 1. The mean age of the alcohol group was 48.2 ± 10.5 years, and the mean age of the drug group was 37.3 ± 10.1 years, with the alcohol group having a significantly higher age at the time of initial diagnosis. The mean years of education were longer in the alcohol group. There was no significant difference in the age of first use between the two groups, but the age of habituation was significantly lower in the drug group. The drug group tended to have more ACEs, higher levels of sense of distrust and sense of rejection, and lower levels of SOC. Cronbach's coefficient alpha of the cumulative frequency of ACEs was 0.692, which was acceptable but not sufficient, and all other scales were above 0.7, indicating sufficient internal consistency.

2. Results of covariance structure analysis

1) Alcohol group

In the alcohol group, the paths ACEs → SOC (-0.09), distrust → AUDIT (-0.07), and SOC → AUDIT (-0.06), for which the standardized coefficients were not significant, were deleted and analyzed again. In the path diagram of the reanalyzed alcohol group, paths are indicated by solid arrows and standardized coefficients are indicated in bold (Figure 1). The goodness-of-fit indices were GFI = 0.993, AGFI = 0.967, CFI = 0.998, and RMSEA = 0.029, indicating a good fit of the model.

The number of ACEs directly affected AUDIT and also affected AUDIT through distrust and sense of rejection. The number of ACEs also affected SOC through distrust and sense of rejection.

Although the direct path from ACEs to

SOC was not significant, the bootstrapping method was used to calculate 95% confidence intervals, and the confidence interval of the standardized coefficient when distrust was mediated between ACEs and SOC did not contain 0 (-0.38, -0.20), indicating that the indirect effect was significant. Furthermore, the confidence interval of the standardized coefficient for the mediation of distrust and sense of rejection between ACEs and SOC did not contain zero (-0.40, -0.23), and the indirect effect was significant. The direct path from distrust to AUDIT was also not significant, but the confidence interval of the standardized coefficient for the case of mediated sense of rejection between distrust and AUDIT did not contain 0 (-0.02, -0.23), and the indirect effect was significant.

Although the direct effect of ACEs on AUDIT was significant, the confidence interval of the standardized coefficient for the mediation of distrust and sense of rejection between ACEs and AUDIT did not include 0 (0.02, 0.14). In addition to the direct effect of ACEs on AUDIT scores, the results also confirmed the partial mediation of the effect of distrust on sense of rejection in AUDIT.

2) Drug group

In the drug group, the paths of ACEs → SOC (-0.05), distrust → DAST (-0.13), and sense of rejection → DAST (-0.02), for which the standardized coefficients were not significant were deleted and analyzed again. In the path diagram of the reanalyzed drug groups, paths are indicated by dashed arrows and standardized coefficients are indicated by fine print (Figure 1). The goodness-of-fit indices were GFI = 0.993, AGFI = 0.966, CFI = 0.998, and RMSEA = 0.033, indicating a good fit of the model. The number of ACEs directly affected DAST and also affected DAST through distrust, sense of rejection, and SOC.

Although the direct path from ACEs to SOC was not significant, 95% confidence intervals were calculated by bootstrapping, and the confidence interval of the standardized coefficient for distrust by using a mediated path between ACEs and SOC that did not include 0 (-0.31, -0.16), indicating that the indirect effect was significant. Furthermore, the confidence intervals for the standardized coefficients when distrust and sense of rejection were mediated between childhood adversity experience and SOC did not contain zero (-0.36, -0.19), and the indirect effect was significant. The direct path from distrust to DAST was also not significant, but the confidence interval of the standardized coefficient, when distrust and DAST were mediated by sense of rejection and SOC, did not contain 0 (0.15, 0.30), and the indirect effect was significant.

Although the direct effect of ACEs on DAST was significant, the confidence interval of the standardized coefficient for the mediated effect of distrust, sense of rejection, and SOC between childhood adversity and DAST did not include 0 (0.06, 0.16). In addition to the direct effect of ACEs on DAST scores, we also found partial mediation of the effect on DAST through distrust, sense of rejection, and SOC.

III. Discussion

1. Characteristics of alcohol and drug groups

The mean AUDIT scores suggest that many of the subjects diagnosed with alcohol use disorders had serious alcohol-related problems; furthermore, the mean DAST scores suggest that many of the subjects diagnosed with substance use disorders had moderate to substantial conditions. Both patients with alcohol use disorders and those with other drug use disorders tended to have a negative sense of trust, a lack of trust in others and in the world, and a strong sense that they themselves were rejected by others, making it difficult for them to cope with stress and seek help from others. This tendency was even more pronounced in the drug group that experienced more childhood adversity.

2. A common process from childhood adversity to an increase in severity of substance use disorders in the alcohol and drug groups.

In both the alcohol group and the drug group, adverse childhood experiences had a direct effect on distrust, sense of rejection, and the severity of substance use disorder. On the other hand, the direct effect of adverse childhood experiences on stress-coping was not significant in both groups, but the effect of adverse childhood experiences on stress-coping through the mediation of distrust and sense of rejection was significant. The concept of SOC was originally proposed in response to the question of what characteristics are common to people who are able to protect their physical and mental health despite being exposed to extreme stressors and experiencing extreme stress; generally speaking, SOC can be developed by providing good life experiences in infancy, adolescence, and later adulthood.46)52) The results of the present study suggest that, even in patients with substance use disorders, the amount of adversity experienced in childhood does not directly decrease SOC, but it may indirectly decrease SOC by increasing distrust and sense of rejection through later life experiences.

3. Differences between alcohol and drug groups

In the alcohol group, ACEs were partially mediated by distrust through

sense of rejection, which affected SOC and AUDIT. The direct paths from distrust to AUDIT and SOC to AUDIT were not significant, but both were significant through the mediation of sense of rejection. Patients with alcohol use disorder were more likely to become "workaholics" due to defenses against dependence and fears of abandonment, and denial of depression and emptiness.38) They also showed over-adapted personality tendencies such as being "serious" and "caring for others"43) and having high public self-consciousness.49) It is not uncommon for patients with alcohol use disorder to feel that they have adapted within the social framework to some extent until middle age, and that they are doing their best at work while drinking. In the present study, the alcohol group also tended to have a sense of distrust due to childhood adversity, but before realizing that their own stress-coping was inadequate, they tended to have a sense of rejection such as "Why don't people accept me even though I am working so hard?"

In the drug group, ACEs were partially mediated by distrust, sense of rejection, and stress coping, which affected DAST. The direct path from distrust to DAST and sense of rejection to DAST was not significant, but both were significant through the mediation of SOC. In the case of patients with illicit drug use disorders, peer pressure to use drugs has an effect on drug abuse.48) If their social group consists of substance abusers, they become more socially isolated. On the other hand, there is also a strong need for peers in the recovery process from drug addiction.33) The results of the present study show that in the case of drug use disorders, distrust due to childhood adversity tends not to be directly linked to sense of rejection. However, distrust was associated with poor stress coping at a relatively young age and a strong feeling of inability to cope with stress, which may lead to a serious dependence on drugs.

4.Significance of this study

The model of the distrustfulness hypothesis, which posits distrust of self and others and low stress-coping as mediating factors that link adversities in one's life history to the severity of a substance use disorder, may have clinical significance in understanding the aggravation process in patients with substance use disorders. The participants in this study came to the hospital with substance-related problems severe enough to be diagnosed as alcohol or drug use disorders, and tended to have higher-than-normal levels of distrust and sense of rejection, and lower stress-coping skills. The higher the cumulative frequency of

adverse childhood experiences, the stronger the tendency. In addition, distrust and sense of rejection were related to the severity of substance use disorder as mediating factors, suggesting that patients with more severe substance use disorders may have more difficulties in establishing trusting relationships with others. Early detection of adverse childhood experiences in adolescence may be important in terms of preventing the onset and severity of substance use disorders in children.

5. Limitations of this study and future issues

Limitations of this study were that the data was from a single institution and only patients with substance use disorders were included.

The future issues are multicenter studies and comparative studies with other disease groups. In this study, we attempted to test the distrustfulness hypothesis from a psychosocial perspective by conducting a cross-sectional survey using psychological scales. There are some neurophysiological findings on the health risks associated with childhood adversity15); however, the accumulation of longitudinal studies and cohort studies, including biological information such as brain imaging and various blood hormone levels, are long-term issues.

The adversity items used in this study were self-administered questionnaires developed by expert consensus by adding the items of the ACE questionnaire used in the ACE Study15) and the unexplicit adverse childhood experiences reported by Kobayashi. 25)26) The questionnaire was developed by expert consensus, and the responses were collected by recalling the subjective experiences of the subjects; thus, some bias was unavoidable. In the present study, we analyzed the total of 17 childhood adversity experiences as a single variable; however, we need to subclassify the 17 items used in the present study.21) Further studies to examine in detail which childhood adversity experiences affect which variables are necessary in the future.

In this study, we attempted a quantitative analysis by focusing on the cumulative frequency of adverse childhood experiences. Since the survey was conducted on patients at a medical institution, it was necessary to limit the questions to those that could be answered in a short time and were not invasive. Further studies consisting of qualitative research based on interviews and case studies are needed to examine the qualitative aspects of childhood adversity experiences and their effects on therapeutic interpersonal relationships and

interpersonal relationships in daily life.

Conclusion.

In this study, we conducted a questionnaire survey on adverse childhood experiences, distrustfulness, sense of rejection, sense of coherence, and substance use disorder severity in first-visit patients with substance use disorder, and tested a hypothetical model based on the distrustfulness hypothesis. The developed and improved model was generally appropriate in terms of goodness-of-fit indices. In both the alcohol and drug groups, adverse childhood experiences affected sense of coherence through the mediation of distrustfulness and sense of rejection. In relation to the severity of substance use disorders, adverse childhood experiences partially influenced the severity directly in the alcohol group; on the other hand, the path from distrustfulness to sense of rejection mediated a significant influence on severity. In the drug group, adverse childhood experiences had a direct effect on severity in part. In addition, a significant path from distrustfulness to sense of coherence had a mediated effect on severity. The model of the distrustfulness hypothesis suggests a process in which childhood adverse childhood experiences lead to increased distrustfulness and sense of rejection, inability to rely on others, reduced stress-coping skills, and compensatory substance use disorders.

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Table 1 Attributes of subjects and mean scores for each scale

	Alcohol group (n=217)		Drug group (n=220)			
	Mean	Standard deviation	Mean	Standard deviation	P value	α coefficient
Age at first examination (years)	48.2	10.5	37.3	10.1	0.000**	
Years of education (years)	13.2	2.6	11.8	2.7	0.000**	
Age of first use (years)	17.6	2.7	19.4	7.5	0.619	
Age of habituation (years)	24.7	8.7	22.6	8.7	0.000**	
Cumulative frequency of adverse childhood experiences	3.5	2.8	5.0	2.7	0.000**	0.692
Distrust	18.6	5.8	21.0	5.4	0.000**	0.834
Sense of rejection	21.0	6.4	22.7	6.9	0.014*	0.885
SOC	51.7	12.7	46.4	12.9	0.000**	0.820
AUDIT score	23.9	9.2				0.849
DAST score			10.9	3.6		0.714

Mann-Whitney's U test (**P < 0.05, **P < 0.01)

SOC: sense of coherence, AUDIT: Alcohol Use Disorders Identification Test, DAST: Drug Abuse Screening Test

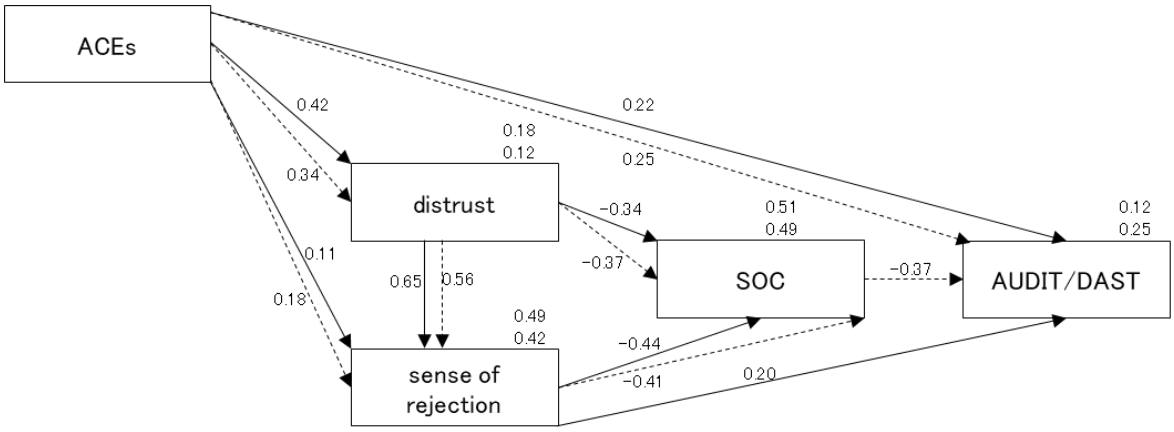

Figure 1 Relationship among childhood adversity experience, distrust, sense of rejection, SOC, AUDIT, and DAST in the alcohol and drug groups

Error variation is omitted. All coefficients are standardized coefficients and significant at the 5% level. Paths and standardized coefficients for the alcohol group are indicated by solid arrows and boldface type in the upper panel, and those for the drug group are indicated by dashed arrows and fine type in the lower panel.

ACEs: adverse childhood experiences,

SOC: sense of coherence, AUDIT: Alcohol Use Disorders Identification Test, DAST: Drug Abuse Screening Test